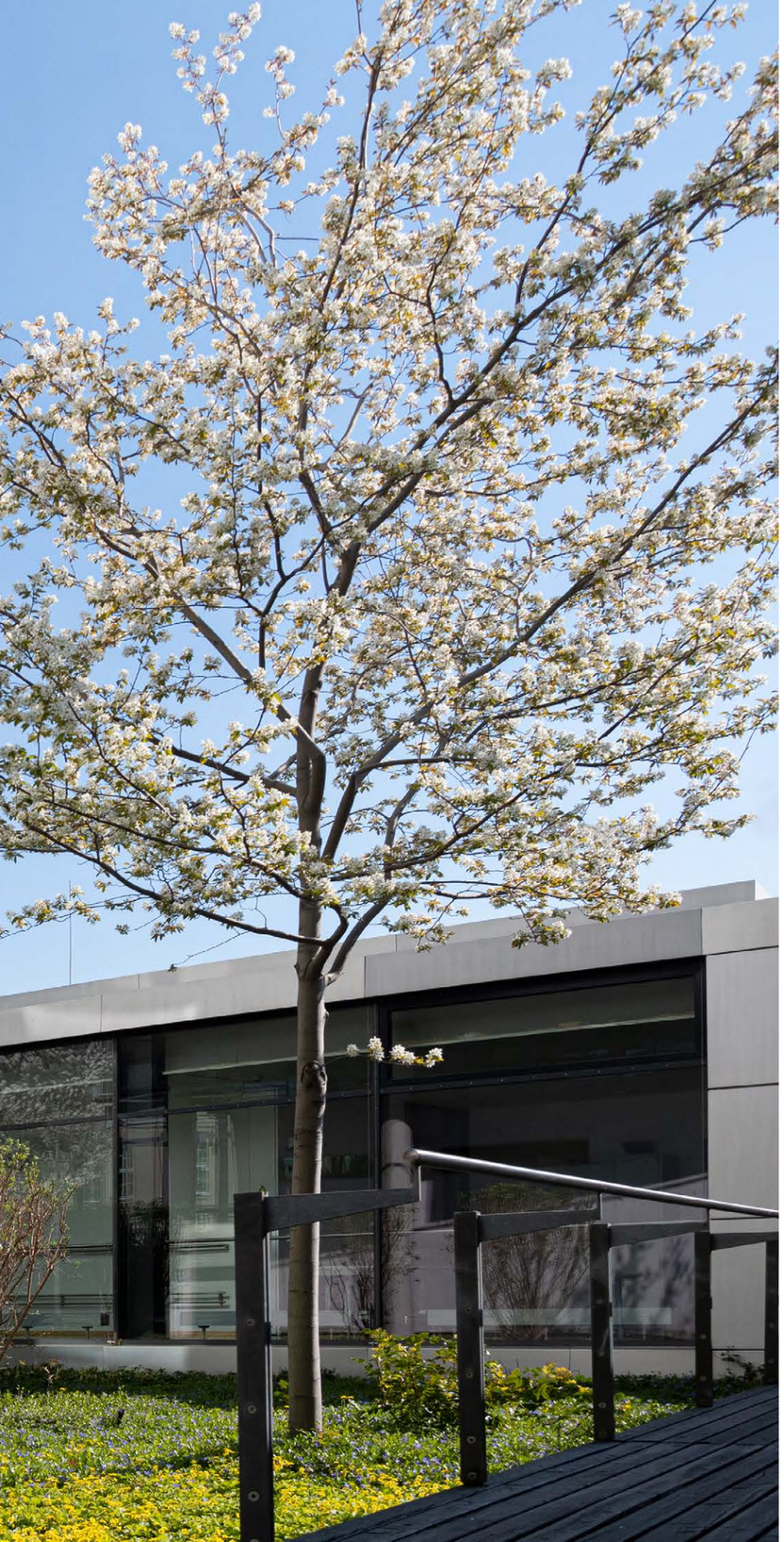

MAX PLANCK INSTITUTE
FOR HUMAN COGNITIVE AND BRAIN SCIENCES

Research Report
for the Scientific Advisory Board

2020–2022

Meaning of icon

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Leipzig, January 2023

Preface

The Max Planck Institute for Human Cognitive and Brain Sciences has continued its pursuit of excellent and internationally renowned research and development over the past three years (2020 to 2022). The Institute currently houses four full departments, ten research groups, and four methods and development units. Around 350 staff members contribute to the lively buzzing atmosphere, cutting-edge science, and the daily multicultural exchange.

The Institute has continued to develop, as it always has, despite the challenges of the pandemic. The newest of our departments, the Department of Psychology headed by Christian F. Doeller, has grown rapidly. Professor Doeller joined the Institute, as its latest director, from Trondheim and the Donders Institute in 2018. He brought with him a prestigious ERC Consolidator grant and initiated several large-scale EU-wide and MPG-wide collaborative projects. The Department of Neurophysics, headed by Nikolaus Weiskopf, has successfully concluded their ERC Consolidator grant held in collaboration with UCL in London, and is currently pursuing follow-up studies. The Department is also running several high-calibre international collaboration projects. Angela D. Friederici's Department of Neuropsychology continues their involvement in an international priority programme funded by the DFG and have secured an ERC Starting Grant as well as a number of other prestigious international grants. The Department of Neurology, under the tutelage of Arno Villringer, secured several new large-scale project grants on obesity and neural rehabilitation. Together with Leipzig University, they started the follow-up of the LIFE population health study (N=10,000) as well as several high-ranking international collaborations.

MPI CBS is one of the leading neuroimaging centres conducting cutting-edge cognitive neuroscience worldwide, supported by and based on top-notch methodological research and developments. But, development means change. In order to strengthen this position – and further evolve – we are committed to reinforcing our research in the domains of computational and cognitive neuroscience. Currently, the Institute is going through due process in order to fill a vacant 5th department on computational neuroscience. The succession appointment for Angela Friederici, who will become Director Emeritus in late summer 2023, will be sought from the field of cognitive neuroscience.

As directors, we feel a strong commitment to support our junior PIs on their way to successful academic careers beyond their time at our Institute. We are therefore very proud of recent successes in this realm. Five group leaders have been appointed professors and will therefore oversee the stepwise outphasing of their respective groups over the next years. Roland Benoit has just been appointed Associate Professor of Psychology and Neuroscience and Fellow of the Institute of Cognitive Science at the University of Colorado Boulder, US; Martin Hebart has been appointed Professor of Computational Cognitive Neuroscience and Quantitative Psychiatry at the University of Gießen, Germany; Gesa Hartwigsen has been appointed Professor of Cognitive including Biological Psychology at Leipzig University, Germany; Julia Sacher has been appointed Professor of Neuroendocrinology at Leipzig University Hospital, Germany; and Veronika Engert was appointed Professor for Social Neuroscience at Jena University Hospital, Germany. In their new postitions, both Hartwigsen and Sacher can build important bridges between MPI CBS and Leipzig University and the University Hospital, respectively.

At the same time, a new and promising Minerva Fast Track Group “Neural Codes of Intelligence”, headed by Stephanie Theves, has started its research in September 2022 and will report for the first time here. In addition, we established a new methods unit, the Neural Data Science and Statistical Computing group, headed by Nico Scherf as group leader, who develops new AI data analysis techniques and supports researchers in all aspects of statistics and analyses. Finally, we have seen a generation change at the helm of administration and IT and have appointed a new head of administration, Sebastian Ziegaus, as well as a new head of our Computing and Database Services, Davide Chiarugi.

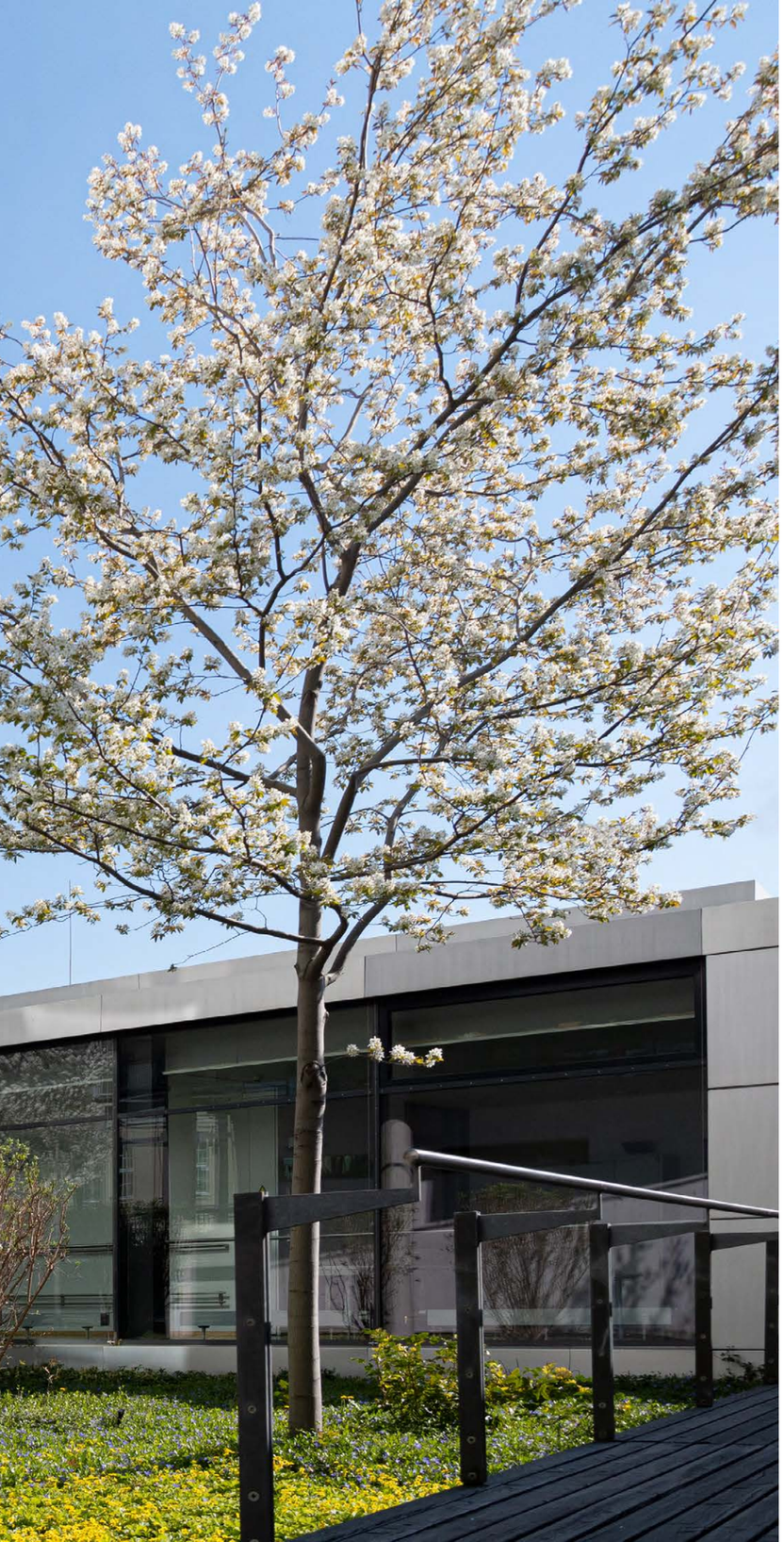
There have also been advances and changes for the Institute’s doctoral students. The International Max Planck Research School on Neuroscience of Communication (NeuroCom) has continued its success in both recruiting promising new doctoral students and seeing the “old” cohorts through to completion. The school will end in 2023 after fourteen very successful years. Since the onset of the IMPRS in 2009, a total of 178 doctoral researchers (59% female, 46% international) from 34 countries have been admitted to the programme. Impressively, almost 45% of the defended projects have received the top mark (summa cum laude).

Our newly funded International Max Planck Research School on Cognitive NeuroImagaing (CoNI) is a brand new graduate programme for international doctoral researchers that covers the highly interdisciplinary and fast-paced fields of cognitive neuroscience, clinical and translational neuroscience, and neuroimaging. Introductory courses and project-specific advanced training provide doctoral researchers with a solid foundation for their theses. An emphasis on neuroimaging and computational modelling strengthens the foundation further and enables new types of doctoral projects at the leading edge of the field. IMPRS CoNI has just started recruitment of its first cohort of PhD students who will start in 2023.

In addition to IMPRS NeuroCom and IMPRS CoNI, the Institute also houses the Max Planck School of Cognition, a top-notch, interdisciplinary, highly competitive doctoral programme involving numerous prestigious German universities and research organisations. Each of our three graduate schools will give some insight into their programmes and structures in this report.

We hope you will enjoy reading this report. It contains up-to-date scientific and administrative information about our Institute and world-class research.

Angela D. Friederici
Arno Villringer
Nikolaus Weiskopf
Christian F. Doeller



View of the inner courtyard

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View of the entrance area

The Max Planck Institute for Human Cognitive and Brain Sciences

The Max Planck Institute for Human Cognitive and Brain Sciences at Stephanstrasse in Leipzig was established on 1 January 2004 by a merger between the former Leipzig-based Max Planck Institute of Cognitive NeuroScience (founded in 1995) and the Munich-based Max Planck Institute for Psychological Research (founded in 1981). The decision to merge the centres of expertise into one followed the development of psychological, neuroscientific, and neurological research increasingly being conducted closely together. The creation of the centre in Leipzig also established exceptional conditions for interdisciplinary behavioural and neurobiological research on human cognition.

The Max Planck Institute for Human Cognitive and Brain Sciences consists of six departments; of these, four are currently active: Neuropsychology, Neurology, Neurophysics, and Psychology. The Institute presently hosts ten research groups, amongst them four Max Planck Research Groups: “Adaptive Memory” (Roland R. Benoit), “Language Cycles” (Lars Meyer), “Pain Perception” (Falk Eippert), and “Vision and Computational Neuroscience” (Martin Hebart), and an Otto Hahn Research Group, “Cognitive Neurogenetics” (Sofie Louise Valk). The Institute also hosts a number of internationally competitive research groups within schemes that have been launched by the MPG to recruit and promote exceptionally

qualified women scientists, such as the Lise Meitner Research Group “Cognition and Plasticity” (Gesa Hartwigsen), and two Minerva Fast-Track Research Groups, “Milestones of Early Cognitive Development” (Charlotte Grosse Wiesmann) and “Neural Codes of Intelligence” (Stephanie Theves, whose group only just started). The Minerva Research Group “EGG (Emotion and NeuroimaGinG) Lab” (Julia Sacher) has just come to a close; the Research Group “Stress and Family Health” (Veronika Engert) is about to conclude in February 2023. Furthermore, there is an independent ERC Research Group "Learning in Early Childhood", led by Michael A. Skeide, that started work in 2020.

We are very proud that, out of these ten research groups, five group leaders have recently been appointed professors and will therefore oversee the stepwise finishing of their respective groups over the next years: Roland Benoit has just been appointed Associate Professor of Psychology and Neuroscience and Fellow of the Institute of Cognitive Science at the University of Colorado Boulder, US; Martin Hebart has been appointed Professor of Computational Cognitive Neuroscience and Quantitative Psychiatry at the University of Gießen, Germany; Gesa Hartwigsen has been appointed Professor of Cognitive including Biological Psychology at Leipzig University, Germany; Julia Sacher has been appointed Professor of Neuroendocrinology at Leipzig University Hospital, Germany; and Veronika Engert was appointed Professor for Social Neuroscience at Jena University Hospital, Germany.

Four methods and development units facilitate scientists’ access to the Institute’s state-of-the-art technical equipment while also conducting research on data acquisition and analysis methods and developing computational and IT approaches: “Nuclear Magnetic Resonance” (Harald E. Möller), “Brain Networks” (Thomas R. Knösche and Burkhard Maess), “Neural Data Science and Statistical Computing” (Nico Scherf), and “Computing and Databases Services” (Davide Chiarugi).

Research foci

The general agenda of MPI CBS is the investigation of the neural bases of human cognitive functions. These are explored by combined assessment of cognition, behaviour, and emotion, and by using neuroscientific tools such as magnetic resonance imaging (MRI), magneto-encephalography (MEG), electro-encephalography (EEG), noninvasive optical imaging, and various transcranial stimulation techniques. Positron emission tomography (PET) is performed in collaboration with Leipzig University Hospital, based upon a joint grant. Besides these neurophysiological and neuroimaging measures, the integration of genetic, autonomic, and other biological markers (e.g. hormones, neuropeptides) has become increasingly important in the Institute’s research.

The Max Planck Institute for Human Cognitive and Brain Sciences in Leipzig provides an exciting framework for these research domains, with the full gamut of cognitive and neuroscientific methodology available under one roof. A defining characteristic of the Institute—and at the same time a basic principle of our research approach—is the dovetailing of research and technical development. The state-of-the-art equipment of the Institute both accentuates Leipzig’s long-standing tradition in psychological research and, additionally, contributes to cutting-edge research within relevant areas. Modern imaging techniques are increasingly being used in combination with traditional psychological approaches. The Institute utilises and, most importantly, develops and optimises these techniques. Hosting the entire spectrum of techniques and approaches that are established within human cognitive science and neurosciences, our Institute offers ideal conditions for its own and guest researchers.

Cooperation agreements and collaborations

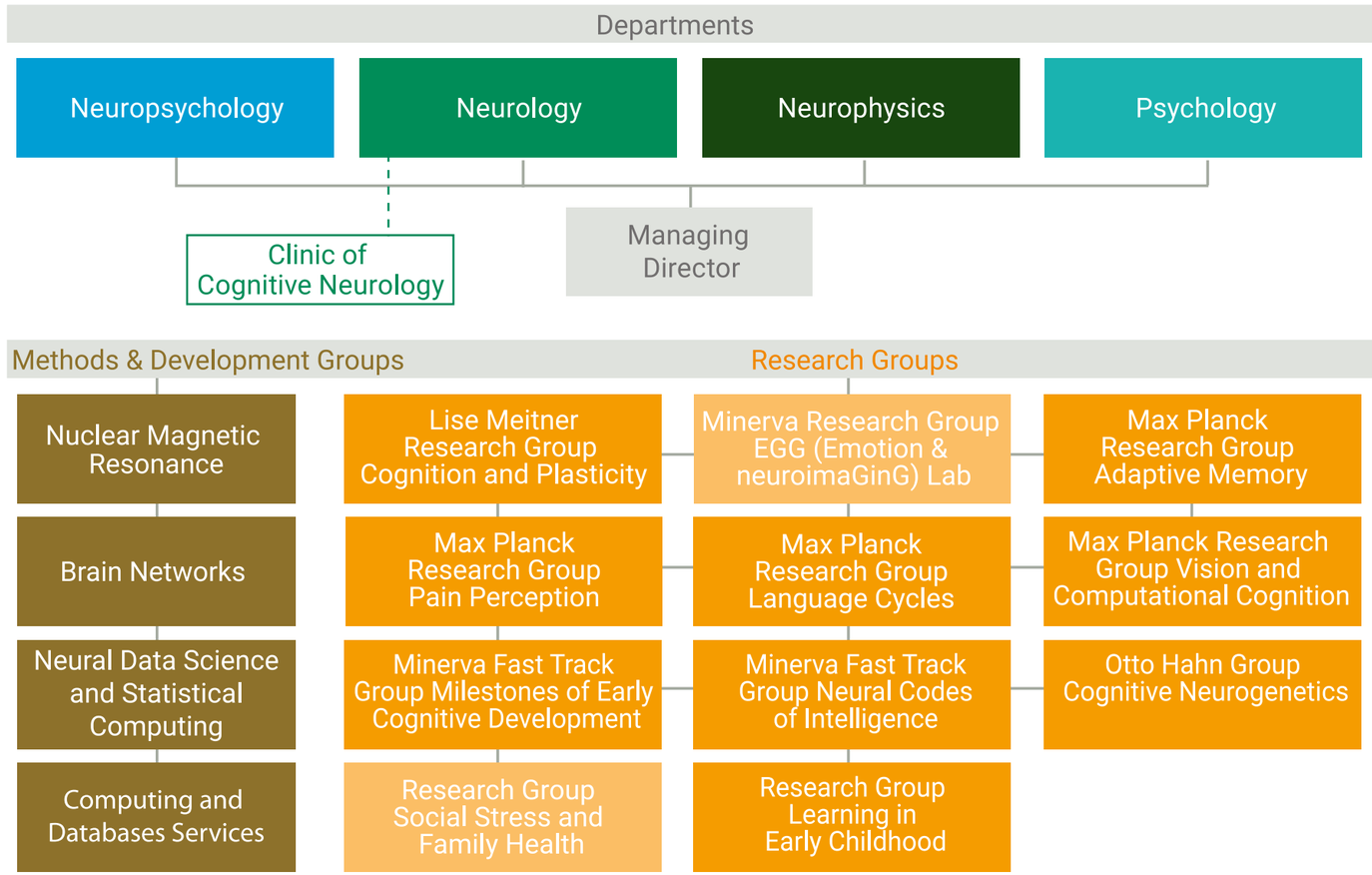
There has been a long-standing collaboration with Leipzig University. The first cooperation agreement between the Max Planck Society and Leipzig University, involving the (then) Max Planck Institute of Cognitive NeuroScience and Leipzig University, goes back to September 1994. In December 2006/January 2007, the Max Planck Society signed a cooperation agreement with Leipzig University and Leipzig University Hospital with regard to the Max Planck Institute for Human Cognitive and Brain Sciences. The purpose of this agreement is to maintain and promote cooperation between the University, the Hospital, and the MPI in the field of cognitive neurology. Above all, this cooperation is implemented through: 1) the management of the Clinic of Cognitive Neurology as part of the hospital by a director of the Max Planck Institute who is also appointed by the University; 2) the exchange of scientific information and experience; 3) the undertaking of joint research projects and cooperation in individual research ventures; 4) the teaching and fostering of junior scientists; and 5) the mutual use of facilities. A new cooperation agreement between all Leipzig Max Planck Institutes and Leipzig University, further extending and strengthening existing collaborations, was signed in 2019.

In 2010, a collaboration agreement with the Institute of Cognitive Neuroscience (ICN) at UCL, UK, was signed, establishing a partnership between the ICN and the International Max Planck Research School on Neuroscience of Communication: Function, Structure, and Plasticity (IMPRS NeuroCom). The agreement includes collaborations in the organisation of the annual IMPRS summer school and student exchange programmes, as well as collaborations between the ICN and MPI CBS. It will be continued by the new International Max Planck Research School on Cognitive NeuroImaging (IMPRS CoNI). IMPRS NeuroCom, which is about to run out at the end of 2023, and the new IMPRS CoNI are interdisciplinary PhD programmes originally initiated by the Max Planck Institute for Human Cognitive and Brain Sciences. Both are based at the Institute and Leipzig University, and also involve the Institute of Cognitive Neuroscience at UCL, UK, and – as a new partner – the Technical University of Dresden, Germany (IMPRS CoNI).

MPI CBS also proudly houses the very successful Max Planck School of Cognition (MPSCog), a collaborative, interdisciplinary and customised doctoral programme that offers outstanding doctoral candidates the tools to gain a superior grasp on the different methods and approaches used in the rapidly evolving field of cognition. The programme, in which all directors are involved and that is headed by Arno Villringer, is characterised by the passion to better understand both human cognition and “mental phenomena” potentially occurring in non-biological systems and agents (artificial intelligence). MPSCog bundles the best cognition researchers from different universities and scientific organisations in a unique setting, also involving international experts in the field like Patrick Haggard from UCL.

All departments hold long-standing collaborations in the form of joint teaching and supervision projects with German and international universities and university hospitals, as well as with non-university research institutions like Helmholtz, Fraunhofer, Bernstein Centers, NIH, or Wellcome Trust. Further collaborative links exist in the shape of joint supervision and assessment of doctoral students between the Max Planck Institute for Human Cognitive and Brain Sciences and several international graduate programmes like the Berlin School of Mind and Brain at Humboldt University Berlin.

Organisational structure



Professor Dr Dr h.c. Angela D. Friederici
Director

Neurocognition of Language

DEPARTMENT OF NEUROPSYCHOLOGY

Language is a uniquely human trait, in particular the ability to combine words into structured sequences.

The human faculty of language is supported by a left hemispheric neural network involving inferior frontal and posterior temporal brain regions, which are connected by white matter fibre tracts. Our research in the past years has focused on the functional and structural specification of this network. We showed that the posterior portion of Broca's area (BA 44) systematically increased its activity when processing syntactic hierarchy, be it in complex constructions or two-word combinations. We demonstrated that during development the maturation of the grey matter of the inferior frontal and posterior temporal language regions, and the white matter fibre tracts connecting them, correlate with the ability to process syntactically complex sentences.

Based on these data and those reported in the literature, a functional neuroanatomical model of language processing was proposed. This model holds that the ability to process hierarchical structured sequences is at the root of the human faculty of language. In our recent research we focused on the ontogenetic and phylogenetic dimensions of the language

faculty, investigating the neuroanatomical prerequisites of language in the prelinguistic human infant and in the non-human primate. This research goes beyond the description of the adult human language network for which we provide further specifications of the functional interplay of brain regions supporting syntactic and semantic processes.

In our recent work we specify the structural underpinnings of the language network, both in human development and across human and non-human primates.

1.1 The Ontogeny and Phylogeny of the Language Network

If we want to keep up the claim that language is a uniquely human trait, we have to describe the ultimate abilities of non-human primates, and moreover, the neuroanatomical differences and similarities between human and non-human primates. Our group has made important progress in this research domain by uncovering a clear spatial extension of BA 44 towards the anterior direction in humans compared to chimpanzees based on cytoarchitectonic analyses. This anterior extension of BA 44 in humans appears to provide space for syntactic processes known to be located there (1.1.1). In a cross species comparison, analysing the dorsal fibre tract going from the auditory cortex to the inferior frontal cortex, we found that this white matter structure was similar between humans, chimpanzees, and macaques. This suggests that this structure supporting auditory information processing was preserved during evolution (1.1.2). The leftward lateralisation of this pathway, however, appears to be a more recent phylogenetic development. In a further study focusing on the evolution of the structural language network, we identified a previously undescribed white matter structure connecting the middle temporal gyrus with frontal areas via the parietal lobe (1.1.3). This structure can be viewed as an evolutionary precursor of the posterior segment of the dorsal pathway. In previous cross species comparisons of basic language-related brain functions, we had shown that macaques are able to process simple structured sequences during perception. Now, we analysed the structure of chimpanzees' production and found a certain systematicity in their call sequences which, however, were much simpler than any human language (1.1.4). These findings suggest that certain neuroanatomical structures, which subserve basic auditory and rule-based processes, remained unchanged in the evolution from non-human to human primates. Other structures, however, those which subserve human syntactic processing, show an evolutionary shift, differentiating human from non-human primates.

At the onset of language development stands the ability to detect systematic relations in the language input, such as non-adjacent-dependencies (NAD). In prior research we had shown that such dependencies in auditory input can be detected by young infants. Here, we investigated infants' memory for such dependencies and found that a memory for morphosyntactic dependencies is already present in six-month-old infants (1.1.5). We furthermore showed that this ability to associatively learn NAD disappears gradually until the age of 3 years, an age at which the controlled processes supported by the prefrontal cortex come into play (1.1.6). During further development the maturation of BA 44 in the left inferior frontal cortex, between 3 and 4 years, is responsible for the children's ability to process syntax, as evidenced by the relation of this region's cortical thickness and syntax performance (1.1.7). In prior studies investigating white matter structure during development, we had reported different trajectories for two dorsal fibre pathways: one targeting BA 6 was present at birth while another targeting the syntax-relevant BA 44 only developed later. Now we have analysed the asymmetry of these pathways and demonstrate a difference between them. Asymmetry was present only in the pathway targeting BA 44, not the one targeting BA 6. The asymmetry of the pathway targeting BA 44 furthermore correlates with language performance (1.1.8). Taken together, these findings indicate that the ability to process language beyond auditory association needs a neural network involving a mature left BA 44 and a fibre tract connecting this area to the temporal cortex in the left hemisphere.

1.1.1 Uncovering the morphological evolution of human Broca's area

Gallardo, G.[1,*], Eichner, C.[1,*], Sherwood, C. C.[2], Hopkins, W. D.[3], Anwander, A.[1], & Friederici, A. D.[1]

[1] Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany, [2] Department of Anthropology, The George Washington University, Washington DC, USA, [3] Department of Comparative Medicine, The University of Texas MD Anderson Cancer Center, Bastrop, TX, USA, * Equal Contribution

Language processing is a human trait, which is supported by a largely left-lateralised brain network. Three key components of this network are Wernicke's region in the temporal cortex and Brodmann Areas (BA) 44 and 45, parts of Broca's area in the inferior frontal cortex. Together these regions functionally subserve syntactic and semantic processes, with BA 44 fostering syntactic processing of hierarchically structured sequences in particular. Cytoarchitectonic homologs of these regions have previously been identified in great apes and other non-human primates. However, how these regions morphologically evolved to support language processing remains unknown. In this work, we study how BA 44 and 45 evolved by comparing their morphology in similar-sized populations of humans and chimpanzees. In both species these brain regions were identified and delineated using the same histological procedure. To compare them, we used state-of-the-art MRI surface reconstruction and registration algorithms that adequately capture and align the brain gyrification between the species (Figure 1.1.1A). Through this approach, we were able to precisely project the chimpanzees' BA 44 & 45 onto the human brain (Figure 1.1.1B). We found that, compared to chimpanzees, humans show an anterior expansion in left BA 44 – a region which has been shown to support syntax. These results suggest that BA 44 has evolved from a purely action-related region in chimpanzees to a more expanded region in humans with a posterior portion supporting action and an anterior portion serving syntactic processes. With these findings we provide a solution for a long-standing debate concerning the structural and functional evolution of Broca's area.

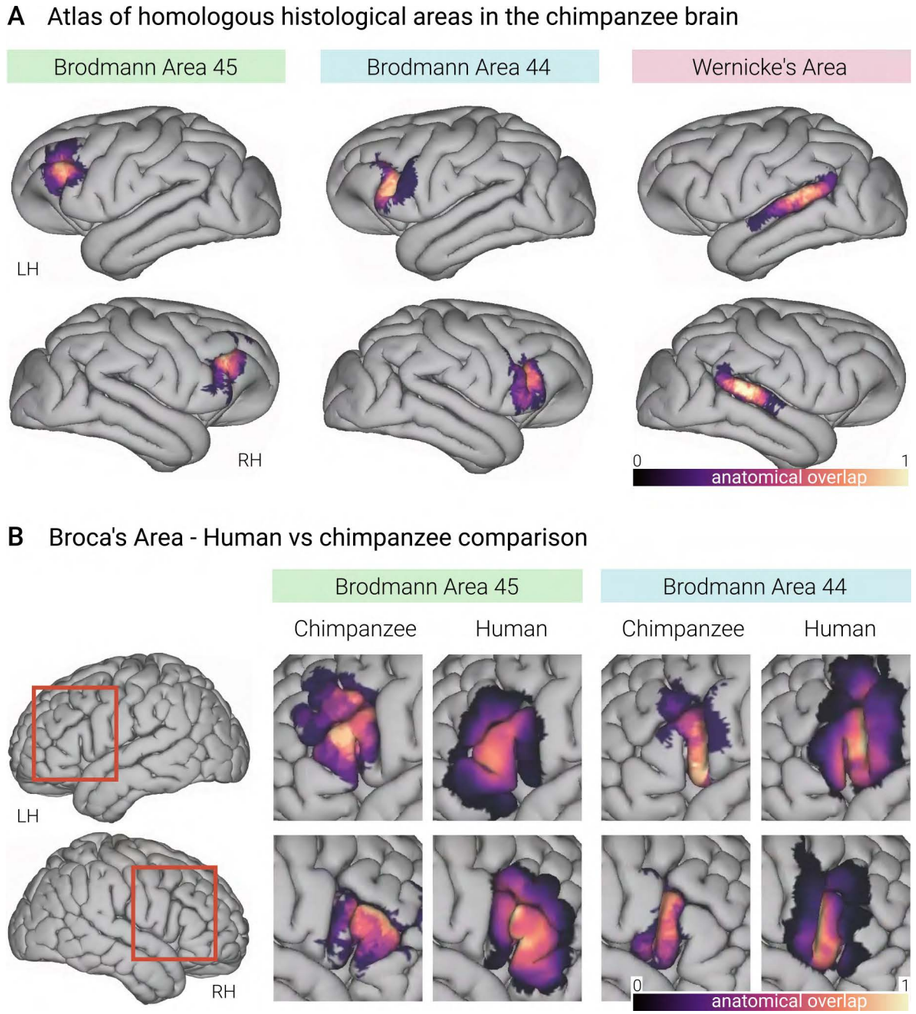


Figure 1.1.1 (A) Probabilistic map of Brodmann 45, 44, and Wernicke's Area in the Juna chimpanzee template. (B) Projection of chimpanzee and human Brodmann Areas 45 and 44 on the MNI human template. In humans, left BA 44 shows an anterior expansion.

1.1.2 The evolution of the arcuate fasciculus: A primate auditory prototype

Balezeau, F.[1,8], Wilson, B.[1,7,8], Gallardo, G.[2], Dick, F.[3], Hopkins, W.[4], Anwander, A.[2], Friederici, A. D.[2], Griffiths, T. D.[1,5,6,9], & Petkov, C. I.[1,9]

[1] Newcastle University Medical School, Newcastle upon Tyne, UK, [2] Max Planck Institute for Cognitive and Brain Sciences, Leipzig, Germany, [3] Birkbeck-UCL Centre for NeuroImaging, Birkbeck University of London, UK, [4] Keeling Center for Comparative Medicine and Research at University of Texas MD Anderson Cancer Center, Bastrop, TX, USA, [5] Wellcome Trust Centre for Neuroimaging, UCL, UK, [6] Department of Neurosurgery, University of Iowa Hospitals and Clinics, Iowa City, IA, USA, [7] Department of Psychology and Yerkes Primate Research Center, Emory University, Atlanta, GA, USA, [8] these authors contributed equally, [9] these authors jointly supervised this work

The human arcuate fasciculus pathway is crucial for language, interconnecting posterior temporal and inferior frontal areas. Whether a monkey homolog exists is controversial and the nature of human-specific specialisation unclear. Prior work investigating this white matter structure suggested differences between species, concerning its termination points in the temporal cortex. Here we used diffusion-weighted MRI in monkeys, apes, and humans to identify homologous pathways originating from the auditory cortex and going to inferior frontal areas. However, the leftwards lateralisation of this pathway was only observed in humans. This discovery establishes a primate auditory prototype for the arcuate fasciculus, reaching from the auditory cortex to the inferior frontal cortex. It reveals its earlier phylogenetic origin and illuminates its remarkable transformation during evolution.

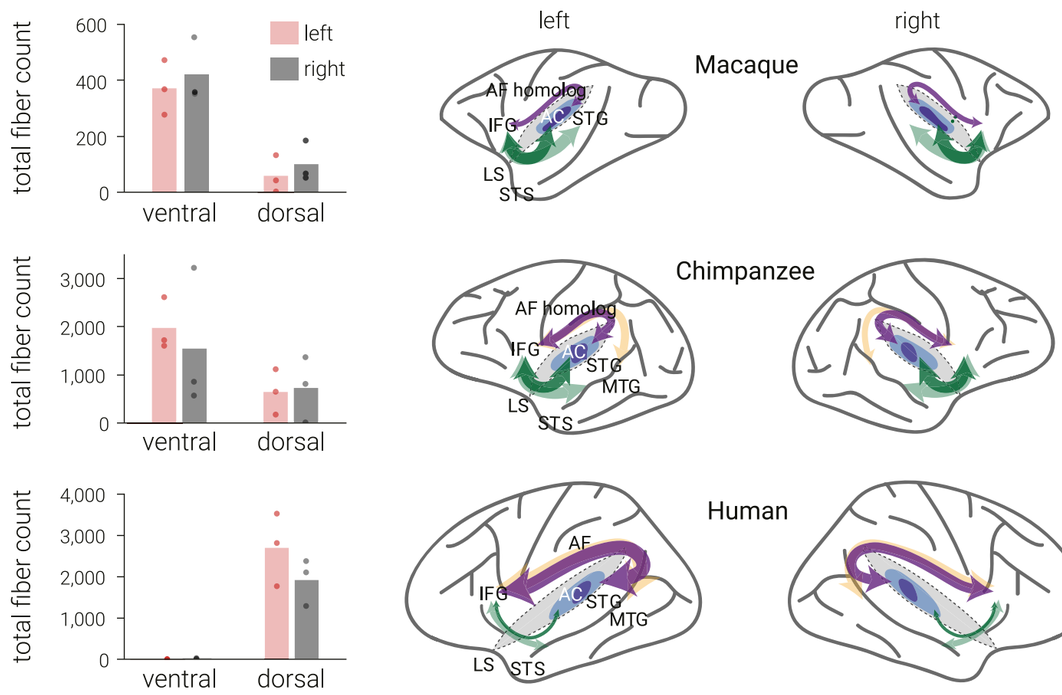


Figure 1.1.2 Summary of auditory dorsal and ventral pathway strength and lateralisation in macaques, chimpanzees, and humans. Left: bar plots showing the individual results and mean fibre counts for the left and right dorsal and ventral pathways for each of the three species. Right: schematic summary of the dorsal (purple) and ventral (dark green) pathway results in macaques, chimpanzees, and humans, overlaid on previous observations (light yellow and light green). The insights into arcuate fasciculus (AF) evolution: homologous ventral (dark green) and dorsal (purple) pathways from the auditory cortex (AC) in all three species, with the AF segment left-lateralised in humans but less so in nonhuman primates.

1.1.3 Evolutionary precursors of the human language network in the chimpanzee brain

Eichner, C.[1], Paquette, M.[1], Müller-Axt, C.[1,2], Bock, C.[3], Gräßle, T.[4], Jäger, C.[1,5], Kirilina, E.[1,6], Lipp, I.[1], Morawski, M.[15], Weiskopf, N.[1,7], Wittig, R. M.[8,9,10], Crockford, C. [8,9,10], Friederici, A. D.[1], & Anwander, A.[1]

[1] Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany, [2] Faculty of Psychology, Technische Universität Dresden, Germany, [3] Alfred Wegener Institute Helmholtz Centre for Polar and Marine Research, Bremerhaven, Germany, [4] Epidemiology of Highly Pathogenic Microorganisms, Robert Koch Institute, Berlin, Germany, [5] Paul Flechsig Institute of Brain Research, Leipzig University, Germany, [6] Center for Cognitive Neuroscience Berlin, Free University Berlin, Germany, [7] Felix Bloch Institute for Solid State Physics, Faculty of Physics and Earth Sciences, Leipzig University, Germany, [8] Department of Human Behavior, Ecology and Culture, Max Planck Institute for Evolutionary Anthropology, Leipzig, Germany, [9] Tai Chimpanzee Project, Centre Suisse de Recherches Scientifiques, Abidjan, Cote d'Ivoire, West Africa, [10] The Ape Social Mind Lab, Institut des Sciences Cognitives Marc Jeannerod, Bron, France

The long-standing question regarding the evolution of human language may only be resolved through comparisons with close living evolutionary relatives, such as chimpanzees. This particularly applies to the structural connectivity of the white matter (WM), which has continuously expanded throughout evolution. However, due to ethical and legal restrictions on chimpanzee research, evolutionary neuroscience currently relies on aged data with limited detail, or on comparisons with evolutionarily distant monkeys.

Using high-field diffusion MRI and an entirely novel reconstruction method, we created an unprecedently detailed MRI brain atlas of the structure and white-matter (WM) connectivity of the chimpanzee from a naturally deceased animal. Our provided open-access resource contains: [i] the highest quality acquisition and description of the connectivity of a great ape brain to date, [ii] the first detailed segmentation of cortical and subcortical grey matter brain structures as well as WM fascicles of the chimpanzee, and [iii] a novel method and software tool to reliably reconstruct complex WM architectures, including crossing fibre environments, for both in-vivo and post-mortem applications.

This unique dataset enabled reconstructions of WM tracts at the highest ever achieved resolution and quality (Figure 1.1.3A). As such, our approach allowed us to identify novel, phylogenetically-relevant details of the chimpanzee connectome. We were able to provide high quality reconstructions of the evolutionary precursors of the human language network. This includes previously undescribed connections in chimpanzees, such as the posterior segment of the dorsal pathway, which provides an indirect connection between the middle temporal gyrus and frontal areas via the parietal lobe (Figure 1.1.3B).

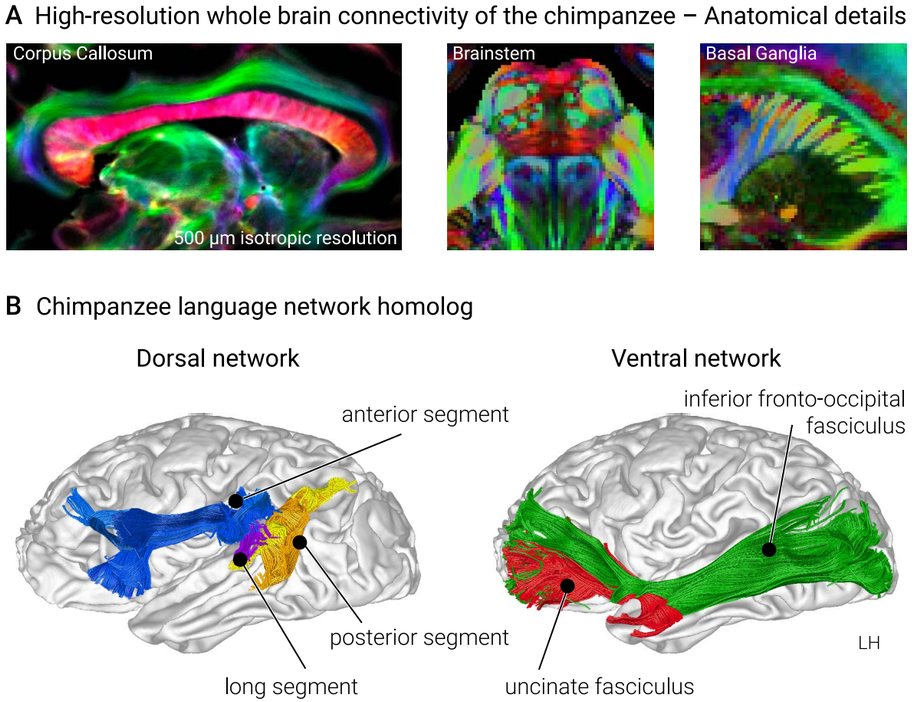


Figure 1.1.3 Detailed structure and connectivity of the chimpanzee's brain. (A) A close-up of anatomical details of the corpus callosum, brainstem, and basal ganglia underlines the achieved diffusion MRI data quality. (B) High-resolution segmentation of WM fibre pathways constituting the homolog of the human language network in the chimpanzee brain.

1.1.4 Chimpanzees produce vocal sequences with ordered and recombinatorial properties

Girard-Buttoz, C.[1,2,3,5], Zaccarella, E.[4,5], Bortolato, T.[1,2,3], Friederici, A. D.[4], Wittig, R. M.[1,2,3], & Crockford, C.[1,2,3]

[1] Institut des Sciences Cognitives Marc Jeannerod, CNRS, Lyon, France, [2] Taï Chimpanzee Project, Centre Suisse de Recherche Scientifique, Abidjan, Ivory Coast, West Africa, [3] Department of Human Behaviour, Ecology and Culture, Max Planck Institute for Evolutionary Anthropology, Leipzig, Germany, [4] Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany, [5] These authors contributed equally

The origins of human language remain a major question in evolutionary science. Unique to human language is the capacity to flexibly recombine a limited set of sounds into words and hierarchical sequences, generating endless new sentences. In contrast, sequence production of other animals appears limited, stunting potential meaning generation. However, studies have rarely quantified flexibility and structure of vocal sequence production across the whole repertoire. Here, we used such an approach to examine the structure of vocal sequences in chimpanzees, known to combine calls into longer, singly-used sequences. Focusing on the structure of vocal sequences, we analysed 4826 recordings of 46 wild adult chimpanzees from Taï National Park. The chimpanzees produced 390 unique vocal sequences. Most vocal units emitted singly were also emitted in two-unit sequences (bigrams), which in turn were embedded into three-unit sequences (trigrams). Bigrams showed positional and transitional regularities within trigrams with certain bigrams predictably occurring in either head or tail positions in trigrams and with specific other units. From a purely structural linguistic perspective, the capacity to organise single units into structured sequences offers a versatile system potentially suitable for expansive meaning generation.

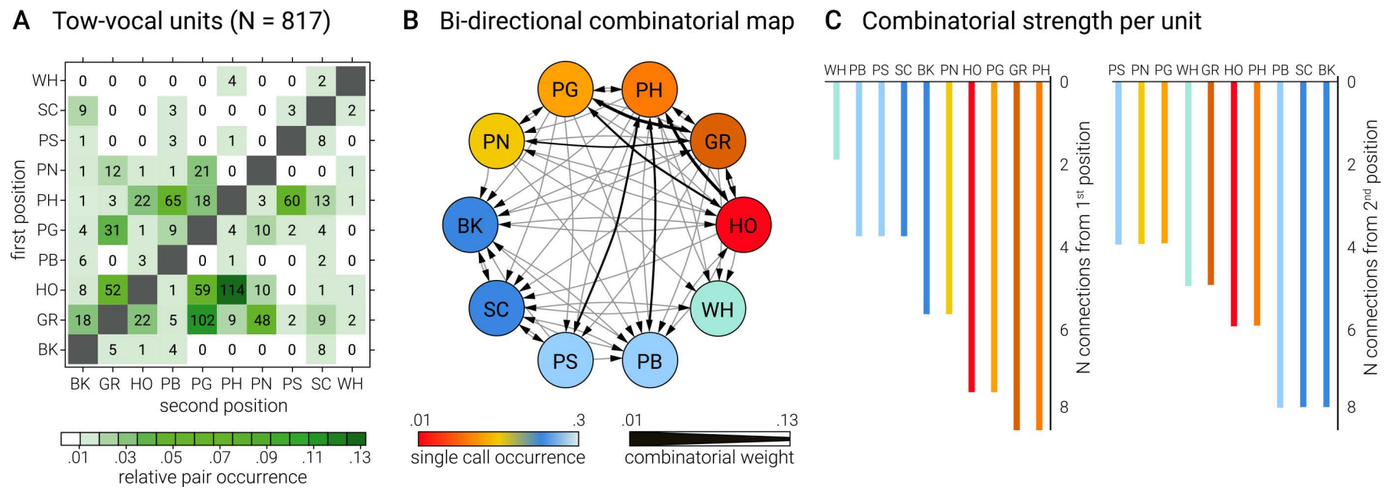


Figure 1.1.4 Bigram flexibility and ordering (N = 817 bigrams and 58 unique bigrams). (A) Frequency distribution for two-unit vocal sequences (bigrams) with units occurring in the first position listed along the y axis and units occurring in the second position listed along the x axis. Colour gradients (white-to-dark-green) represent the relative occurrence of each bigram within the two-unit set. In each cell, the absolute frequency count for each bigram is conversely reported. (B) The bigram combinatorial network with the ten single units depicted as circled nodes and colour gradients (hot-to-cold) representing the number of times a certain unit is found in the bigram set. This network was also used for the calculation of the Betweenness Centrality among the units. The size of the directional edges (arrows) expresses the number of times the specific bigram is found in the sample (thick-to-thin). (C) The number of different single units with which each single unit forms a bigram in the sample, as the first unit (left) or second unit (right).

1.1.5 Memory for non-adjacent dependencies in the first year of life: Sleep changes the nature of representation

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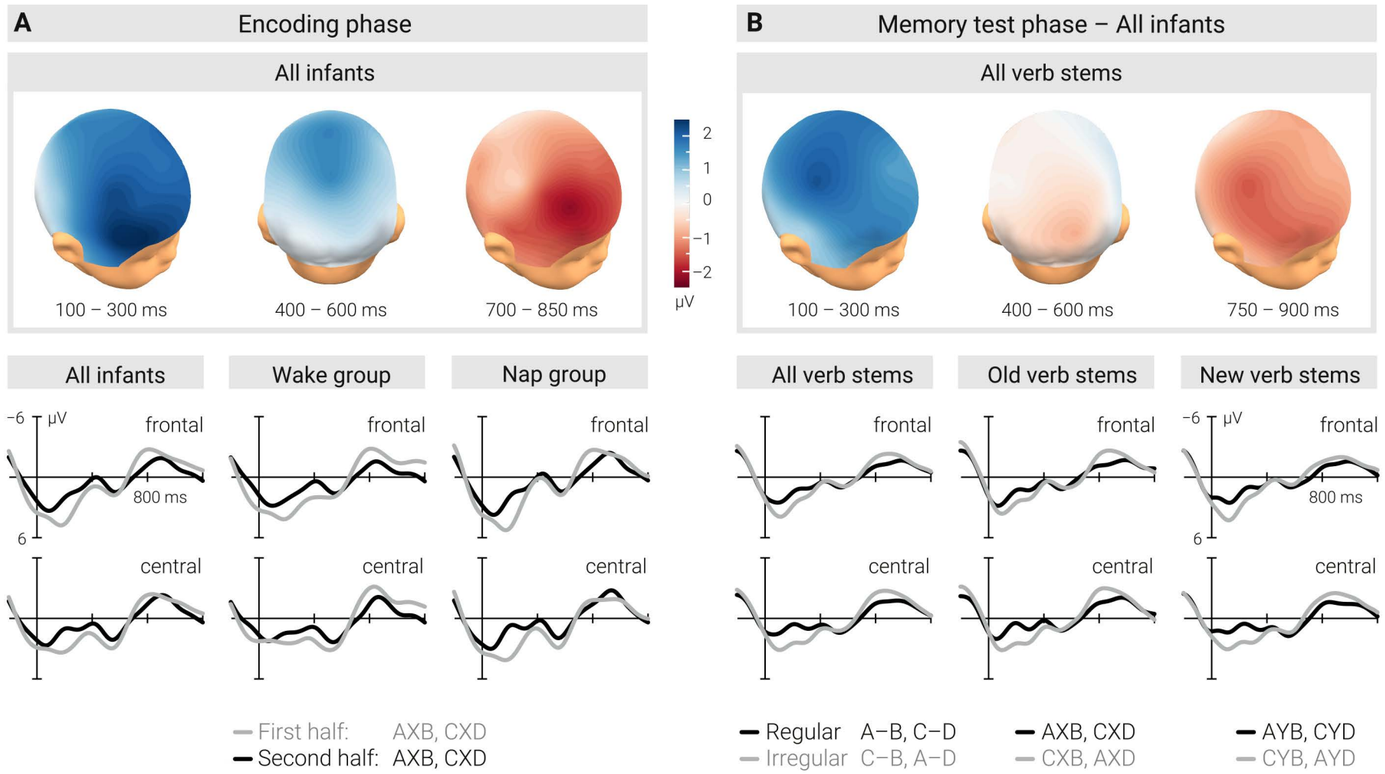
Grammar learning involves memory for nonadjacent dependencies (NADs). Encoding of NADs has been observed in very young infants but their memory of NADs has remained unexplored. Here we investigated whether 6- to 8-month-olds retain NADs and if sleep after encoding affects this memory. German infants were familiarised with two morpho-syntactic NADs (AXB, CXD) presented in sentences of an unknown natural language (e.g., sta-X-ando, può-X-are, with X representing different verb stems in Italian). Brain responses after a retention period revealed memory of NADs, independent of whether infants had napped or stayed awake in this period. During sleep, a new form of generalised memory evolved from the initially represented dependencies between sounds. Infants with high, left, frontal spindle activity during sleep showed an additional brain response indicating memories of individual speech phrases. Results imply that infants as young as 6 months are equipped with memory mechanisms for grammar learning. They also suggest that consolidation of highly specific information can occur parallel to changes in the nature of generalised memory.



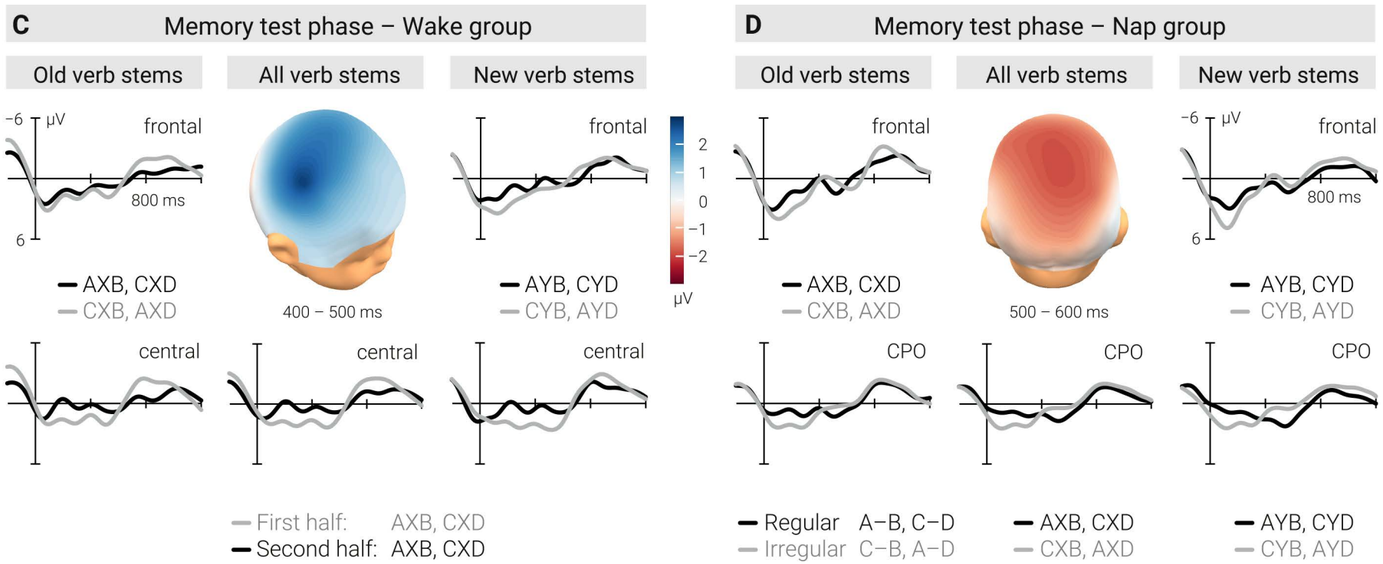


Figure 1.1.5 Familiarity and memory effects. ERPs and the spatial distribution of the effects of the encoding and memory test phases, time-locked to the onset of the suffixes. Negativity is plotted upward. (A) Top: The familiarity effects of the encoding phase in the overall group (N = 85 infants). Bottom: ERPs over the frontal and central regions for the first half (grey lines) and the second half (black lines) of the encoding phase in the overall group, the wake group (N = 37 infants), and the nap group (N = 48 infants). Voltage maps in top panel represent ERP differences between the responses in the first and the second half of the encoding session. (B) Top: The memory effects at early and late latencies, no memory effect at middle latency in the overall group. Bottom: ERPs over frontal and central regions for regular (black lines) and irregular (grey lines) sentences averaged across all phrases, phrases with old verb stems, and phrases with new verb stems. Voltage maps in top panel represent ERP differences between irregular and regular sentences for all verb stems. (C) The mid-latency memory effect in the wake group (voltage map as in B) and ERPs over frontal and central regions for old and new verb stems. (D) The mid-latency memory effect in the nap group (voltage map as in B) and ERPs over frontal and CPO regions for old and new verb stems. The CPO region included the central and parietal-occipital regions.

1.1.6 Gradual development of non-adjacent dependency learning during early childhood

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In order to become proficient native speakers, children have to learn the morpho-syntactic relations between distant elements in a sentence, so-called non-adjacent dependencies (NADs). Previous research suggests that NAD learning in children comprises different developmental stages. Until 2 years of age, children are able to learn NADs associatively under passive listening conditions while, starting around the age of 3–4 years, children fail to learn NADs during passive listening. To test whether the transition between these developmental stages occurs gradually, we tested children's NAD learning in a foreign language using event-related potentials (ERPs). We found ERP evidence of NAD learning across the ages of 1, 2, and 3 years. The amplitude of the ERP effect representing NAD learning, however, decreased with age. These findings might indicate a gradual transition in children's ability to learn NADs associatively. Cognitively, this transition might be driven by children's increasing knowledge of their native language, hindering NAD learning in novel contexts. Neuroanatomically, maturation of the prefrontal cortex might play a crucial role, promoting top-down learning and affecting bottom-up associative learning. In sum, our study suggests that NAD learning under passive listening conditions undergoes a gradual transition between different developmental stages during early childhood.

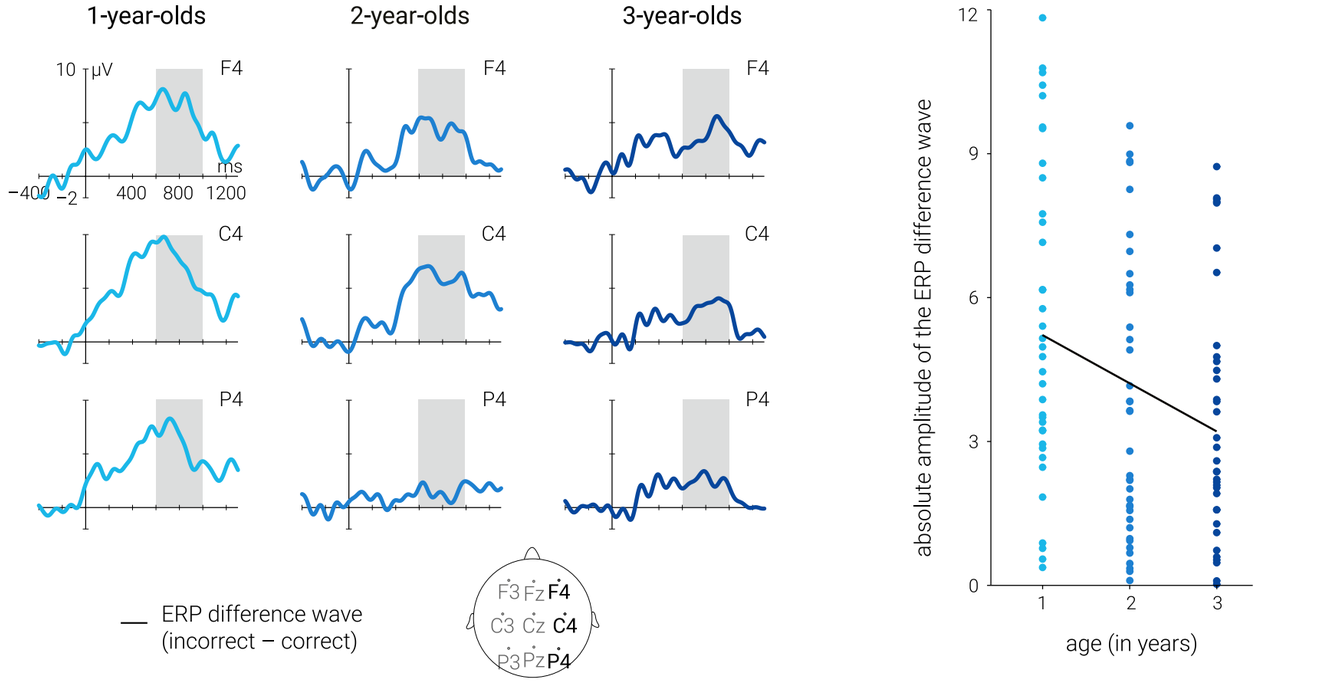

Figure 1.1.6 Grand-average ERP difference waves (incorrect - correct) for the three age groups. To account for the absolute amplitudes used in the analyses, the ERP difference wave for the children with negative polarity is flipped for visualization purposes. Grey bars highlight the time window from which the absolute amplitude was extracted.

1.1.7 Children's syntax is supported by the maturation of BA 44 at 4 years, but of the posterior STS at 3 years of age

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Within the first years of life children learn major aspects of their native language. However, the ability to process complex sentence structures (i.e. syntax), a core faculty in human language, has been found to emerge slowly. A milestone in the acquisition of syntax is reached around the age of 4, when children learn a variety of syntactic concepts, including, for example, subordinate clauses. Here, we ask which maturational changes in the child's brain underlie the emergence of syntactic abilities around this critical age. We relate markers of cortical brain maturation to 3- and 4-year-olds' syntactic abilities, in contrast to other language abilities. Our results show that distinct cortical brain areas in the left hemisphere support syntax in the two age groups. While 3-year-old's syntactic abilities were associated with increased surface area in the most posterior part of the left superior temporal sulcus, 4-year-old children showed an association with cortical thickness in the left posterior part of Broca's area, i.e. BA 44. The present findings suggest that syntactic abilities rely on the maturation of distinct cortical regions in 3- compared to 4-year-olds. The observed shift, to more mature regions involved in syntax, may underlie the behavioural milestones in syntax acquisition around 4 years of age.

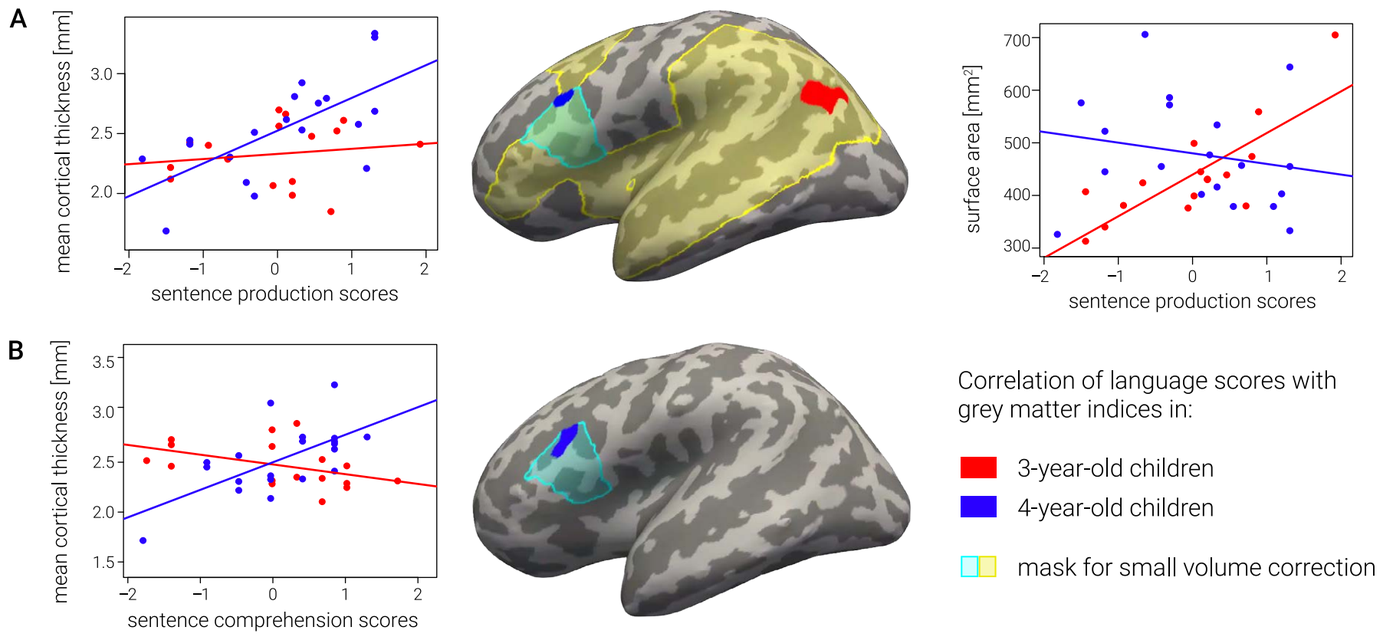

Figure 1.1.7 (A) Linear correlation of sentence production abilities of children (3-year-olds: red; 4-year-olds: blue) with surface area/ cortical thickness in the preregistered mask of language-related ROIs (light yellow) and of left BA 44 (light blue). (B) Linear correlation of sentence comprehension abilities of 4-year-old children (blue) with cortical thickness in the mask of left BA 44 (light blue). The correlations were independent of sex, non-verbal IQ, and estimated Total Intracranial Volume (eTIV). All clusters are reported after multiple comparison correction at a cluster-forming threshold of $p < 0.01$ and clusterwise threshold of $p < 0.05$ and displayed on the inflated cortex of the common group template.

1.1.8 Lateralisation of the dorsal fibre tract targeting Broca's area predicts language development

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The functional brain network for language appears to already be lateralised toward the left hemisphere in an early developmental stage. However, whether and how this is paralleled by the asymmetry of white matter connections in the language network remains an open question. The structural brain network for language contains, among others, two dorsal fibre tracts, one targeting the posterior portion of Broca's area (BA 44), and the other targeting the precentral gyrus (BA 6). Here we demonstrate, in a large sample of preschool children (3 to 6 years; N = 156), that local microstructural asymmetry along the BA 44-targeting fibre tract significantly correlates with age and language performance. However, asymmetry of the BA 6-targeting fibre bundle and two control fibre bundles did not. The anterior-horizontal part of the BA 44-targeting fibre tract correlated with age but not with language performance, whereas its posterior-ventral part correlated with language performance. Our findings show that the leftward asymmetry of the fibre tract connecting Broca's area with the temporal cortex develops in early childhood and is related to early language development.

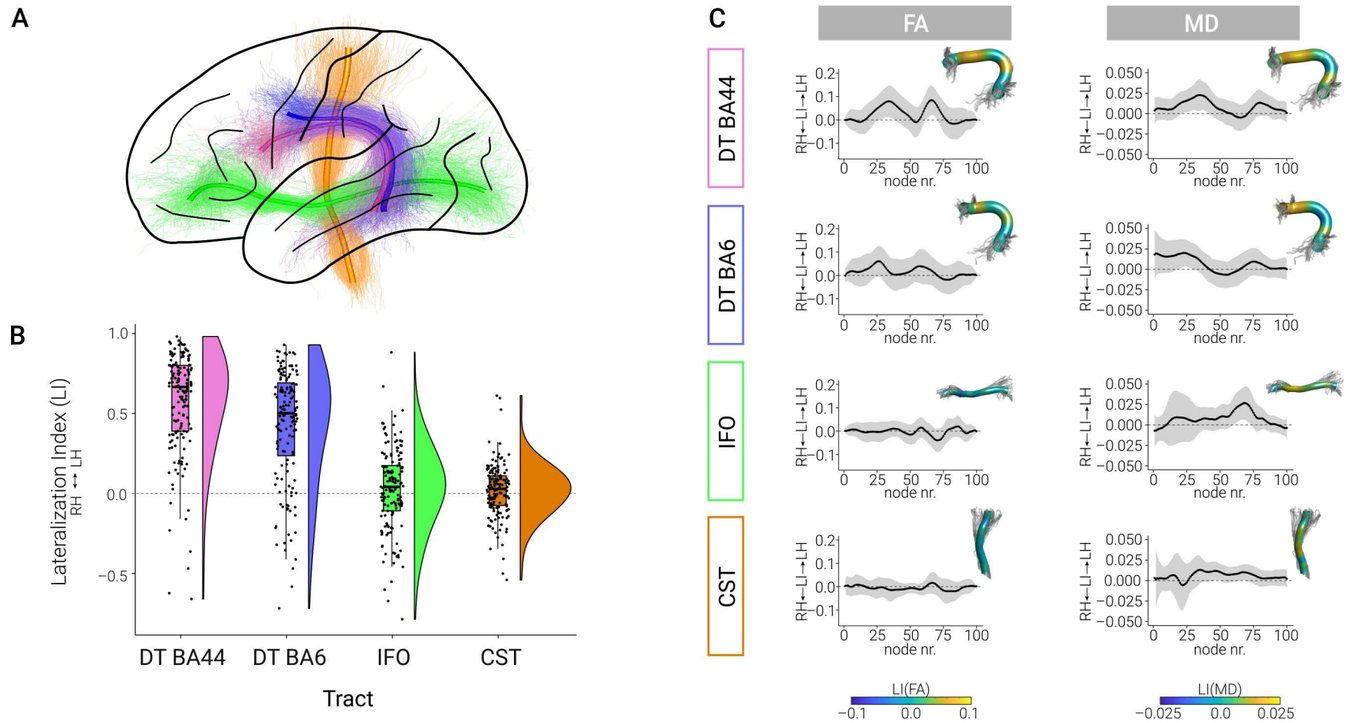

Figure 1.1.8 (A) Tractography reconstructions for the dorsal tract targeting BA 44 (DT BA 44; magenta), the dorsal tract targeting BA 6 (DT BA 6; blue), the ventral tract (IFO; green), and the corticospinal tract (CST; orange) using automated fibre quantification software (39). For each tract the figure displays a random sample of 500 streamlines (thin lines) across all subjects, alongside the respective centroid tract (bold lines), used for the subsequent analyses. (B) Summary of tract-wise macrostructural asymmetry. A positive lateralisation index (LI) indicates leftward asymmetry. (C) Localised microstructural lateralisation profiles for fractional anisotropy (FA) and mean diffusivity (MD). The grey-filled areas indicate the respective local standard deviations. For visualisation, microstructural lateralisation indices are additionally plotted on a representative tract.

1.2 The Functional Neuroanatomy of the Language Network

The functional neuroanatomical language network consists of a number of regions in the inferior frontal and posterior temporal cortex, which are connected via dorsal and ventral fibre tracts allowing information transfer between them.

Syntactic processes are known to involve BA 44 in the IFG and the posterior temporal cortex. This was confirmed in an fMRI study using a specifically designed novel artificial grammar, which tested for hierarchical structure building (1.2.1). Semantic processes in contrast are taken to involve the temporal cortex, the angular gyrus, and BA 45. The timing and the interplay of the different regions within the syntactic and semantic network are still an open issue, which we investigated in two studies using a combined Transcranial Magnetic Stimulation and Electroencephalography (TMS-EEG) approach. The first study focused on syntactic processes and tested the causal role of Broca's area in syntactic prediction. Interestingly, we found no causal effect on the syntax-related ERP component when stimulating Broca's area during the first word in two-word constructions. This suggests that Broca's area may not be involved in top-down prediction but rather in bottom-up integration processes (1.2.2). This interpretation was supported by a behavioural syntactic priming study showing that the observed priming effect was not due to enhancement of the syntactic fit of two subsequent elements (prelexical prediction), but due to an inhibition of their misfit (postlexical integration) (1.2.3). The second TMS-EEG study focused on semantic prediction and the resulting expectancy as evidenced in the modulation of the ERP N400 effect. The results of this study indicate an involvement of the left posterior temporal cortex and the posterior IFG, with a clear processing order of the IFG following the temporal cortex during semantic processes (1.2.4). These TMS-EEG findings clearly advance our knowledge about the dynamics of the functional interplay of the different brain regions within the language network. In a patient-based study the different contributions of the frontal and temporal regions to semantic composition were investigated. Data from patients suffering from a left-hemispheric stroke suggest that the temporal cortex supports semantic combinatorics, whereas the anterior inferior frontal cortex comes into play when semantic decisions are made (1.2.5).

Last but not least, we asked whether plasticity of the structural language network is a function of native and second language learning. Second language learning in an intensive training across 6 months revealed changes in the white matter of semantic- and phonology-related brain systems, but not in the syntax-related system (1.2.6). In the native language training study, we found effects of multi-day training of syntactically complex sentences in the white matter network. The connectivity pattern before training revealed individual differences that predicted individual language performance, suggesting an anatomical predisposition for the ability to process and learn language (1.2.7).

1.2.1 Hierarchical syntactic processing is beyond mere associating: fMRI evidence from a novel artificial grammar

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[1] College of Chinese Language and Culture, Beijing Normal University, China, [2] Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany, [3] Department of Audiology and Phoniatrics, Charité – Berlin University of Medicine, Germany

Grammar is central to any natural language. In the past decades, artificial grammar of the A^nB^n type, in which a pair of associated elements can be nested in another pair, was considered as a model to mimic human language syntax without semantic interference. However, such a grammar relies on mere association mechanisms, insufficient to reflect the hierarchical nature of human syntax. Here, we tested how the brain imposes syntactic hierarchies according to the category relations on linearized sequences. We designed a novel artificial "Hierarchical syntactic structure-building Grammar" (HG) and compared that to the A^nB^n grammar as a "Nested associating Grammar" (NG) based on multilevel associations. Thirty-six healthy native German speakers were randomly assigned to one of the two grammars. After successfully completing an explicit, behavioural learning session, both groups performed a grammaticality judgment task in the MRI scanner with auditorily presented word sequences generated by the corresponding grammar. Compared to the NG group, we found that the HG group showed: (a) significantly higher involvement of Brodmann area (BA) 44, the posterior part of Broca's area in the inferior frontal gyrus (IFG), and the posterior superior temporal gyrus (pSTG) in the left hemisphere, and (b) qualitatively distinct connectivity between the two regions. Thus, the present study demonstrates that the build-up process of syntactic hierarchies critically relies on a distinctive left-hemispheric syntactic network involving BA 44 and pSTG. This indicates that our novel artificial grammar constitutes a suitable experimental tool to investigate syntax-specific processes in the human brain.

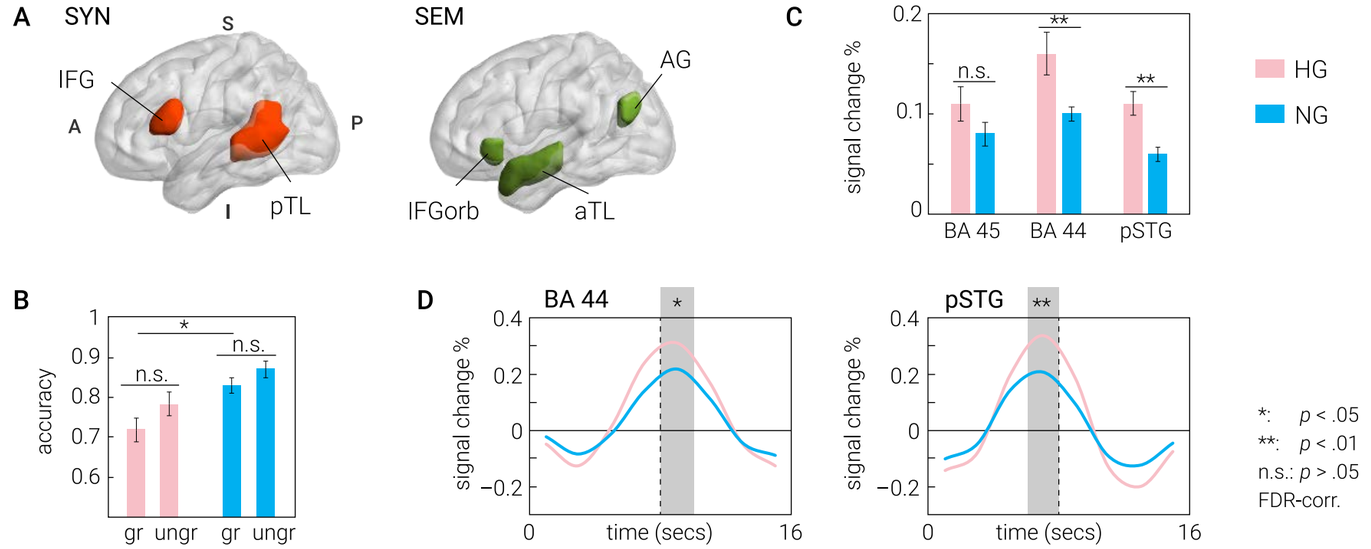

Figure 1.2.1 (A) Syntactic network (SYN) and semantic network (SEM) from the 220 participant-based, functional, left-hemisphere language atlas (on the basis of Fedorenko et al., 2010; https://evlab.mit.edu/funcloc/download-parcels). (B) Behavioural results in the scanning session: gr, grammatical; ungr, ungrammatical condition. (C) Signal intensity analysis results for HG (hierarchical syntactic structure-building grammar, pink) and NG (nested associating grammar, blue) in BA 45, BA 44, and posterior superior temporal gyrus (pSTG). (D) Peak analysis results for BA 44 and pSTG.

1.2.2 Neurostimulation of Broca's area does not interfere with syntactic predictions: A combined TMS-EEG approach

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Syntactic prediction on the basis of word category information has been proposed as the key mechanism supporting the fast syntactic processes in language. Previous functional neuroimaging studies point towards Broca's area in the left inferior frontal gyrus (IFG) as one fundamental cortical region involved in categorical prediction during incremental language processing in a top-down manner. Causal evidence for this hypothesis is, however, still missing. In this study, we combined EEG and TMS to test whether Broca's area is functionally relevant in predictive mechanisms for language. We transiently perturbed Broca's area during the first word in a two-word construction, while simultaneously measuring the event-related potential (ERP) correlates of syntactic processing (early syntactic negativity (ESN) and P600). We reasoned that if Broca's area is involved in predictive mechanisms for syntax, disruptive TMS during the first word would mitigate the difference in the ERP responses for predicted and unpredicted categories in basic two-word constructions. We found that the perturbation of Broca's area at the predictive stage did not affect the ERP correlates of basic composition. We discuss the results considering an alternative account of the role of Broca's area in syntactic processing, namely, a bottom-up integration of words into constituents, within the language network.

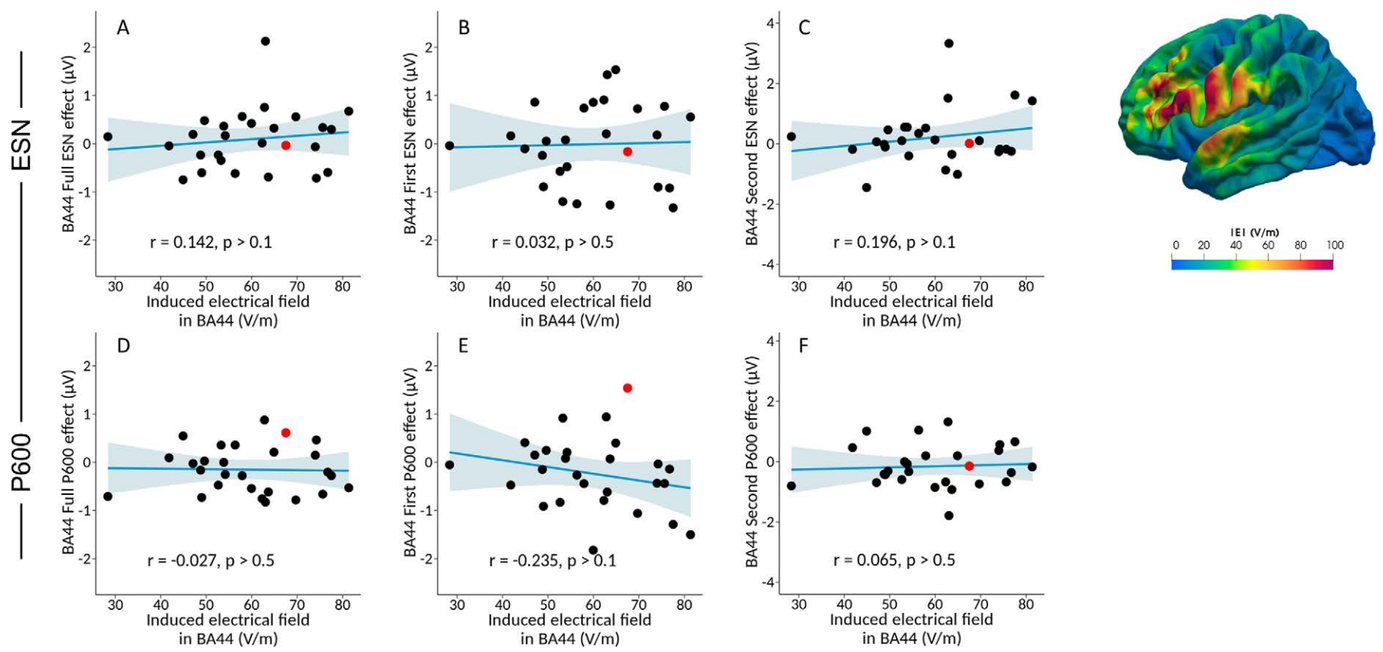

Figure 1.2.2 (A) Analysis of the correlation between the Full $ESN_{BA\ 44}$ effect (Full $ESN_{BA\ 44}$ – Full ESN_{sham}) and the induced electrical field in BA 44. (B) Separate correlation analyses for the First $ESN_{BA\ 44}$ effect. (C) Second $ESN_{BA\ 44}$ effect. (D) Full $P600_{BA\ 44}$ effect. (E) First $P600_{BA\ 44}$ effect. (F) Second $P600_{BA\ 44}$ effect. The plotted brain illustrates the reconstructed TMS-induced electrical field from the BA 44 session for a single subject, highlighted in red in the scatter plots. ESN = early syntactic negativity.

1.2.3 Testing the automaticity of syntax using masked visual priming

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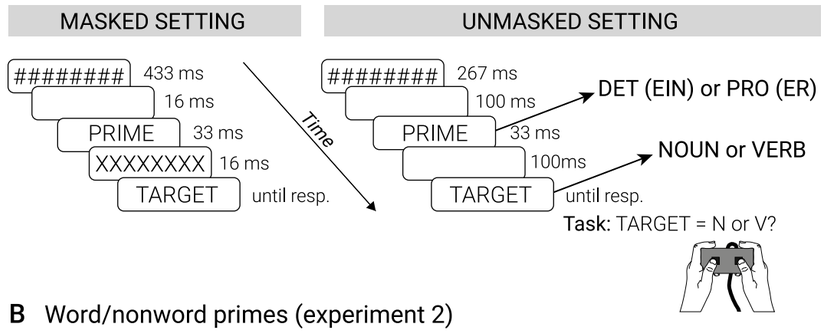
[1] Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany, * shared co-first authorship

Language comprehension proceeds at a very fast pace. It is argued that context influences the speed of language comprehension by providing informative cues. How syntactic contextual information influences the processing of incoming words is, however, less known. Here we employed a masked syntactic priming paradigm in four behavioural experiments, in the German language, to test whether masked primes automatically influence the categorisation of nouns and verbs. We found robust syntactic priming effects with masked primes but only when verbs were morpho-syntactically marked. Furthermore, we found that, compared to baseline, primes slow down target categorisation when the relationship between prime and target is syntactically incorrect, rather than speeding it up when the relationship is syntactically correct. This argues in favour of an inhibitory nature of syntactic priming. Overall, the data indicate that humans automatically extract syntactic features from the context to guide the analysis of incoming words during online language processing.

A Syntactic priming task



B Word/nonword primes (experiment 2)

		TARGET		TARGET	
		NOUN	VERB	NOUN	VERB
PRIME	DET	EIN BART *a beard*	*EIN KAUT *a chews*	**FTN** BART	**FTN** KAUT
	PRO	*ER BART *he beard*	ER KAUT *he chews*	**FR** BART	**FR** KAUT

C Results (experiment 2)

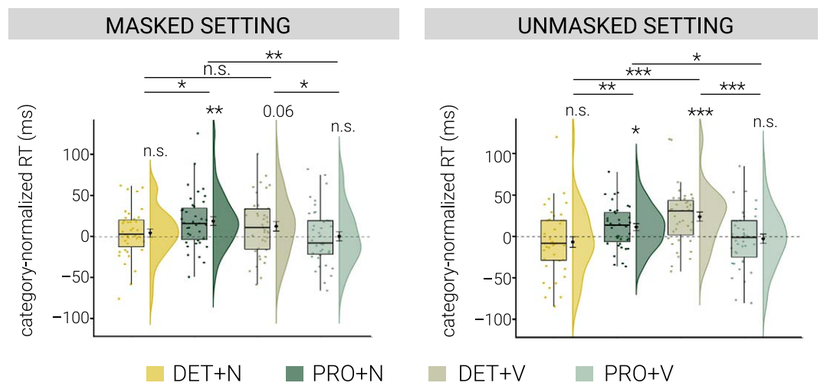


Figure 1.2.3 (A) Time-course of stimulus presentation in the Syntactic Priming task, in both masked and unmasked settings, across four behavioural experiments. Participants were asked to judge the category of target stimulus (noun or verb) via button press. Accuracy and reaction time responses were recorded. (B) In experiment 2 the non-word prime effect was subtracted from the real-word prime effect to account for category bias (category-normalisation procedure). DET = determiner, PRO = pronoun, REAL = real-word prime, NON = non-word prime. The asterisks indicate ungrammaticality. (C) Results of the post-hoc analysis of the Prime × Target's Category interaction showing significant inhibition in the ungrammatical conditions (one-sample t tests against log(1) = 0) in the masked and unmasked settings after the category-normalisation procedure. The dotted line displays the baseline. The dots correspond to the individual raw observations. The median values are displayed within the boxplots. The mean values and the error bars, indicating ± 1 standard error of the mean, are shown to the right of the boxplots. For visualisation purposes, we show non-log-transformed RTs. The FDR approach (Benjamini & Hochberg, 1995) was used to correct p values for Type I error. (***p < .001. **p < .01. *p < .05. n.s. = non-significant).

1.2.4 Causal evidence from TMS-EEG for a coordinated temporal interplay within the language network

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Sentence comprehension is supported by a coordinated interplay within a left-dominant brain network, including the posterior inferior frontal gyrus (pIFG), posterior superior temporal gyrus and sulcus (pSTG/STS), and the angular gyrus (AG). Semantic expectancy is a key factor for sentence comprehension and is associated with a modulation of the electrophysiological event-related N400 response. In two experiments, we probed the functional and temporal specificity of language-related brain regions during the auditory processing of short sentences (i.e., pronoun-verb-article-noun) and related this to the N400 response. Adapting a condition-and-perturb approach, we found that reducing neural excitability of left AG, via continuous theta burst stimulation (cTBS), led to disruptive effects when either the pIFG and pSTG/STS were stimulated with repetitive transcranial magnetic stimulation (rTMS). More specifically, rTMS applied to these regions at the mid-sentence verb position led to disrupted performance, indicating their functional involvement. Moreover, varying the point of stimulation, we found that the pSTG/STS showed functional relevance in an earlier processing time-window relative to the pIFG. These findings provide the first causal evidence that these brain regions jointly contribute to sentence-based semantic processing, with a clear processing order of left pSTG/STS followed by left pIFG.

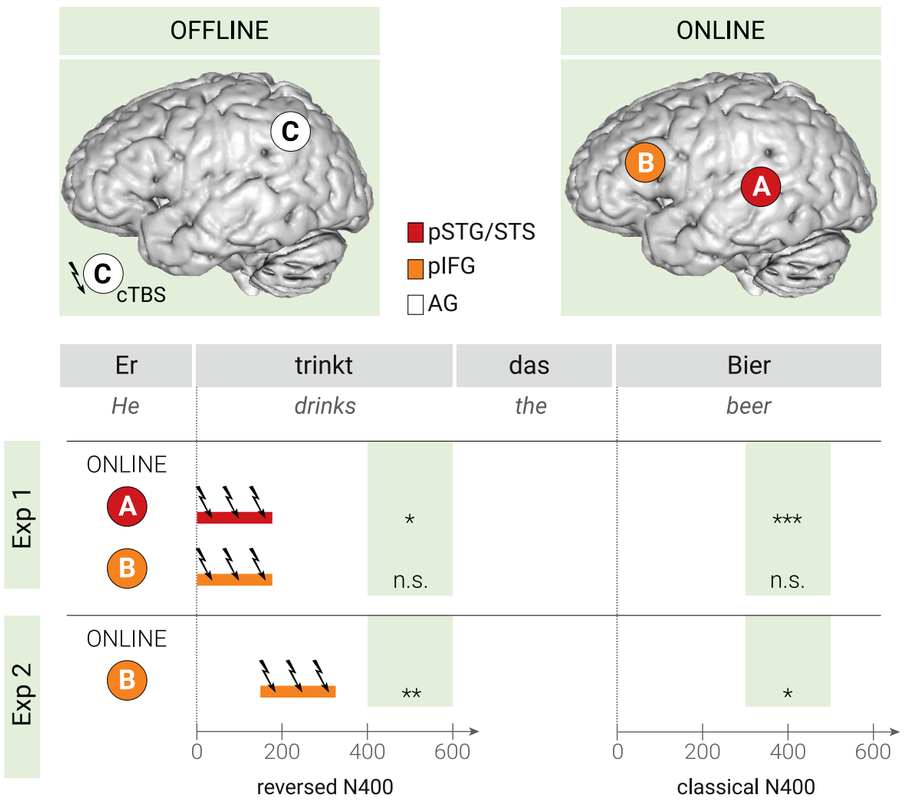

Figure 1.2.4 Overview of the electrophysiological findings of Experiment 1 and 2. After the excitability of the left AG was temporarily reduced using offline cTBS, both the left pSTG/STS and left pIFG revealed disruptive effects of online rTMS on the reversed N400 at the mid-sentence verb position. A 3-pulse burst of online rTMS (10 Hz) was either applied at an early (Experiment 1) or later time-point (Experiment 2) relative to verb onset. Interestingly, the left pSTG/STS showed functional relevance in the earlier time-window (i.e., 0-200 ms), whereas the functional relevance of the left pIFG emerged later (i.e., 150-350 ms). Crucially, both rTMS protocols outlasted the stimulation duration and had an impact on the reversed N400 effect at the mid-sentence verb (i.e., 400 - 600 ms) as well as the classical N400 effect at the sentence-final noun (i.e., 300 - 500 ms), indicating their functional relevance in sentence-based semantic processing. Significance codes: *** < 0.001, ** < 0.01, * < 0.05

1.2.5 Dissociable contributions of frontal and temporal brain regions to basic semantic composition

Graessner, A.[1], Zaccarella, E.[1], Friederici, A. D.[1], Obrig, H.[1,2]*, & Hartwigsen, G.[1]*

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Semantic composition is the ability to combine single words to form complex meanings and is an essential component for successful communication. Evidence from neuroimaging studies suggests that semantic composition engages a widely distributed left-hemispheric network, including the anterior temporal lobe, the inferior frontal gyrus, and the angular gyrus. To date, the functional relevance of these regions remains unclear. We investigated the impact of lesions to key regions in the semantic network on basic semantic composition. We conducted a multivariate lesion-behaviour mapping study in 36 native German speaking participants with chronic lesions to the language network after left-hemispheric stroke. During the experiment, participants performed a plausibility judgement task on auditorily presented adjective-noun phrases that were either meaningful ('anxious horse'), anomalous ('anxious salad') or had the noun replaced by a pseudoword ('anxious gufel'), as well as a single-word control condition ('horse'). We observed that reduced accuracy for anomalous phrases was associated with lesions in left anterior inferior frontal gyrus, whereas increased reaction times for anomalous phrases correlated with lesions in anterior-to-mid temporal lobe. These results indicate that the anterior inferior frontal gyrus is relevant for accurate semantic decisions, while anterior-to-mid temporal lobe lesions lead to slowing of the decision for anomalous two-word phrases. These differential effects of lesion location support the notion that the anterior inferior frontal gyrus affords executive control for decisions on semantic composition while anterior-to-mid temporal lobe lesions slow the semantic processing of the individual constituents of the phrase.

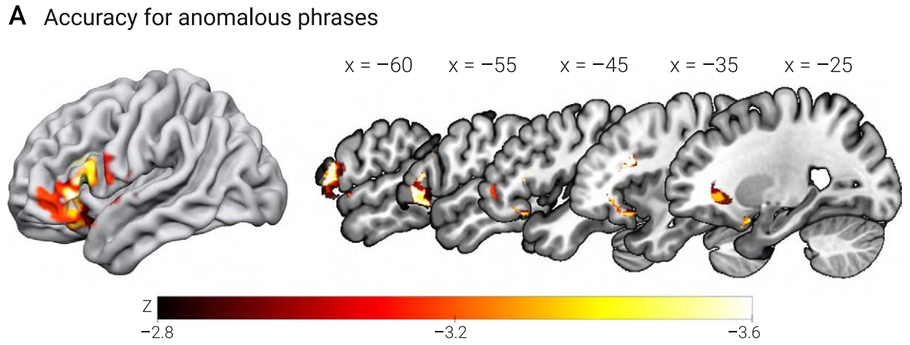

Figure 1.2.5 (A) Support Vector Regression-lesion Symptom Map results for the accuracy data in the anomalous condition. Lower accuracy for anomalous phrases (controlled for all other conditions) correlated with a lesion cluster spanning the left inferior frontal gyrus and temporal pole. Thresholded voxelwise at $p < 0.005$ and clusterwise at FWE $p < 0.05$, with lesion size and the two other conditions regressed out of both behavioural and lesion data. (B) Support Vector Regression-Lesion Symptom Map (SVR-LSM) results for reaction times in the anomalous condition. Slower reaction times for anomalous phrases (controlling for all other conditions) correlated with lesions in the left anterior temporal lobe and middle temporal gyrus. Thresholded voxelwise at $p < 0.005$ and clusterwise at FWE $p < 0.05$, with lesion size regressed out of both behavioural and lesion data.

1.2.6 Structural changes in the language network induced by second language learning

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Adult second language learning (L2) has been confirmed to induce neuroplastic changes in the human brain. Yet, it remains unclear how the structural language connectome changes across time. In this study, we attempted to answer this question by investigating the longitudinal changes of the white matter connectome in native Arabic-speaking adults who learned German over a period of 6 months. Changes mainly occurred in the second half (3 - 6 months) of our study. Significantly increased connectivity was observed within the sub-networks in bilateral temporal-parietal semantic and phonological-related systems as well as right temporal-frontal pathways. Interestingly, the syntax-related network did not change significantly. Over the same time-period, the inter-hemispheric connections showed a significant decrease in connectivity that was correlated with L2 (German) proficiency. The above findings suggest that in the first 6 months of L2-learning the dynamic changes in the language network are restricted to sub-networks related to lexical processing, and that successful L2-language acquisition in adulthood requires right-brain involvement. The reduced interhemispheric connectivity found during learning could have played a key role in this rightward shift. Taken together, our study highlights the timeline of structural changes in language-related networks driven by learning a second language.

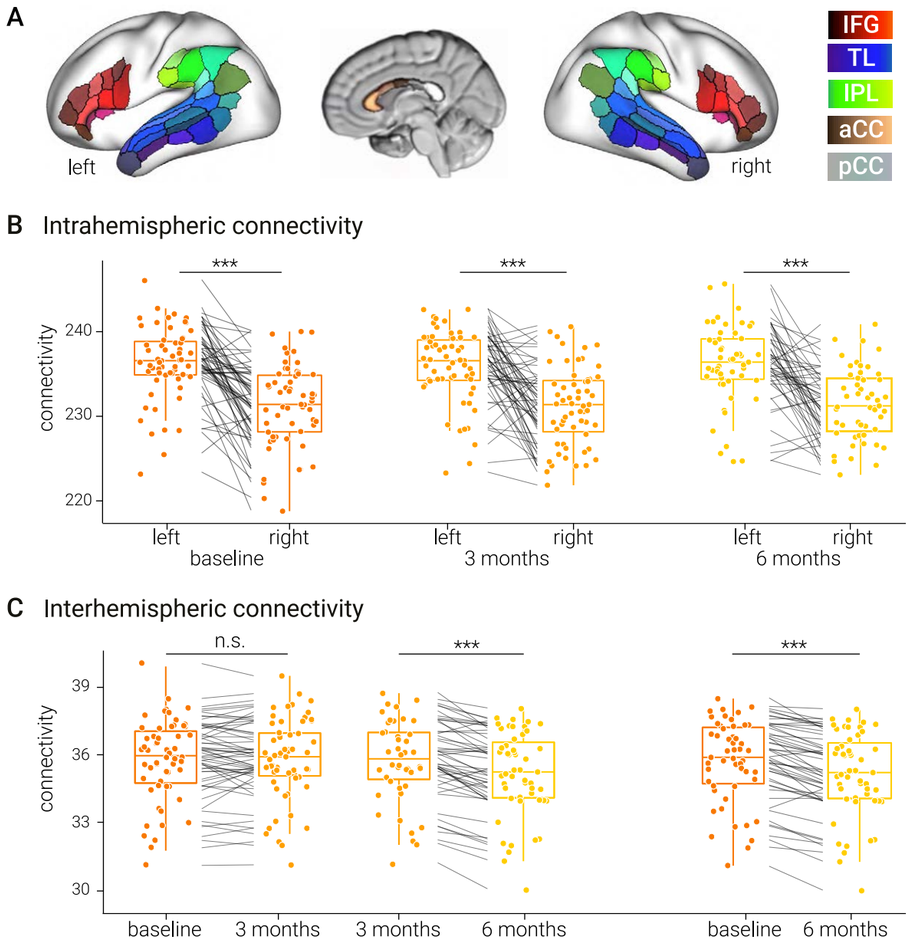

Figure 1.2.6 Longitudinal change of the intra- and interhemispheric connection strength of the language network. (A) Areas in the language network of the left and right hemisphere including Corpus callosum (CC) subregions. (B) Intra-hemispheric network strength at each time point during the learning period. ** $p < 0.01$. (C) Longitudinal changes of inter-hemispheric connectivity strength. *** $p < 0.0005$. LH: left hemisphere, RH: right hemisphere.

1.2.7 White matter brain structure predicts language performance and learning success

Sánchez, S. M.[1,2], Schmidt, H.[2,3], Gallardo, G.[2], Anwander, A.[2], Brauer, J.[2,4], Friederici, A. D.[2], & Knösche, T. R.[2,5]

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Individual differences in the ability to learn a new language have long been discussed. Less attention has been paid to individual differences in processing one's native language. Here we investigated the relationship between long-range white matter connectivity of the brain, as revealed by diffusion tractography, and the ability to process syntactically complex sentences in the participants' native language as well as the improvement thereof by multi-day training. We identified specific network motifs by singular value decomposition that indeed related white matter structural connectivity to individual language processing performance. First, for two such motifs, one in the left and one in the right hemisphere, individual prevalence significantly predicted the individual language performance. This suggests an anatomical predisposition for the individual ability to process syntactically complex sentences. Both motifs comprised a number of cortical regions, but seemed to be dominated by areas known for their involvement in working memory rather than the classical language network itself. Second, we identified another left hemispheric network motif, where the change of prevalence over the training period significantly correlated with the individual change in performance, thus reflecting training-induced white matter plasticity (see Figure 1.2.7). This motif comprises diverse cortical areas including regions known for their involvement in language processing, working memory, and motor functions. The present findings suggest that individual differences in language processing and learning can be explained, in part, by individual differences in the brain's white matter structure. Thus, brain structure may be considered as a crucial factor when discussing variations in human cognitive performance more generally.

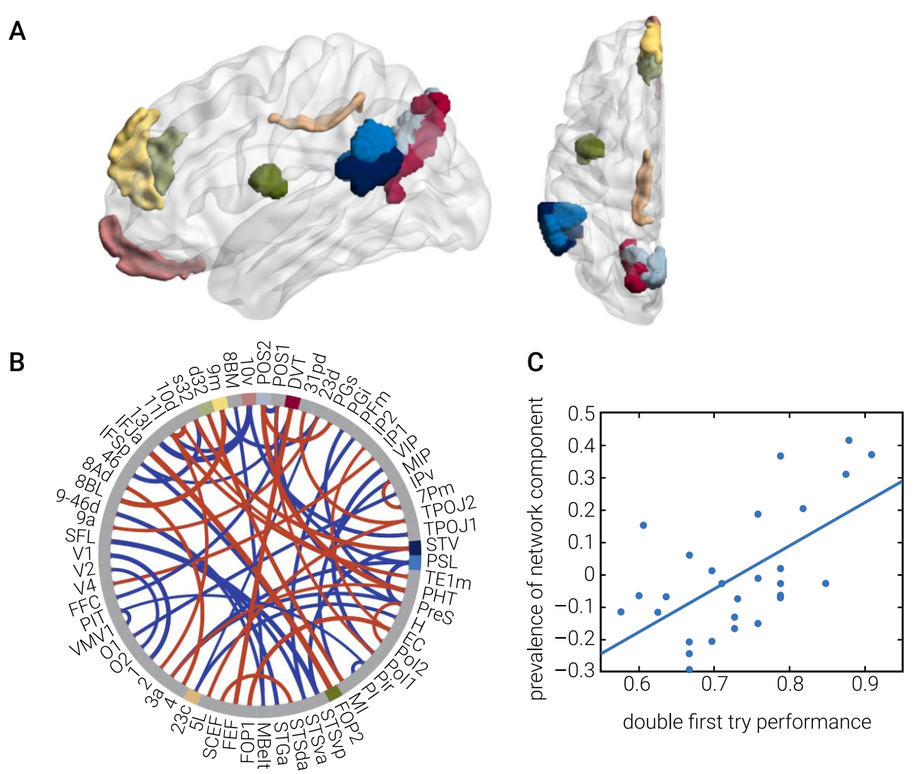

Figure 1.2.7 Network motif 1 in the left hemisphere, whose prevalence before the training correlated with the baseline performance on day 1. (A) Sagittal and axial view of nine brain areas where the network component had highest (absolute) connectivity. (B) Chord plot of the strongest connections in the network motif, with line thickness indicating the absolute weight of the connection within the motif and the colour indicating the sign (red: positive, blue: negative). Plotted are 67 of the 185 brain areas. The main constituents of the network motif (panel A) are highlighted in colour. (C) Regression plot of network prevalence before the training (right singular vector V) against the performance of subjects during the first day of training on the double centre embedding task (r = 0.567, p = 0.046).

Congresses, Workshops, and Symposia

2021

- Friederici, A. D., Maran, M., Papitto, G., Schroën, J. A. M., Trettenbrein, P. C., van der Burght, S., & Zaccarella, E. (May – September). *Leipzig Lectures on Language.* Online lecture series. Max Planck Institute for Human Cognitive and Brain Sciences Leipzig, Germany. https://www.cbs.mpg.de/leipzig-lectures-on-language
- Friederici, A. D., Maran, M., Papitto, G., Schroën, J. A. M., Trettenbrein, P. C., van der Burght, S., & Zaccarella, E. (October). *Leipzig Lectures on Language.* End-of-year symposium. Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, German. https://www.cbs.mpg.de/leipzig-lectures-on-language
- Govaart, G., & Paul, M. (June). *Reproducibility and transparency in EEG research: Current developments.* Virtual Symposium organized at Psychologie und Gehirn (PuG 2021).

2022

- Eichner, C. (May). *Evolution of Brain Connectivity.* Workshop. Max Planck Institute for Human Cognitive and Brain Sciences Leipzig, Germany.
- Papitto, G., Trettenbrein, P. C., Friederici, A. D., & Zaccarella, E. (September). *Segregation and overlap between language and action: Neurobiological and theoretical perspectives.* Joint Conference on Language Evolution. Kanazawa, Japan.

Degrees

PhD Theses

2020

- Cheung, V. K. M. *The neurocognitive basis of musical expectancy and pleasure: A computational modelling approach.* Leipzig University, Germany.
- Qi, T. *The brain structure during language development: Neural correlates of sentence comprehension in preschool children.* Leipzig University, Germany.

2021

- Ekerdt, C. *How language shapes the developing brain. An investigation of the white matter structures underlying language acquisition.* Leipzig University, Germany.
- Kühn, C. *Training-induced plasticity in the developing brain of preschoolers during sensitive periods in language acquisition.* Leipzig University, Germany.
- van der Burght, C. *The central contribution of prosody to sentence processing: Evidence from behavioural and neuroimaging studies*. Leipzig University, Germany.

2022

- Chien, P.-J. *Neural bases of linguistic pitch in a tonal language: Intonation, lexical tone, and the role of language experience.* Leipzig University, Germany.
- Paul, M. *Non-adjacent dependency learning: Development, domain differences, and memory.* Leipzig University, Germany.

Appointments

2020

- Skeide, M. A. *ERC Group Leader.* Max Planck Institute for Cognitive and Brain Sciences, Leipzig, Germany.
- Skeide, M. A. *Heisenberg Fellow,* German Research Federation (DFG). Max Planck Institute for Cognitive and Brain Sciences, Leipzig, Germany.
- Zaccarella, E. *Substitute Professor (W3),* Department of Linguistics, Faculty of Human Sciences, University of Potsdam, Germany.

2022

- Friederici, A. D. *Board member of the International Max Planck Research School on Cognitive NeuroImaging (IMPRS CoNI),* Max Planck Institute for Cognitive and Brain Sciences, Leipzig, Germany.
- Männel, C. *W2 Professorship,* Clinic for Audiology and Phoniatrics, Charité – Berlin University of Medicine, Germany.
- Schaadt, G. *W2 Professorship,* Department of Special Education, Free University of Berlin, Germany.

Awards

2020

- Schroën, J. A. M. *Poster Award.* Transcranial Brain Stimulation in Cognitive Neuroscience Workshop. Trento University, Rovereto, Italy.

2021

- Friederici, A. D. *The Huttenlocher Award of the Flux Society*.
- Govaart, G., & Paul, M. *IGOR Prize for Open and Reproducible Science 2021 for the symposium "Reproducibility and transparency in EEG research: current developments" at the 46th Annual Meeting "Psychologie und Gehirn",* Tübingen, Germany.

Publications

Books & Book Chapters

Cheung, V. K. M. (2020). The neurocognitive basis of musical expectancy and pleasure: A computational modelling approach. *MPI Series in Human Cognitive and Brain Sciences*: Vol. 210. Leipzig: Max Planck Institute for Human Cognitive and Brain Sciences.

Ekerdt, C. (2021). How language shapes the developing brain: An investigation of the white matter structures underlying language acquisition. *MPI Series in Human Cognitive and Brain Sciences*: Vol. 217. Leipzig: Max Planck Institute for Human Cognitive and Brain Sciences.

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Kuhnke, P. (2021). The neural basis of conceptual knowledge retrieval: Insights from fMRI & TMS in the healthy human brain. *MPI Series in Human Cognitive and Brain Sciences*: Vol. 214. Leipzig: Max Planck Institute for Human Cognitive and Brain Sciences.

Paul, M. (2022). Non-adjacent dependency learning: Development, domain differences, and memory. *MPI Series in Human Cognitive and Brain Sciences*: Vol. 219. Leipzig: Max Planck Institute for Human Cognitive and Brain Sciences.

Qi, T. (2020). The brain structure during language development: Neural correlates of sentence comprehension in preschool children. *MPI Series in Human Cognitive and Brain Sciences*: Vol. 207. Leipzig: Max Planck Institute for Human Cognitive and Brain Sciences.

Van der Burght, C. (2021). The central contribution of prosody to sentence processing: Evidence from behavioural and neuroimaging studies. *MPI Series in Human Cognitive and Brain Sciences*: Vol. 213. Leipzig: Max Planck Institute for Human Cognitive and Brain Sciences.

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Professor Dr Arno Villringer
Director

2

Plasticity

DEPARTMENT OF NEUROLOGY

Our mission is to prevent and treat stroke and dementia.

We **aim** to elucidate the mechanisms underlying:

(i) the development of **risk factors** (obesity, hypertension) and their short- and long-term effects on brain structure and function,

(ii) the pathophysiology of **brain lesions** underlying stroke and dementia and their impact on sensorimotor function and cognition, and

(iii) learning and recovery after stroke (**rehabilitation**).

Our **translational goals** are to:

(i) develop early biomarkers and intervention strategies to prevent the development of risk factors,

(ii) interrupt risk factor-dependent processes leading to stroke and dementia, and

(iii) improve recovery from stroke.

Each research topic is closely related to the others.

Risk Factors (Chapter 2.1). The interaction between body and brain is a central theme of our work. We hypothesise that detrimental, self-reinforcing interactions between gut and brain as well as heart and brain ("vicious cycles") trigger and further promote the development of the risk factors obesity and hypertension, which we conceptualise as "learned" behavioural changes. To test these hypotheses, we use a combination of cognitive/behavioural, vascular, metabolic, and neuroimaging approaches (e.g., Schlögl et al., 2016, Lancet Diabetes Endocrinol, 4, 695–705). The study of physiological interactions in healthy participants provides a unique window into understanding critical signalling pathways, such as the effects of baroreceptor signalling on cognition and perception (Al et al., 2020, PNAS). At the same time, the development of computational models can provide a mechanistic framework for neuronal interactions, e.g., related to dopaminergic neurotransmission (Wiencke et al., 2020, PLoS Comput Biol), with the goal of understanding maladaptive changes underlying behavioural manifestation of risk factors as "vicious cycles". In this context, ongoing research projects aim to decipher the role of the body's response to psychological or physiological stress as a common maladaptive mechanism of various risk factors.

Brain Lesions (Chapter 2.2). While we seek to understand the neural correlates of behaviours that lead to the development of risk factors, we are also investigating where, when, and how established risk factors lead to brain damage (e.g., Lampe et al., 2019, Ann Neurol; Schaare et al., 2019, Neurology). We specifically study the consequences of pathologic heart-brain interactions (Müller et al., 2020, Circ Res) and seek to understand pathophysiology by taking advantage of multi-modal studies of the brain, including regional cerebral blood flow, metabolism, and molecular markers. Using machine learning on large structural MRI data sets, we have already been able to establish neurobiological links between a form of dementia (bvFTD) and psychosis (Koutsouleris et al., 2022, JAMA Psychiatry). We also identify and validate innovative non-invasive electrophysiological markers of pathological brain activity such as phase-amplitude coupling of beta and gamma oscillations and beta bursts, which can potentially serve as early biomarkers of neurodegeneration (Gong et al., 2021, Brain; Zhang et al., 2021, NeuroImage).

Rehabilitation (Learning and Recovery) (Chapter 2.3). Looking at our patients with acquired brain injuries, the third focus of our research is on understanding learning and recovery of brain function, particularly the somatosensory/sensorimotor system. We are investigating the neural correlates of motor learning in healthy young and elderly participants, post-stroke individuals, and Parkinson's patients, and examining the effects of cardiovascular training, brain computer interfaces (BCI), drugs modulating the dopaminergic or serotonergic system, and transcranial stimulation. For example, we have demonstrated improvements in motor learning when coupled with cardiovascular training (Lehmann et al., 2020, J Neurosci). In the context of transcranial stimulation, we have resolved some of the earlier conflicting results by demonstrating positive and negative effects of the same transcranial direct current stimulation in individuals after stroke (Muffel et al., 2022, Brain Stimul). In order to stratify stroke patients for the following motor rehabilitation, we also develop novel

approaches based on the combination of tractography and multi-muscle TMS mapping (Nazarova et al., 2021, Stroke). Building on close collaborations with the Department of Neuropsychology at our Institute, Leipzig University Hospital, and national networks, clinicians in our Clinic for Cognitive Neurology are working to understand aphasia and language recovery support (Martins et al., 2019, Brain, 142, 3217–3229; Hartwigsen et al., 2020, eLife; Lorenz et al., 2022, Cortex). In other collaborations with the clinic, we are investigating the potential of virtual reality in the treatment of patients with neglect and the efficacy of music therapy and its foundations.

Setting, participants, approaches: We conduct our research together with our partner institution, the Clinic for Cognitive Neurology at Leipzig University Hospital (100 m walking distance, clinical service headed by Hellmuth Obrig). We conduct (longitudinal) observational studies on large population-based databases (UK biobank, German national cohort) including our own LIFE cohort (N = 10,000) and patient cohorts of our Clinic for Cognitive Neurology, as well as proof-of-concept interventional trials in groups of young and older healthy volunteers. We use a combination of behavioural/cognitive approaches in conjunction with a wealth of (computational) neuroimaging and neurointerventional MR-based (3T to 7T), electrophysiological (MEG, EEG, TMS, and TDCS), and optical (fNIRS) methods and focused ultrasound.

Method development: To best answer the above scientific questions, we are investing in methodological advances. For example, in recent years we have developed more naturalistic neuroimaging approaches that combine mobile imaging (EEG, fNIRS) with virtual reality (Hofmann et al., 2021, eLife). We have also implemented a smartphone-friendly user interface in existing apps to assess eating behaviour in “real life” (Medawar et al., in press, NPJ Science of Food). Applying explainable AI to neuroimaging data is another contribution of our group, achieved in cooperation with Technical University, Berlin (Hofmann et al., 2022, NeuroImage). We have continued our work on developing methods for non-invasive assessment of brain perfusion in acute stroke (Lv et al., 2013, Ann Neurol, 73, 136–140; Khalil et al., 2017, Stroke, 48, 925–931; Hu et al., 2021, Hum Brain Mapp) and oxygen consumption (Fan et al., 2020, J Cereb Blood Flow Metab). Using innovative EEG/MEG-data analyses and computational modelling, Vadim Nikulin’s group has provided a unifying explanation for the generation of evoked activity and ongoing oscillations (Iemi et al., 2019, eLife, 8, e43620; Studenova et al., 2022, PLoS Comput Biol). They also developed a novel approach allowing unprecedented non-invasive detection of single-trial excitatory-postsynaptic currents in pyramidal cells using machine learning for early somatosensory responses (Stephani et al., 2021, eLife). His group has also developed new methods for separating cross-frequency coupled sources in the brain (Idaji et al., 2020, NeuroImage) and a method to eliminate spurious interactions due to the harmonic components in neuronal data (Idaji et al., 2022, NeuroImage). Finally, we are collaborating with a group at Leipzig University, the Fraunhofer Institute for Biomedical Engineering (IBMT), and several companies, and with the support of a new 7 million Euro grant from the Federal Ministry of Education and Research, will develop ultrasound-based neuromodulation with the goal of non-invasive deep brain stimulation.

Mentoring: Coaching, mentoring, and maintaining the mental health of all department employees is a top priority. All graduate students are advised to participate in a graduate programme (Arno Villringer has founded two of them where he is still the speaker: the Max Planck School of Cognition and the Berlin School of Mind and Brain), and mentoring continues thereafter. We are pleased to report that four former members of the department have moved to professorship/faculty positions in the past three years, bringing the total number of former members of the group who have achieved this to 36.

Open Science, Society: We are committed to good scientific practice and are advocates of open science. Next to open preprints, we have recently adopted code-sharing, open data, and pre-registration of empirical studies as a standard for all our work. Members of the department are active and driving forces in the Institute's Open Science Initiative, ReproducibiliTEA, the Code Review Club, Green Team, and Equality and Diversity Team. We are grateful to the Max Planck Society and other public funders for their continued support. While we greatly appreciate this support for our curiosity-driven basic research, we are also aware that our research addresses topics with potentially large societal implications, as demonstrated, for example, by the striking relationship between social status, inequality, and the prevalence of risk factors. We are committed to "giving back" to society as much as possible, as expressed through a series of communications and events for the general public.

Publications: We think that our work has had impact on the fields of brain imaging, blood flow, and metabolism given that since 2020 a total of 63 papers have been published in leading journals such as *NeuroImage* (34), *NeuroImage Clinical* (7), *Human Brain Mapping* (13), *Journal of Cerebral Blood Flow and Metabolism* (6), *Circulation Research* (1), *European Heart Journal* (1), and *Stroke* (1). Other studies have appeared in leading journals with wider coverage, such as *eLife* (4), *Brain* (1), *Annals of Neurology* (2), *JAMA Psychiatry* (1), *JAMA Network Open* (2), *Neurology* (1), *Biological Psychiatry* (4), *Nature Communications* (2), *PNAS* (2), *Cell Reports* (1), *Journal of Neuroscience* (5), *Cerebral Cortex* (7), *PLOS Computational Biology* (3), and *Nature Protocols* (2). As part of large consortia, there are additional publications in *Nature* (2), *Molecular Psychiatry* (1), *Nature Communication* (1), *JAMA Neurology* (1), and *Stroke* (1). Highlighting these publications in no way implies that we are not fully convinced of the scientific value of all other work; the full publication record of the last three years is given at the end of this Department's report.

2.1 Risk Factors

The **central thesis** of this research focus is that **vicious cycles of brain-body interactions** are crucial for the development of the risk factors obesity and hypertension.

In the development of **obesity**, such a hypothesised cycle of body-brain interactions involves the gut-brain axis and is illustrated in Figure 2.1.1.2 below (in Chapter 2.1.1); Veronica Witte's group is investigating the interactions between eating behaviours, the microbiome, and metabolic parameters, as well as cognitive and brain functions (see Chapter 2.1.1).

In the development of **hypertension**, the hypothesised cycle involves heart-brain interactions. Our work here builds on findings that blood pressure modulations and heart-brain interactions are associated with changes in perception (somatosensory and pain) and emotion that may lead to greater well-being at higher blood pressure (Schaare et al., MedRxiv), with baroreceptor activity as a mediator. To understand the basic mechanisms, we examine perception and emotion (including stress) in the context of heart-brain interactions and blood pressure (see Chapters 2.1.2 and 2.1.3).

2.1.1 Eating behaviour, diet, and obesity: A brain-body crosstalk

Medawar, E.[1], Thieleking, R.[1], Hofmann, S.[1], Lammer, L.[1,2], Beyer, F.[1,2], Vartanian, M.[1], Endres, K.[1], Janssen, L.[1], Villringer A.[1,2], & Witte A. V.[1,2]

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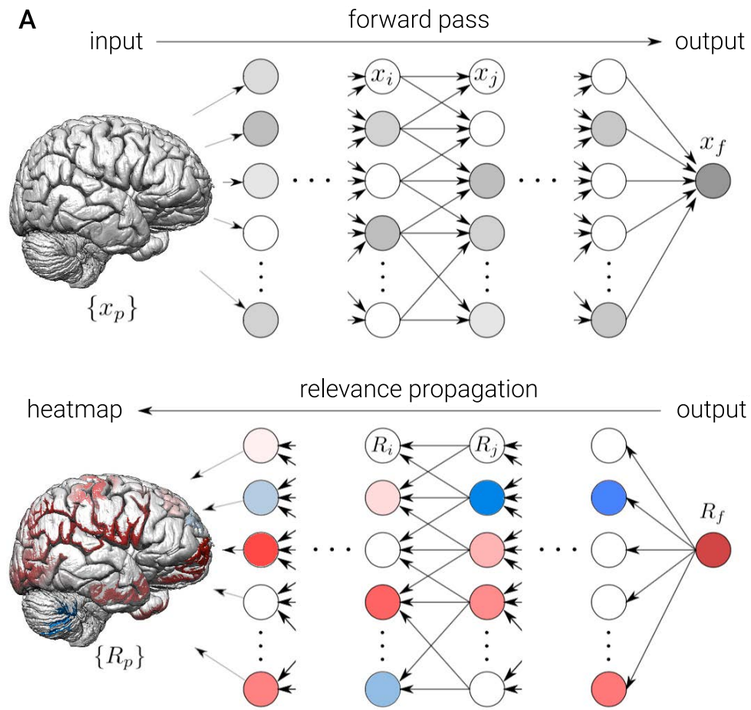
Overeating and weight gain have been linked to abnormal functionality of homeostatic brain networks and alterations in higher cognitive functions such as reward evaluation, executive functions, and learning and memory. At the same time, there is evidence that modifiable factors such as obesity and diet influence the gut-brain axis and modulate brain health and cognition through multiple pathways. Using neuroimaging data from epidemiological studies and randomised clinical trials, we aimed to elucidate the underlying neurobehavioural mechanisms.

We analysed behavioural data from ~10,000 and multi-modal 3T MRI data from ~2,600 randomly selected adults (47% female, 18–80 years old, BMI 18–47 kg/m2) from the LIFE-Adult study, a comprehensively phenotyped population-based cohort (Engel et al., 2022). Interindividual differences in eating behaviour and diet were related to personality traits (Medawar et al., 2020) and to cortical thickness of the orbitofrontal cortex (Beyer et al., 2019, Hum Brain Mapp, 40, 9, 2747–2758), suggesting crucial brain-behaviour relationships across the lifespan. Because higher BMI was related to increased micromovements of the head during MRI, which led to image artifacts, obesity studies need to closely monitor head movements (Beyer et al., 2020; Heinrich et al., 2022). Although the exact mechanisms are not yet clear, preliminary correlation analyses suggest that the gut microbiota is related to differences in eating behaviours and weight loss success two years after bariatric surgery. This suggests a modulatory role of the gut-brain axis in food craving and executive functions (Medawar et al., 2021).

In another project of our group, using a novel deep learning ensemble architecture, we observed that conditions associated with weight gain, such as visceral fat, hypertension, and type 2 diabetes, were related to higher brain age in this cohort (Hofmann et al., 2022). In our publicly available code, we also provide 3D image reconstructions showing the brain regions of each subject that provide relevant information for predicting brain age, such as lesioned white matter or enlarged ventricles in older participants (Figure 2.1.1.1). This new window into deep-learning techniques thus provides the ability to predict the progression of cognitive aging for each individual and also contributes to explaining the underlying mechanisms of lifestyle-related brain aging using a data-driven, unsupervised methodology.

Overall, our findings support the view that diet, overweight, and obesity in the general population are intertwined with markers of brain health and cognition via body-brain communication (Medawar and Witte, 2022) (Figure 2.1.1.2). Intervention studies, meta-analyses, and longitudinal cohort studies are currently underway to further distinguish between causality and correlation in obesity and nutrition brain research.



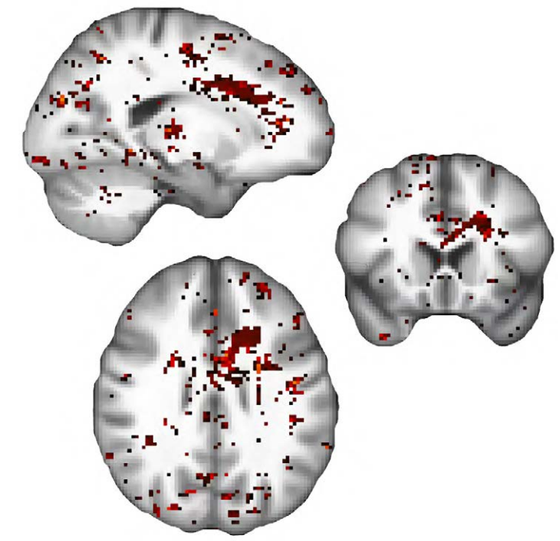


Figure 2.1.1.1 Schematic of explainable 'brain age' prediction, and areas predictive for accelerated brain aging in type 2 diabetes. (A) Upper panel, forward pass: Raw MRI images serve as input to a deep learning canonical neural network (CNN) that predicts chronological age with high accuracy (mean error of +/- 3.5 years). A negative and positive brain age deviance from chronological age ('younger' or 'older' brain age) relates to de- or accelerated cognitive aging. Lower panel, relevance propagation: Using layer-wise weighted relevance propagation (LRP) from the output 'neuron' back to the individual's input space, a novel algorithm highlights areas in the raw MRI image that are most relevant for lower (younger, blue) or higher (older, red) brain age prediction. (B) Using LRP combined with ensemble CNNs, we show significantly associated brain areas in the white matter on fluid-attenuated inversion recovery (FLAIR) MRI, relevant for accelerated brain age in type 2 diabetes mellitus in the LIFE-Adult study (*N* = 2,637; 18–82 years). For details, see Hofmann et al., 2022.

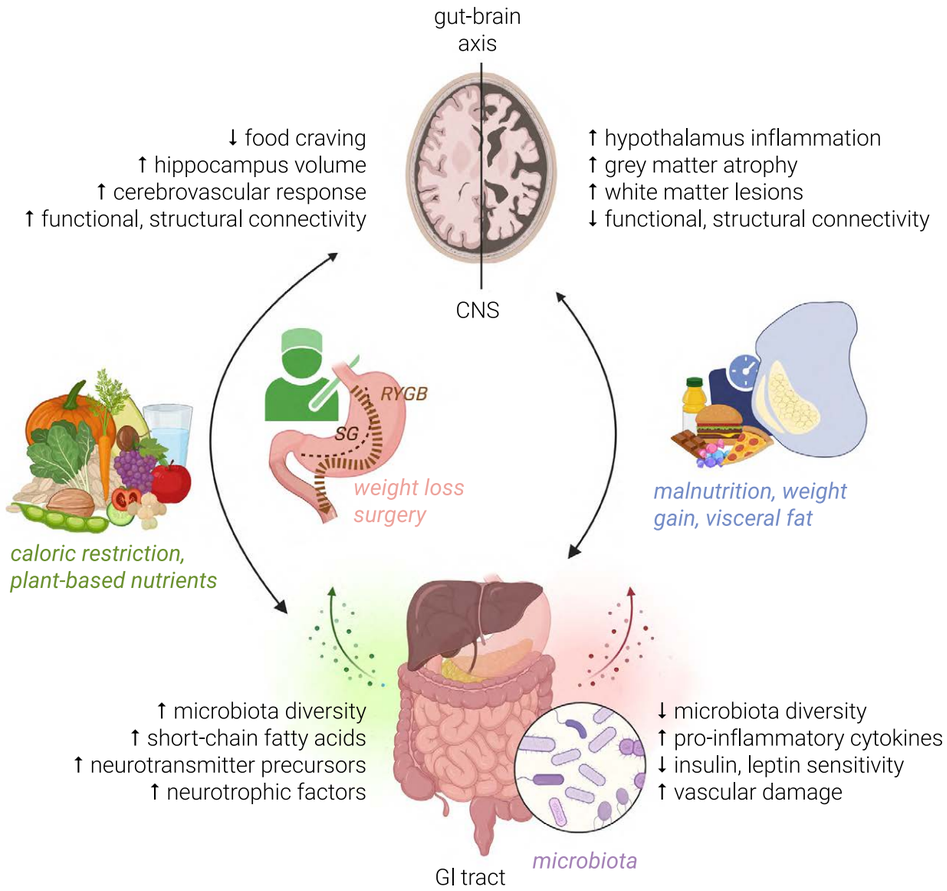


Figure 2.1.1.2 Modifiable factors of a bi-directional gut-brain axis cross-talk and their relevance to obesity and brain health, serving as a theoretical framework for the group's research agenda. Right: Malnutrition, weight gain, and visceral fat accumulation are linked with detrimental structural and functional brain changes as well as disbalance in microbiota, inflammation, metabolic, and vascular factors. Left: Weight loss and plant-based dietary factors might link to improved structural and functional brain changes as well as beneficial microbiota and metabolic mediators of brain health. CNS, central nervous system, GI, gastrointestinal, RYGB, gastric bypass, SG, sleeve gastrectomy. Figure created with biorender.com, taken from Medawar & Witte, 2022.

2.1.2 Cardio-respiratory function and somatosensory perception

Al, E.[1,2,3], Grund, M.[1], Nierhaus, T.[1,5], Forschack, N.[1,6], Stephani, T.[1], Forster, C.[1], Enk, L.[1], Hardikar, S.[1], Azanova, M.[1], Chen, X.[1], Panagoulas, E.[1], Steinfath, P.[1], Nikulin, V.[1], & Villringer, A.[1,2,3,4]

[1] Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany, [2] Max Planck School of Cognition, Germany, [3] Berlin School of Mind and Brain, Germany, [4] Einstein Center Neurosciences, Berlin, Germany, [5] Free University of Berlin, Germany, [6] Institute of Psychology, Leipzig University, Germany

The goal of this line of research is to understand the pathways and mechanisms by which the interplay of respiration, heart, and brain function influences somatosensory perception.

One hypothesised pathway is *baroreceptor* activation, which triggers modulation of neuronal activity with each heartbeat. In support of this hypothesis, we have shown that conscious somatosensory perception is weaker in the early phase of the cardiac cycle (systole, high baroreceptor activity) than in the late phase (diastole, low baroreceptor activity), and that this effect is associated with an attenuated P300 in the somatosensory evoked potential (Al et al., 2020). We confirmed this finding in two replication studies (Al et al., 2021; Grund et al., 2022). We interpret this difference in the context of predictive coding, i.e., the predicted pulse-associated activation of tactile receptors throughout the body is suppressed.

A second proposed explanation for the modulations in perception is a *shift between interoception and exteroception*. We tested this by relating an index of the strength of interoception – the representation of the heart in the brain, the heart evoked potential (HEP) – to somatosensory perception and somatosensory evoked potentials (SEPs). We showed that the amplitude of the HEP is inversely related to conscious somatosensory perception and that, consistent with a modulation of attention, this is already reflected in an early SEP component (P50) (Al et al., 2020; Al et al., 2022). We furthermore show that conscious perception also varies during the respiratory cycle. Interestingly, when performing a somatosensory detection task, respiration and the respiration-associated modulation of the heart frequency become aligned with the task, such that the time point of the somatosensory stimulation coincides with the period "end-of-inspiration–onset-of-expiration" (Figure 2.1.2A, Grund et al., 2022). This is also the period when heart frequency is the highest (Figure 2.1.2B). Interestingly, the group in Münster (Kluger et al., 2021, eLife, 10, e70907) has recently shown, using MEG, that shortly before and within this period of the respiratory cycle, alpha rhythm strength is the lowest, offering an explanation via increased excitability. The latter finding is consistent with the work on alpha rhythm and cortical excitability by our group (Schubert et al., 2009, J Cogn Neurosci, 21, 2407–2419; Becker et al., 2011, J Neurosci, 31, 11016–11027; Forschack et al., 2017, J Neurosci, 37, 6983–6994; Al et al., 2020; Stephani et al., 2021) and other groups (for a review see Samaha et al., 2020, Trends Cogn Sci, 24(8), 639–653). In joint work with the group in Münster, we are now showing converging evidence from MEG and EEG recordings that not only modulation of alpha rhythm, but also respiration-associated modulation of the aperiodic 1/f slope (another recently proposed (M)EEG-index of cortical excitability) indicates a strong coupling of respiration phase and cortical excitability, in good agreement with the modulation of perception across the respiratory cycle (Kluger et al., 2022, bioRxiv 2022).

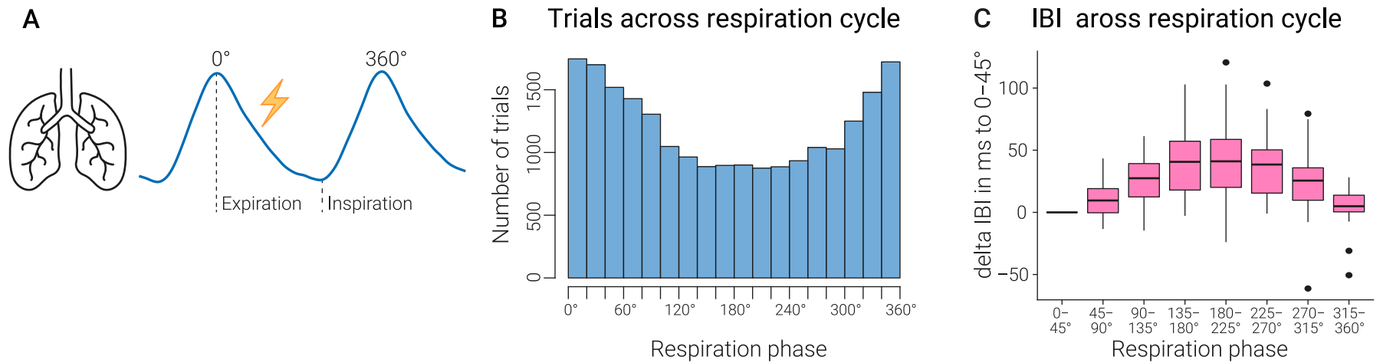


Figure 2.1.2 (A) Somatosensory stimulation could be delivered at a specific phase of the respiratory cycle. (B) Distribution of mean stimulus onsets (of a somatosensory detection task involving near-threshold stimuli) relative to the respiratory cycle. The figure indicates the cumulative number of trials across all trials and participants for the relative position of the stimulus onset within the respiratory cycle binned in 20° intervals from 0° to 360°. The Rayleigh test across all trials and participants was significant. (C) The figure shows IBI differences for each eighth section of the respiratory cycle relative to the first eighth (0°–45°). Modified from Grund et al., 2022.

2.1.3 Brain-body physiology of (naturalistic) affective states

Babayan, A.[1], Erbey, M.[1,2], Fourcade, A.[1], Hofmann, S.[1], Klotzsche, F.[1,2], Kumral, D.[1,2], Reinelt, J.[1], Röbbig, J.[1], Schaare, L. H.[1], Tromp, J.[1,2], Uhlig, M.[1], Villringer, A.[1,2], & Gaebler, M.[1,2]

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We aim at an understanding of the interplay of neural and other bodily systems (cardio-respiratory, endocrine) during affective states, including stress, in healthy humans. The development and progression of risk factors leading to mental and physical disease is thought to be related to affective states, specifically stress (Chrousos & Gold, 1992, JAMA, 267(9), 1244–1252), and their (patho-)physiology. In the "Leipzig Study for Mind-Body-Emotion Interactions" (LEMON) (Babayan et al., 2019, Sci Data, 6, 180308), we compared emotional processing of healthy younger and older adults. Age differences in the regulation of emotion by preferentially processing positive information (e.g., faces; Erbey et al., 2020) and by cognitively reappraising negative experiences (e.g., anger; Röbbig et al., 2021) were linked to additional inter-individual differences (such as the future time perspective; Erbey et al., 2020) as well as contextual factors (such as the emotional intensity; Röbbig et al., 2021). For acute psychosocial stress, we had previously reported changes in subjective, autonomic, endocrine, and functional connectivity stress measures as well as links between them (Bae et al., 2019, Psychoneuroendocrinology, 101, 35–41; Reinelt et al., 2019, NeuroImage, 199, 680–690). Surprisingly, we now additionally found rapid stress-related volumetric brain changes in several regions, including anterior/mid-cingulate and insular cortices (Uhlig et al., 2023).

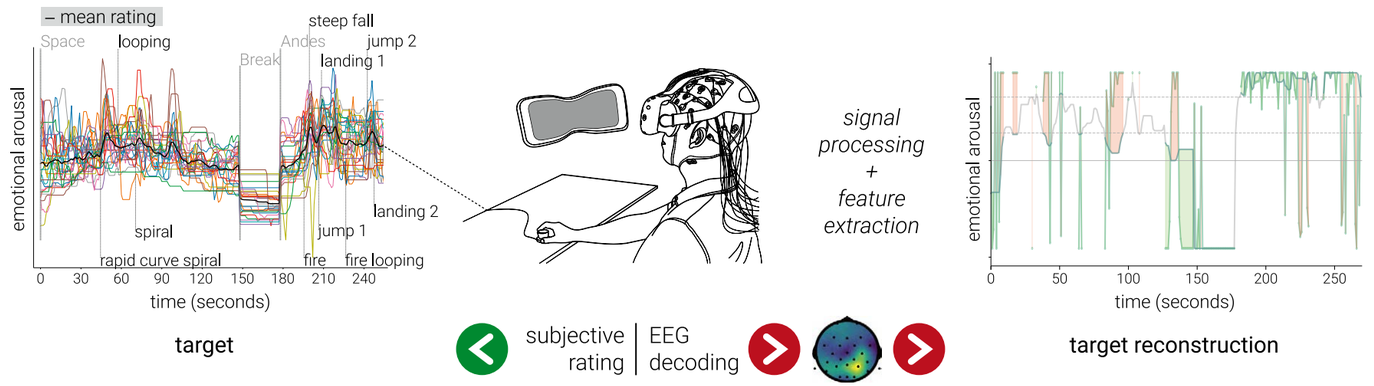

Figure 2.1.3 Approach to decode subjective affect (e.g., emotional arousal) from brain (and body) physiology (e.g., EEG) under naturalistic stimulation. Example adapted from Hofmann et al. (2021), in which an immersive virtual reality (iVR) experience that included rollercoasters served as affective stimulus. Left: Coloured lines: individual participants; black line: mean across participants; vertical lines (light grey): beginning of the three phases of the iVR experience (Space Coaster, Break, Andes Coaster); vertical lines (dark grey): manually labelled salient events (for illustration); Right: Phases of higher (red shading) and lower (green shading) emotional arousal, reconstructed from parieto-occipital alpha power.

Methodologically, in the last few years, we have developed an immersive virtual reality (VR) setting to enable naturalistic (i.e., dynamic, interactive, situated) studies with full experimental control and synchronous assessment of behavioural and physiological measures. We induced emotions with VR (using a rollercoaster experience) to confirm the link between subjective emotional arousal and parieto-occipital alpha power under more naturalistic conditions (Figure 2.1.3, Hofmann et al., 2021). We are currently working on integrating and jointly analysing peripheral physiological (particularly cardiac) signals (Quintero et al., 2022, Proceedings of the 2022 IEEE Conference on Virtual Reality and 3D User Interfaces Abstracts and Workshops (VRW), 46–47; Quintero et al., 2021, Proceedings of the 2021 IEEE International Symposium on Mixed and Augmented Reality (ISMAR)). In collaboration with the Clinic for Cognitive Neurology in Leipzig, we are also developing VR applications for the diagnostics and rehabilitation of cognitive impairments (Krohn et al., 2020). Systematic evaluation of 3D stimulus material (Tromp et al., 2020) and interaction techniques (Masurovsky et al., 2020) are thereby required for such a novel technology and particularly its use with older participants or patients.

2.2 Brain Lesions

The **central question** of this research focus concerns the mechanisms that lead to brain damage and impaired function, which are potential targets for intervention. Following our work on heart-brain interactions (see Chapters 2.1.2 and 2.1.3), we examine gradual changes during ageing and in patients with heart disease and hypothesise that disturbances in heart-brain communication are a driving factor in diseases that have traditionally been considered only "neurological" or "cardiac" disorders (Chapter 2.2.1). By combining multi-modal structural, molecular, and functional imaging, including positron emission tomography (PET) with molecular/biochemical information from serum, genetics, and cerebrospinal fluid, Matthias Schroeter's group characterises brain damage in dementia patients (Chapter 2.2.2). Vadim Nikulin's group is developing and using new electrophysiological markers of brain function to identify early markers of (potential) functional brain damage. For example, in a subset of "healthy" elderly participants, we find a new electrophysiological marker previously associated with Parkinson's disease that opens a window for potential preclinical diagnosis (Chapter 2.2.3, see also parallel work in Nikolaus Weiskopf's department on iron quantification in the substantia nigra).

2.2.1 Brain damage and heart-brain interactions

Khalil, A.[2], Müller, K.[1], Kumral, D.[1,4], Villringer, K.[2], Laufs, U.[3], Wachter, R.[3], Schroeter, M.L.[1,3], & Villringer, A.[1,2,3]

[1] Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany, [2] Charité – Berlin University of Medicine, Germany, [3] Leipzig University Hospital, Germany, [4] Department of Psychology, University of Freiburg, Germany

The goal of this line of research is to identify brain damage and underlying mechanisms related to heart-brain interactions. One focus of our work has been on patients with chronic heart failure (Villringer & Laufs, 2021). In a sub-analysis of the LIFE cohort (n = 2,490), we found that the presence and duration of heart failure were independently associated with white matter lesions (WML) (Stegmann et al., 2021). In another study, we identified the PR interval in the ECG as another contributing factor (Kornej et al., 2022). In a deeply phenotyped cohort of patients with chronic heart failure (without previous stroke) diffuse brain atrophy (operationalised as decrease in grey matter density: GMD) was identified that correlated with cardiac ejection fraction and with NT-proBNP (N-terminal brain natriuretic peptide prohormone), a biomarker used for screening, diagnosis, and prognosis of heart failure (Müller et al., 2020, Circ Res). Additional analyses based on resting-state fMRI recordings in the same patients suggest a link between heart failure and precuneus disconnection from other brain regions associated with social and executive functions (Schroeter et al., in revision). We are currently investigating whether the heart evoked potential (HEP), which serves as an index of heart-brain interaction (see Chapter 2.1.2), is affected in chronic heart failure. In a recent study of patients with atrial fibrillation, we showed that the HEP is indeed dramatically reduced (Kumral et al., 2022), consistent with a disturbance of heart-to-brain signalling (Figure 2.2.1). With regard to the vascular and metabolic mechanisms of brain injury in stroke in humans, we have continued our methodological work in close collaboration with the group at Charité in Berlin (A. Khalil, K. Villringer, J. Fiebach, J. Scheitz) and collaborators at Stanford (A. Fan) and Montréal (C. Gauthier). In particular, we further validated our proposed non-invasive assessment of cerebral blood flow based on time delay analysis of resting-state fMRI data (Lv et al., 2013, Ann

Neurol, 73, 136–140) to show that it allows non-invasive tracking of reperfusion (Khalil et al., 2020). We have also improved the method by showing that independent component analysis can identify the hypo-perfused brain region (Hu et al., 2021) and that the measurement time can be reduced to 204 seconds and still provide sufficient diagnostic quality for clinical decision making (Tanrıtanır et al., 2020). In a feasibility study, we also demonstrated the ability of MRI to assess oxygen consumption in an acute stroke clinical setting. We showed that QSM-MRI can non-invasively quantify oxygen extraction fraction (OEF) in stroke patients, relates to perfusion status, and is sensitive to OEF changes over time (Fan et al., 2020).

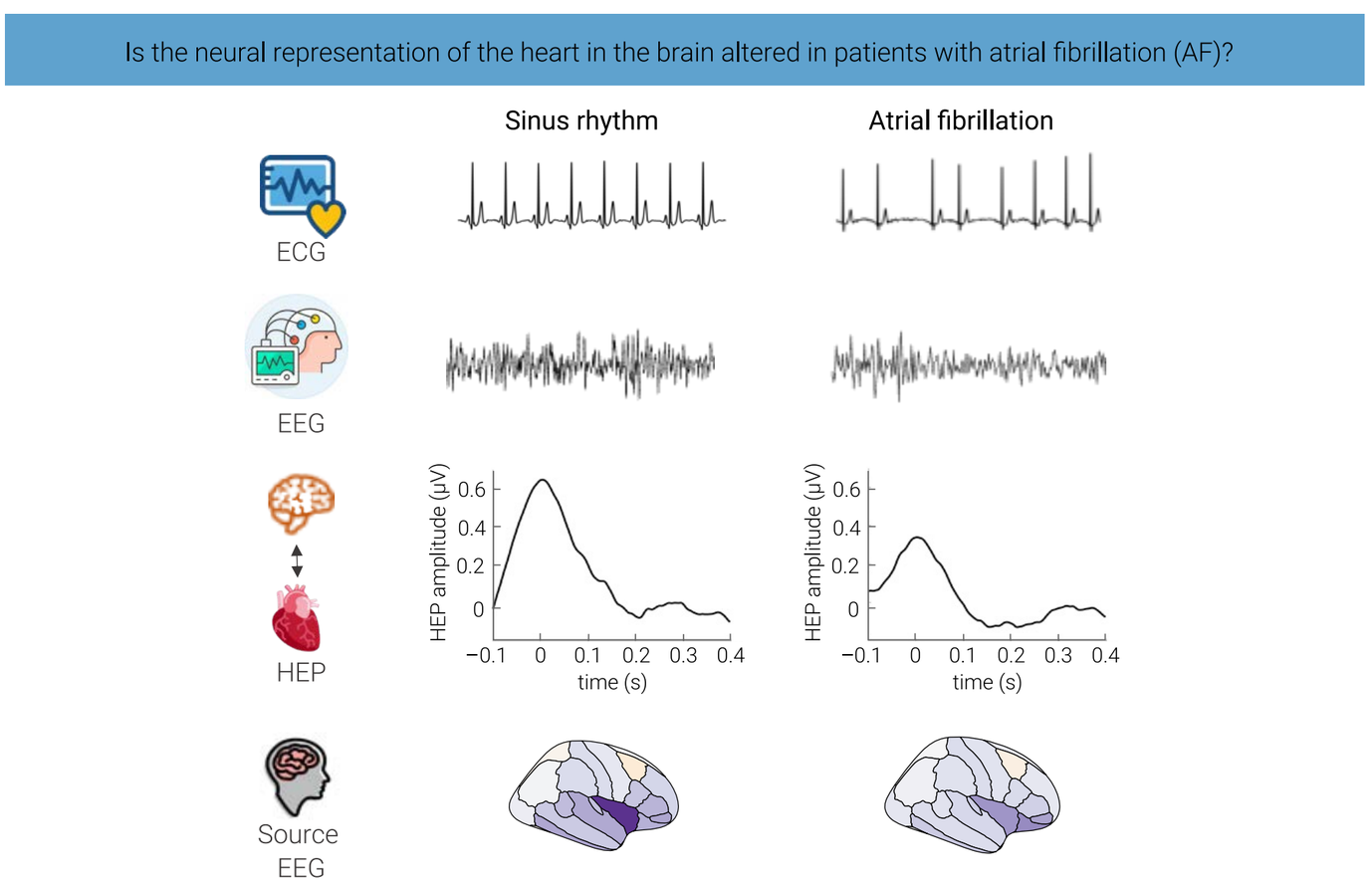

Figure 2.2.1 Attenuation of the heart evoked potential (HEP) in patients with atrial fibrillation. Modified from Kumral et al., 2022.

2.2.2 Predicting dementia – From in-depth-phenotyping and imaging to differential diagnosis and treatment

Müller, K.[2], Lampe, L.[1,2], Ballarini, T.[2], Kynast, J.[2], Albrecht, F.[2], Polyakova, M.[1,2] Villringer, A.[1,2], & Schroeter, M. L.[1,2]

[1] Clinic for Cognitive Neurology, Leipzig University Hospital, Germany, [2] Max Planck Institute for Human Cognitive and Brain Sciences, Germany

The goals of this line of research are to develop biomarkers for early and differential diagnosis and treatment efficacy of dementia from multi-modal imaging, serum, genetics, and cerebrospinal fluid. We are involved in several multi-centre studies such as the Consortium for FrontoTemporal Lobar Degeneration (FTLD) and the GENetic Frontotemporal Initiative (GENFI). Beside characterising disease-specific atrophy and connectivity changes with functional and structural MRI, we have investigated histopathology and molecular underpinnings in-vivo with tau and amyloid positron emission tomography (Aghakhanyan et al., 2022; Ballarini et al., 2020; Beyer et al., 2020; Brendel et al., 2020; Franzmeier et al., 2022, Nat Commun, 13(1); Katzdobler et al., 2022; Messerschmidt et al., 2022; Mueller et al., 2020; Oeckl et al., 2022; Song et al., 2021). Moreover, we have investigated genetic correlates of neurodegenerative diseases with a focus on frontotemporal lobar degeneration (Wagner et al., 2021) and developed diagnostic tools focused on language/speech functions and social cognition – a cognitive function under-investigated so far (Kynast et al., 2020; Kynast et al., 2021; Schroeter, 2022; Seckin et al., 2022; Staiger et al., 2021). Machine learning enables us to support individual patient care by predicting differential diagnosis, symptoms, disease course (Anderl-Straub et al., 2021; Lampe et al., 2022; Lombardi et al., 2021; Schroeter et al., 2020, Cortex; Schroeter et al., 2020, Front Aging Neurosci; Tetreault et al., 2020), and treatment efficacy, in particular for Parkinson's disease (Ballarini et al., 2019, NeuroImage Clin, 21).

Two recent findings are given in Figure 2.2.2. Figure 2.2.2A illustrates the neural correlates of social cognition that we have extracted with systematic quantitative meta-analyses in the NeuroQualia project, namely the frontomedian cortex, insula, amygdala, and temporoparietal areas (Eslinger et al., 2021). This human affectome project aims at developing a comprehensive and common functional model for emotions and feelings. Figure 2.2.2B illustrates our pioneering trans-diagnostic study, where we cross-validated behavioural variant frontotemporal dementia and schizophrenia, sharing clinical symptoms and neural correlates. Beyond the categorical limitations of current clinical frameworks, we thus have re-conceptualised syndrome definitions, here Bleuler's dementia praecox framework for schizophrenia (Koutsouleris et al., 2022).

In order to make our findings and diagnostic capabilities available to a wider range of people, including those in rural areas, we are currently in the process of developing and validating telemedicine-based dementia diagnosis, for which we recently received a grant (TeleDem).

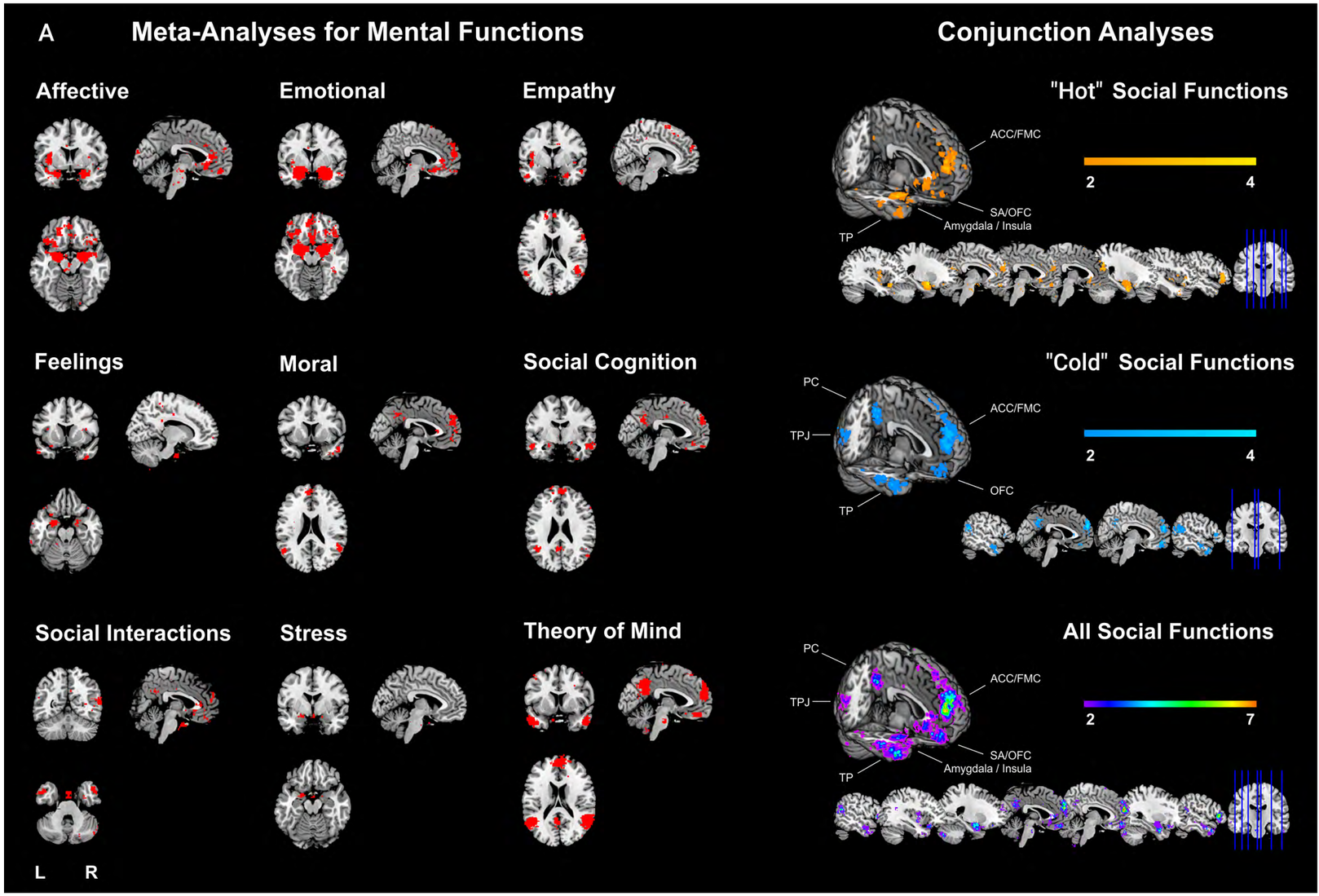

Figure 2.2.2 (A) shows the neural correlates of social cognition that we have extracted with systematic quantitative meta-analyses in the NeuroQualia project (Eslinger et al., 2021).

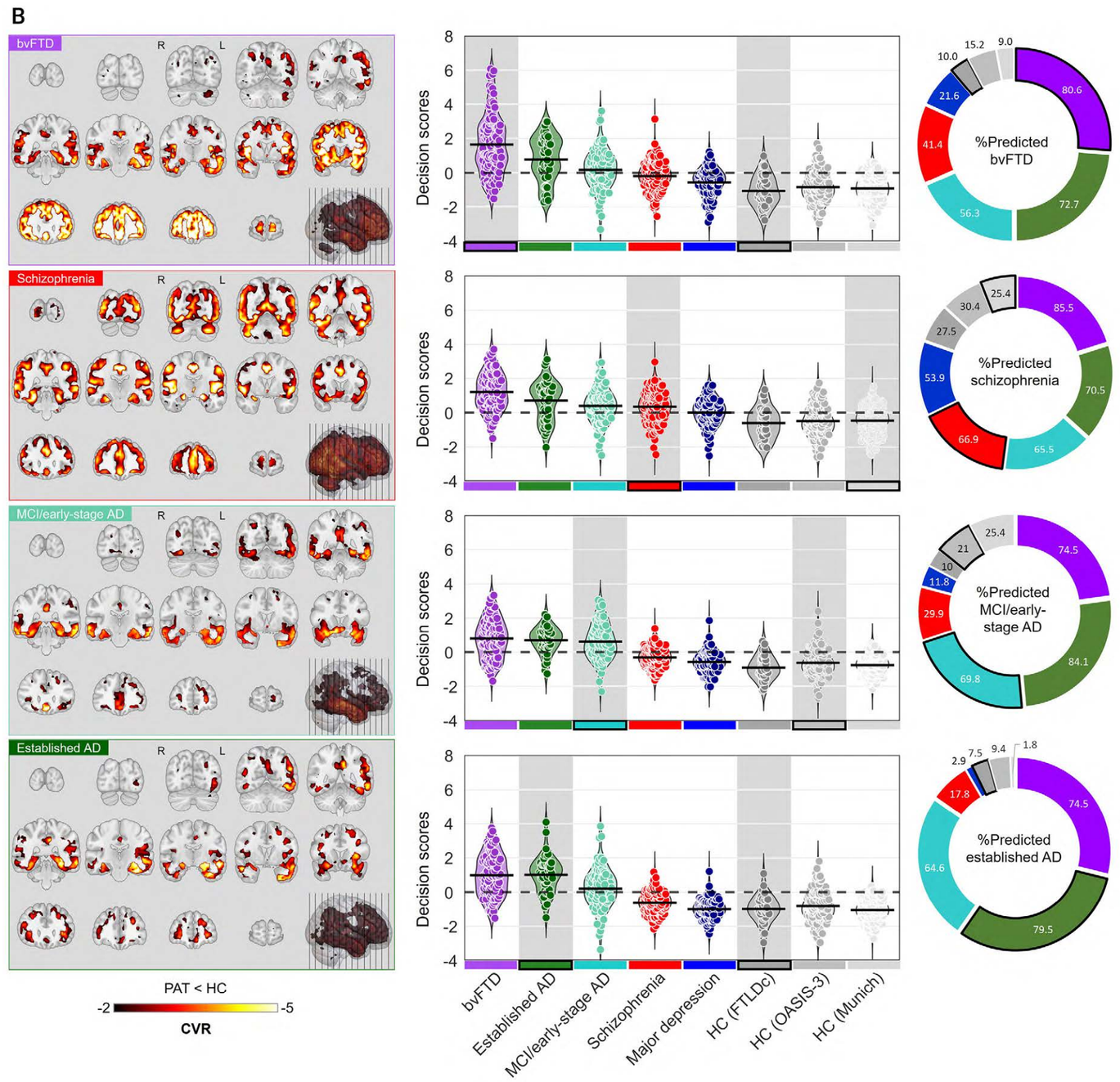

Figure 2.2.2 (B) illustrates our pioneering trans-diagnostic study where we cross-validated behavioural variant frontotemporal dementia and schizophrenia, sharing clinical symptoms and neural correlates (Koutsouleris et al., 2022).

2.2.3 Neural interactions and dynamics in health and neurological disorders

Cesnaite, E.[1], Chen, Y.[1], Gerster, M.[1], Gippert, M.[1], Idaji, M. J.[1], Kapralov, N.[1], Stephani, T.[1], Studenova, A.[1], Zhang, J. [1], Villringer, A.[1], & Nikulin, V.[1]

[1] Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany

Brain responses to the same stimulus or during the performance of the same movement are never the same – the phenomenon is referred to as neuronal variability. The investigation of neurophysiological processes, underlying such variability, is at the core of our group's research, both in healthy participants and patients with neurological disorders such as stroke and Parkinson's disease.

To this end, we have recently established a novel methodology allowing the non-invasive tracking of the variability in the strength of excitatory-postsynaptic currents (reflected in N20 component; Figure 2.2.3A) in somatosensory cortex (Stephani et al., 2021). This unprecedented level of neurophysiological insight provided an independent and much sought after confirmation of the inhibitory nature of alpha oscillation. Moreover, we showed for the first time that the currently held canonical belief that stronger evoked responses should correspond to stronger perception is not valid and that weaker responses can be associated with stronger perception.

Using computational modelling and analysing temporal variability of neuronal oscillations in EEG data, we provided solid evidence for the existence of a baseline-shift mechanism for the generation of evoked responses (ER) (Studenova et al., 2022). It is a general mechanism providing a unification of neuronal oscillations and ER. Using this framework, we have now established a mechanistic link between the two most frequently studied electrophysiological phenomena: the P300 ER and alpha oscillations (Figure 2.2.3B).

Since cortical excitability has been shown earlier to be a major driving force of behavioural and neuronal variability, we have utilised a recently proposed measure for cortical excitability (1/f spectral slope) and scrutinised its efficacy for the detection of neuronal dynamics in Parkinson's disease (PD) (Figure 2.2.3D; Gerster et al., 2022). We have also shown that abnormal cortical excitability, associated with increased phase-amplitude coupling (PAC), is present not only in PD but also in some seemingly healthy elderly participants (Figure 2.2.3C; Zhang et al., 2021), thus making PAC a promising potential biomarker for the detection of prodromal PD. In order to separate genuine (e.g., PAC) from spurious non-linear interactions, we have also presented a new approach called Harmoni (Figure 2.2.3E; Idaji et al., 2022).

Having developed and tested an array of such diverse electrophysiological approaches, as a next step, we aim to apply them to the estimation of pathological neuronal dynamics in stroke and PD as well as to use them as biomarkers for patient stratification and to track the efficacy of therapeutic brain stimulation.

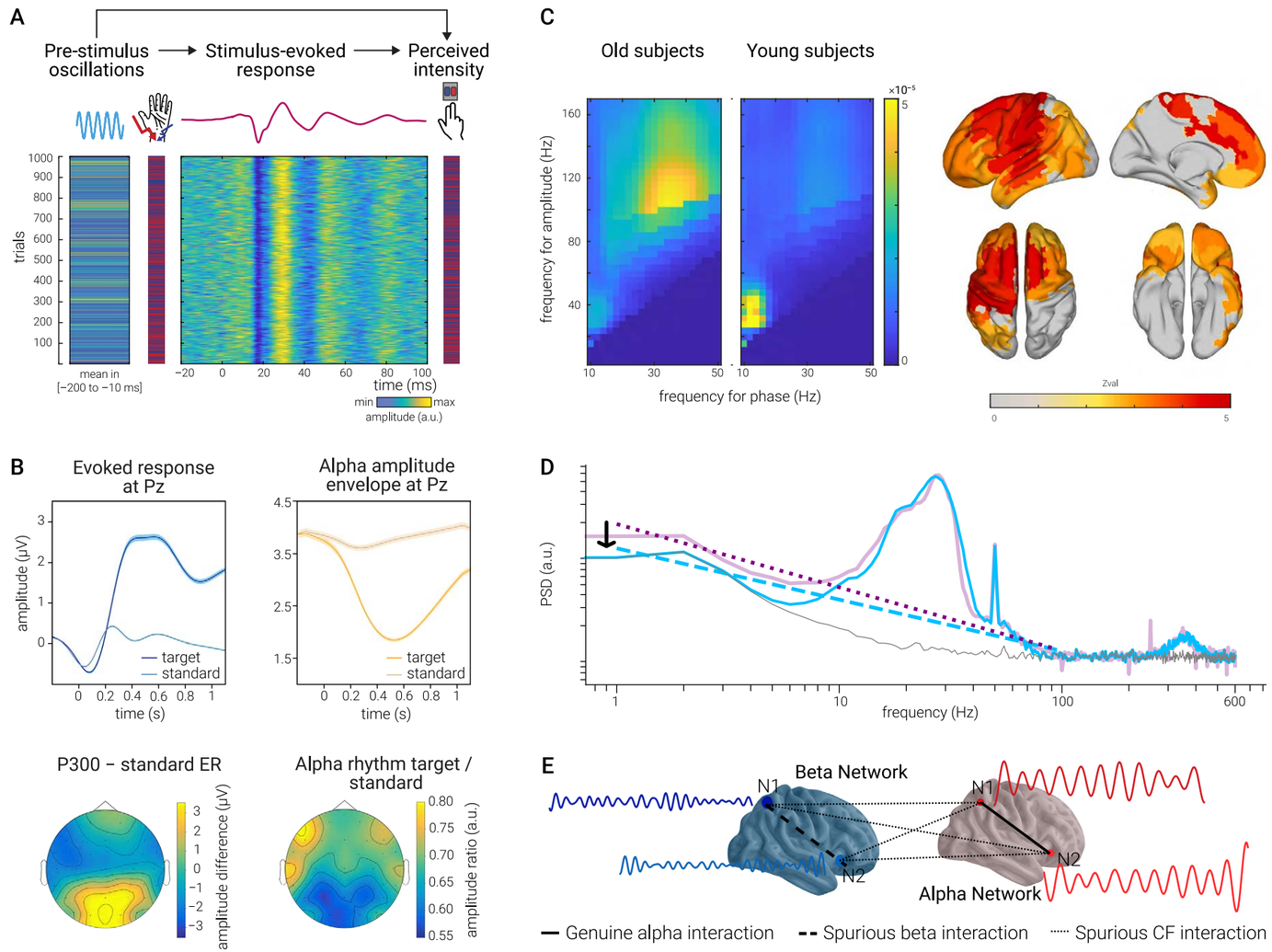

Figure 2.2.3 Neuronal variability in health and disease. (A) Non-invasive tracking of excitatory postsynaptic currents (N20 at 20 ms latency) with EEG. The variability in this component was related to oscillations and behaviour. (B) Baseline-shift mechanism predicts both spatial and temporal similarity in the dynamics of oscillations and ERs. (C) Phase-amplitude coupling between beta and gamma oscillations as a potential biomarker for prodromal stage of PD. (D) Challenges in inferring E/I ratio in subthalamic nucleus in patients with PD. (E) Detection of genuine cross-frequency interactions and their separation from non-sinusoidal shape of neuronal oscillations.

2.3 Rehabilitation: Learning, Recovery, and Plasticity

The **central question** of this research focus concerns the mechanisms that enable learning, particularly in post-stroke recovery. Here, we build heavily on the close interaction with the Clinic for Cognitive Neurology at Leipzig University Hospital.

A major focus is on mechanisms of **sensorimotor learning** in healthy adults and post-stroke patients, as well as on ways to improve the latter using brain computer interface (BCI), transcranial stimulation methods, and neuromodulatory drugs such as SSRIs or l-Dopa (Bernhard Sehm's group, see Chapter 2.3.1 A). This research focus also benefits from several ongoing collaborations (Chapter 2.3.1 B) with members of the sports science faculties at the Universities of Leipzig (Patrick Ragert's group) and Magdeburg (Marco Taubert's group), Christopher Steele and Claudine Gauthier at Concordia University, Montréal, Canada, and the Technical University of Berlin (Klaus-Robert Müller) in the field of BCI and machine learning.

Hellmuth Obrig (Head of Clinical Service of the Clinic for Cognitive Neurology) and his group focus on basic research and clinical interventions in patients with **aphasia**, building on a long-standing collaboration with the Department of Neuropsychology (Angela Friederici) and Gesa Hartwigsen's research group (Chapter 2.3.2). Angelika Thöne-Otto, Head of the Neuropsychology Unit at the Clinic for Cognitive Neurology at Leipzig University Hospital, and her colleagues are developing new VR-based tools to better diagnose and treat patients with hemispatial **neglect** (Chapter 2.3.3). A group led by Annerose Engel at the Clinic for Cognitive Neurology is focusing on **music-based therapy**. In parallel, Thomas Fritz is developing and using new music-based fitness devices for improved rehabilitation – also as part of a spin-off company he founded – and his group at the Institute is investigating the physiological basis of these effects (Chapter 2.3.4). A major method development for MRI-guided focused ultrasound stimulation, with the vision of achieving non-invasive deep brain stimulation, being pursued under a recently awarded major grant, is briefly outlined in Chapter 2.3.5.

2.3.1 Neuroplasticity, motor learning and motor recovery: Part A

Grigoryan, K. A.[1], Gippert, M.[1], Shih, P. C.[1], Gundlach, C.[1], Muffel, T.[1], Kalloch, B.[1], Nazarova M.[4], Asamolova, N.[1], Flores, A.[1], Steele, C.[1,2], Villringer, A.[1], Nikulin V.[1], & Sehm, B.[1,3]

[1] Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany, [2] Department of Psychology, Concordia University, Montreal, QC, Canada, [3] Clinic for Neurology, Halle University Hospital, Germany, [4] Martinos Center, Massachusetts General Hospital, Harvard Medical School, Boston, USA

In our work, we investigate the underlying mechanisms of brain changes in healthy individuals and patients with sensorimotor deficits as a result of stroke. Our goal is to improve learning and recovery through a better understanding of the factors contributing to neuroplasticity by developing individualised intervention approaches based on (patho-)physiological principles.

We use kinematic assessments of complex sensorimotor functions using a robotic device in an augmented reality environment. In healthy subjects, we show that a sequence involving an active pre-movement of the contralateral arm (video, see right-hand column) (Gippert et al., bioRxiv) or an imagined pre-movement of the same arm (Gippert et al., in prepa-

ration) improves sensorimotor adaptation. Thus, motor adaptation is not an isolated process but is strongly influenced by preceding events such as movements of other body parts and even by mental simulation of the movement (Figure 2.3.1A and B).

In addition, we investigated the control mechanisms of bi-manual coordination (video, see right-hand column) in healthy individuals and their decline with age (Shih et al., 2021). In stroke patients, we show that the side of the lesion critically affects performance and suggest hemispheric specialisation in bi-manual motor control (Shih et al., in preparation) – an idea that promotes an individualised treatment approach in patients (Figure 2.3.1C).

We use brain computer interface (BCI) (video, see right-hand column) and transcranial electrical stimulation (tES) to modulate brain function and induce plasticity. By combining tES with simultaneous functional MRI we study network effects in healthy individuals (Gundlach et al., 2020; Ekhtiari et al., 2022). We show that frequency-adapted stimulation induces a locally-specific decrease in whole-brain functional connectivity of the left S1, highlighting the potential of tES to induce highly specific changes in the brain (Gundlach et al., 2020) (Figure 2.3.1D).

In a clinical study of post-stroke patients, we investigated the modulatory potential of tES on several kinematic parameters during different tasks (video, see right-hand column). This comprehensive behavioural characterisation shows that improvement of some functions comes at the expense of a reduction of others. Thus, we provide a novel picture of a homeostatic response of the damaged brain to external stimulation and unify previous heterogeneous results into one framework (Muffel et al., 2022).

In addition, we investigated possible reasons for the heterogeneous response to tES using modelling approaches. We show that age-related changes in brain structure and lesions affect the current distribution of tES and therefore represent an important source of variability (Kalloch et al., 2022; Figure 2.3.1).

We have shown that corticospinal connectivity has a critical impact on the potential to recover from stroke (Nazarova et al., 2021). We have also investigated how focal lesions cause not only local destruction but also disruption of connectivity to neighbouring and distant brain areas and how this relates to behavioural deficits (Zayed et al., 2020, 42nd Annual International Conference of the IEEE Engineering in Medicine & Biology Society (EMBC), 1701–1704; Figure 2.3.1F).

The next steps are to effectively utilise neuroplastic mechanisms through precise interventions based on the individual functional and structural characteristics of the patient's brain.

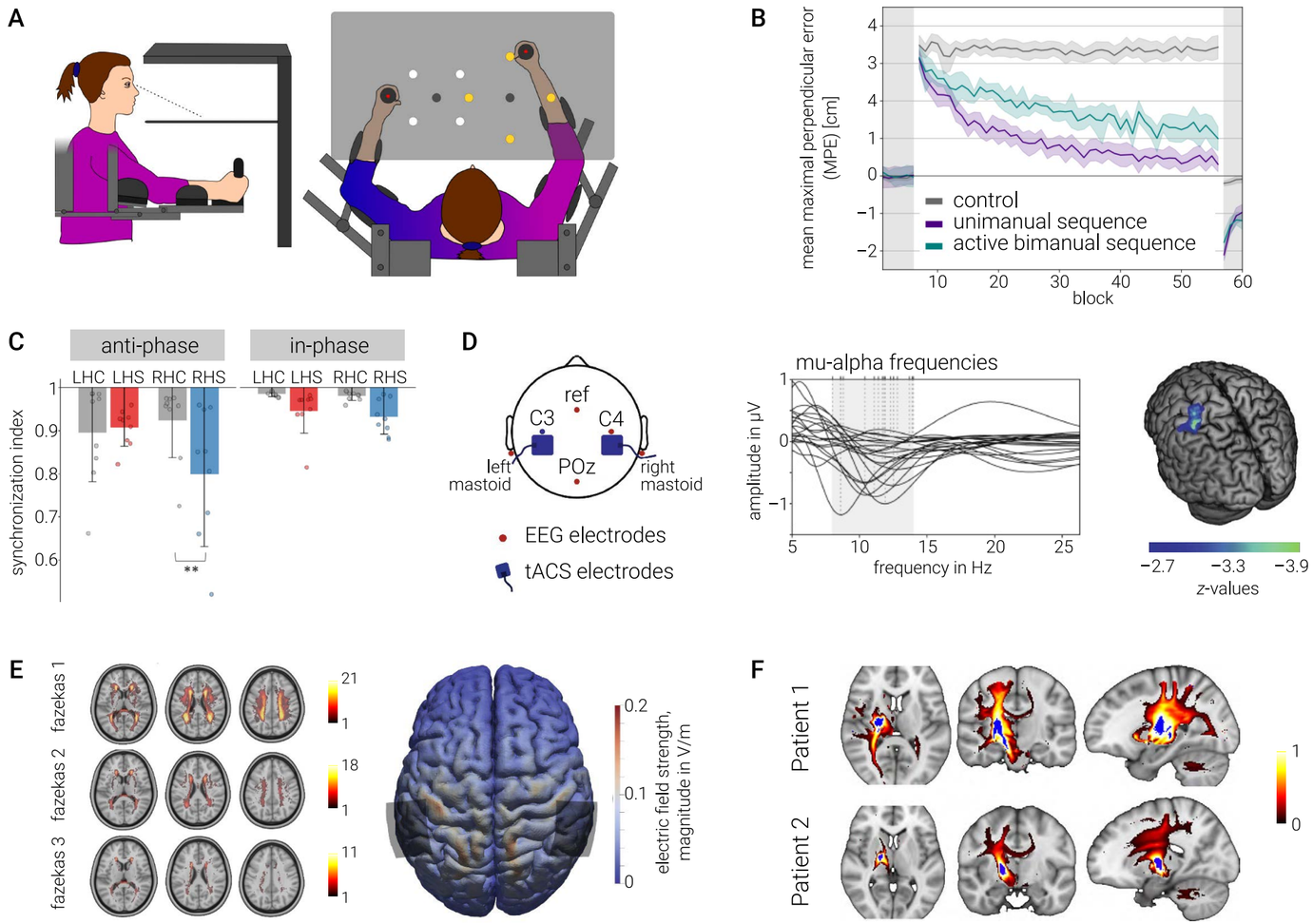

Figure 2.3.1 (A) Setup of kinematic assessment that is deployed in behavioural tasks capturing different aspects of sensorimotor function and impairment. (B) Sensorimotor adaptation is facilitated when embedded into a sequence of events, encompassing ipsi- and contralateral as well as imagined pre-movements. (C) Bi-manual coordination after stroke is differentially impaired in patients with left- vs. right-sided lesions (LHC = left hemisphere controls; LHS = left hemisphere stroke; RHC = right hemisphere controls; RHS = right hemisphere stroke). (D) tES applied at individual frequencies induces local and functional specific changes in whole-brain network architecture. (E) Structural brain aging and lesions (white matter lesions, Fazekas 1 to 3) affect current distributions of tES thus contributing to outcome variability. (F) Structural disconnectivity profiles in two patients with similar subcortical lesions: The disconnection of adjacent and remote brain regions goes far beyond the structural damage of the local tissue destruction (lesion in blue, disconnectivity from yellow to red).

2.3.1 Neuroplasticity, Motor Learning and Motor Recovery: Part B

Ragert, P.[1,2], Nikulin, V.[1], Kenville, R.[1,2], Maudrich, T.[1,2], Sehm, B.[1,5], Lehmann, N.[1,3], Taubert, M.[1,3], Jäger, A.-T.[1], Müller, K.-R.[6], Vidaurre, C.[6], Gauthier, C.[4], Steele, C.[4], Paul, K.[1,7], Cnossen, F.[7], Lanzer, P.[8], Nierhaus, T.[1,9], Villringer, A.[1]

[1] Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany, [2] Sports Faculty, Leipzig University, Germany, [3] Sports Faculty, Otto von Guericke University of Magdeburg, Germany, [4] Department of Psychology, Concordia University, Montreal, QC, Canada, [5] Clinic for Neurology, Halle University Hospital, Germany, [6] Technical University, Berlin, Germany, [7] University of Groningen, the Netherlands, [8] Medical Center, Bitterfeld, Germany, [9] Free University of Berlin, Germany

Our work on motor learning benefits from several, long-standing collaborations: Together with Nico Lehmann and Marco Taubert at the University of Magdeburg, we continued our – clinically highly relevant – work on the interaction between cardiovascular exercise (CE) and motor learning. We demonstrated a learning boost by CE on motor learning and showed that this was mediated by CE-induced increases in cerebral blood flow in frontal brain regions and changes in white matter microstructure in frontotemporal fibre tracts (Lehmann et al., 2020). CE also altered the trajectory of learning-related changes in white matter microstructure among parieto-occipital and primary sensorimotor areas of the right hemisphere and these changes correlated with improved learning after CE (Lehmann et al., 2022).

In collaboration with Christopher Steele and Claudine Gauthier (Concordia University, Montréal, Canada), we were able to separate – using 7T MRI – learning-related changes in functional connectivity (SMA) during learning of visuomotor sequences from motor execution-related findings in superior parietal cortex (SPC) (Jäger et al., 2022). We were also able to show changes in WM microstructure in pathways underlying primary motor and sensorimotor cortex (Tremblay et al., 2021). In a clinically-relevant complex learning task, a group of medical students learned to perform a simulator-assisted endovascular procedure (carotid artery catheterisation). Using fMRI, we demonstrated that visuomotor transformations in the intraparietal sulcus mediated the acquisition of this endovascular medical skill (collaboration also with Fokie Cnossen, Groningen, and Peter Lanzer, Bitterfeld, Germany) (Paul et al., 2022).

In collaboration with Patrick Ragert's group at the Faculty of Sports Science, Leipzig University, Germany, we investigated mechanisms of neural motor control relevant to both sport and clinical work, such as intermuscular coherence between homologous muscles during dynamic and static movements (Kenville et al., 2020) and neural correlates of inhibitory control during mirror movements. We found that δ-power in frontal regions may reflect executive processes that exert inhibitory control over unintended motor performance (Maudrich et al., 2020).

In collaboration with Klaus-Robert Müller and Carmen Vidaurre (Technical University Berlin), we investigated the effects of performing BCI (which we also use clinically) on measures of brain structure and function. After only one hour of applying two different types of BCI (either based on EEG rhythms modulated by motor imagery or ERPs triggered by visual stimuli), we found increased T1-weighted MR signals in the grey matter of the respective target brain regions (Nierhaus et al., 2021). The observed spatial specificity of BCI-induced brain plasticity holds promise for therapeutic interventions tailored to individual functional deficits.

2.3.2 Language and plasticity

Regenbrecht, F.[1], Pino, D.[1,2], & Obrig, H.[1,2]

[1] Clinic for Cognitive Neurology, Leipzig University Hospital, Germany, [2] Max Planck Institute for Human Cognitive and Brian Sciences, Leipzig, Germany

Our goal is to develop approaches to better treat people with aphasia (PWA)/communication disorders. The targeted optimisation of interventions to alleviate symptoms in PWA can additionally contribute to answering basic (patho)linguistic questions. With the help of the clinic's interdisciplinary diagnostic and therapeutic team, we invite PWA and patients with cognitive communication disorders to investigate the neural basis of (impaired) language comprehension and production. In collaboration with researchers from the Department of Neuropsychology, a wide range of topics from language development (Werwach et al., 2022) to psycholinguistic issues are addressed. Currently, a focus is on lexical-semantic processing (Pino et al., 2022; Graessner et al., 2021), examining facilitation and interference effects within the mental lexicon (van Scherpenberg et al., 2020 & 2021). For example, we demonstrated differential effects of lesion location on word retrieval in a picture naming task in the presence of distracter words (see Figure 2.3.2, Pino et al., 2022). Given that confrontational naming is a cornerstone of aphasia rehabilitation, this may be relevant to the development and evaluation of novel therapeutic procedures. In addition, exploring web-based approaches to PWA will allow scientific and therapeutic efforts to be extended to a larger and more diverse population (Stark et al., 2022).

The most challenging task – providing clinically meaningful studies on therapy enhancement – is being addressed jointly within national research networks and the German Aphasia Society. Projects address therapy optimisation (Breitenstein et al., 2017, Lancet, 389, 1528–1538; follow-up proposal submitted). Besides the novel structured assessment and treatment schemata developed within these studies, the critical question is the minimally effective dose of aphasia treatment in chronic PWA. Moreover, therapy augmentation by brain stimulation (TDCS) is the focus of an on-going national RCT.

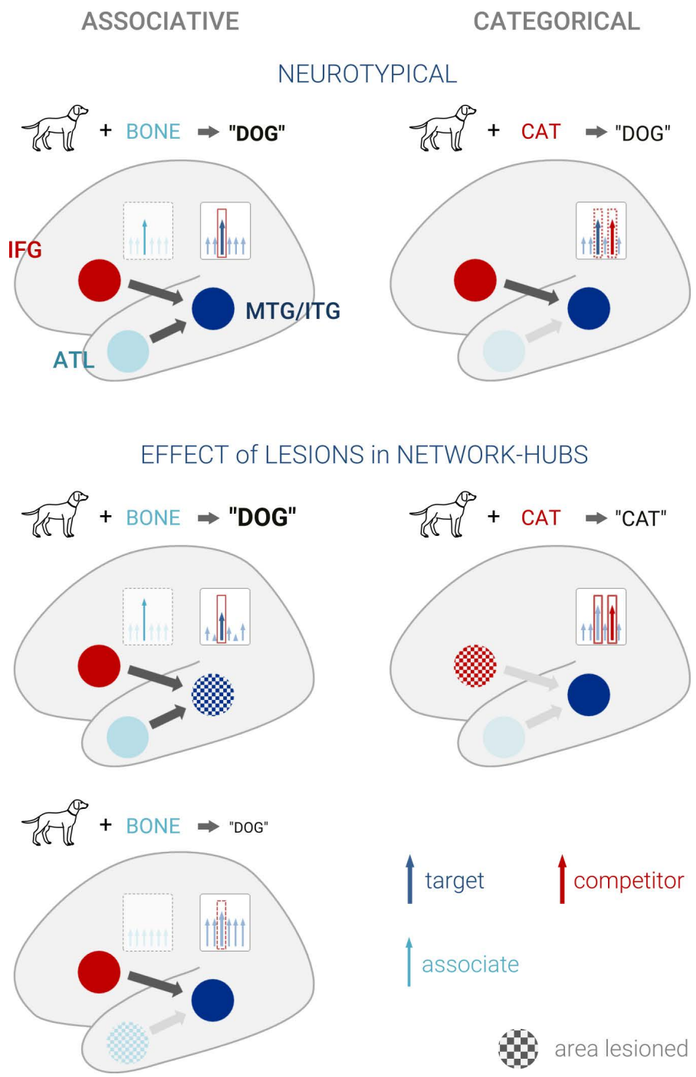

Figure 2.3.2 Example of how research in people with an acquired brain lesion in the (extended) language network can contribute to models of lexico-semantic retrieval/selection. The sketch summarises how lesion patterns may modulate aspects of this capacity central to language-based communication. Results from a picture-word interference task in which a distractor word was associatively or categorically related to the to-be-named target picture. IFG-inferior frontal gyrus; MTG/ITG middle/inferior temporal gyrus; ATL anterior temporal lobe. Adapted from Pino et al., 2022.

2.3.3 Digital technologies in neuropsychological rehabilitation

Belger, J.[1,2], Blume, M.[1], Quinque, E. M.[1], Gaebler, M.[1], Klotzsche, F.[2], Weicker, J.[1,2], & Thöne-Otto, A.[1,2]

[1] Clinic for Cognitive Neurology, Leipzig University Hospital , Germany, [2] Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany

The research goal of our group is to improve the care of patients with neuropsychological deficits by using digital technologies. In a joint project with the Fraunhofer Institute for Telecommunications – Heinrich Hertz Institute (HHI) in Berlin, the Clinic for Neurology of the Charité in Berlin, and the Magdeburg-based company Hasomed®, we are evaluating the use of virtual reality (VR) in neuropsychological rehabilitation. We developed an app for testing and training spatial memory (imVMT) (video, see right-hand column) and executive functions. The successful initial evaluation was conducted in healthy younger and older individuals (Gaebler et al., 2020). Subsequently, feasibility studies were conducted in our Clin-

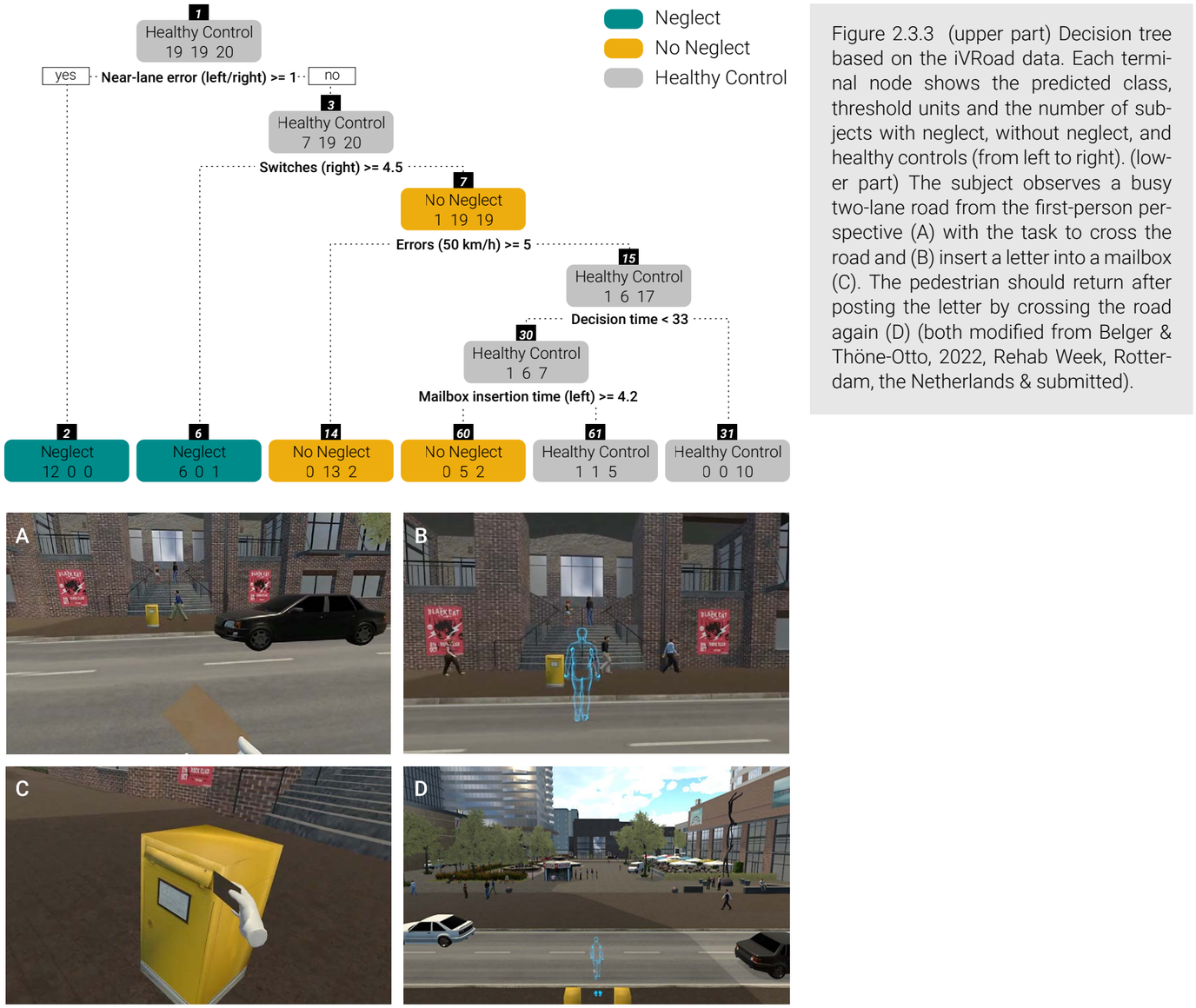

Figure 2.3.3 (upper part) Decision tree based on the iVRoad data. Each terminal node shows the predicted class, threshold units and the number of subjects with neglect, without neglect, and healthy controls (from left to right). (lower part) The subject observes a busy two-lane road from the first-person perspective (A) with the task to cross the road and (B) insert a letter into a mailbox (C). The pedestrian should return after posting the letter by crossing the road again (D) (both modified from Belger & Thöne-Otto, 2022, Rehab Week, Rotterdam, the Netherlands & submitted).

ic for Cognitive Neurology in a mixed group of neurological patients (Belger et al., 2021, IEEE Conference on Virtual Reality and 3D User Interfaces Abstracts and Workshops (VRW), 723–724).; Thöne-Otto et al., 2022; Blume et al., 2020). All tasks showed excellent feasibility and acceptance. In a follow-up project, we developed a virtual road crossing task *iV-Road* (video, see right-hand column) with the aim to investigate visuospatial neglect in chronic stroke patients. Again, the task was well tolerated. Based on the application of forest plot analyses through machine learning, we identified critical behavioural variables that detect visuospatial neglect more sensitively than traditional paper-pencil tasks (Belger & Thöne-Otto, 2022, Rehab Week, Rotterdam, the Netherlands; see Figure 2.3.3).

VR has high potential to improve neurological rehabilitation, not only in terms of ecologically valid neurocognitive testing and rehabilitation, but also in terms of motor rehabilitation, pain management, and anxiety management (Quinque et al., in press). As digital technologies increase the possibilities of self-directed remote training, in another research project we investigated what motivational and cognitive requirements need to be met in order to develop internet-based cognitive training suitable for stand-alone use in neurological patients (Weicker et al., 2020).

2.3.4 Optimising rehabilitation success with music

Vidal, M.[1,2,3], Schneider, L.[1], Montgomery, M.[1,2], & Fritz, T. H.[1,2]

[1] Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany, [2] Institute for Psychoacoustics and Electronic Music (IPEM), Ghent University, Belgium, [3] Department of Statistics and O.R. and Institute of Mathematics, University of Granada, Spain

We are investigating the neural mechanisms underlying the effect of music on emotions and related brain functions, with the goal of developing and evaluating new music-based rehabilitation interventions. We exploit the concept that music modulates arousal via the emotional motor control system (as opposed to the voluntary motor control system, Figure 2.3.4A).

In a recent study, we compared arousal due to movement to actively control music (singing) and moving along to music (body sway), hypothesising that actively controlling music will more strongly engage participants emotionally and lead to a qualitatively different pattern of pupil activity. We found that active participation in the music performance during singing enhanced cholinergic pupillary dilations and that being able to move with the body to the music during singing further enhanced the effect of the music performance (singing) on pupillary activity (Figure 2.3.4B).

In a therapeutic setting, we developed a method to maximise musically-induced arousal during music performance with physically demanding music fitness movements. We observed that the systematic combination of exercise and music-making, and the corresponding increase in emotional arousal during the interventions, positively influenced cognitive and physiological parameters relevant to rehabilitation success, including the perception of effort (Fritz et al., 2013, PNAS, 110, 17784–17789), physical pain (Fritz et al., 2018, Front Psychol, 8), mood (Fritz et al., 2013, Front Psychol, 4), social integration (Fritz et al., 2015, Front Hum Neurosci, 9), fear (Schneider et al., 2022, Front Pain Res, 3), divergent thinking ability (Fritz et al., 2019, Front Psychol, 11), and endurance (Rehfeld et al., 2022). In a recent study, we furthermore demonstrated the efficacy of this musical arousal intervention in improving short-term memory function in older adults with dementia (Strong et al., 2022, Brain Sci, 12).

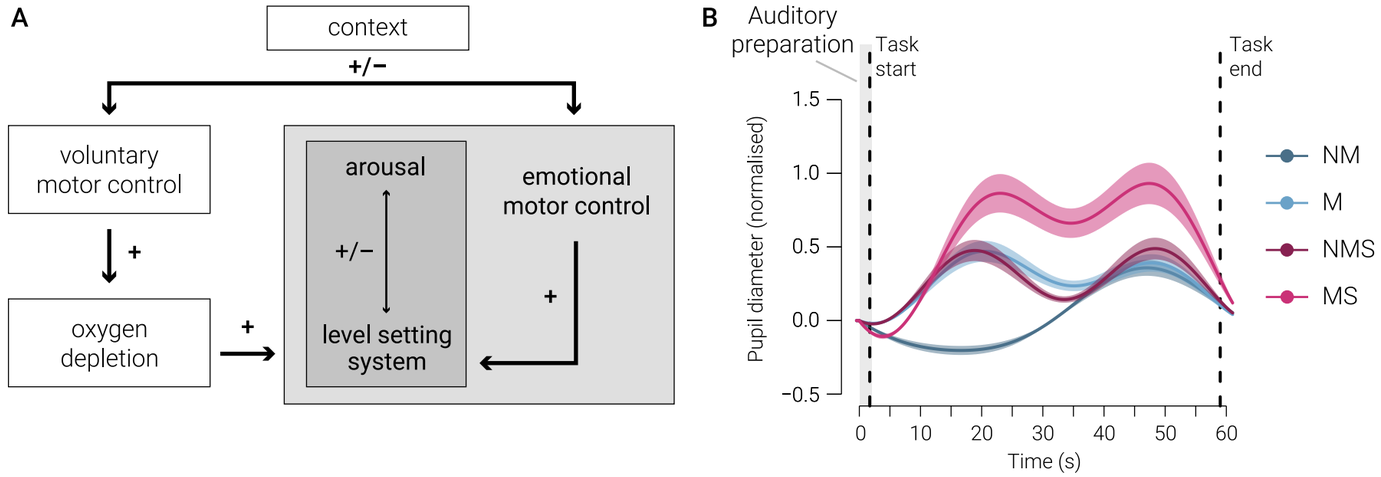

Figure 2.3.4 (A) Interaction of voluntary and emotional motor control. (B) Pupil response during conditions with different task emotionality determined by musical performance, NM – no movement, M – body sway to music, NMS – singing with no body sway allowed, MS – singing with body sway allowed (under review).

2.3.5 Low intensity focused ultrasound stimulation

Nierhaus, T.[1,2], Nikulin, V.[1], Tretbar, S.[3], Melzer, A.[4], & Villringer, A.[1]

[1] Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany, [2] Free University of Berlin, Germany, [3] Fraunhofer Institute for Biomedical Engineering IBMT, Sulzbach, Germany, [4] Innovation Center Computer Assisted Surgery (ICCAS), Leipzig University, Germany

The goal of this project is to develop and test low-intensity focused ultrasound (LIFU) for non-invasive deep brain stimulation, overcoming limitations of current electrophysiological stimulation methods such as TMS or TDCS with respect to 3D focusing. Previous studies provided preliminary evidence that focused ultrasound could be used for non-invasive modulation of neuronal activity in humans (Legon et al., 2014, Nat Neurosci, 17, 322–329). However, further validation is needed to disentangle the effects of tFUS due to concomitant factors such as electrical, mechanical, and acoustic effects associated with device operation. We performed a pilot study using a prototype system (Fraunhofer Institute) that allowed the adjustment of focus depth using beamforming. We demonstrate that evoked activity due to tFUS associated noise is eliminated by auditory masking. When using white noise masking it is possible to observe a differential modulation of EEG depending on the stimulation depths (focus 30 mm vs. 100 mm): While alpha power is suppressed for tFUS with 100 mm focus, tFUS with 30 mm focus shows a synchronisation (Figure 2.3.5). Together with ICCAS, IBMT Fraunhofer, and two companies (Localite, MR instruments), we acquired a 7 million Euro grant from the Federal Ministry of Education and Research (BMBF) to develop LIFU guided by MRI further.

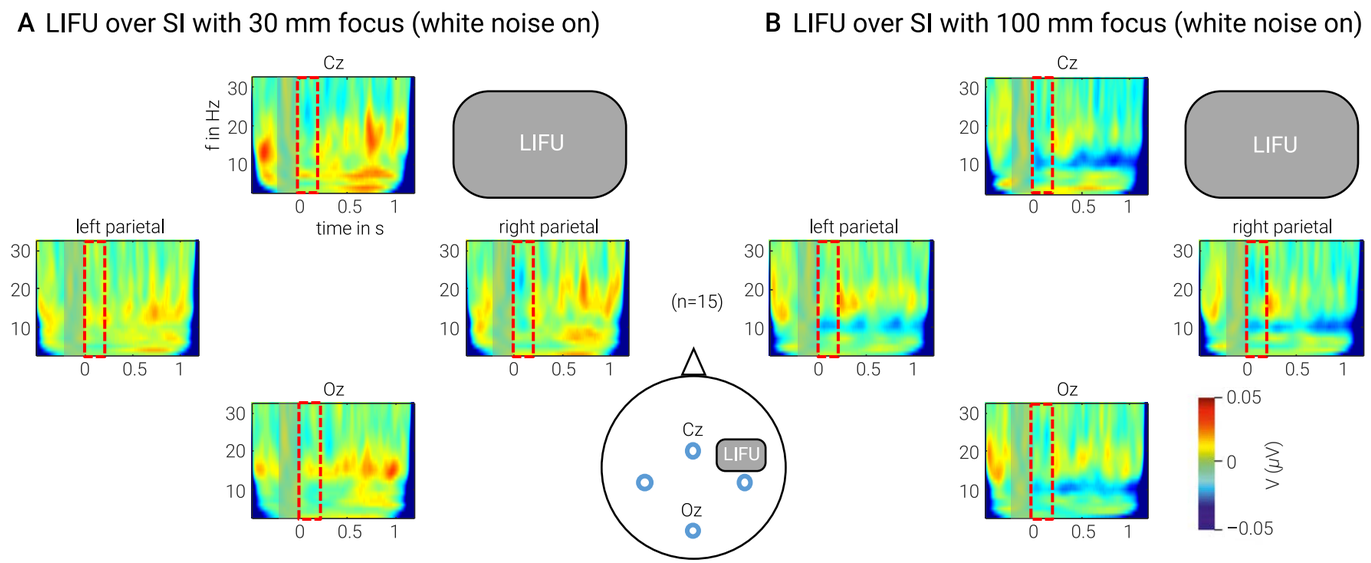

Figure 2.3.5 Time-Frequency analysis (EEG) during LIFU stimulation at different depth of focus (30 mm left, 100 mm right): Compared to baseline (200 ms pre stimulation, grey shaded area) oscillatory activity synchronises for focus depth 30 mm and desynchronises for focus at 100 mm. Red dashed rectangle illustrates the 200 ms LIFU stimulation period. Lower middle plot shows electrode and LIFU position on the scalp. Left and right parietal electrodes correspond to CP3 and CP4. X- and Y-axis are time (seconds) and frequency (Hz), respectively.

Congresses, Workshops, and Symposia

2020

- Hofmann, S. (January). *Generative Adversarial Networks (GANs): A Primer.* Workshop. CBS CoCoNut. Max Planck Institute for Human Cognitive and Brain Sciences. Leipzig, Germany.
- Hartmann, H., & Medawar, E. (May). *Max Planck Sustainability Network Meeting "Climate Change of Mind"*. Annual Meeting. Max Planck Institute for Human Cognitive and Brain Sciences. Leipzig, Germany.
- Schroeter, M. L. (June). *Big data and machine learning personalize neuropsychiatric disorders: Ready for clinical translation?* Symposium. 26th Annual Meeting of the Organization for Human Brain Mapping (OHBM). Virtual.
- Hofmann, S. (July). *Dynamical Systems Approaches to Neuroscience: A Hands-On Introduction via PyRates*. Workshop. CBS CoCoNut. Max Planck Institute for Human Cognitive and Brain Sciences. Leipzig, Germany.
- Hofmann, S. (August). Primer on Structural Equation Modeling. Workshop. CBS CoCoNut. Virtual.
- Beyer, F., Medawar, E., Hofmann, S., & Witte, V. (October). *OMEGA Lab conference 2020 "Brain plasticity – influences of lifestyle and aging"*. Conference. Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany.
- Sehm, B. (October). *Stroke Alliance Saxony-Anhalt.* Symposium. Martin Luther University Halle, Germany.
- Hofmann, S. (November). *General Meeting of Max Planck PhDNet.* Meeting. Dresden, Germany. Virtual.
- Villringer, A., & Lachmann, U. (December). *11. Prophylaxe-Seminar des Kompetenznetzes Schlagfanfall.* [*11th Prophylaxis Seminar of the Competence Network Stroke*]. Symposium. Competence Network Stroke (KNS), Berlin, Germany.

2021

- Villringer A., & Babayan, A. (March). *8th MindBrainBody Symposium*. MindBrainBody Institute at Berlin School of Mind and Brain, Germany. Virtual.
- Babayan, A., & Revina, Y. (April). *Girls' and Boys' Day. Future Day.* Workshops. Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany. Virtual.
- Grigoryan, K. A. (April). *Controlling computers with our brains.* Workshop. Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany.
- Hofmann, S., & Medawar, E. (April). *Graph Theory: A primer*. Workshop. CBS CoCoNut. Virtual.
- Nikulin, V. (May). *MEGNord conference*. Conference. Moscow, Russian Federation.
- Sehm, B. (October). *Stroke Alliance Saxony-Anhalt*. Symposium. Martin Luther University Halle, Germany.
- Nikulin, V. (October). *VII. International school for young scientists. Active and passive methods of brain research*. Conference. Moscow, Russian Federation.
- Villringer, A., & Lachmann, U. (December). *12. Prophylaxe-Seminar des Kompetenznetzes Schlagfanfall.* [*12th Prophylaxis Seminar of the Competence Network Stroke*]. Symposium. Competence Network Stroke (KNS), Berlin, Germany

2022

- Babayan, A., & Revina, Y. (April). *Girls' and Boys' Day. Future Day*. Workshops. Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany. Virtual and presence modes.
- Villringer, A., & Babayan, A. (March). *9th MindBrainBody Symposium.* Symposium. MindBrainBody Institute at Berlin School of Mind and Brain, Germany. Virtual.
- Hofmann, S. (June). *Sustainability and Environment Action (SEA)*. OHBM Symposium. Glasgow, UK.
- Schroeter, M. L. (June) *Re-conceptualizing neuropsychiatric diseases with meta-Analytical data mining*. Symposium. 28th Annual Meeting of the Organization for Human Brain Mapping (OHBM), Scotland, UK.
- Obrig, H. (June). *Aspects of clinical research using optical imaging (fNIRS) and structural MRI.* Workshop. 11th IMPRS NeuroCom Summer School in Cognitive Neuroscience. International Max Planck Research School on Neuroscience of Communication: Function, Structure, and Plasticity (IMPRS NeuroCom), Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany.

- Meyer, L. & Nikulin, V. (June). *Promises, Practices, and Pitfalls of Current M/EEG Analysis Approaches.* Workshop. 11th IMPRS NeuroCom Summer School in Cognitive Neuroscience. International Max Planck Research School on Neuroscience of Communication: Function, Structure, and Plasticity (IMPRS NeuroCom), Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany.
- Belger, J., & Thöne-Otto, A. (September). *Virtuelle Realität in der Neuropsychologie.* [*Virtual reality in neuropsychology*]. Symposium. German Society for Neuropsychology (GNP), Marburg, Germany.
- Sehm, B. (October). *Stroke Alliance Saxony-Anhalt*. Symposium. Martin Luther University Halle, Germany.
- Witte, V. (October). *OMEGA Lab Retreat*. Workshop. Bad Belzig, Germany.
- Villringer, A., & Lachmann, U. (December). *13. Prophylaxe-Seminar des Kompetenznetzes Schlagfanfall.* [*13th Prophylaxis Seminar of the Competence Network Stroke*]. Symposium. Competence Network Stroke (KNS), Berlin, Germany.

Degrees

PhD Theses

2020

- Ballarini, T. *Magnetic resonance imaging biomarkers for cinical symptoms and therapy in Parkinson's disease.* Leipzig University, Germany.
- Beyer, F. *Body mass index relates to brain structure and function – a population-based neuroimaging approach.* Leipzig University, Germany.
- Hudl, N. *Neural correlates of working memory training: fMRI analyses in healthy older adults.* Leipzig University, Germany.
- Meemken, M. *Implicit and explicit appetitive outcome-learning in obesity.* Leipzig University, Germany.
- Schaare, L. *Blood pressure and brain structure in early adulthood.* Leipzig University, Germany.

2021

- Baczkowski, B. *Inferring risk in the absence of threat: On the interaction of Pavlovian threat memory with the pre-existing knowledge of environmental structure.* Leipzig University, Germany.
- Bloechl-Sevinchan, M. *Situating determinant of mental health and well-being during ageing within a lifespan perspective.* University of Muenster, Germany.
- Kalloch, B. *Towards individualized transcranial electric stimulation therapy through computer simulation.* Leipzig University, Germany.
- Kenville, R. *Compound motor control: Non-invasive approaches to uncover principles and mechanisms.* Leipzig University, Germany.
- Kube, J. *Behavioral adaptation and the processing of positive and negative action consequences in obesity.* Leipzig University, Germany.
- Kumral, D. *Variability in heart and brain activity across the adult lifespan.* Charité – Berlin University of Medicine, Germany.
- Maudrich, T. *Physiological mirror activity: Neural correlates and mechanisms.* Leipzig University, Germany.
- Shih, P.-C. *Bilateral upper-limb coordination in aging and stroke.* Leipzig University, Germany.
- Reinelt, J. *Mind-Brain-Body Interactions after Acute Psychosocial Stress.* Leipzig University, Germany.
- Weicker, J. *Development and evaluation of an adaptive working memory training intervention.* Leipzig University, Germany.

2022

- Akbal, Z. *Live-body experiences in virtual reality (VR): A phenomenology of the virtual body.* University of Potsdam, Germany.
- Al, E. *The impact of heart-brain interactions on somatosensory perception.* Charité – Berlin University of Medicine, Germany.

- Grund, M. *Neural correlates of conscious and unconscious somatosensory processing.* Leipzig University, Germany.
- Idaji, M. J. *New machine learning methods for modeling nonlinear interactions in neural data – Towards separation and detection of genuine cross-frequency synchronized sources.* Technical University Berlin, Germany.
- Molloy, E. *Behavioral, functional, and neurophysiological response to one week administration of escitalopram.* Leipzig University, Germany.
- Paul, K. I. *Unravelling early endovascular skill acquisition.* University of Groningen, the Netherlands.
- Poessel, M. *The association between metabolic health status and smell perception in obesity: Behavioral and brain anatomical correlates.* Leipzig University, Germany.

MD Theses

2020

- Thomas, K. *Volumetrische Charakterisierung und Analyse mikrostruktureller Maße des Hypothalamus im Rahmen von Adipositas.* [*Volumetric characterization and analysis of microstructural measures of the hypothalamus in the context of obesity*]. Leipzig University, Germany.
- Maleka, L. A. *Der modulierende Einfluss von musikalischem Feedback auf das unilaterale repetitive Handtraining von Patienten nach Schlaganfall.* [*The modulatory influence of musical feedback on unilateral repetitive hand training of patients after stroke*]. Leipzig University, Germany.

2021

- Bormann, J. *Wortklassenprädiktion im syntaktischen Kontext – eine Studie bei Patienten mit linkshemisphärieller Läsion im Sprachnetzwerk.* [*Word class prediction in syntactic context – a study in patients with left hemispheric lesion in the language network*]. Leipzig University, Germany.
- Kunzendorf, S. *The psychophysiology of heart-brain-interactions: How active information sampling is modulated across the cardiac cycle.* Charité – Berlin University of Medicine, Germany.
- Rausch, F. *The interplay between a dietary preference for fat and sugar, gene expression in the dopamine system and executive cognition in humans.* Leipzig University, Germany.
- Seidel-Marzi O. *Neurodiagnostics in sports: Investigating the brain's potential to optimize performance in athletes.* Leipzig University, Germany.

2022

- Heinrich, M. *Oestradiol moderates the association of visceral fat on brain structure and cognitive function in women*. Leipzig University, Germany.
- Paul, L. *The effect of an acute phenylalanine/tyrosine depletion on reinforcement learning in humans differing in the intake of fat and sugar*. Leipzig University, Germany.

Appointments

2020

- Männel, C. *W2 Professorship*, Clinic for Audiology and Phoniatrics, Charité – Berlin University of Medicine, Germany.

2021

- Martins, M. *Assistant Professorship*, School of Collective Intelligence, Mohammed VI Polytechnic University, Morocco.

2022

- Sacher, J. *W2 Professorship*. Professor for Cognitive Neuroendocrinology, Leipzig University Hospital, Germany.
- Schaadt, G. *W2 Professorship*, Free University Berlin, Germany.
- Witte, V. *W3 Professorship (pending)*, Neuroanatomy, University of Hamburg, Germany.

Awards

2020

- Al, Esra. *Young Scientist Award.* Deutsche Gesellschaft für Psychophysiologie und ihre Anwendung (DGPA), Germany.
- Zsido, R. *Interdisciplinary Life Science Fellowship*. Joachim Herz Foundation, Hamburg, Germany.

2021

- Al, E. *QUEST 1,000 € NULL Results and Replication Study Award*. Berlin Institute of Health at Charité – Berlin University of Medicine, Germany.
- Babayan, A., Pfeifer, F., & Revina, Y. *GOLD for Gender Equality Plan 2021–2023 of the Max Planck Institute for Human Cognitive and Brain Sciences*. Max Planck Society, Munich, Germany.
- Beyer, F. *t.e.a.m. für Postdoktorandinnen [t.e.a.m. for female postdocs]*. Mentoring programme at Leipzig University, Germany.
- Beyer, F. *Walter-Benjamin-Programm*. German Research Foundation (DFG), Bonn, Germany.
- Grigoryan, K. A. *Member of the winning team of RoX Digital health Hackathon*. Berlin, Germany.
- Kapralov, N. *Second Prize*. The Eighth International Olympiad in Cryptography (NSUCRYPTO-2021), Russia.
- Stephani, T. *Experimental Design Award.* IMPRS NeuroCom, London/Leipzig, UK/Germany.
- Vartanian, M. *Scholarship of the Friedrich Naumann Foundation*. Potsdam, Germany.
- Waltmann, M. *Poster Prize.* German Society for Child and Adolescent Psychiatry, Psychosomatics and Psychotherapy (DGKJP), Berlin, Germany.
- Weicker, J. *Promotion award*. Gesellschaft für Neuropsychology (GNP), Germany.
- Witte, V. *t.e.a.m. für Postdoktorandinnen [t.e.a.m. for female postdocs]*. Mentoring programme at Leipzig University, Germany.
- Zhang, J. *Paper of the month.* Collaborative Research Centre TRR 295 ReTune, Germany.
- Zsido, R. *Dr Margarete Blank Publication Prize*. Leipzig University, Germany.

2022

- Al, E. *Research Excellence Award*. Neuroergonomics & NYC Neuromodulation conference, New York City, USA.
- Flores, A. *Best scientific project presentation*. Department of Neurology, Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany.
- Gerster, M. *NENS exchange grant*. Federation of Neuroscience Societies (FENS), Brussels, Belgium.
- Gerster, M. *Best procedure idea presentation.* Department of Neurology, Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany.
- Gippert, M. *Best paper presentation*. Department of Neurology, Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany.
- Medawar, E. *Merit Award for Poster*. Meeting of Organization for Human Brain Mapping (OHBM), Glasgow, Scotland, UK.
- Medawar, E. *Best Poster Prize*. Meeting of Society for the Study of Ingestive Behavior (SSIB), Porto, Portugal.

Publications

Books & Book Chapters

Becker, R., Mayhew, S., Ritter, P., & Villringer, A. (2023). Visual system. In C. Mulert & L. Lemieux (Eds.), *EEG - fMRI* (2nd Ed., pp. 565–589). Cham: Springer International Publishing. https://doi.org/10.1007/978-3-031-07121-8_23

Fritz, T. H. (2020). Warum Musik verbindet: Untersuchung aus neurowissenschaftlicher Perspektive. In K. Bradler & A. Michel (Eds.), *Musik und Ethik: Ein Symposium an der Brandenburgischen Technischen Universität Cottbus-Senftenberg* (pp. 71–78). Münster: Waxmann.

Fritz, T. H. (2021). Why do people exercise to music? In W. F. Thompson & K. N. Olsen (Eds.), *The science and psychology of music: From Beethoven at the office to Beyoncé at the gym* (pp. 284–289).

Hudl, N. (2020). Neural correlates of working memory training: fMRI analyses in healthy older adults. *MPI Series in Human Cognitive and Brain Sciences*: Vol. 205. Leipzig: Max Planck Institute for Human Cognitive and Brain Sciences.

Kenville, R. (2021). Compound motor control: Non-invasive approaches to uncover principles and mechanisms. *MPI Series in Human Cognitive and Brain Sciences*: Vol. 215. Leipzig: Max Planck Institute for Human Cognitive and Brain Sciences.

Kube, J. (2020). Behavioral adaptation and the processing of positive and negative action consequences in obesity. *MPI Series in Human Cognitive and Brain Sciences*: Vol. 212. Leipzig: Max Planck Institute for Human Cognitive and Brain Sciences.

Maudrich, T. (2021). Physiological mirror activity: Neural correlates and mechanisms. *MPI Series in Human Cognitive and Brain Sciences*: Vol. 216. Leipzig: Max Planck Institute for Human Cognitive and Brain Sciences.

Ritter, P., Rothlübbers, S., Becker, R., Freyer, F., & Villringer, A. (2023). EEG quality: The image acquisition artefact. In C. Mulert & L. Lemieux (Eds.), *EEG - fMRI* (2nd Ed., pp. 189–212). Cham: Springer International Publishing. https://doi.org/10.1007/978-3-031-07121-8_9

Shih, P.-C. (2022). Bilateral upper-limb coordination in aging and stroke. *MPI Series in Human Cognitive and Brain Sciences*: Vol. 218. Leipzig: Max Planck Institute for Human Cognitive and Brain Sciences.

Vartanian, M., Khorsandi, S., Sancho Escanero, L., Acedo-Carmona, C., & Christensen, J. F. (2022). Human flourishing through dance practice. In T. Chemi, E. Brattico, L. Overby Fjorback, L. Harmat, T. Chemi, E. Brattico, L. O. Fjorback, & L. Harmat (Eds.), *Arts and Mindfulness Education for Human Flourishing*. London: Routledge.

Villringer, A. (in press). Neuronale Grundlagen der Plastizität des Gehirns. In H. Frommelt & A. Thöne-Otto (Eds.), *NeuroRehabilitation* (3rd ed.). Heidelberg: Springer.

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Journal Articles

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Index of Published Figures

Figure 2.1.1.1

(part A) Adapted from Hofmann, S. M., Beyer, F., Lapuschkin, S., Goltermann, O., Loeffler, M., Müller, K.-R., Villringer, A., Samek, W., & Witte, A. V. (2022). Towards the interpretability of deep learning models for multi-modal neuroimaging: Finding structural changes of the ageing brain. *NeuroImage, 261*. https://doi.org:10.1016/j.neuroimage.2022.119504

Figure 2.1.1.2

(part B) Adapted from Medawar, E., & Witte, A. (2022). Impact of obesity and diet on brain structure and function: A gut–brain–body crosstalk. *Proceedings of the Nutrition Society, 81*(4), 306–316. https://doi.org/10.1017/S0029665122002786

Figure 2.1.2

(part A, B, and C) Adapted from Grund, M., Al, E., Pabst, M., Dabbagh, A., Stephani, T., Nierhaus, T., Gaebler, M., & Villringer, A. (2022). Respiration, heartbeat, and conscious tactile perception. *The Journal of Neuroscience*, *42*(4), 643–656. https://doi.org/10.1523/JNEUROSCI.0592-21.2021

Figure 2.1.3

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Figure 2.2.1

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Figure 2.2.2

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(part B) Adapted from Koutsouleris, N., Pantelis, C., Velakoulis, D., McGuire, P., Dwyer, D. B., Urquijo-Castro, M. F., Paul, R., Dong, S., Popovic, D., Oeztuerk, O., Kambeitz, J., Salokangas, R. K. R., Hietala, J., Bertolino, A., Brambilla, P., Upthegrove, R., Wood, S. J., Lencer, R., Borgwardt, S., Maj, C., Nöthen, M., Degenhardt, F., Polyakova, M., Mueller, K., Villringer, A., Danek, A., Fassbender, K., Fliessbach, K., Jahn, H., Kornhuber, J., Landwehrmeyer, B., Anderl-Straub, S., Prudlo, J., Synofzik, M., Wiltfang, J., Riedl, L., Diehl-Schmid, J., Otto, M., Meisenzahl, E., Falkai, P., Schroeter, M. L., International FTD-Genetics Consortium (IFGC), the German Frontotemporal Lobar Degeneration (FTLD) Consortium, & the PRONIA Consortium (2022). Exploring links between psychosis and frontotemporal dementia using multimodal machine learning: Dementia Praecox revisited. *JAMA Psychiatry*, *79*(9), 907–919. https://doi.org/10.1001/jamapsychiatry.2022.2075

Figure 2.2.3

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Figure 2.3.1 Part A

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Figure 2.3.2

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Figure 2.3.3

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Figure 2.3.4

(part A). Unpublished figure

(part B). Manuscript under review

Figure 2.3.5

Unpublished figure

Professor Dr Nikolaus Weiskopf
Director

3

Imaging the Anatomical and Functional Brain Micro-Organisation

DEPARTMENT OF NEUROPHYSICS

Our vision is to develop and apply non-invasive magnetic resonance imaging (MRI) methods to reliably characterise the detailed anatomical and functional micro-organisation of the human brain.

Understanding the normal and diseased human brain crucially depends on reliable knowledge of its anatomical microstructure and functional micro-organisation (e.g., cortical layers, columns and stripes, cyto-/myeloarchitecture; Figure 3.1.1). To date, the micro-organisation can only be determined using invasive methods, such as post-mortem histology or invasive electrophysiology. This limits neuroscience, clinical research, and diagnosis.

The non-invasive characterisation of the brain micro-organisation and its changes in health and disease poses significant challenges. Several orders of magnitude of spatial scale need to be spanned and the multitude of different anatom-

ical and physiological structures need to be captured and integrated (Figure 3.1.1). MRI is well suited to achieve this. It is non-invasive and offers exquisite soft tissue contrast, which can be tailored to specific microstructural aspects, since it is sensitive to water-tissue interactions acting at different spatial and temporal scales (Figure 3.1.2).

Micro-organisation imaging requires unprecedented spatial resolution, minimal artifact levels and high tissue specificity. To address these extraordinary methodological challenges, we pursue an integrated interdisciplinary approach consisting of:

1. MR physics developments (3.1),
2. biophysical modelling and data processing (3.2),
3. neuroscientific proof-of-concept and validation studies (3.3).

The successful development of in-vivo histology using MRI (hMRI) of the anatomical and fMRI of the functional micro-organisation hold great potential for research and clinical applications. For the first time investigations of the structure-function relationship and plasticity at the microstructural level become feasible in the human brain on a large scale. This will allow for an improved understanding of how brain structure determines function and functional demands affect structure. Microstructure imaging is expected to provide sensitive biomarkers of nervous system changes due to trauma or neurodegeneration, providing important early biomarkers in personalised medicine and clinical trials.

Over the last three years the research in the Department of Neurophysics has placed increasing emphasis on applications of the recently developed methods. Mesoscopic functional and anatomical features of the cortex were characterised (e.g. V2 stripes in 3.3.1 and cortical layers in 3.3.2). Novel quantitative markers that offer cellular sensitivity and are derived from first biophysical principles led to a re-interpretation of established nigrosome imaging markers of the substantia nigra (3.3.3). The methods were also translated to, and applied for, imaging hominoid brains to improve our phylogenetic and ontogenetic understanding (3.3.4, 3. 3.5).

Developments in the field of MR physics have continued improving resolution and data quality, enabling robust data acquisition at ultra-high resolution (e.g., parallel transmit use for quantitative mapping, 3.1.1; 600 µm resolution T2 mapping, 3.1.2). The entire spectrum of biophysical models from *ab initio* modelling of iron contrast to data-driven semi-empirical modelling of myelin contrast was further advanced towards a more specific view of the brain's microstructure (e.g., 3.2.1, 3.2.2).

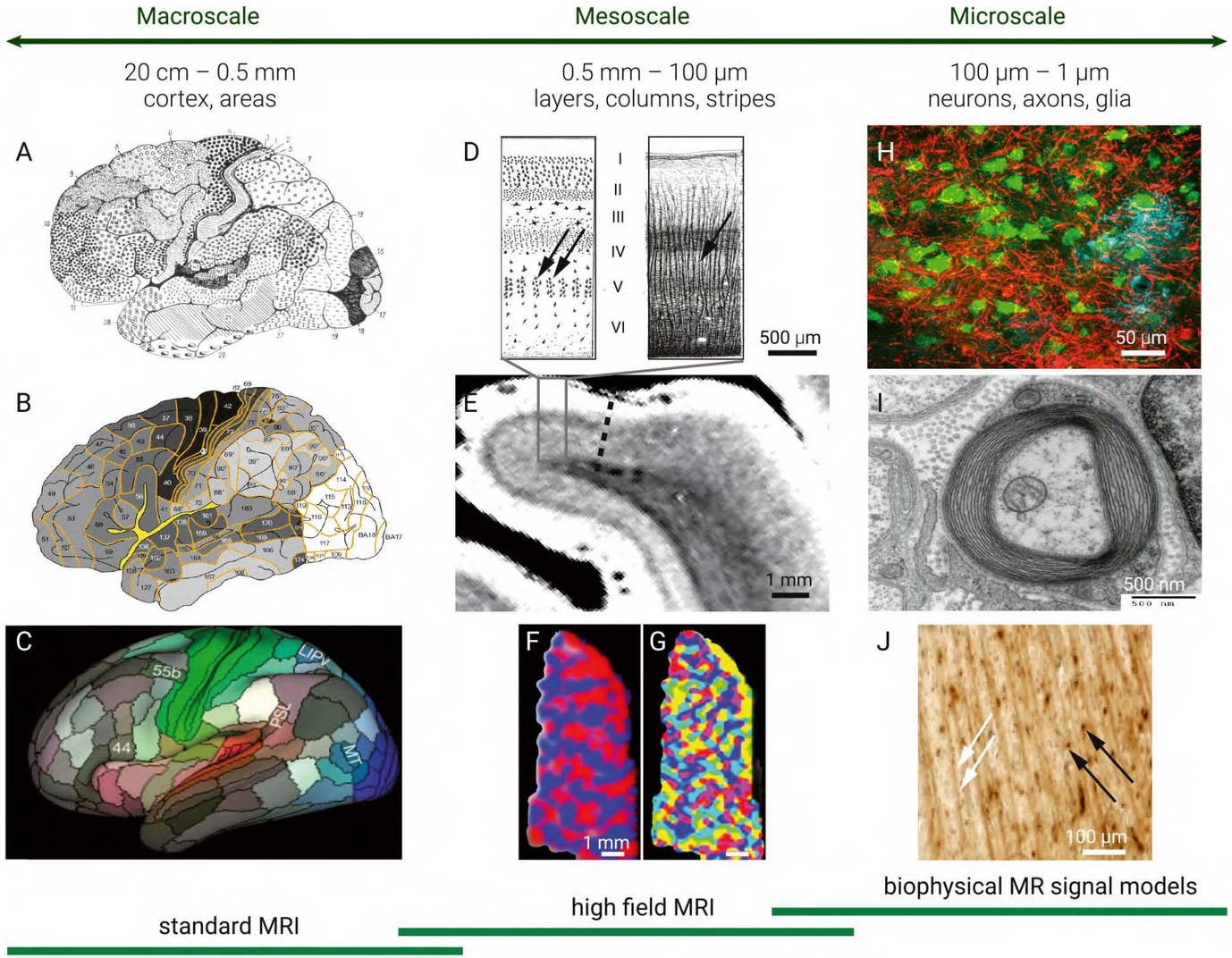

Figure 3.1.1 Imaging the brain micro-organisation.
(A) Examples of neocortical organisation on the macroscopic (A–C), mesoscopic (D–G), and microscopic (H–J) scales, spanning five orders of magnitude in resolution and various structural features. (A) cytoarchitectonic parcellation, (B) myeloarchitectonic parcellation, (C) recent in-vivo cortical parcellation based on combining structural and functional MRI. The neocortex can be subdivided into six distinct layers based on cytoarchitecture (D, left) or myeloarchitecture (D, right). Mesoscopic ontogenetic columns (columns of increased neuron cell body density and decreased myelin density) are indicated by arrows in (D). (E) High resolution T2*-weighted MR image showing distinct cortical layers. Functional units are also found on the mesoscopic scale. Examples of these functional cortical columns are (F) ocular dominance and (G) orientation preference columns in human visual cortex. On the microscopic scale, neuronal cell bodies, myelinated fibres, and glial cells are important constituents of the cortex. (H) Microscopy shows neuronal cell bodies, myelinated fibres and astroglia. (I) Myelin sheath around axonal fibres imaged using electron microscopy. (J) Iron localised in oligodendrocytes and myelinated fibres. Reprinted from Edwards et al. (2018, Neuroimage, 182, 184-206), which also provides a comprehensive list of references for the different subfigures.

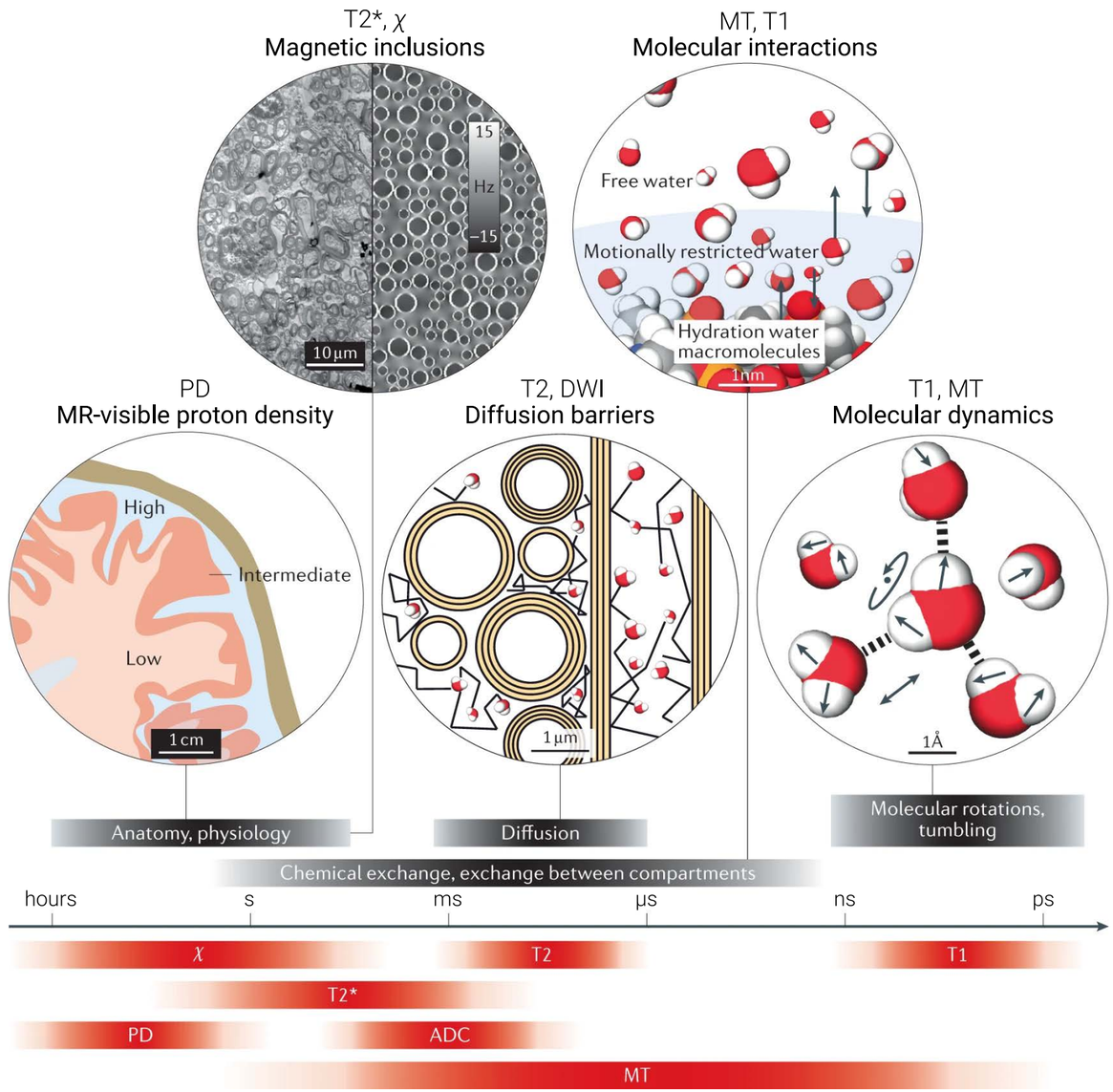

Figure 3.1.2 Foundations of MRI-based in-vivo histology (hMRI): Quantitative magnetic resonance imaging parameters reflect water–tissue interactions on multiple temporal and spatial scales. Upper part: microstructural tissue components and water–tissue interactions influencing quantitative magnetic resonance imaging (qMRI) parameters, along with their characteristic length scales. Lower part: timescale of processes impacting qMRI parameters. The proton density (PD) reflects the content of magnetic resonance (MR)-visible free water in the tissue. Diamagnetic and paramagnetic tissue components induce local variations of the magnetic field in their proximity, resulting in effective transverse relaxation time (T2*) through static dephasing and motional narrowing mechanisms. Cell membranes and myelinated fibres act as diffusion barriers, hindering water diffusion (and reducing the apparent diffusion coefficient (ADC)) detected by diffusion-weighted imaging (DWI) in an anisotropic fashion. Magnetisation transfer (MT) between freely tumbling water, bound water and less mobile macromolecular protons strongly influences MT and longitudinal relaxation time (T1) parameters. Molecular tumbling modulating dipolar interactions with neighbouring nuclear and unpaired electron spins are the main contributors to the longitudinal relaxation process (T1). χ, magnetic susceptibility; T2, transverse relaxation time. Reprinted from Weiskopf et al. (2021, Nature Reviews Physics, 3, 570–588).

3.1 MR Physics Developments

MR Physics Developments focused on developments on the 7T and 3T Connectom MRI platforms (300mT/m high performance gradient system, which is one of four worldwide), since they offer superior contrast/signal-to-noise ratio (CNR/SNR). The advanced parallel transmit capabilities of the newly installed 7T Siemens Terra MRI scanner were leveraged for reducing bias in multi-parameter mapping and extending the high quality imaging volume (MPM, 3.91.1). Novel k-space acquisition schemes and image reconstruction methods helped us to significantly reduce scan time and enabled the acquisition of T2 maps with the unprecedented isotropic resolution of 600 µm (3.1.2). Moreover, compressed sensing, low rank reconstruction, and deep learning reconstruction-based methods were developed to improve the image quality, increase the reconstruction speed, and enhance the flexibility of acquisition schemes (e.g., 3.1.3). For additional MR Physics Development projects (e.g. post-mortem imaging, ultra-high resolution fMRI), see our website.

3.1.1 Parallel transmit kT-points pulses improve 500µm resolution quantitative multi-parameter mapping (MPM) at 7T

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[1] Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany, [2] Siemens Healthcare GmbH, Erlangen, Germany, [3] Spinal Cord Injury Center Balgrist, University Hospital Zurich, Switzerland, [4] Felix Bloch Institute for Solid State Physics, Leipzig University, Germany

Adapted from Pine et al., submitted to ISMRM 2023.

Quantitative multi-parameter mapping (MPM) can provide detailed information about brain microstructure, measuring (Vaculčiaková et al., 2022): longitudinal relaxation rate (R1), proton density (PD) and effective transverse relaxation rate R2*. It is based on a combination of 3D multi-echo gradient echo (GRE) acquisitions, $B1^+$ radio-frequency (RF) transmit field mapping and modelling. Despite including $B1^+$ mapping in the quantification, bias and shading artifacts can be observed at 7T. We integrated the pTx kt-points approach (Cloos et al., 2012) for non-selective excitation with high $B1^+$ homogeneity in the GRE and AFI $B1^+$ mapping acquisitions.

The performance of the kt-points MPM approach was compared to the conventional MPM approach in a group of 8 volunteers at 7T. Data were acquired with two different non-selective RF excitation pulses: pTx 4 kt-points (220µs sub-pulses) and sinc pulses (180, 1368µs pulse durations, BWT 6), here called pTx and True Form acquisition, respectively. The MPM acquisition entailed two in-house built 3D multi-echo GRE with PD- and T1-weighting (with nominal excitation flip angles of 8° and 24° respectively for the True Form measurement, and 7° and 22° for the pTx measurement) with 500µm isotropic resolution and 2x2 GRAPPA acceleration. Maps of the local flip angle distribution were estimated from an in-house built AFI acquisition (Lutti et al., 2012), which used the same type of RF excitation pulse to ensure direct comparability and applicability of RF transmit maps.

Data were processed using the open source hMRI toolbox (Tabelow et al., 2019). It resulted in local flip angle maps, R1, PD and R2* maps. Maps were transformed to MNI group space for further analysis using DARTEL as implemented in the hMRI toolbox. The voxel-wise mean, standard deviation (SD) and coefficient of variation (CoV) were calculated across the group for each method to compare noise and bias characteristics.

The pTx approach significantly improved the excitation flip angle homogeneity across the brain (Figure 3.1.1.1). This improvement translated to lower bias (Figure 3.1.1.2) and reduced CoV (Figure 3.1.1.3) in R1 maps. The pTx approach also improved CoV of the PD maps but not for R2* maps (Figure 3.1.1.4). Improvements were most conspicuous in areas typically suffering from signal dropouts due to low effective flip angles such as the inferior temporal lobes or parts of the cerebellum. The negligible impact on R2* maps can be explained by the small dependence of R2* fits on the initial signal intensity.
The improvements indicate a larger effective coverage and sensitivity for anatomical studies. The approach can be readily deployed and integrated in the scanning and data processing workflow as it only adds ca. 2.5 mins scan time, runs on the scanner console and is compatible with established quantitative MRI processing pipelines (e.g., hMRI toolbox).

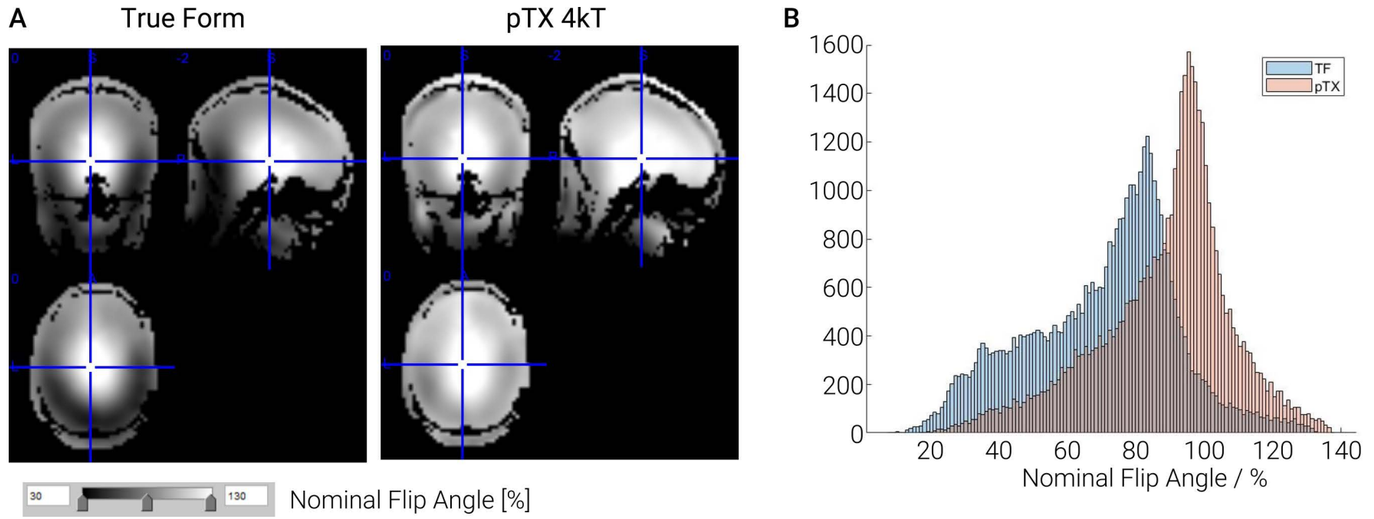

Figure 3.1.1.1 Local excitation flip angle distribution for the True Form and pTx 4 kt-points approach as measured with AFI for a single subject. (A) Exemplary map of local actual flip angle relative to nominal flip angle, (B) Histogram of relative actual flip angles across entire brain. The pTx pulses achieved a higher homogeneity and recovered excitation effectiveness in cerebellar and basal brain regions.

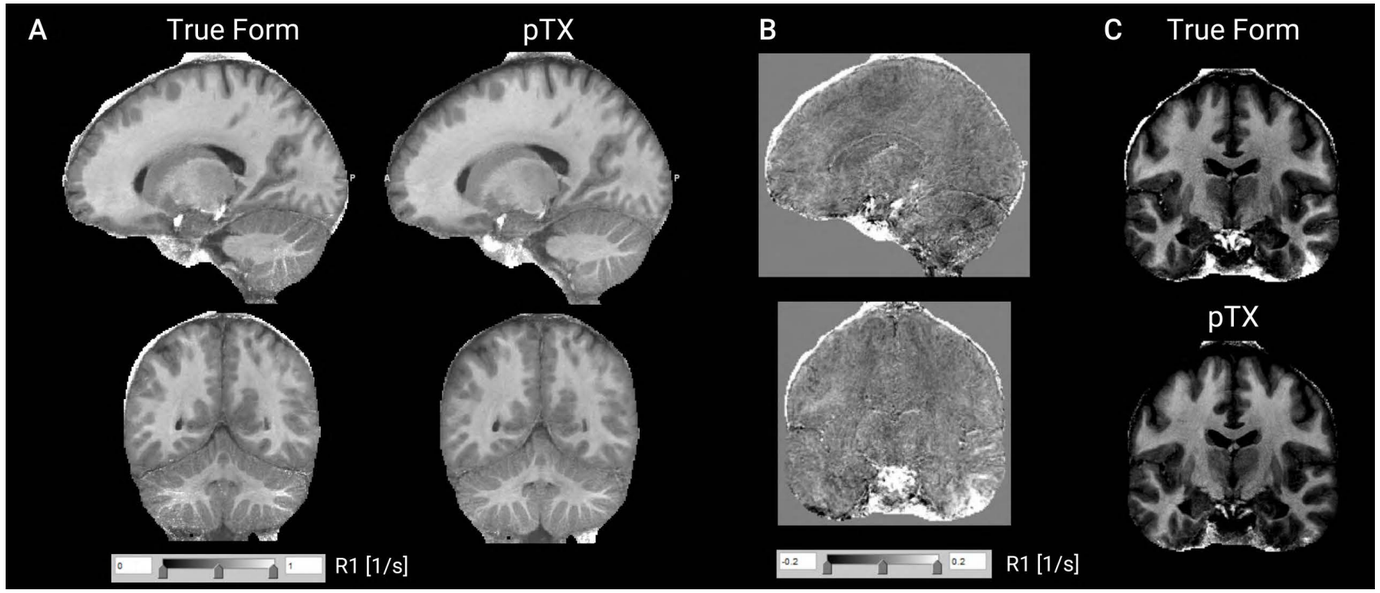

Figure 3.1.1.2 Group averaged R1 maps for the True Form and pTx 4 kt-points approach. (A) Mean across the group. (B) Group difference between True Form and pTx 4 kt-points approach. (C) Means for slices presented in B. Asymmetric bias is visible in the cerebellum and temporal lobes.

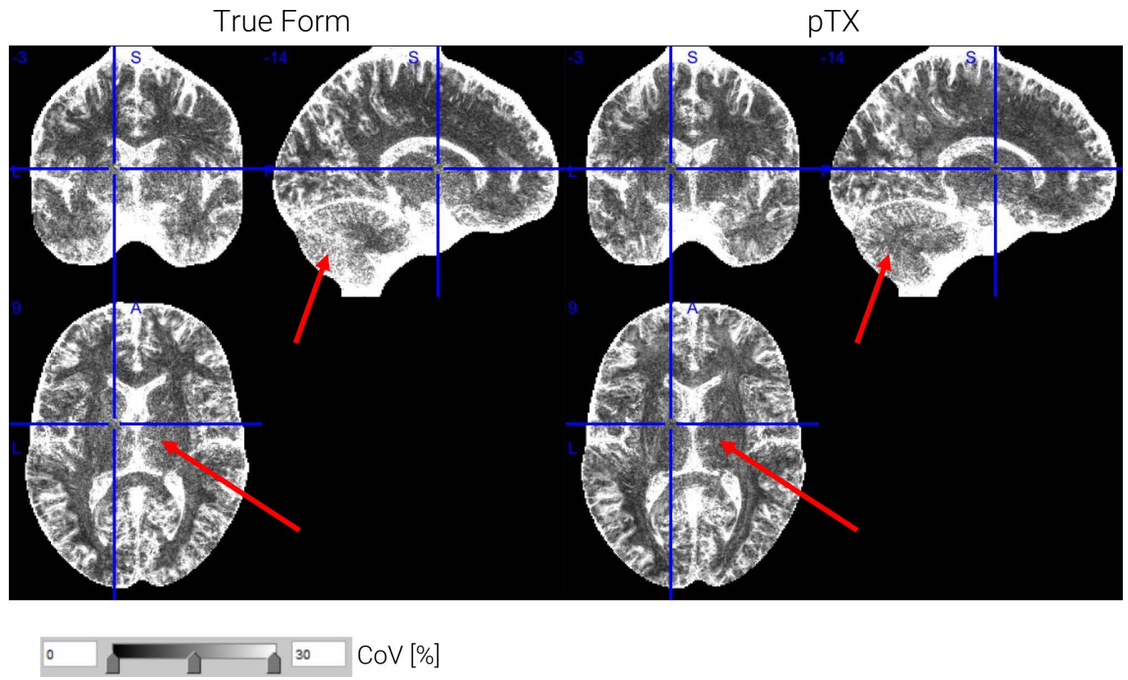

Figure 3.1.1.3 Group averaged coefficient of variation (CoV) of R1 maps for the True Form (left) and pTx 4 kt-points (right) approach. Similar to the reduced bias (Figure 3.1.1.2) reductions of CoV were observed in the cerebellum, temporal lobes but also in the center of the brain.

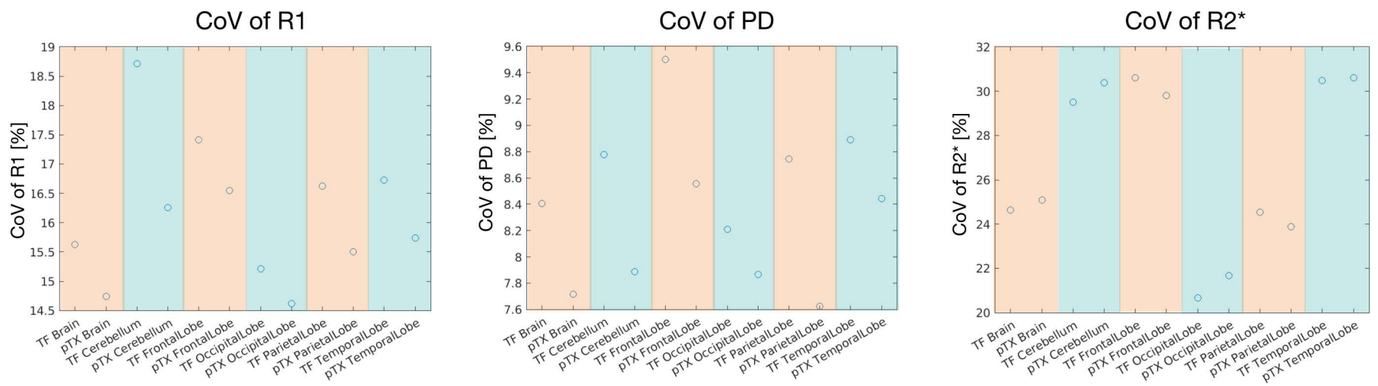

Figure 3.1.1.4 Median of coefficient of variation (CoV) of parameter maps in different regions of interest for the True Form (TF) and pTx 4 kt-points approach. Most consistent improvements in CoV using the pTx approach were observed for R1.

3.1.2 High-resolution quantitative T2 mapping in-vivo at high field 7T

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Accurate and robust quantification of relaxation parameters is crucial for studying the microstructural composition of the human brain in-vivo (Edwards et al., 2018). Measurements across cortical layers require high resolution, resulting in long scan times and/or the need for sophisticated analysis methods when estimating T2. We addressed these issues by combining a multi-echo (ME) spin-echo (SE) sequence with the echo-modulation curve (EMC) approach for T2 estimation based on pre-calculated dictionaries (Ben-Eliezer et al., 2015) and a conventional SE acquisition for reference.

The EMC dictionaries were simulated for a range of input parameters (Figure 3.1.2.1). Measurements were performed on a Siemens Terra 7T Scanner with 2x GRAPPA acceleration. The MESE acquisitions (0.6mm isotropic voxels) were scanned in ~14min. Additionally, we acquired a modified MESE sequence using lower refocusing pulse flip angles (140°). Reference SE measurements (TE=11.6, 20, 35, 50ms) were acquired with in-plane resolution of 1.2mm x 1.2mm and total scan time of ~28min.

In the resulting echo magnitude images (Figure 3.1.2.2), signal reduction due to ($B1^+$) transmit field variation was visible, especially in temporal brain regions and subcortical structures. To reduce bias due to the non-central χ noise distribution, which resulted in apparent T2 overestimation, a majorise-minimise algorithm was used (Varadarajan and Haldar, 2015) for denoising (Figure 3.1.2.3).

T2 was estimated by voxel-wise matching to the EMC dictionary (Figure 3.1.2.4). Bias introduced by a low $B1^+$ field was not fully removed. Nonetheless, the resulting MESE quantitative T2 estimates showed good agreement with literature values (Seginer and Schmidt, 2022) and to the SE reference while exhibiting great detail from the, to our knowledge, unmatched isotropic resolution of 0.6mm. The EMC method also demonstrated robustness against $B1^+$ variations (Figure 3.1.2.4). Future work will address the robustness of the method while extending the field of view to whole brain acquisition including areas with the most prominent $B1^+$ variations at 7T.

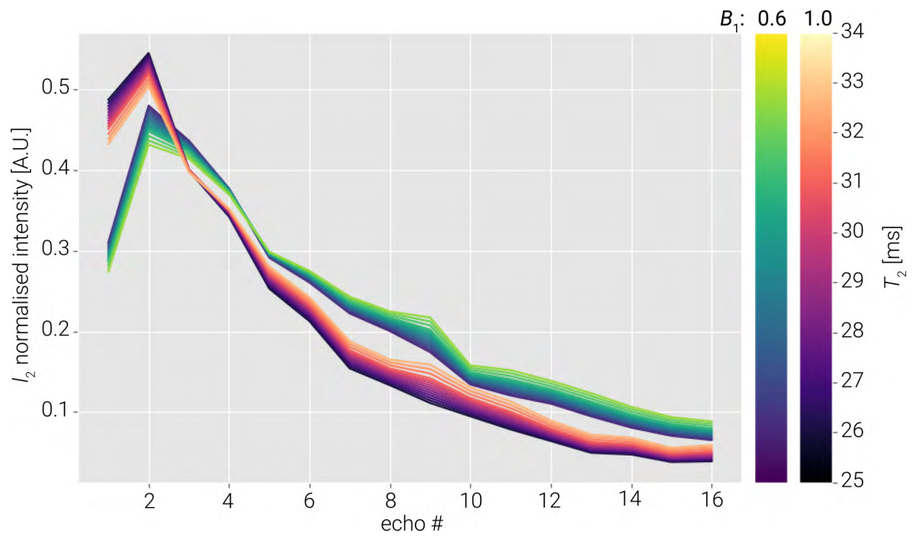

Figure 3.1.2.1 Exemplary signal response curves for a range of T2 values. The formation and characteristics of stimulated echoes is plotted for two distinct transmit field efficiencies (red vs green). The signal course deviates drastically from a mono-exponential decay.

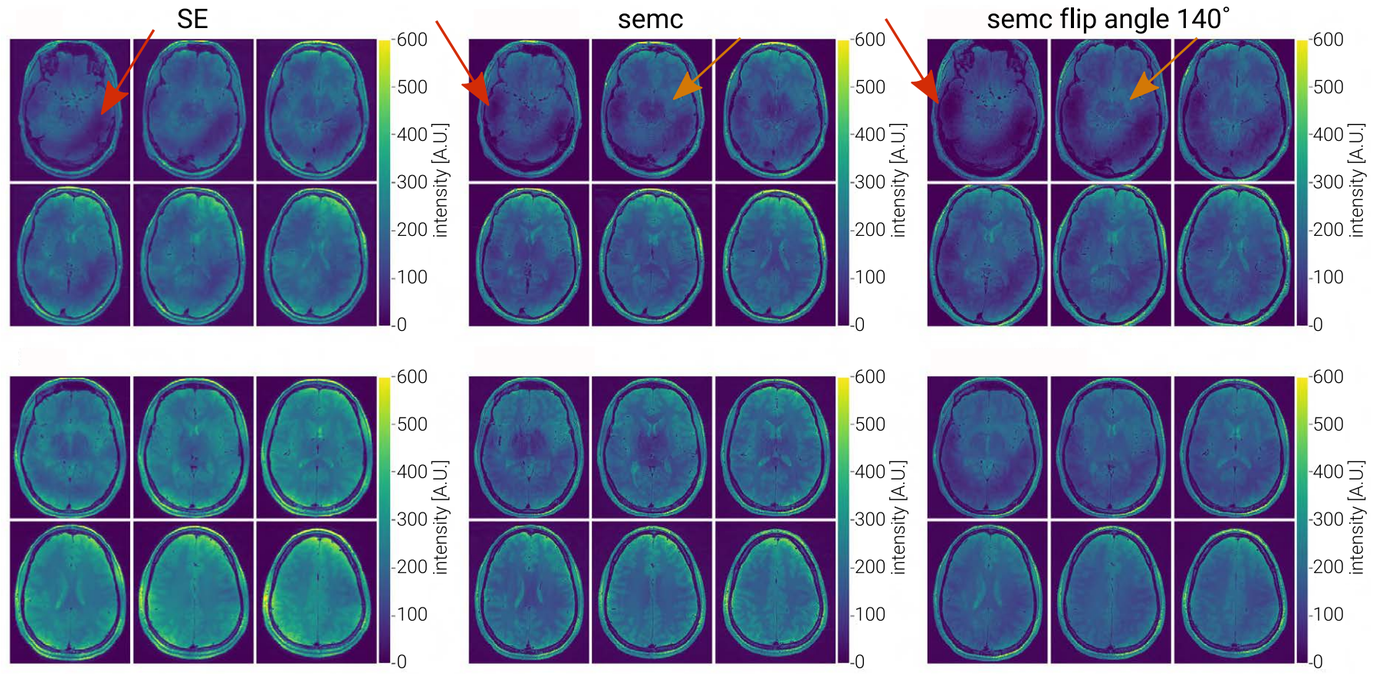

Figure 3.1.2.2 Echo magnitude images of the first echo for a selection of slices for the 3 different acquisitions for 2 different subjects (Top / Bottom). (Left) spin echo. (Middle) MESE. (Right) MESE with reduced refocusing pulse flip angle. Note the signal variation due to an inhomogeneous transmit field, with severe signal dropout in lateral and temporal brain regions (red arrows). Comparing fully refocused (middle) and reduced flip angle refocused (right) images it appears the latter mitigates signal dropout (orange arrows).

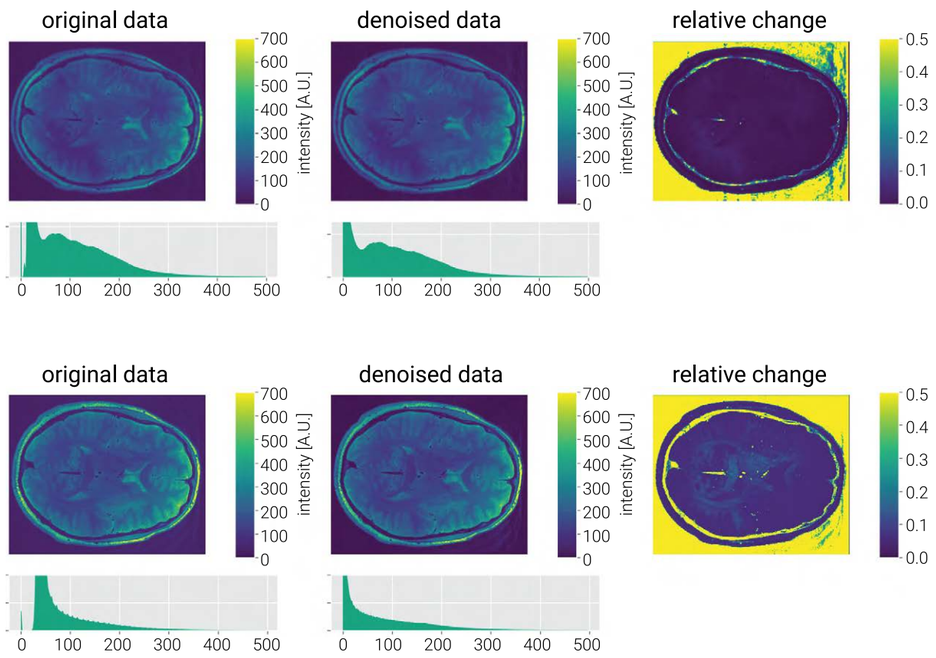

Figure 3.1.2.3 Non-central χ noise characteristics are arising from root-sum-of-squares coil combination when computing magnitude images. Due to the noise characteristics, low signal-to-noise ratio (SNR) voxels are affected more strongly than high SNR voxels. This results in an intensity shift in low signal regions from zero towards the noise mean of the distribution, as can be seen in the intensity histograms below the unprocessed data. With higher SNR the noise characteristics approach Gaussian behaviour. The denoising process adjusts the voxel signal value based on its relative SNR, leading to a shift in lower SNR voxels, as seen in the histograms below the denoised data. (Top) spin echo magnitude image with relatively high SNR. (Bottom) MESE acquisition with generally lower SNR levels.

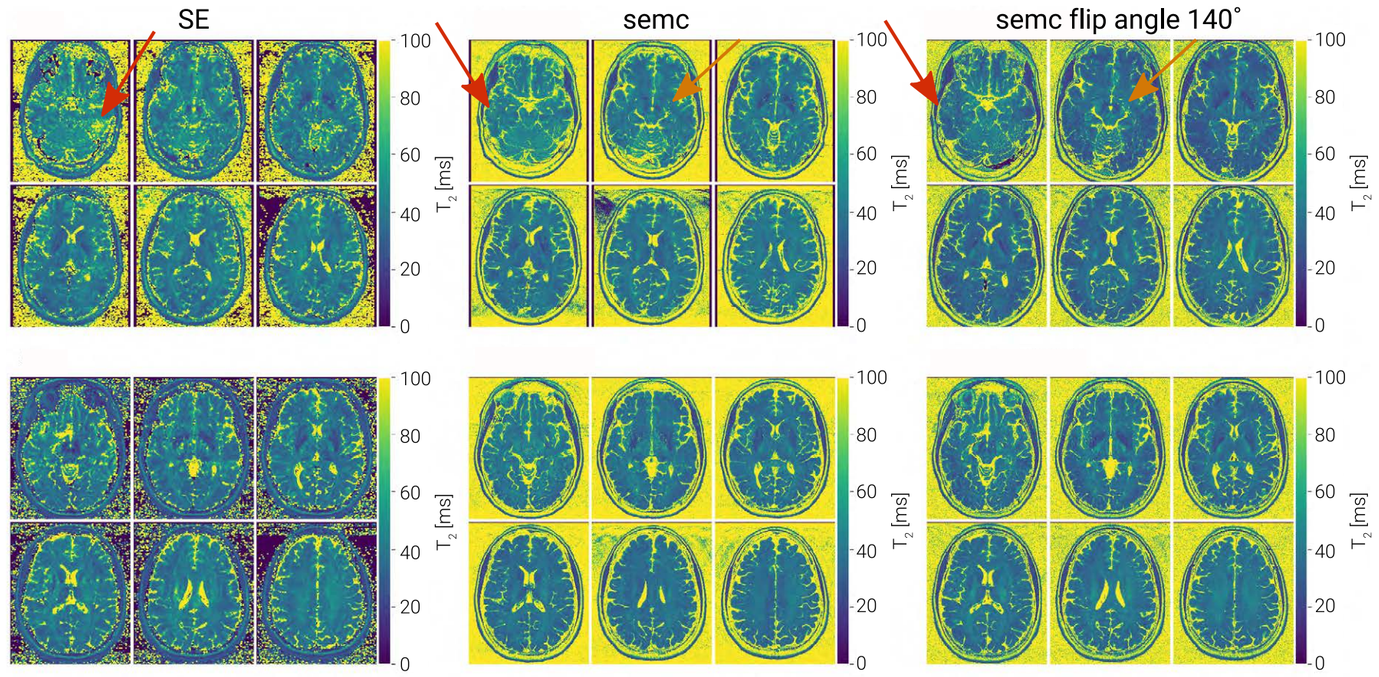

Figure 3.1.2.4 T2 maps estimated after application of the same denoising pipeline via (left) mono-exponential signal decay modelling and (middle and right) EMC dictionary curve matching. The B1+ transmit field bias was not fully corrected by the EMC method. Note (red arrows) the strong signal dropout, i.e., low SNR caused by inefficient excitation can lead to absence of image features (orange arrows).

3.1.3 Evaluating different k-space undersampling schemes with iterative and deep learning image reconstruction for fast multi-parameter mapping (MPM)

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Adapted from Podranksi et al., submitted to ISMRM 2023.

The well-established approaches to speeding up microstructural imaging using quantitative multi-parameter mapping (MPM, (Vaculčiaková et al., 2022)) rely on Cartesian undersampling. Image reconstruction of the underlying multi-echo gradient echo (ME-GRE) data is performed echo by echo. This study explored different k-space undersampling schemes, i.e., elliptical Poisson disc compressed sensing (CS) and CAIPIRINHA, in comparison to equi-spaced Cartesian. The performance of iterative image reconstruction (ENLIVE, (Holme et al., 2019)) and machine learning based Deepcomplex-MRI (DCMRI, (Wang et al., 2020)) on these datasets was evaluated.

Fully sampled, 1mm isotropic resolution MPM datasets (a pair of PD- and T1-weighted 3D ME-GRE acquisitions with 8 equidistant echoes) were acquired on eleven healthy volunteers employing prospective motion correction at 3T. Fourier transform was applied in the readout direction, resulting in a stack of 2D k-space planes/slices. The resulting 2D k-space planes for each volume were processed separately, retrospectively undersampled and fed into the different reconstruc-

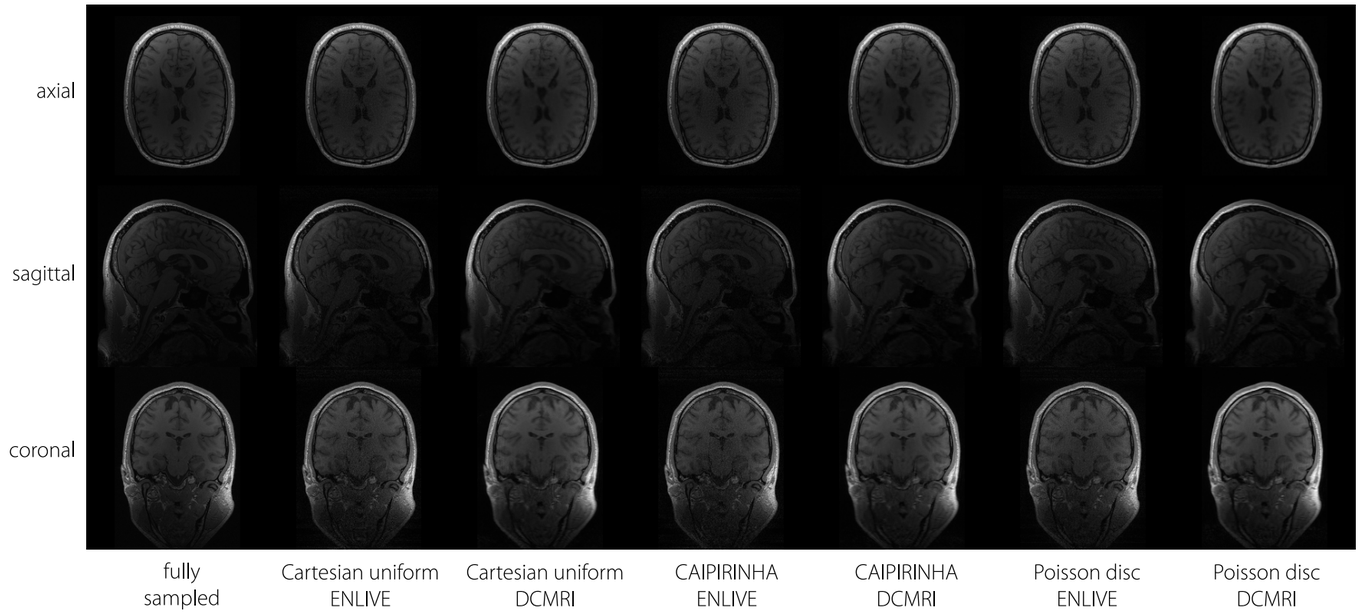

Figure 3.1.3.1 T1-weighted images of a single volunteer retospectively undersampled with 9x acceleration using different k-space undersampling schemes and reconstructed using ENLIVE and DCMRI. Undersampling with 3x3 patterns (Cartesian and CAIPIRINHA) or 9x undersampled Poisson disc, each with fully sampled auto-calibration region in k-space center spanning 6.5% of the sampling matrix. ENLIVE tended to shift the average image intensity for slices with little overall signal (inferior and superior) leading to stripe like effects in affected regions of the coronal and sagittal views.

tion algorithms using all 8 echoes stacked together. The dataset of one volunteer was held back for evaluation. Results were compared against root sum of squares, coil-combined, fully-sampled reference data in terms of peak signal-to-noise ratio (PSNR), structural similarity metrics (SSIM), and qualitative appearance.

ENLIVE was applied using default parameters with 12 iterations in about 40 minutes per volume on 128 compute cores. DCMRI was adapted to process all 8 echoes simultaneously by introducing an additional input/output dimension and modifying the necessary data preparation steps. The residual blocks were adjusted to use convolutions with 64 output channels for the hidden states. The training was performed separately for each sampling pattern employing an accelerated High-Performance-Computing node with 4x NVIDIA A100 GPU (40 GB HBM2 memory) for about 12 hours each. After training, inference for each volume was performed in less than 4 minutes on a single GPU.

In general, image quality was rather high even at high 9x acceleration factors (Figure 3.1.3.1). Average PSNR and SSIM were comparable between k-space schemes and reconstruction methods (Figures 3.1.3.2A and 3.1.3.2B). A steeper decrease with higher acceleration factors was noticeable for DCMRI. One potential explanation is little robustness of the DCMRI architecture to very noisy data that might be handled by introducing batch normalisation or dropout layers and potentially focusing stronger on image foregrounds during training. Independent of the method, a similar quality reduction was found for longer echo times (Figures 3.1.3.2C and 3.1.3.2D).

Visual inspection shows that Cartesian and CAIPIRINHA sampling schemes resulted in more structured artifacts specifically when using DCMRI reconstruction (Figure 3.1.3.3). ENLIVE tends to enhance noise and shift the average image

intensity for slices with little signal, leading to visible stripe-like structures at the top and bottom in the coronal and sagittal views (Figures 3.1.3.1 and 3.1.3.4).

We compared state-of-the-art ENLIVE to multi-echo DCMRI, which showed high image quality even at 9x acceleration. The much shorter reconstruction time of DCMRI promises to facilitate routine high throughput applications and online visual image inspection. Future work will concentrate on establishing advantages of joint multi-echo DCMRI and ENLIVE reconstruction for calculation of MPMs and applying DCMRI to high-resolution data that suffers from long reconstruction runtimes.

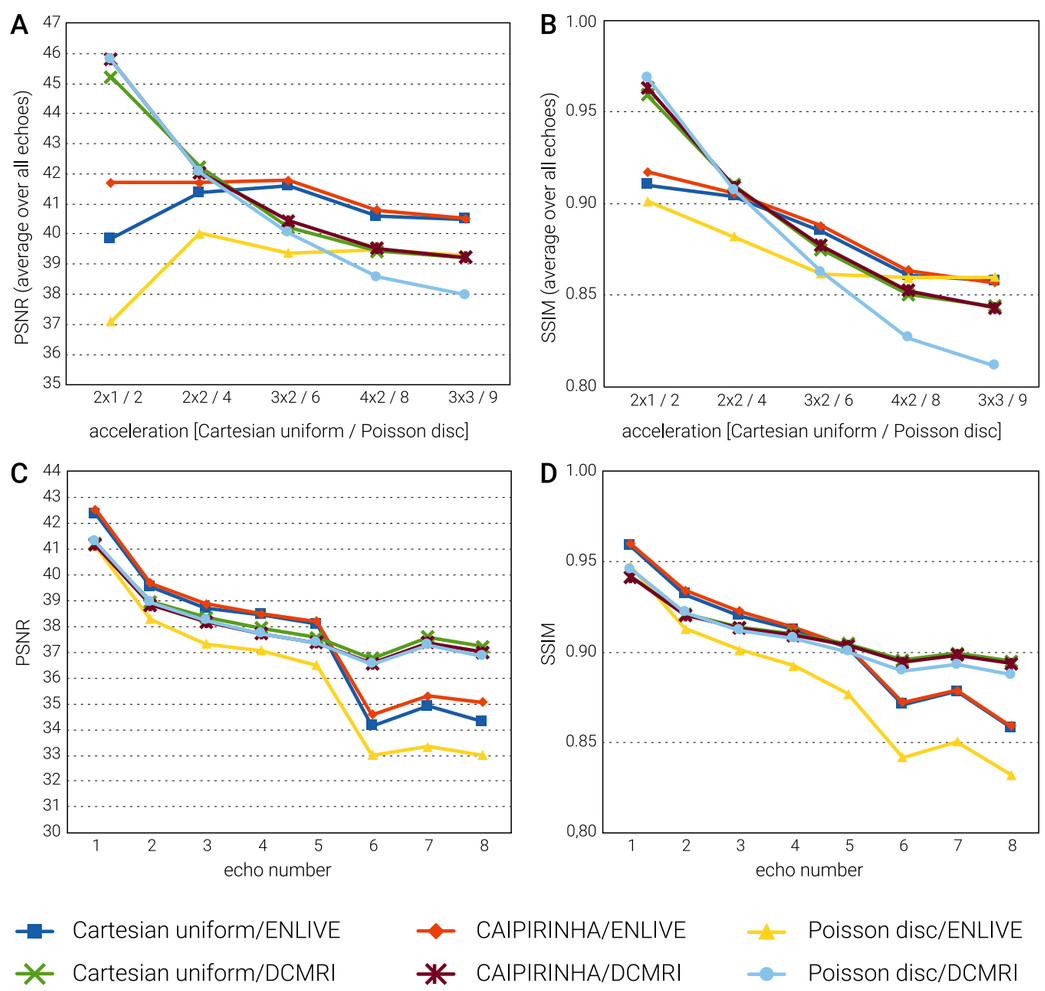

Figure 3.1.3.2 Quantitative metrics for different k-space undersampling schemes and reconstruction methods. PSNR (A) and SSIM (B) for different acceleration factors. DCMRI yields higher SSIM and PSNR than ENLIVE at low acceleration but shows a steeper decrease in SSIM with increasing acceleration than ENLIVE. PSNR (C) and SSIM (D) for images at different echo times for Cartesian/CAIPIRINHA or Poisson disc accelerations showed a reduction in PSNR and SSIM with increasing echo times. DCMRI is slightly more stable across echoes than ENLIVE.

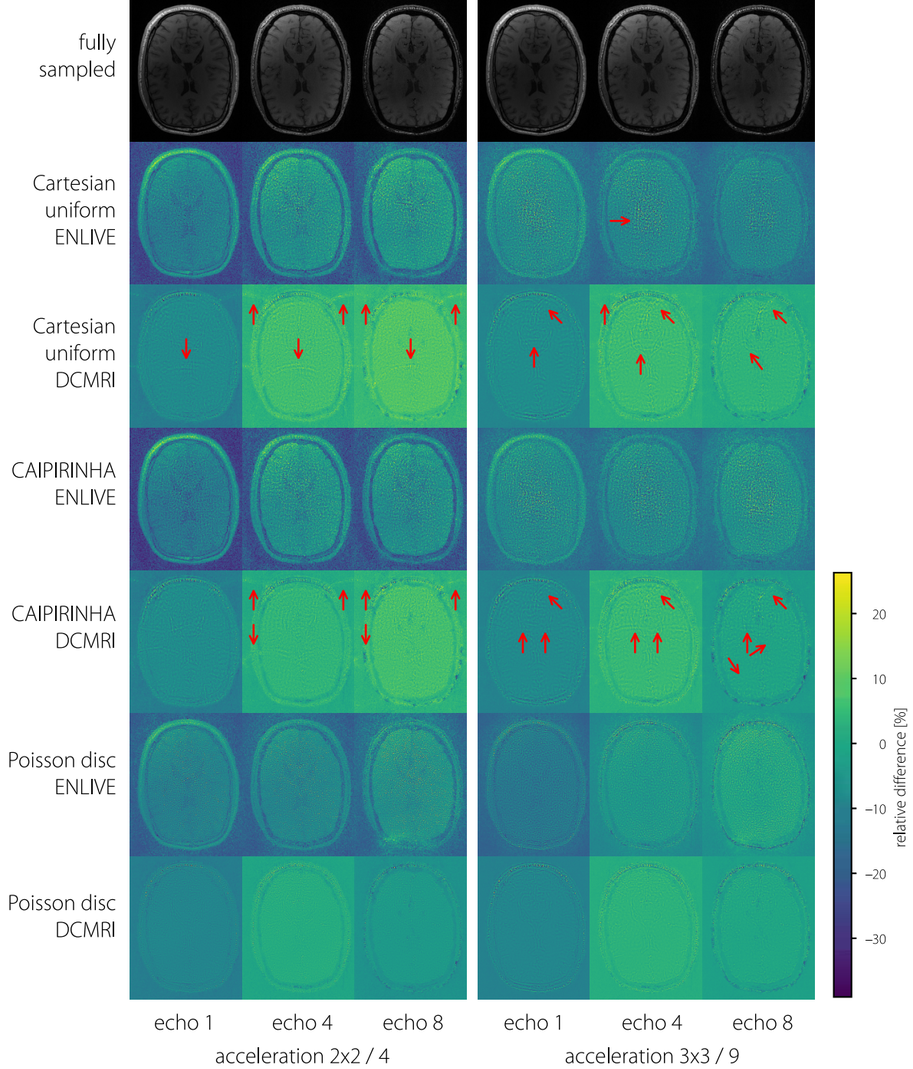

Figure 3.1.3.3 Relative difference between a specific combination of undersampling scheme and reconstruction method and the fully sampled reference for echoes 1, 4 and 8 (last) of an exemplary slice of the T1-weighted test dataset. Cartesian and CAIPIRINHA sampling show residual aliasing with higher acceleration – more pronounced in DCMRI reconstructions (red arrows). ENLIVE suffers from noise degradation at high acceleration while DCMRI produces overly smooth reconstructions. Artifacts are less apparent for longer echo times, since they are masked by the generally lower SNR.

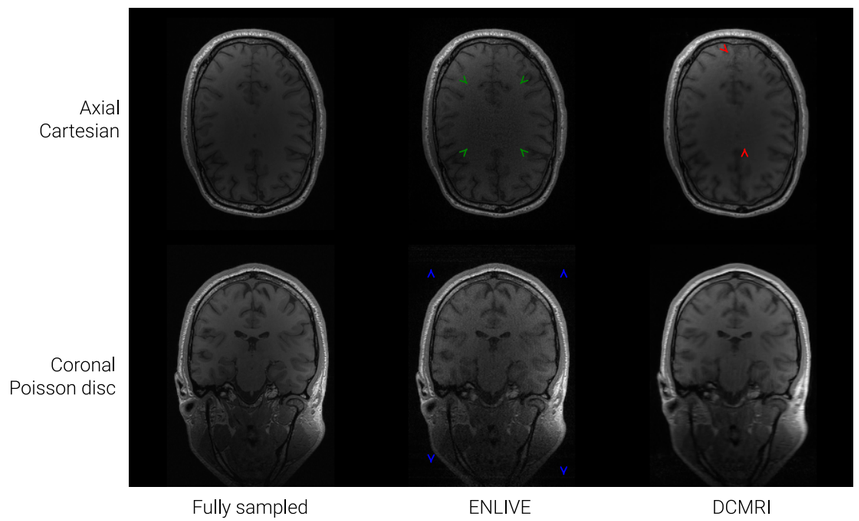

Figure 3.1.3.4 Detailed view of exemplary reconstructions from Cartesian 3x3 undersampling (axial view, top row) and reconstructions from Poisson disc 9x undersampling (coronal view, bottom row) in comparison to fully sampled data (left column). ENLIVE (center column) shows central noise enhancement (green arrows) and voxel intensity shifts between axial 2D reconstruction planes with little signal (blue arrows). DCMRI reconstruction (right column) is generally smoother and shows residual ghosting for Cartesian undersampling (red arrows).

3.2 Biophysical Modelling and Data Processing

The development of unified biophysical models is central for the success of non-invasive imaging of the brain's micro-organisation. They effectively integrate and leverage the wide range of contrasts (e.g., diffusion, relaxometry, magnetisation transfer contrasts) for inferring the underlying microstructure from MRI, even when the microstructural features are smaller than the nominal voxel size (Figures 3.1.1 and 3.1.2). The use of multiple contrasts improves the micro-organisation estimates from MRI, since they provide different perspectives of the underlying microstructure and improve the conditioning of the notoriously difficult model inference.

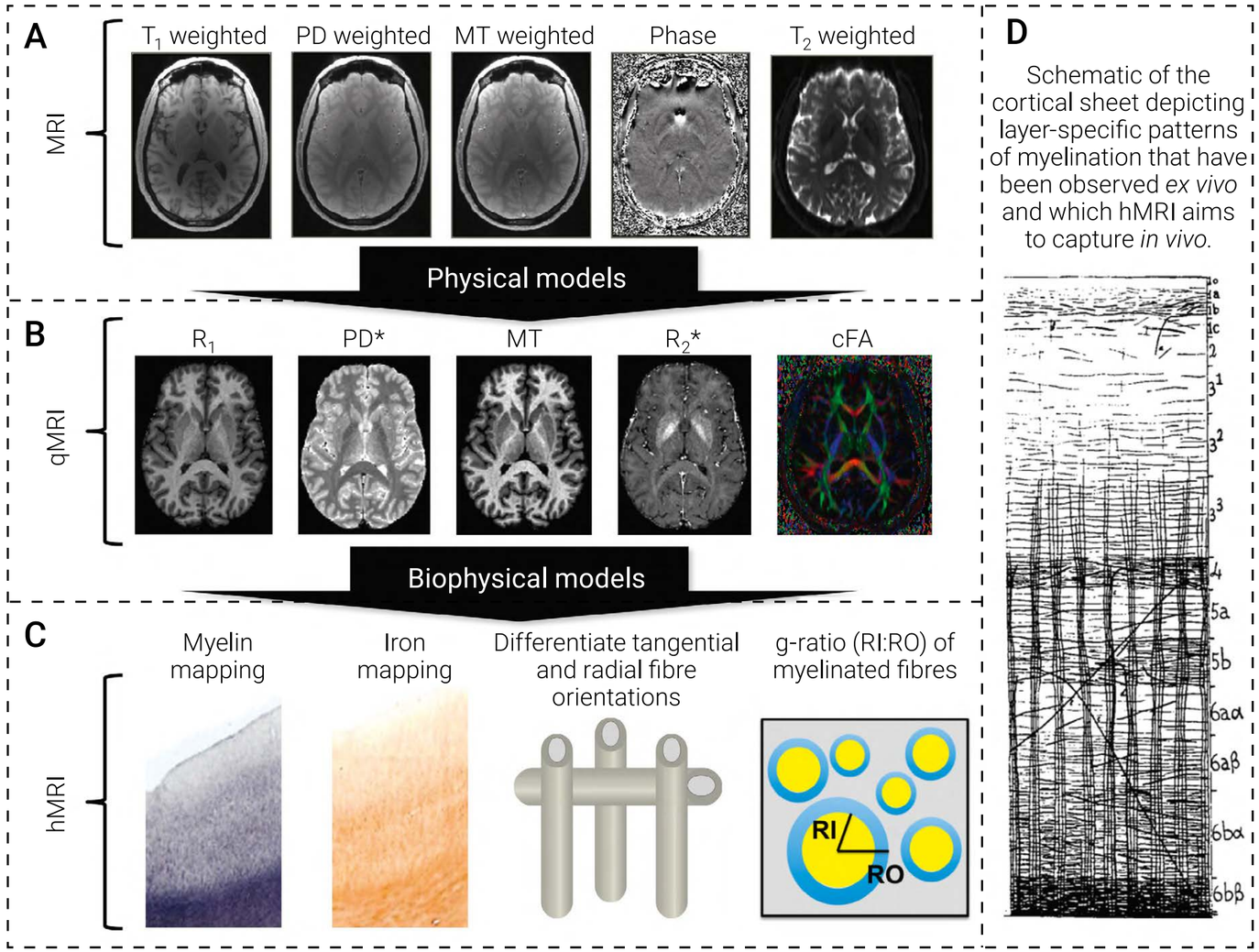

Figure 3.2.1 From standard MRI to in-vivo histology using MRI (hMRI). (A) MRI offers a multitude of contrasts that can be weighted towards particular MRI parameters, for example, proton density (PD), magnetisation transfer (MT) rate, longitudinal and transverse relation time (T_1 and T_2), and susceptibility effects as visible in the phase MR signal. (B) Quantitative MRI (qMRI) uses physical models to calculate quantitative parameter maps that depend nontrivially on the underlying tissue microstructure. (C) hMRI uses biophysical models to convert MRI or qMRI data to specific biological metrics such as myelin density, iron density, fibre orientation or g-ratio. This even allows for studying microstructural features that are smaller than the nominal voxel size by providing aggregate measures of them. (D) Ultimatively, hMRI may provide a detailed microstructural description of the brain, here, for example, the myeloarchitectural description of the cortical sheet. (reprinted from (Weiskopf et al., 2015, Curr. Opin. Neurol., 28, 313–322))

An example for a generative model based on first principles is the description of neuromelanin-iron induced contrast in the substantia nigra, which is informed by advanced histology such as X-ray fluorescence and PIXE measurements (3.2.1, (Brammerloh et al., 2021)). Another example, which is based on a data-driven semi-empirical model, is the prediction of myelination-related contrast in the cortex based on differing lipid compositions measured by MALDI (3.2.2). The integration of in-vivo MRI group data and gene expression atlases demonstrates an association of quantitative MRI parameters with cytoarchitecture and supports a differential microstructural sensitivity of different MRI parameters (3.2.3). The biophysical modelling is complemented by developments in the field of image and data processing, which allow for high quality estimation, registration and segmentation of ultra-high resolution datasets. Further information on the data processing methods, biophysical modelling and accompanying open source software can be found on our website.

3.2.1 In-situ magnetometry of human dopaminergic neurons using super-resolution MRI and ion-beam microscopy

Brammerloh M.[1,2], Kirilina, E.[1,3], Sibgatulin, R.[4], Herrmann, K-H.[4], Reinert, T[1,2], Jäger, C.[1,5], Pelicon, P.[6], Vavpetič, P.[6], Pine, K. J.[1], Müller, R.[1], Deistung, A.[7], Morawski, M.[5], Falkenberg, G.[8], Brueckner, D.[8], Reichenbach, J.[4], & Weiskopf, N. [1,2]

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Dopaminergic neurons in substantia nigra rely on iron as a cofactor for dopamine synthesis. However, they are vulnerable to oxidative stress when reactive iron is present in high concentrations. Dopaminergic neurons (DNs) contain the neuroprotective biopolymer neuromelanin. Neuromelanin binds excess cellular iron in two binding sites: a monoatomic pool, and a multi-atomic pool, both with distinct magnetic properties and iron affinities (Zucca et al., 2015). The high iron concentration in DNs enables MRI to detect these neurons and possibly quantify them in-vivo.

However, the magnetic properties of iron bound to neuromelanin in dopaminergic neurons are poorly understood. Prior research merely studied these properties in extracted neuromelanin. Neuromelanin extraction is known to perturb iron storage in the biopolymer and to alter its iron distribution. Hence, the magnetic properties after extraction probably do not accurately reflect the magnetic properties in-vivo. Therefore, a quantitative link between macroscopic in-vivo MRI iron measures and cellular iron concentrations is still missing.

We used 22-µm-resolution post-mortem MR microscopy on human substantia nigra tissue at 9.4T combined with ion and electron beam microscopy, using proton-induced X-ray emission (PIXE) and X-ray fluorescence (XRF), and to characterize the magnetic properties of neuromelanin directly in DNs (Figure 3.2.1.1) in-situ. Due to their high iron content, individual neuromelanin-rich neurons were detectable in multi-echo gradient echo images as point-like structures with low image intensity and dipole-like phase perturbations (Figure 3.2.1.1B, 3.2.1.1C). Thus, MRI microscopy provides 3D cellular maps of the entire SN (Figure 3.2.1.2) with histological quality.

We determined the dipole moments of 24 neurons by fitting complex-valued multi-echo gradient echo images. We devised a super-resolution model of the MRI signal around isolated magnetic spheres, fitting the sphere's magnetic moment and its location at subvoxel resolution. The total iron content of the same individual neurons was determined using proton-induced X-ray emission microscopy. We characterised the susceptibility of iron in DNs (Figure 3.2.1.2) and estimated that the R2* and susceptibility contribution of DNs are within reach of in-vivo MRI. Comparing R2* values in nigrosomes recorded at field strengths ranging from 1.5T to 9.4T, we demonstrated that the susceptibility of DNs is approximately independent of static magnetic field strength. Thus, the susceptibility values obtained in this study at ultra-high fields can be applied at clinical field strength.

MR microscopy DN visualisation is a promising tool for 3D histology of nigral anatomy without using contrast agents or tissue clearing. We estimated the magnetic susceptibility of neuromelanin-bound iron inside dopaminergic cells. This value was close to the susceptibility of the mono-atomic iron binding site in neuromelanin. The estimated susceptibility values allow us to interpret in-vivo nigral magnetic susceptibility and R2* measures in terms of cellular iron concentrations. Our results are a crucial step toward in-vivo nigrosome visualisation and in-vivo quantification of DNs for diagnostics.

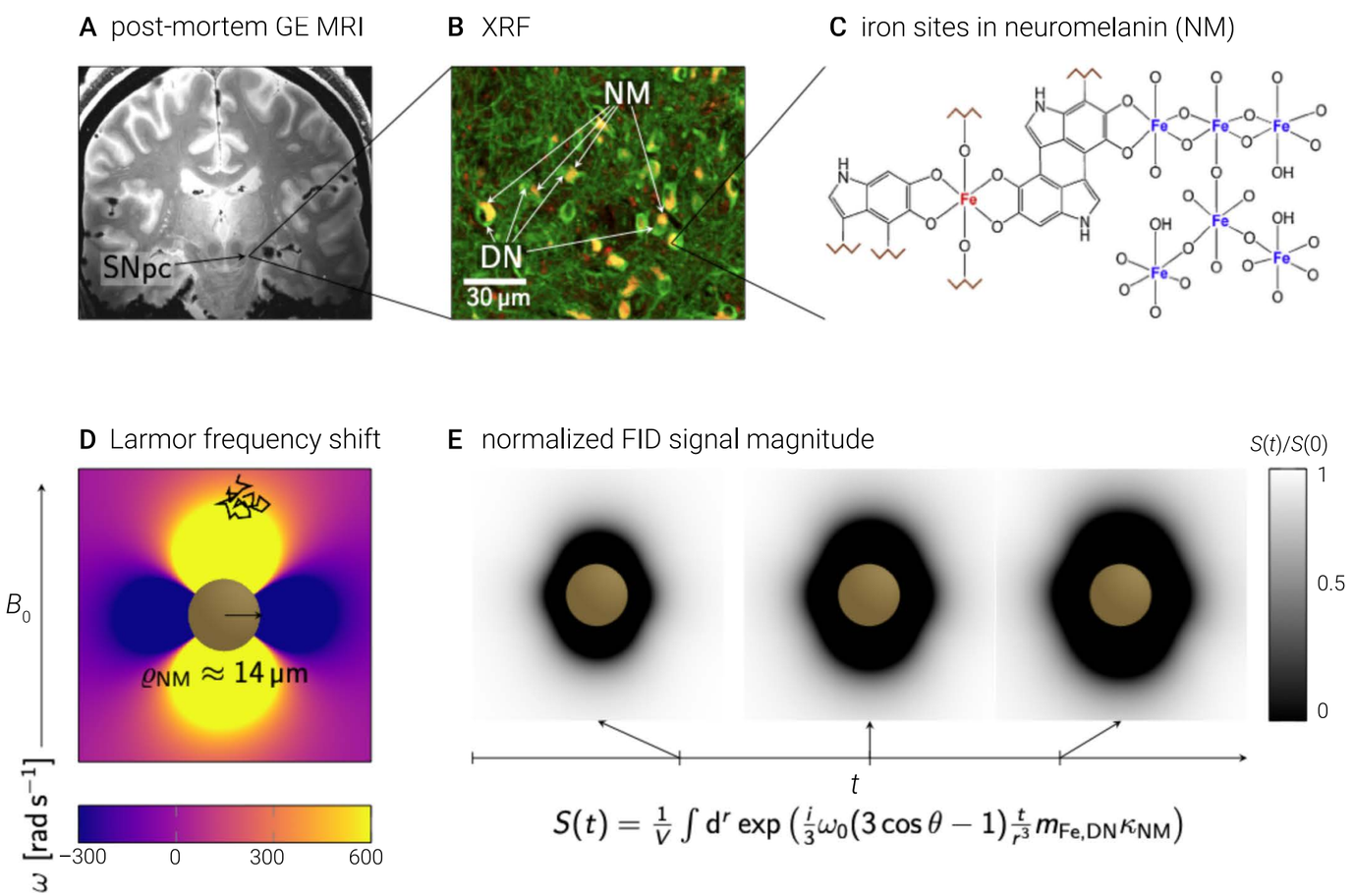

Figure 3.2.1.1 Biophysical modelling of the magnetism of a neuromelanin cluster in a dopaminergic neuron's soma. (A) An iron-sensitive gradient echo (GE) MRI image shows the substantia nigra pars compacta (SNpc) as an oval hypointense region in the brainstem. (B) Dopaminergic neurons (DNs, green) contain clusters of iron-rich pigment neuromelanin (NM, yellow). DNs were stained with nickel-enhanced anti-tyrosine-hydroxylase immunohistochemistry. We show an overlay of nickel (green) and iron (red) concentration maps acquired with X-ray fluorescence (XRF) microscopy, which shows iron-rich NM within the nickel-marked DN somata as yellow. (C) Neuromelanin has two iron binding sites with distinct magnetic properties and an unknown share of the total iron load: a mono-nuclear (red) and a crystalline pool (blue). That potentially enables MRI to detect the distribution of iron between the pools, which contributes distinctly to relaxation. (D) We approximated neuromelanin clusters as magnetised spheres to model their effect on the MRI signal. Histology provided an estimate of the cluster's radius, ρ_{NM}. The resulting cross-shaped magnetic dipole field around the NM cluster determines the Larmor frequency sensed by water protons diffusing in their vicinity (indicated with a black line). (E) In a GE experiment, the spatial variation in Larmor frequencies around the NM cluster leads to loss of phase coherence, creating a dephased volume. The signal S(t) is calculated by integrating the mesoscopic Green's function.

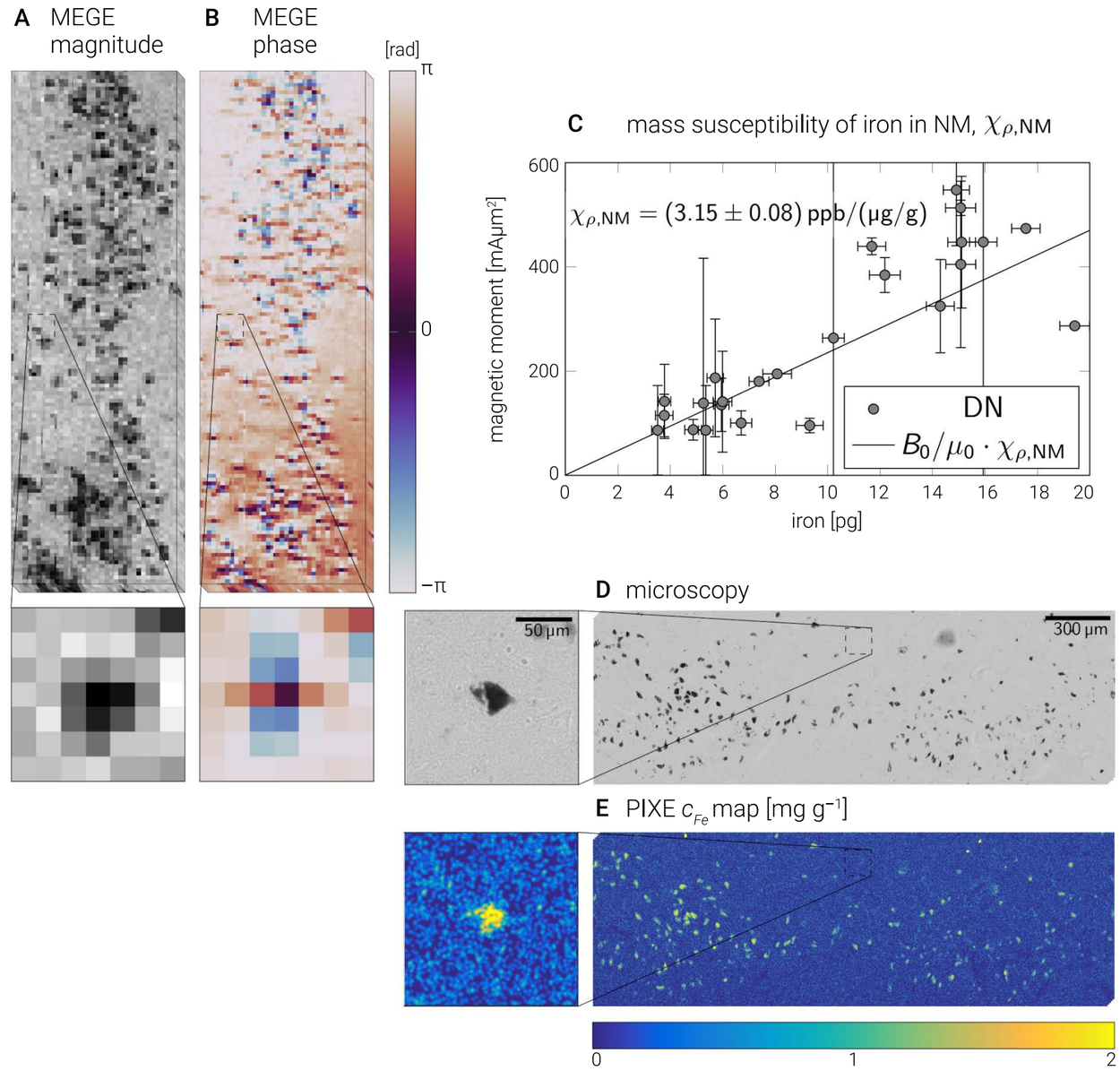

Figure 3.2.1.2 Mass susceptibility of iron in neuromelanin (NM, C) estimated from complex-valued MRI signal (A, B) and quantitative iron histology (D, E). (A, B) Individual dopaminergic neurons appear as dot-like hypointensities in multi-echo gradient echo (MEGE) magnitude data and as cross-shaped dipoles in MEGE phase data. A simulation of the complex-valued MRI signal was used to estimate the magnetic moment of individual dopaminergic neurons (exemplary neuron shown in the inset). (C) The mass susceptibility of iron in NM was found to be 3.15±0.08 ppb / (µg iron / g tissue), combining estimates of the magnetic moment and iron content. Each dot represents one neuron. (D, E) Dopaminergic neurons show an increased iron concentration on elemental maps obtained with proton-induced X-ray emission (PIXE). We quantified the iron content of individual dopaminergic neurons in 3D, covering entire neurons. As the neurons were taller than our histological section thickness, this approach mitigates a partial volume effect.

3.2.2 Grasping myelin complexity: Combining spatially resolved brain lipid mass spectrometry with multimodal quantitative magnetic resonance imaging

Lipp, I.[1], Kirilina, E.[1], Jung, S.[1,2], Wachendorf, J.[3], Jäger, C.[1,4], Terzi, M.N.[3,5], Edwards, L. J.[1], Pine, K. J.[1], Bidmon, H-J.[6], Axer, M.[2,5], Huesgen, P. F.[3,7,8], & Weiskopf, N.[1,9]

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Myelin plays a crucial role for brain function, facilitating axonal conduction, enabling the fine tuning of neural circuits and providing trophic support for axons. Myelin's multiple functions are facilitated by its complex composition comprising a large variety of lipids, proteins and trapped water. Quantitative magnetic resonance imaging (qMRI) is a sensitive tool for mapping brain myelination, enabling in-vivo studies on cortical myeloarchitecture, developmental myelination and myelin breakdown in pathology. The mechanisms of myelin-induced MRI contrast are complex and incompletely understood. Particularly, the sensitivity of MRI myelin markers to myelin composition is largely unexplored.

Here, we related quantitative MRI parameters in the human brain to myelin content and composition using a combination of quantitative MRI and matrix-assisted laser desorption/ionization mass spectrometry imaging (MALDI-MSI) of lipids in post-mortem human brain tissue (Figure 3.2.2.1). We showed that lipid compositions of myelin within and between the cortical grey matter and white matter are systematically different (Figure 3.2.2.2). We demonstrated that lipids can be clustered in subgroups with similar spatial distributions (Figure 3.2.2.3). We introduce a novel semi-quantitative myelin marker based on the first principal component of multi-dimensional MALDI-MSI lipid maps, which can be used across the entire brain unlike conventional histology and can be used to validate myelin-sensitive quantitative MRI parameters (Figure 3.2.2.1D).

We show that general linear modelling, accounting for the distribution of multiple lipids, provides an even better description of myelin sensitive qMRI parameters (Figure 3.2.2.5), pointing towards the differential sensitivity of quantitative MRI to different lipid types in tissue. The MALDI-MSI approach captures myelin molecular complexity, improves specificity and quantification of myelin mapping. It is an important step towards quantitative MRI markers of myelin content and composition, i.e. non-invasive lipidomics.

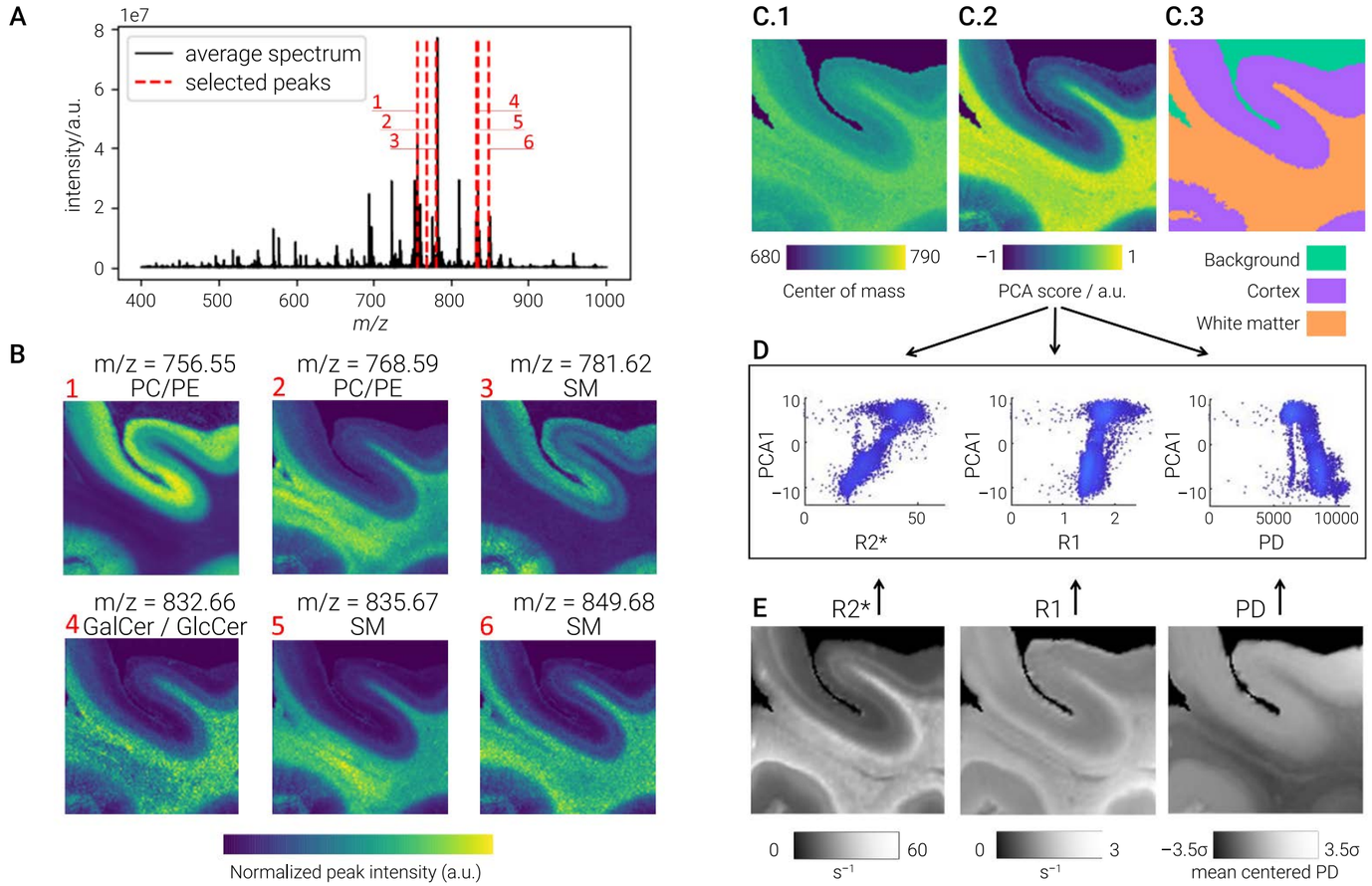

Figure 3.2.2.1 Complex myelin lipid composition revealed by MALDI-MSI. After quantitative MRI scanning, post-mortem tissue samples were sectioned and histology was performed. Lipids with different mass to charge ratio were mapped by MALDI-MSI. Here, the pipeline is illustrated using an example dataset from the primary visual cortex (V1). The average mass over charge spectrum across all pixels is shown in (A). Examples of MALDI-MSI maps of several lipids from different lipid classes illustrate distinct spatial distributions in (B): While the lipids with the mass to charge ratio (m/z, atomic mass / electron charge) 756.55 and 781.62 are mostly present in the cortex, other lipids are mostly localised in white matter. Some of those are specifically expressed in specific white matter tracts (here, the lipids with m/z 835.67 and 768.59), others have lower occurrences in the same tract (here, the lipids with m/z 832.66 and 849.68). The most likely identity of each lipid as derived from METASPACE (https://metaspace2020.eu/) for each m/z value is provided (SM: sphingomyelin, GalCer: galactocerebroside, GlcCer: glucosylceramide, PC: phosphatidylcholine, PE: phosphatidylethanolamine). Note that several lipid species can contribute to the same m/z value. The dimensionality of the MALDI peak maps was reduced by a principal component analysis (C.2), which suggested that more than 40% of the spatial variance can be explained by the first principal component (PCA1). The component score of this main component results in a semi-quantitative myelin map, which was then spatially correlated (D) with the quantitative MRI maps shown in (E). Spatial clustering based on the lipid composition (shown in (C.3)) of the tissue using the MALDI-MSI data revealed different lipid compositions in cortex and white matter. This also manifests in the general measured mass distribution and allows us to discern cortical grey and white matter by mapping.

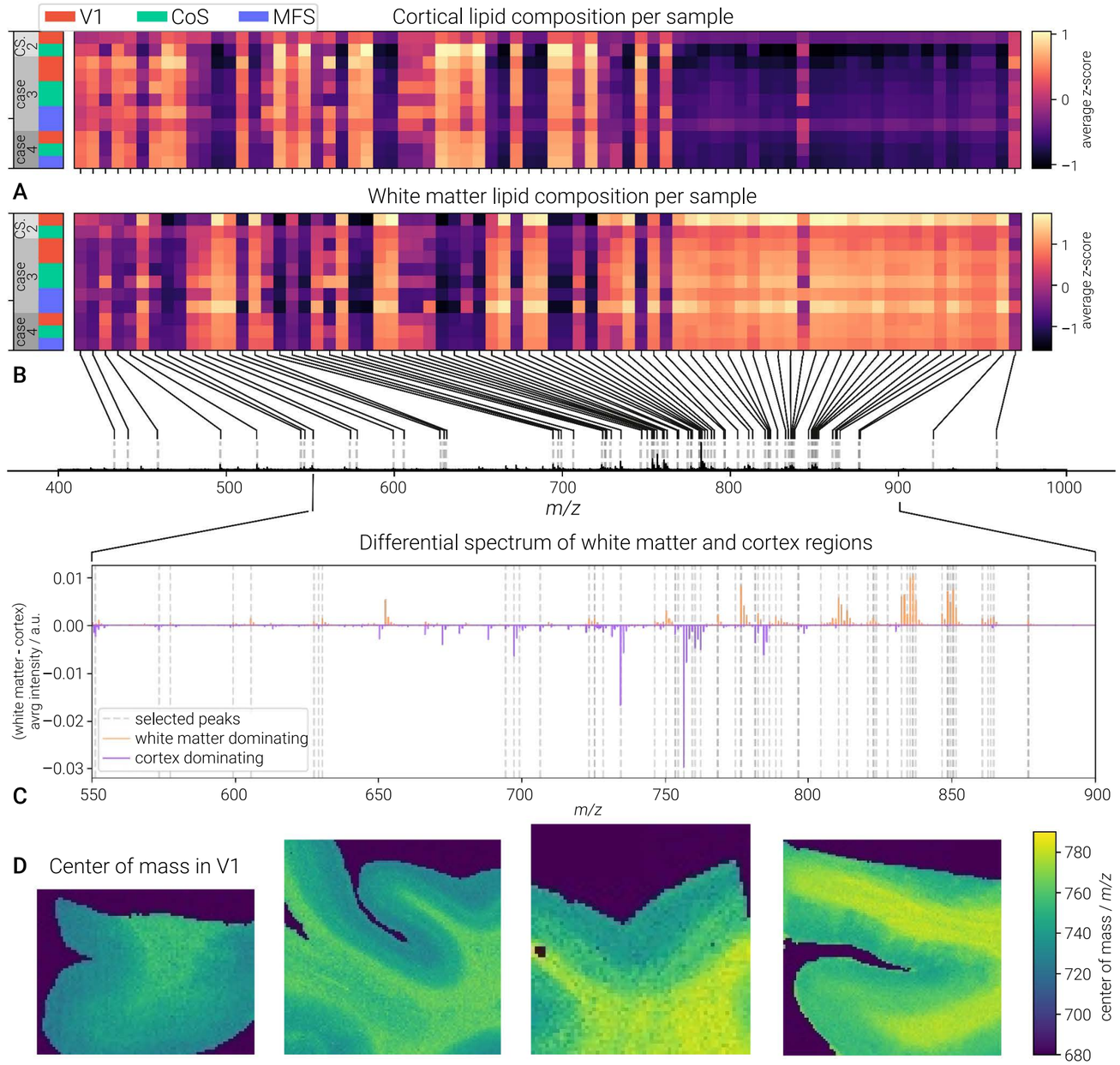

Figure 3.2.2.2 White matter and cortex have different lipid composition. (A) and (B) show the intensity distribution of the selected lipids in the cortex and white matter regions respectively. Each row represents the average intensity (z-standardised for comparability) of all peaks across the selected region in 11 investigated brain tissue samples (11 rows). Lipids of higher m/z dominate in white matter regions, while lower mass lipids dominate in cortical regions. Subtracting the average spectra of all cortex regions from the average spectra of all white matter regions conveys this characteristic difference throughout the measured mass domain (C). This characteristic in lipid mass can be visualised by calculating the center of mass for each pixel's spectrum. (D) shows the distribution of the center of mass for all V1 measurements of the three cases. As undesired matrix molecules dominate for $m/z < 550$ the center of mass was calculated on the range of $550 < m/z < 900$. Acronyms: **V1**: primary visual cortex, **CoS**: collateral sulcus, **MFS**: midfusiform sulcus.

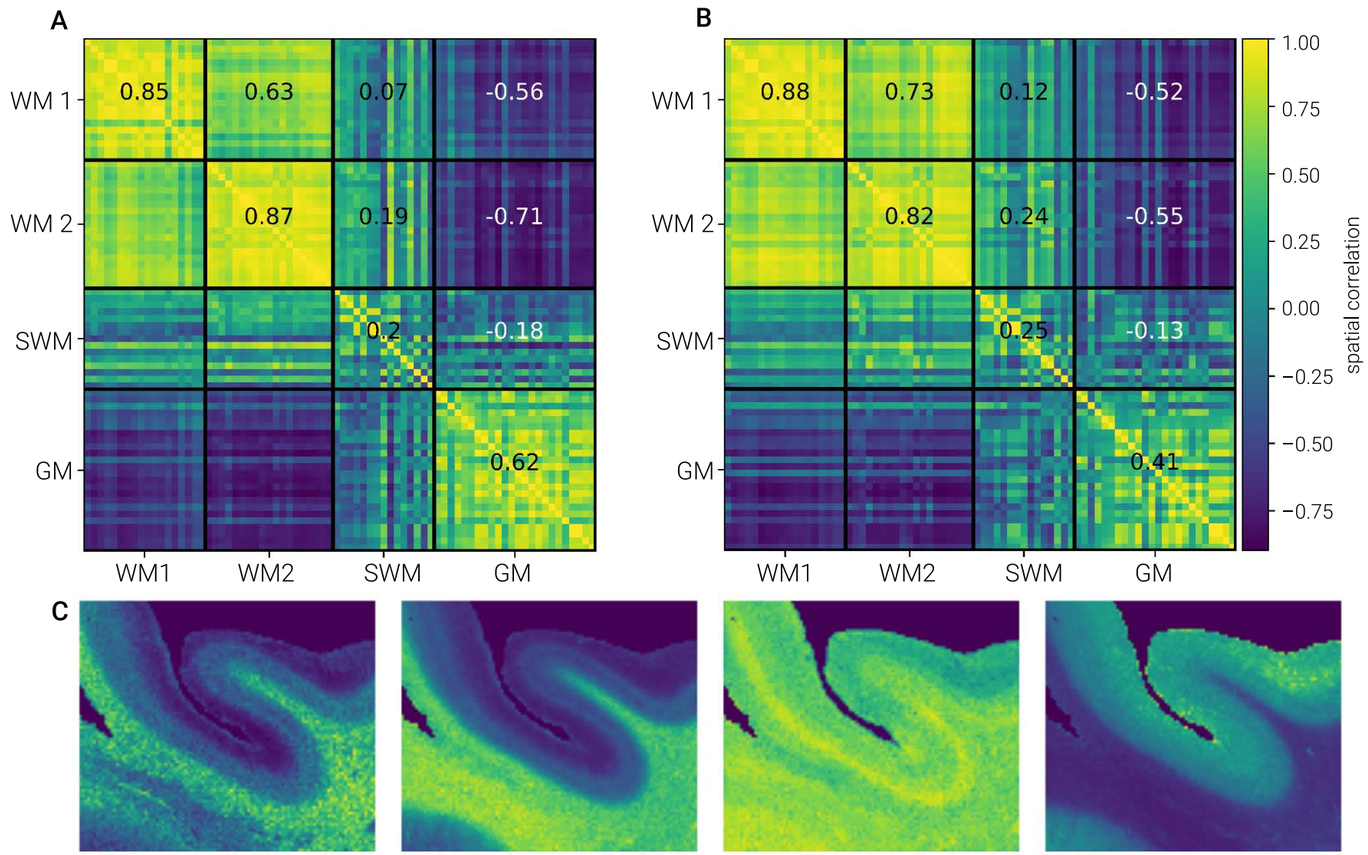

Figure 3.2.2.3 Lipid groups show distinct anatomical distribution within white matter and between white and grey matter. A matrix of spatial correlation between all selected lipids, demonstrates the presence of four clusters of lipids determined by hierarchical clustering based on spatial correlations. (A) shows the sorted correlation matrix results obtained for the sample with best SNR, best tissue quality and largest coverage of white and grey matter regions, which was used to calculate the uniform hierarchical clustering (primary visual cortex and underlying white matter). (B) The averaged correlation matrix for all selected samples. Four clusters were detected containing lipids with similar spatial distributions. (C) Lipid peak maps averaged across all lipids within four clusters. Two white matter clusters (WM1 and WM2) contained lipids mostly localised within white matter, but showing different distributions. The superficial white matter (SWM) cluster includes lipids measured throughout the tissue. The grey matter (GM) cluster includes lipids dominant in cortical grey matter.

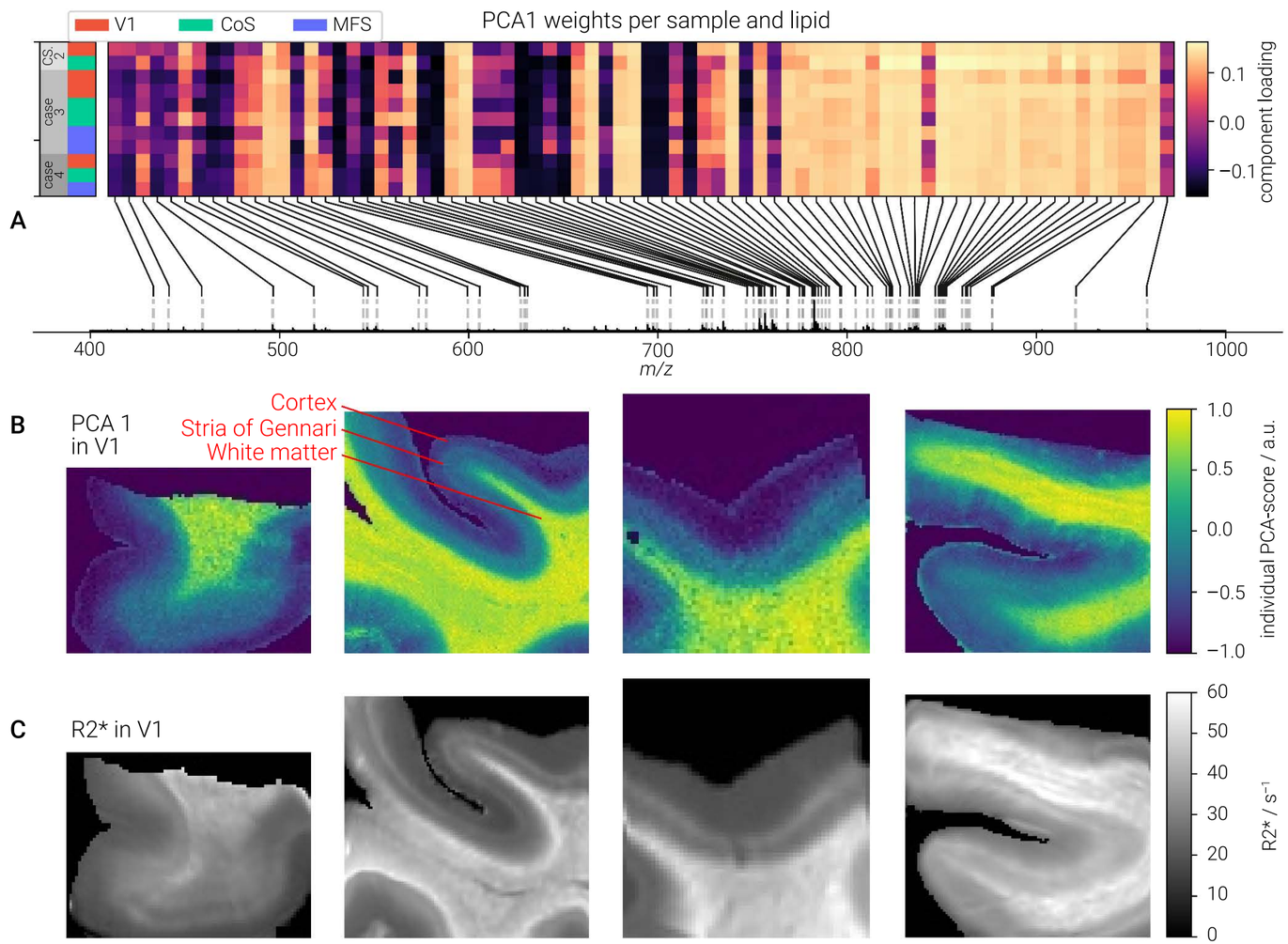

Figure 3.2.2.4 First principal component of all lipid peaks detected by MALDI-MSI. PCA1 is a semiquantitative marker of myelination. The first principal component map (PCA1) of the MALDI-MSI measurements is shown (B) alongside the coregistered *R2** qMRI measurements (C) for four tissue blocks all containing primary visual cortex V1. The respective weights for all lipids are plotted as a heatmap (A). Each row represents the component loadings of all selected peaks in one of 11 tissue blocks. This lipid composition is comparatively consistent across datasets, as suggested by the similar pattern across rows. The myelo-architectonic landmarks, such as stria Gennari, are visible in the semi-quantitative myelin map.

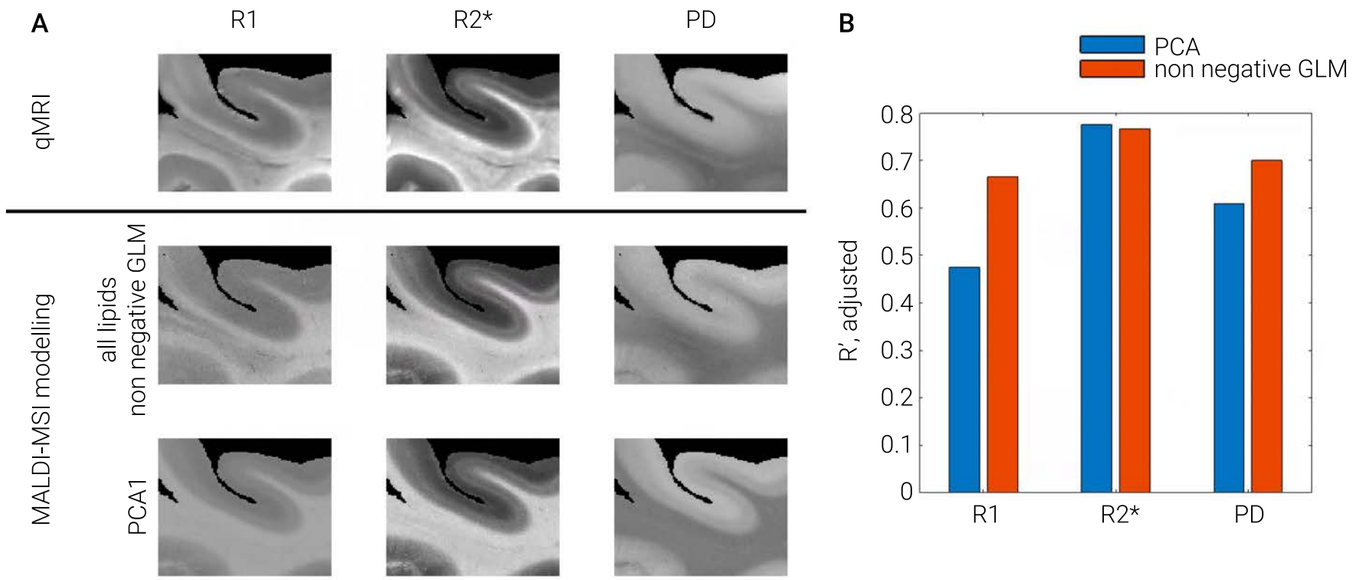

Figure 3.2.2.5 Modelling qMRI parameters by lipid distribution maps. (A) The registered qMRI measurements *R2**, *R1* and *PD* (upper row) for one sample were fitted using non-negative GLM based on all 76 selected lipid maps (middle row), and only the first PCA component (bottom row). (B) The variance in qMRI parameters explained by lipids quantified as the average R2 value through all samples, adjusted for the number of degrees of freedom in each model. Taking into account all lipids substantially improves the model prediction, particularly for R1, pointing towards the sensitivity of qMRI parameters to lipid composition of myelin.

3.2.3 Using cell type-specific gene expression to explore cell type associations of quantitative MRI maps of human neocortex

Edwards, L. J.[1], McColgan, P. [1,2], Helbling, S. [1,3], Zarkali, A. [4], Vaculčiaková, L. [1], Pine, K. J.[1], Dick, F.[5], & Weiskopf, N. [1,6]

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Adapted from Edwards et al., Cerebral Cortex, 2022.

Quantitative MRI (qMRI) parameters in the cortex are sensitive to underlying biological substrates. To investigate their specificity to different neocortical cell types, we compared the in-vivo spatial distribution of the qMRI parameters longitudinal relaxation rate (R1), effective transverse relaxation rate (R2*), and magnetisation transfer saturation (MTsat) to gene expression from the Allen Human Brain Atlas (Hawrylycz et al. 2012), then combined this with public lists of genes enriched in specific human brain cell types (Edwards et al. 2022). As qMRI parameters are magnetic field strength-dependent, we used high resolution MRI data from 3T and 7T.

Optimal linear combinations of genes were found which capture the spatial distribution of the qMRI parameters using partial least squares (PLS) regression. Two PLS components were estimated, and components were only analysed fur-

ther when they explained more than 10% of the spatial variance of the respective qMRI parameter. Bootstrapping was used to obtain gene lists of the highest-weighted genes in each respective PLS component. The qMRI parameters and the PLS components are shown in Figure 3.2.3.1.

The gene lists for each qMRI parameter were then combined with cell type-specific gene lists using expression weighted cell type enrichment (EWCE) analysis (Skene and Grant 2016), which examines whether the genes in the qMRI-parameter list show enhancement in a given cell type-specific list greater than expected by chance (FDR-corrected $p < 0.05$). Cell type associations which reproduced in two independent cell type-specific gene lists were taken to be robust.

The associations are summarised in Figure 3.2.3.2. All qMRI parameters were associated with cytoarchitecture. Further, there were differential associations between the parameters, which shows the potential for deriving more specific biomarkers for different cell types by combining the parameters. This could have important implications in neuroscience and clinical studies.

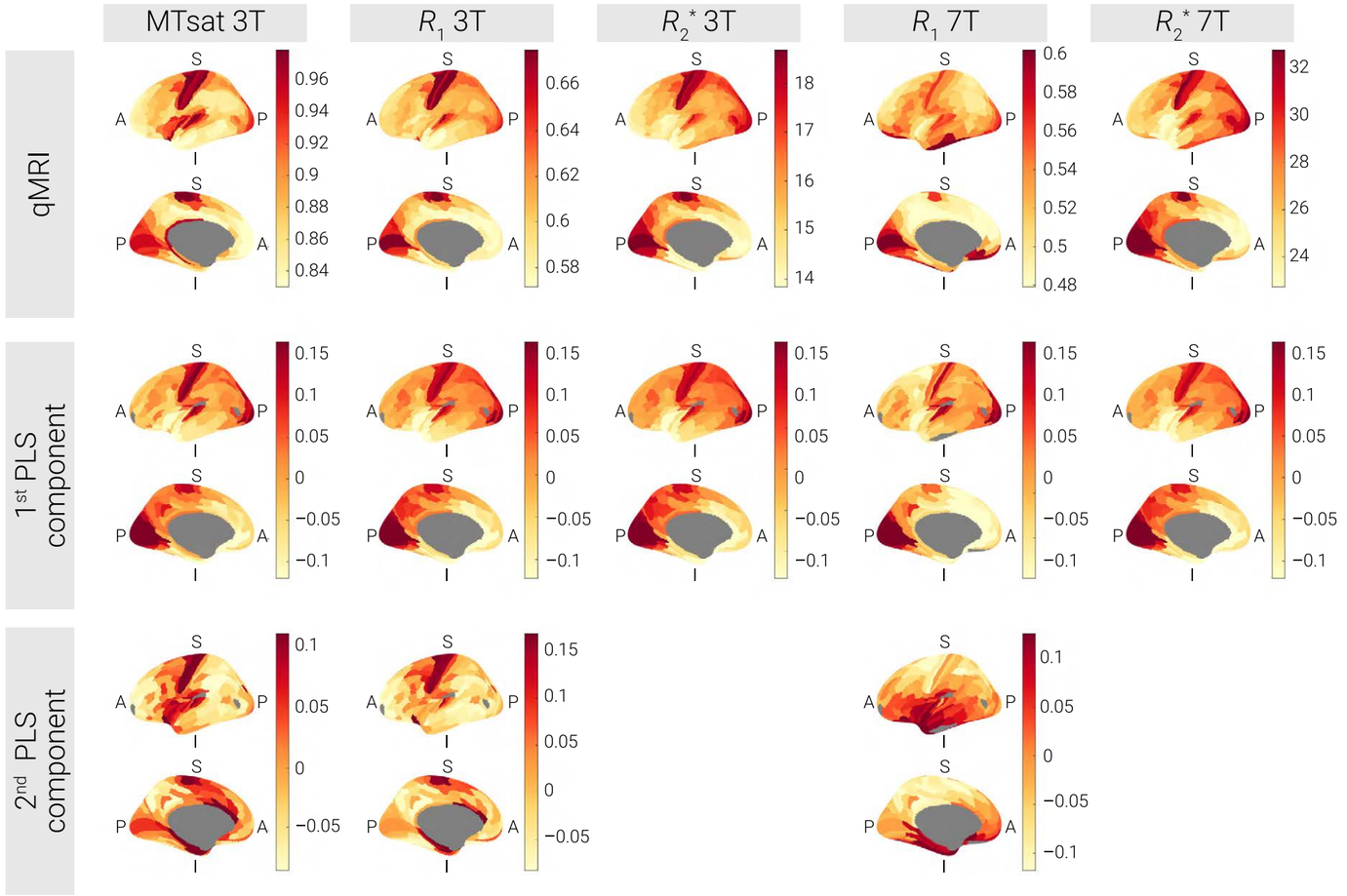

Figure 3.2.3.1 Spatial distribution of the qMRI parameters and the respective PLS components. The PLS components are very similar to the qMRI parameters and capture well the differences between them. Only PLS components which explain more than 10% of the spatial variance of the respective qMRI parameter are shown. R1 and R2* in / s, MTsat in percent units, PLS components in arbitrary units.

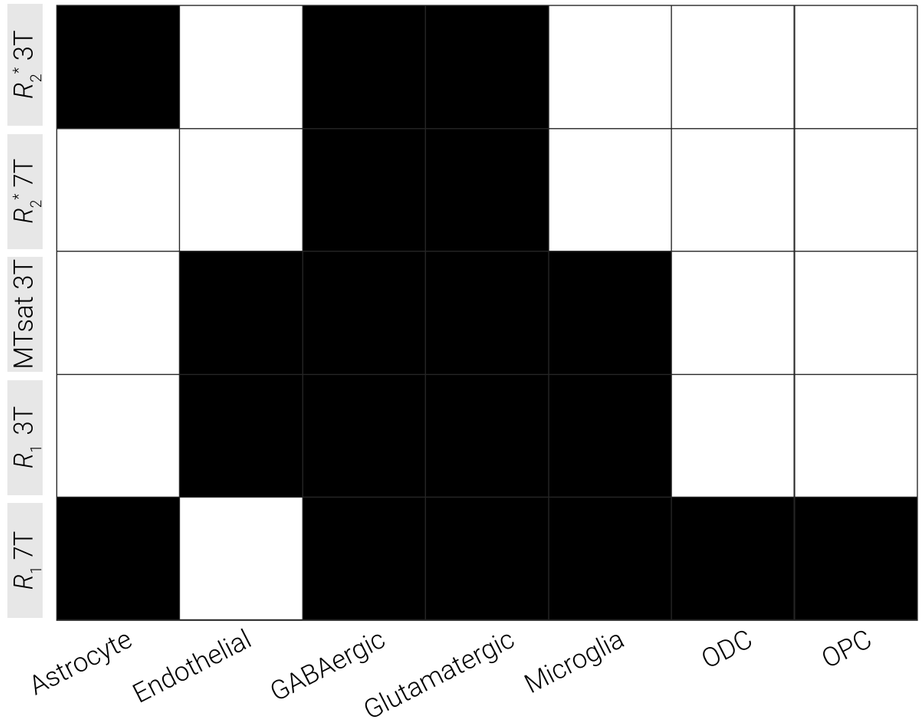

Figure 3.2.3.2 Summary of the robust cell-type associations of the qMRI parameters. The investigated cell types are listed along the bottom row. Robust associations are shown in black. ODC: oligodendrocyte. OPC: oligodendrocyte precursor cell.

3.3 Neuroscientific Applications and Validation

The non-invasive imaging of brain micro-organisation offers possibilities for a wide range of neuroscientific studies. At the same time the newly developed imaging methods and biophysical models require careful validation. This section provides examples of different in-vivo and post-mortem studies pursuing these goals.

Ultra-high resolution fMRI and multi-parameter mapping at 7T are combined for investigating the structure-function relationship in the secondary visual cortex at the level of mesoscopic stripes (3.3.1). Similarly, laminar fMRI is used to study layer-specific activity in working memory (3.3.2). Leveraging the high quality diffusion imaging on the Connectom MRI scanner allows us to map the short association fibres (SAF) and short range connectivity in Broca's area for the first time, improving our understanding of the language network (3.3.6).

High-resolution imaging in conjunction with biophysical modelling, quantitative histology, and a newly developed atlas is used for a more precise delineation of nigrosome 1 in the substantia nigra, which plays a major role in Parkinson's disease (3.3.3). This helps us to demonstrate that the widespread equation of the hyperintense part of the radiological swallow tail sign with nigrosome 1 is inaccurate (3.3.3).

The approaches for myelin and iron mapping were also exploited for comprehensive post-mortem imaging of hominoid brains (3.3.4, 3.3.5) as part of the Evolution of Brain Connectivity (EBC) project in collaboration with our Institute's Department of Neuropsychology, MPI for Evolutionary Anthropology (Leipzig), Paul Flechsig Institute of Brain Research (Leipzig University) and Robert Koch Institute (Berlin). For additional application and validation projects, see our website (Validation and Application, Neuroanatomy).

3.3.1 High resolution quantitative and functional MRI indicate lower myelination of thin and thick stripes in human secondary visual cortex

Haenelt, D.[1,2], Trampel, R.[1], Nasr, S.[2,3], Polimeni, J. R.[2,3,4], Tootell, R. B. H.[2,3], Sereno, M. I.[5], Pine, K. J.[1], Edwards, L. J.[1], Helbling, S.[1,6], & Weiskopf, N.[1,7]

[1] Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany, [2] Athinoula A. Martinos Center for Biomedical Imaging, Massachusetts General Hospital, Boston, USA, [3] Department of Radiology, Harvard Medical School, Boston, USA, [4] Harvard-MIT Division of Health Sciences and Technology, Massachusetts Institute of Technology, Boston, USA, [5] Department of Psychology, College of Sciences, San Diego State University, USA, [6] Ernst Strüngmann Institute for Neuroscience in Cooperation with Max Planck Society, Frankfurt am Main, Germany, [7] Felix Bloch Institute for Solid State Physics, Leipzig University, Germany

Recent developments in ultra-high field MRI (≥ 7T) allow the study of columnar features of the human brain non-invasively. For example, the thin-thick-pale stripe pattern in extrastriate cortex V2 (Tootell et al., 1983) can be delineated with high-resolution fMRI (Nasr et al., 2016). Based on histological studies, these stripes also vary in myelin content although it is still debated which stripe type is more myelinated (Horton et al., 1997).

Here, we used quantitative MRI (qMRI) (Weiskopf et al., 2021) in conjunction with fMRI to study myelination differences between stripe types using the longitudinal (R1) and effective transverse (R2*) relaxation rates (further details reported in Haenelt et al. (2022, bioRxiv, Preprint). Four participants were invited to multiple scanning sessions on a 7T MRI scanner over different days. Thin and thick stripes were localised by exploiting their different sensitivity to colour and binocular disparity, respectively. All functional data were acquired with a nominal isotropic voxel size of (0.8 mm)^3. For qMRI, we used the MPM protocol (Vaculčiaková et al., 2022) and acquired data with isotropic 0.5 mm resolution.

Figure 3.3.1.1 shows exemplary activation maps for thin and thick stripes, respectively. Based on the functional definition of these stripes, R1 and R2* in thin/thick stripes were compared to whole V2 excluding the other stripe type (thick/thin) and therefore containing pale stripe contributions, which is shown in Figure 3.3.1.2.

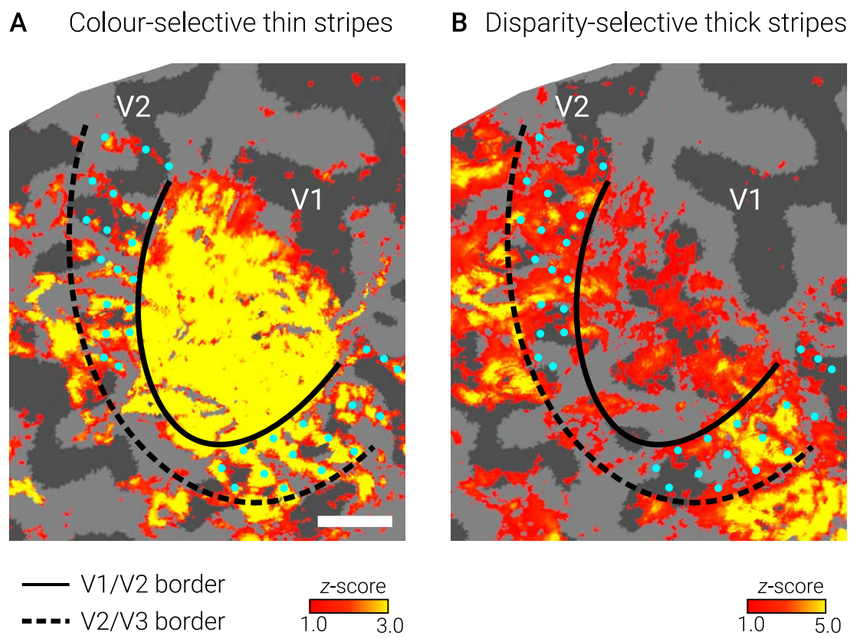

Figure 3.3.1.1 Activation maps for colour-selective thin and disparity-selective thick stripes. Thin stripes (contrast: colour > luminance) and thick stripes (contrast: depth > no depth) are shown as thresholded activation maps in (A) and (B), respectively. Both maps are illustrated on the flattened surface mesh of the right hemisphere for one representative participant showing stimulated portions of V1 and V2. In V2, patchy stripes can be identified, which run through V2 oriented perpendicular to the V1/V2 border. Manually drawn cyan dots mark activated regions in (A) to illustrate the alternating activation pattern between (A) and (B). Scale bar: 1 cm.

Our results indicate lower myelination of both thin and thick stripes and therefore stronger myelination of pale stripes. To the best of our knowledge, this is the first study that shows myelination differences using qMRI at the spatial scale of columnar systems in the living human brain.

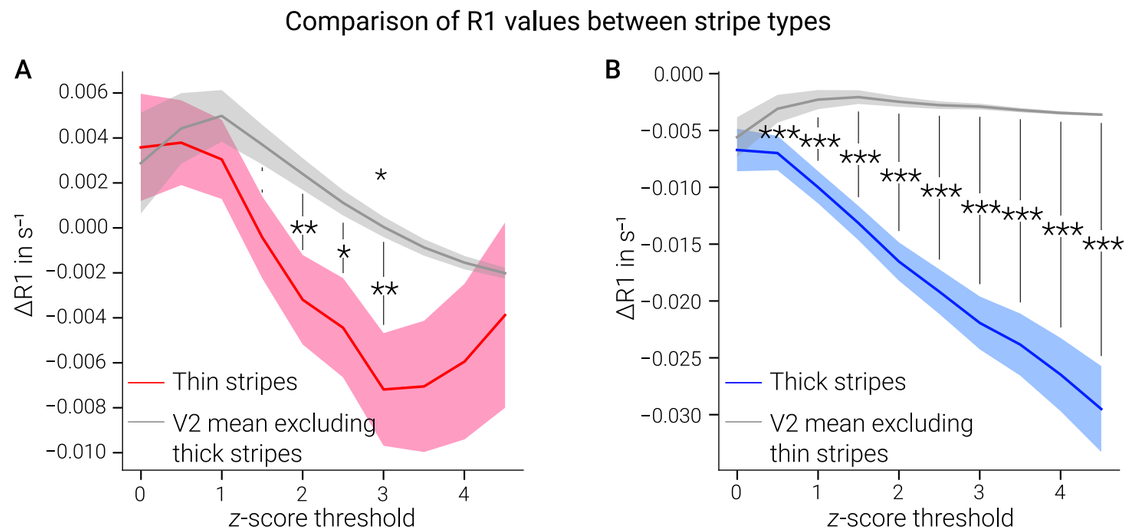

Figure 3.3.1.2 Comparison of quantitative R1 and R2* values between V2 stripe types. Cortical R1 (A)–(B) and R2* (C)–(D) values in thin stripes (red), thick stripes (blue) and whole V2 excluding the other stripe type (grey; and therefore containing contributions from pale stripes) are shown for various z-score threshold levels, which were used to define thin and thick stripe ROIs based on fMRI. Quantitative parameters are plotted as deviation from the mean within V2 after removing variance from local curvature. Statistical significance was assessed by permutation testing. R1 in thin/thick stripes were lower than surrounding grey matter, which points towards heavier myelination of pale stripes. No effects were found for R2*. Shaded areas indicate one standard deviation of the generated null distribution used for permutation testing.

3.3.2 Probing the laminar circuitry of the dlPFC during the attentional modulation of working memory

Lorenz, R.[1,2,3], Chaimow, D.[1], Degutis, J. K.[1,4], Assem, M.[3], Duncan, J.[2], & Weiskopf, N.[1,5]

[1] Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany, [2] MRC Cognition and Brain Sciences Unit, University of Cambridge, UK, [3] Stanford University, CA, USA, [4] Charité – Berlin University of Medicine, Germany, [5] Felix Bloch Institute for Solid State Physics, Leipzig University, Germany

The neural mechanisms of selectively attending to information held in working memory (WM) are not well understood. This high-resolution fMRI study at 7T uses multivariate pattern analysis (MVPA) to investigate the layer-specificity of information processing in the dorsolateral prefrontal cortex (dlPFC) during the attentional modulation of WM. Recent findings about the dissociable functional role of distinct cortical layers led us to hypothesise that attended items can be decoded more strongly than unattended items held in WM in the superficial layers of the dlPFC as these layers have been proposed to act as a WM buffer (Bastos et al., 2018). Contrarily, we hypothesised that subjects' motor response can be decoded more strongly in deep layers of the dlPFC as those are suggested to be involved in governing action selection/execution (Finn et al., 2019). In a discovery sample we acquired BOLD fMRI data from 4 subjects while they performed a retro-cue working memory paradigm (Figure 3.3.2.1). We focused all analyses on the left dlPFC, closely following (Finn et al., 2019) and defined an ROI by selecting regions in dlPFC that are part of the frontoparietal network (FPN; Ji et al., 2019). To assess whether findings are specific to FPN, we selected an anatomically and functionally sim-

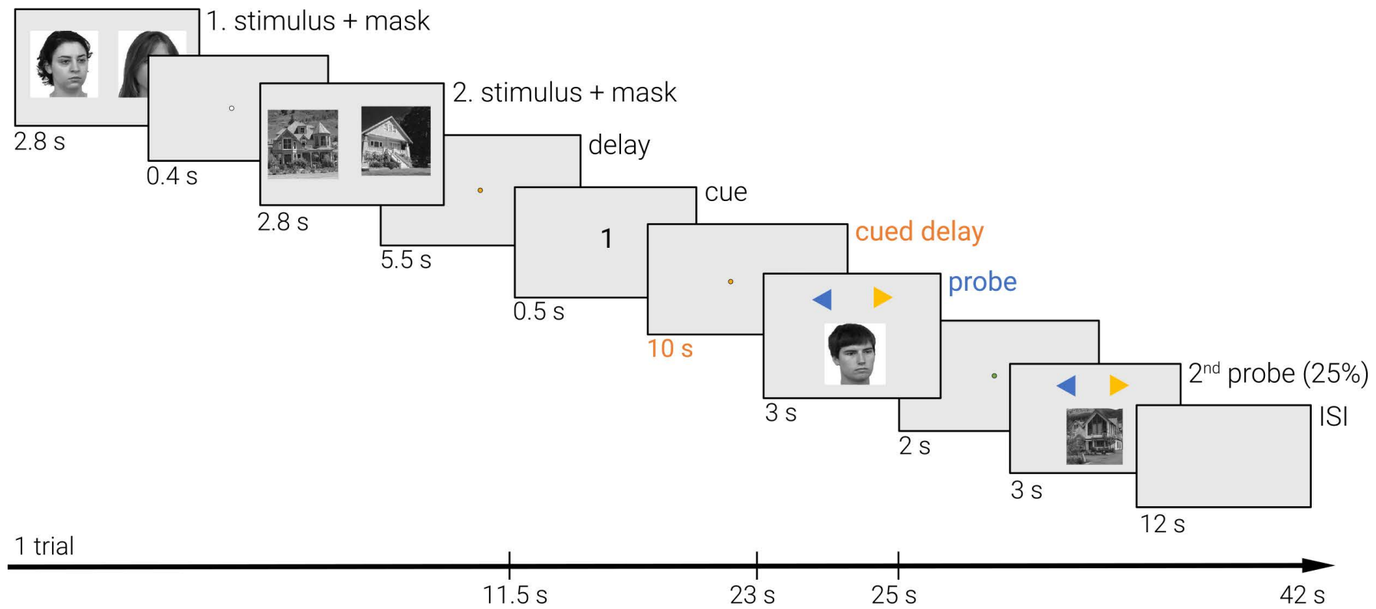

Figure 3.3.2.1 The retro-cue working memory paradigm consists of a slow event-related design with 16 trials per run. For each trial, subjects are presented with two sets of images (consisting of two images from either the house or face category). Subjects are then presented with a retro-cue that indicates whether the first or second set will be relevant for the probe period (i.e., attended category). Following the cued delay period, subjects are presented with an image that is always from the attended image set and need to indicate whether this probe is a match using the index or middle fingers of their right hand. In 25% of the trials, subjects are also probed about the unattended image set.

ilar set of control regions belonging to the cingulo-opercular network (COP). We observed better decoding of attended items in both superficial and deep layers of the dlPFC compared to unattended items (Figure 3.3.2.2a). We did not see any decoding difference between attended and unattended items for the control regions (Figure 3.3.3.2b). We also observed better decoding for the motor response in the probe period in deep than superficial layers of the dlPFC. While results are in line with our hypotheses on the laminar circuitry of the dlPFC involved in WM, they are not yet conclusive due to the small sample. We used this discovery sample to inform a study pre-registration and acquired data of 25 subjects that we are currently analyzing.

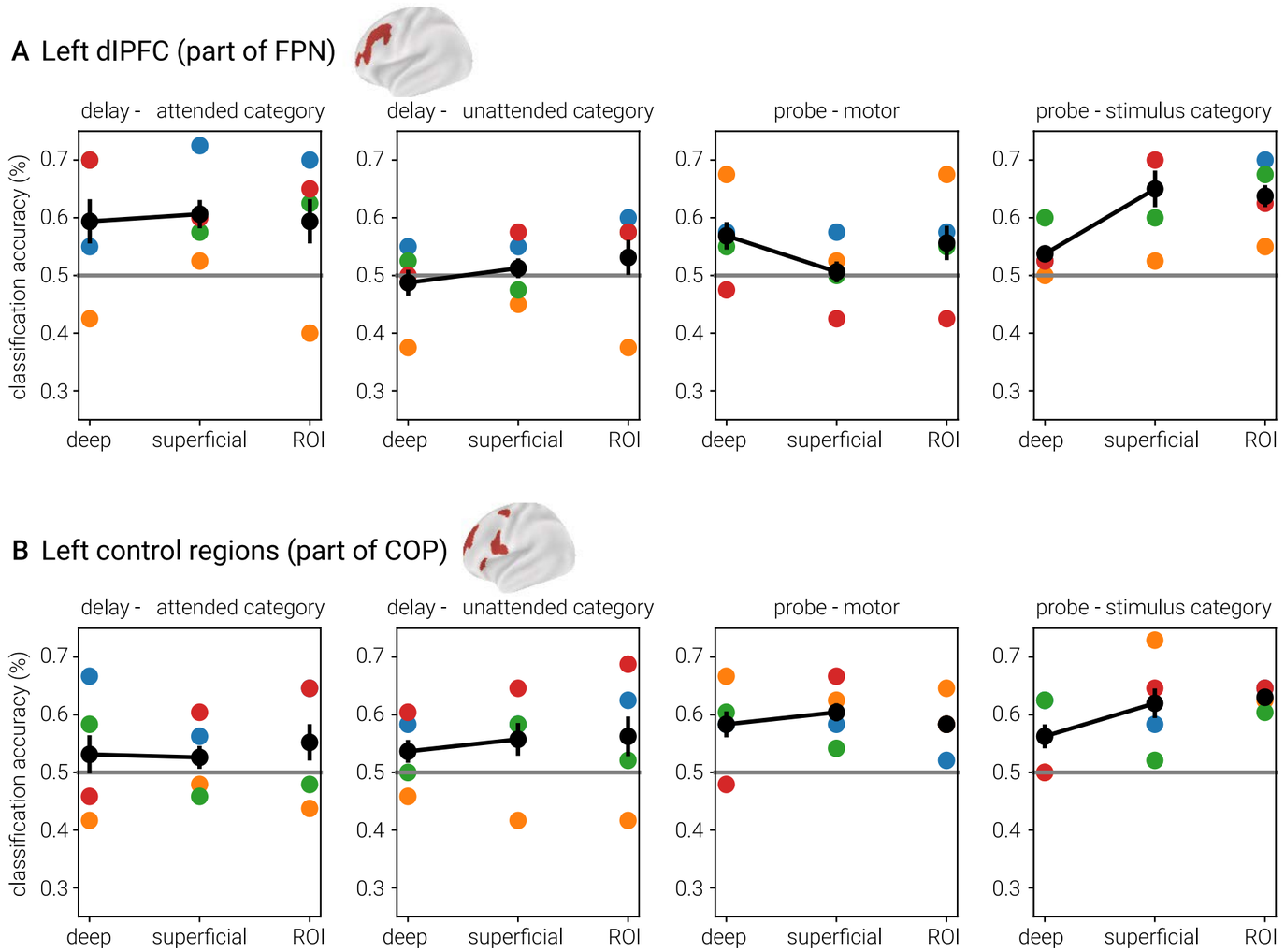

Figure 3.3.2.2 Mean layer-wise decoding accuracy across all parcels of the left dlPFC (part of the FPN) (A) and for comparison, across a control set of frontal parcels (part of the COP) (B). For comparison, we also included mean decoding accuracy across entire parcels ("ROI", i.e., not layer-wise). Coloured dots correspond to the four individual subjects.

3.3.3 Swallow tail sign and nigrosome 1: Close but not quite the same

Brammerloh, M.[1,2], Kirilina, E.[1,3], Alkemade, A.[4], Bazin, P.-L.[1,5], Jantzen, C.[1], Jäger, C. [1,5], Herrler, A.[6], Pine, K. J.[1], Gowland, P.[7], Morawski, M.[1,5], Forstmann, B.[5], & Weiskopf, N.[1,2]

[1] Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany, [2] Felix Bloch Institute for Solid State Physics, Leipzig University, Germany, [3] Center for Cognitive Neuroscience Berlin, Free University Berlin, Germany,[4] Integrative Model-based Cognitive Neuroscience Research Unit, University of Amsterdam, NL, [5] Paul Flechsig Institute of Brain Research, Leipzig University, Germany, [6] Department of Anatomy and Embryology, Maastricht University, NL, [7] Sir Peter Mansfield Imaging Centre, School of Physics & Astronomy, University of Nottingham, UK

Adapted from Brammerloh et al., Swallow tail sign: revisited, 2022, Radiology.

The loss of the radiologic swallow tail sign (ST) on MRI scans of the substantia nigra is a promising diagnostic marker of Parkinson's disease, although its anatomic underpinning is unclear. An early influential study showed that the hyperintense inner part of the swallow tail sign on T2*-weighted images (STh) corresponds to iron-poor areas in substantia nigra and suggested it to equal nigrosome 1, the region affected earliest and strongest in Parkinson's disease (Blazejewska et al., 2013). That would render the STh a cellularly specific marker. However, recent post-mortem tissue studies have challenged this interpretation, reporting that nigrosome 1 is hypointense in T2*-weighted images (e.g. (Brammerloh et al., 2021).

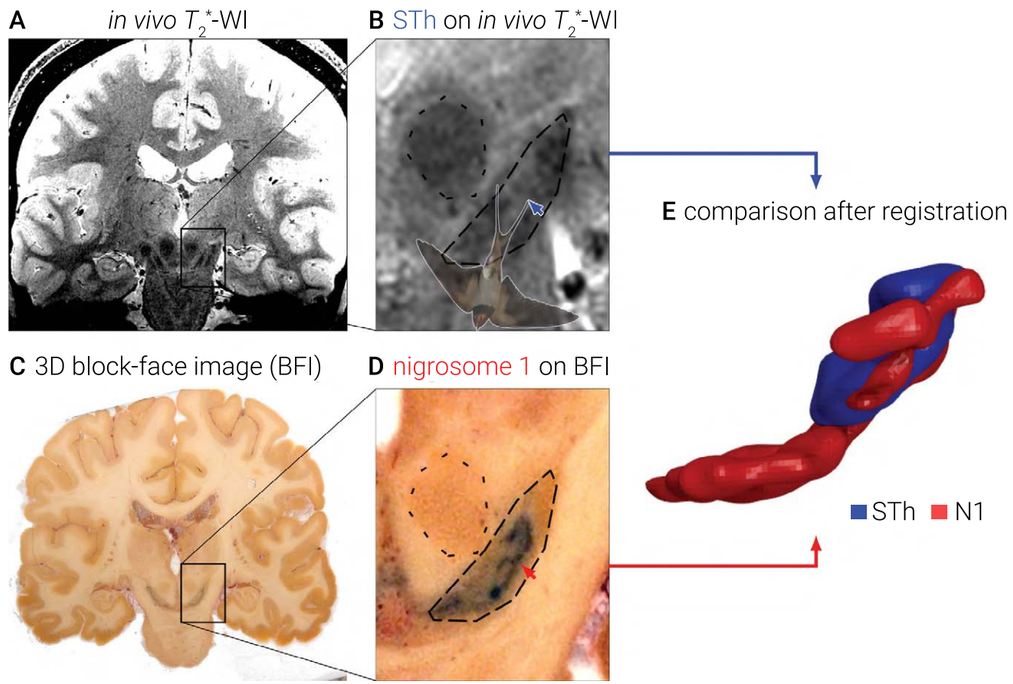

Figure 3.3.3.1 We revealed the spatial relation of the radiological swallow tail sign (ST) and nigrosome 1 (N1), combining in-vivo MRI (A) and post-mortem 3D histochemistry (C). On in-vivo T2*-WI, the hyperintense inner part of the swallow tail sign (STh, blue arrow) was segmented as a hyperintense patch in the substantia nigra (SN), surrounded by larger hypointense structures that resemble the tail of a swallow (B). The boundary of the substantia nigra is indicated with long dashes, and the boundary of the red nucleus with short dashes (B, D). The dopaminergic region N1 was segmented as a dark-pigmented stripe on 3D block-face (BFI) images (red arrow, D). An affine, landmark-based co-registration of in-vivo and post-mortem data enabled the comparison of the radiological ST and histologically defined N1 (E).

We demonstrated that nigrosome 1 and the radiologic STh are partially overlapping but distinct (video, see right-hand column), combining published 7T in-vivo and post-mortem MRI with 3D block-face imaging and immunohistochemistry (Kirilina et al., 2020; Alkemade et al., 2022). We delineated the STh in in-vivo T2*-weighted images (Figures 3.3.3.1B, 3.3.3.2B) and nigrosome 1 in block-face images (Figure 3.3.3.1D, 3.3.3.1E). STh was ovoid-shaped for all participants, while nigrosome 1 was consistently flat and disk-like (Figure 3.3.3.1E). Nigrosome 1 was significantly thinner (p = .001) and longer (p = .003) than the STh (Figure 3.3.3.2F). Coregistration of in-vivo and post-mortem T2*-weighted MRI scans to block-face images showed that nigrosome 1 only partly overlapped with STh for all possible combinations of data sets (Figure 3.3.3.2F).

Therefore, we demonstrated that the widespread equation of the STh and nigrosome 1 is inaccurate as the structures are only partially overlapping. Therefore, STh and nigrosome 1 probably correspond to distinct structures and should not be used synonymously. The cellular underpinnings of the STh should be further investigated. A more accurate link to substantia nigra anatomy will improve its value for diagnostics and disease monitoring.

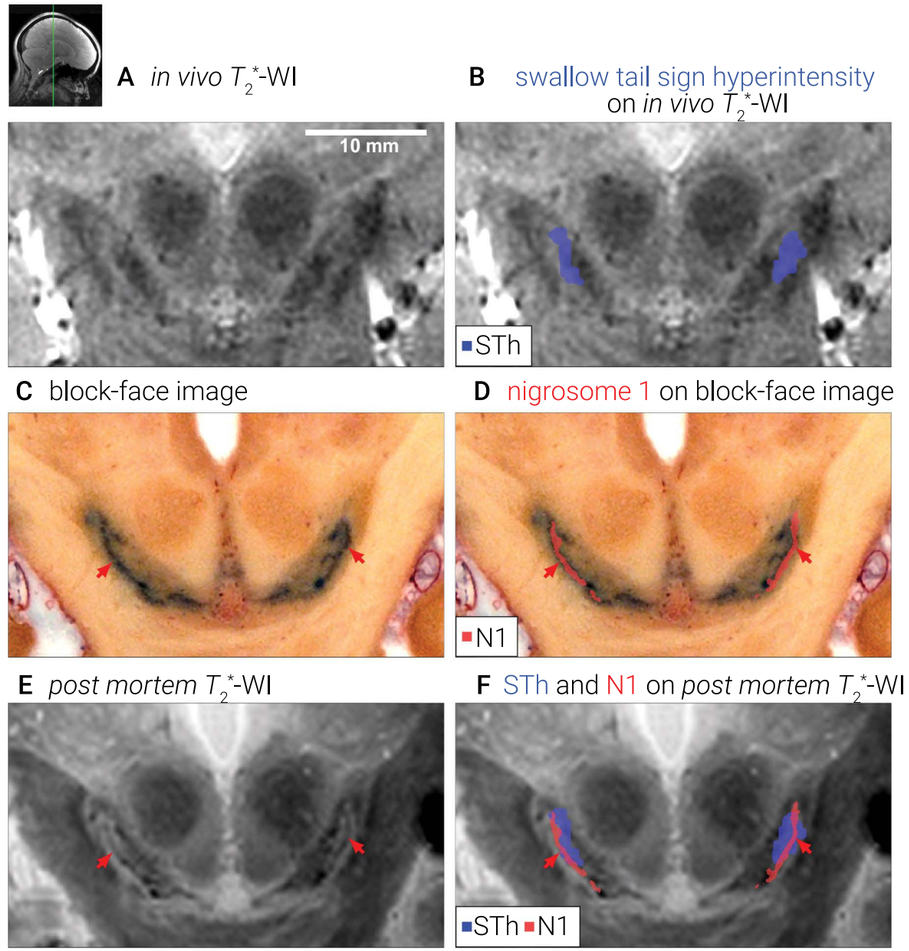

Figure 3.3.3.2 The hyperintense inner part of the swallow tail sign (STh) and nigrosome 1 (N1) overlap partially but show different geometry. (A, B) On in-vivo T2*-WI, the oval STh (Figure 1C) was segmented consistently. (C, D) Oblique coronal sections showed N1 (red arrows) as an elongated, bent stripe. N1 was significantly thinner (p < .001) and longer (p = .003) than the ST. (E) On post-mortem T2*-WI, N1 appeared consistently as a hypointense stripe (red arrows). (F) After co-registration to post-mortem T2*-WI, N1 (red arrows) and STh appeared as distinct, partly overlapping structures.

3.3.4 Lifespan trajectory of chimpanzee brains characterised by magnetic resonance imaging histology

Lipp, I.[1], Kirilina, E.[1,2], Jäger, C.[1,3], Morawski, M.[1,3], Jauch, A.[1], Pine, K.J.[1], Edwards, L.J.[1], Helbling, S.[1,4], Rose, D.[1], Helms, G.[1,5], Eichner, C.[1], Deschner, T.[6,7], Gräßle, T.[8], the EBC consortium, Gunz, P.[9], Düx, A.[8,10], Anwander, A.[1], Friederici, A.D.[1], Wittig, R. M. [9,11,12], Crockford, C.[9,11,12], & Weiskopf, N.[1,13]

[1] Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany, [2] Center for Cognitive Neuroscience Berlin, Free University Berlin, Germany, [3] Paul Flechsig Institute for Brain Research, Leipzig University, Germany, [4] Ernst Strüngmann Institute for Neuroscience in Cooperation with Max Planck Society, Frankfurt am Main, Germany, [5] Department of Clinical Sciences and Medical Radiation Physics, Lund University, Sweden, [6] Institute for Cognitive Sciences, University of Osnabrueck, Germany, [7] Ozouga Chimpanzee Project, Loango NP, Gabon, [8] Epidemiology of Highly Pathogenic Microorganisms, Robert Koch Institute, Berlin, Germany, [9] Max Planck Institute for Evolutionary Anthropology, Leipzig, Germany, [10] Helmholtz Institute for One Health, Greifswald, Germany, [11] Institute of Cognitive Science Marc Jeannerod, CNRS, Lyon, France, [12] Taï Chimpanzee Project, Centre Suisse de Recherches Scientifiques, Abidjan, Ivory Coast, [13] Felix Bloch Institute for Solid State Physics, Leipzig University, Germany

Understanding the evolutionary and ontogenetic changes in the brain that led to the development of unique human skills and abilities requires comparative neuroscience in primates. Reaching species-specific developmental milestones is facilitated by myelination and maturation of corresponding brain areas. Therefore, comparison of brain trajectories within hominoid lineage provides key insights into the evolution of the human brain. However, due to practical and ethical challenges, data on brain maturation in humans' closest living relatives, the great apes, are scarce and mostly limited to morphological analyses. Here, we studied the lifespan trajectory of chimpanzee brains, using a subset of 17 whole brains from a unique sustainably collected dataset containing 32 whole brains from captive and wild chimpanzees between one month and 52 years of age who died of natural causes (as part of the collaborative EBC project; *Gräßle et al., 2022*). Using ultra-high resolution quantitative magnetic resonance imaging (MRI; (Vaculčiaková et al., 2022), we mapped cortical myelination and iron accumulation as well as intracortical gradients, reflecting cortical myeloarchitecture (Figure 3.3.4.1A). Quantitative MRI results were in line with histology across brain regions (Figure 3.3.4.1B). Magnetisation transfer saturation maps showed a steady increase in cortical myelination from childhood to adulthood. The time constant to reach the 30% level of adult cortical maturation varied between 1.5 and 3 years between cortical areas, demonstrating a pattern of cortical maturation in the chimpanzee brain (Figure 3.3.4.2). The reported maps and developmental curves provide a foundation for future comparative neuroscience research and are an essential step towards comprehensive reconstruction of how the human brain evolved.

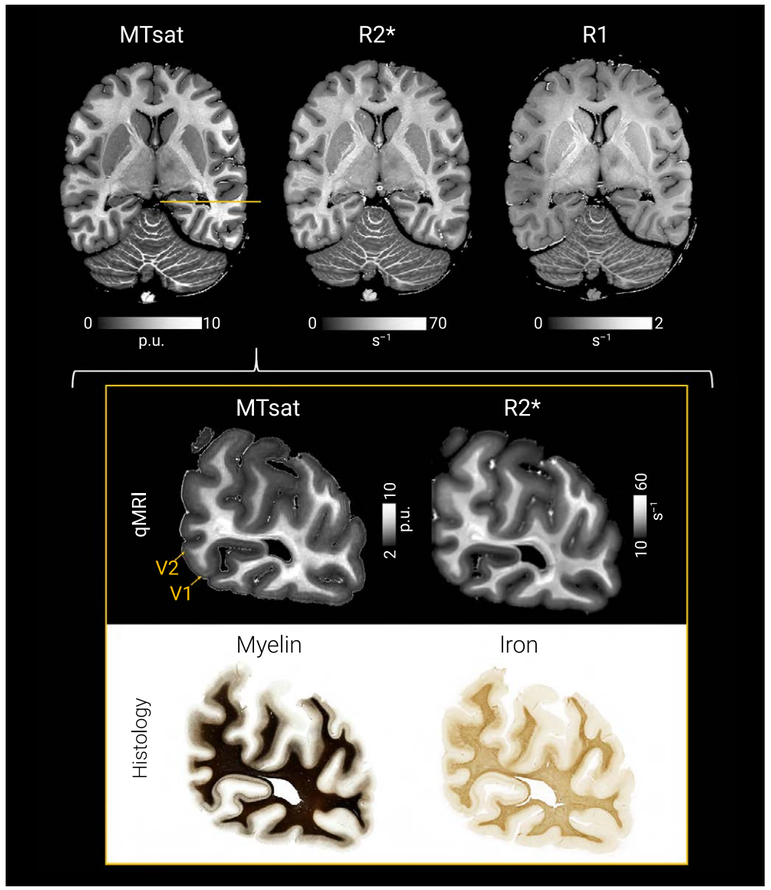

Figure 3.3.4.1 Top: Example 300µm isotropic resolution quantitative MRI dataset from a 45 year old male chimpanzee collected in the wild after natural death. Axial slices for each of the three quantitative contrasts: magnetisation transfer saturation (MTsat), effective transverse relaxation rate (R2*), and longitudinal relaxation rate (R1) are shown. All parameters show an exquisite contrast between grey and white matter. The high resolution allows for identifying neuroanatomical features in detail (e.g., cortical sheet, basal ganglia, cerebellar folia) and to assess differences in microstructure between cortical areas and across cortical depth. Bottom: Quantitative MRI parameters MTsat (myelin-sensitive) and R2* (myelin- and iron-sensitive) and histological stainings of coronal sections of the occipital lobe in a 12 year old male chimpanzee who died in a sanctuary. Myelin was visualised with a Gallyas Silver stain (note the stain saturates in the white matter). A diaminobenzidine-enhanced Perls' stain was used to visualise iron. Primary (V1) and secondary (V2) visual cortices are pointed out.

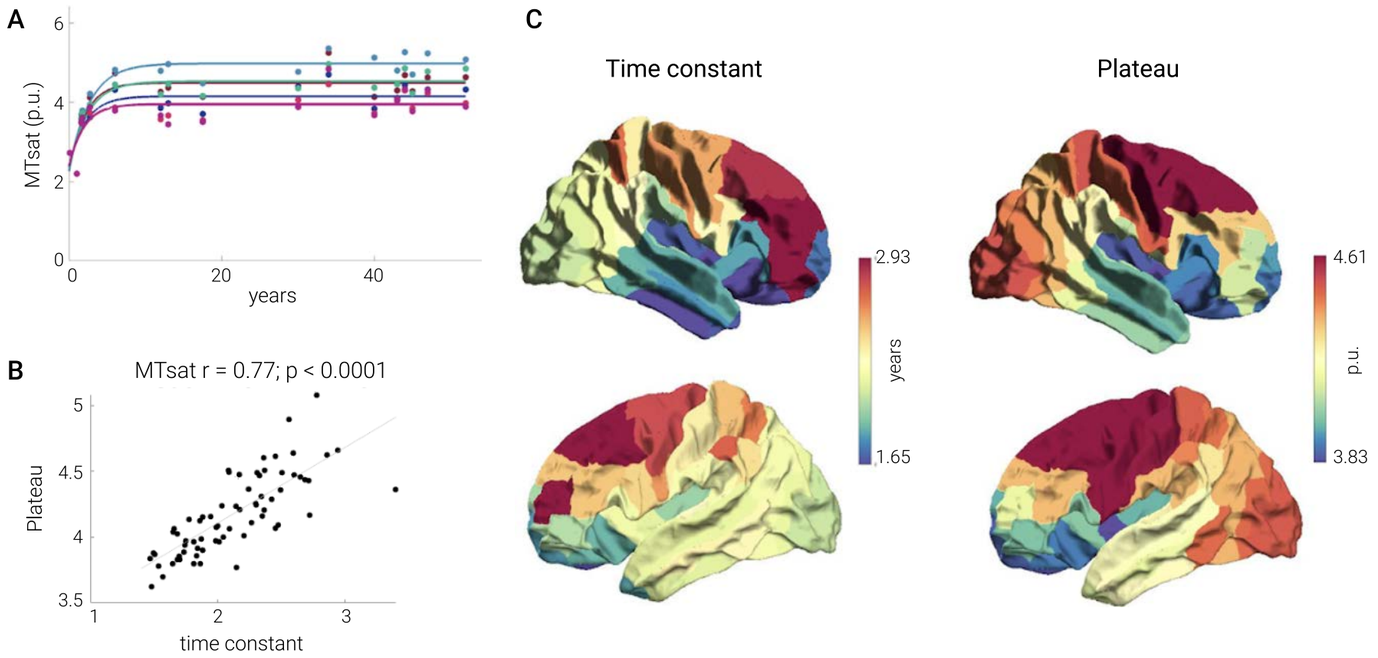

Figure 3.3.4.2 Developmental maturation of the chimpanzee cortex. (A) For various regions from the BB38 cortical chimpanzee atlas (Ardesch et al., 2019), the individual data points and fitted developmental curves for the myelin-sensitive parameter MTsat (left) are shown. The exponential saturation model by Hallgren and Sourander, 1958. was fit to the data points to quantify developmental trajectories. (C) The developmental time constant is plotted across all atlas regions. A higher time constant indicates a slower developmental increase. The plateau reached during development is also shown. The spatial distributions between time constant and plateau show some correspondence, confirmed by a correlation analysis (B) across all regions between time constant and plateau (Note that regions with no significant model prediction and regions whose values deviated more than 3 scaled median absolute deviations from the median for either measure were excluded from these calculations). The relationship indicates that more strongly myelinated regions take longer to fully myelinate.

3.3.5 Iron Accumulation of Dopaminergic Neurons across the Chimpanzee's Life Span.

Kirilina, E.[1], Reinert, T[1,2], Jäger, C.[1,2], Büttner, F.[1,3], Brammerloh, M.[1], Lipp, I.[1], Morawski, M.[1,2], Wittig, R.[4,5], Crockford, C.[4], Falkenberg, G.[6], Brueckner, D.[6], & Weiskopf, N.[1,7]

[1] Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany, [2] Paul Flechsig Institute of Brain Research, Leipzig University, Germany, [3] Faculty of Physics and Earth Sciences, Leipzig University, Germany, [4] Institute of Cognitive Science Marc Jeannerod, CNRS, Lyon, France, [5] Taï Chimpanzee Project, Centre Suisse de Recherches Scientifiques, Abidjan, Ivory Coast, [6] German Electron Synchrotron (DESY), Hamburg, Germany, [7] Felix Bloch Institute for Solid State Physics, Leipzig University, Germany

The neurotransmitter dopamine plays a key role in human brain function, regulating motor control and reward-driven behaviour. Dopamine synthesis is catalysed by iron and involves generation of highly reactive iron species and toxic quinone biproducts. Dopaminergic neurons (DN) in substantia nigra are therefore vulnerable to both iron deficit and iron excess. DN are equipped with the neuroprotective iron-chelating polymer neuromelanin, which minimises the cytosolic levels of quinones and reactive iron but eventually becomes neurotoxic when being oversaturated with iron in age. However, the levels of iron causing pathology in human DN are not yet known, and the life-span trajectory of cellular iron levels in DN has not yet been characterised, mainly since methods for non-invasive monitoring of DN iron are missing. Post-mortem histological studies in humans cover old age only. Rodent and macaque animal models do not provide adequate information due to the short life expectancy of these species and much lower iron levels as compared to humans. For the first time we studied the iron accumulation in a unique primate animal model: Post-mortem chimpanzee brains were collected in an ethical way and with sustainable practices (as part of the collaborative EBC project). Quantitative MRI of whole brains with unprecedented resolution of 0.3 mm (Figure 3.3.5.1) were combined with cellular iron quantification on histological slices using X-ray fluorescence (Figure 3.3.5.2, at DESY, Hamburg) on a subset of animals with ages spanning the chimpanzee lifespan from one month to 44 years old. The iron concentration in the neuromelanin increased from 70 ppm at birth to 400 ppm at senior age. The life span was well described with an exponential saturation curve, proposed previously by Hallgren and Sourander (Hallgren and Sourander, 1958) for iron accumulation in other human brain regions (Figure 3.3.5.3).

For the first time, we quantified the nigral anatomy and iron accumulation in dopaminergic neurons across the entire life span of chimpanzee brains providing the closest possible animal model of the human dopaminergic system. This data can now be used to inform a novel MRI-based biomarker of iron-rich dopaminergic neurons (Brammerloh et al., 2021). This biomarker will be of paramount importance for basic neuroscience of dopaminergic system and for early-stage diagnostics of neurodegenerative diseases.

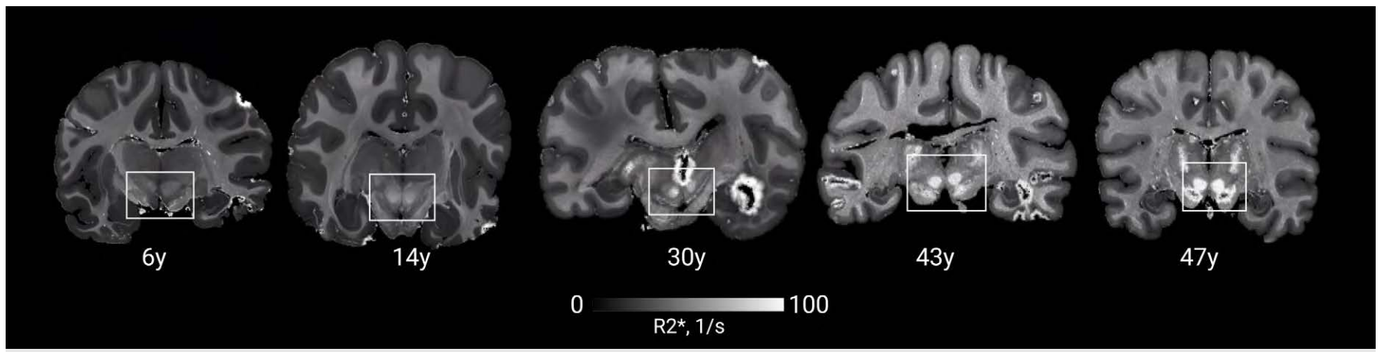

Figure 3.3.5.1 Ultra-high resolution (300µm isotropic resolution) quantitative MRI of chimpanzee brains across lifespan show age-related iron accumulation in substantia nigra and in dopaminergic neurons, reflected in increasing R2* values with age.

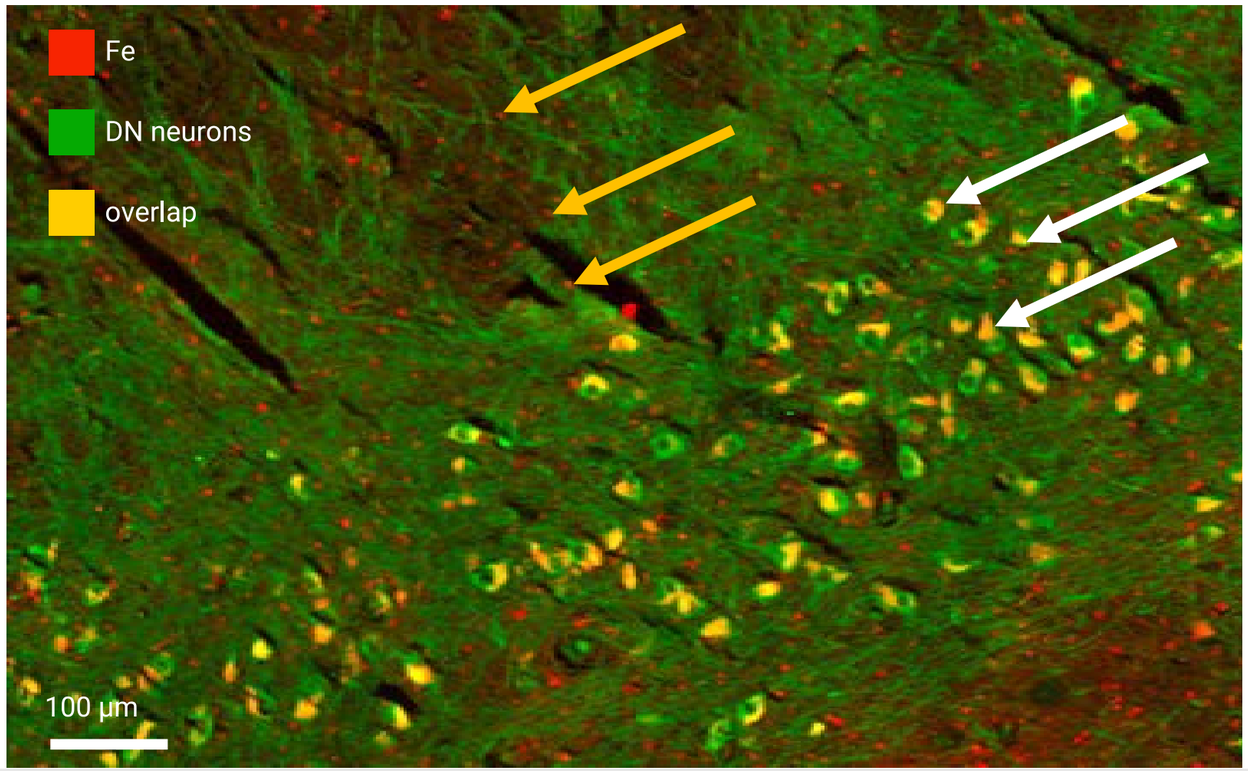

Figure 3.3.5.2 Quantitative maps of iron (red colour) in substantia nigra of adult chimpanzee obtained with micrometer resolution using X-ray fluorescence (XRF) allows measurements of intracellular iron concentrations across macroscopic regions. Dopaminergic neurons were stained using Ni-enhanced immunohistochemistry against tyrosine hydroxylase and were visible as Ni-enhanced structures (green colour). Bodies of dopaminergic neurons show very high iron concentration (white arrows). Bodies of oligodendrocytes are visible as iron-rich hotspots without prominent tyrosine hydroxylase staining (yellow arrow).

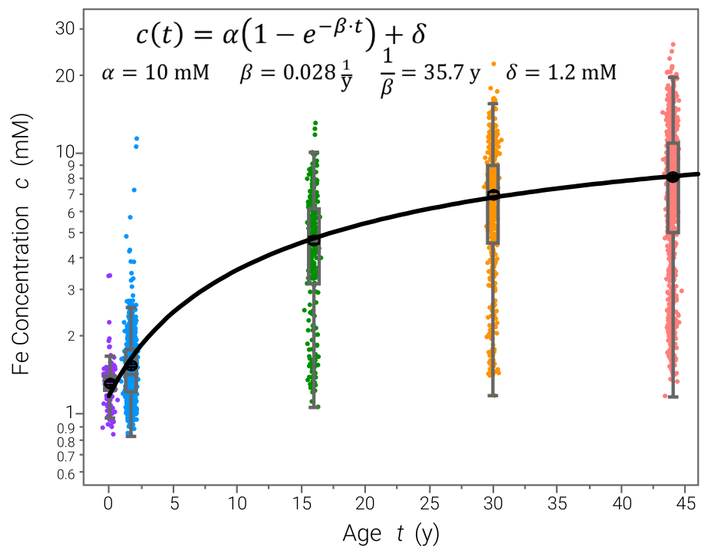

Figure 3.3.5.3 Age-dependent iron accumulation in dopaminergic neurons quantified using X-ray fluorescence (XRF) across the chimpanzee lifespan. Dots represent iron concentration in single neurons measured in brains of five animals with different ages (dots of different colour). The circles represent the median of the distributions and the boxes show interquartile intervals. The age-dependence of mean neuronal iron concentration is described well by exponential saturation model with the time constant of 35.7 years.

Acknowledgments: We acknowledge DESY (Hamburg, Germany), a member of the Helmholtz Association HGF, for the provision of experimental facilities. Parts of this research were carried out at PETRA III using microprobe at beamline P06. Beamtime was allocated for proposal I-20211534.

3.3.6 Short-range connectivity within Broca's area

Damm, J.[1], Kirilina, E.[1], Zaccarella, E.[2], Movahedian Attar, F.[1], Chaimow, D.[1], Schmidt, M.[1], Friederici, A. D.[2], & Weiskopf, N.[1,3]

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Short-range connections in the language network are largely unexplored. Broca's area in the left inferior frontal gyrus is a central node of the language network (Friederici, 2012). The area is divided anatomically into two cytoarchitectonically defined regions: Brodmann Area (BA) 44 and BA 45. The two regions are tightly functionally connected and may inhibit each other during language processing depending on the type of linguistic information under analysis. The left BA 44—which has been shown to support syntactic processes (Makuuchi et al., 2009; Zaccarella & Friederici, 2015) — inhibits left BA 45 when syntactic information is strongly relevant to the tasks (Wu et al., 2019). The left BA 45—which is conversely highly sensitive to semantic information (Goucha & Friederici, 2015)—inhibits the left BA 44 when semantic processing is started off (Wu et al., 2019). BA 44, moreover, appears to be structurally (Amunts et al. 2010) and functionally (Clos et al., 2013) heterogeneous across the anterior-posterior axis, contributing to syntactic processing in the most anterior part (aBA 44) and to motor-related functions in the most posterior part (pBA 44) along BA 6 (Papitto, Friederici & Zaccarella, 2020).). Overall, the functional interaction between BA 44, BA 45, and their functional subdivisions suggests the presence of short direct white matter connections between these areas.

Short-range connectivity (short-range association fibres, SAF) within and between Broca's area subdivisions remains unexplored due to the challenges in mapping SAF, which requires ultra-high resolution Diffusion Weighted Imaging (DWI) and dedicated fibre models. We recently developed and validated a robust and sensitive method for mapping SAF using ultra-strong gradients of the Connectom scanner (Movahedian Attar et al., 2020). Here, we apply this method to map short range connectivity between Broca's area subdivisions.

We analyzed DWI data of five healthy (1f, 26 ± 3.87y) right-handed (mean laterality quotient: 89 ± 13.89%; Oldfield, 1971) adults from (Movahedian Attar et al., 2020). Areas BA 44 and BA 45 were identified on the cortical surface from a segmented anatomical T1w image, using the Julich-Brain Cytoarchitectonic Atlas (Amunts et al., 2020).

Fibre tracts connecting BA 44 and BA 45 were detected bilaterally in all investigated participants. Four out of five subjects showed left-lateralised short-range connectivity between BA 44 and BA 45 (Figure 3.3.6.1). Furthermore, we detected a stronger connectivity between aBA 44 and BA 45 than between pBA 44 and BA 45 in both hemispheres, corresponding well to the previously described functional subdivisions within BA 44.

The ability to map short-range connections within the language network promises to close the gaps in the current models of the language processing network.

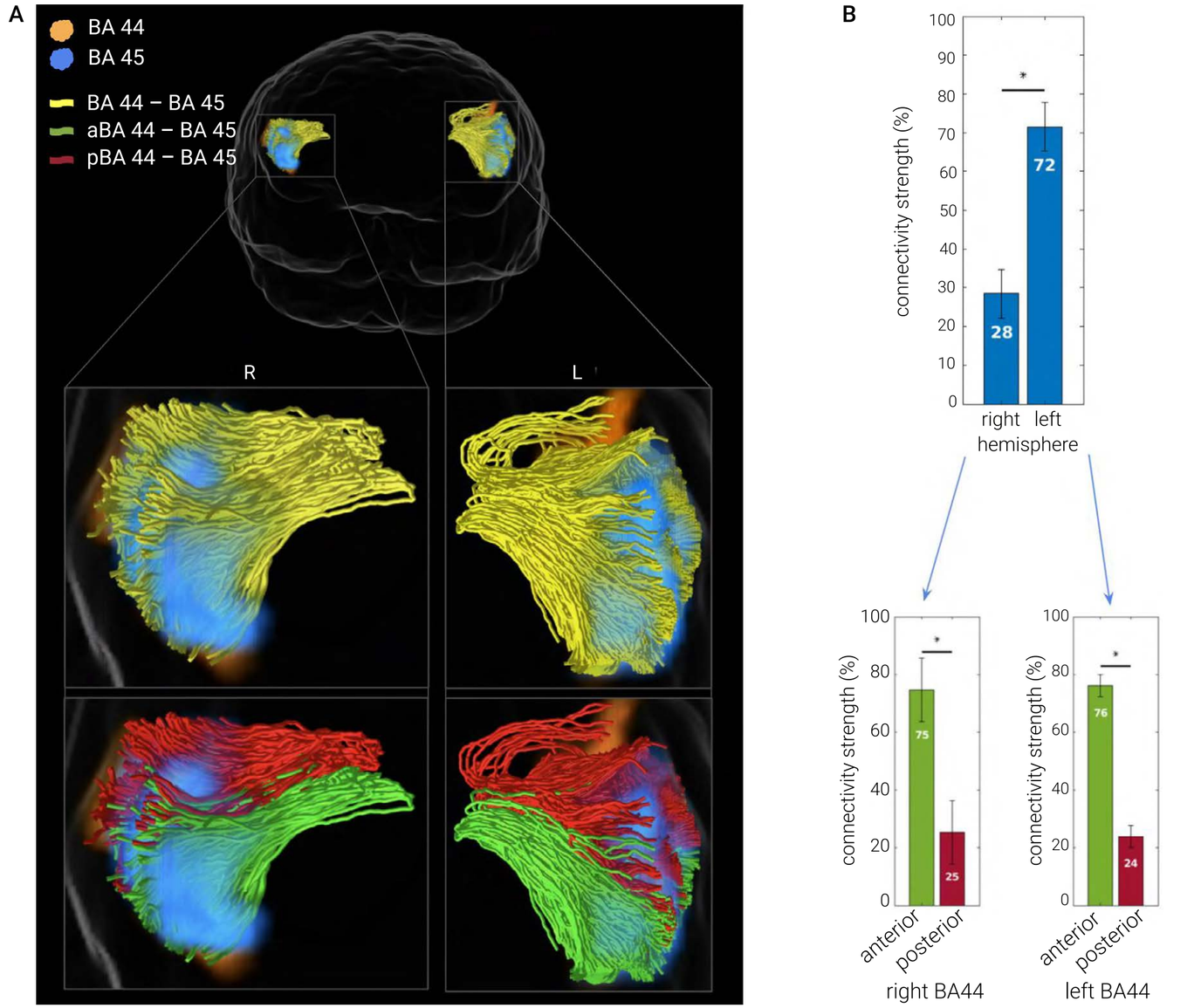

Figure 3.3.6.1 Short-range connections between subdivisions of Broca's area mapped in-vivo in the left (L) and right (R) hemisphere using submillimeter resolution diffusion-weighted tractography. (A) Short-range association fibres for one representative participant (f, 27y, laterality quotient: 100%) mapped between BA 44 and BA 45 (middle row; streamline length$_L$: 13.8 ± 11.8mm, streamline length$_R$: 17.8 ± 12.5mm) and between anterior and posterior parts of BA 44 (aBA 44, pBA 44) and BA 45 (bottom row) with a maximum length of 60mm to exclude spurious fibre tracts. (B) Mean relative connectivity strength in the group of five participants differentiating aBA 44 - BA 45 and pBA 44 - BA 45 short-range connectivity. The ratio of streamline counts derived from probabilistic tractography were used to define the connectivity.

Congresses, Workshops, and Symposia

2020

- Weiskopf, N. (October). *Neurophysics Retreat 2020*. Retreat. Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany. Virtual.

2021

- Eippert, F., Valk, S. L., & Weiskopf,N. (July). *Career building. Expertise session II.* 10th IMPRS NeuroCom Summer School in Cognitive Neuroscience. International Max Planck Research School on Neuroscience of Communication: Function, Structure, and Plasticity (IMPRS NeuroCom), Max Planck Institute for Human Cognitive and Brain Sciences & ICN, Leipzig & London, Germany & UK. Virtual.
- Weiskopf, N. (October). *Neurophysics Retreat 2021*. Retreat. Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany.

2022

- Lipp, I. (June). *Quantitative MRI for in-vivo histology from six perspectives.* OHBM Educational Course. Annual Meeting Organization for Human Brain Mapping, Scottish Event Center, Glasgow, UK.
- Trampel, R. & Weiskopf, N. (June). *From protons to segmentation of neuroanatomical structures- Hands on 7T.* Workshop. 11th IMPRS NeuroCom Summer School in Cognitive Neuroscience. International Max Planck Research School on Neuroscience of Communication: Function, Structure, and Pasticity (IMPRS NeuroCom), Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany.
- Weiskopf, N. & Krieghoff, V. (June). *11th IMPRS NeuroCom Summer School in Cognitive Neuroscience.* International Max Planck Research School on Neuroscience of Communication: Function, Structure, and Pasticity (IMPRS NeuroCom), Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany.
- Weiskopf, N. (October). *Neurophysics Retreat 2022*. Retreat. St. Augustine's Monastery, Erfurt, Germany.
- Kirilina E., & Weiskopf, N. (October). *Detecting Parkinson's disease at early stage with MRI: Recent advances and promising approaches.* Symposium. Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany.

Degrees

PhD Theses

2021

- Gast, R. *Phase transitions between asynchronous and synchronous neural dynamics: Theoretical insight into the mechanisms behind neural oscillations in Parkinson's disease.* Leipzig University, Germany.

Appointments

2020

- Weiskopf, N. *Adjunct Professor, Center for Medical Physics and Biomedical Engineering*, Medical University of Vienna, Austria
- Weiskopf, N. *Spokesperson of the International Max Planck Research School on Neuroscience of Communication: Function, Structure, and Plasticity (IMPRS NeuroCom)*, Max Planck Institute for Cognitive and Brain Sciences, Leipzig, Germany.

2022

- Kirilina, E. *Research Group Leader (W2)*, Department of Neurophysics, Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany
- Weiskopf, N. *Spokesperson and Board member of the International Max Planck Research School on Cognitive NeuroImaging (IMPRS CoNI)*, Max Planck Institute for Cognitive and Brain Sciences, Leipzig, Germany.

Awards

2020

- Brammerloh, M., *International Society for Magnetic Resonance in Medicine Magna Cum Laude Merit Award.* ISMRM, USA

2021

- Brammerloh, M. *Gorter Prize, 3rd place.* German Section of the International Society for Magnetic Resonance in Medicine, Germany
- Lipp, I. *Sign UP! Careerbuilding.* Max Planck Society and European Academy for Women in Politics and Economics Berlin, Munich/Berlin, Germany
- Pine, K. J. *Best Abstract Award (cum laude)* European Society for Magnetic Resonance in Medicine and Biology (ESMRMB)

2022

- Kirilina E. *International Erwin L. Hahn Institute Award 2022 for the category BRAIN.* Erwin L. Hahn Institute for MRI, Essen, Germany

Publications

Books & Book Chapters

Linden, D., Goebel, R., & Weiskopf, N. (2021). A brief history of real-time fMRI neurofeedback. In M. Hampson (Ed.), *fMRI Neurofeedback* (pp. 1–19). Elsevier. https://doi.org/10.1016/B978-0-12-822421-2.00005-3

Journal Articles

Aldusary, N., Traber, G. L., Freund, P., Fierz, F. C., Weber, K. P., Baeshen, A., Alghamdi, J., Saliju, B., Pazahr, S., Mazloum, R., Alshehri, F., Landau, K., Kollias, S., Piccirelli, M., & Michels, L. (2020). Abnormal connectivity and brain structure in patients with visual snow. *Frontiers in Human Neuroscience*, *14*. https://doi.org/10.3389/fnhum.2020.582031

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Bazin, P.-L., Alkemade, A., Mulder, M. J., Henry, A. G., & Forstmann, B. U. (2020). Multi-contrast anatomical subcortical structures parcellation. *eLife*, *9*. https://doi.org/10.7554/eLife.59430

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4

Professor Dr Christian F. Doeller
Director | Managing Director

Space for Cognition

DEPARTMENT OF PSYCHOLOGY

The fundamental question in cognitive neuroscience—what are the key coding principles of the brain enabling human thinking—still remains largely unanswered. In our long-term aim to tackle this question, we use two model systems: human memory and the neural population code for space, representing the summed activity of neurons signalling an individual's position in its environment. Firstly, we will provide a summary of our research approach. Secondly, along the lines of show-case examples of ongoing or recently finished projects, in the following section, we will give an overview of our key research areas including: (1) space and memory, (2) time, (3) knowledge acquisition and structure learning, (4) value-based decision making, and (5) vision and Neuro-AI.

The SatNav in the brain: One of the most fascinating discoveries in neuroscience was the Nobel prize awarded identification of spatially responsive cells in the hippocampal formation (HF). Hippocampal place cells, and grid cells in nearby entorhinal cortex (EC), work in concert with other spatially tuned cell types to signal position, direction, distance and speed. Together, they provide a spatial map, the brain's SatNav, the most intriguing coding scheme outside the sensory system. But what are the corresponding neural coding mechanisms in humans? We, together with others, have made important steps towards answering this question.

Spatial maps in humans: We have been instrumental, along with others, in translating neural coding mechanisms underlying wayfinding, from rodent electrophysiology to the systems level in humans. By combining fMRI with virtual reality (VR), we have demonstrated that similar spatial maps exist in the human brain. Our discoveries include a continuous, grid-like code of space in the human network for episodic memory (Doeller et al., 2010, Nature), the identification of the human homologue of medial and lateral EC (Navarro-Schröder et al., 2015, eLife), and the breakdown of the grid system in a human genetic model of Alzheimer's disease (Kunz et al., 2015, Science). Despite the wealth of studies on spatial coding in the HF, whether similar coding principles support cognitive operations beyond the spatial domain remains one of the most exciting questions in cognitive neuroscience.

From spatial maps to mnemonic maps: Is mnemonic information represented in cognitive maps? We identified the neural mechanisms of insight-triggered reconfiguration (Milivojevic et al., 2015, Curr Biol), theta-driven integration (Backus et al., 2016, Curr Biol) and mnemonic scaling of non-spatial mnemonic space (Collin et al., 2015, Nat Neurosci). We have identified a crucial learning rule in the HF (Doeller et al., 2008, PNAS; Doeller & Burgess, 2008, PNAS) and provided evidence that memories are not stored in isolation but rather in hierarchical networks (along the hippocampal long-axis; Collin et al.) and spatio-temporal event maps (Deuker et al., 2016, eLife). We have also described attractor dynamics (Steemers et al., 2016, Curr Biol) and mnemonic convergence (Backus et al., 2016, Nat Comm) as neural mechanisms for the access of stored information. Finally, we have identified how directional codes in the brain relate to memory (Nau et al., 2020, Nat Comm) and discovered how HF remapping and EC realignment supports context-dependent memory (Julian & Doeller, 2021, Nat Neurosci).

Cognitive spaces: Our long-term framework is concerned with the key idea that this navigation system in the brain—potentially as a result of evolution—provides a fundamental neural metric for human cognition, see Bellmund et al., 2018, Science; Nau et al., 2018, TICS; Kaplan et al., 2017, TINS; and Bottini & Doeller, 2020, TICS, for a summary of our theoretical account. Specifically, we propose that the brain represents our experiences in so-called 'cognitive spaces'. For illustration, consider the simple example of describing cars, which you might do along two dimensions, their engine power and their weight. Depending on the two features, racing cars, for instance, would occupy a region characterised by high power and low weight, whereas campers comprise low power and high weight. We test the overarching hypothesis that—akin to representing places and paths in a spatial map—similar coding principles are involved in the formation of such cognitive spaces. Importantly, in our experimental framework, we investigate whether these domain-general principles support a broad range of our fundamental cognitive functions ranging from spatial navigation, memory formation, learning, imagination, and perception to time processing, decision making, action control and knowledge acquisition. In a series of key experiments, we have demonstrated spatial distance coding in the HF while learning abstract concepts (Theves et al., 2019, Curr Biol; Theves et al., 2020, J Neurosci) and identified the role of the HF and prefrontal regions in representing abstract hierarchies (Theves et al., 2021, J Neurosci) and in adaptively guiding reward generalisation (Garvert et al., in press, Nat Neurosci). Furthermore, we provided evidence for grid-like coding during mental simulation (Bellmund et al., 2016, eLife) and visual exploration (Nau et al., 2018, Nat Neurosci). We have also found that such coding is reflected in oscillatory dynamics (Staudigl et al., 2018, Curr Biol) and in the deformation of mnemonic responses in environments with concurrent deformations of the grid code (Bellmund et al., 2020, Nat Hum Behav). Finally, we observed mapping of temporal structure of episodic memories (Bellmund et al., 2022, Nat Comm) and task regularities (Polti et al., 2022, eLife) in the HF, in particular in the lateral EC (Bellmund et al., 2019, eLife).

Translation: Our key translational research is largely expressed in two pillars: We are developing AI-based deep neural network technology as analysis and discovery tools for neuroscience (Frey et al., 2021, Nat Neurosci; Frey et al., 2021,

eLife), and work towards novel neural-coding biomarkers for early detection of hippocampal-entorhinal neurodegeneration such as Alzheimer's disease (Kunz et al., 2015, Science) and more recently for our understanding of the long-COVID syndrome.

The tools: Discoveries are only made possible through innovative technologies. Our central research tools are functional magnetic resonance imaging (fMRI) as well as magnetoencephalography (MEG). We further combine neuroimaging with multivariate analysis approaches to quantify properties of representational spaces, machine learning analysis techniques, deep neural networks and a wide variety of cognitive tasks.

Neuroimaging. Space-resolved fMRI, as the central, high-throughput research tool, is complemented by time-resolved MEG to take advantage of the high temporal resolution and fine-grained information of multidimensional oscillatory data.

Virtual reality and cognitive tasks. To examine cognition in a realistic manner, we leverage virtual reality technology (both desktop-based and natural navigation in virtualizer and tracking labs) to simulate spatial navigation as well as life-like cognitive tasks. A wide array of cognitive tasks are used, ranging from psychophysics and eyetracking to realistic knowledge acquisition tasks.

Organisational structure: The Department started its work in September 2018. In addition to the main site of the lab at MPI CBS in Leipzig, we have significant research activities at the Kavli Institute at NTNU, Trondheim, Norway, in particular at the Kavli Institute's Jebsen Centre for Alzheimer's Disease, founded in 2020. While our MPI and Kavli sites focus on distinct research areas (basic cognitive neuroscience at MPI CBS vs translational neuroscience at Kavli), they are complementary, with a multitude of interactions between them. Furthermore, we have a strong network of national and international collaborators, with particularly strong hubs of jointly supervised doctoral and postdoctoral researchers in Berlin (MPI for Human Development and Charité – Berlin University of Medicine), Rovereto (CIMeC, University of Trento, Italy), and London (UCL).

4.1 Research Area SPACE & MEMORY

4.1.1 Remapping and realignment in the human hippocampal formation predict context-dependent spatial behaviour

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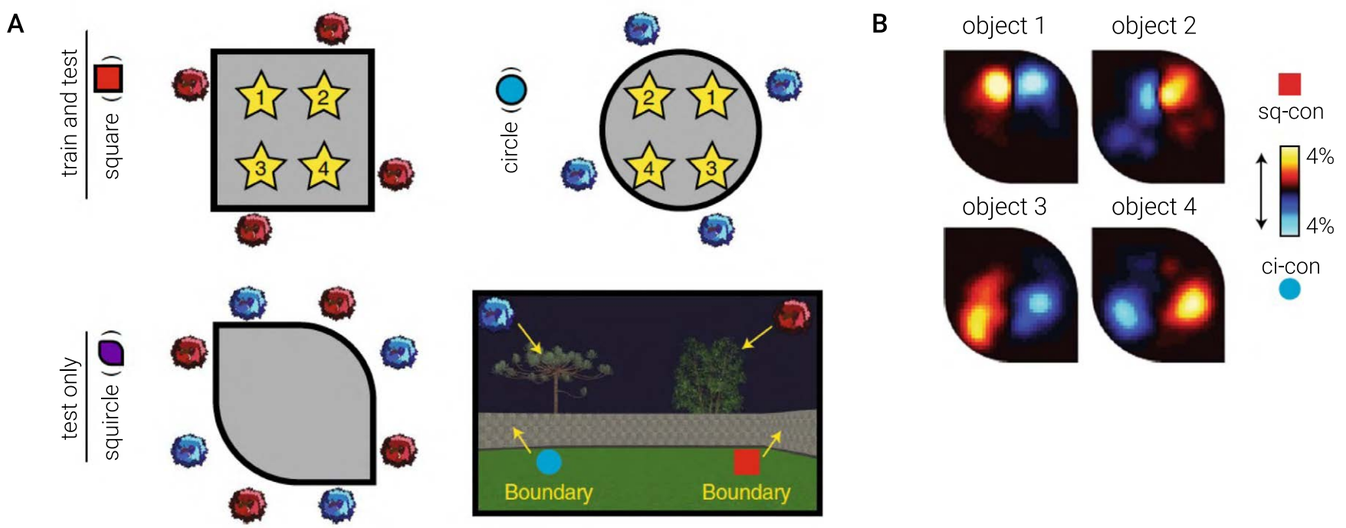
To guide spatial behaviour, the brain must retrieve memories that are appropriately associated with different navigational contexts. Contextual memory might be mediated by cell ensembles in the hippocampal formation that alter their responses to changes in context, processes known as remapping and realignment in the hippocampus and entorhinal cortex, respectively. However, whether remapping and realignment guide context-dependent spatial behaviour is unclear. To address this issue, human participants learned object-location associations within two distinct virtual reality environments and subsequently had their memory tested during functional MRI (fMRI) scanning. Entorhinal grid-like representations showed realignment between the two contexts, and coincident changes in fMRI activity patterns consistent with remapping were observed in the hippocampus. Critically, in a third ambiguous context, trial-by-trial remapping and realignment in the hippocampal-entorhinal network predicted context-dependent behaviour. These results reveal the hippocampal-entorhinal mechanisms mediating human contextual memory and suggest that the hippocampal formation plays a key role in spatial behaviour under uncertainty (Julian, et al., 2021, Nat Neurosci).



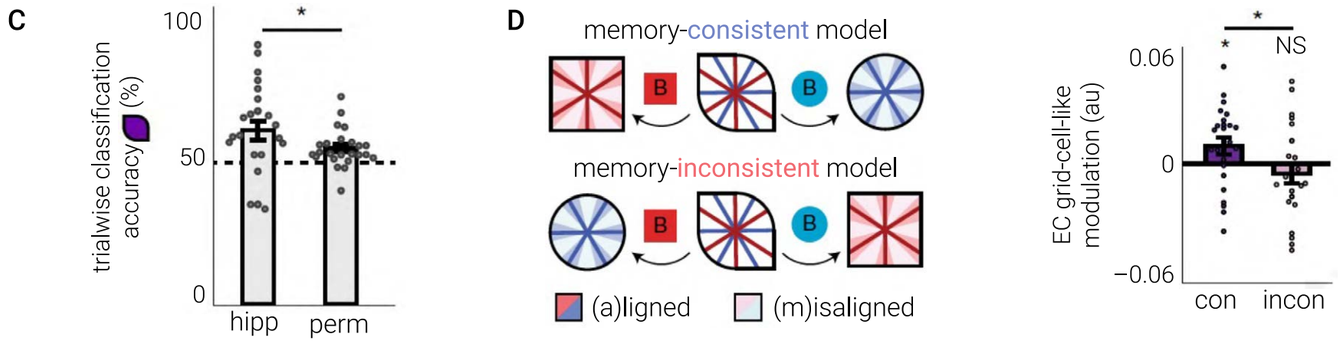


Figure 4.1.1 Context-dependent remapping and realignment in the human hippocampal formation. (A) Context-dependent spatial memory task. Participants learned four object locations in two arenas ('Square' and 'Circle'). Memory for object locations was also tested in a third half-square, half-circular arena ('Squircle'). (B) Contextual memory retrieval in the ambiguous Squircle context. Heat maps depicting the difference in Square- and Circle-consistent recalled locations in the Squircle, separately for each of the four target objects. (C) Hippocampal remapping distinguishes between contexts and predicts memory-guided behaviour. Trial-wise hippocampal Square- vs Circle-consistent Squircle contextual memory classification accuracy was significantly higher than in a permutation test. (D) Entorhinal grid-like realignment predicts memory-guided behaviour. Two grid-like models were fit, one that assumed that the grid orientation changed on a trial-by-trial basis consistent with contextual memory (Con) and another that assumed that grid orientation changed inconsistent with contextual memory (Incon), left. The Con model significantly fit the data better than the Incon model (right).

4.1.2 Deforming the metric of cognitive maps distorts memory

Bellmund, J. L. S.[1,2,3], de Cothi, W.[4,5], Ruiter, T. A.[2,6], Nau, M.[3], Barry, C.*[,5], & Doeller, C. F.*[,1,2,7]

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Environmental boundaries anchor cognitive maps that support memory. However, trapezoidal boundary geometry distorts the regular firing patterns of entorhinal grid cells, proposedly providing a metric for cognitive maps. Here we test the impact of trapezoidal boundary geometry on human spatial memory using immersive virtual reality. Consistent with reduced regularity of grid patterns in rodents and a grid-cell model based on the eigenvectors of the successor representation, human positional memory was degraded in a trapezoid environment compared with a square environment—an effect that was particularly pronounced in the narrow part of the trapezoid. Congruent with changes in the spatial frequency of eigenvector grid patterns, distance estimates between remembered positions were persistently biased, revealing distorted memory maps that explained behaviour better than the objective maps. Our findings demonstrate that environmental geometry affects human spatial memory in a similar manner to rodent grid-cell activity and, therefore, strengthen the putative link between grid cells and behaviour along with their cognitive functions beyond navigation (Bellmund, et al., 2020, Nat Hum Behav).

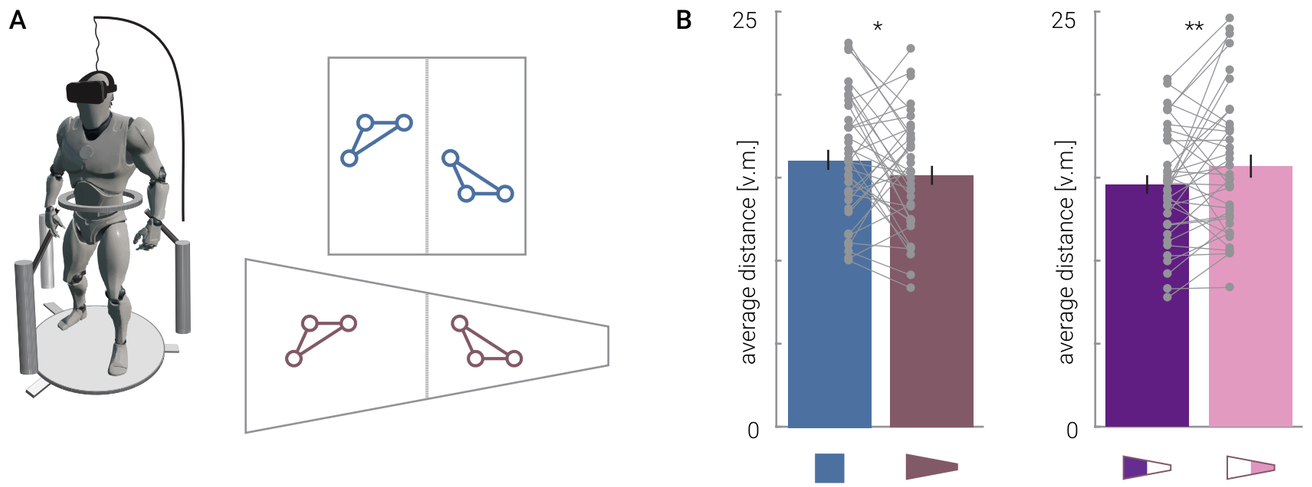

Figure 4.1.2 Boundary geometry distorts memory. (A) Schematic of the immersive virtual reality setup with a head-mounted display and a motion platform, which translated physical steps and rotations into virtual movement (left). An example configuration of object positions (circles), right. Two triplets of objects were positioned in each environment with one triplet in each half of each environment, yielding four triplets with matched distances between positions. (B) Distortion of distance estimates. Taking advantage of matched distances between object positions, estimated distances were averaged and compared between environments. Identical distances were estimated to be shorter in the trapezoid than in the square and to be longer in the narrow part of the trapezoid than in the broad part, in line with the lower radial frequencies of the successor representation grid patterns in the trapezoid (not shown).

4.1.3 Adaptive cognitive maps for curved surfaces in the 3D world

Kim, M.[1], & Doeller C. F.[1,2,3]

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Terrains in a 3D world can be undulating. Yet, most prior research has exclusively investigated spatial representations on a flat surface, leaving a 2D cognitive map as the dominant model in the field. Here, we investigated whether humans represent a curved surface by building a dimension-reduced flattened 2D map or a full 3D map. Participants learned the location of objects positioned on a flat and curved surface in a virtual environment by driving on the concave side of the surface (Experiment 1), driving and looking vertically (Experiment 2), or flying (Experiment 3). Subsequently, they were asked to retrieve either the path distance or the 3D Euclidean distance between the objects. Path distance estimation was good overall, but we found a significant underestimation bias for the path distance on the curve, suggesting an influence of potential 3D shortcuts, even though participants were only driving on the surface. Euclidean distance estimation was better when participants were exposed more to the global 3D structure of the environment by looking and flying. These results suggest that the representation of the 2D manifold, embedded in a 3D world, is neither purely 2D nor 3D. Rather, it is flexible and dependent on the behavioural experience and demand (Kim, et al., 2022, Cognition).

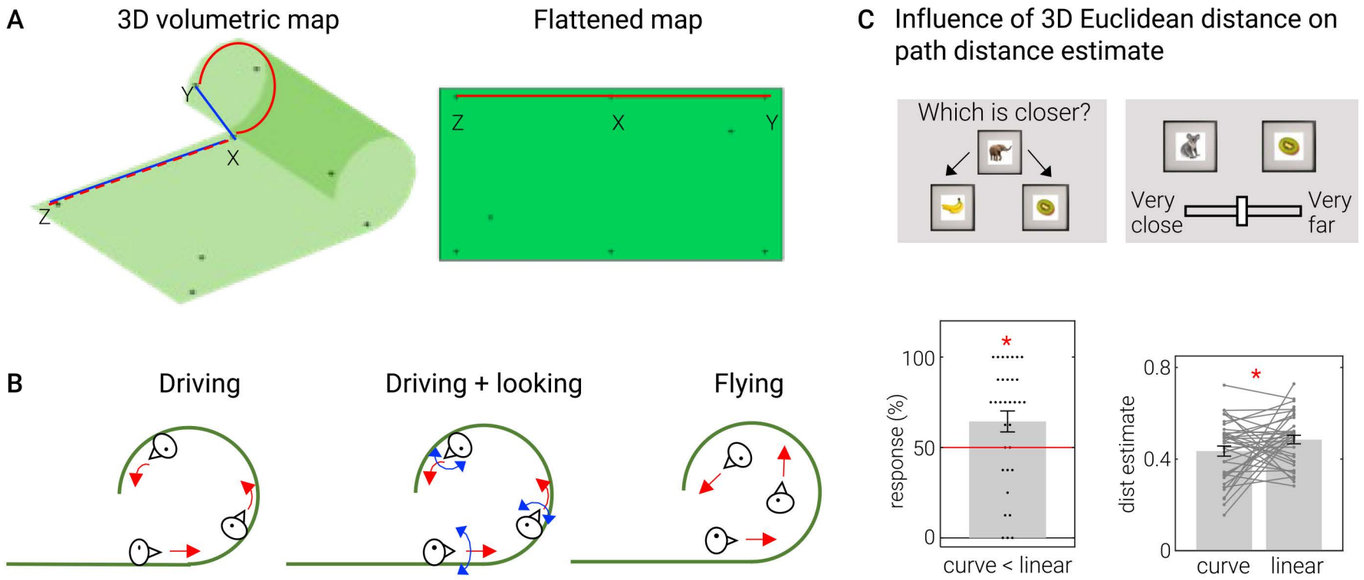

Figure 4.1.3 Cognitive maps for a curved surface. (A) We investigated whether people build a volumetric map (less information efficient, more flexible) or a dimension-reduced surface map (more information efficient) when they navigate on a 2D manifold in a 3D world. (B) We used a desktop-based VR with various movement methods such as driving (Exp 1), driving with additional viewing (Exp 2), and flying (Exp 3). (C) Participants showed a bias in underestimating the path length on the curve section compared to the linear section. This suggests the influence of automatically encoded 3D Euclidean distance even when people only move on the surface, rejecting the pure surface map hypothesis. Performance on path and Euclidean distance estimation and self-reported encoding strategy imply that people utilise a hybrid form of the map.

4.1.4 Dissociating distinct cortical networks associated with subregions of the human medial temporal lobe using precision neuroimaging

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Tract-tracing studies in primates indicate that different subregions of the medial temporal lobe (MTL) are connected with multiple brain regions. However, no clear anatomical framework defining the boundaries of human mnemonic functions exists. This gap in knowledge originates in notoriously low MRI data quality in the anterior human MTL and in group-level blurring of idiosyncratic anatomy between adjacent brain regions, such as entorhinal and perirhinal cortices, and parahippocampal areas TH/TF. Using MRI, we intensively scanned four human individuals and collected whole brain data with unprecedented MTL signal quality. Following detailed exploration of cortical networks associated with MTL subregions within each individual, we discovered three biologically meaningful networks associated with the entorhinal cortex, perirhinal cortex, and parahippocampal area TH, separable from area TF. Our findings define the anatomical constraints within which human mnemonic functions must operate and are meaningful for examining the evolutionary trajectory of the MTL connectivity across species.

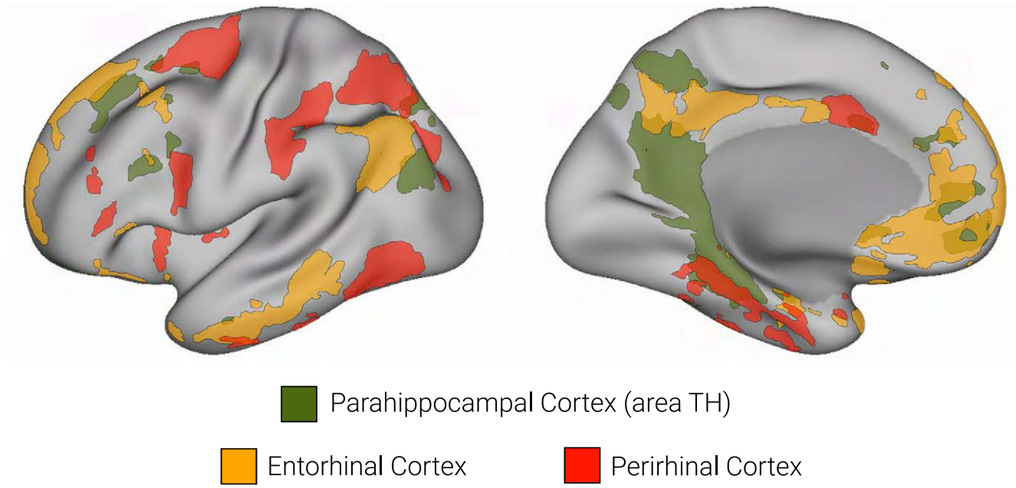


Figure 4.1.4 Subregions of the human MTL are associated with distinct distributed brain networks. A surface map showing a schematic whole-brain neuroanatomical architecture of the distributed cortical brain networks linked to the human parahippocampal, perirhinal and entorhinal cortices.

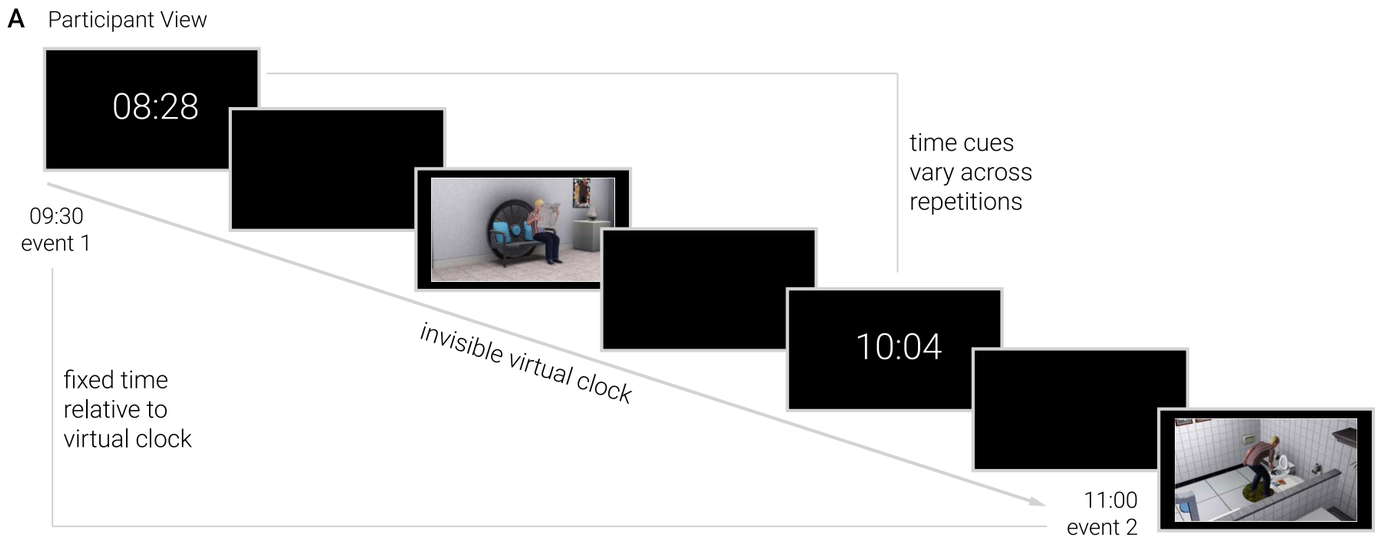
4.2 Research Area TIME

4.2.1 Mnemonic construction and representation of temporal structure in the hippocampal formation

Belllmund, J. L. S.[1], Deuker, L.[2], Montijn, N. D.[3], & Doeller, C. F.[1,4,5]

[1] Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany[2], [2] Donders Institute for Brain, Cognition and Behaviour, Radboud University, Nijmegen, the Netherlands, [3] Department of Clinical Psychology, Utrecht University, Utrecht, the Netherlands, [4] Kavli Institute for Systems Neuroscience, Centre for Neural Computation, The Egil and Pauline Braathen and Fred Kavli Centre for Cortical Microcircuits, Jebsen Centre for Alzheimer's Disease, Norwegian University of Science and Technology (NTNU), Trondheim, Norway, [5] Wilhelm Wundt Institute for Psychology, Leipzig University, Germany

The hippocampal-entorhinal region supports memory for episodic details, such as temporal relations of sequential events and mnemonic constructions combining experiences for inferential reasoning. However, it is unclear whether hippocampal event memories reflect temporal relations derived from mnemonic constructions, event order, or elapsing time, and whether these sequence representations generalise temporal relations across similar sequences. Here, participants mnemonically constructed times of events from multiple sequences using infrequent cues and their experience of passing time. After learning, event representations in the anterior hippocampus reflected temporal relations based on constructed times. Temporal relations were generalised across sequences, revealing distinct representational formats for events from the same or different sequences. Structural knowledge about time patterns, abstracted from different sequences, biased the construction of specific event times. These findings demonstrate that mnemonic construction and the generalisation of relational knowledge combine in the hippocampus, consistent with the simulation of scenarios from episodic details and structural knowledge (Bellmund, et al., 2022, Nat Comm).



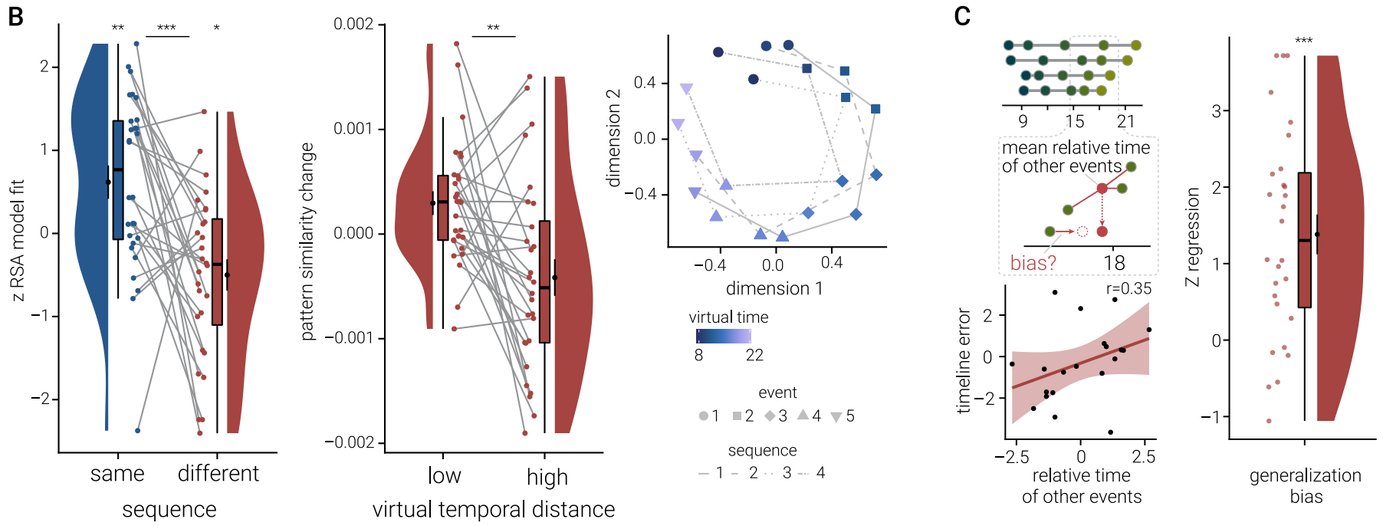


Figure 4.2.1 Representation of temporal structure in the hippocampal formation. In a day learning task, participants learned four sequences (virtual days) of five events each and inferred when events took place relative to a virtual clock. Participants had to mentally construct event times by combining their experience of elapsing real time with the time cues. (B) Left: The anterior hippocampus generalises temporal relations across sequences. Z-values show results of participant-specific linear models quantifying the effect of virtual time for event pairs from the same sequence (blue) and from different sequences (red). Temporal distance is negatively related to hippocampal representational change for event pairs from different sequences. Middle: To illustrate the effect, average pattern similarity change values are shown for across-sequence event pairs that are separated by low and high temporal distances based on a median split. Right: Multidimensional scaling results show low-dimensional embedding of the event sequences. (C) Structural knowledge biases construction of event times. Top left: The generalisation bias quantifies the influence of structural knowledge on the construction of individual event times. For each event, the mean time of events at the same sequence position in the other sequences was calculated to test whether event times were biased towards the relative time of other events. Bottom left: The scatterplot illustrates the generalisation bias for an example participant. Each circle corresponds to one event and the regression line highlights the relationship between the relative time of other events and the errors in constructed event times. Right: The relative time of events from other sequences predicted signed event time construction errors. Positive values indicate that when other events took place late relative to a specific event, the time of that event was estimated to be later than when other events were relatively early.

4.2.2 Rapid encoding of task regularities in the human hippocampus guides sensorimotor timing

Polti, I.*[1,2], Nau, M.*[1,2], Kaplan, R.[1,3], van Wassenhove, V.[4], & Doeller, C. F.[1,2,5]

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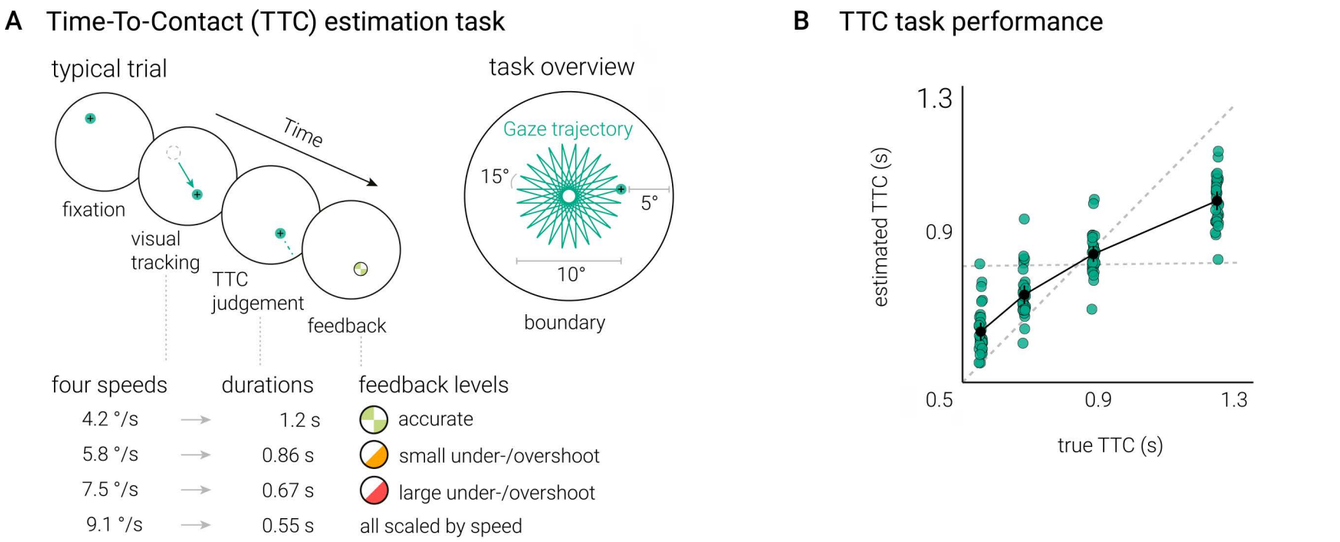
The brain encodes the statistical regularities of the environment in a task-specific yet flexible and generalisable format. Here, we seek to understand this process by bridging two parallel lines of research, one centred on sensorimotor timing, and the other on cognitive mapping in the hippocampal system. By combining functional magnetic resonance imaging (fMRI) with a fast-paced time-to-contact (TTC) estimation task, we found that the hippocampus signalled behavioural feedback received in each trial as well as performance improvements across trials, along with reward-processing regions. Critically, it signalled performance improvements independent from the tested intervals, and its activity accounted for the trial-wise regression-to-the-mean biases in TTC estimation. This is in line with the idea that the hippocampus supports the rapid encoding of temporal context even on short time scales in a behaviour-dependent manner. Our results emphasise the central role of the hippocampus in statistical learning and position it at the core of a brain-wide network updating sensorimotor representations in real time for flexible behaviour (Polti, et al., 2022, eLife).



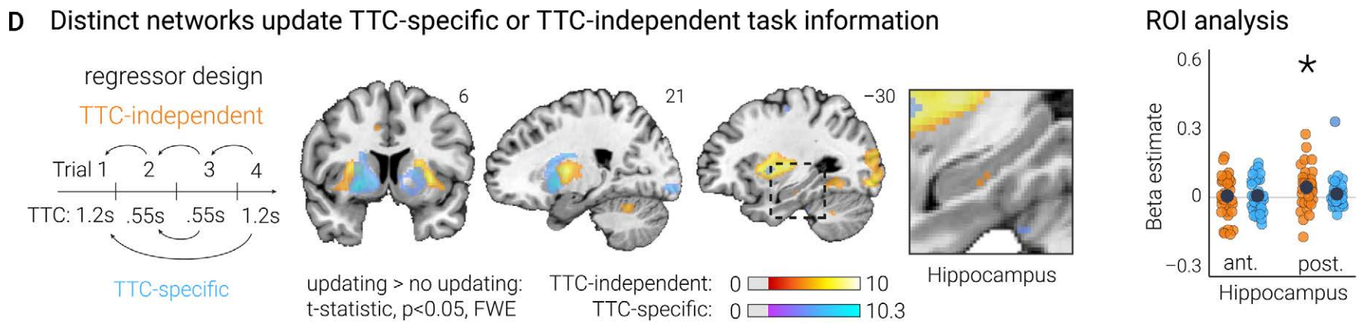


Figure 4.2.2 Encoding of task regularities in the HF. (A) Participants fixated a visual target moving at a constant speed in a predefined direction. Across trials, 24 directions and 4 speeds were tested, leading to 4 different target durations. After the target stopped moving, participants estimated the time when it would have hit a visual boundary, indicated via button click (Time-To-Contact, TTC). (B) Participants' TTC estimates regressed towards the grand-mean of the TTC distribution (horizontal dashed line). (C) Left: Activity in each trial modelled with a separate regressor as a function of feedback received in the previous trial. Right: Independent regions-of-interest (ROI) analysis. Negative values indicate that smaller errors, and higher-accuracy feedback, led to stronger activity. (D) Left: Two parametric regressors per run modelled the improvement in behavioural performance since the last trial independent of the tested TTC (TTC-independent) or the improvement since the last trial when the same target TTC was tested (TTC-specific). Middle: Voxel-wise analysis. Right: ROI analysis.

4.2.3 Entorhinal grid-like signals reflect temporal context for human timing behaviour

Polti, I.*[1,2], Nau, M.*[1,2], Kaplan, R.[1,3], van Wassenhove, V.[4], & Doeller, C. F.[1,2,5]

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An important ability for successful interaction with the environment is the estimation of magnitudes such as the duration of an event. To improve duration estimates, the brain must compensate for sensory uncertainty, which it does by encoding the statistical regularities that link co-occurring stimuli and tasks (i.e., temporal context). The entorhinal cortex (EC) supports the encoding of such task regularities, which has been suggested to rely on grid cells that the EC is known to harbour. On the population level, grid cells exhibit a six-fold rotational symmetry as a function of gaze direction, which is thought to be measurable with functional magnetic resonance imaging (fMRI). Here, we therefore tested whether temporal context modulates grid-like fMRI activity in the human EC, and characterised in detail its relationship to behavioural performance in a time-to-contact (TTC) estimation task. We indeed found that EC activity signalled the accuracy as well as biases in timing behaviour, and that grid-like activity reflected timing errors consistent with temporal-context encoding. Importantly, our findings are well explained by Bayesian models of time perception, suggesting that the human EC contributes to the adaptation of internal timing mechanisms to the temporal statistics of the environment.

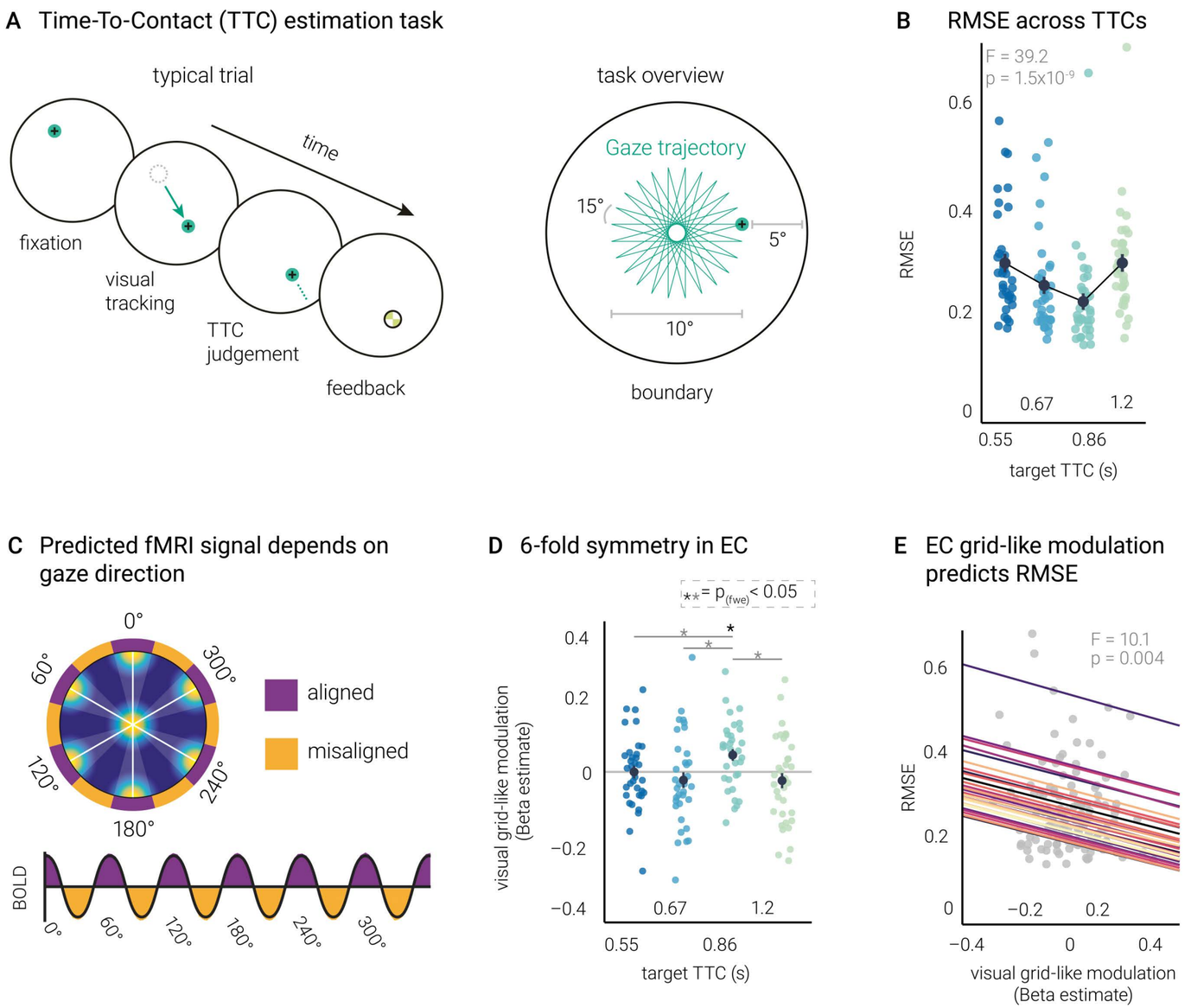

Figure 4.2.3 Grid-like representations for temporal context. (A) Participants fixated a visual target moving at a constant speed in a predefined direction. Across trials, 24 directions and 4 speeds were tested, leading to 4 different target durations. After the target stopped moving, participants estimated the time when it would have hit a visual boundary, indicated via button click (Time-To-Contact, TTC). (B) TTC estimation Root-Mean-Square Error (RMSE) across target TTCs. (C) The hexadirectional signal was cross-validated across data partitions. Putative grid-orientation was estimated using half of the data and then used to contrast orientation-aligned vs. orientation-misaligned gaze movements in the other half (odd vs even runs). (D) Amplitude of the Entorhinal Cortex (EC) hexadirectional signal in held-out data expressed as beta estimates. There were consistent differences in EC fMRI activity for aligned vs. misaligned directions across target TTCs. (E) Stronger within-subject EC visual grid-like modulation predicts lower TTC RMSE. Separate regression lines plotted for each participant (coulor-coded).

4.3 Research Area KNOWLEDGE ACQUISITION & STRUCTURE LEARNING

4.3.1 Mental search of concepts is supported by egocentric vector representations and restructured grid maps

Viganò, S.[1,2], Bayramova, R.[1], Doeller, C. F.*[,1,3,4], & Bottini, R.*[,2]

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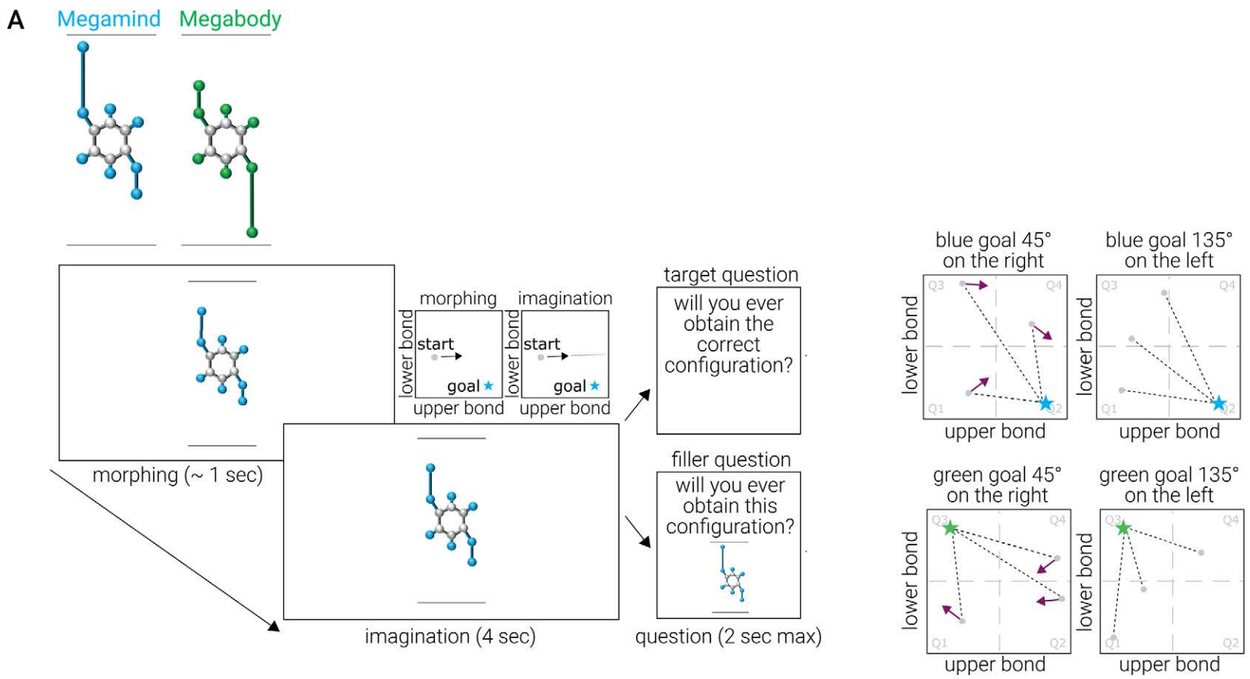
The human hippocampal-entorhinal system is known to represent both spatial locations and abstract concepts in memory in the form of allocentric cognitive maps. Using fMRI, we show that the human parietal cortex evokes complementary egocentric-like vector representations in conceptual spaces during goal-directed mental search, akin to those observable during physical navigation to determine where a goal is located relative to oneself. Concurrently, grid-like representations, a neural signature of allocentric cognitive maps in entorhinal, prefrontal, and parietal cortices, are restructured as a function of conceptual goal proximity, akin to rodent grid cells firing around reward locations during spatial exploration. These brain mechanisms might support flexible and parallel readout of where target conceptual information is stored in memory, capitalising on complementary reference frames.



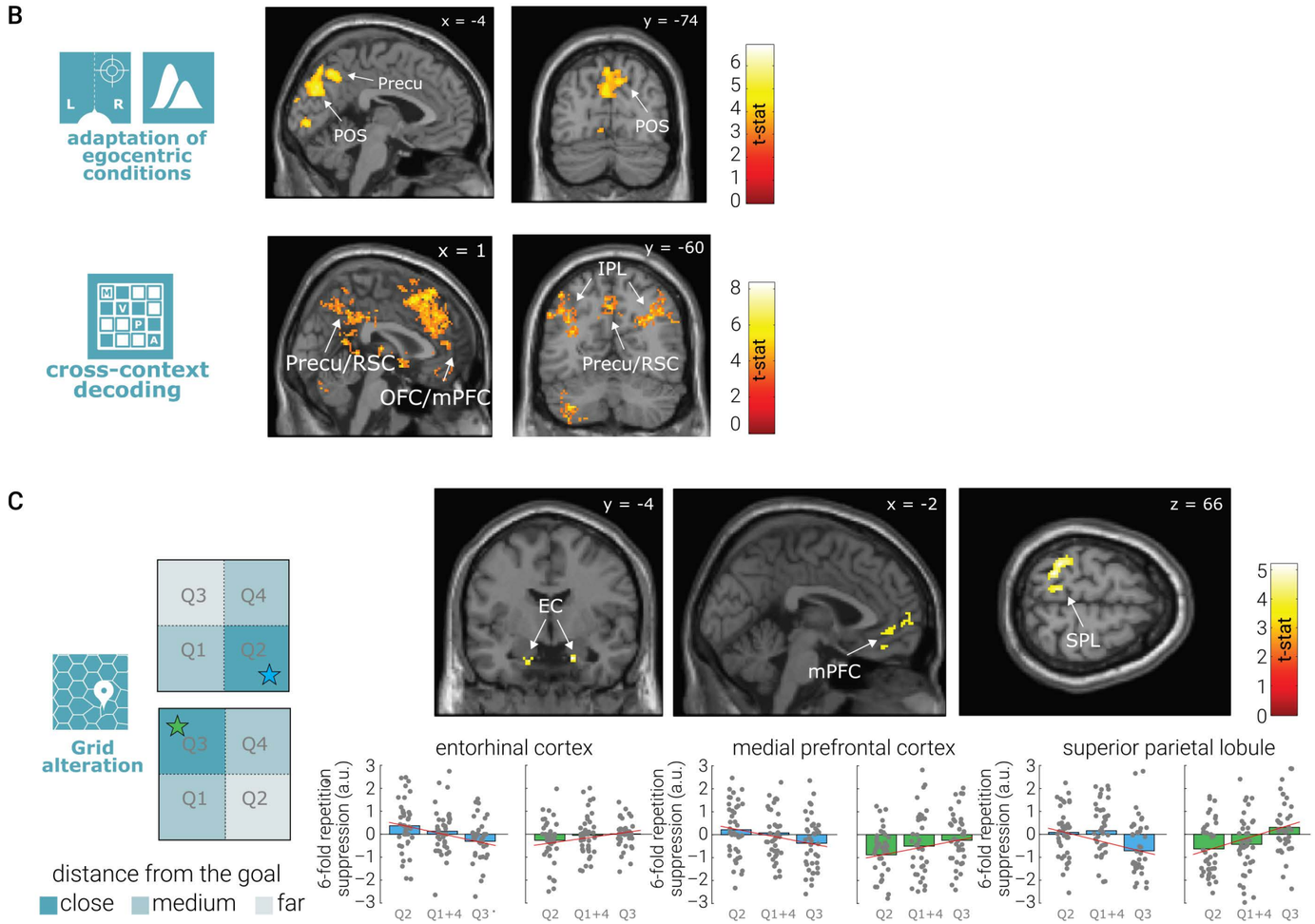


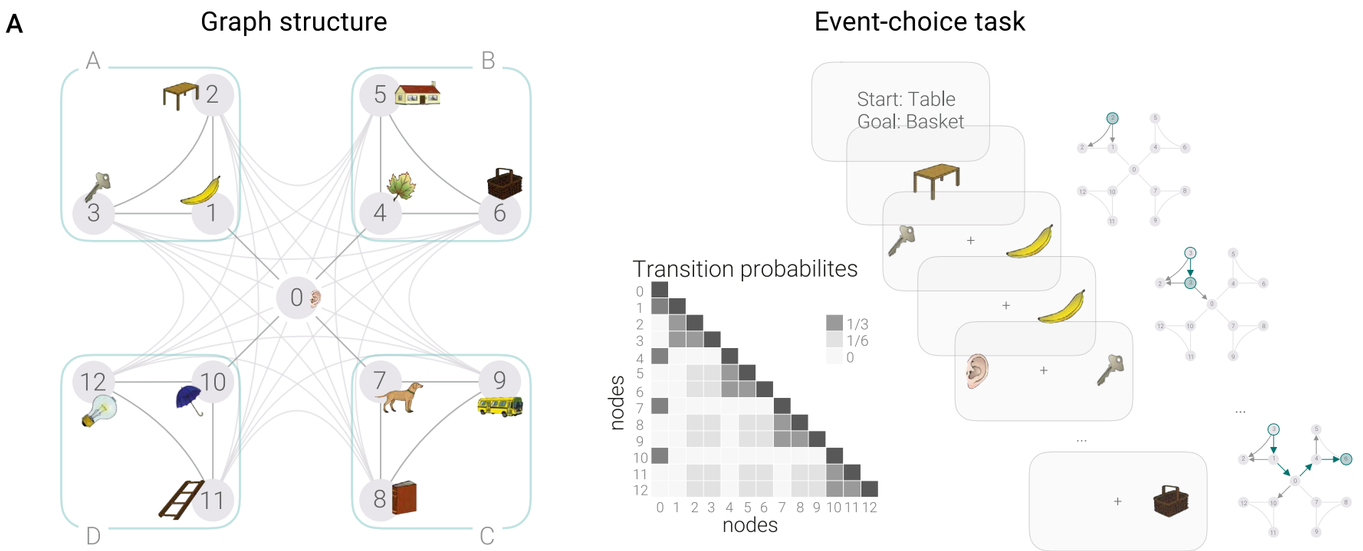
Figure 4.3.1 Egocentric and allocentric concept representations. (A) Participants learned to navigate two conceptual spaces where they had to find two goal "molecules", defined by specific upper bond/lower bond ratios. In doing so, they could have the goal on either the left or right, or they could be close or far from the goal. (B) Both fMRI adaptation and multivariate cross-context decoding revealed that the medial parietal cortex represented the position of the conceptual goal in egocentric-like terms, differentiating whether it was on one side or the other compared to the current stimulation. (C) At the same time, the grid-like signal, a typical signature of allocentric coding, was modulated by goal proximity in the entorhinal cortex, medial prefrontal cortex, and superior parietal lobule, as revealed by fMRI repetition suppression.

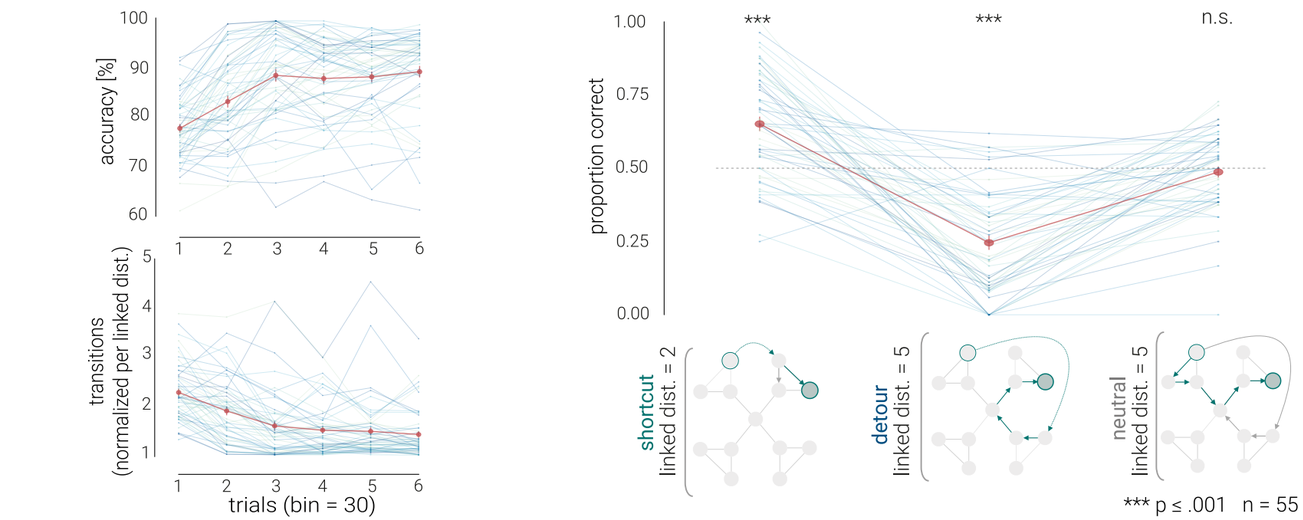
4.3.2 Integrating knowledge about structure and reward contingencies for generalisation and inference

Deilmann, F. F.[1], Theves, S.[1], Garvert, M. M.[1], & Doeller, C. F.[1,2,3]

[1] Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany, [2] Kavli Institute for Systems Neuroscience, Centre for Neural Computation, The Egil and Pauline Braathen and Fred Kavli Centre for Cortical Microcircuits, Jebsen Centre for Alzheimer's Disease, Norwegian University of Science and Technology (NTNU), Trondheim, Norway, [3] Wilhelm Wundt Institute for Psychology, Leipzig University, Germany

The hippocampal-entorhinal system is remarkably efficient in organising relations between sensory stimuli, such as state transition probabilities, in a cognitive map. Such knowledge representation is assumed to enable fast learning of novel relations and the generalisation of reward, likely facilitating goal-directed behaviour. However, in addition to experienced transition probabilities, objects may simultaneously share other types of relational information, such as reward contingencies. This fMRI study investigates how the neural representation of relational knowledge is influenced by a subsequently learned latent reward structure and whether the structural relations between objects still are represented veridically. Participants first acquired knowledge about object relations based on object transitions that follow a hidden graph structure. In a subsequent decision-making task, each object was associated with fluctuating reward values. Critically, two parts of the graph structure shared the same reward contingencies (orthogonal to the initial graph representation). Behavioural data suggest that participants successfully acquire structural knowledge and can utilise it to find shortcuts when transitioning around the graph. Model-based analysis revealed that participants can extract the additional underlying latent reward structure and generalise over states sharing the same reward contingencies. Furthermore, they can apply their acquired structural knowledge to correctly infer current reward values of objects whose values they never directly experienced. Preliminary RSA results revealed hippocampal and vmPFC activation patterns reflecting structure and reward contingency representations. This suggests participants represent both experienced transitions and shared reward contingencies between objects. Moreover, they can combine both types of information for generalisation and inference.





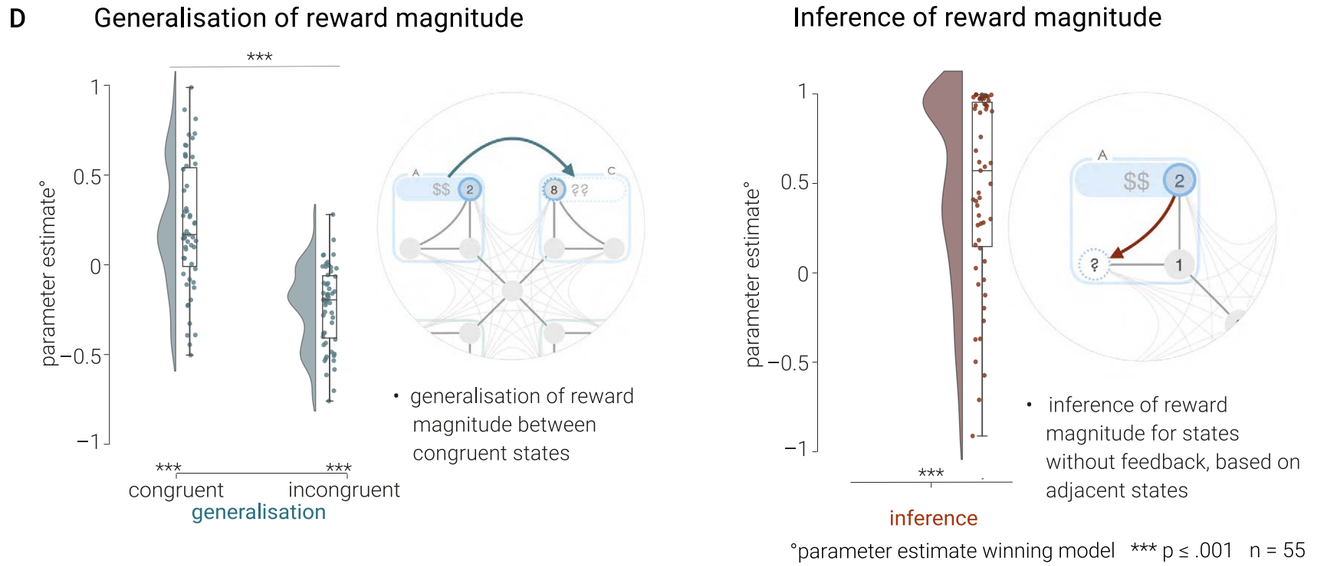


Figure 4.3.2 Representing structure and reward contingencies for generalisation. (A) Structure Learning. Graph structure nodes represent visual objects and edges possible transitions. In the event-choice task participants could choose between two upcoming objects to ultimately reach a goal object. (B) Structure Learning Behaviour. Participants successfully acquired relational knowledge (accuracy and transitions to reach a goal object) and used it to find shortcuts when transitioning around the graph structure (shortcut preference) (C) Value Learning. Each highlighted node was rewarded with a specific value in a 2AFC-task, derived from a hidden reward drift function. Importantly, two clusters share the same reward contingencies (depicted by the same colour) (D) Value Learning Behaviour. Reinforcement-Learning model parameter estimates suggest generalisation of objects' value beliefs for congruent but not for incongruent objects. Inference parameter estimates demonstrate correct inferred value beliefs for objects without feedback, based on adjacent nodes.

4.4 Research Area VALUE-BASED DECISION MAKING

4.4.1 Hippocampal spatio-predictive cognitive maps adaptively guide reward generalisation

Garvert, M. M.[1,3], Saanum, T.[2], Schulz, E.[2], Schuck, N. W.[3], & Doeller, C. F.[1,4,5]

[1] Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany, [2] Max Planck Institute for Biological Cybernetics, Tübingen, Germany, [3] Max Planck Institute for Human Development, Berlin, Germany, [4] Kavli Institute for Systems Neuroscience, Centre for Neural Computation, The Egil and Pauline Braathen and Fred Kavli Centre for Cortical Microcircuits, Jebsen Centre for Alzheimer's Disease, Norwegian University of Science and Technology (NTNU), Trondheim, Norway, [5] Wilhelm Wundt Institute for Psychology, Leipzig University, Leipzig, Germany

The brain forms cognitive maps of relational knowledge, an organising principle thought to underlie our ability to generalise and make inferences. However, how can a relevant map be selected in situations where a stimulus is embedded in multiple relational structures? Here, we find that both spatial and predictive cognitive maps influence generalisation in a choice task, where spatial location determines reward magnitude. Mirroring behaviour, the hippocampus not only builds a map of spatial relationships but also encodes the experienced transition structure. As the task progresses, participants' choices become more influenced by spatial relationships, reflected in a strengthening of the spatial and a weakening of the predictive map. This change is driven by orbitofrontal cortex, which represents the degree to which an outcome is consistent with the spatial rather than the predictive map and updates hippocampal representations accordingly. Taken together, this demonstrates how hippocampal cognitive maps are used and updated flexibly for inference (Garvert et al., in press, Nat Neurosci).

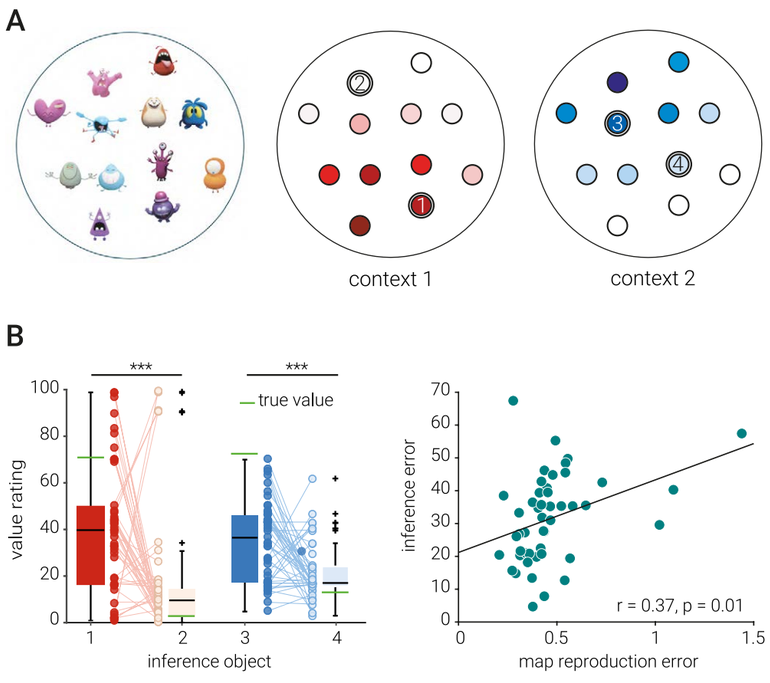


Figure 4.4.1 Hippocampal cognitive maps guide reward generalisation. (A) Experimental design: Spatial position of monsters during the virtual reality navigation task and value distribution associated with the same monsters in context 1 and 2 in the choice task of the experiment. Darker colours indicate higher values. Numbered circles indicate the location of inference stimuli that were never presented during the choice task. (B) Value rating for the inference stimuli at the end of the study (left). Correlation between the map reproduction and inference ratings (right).

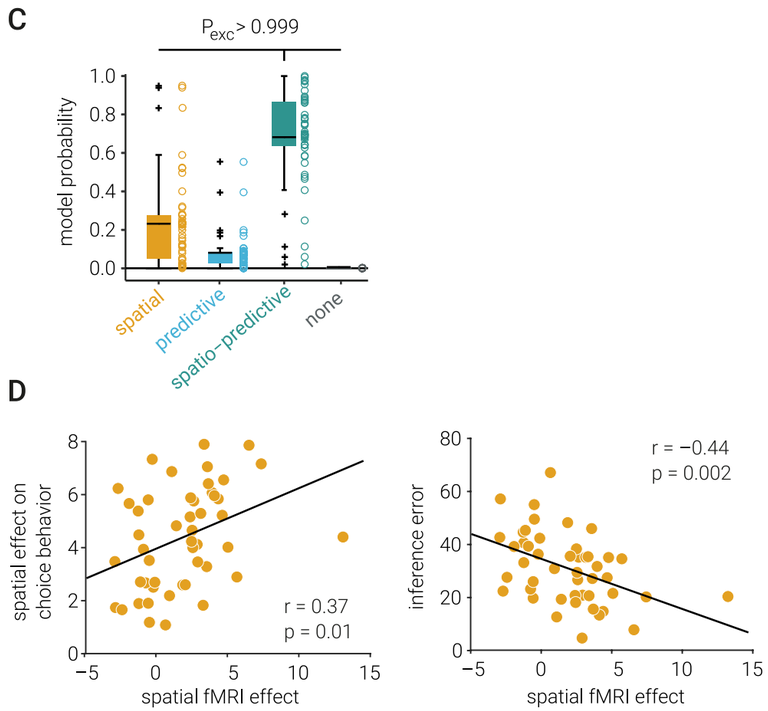


Figure 4.4.1 (C) Modelling results suggest that participants generalised over spatial and predictive stimulus relationships. The winning model generalises values according to a combination of spatial and predictive relationships between stimuli. (D) fMRI results: Spatial and predictive cognitive maps in the hippocampal formation are related to generalisation and inference. Left: Correlation between the spatial fMRI cross-stimulus enhancement effect and the spatial effects governing decisions in the choice task. Right: Correlation between the spatial fMRI cross-stimulus enhancement effect and the inference error.

4.4.2 Representing values for prospective decision making

Nitsch, A.[1], Garvert, M. M.[1], Bellmund, J. L. S.[1], Schuck, N. W.[2], & Doeller, C.F.[1,3,4]

[1] Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany, [2] Max Planck Institute for Human Development, Berlin, Germany, [3] Kavli Institute for Systems Neuroscience, Centre for Neural Computation, The Egil and Pauline Braathen and Fred Kavli Centre for Cortical Microcircuits, Jebsen Centre for Alzheimer's Disease, Norwegian University of Science and Technology (NTNU), Trondheim, Norway, [4] Wilhelm Wundt Institute for Psychology, Leipzig University, Leipzig, Germany

Everyday decisions require us to predict how valuable different choice options will be in the future. Prediction of future values is facilitated by an internal model representing state transitions and associated reward contingencies in a task. Recently, it has been suggested that the hippocampal-entorhinal system represents relationships between states in a cognitive map, enabling prediction of future states by facilitating the computation of distances and directions. It is unclear whether such a map-like representation would code for abstract value dimensions during prospective decision making. Here, we aim to test the idea that the hippocampal-entorhinal system integrates relational information about changing values of choice options in an abstract value space. To this end, we combined fMRI with a novel decision task which required participants to track and predict changing values of two options over a sequence of time points. Crucially and unbeknownst to participants, such a sequence formed a trajectory through an abstract two-dimensional value space. Recognising the direction of the particular trajectory allowed for prediction of future values of the two options. Behavioural results show that participants are able to integrate and extrapolate changes along the two value dimensions to guide prospective decision making. Preliminary fMRI results reveal an entorhinal grid code while participants traverse the abstract value space, suggesting the formation of a map-like representation. Ultimately, this study can help us elucidate whether hippocampal-entorhinal cognitive maps support efficient prospective value-based decision making.

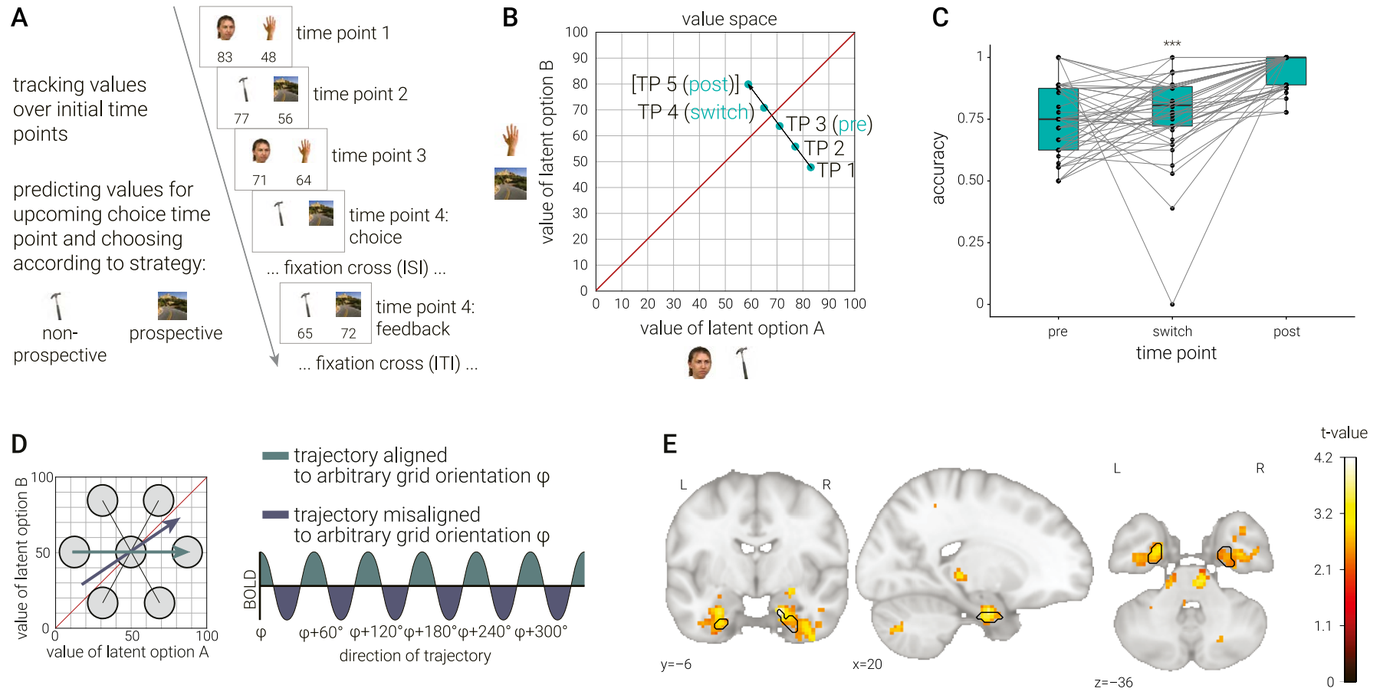


Figure 4.4.2 Representing values for prospective decision making. (A) In the decision task, participants track and predict changing values of two latent options A and B over a sequence of time points. Their goal is to choose the option which will be more valuable at a future choice time point (prospective vs. non-prospective decision). (B) A sequence of time points forms a trajectory through an abstract two-dimensional value space. Trajectories crossing the diagonal of the value space involve switches of the more valuable option (switch trajectory). (C) Participants detected switches significantly more often than expected by chance. (D) The regular hexagonal firing pattern of grid cells translated to a hexadirectional signal in fMRI as a function of trajectories through space. (E) Grid-like hexadirectional modulation in entorhinal cortex during trajectories in value space (black outline depicting significance after entorhinal small volume correction)

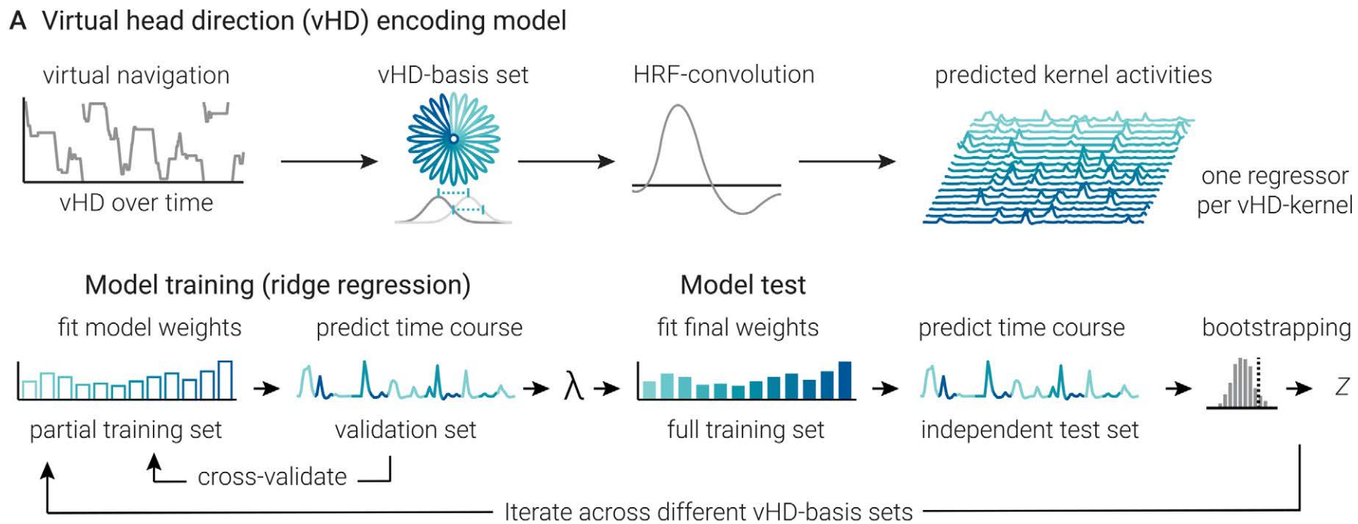
4.5 Research Area VISION AND NEURO-AI

4.5.1 Behaviour-dependent directional tuning in the human visual-navigation network

Nau, M.[1,2], Navarro Schröder, T.[1], Frey, M.[1,2], & Doeller, C. F.[1,2,3]

[1] Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany, [2] Kavli Institute for Systems Neuroscience, Centre for Neural Computation, The Egil and Pauline Braathen and Fred Kavli Centre for Cortical Microcircuits, Jebsen Centre for Alzheimer's Disease, Norwegian University of Science and Technology (NTNU), Trondheim, Norway, [3] Wilhelm Wundt Institute for Psychology, Leipzig University, Germany

The brain derives cognitive maps from sensory experience that guides memory formation and behaviour. Despite extensive efforts, it still remains unclear how the underlying population activity unfolds during spatial navigation and how it relates to memory performance. To examine these processes, we combined 7T-fMRI with a kernel-based encoding model of virtual navigation to map world-centred directional tuning across the human cortex. First, we present an in-depth analysis of directional tuning in visual, retrosplenial, parahippocampal and medial temporal cortices. Second, we show that tuning strength, width, and topology of this directional code during memory-guided navigation depend on successful encoding of the environment. Finally, we show that participants' locomotory state influences this tuning in sensory and mnemonic regions such as the hippocampus. We demonstrate a direct link between neural population tuning and human cognition, where high-level memory processing interacts with network-wide visuospatial coding in the service of behaviour (Nau, et al., 2020, Nat Comm).



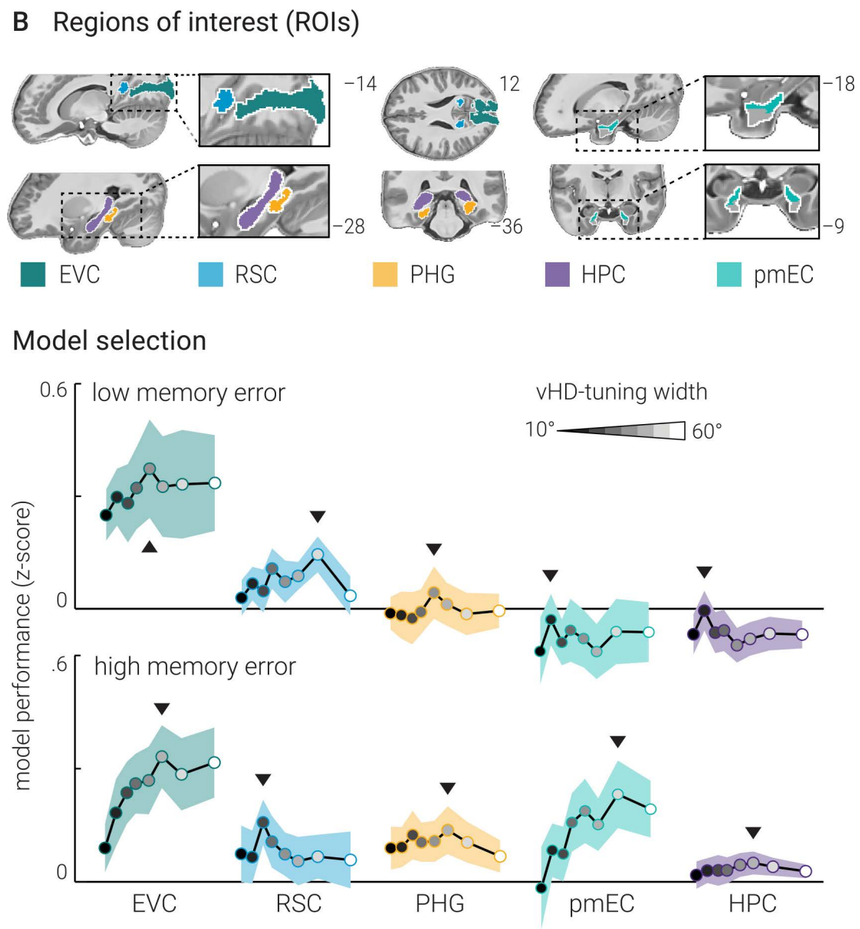


Figure 4.5.1 Directional tuning revealed by a kernel-based encoding model of virtual navigation. (A) Top: Virtual head direction (vHD) encoding model. We modelled vHD using multiple basis sets of circular–Gaussian kernels covering the full 360°. Given the observed vHD, we generated predicted time courses (regressors) for all kernels in each basis set. The resulting regressors were convolved with the hemodynamic response function to link the kernel activity over time to the fMRI signal. Bottom: Model training. We estimated voxel-wise weights for each regressor in a training data set. Weights were estimated in the partial training set and then used to predict the time course of the validation set. Model test: we used the final model weights to predict each voxel's time course in an independent test set and additionally converted model performance into Z scores via bootstrapping for statistical testing. (B) Region-of-interest (ROI) analysis. For scene-processing and navigation regions (early visual cortex (EVC), retrosplenial cortex (RSC), parahippocampal gyrus (PHG), posteromedial entorhinal cortex (pmEC), and the hippocampus (HPC)), we plot the model performance (Z score) at the ROI level for all basis sets. Each dot represents the group-average model performance for one basis set, with darker colours representing narrow kernels and lighter colours representing wider kernels. The following kernel widths were tested: 10°, 15°, 20°, 24°, 30°, 36°, 45°, and 60°. The black triangles mark the basis set that leads to the optimal model performance.

4.5.2 Magnetic resonance-based eye tracking using deep neural networks

Frey, M.*[1,2], Nau, M.*[1,2], & Doeller, C. F.[1,2,3]

[1] Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany, [2] Kavli Institute for Systems Neuroscience, Centre for Neural Computation, The Egil and Pauline Braathen and Fred Kavli Centre for Cortical Microcircuits, Jebsen Centre for Alzheimer's Disease, Norwegian University of Science and Technology (NTNU), Trondheim, Norway, [3] Wilhelm Wundt Institute for Psychology, Leipzig University, Leipzig, Germany, * equal contribution

Viewing behaviour provides a window into many central aspects of human cognition and health and it is an important variable of interest or confound in many functional magnetic resonance imaging (fMRI) studies. To make eye tracking freely and widely available for MRI research, we developed DeepMReye, a convolutional neural network (CNN) that decodes gaze position from the magnetic resonance signal of the eyeballs. It performs cameraless eye tracking at subimaging temporal resolution in held-out participants with little training data and across a broad range of scanning protocols. Critically, it works even in existing datasets and when the eyes are closed. Decoded eye movements explain network-wide brain activity also in regions not associated with oculomotor function. This work emphasises the importance of eye tracking for the interpretation of fMRI results and provides an open source software solution that is widely applicable in research and clinical settings (Frey, et al., 2021, Nat Neurosci).

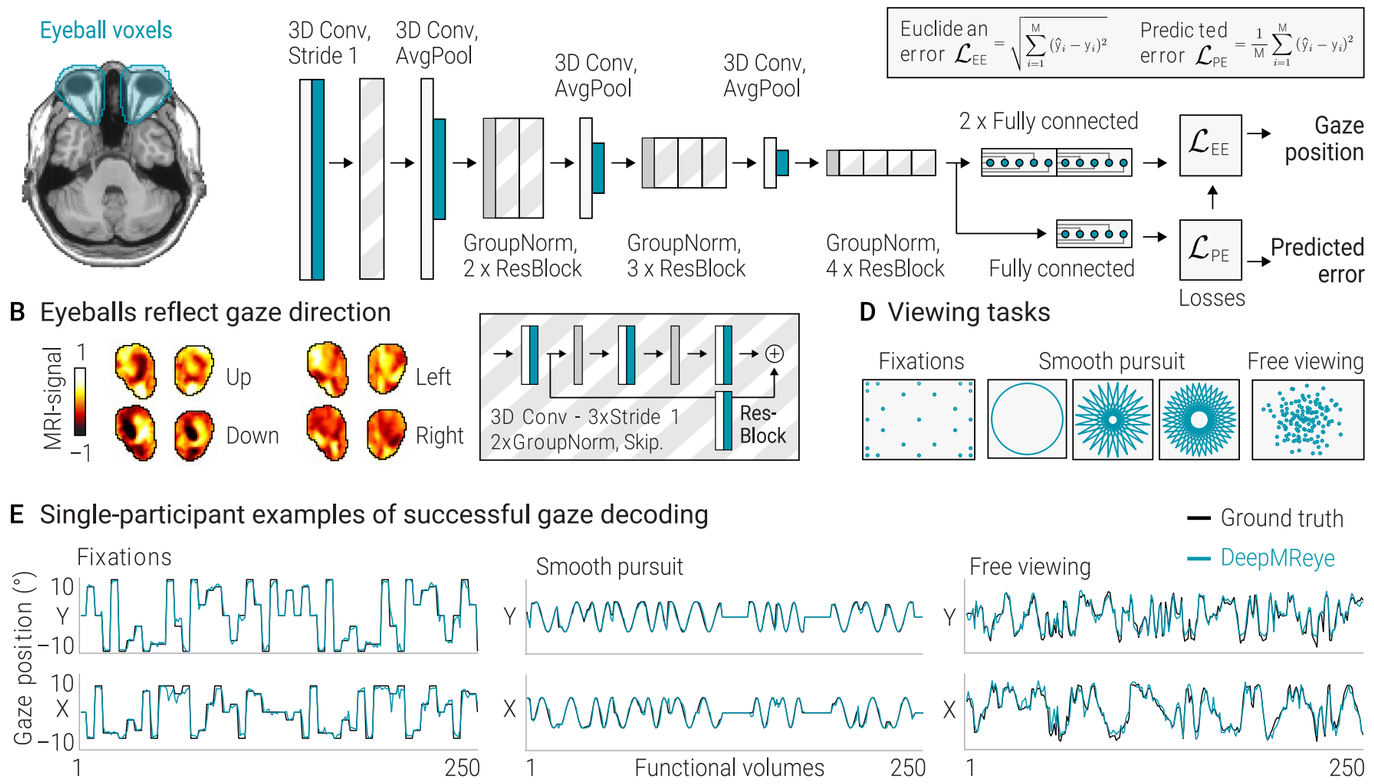


Figure 4.5.2 Eye tracking using deep neural networks. Model architecture and input. (A) Manually delineated eye masks superimposed on a structural template. (B) Eyeball MR signal reflects gaze direction. The normalised MR signal of eye mask voxels of a sample participant who fixated on a target on the left, right, top or bottom of the screen are plotted. (C) CNN architecture. The model takes the eye mask

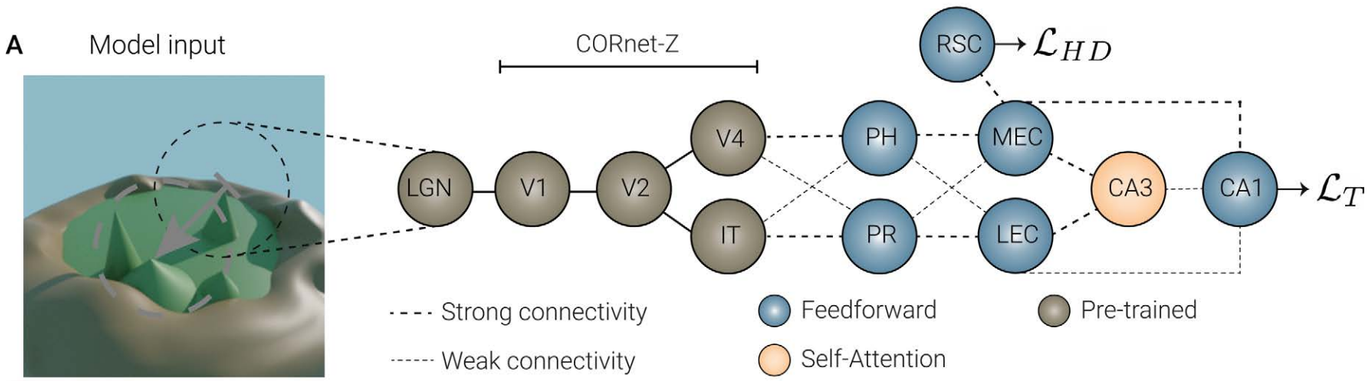
voxels as three-dimensional (3D) input and predicts gaze position as a two-dimensional (2D; X, Y) regression target. It performs a series of 3D convolutions (3D Conv) with group normalisations (GroupNorm) and spatial downsampling via average pooling (AvgPool) in between. Residual blocks (ResBlock) comprise an additional skip connection. The model is trained across participants using a combination of two loss functions: (1) the Euclidean Error (EE) between the predicted and the true gaze position and (2) the error between the EE and a predicted error (PE). It outputs gaze position and the PE as a decoding confidence measure for each repetition time (TR). (D) Schematics of viewing priors. We trained and tested the model on data from 268 participants performing fixations, smooth pursuit on circular or star-shaped trajectories and free viewing. (E) Across-participant gaze decoding results. Single-participant examples of successful gaze decoding for three viewing behaviours.

4.5.3 Probing neural representations of scene perception in a hippocampally dependent task using artificial neural networks

Frey, M.[1,2], Doeller, C. F.[1,2,3] & Barry, C.[4]

[1] Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany, [2] Kavli Institute for Systems Neuroscience, Centre for Neural Computation, The Egil and Pauline Braathen and Fred Kavli Centre for Cortical Microcircuits, Jebsen Centre for Alzheimer's Disease, Norwegian University of Science and Technology (NTNU), Trondheim, Norway, [3] Wilhelm Wundt Institute for Psychology, Leipzig University, Germany , [4] Research Department of Cell and Developmental Biology, UCL, UK

Deep artificial neural networks (DNNs) trained through backpropagation provide effective models of the mammalian visual system, accurately capturing the hierarchy of neural responses through primary visual cortex to inferior temporal cortex (IT). However, the ability of these networks to explain representations in higher cortical areas is relatively lacking and considerably less well researched. For example, DNNs have been less successful as a model of the egocentric to allocentric transformation embodied by circuits in retrosplenial and posterior parietal cortex. We describe a novel virtual environment inspired by a hippocampally dependent task, designed to probe the ability of DNNs to transform scenes viewed from different egocentric perspectives. Using a network architecture inspired by the connectivity between temporal lobe structures and the hippocampus, we demonstrate that DNNs trained using a triplet loss can learn this task. Moreover, by enforcing a factorised latent space, we were able to split information propagation into "what" and "where" pathways, which we use for the reconstruction of the input. This allowed us to beat the state-of-the-art for unsupervised object segmentation on the CATER, MOVi-A and MOVi-B benchmarks.



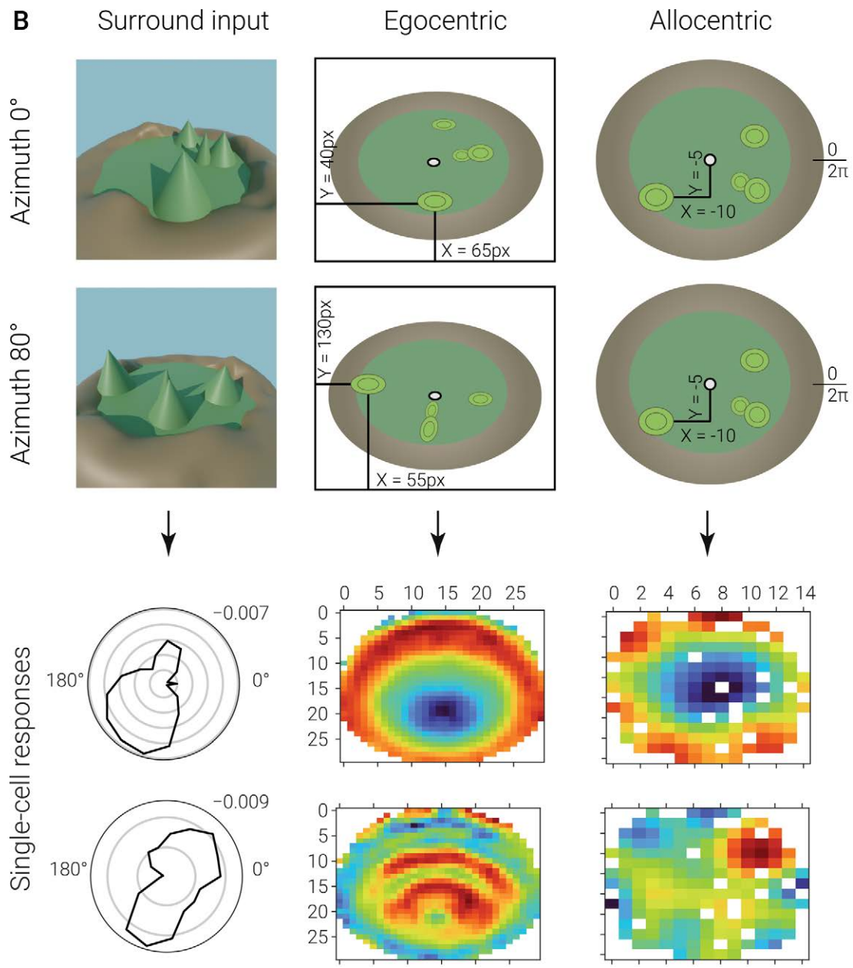


Figure 4.5.3 Using artificial neural networks to understand scene representation. (A) Task design and model architecture. We adapt the 4-Mountains-Test using a simplified task design with one to four objects with circular symmetry and a global reference frame. We then designed a biologically inspired model architecture, for which we took visual cortex responses from pre-trained CORnet-Z and fed them through perirhinal (PR) and parahippocampal (PH) cortices. Retrosplenial cortex uses an auxiliary loss to decode head direction. Medial entorhinal (MEC) and lateral entorhinal cortex (LEC) use a disentangled latent space to separate object from location information. Both are integrated within the hippocampus, with CA3 using a self-attention layer across both time and space. (B) Single-cell representations across different reference frames. Top: Illustration of egocentric and allocentric schemas. The left side shows two snapshots from the same scene using different viewpoints. The panels to the right depict the egocentric and allocentric schema for the respective snapshot. Black lines indicate screen coordinates for the same object in the egocentric view and world coordinates in the allocentric view. Note that by definition the allocentric, world-centred schema is the same for both snapshots. The two panels on the right show reference frames for the 'within' snapshots, for either the position (left) or the observer's head direction (right). Bottom) Example representations from nodes within the network, across each reference frame, showing activity of two neurons for azimuth, egocentric object position and allocentric object position.

Congresses, Workshops, and Symposia

2020

- Doeller, C. F., & Garvert, M. (regular). *Mind Meeting Seminar Series.* Seminar Series. Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany.

2021

- Doeller, C. F., & Theves, S. (regular). *Mind Meeting Seminar Series.* Seminar Series. Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany.
- Kim, M. (July). *Experimental Design*. Workshop. 10th IMPRS NeuroCom Summer School in Cognitive Neuroscience. International Max Planck Research School on Neuroscience of Communication: Function, Structure, and Plasticity (IMPRS NeuroCom), Max Planck Institute for Human Cognitive and Brain Sciences & ICN, Leipzig & London, Germany & UK. Virtual.
- Pettini, L., Rapp, J., Jostock, E., Kriebel, H., & Schwarzenbeck, H. (October). *Max Planck School Day*. Harnack Haus, Berlin, Germany.
- Morgan T., Vizioli L. (main organisers), Bergmann J., Berman A., Bollmann S., Chaimow D., Nothnagel N., Scheeringa R., Huber R., & van Kemenade B. (board members) (April and September). *Third and fourth layer fMRI dinner*. Virtual.

2022

- Doeller, C. F., & Theves, S. (regular). *Mind Meeting Seminar Series.* Seminar Series. Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany.
- Kim, M. (June). *Model-based fMRI: a non-invasive way to probe the grid code in the human brain.* Workshop. 11th IMPRS NeuroCom Summer School in Cognitive Neuroscience. International Max Planck Research School on Neuroscience of Communication: Function, Structure, and Plasticity (IMPRS NeuroCom), Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany.
- Barnaveli, I. (July). *Virtual Reality in Neuroscience Research*. Workshop. Max Planck School of Cognition, Leipzig, Germany.
- Seung, S., & Gramann K. (June). *Mobile Brain-Body Imaging Workshop*. Schwarz Center of Cognitive Neuroscience, UC San Diego, USA.
- Pettini, L. (September). *Max Planck School Day*. Harnack Haus, Berlin, Germany.

Degrees

PhD Theses

2020

- Nau, M. *Perception and the Cognitive Map: Deriving a stable world from visual inputs*. Norwegian University of Sciences and Technology (NTNU), Trondheim, Norway.
- Theves, S. *Mapping conceptual knowledge acquisition in the hippocampal system.* Radboud University, Nijmegen, the Netherlands.

2021

- de Haas, N. *Mapping space, episodes and values in the hippocampus.* Radboud University, Nijmegen, the Netherlands.
- Syversen, I. F. *Application of advanced MRI methods in cancer and neuroimaging.* Norwegian University of Science and Technology (NTNU), Trondheim, Norway.
- Huber, S. A. *Functional Parcellation of the Human Hippocampus.* University of Regensburg, Germany (MD doctoral thesis project supervision).

2022

- Ottink, L. *Mental maps with and without vision: Forming cognitive maps of space based on the visual and haptic senses.* Radboud University, Nijmegen, the Netherlands.

Appointments

2020

- Garvert, M. *Associate Fellow of the ZiF research group 'Cognitive behavior of humans, animals, and machines: A situation model perspective'*. University of Bielefeld, Germany.

2021

- Navarro Schröder, T. *Associate Professor*. Kavli Institute for Systems Neuroscience, Norwegian University of Science and Technology (NTNU), Trondheim, Norway.
- Theves, S. *Minerva Fast Track Research Group Leader* (awarded 2021; starting 2022). Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany.

2022

- Doeller, C. F. *Honorary Professor of Cognitive Neuroscience of Learning and Memory*. Technical University (TU) Dresden, Germany (official start 2023).
- Doeller, C. F. *Board member of the International Max Planck Research School on Cognitive NeuroImaging (IMPRS CoNI)*, Max Planck Institute for Cognitive and Brain Sciences, Leipzig, Germany.

Awards

2020

- Nau, M. *Elsevier/Vision Research Award*. Vision Science Society (VSS), USA.
- Nau, M. *Trainee Professional Development Award*. Society for Neuroscience (SfN), Washington, D.C., USA.

2021

- Kim, M. *Group Award for best experimental design*. IMPRS Summer School 2021, London, UK (virtual).
- Nau, M. *Invited participant at the 4th World Laureate Forum*. Shanghai, China.
- Nau, M. *Otto Hahn Medal*. Max Planck Society, Munich. Germany.
- Theves, S. *Invited participant at the 4th World Laureate Forum*. Shanghai, China.
- Theves, S. *Otto Hahn Medal*. Max Planck Society, Munich, Germany.
- Schäfer, T. *Poster Award*. IMPRS Summer School 2021, London, UK (virtual).

2022

- Bécu, M. *selected for Kavli NDI-X Speaker Series*: *"Modulation of object and geometry spatial coding in human aging"*. Kavli NDI Johns Hopkins University, School of Medicine, Baltimore, MD, US.
- Kim, M. *European Brain and Behaviour Society Travel Award.* European Brain and Behaviour Society, Lausanne, Switzerland.
- Theves, S. *Postdoctoral Fellow Award*. Annual Meeting of the Society for Cognitive Neuroscience, San Francisco, US.
- Doeller, C. F. *Elected member of the Royal Norwegian Society of Sciences and Letters.* Trondheim, Norway (official start 2023).

Publications

Books & Book Chapters

de Haas, A. N. (2021). *Mapping space, episodes and values in the hippocampus*. Nijmegen, the Netherlands: Radboud University.

Jeung, S., Hilton, C., Berg, T., Gehrke, L., & Gramann, K. (2022). Virtual reality for spatial navigation. In *Current Topics in Behavioral Neurosciences*. https://doi.org/10.1007/7854_2022_403

Julian, J. B., & Doeller, C. F. (2020). Context in spatial and episodic memory. In D. Poeppel, G. R. Mangun, & M. S. Gazzaniga (Eds.), *The Cognitive Neurosciences* (6th ed., pp. 217–232). Cambridge, MA: MIT Press.

Nau, M. (2020). *Perception and the cognitive map: Deriving a stable world from visual inputs*. Trondheim, Norway: Norwegian University of Science and Technology.

Ottink, L. (2022). *Mental maps with and without vision: Forming cognitive maps of space based on the visual and haptic senses*. Nijmegen, the Netherlands: Donders Institute for Brain, Cognition and Behaviour, Radboud University.

Sonntag, H. (2020). The effect of uncertainty in MEG-to-MRI coregistrations on MEG inverse problems. *MPI Series in Human Cognitive and Brain Sciences*: Vol. 204. Leipzig: Max Planck Institute for Human Cognitive and Brain Sciences.

Syversen, I. F. (2021). *Applications of advanced MRI methods in cancer and neuroimaging*. Trondheim, Norway: Norwegian University of Science and Technology.

Theves, S. (2020). *Mapping conceptual knowledge acquisition in the hippocampal system*. Nijmegen, the Netherlands: Donders Institute for Brain, Cognition and Behaviour, Radboud University.

Theves, S., Grande, X., Düzel, E., & Doeller, C. F. (in press). Pattern completion and the Medial Temporal Lobe Memory System. In *Oxford Handbook of Human Memory*. Oxford: Oxford University Press.

Journal Articles

Baram, A. B., Muller, T. H., Nili, H., Garvert, M., & Behrens, T. E. J. (2021). Entorhinal and ventromedial prefrontal cortices abstract and generalize the structure of reinforcement learning problems. *Neuron*, *109*(4), 713–723.e7. https://doi.org/10.1016/j.neuron.2020.11.024

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Bellmund, J. L. S., de Cothi, W., Ruiter, T. A., Nau, M., Barry, C., & Doeller, C. F. (2020). Deforming the metric of cognitive maps distorts memory. *Nature Human Behaviour*, *4*(2), 177–188. https://doi.org/10.1038/s41562-019-0767-3

Bellmund, J. L. S., Deuker, L., Montijn, N. D., & Doeller, C. F. (2022). Mnemonic construction and representation of temporal structure in the hippocampal formation. *Nature Communications*, *13*(1). https://doi.org/10.1038/s41467-022-30984-3

Bellmund, J. L. S., Polti, I., & Doeller, C. F. (2020). Sequence memory in the hippocampal-entorhinal region. *Journal of Cognitive Neuroscience*, *32*(11), 2056–2070. https://doi.org/10.1162/jocn_a_01592

Bottini, R., & Doeller, C. F. (2020). Knowledge across reference frames: Cognitive maps and image spaces. *Trends in Cognitive Sciences*, *24*(8), 606–619. https://doi.org/10.1016/j.tics.2020.05.008

Bottini, R., & Doeller, C. F. (2020). Language experience in cognitive maps and image spaces. *Trends in Cognitive Sciences*, *24*(11), 855–856. https://doi.org/10.1016/j.tics.2020.08.003

Brahms, M., Heinzel, S., Rapp, M., Reisner, V., Wahmkow, G., Rimpel, J., Schauenburg, G., Stelzel, C., & Granacher, U. (2021). Cognitive-postural multitasking training in older adults: Effects of input-output modality mappings on cognitive performance and postural control. *Journal of Cognition*, *4*(1). https://doi.org/10.5334/joc.146

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Ortiz-Tudela, J., Bergmann, J., Bennett, M., Ehrlich, I., Muckli, L., & Shing, Y.-L. (2022). Concurrent contextual and time-distant mnemonic information co-exist as feedback in the human visual cortex. *NeuroImage*. https://doi.org/10.1016/j.neuroimage.2022.119778

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Petković, B., Ziolkowski, M., Kutschka, H., Toepfer, H., & Haueisen, J. (2022). Accuracy assessment of simplified computation of active and passive magnetic shielding for optically pumped magnetometers. *IEEE Transactions on Magnetics*, *58*(9). https://doi.org/10.1109/TMAG.2022.3161736

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Reznik, D., Guttman, N., Buaron, B., Zion-Golumbic, E., & Mukamel, R. (2021). Action-locked neural responses in auditory cortex to self-generated sounds. *Cerebral Cortex*, *31*(12), 5560–5569. https://doi.org/10.1093/cercor/bhab179

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Thomas, L., Lockwood, P. L., Garvert, M., & Balsters, J. H. (2022). Contagion of temporal discounting value preferences in neurotypical and autistic adults. *Journal of Autism and Developmental Disorders*, *52*(2), 700–713. https://doi.org/10.1007/s10803-021-04962-5

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Figure 4.1.2

Adapted from Bellmund, J. L. S., Cothi, W., de Ruiter, T. A., Nau, M., Barry, C.*, & Doeller, C. F.* (2020). Deforming the metric of cognitive maps distorts memory. *Nature Human Behaviour*, 4(2), 177–188

Figure 4.1.3

Adapted from Kim, M., & Doeller, C. F. (2022). Adaptive cognitive maps for curved surfaces in the 3D world. *Cognition*, 225, 105-126

Figure 4.2.1

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Figure 4.2.2

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Figure 4.4.1

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Figure 4.5.1

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Figure 4.5.2

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5.1

Dr Roland G. Benoit

Max Planck Research Group Adaptive Memory

(commenced July 2016)

Our research seeks to understand how the human memory systems retain and use knowledge of the past in an adaptive manner. Specifically, we focus on three research areas:

(i) Memory suppression

Unpleasant experiences often turn into memories that involuntarily intrude into our awareness. However, we can actively control such unwanted memories by suppressing their retrieval (e.g., Benoit et al., 2015). In recent years, we have examined the sustained consequences of this process. Our meta-analysis corroborates that suppression does not merely prevent intrusions in a transient fashion. Over time, it also causes forgetting. Though, this is deficient in individuals with depression and anxiety (Stramaccia et al., 2021). Suppression induces forgetting by hindering the reinstatement of previously suppressed neural representations (Meyer, & Benoit, 2022).

(ii) Episodic simulation

Our memory systems allow us to imagine the possible future. They provide stored details and the constructive processes to recombine these details into simulations of novel episodes (Schacter, Benoit, & Szpunar, 2017). Such episodic simulation fosters farsighted decisions (Figure 5.1.1; Rösch et al., 2022). We also learn from imagined events much like we learn from actual events (Benoit et al., 2019; Paulus et al., 2022). Our research examines the computational and neural basis of such simulation-based learning (Figure 5.1.2).

(iii) The core network

Episodic memory and simulation are largely based on a common core network. Our work is focused on understanding the interactions and unique contributions of its individual regions. For example, the medial prefrontal cortex (PFC) encodes schemas of our environment (Benoit et al., 2019). These schemas do not represent the environment in an objective fashion. Instead, they emphasise what is particularly valuable (Paulus et al., 2020). We examine the *de novo* emergence of schemas (Figure 5.1.3) and how they allow us to anticipate the imminent future. We also examine how prior knowledge guides retrieval via interactions between the PFC and the medial temporal lobes (Figure 5.1.4.1 & Figure 5.1.4.2).

Taken together, our research adds to our understanding of the cognitive and neural processes that are fundamentally involved in controlling our memories and in the mental creation of our future.

5.1.1 Promoting farsighted decisions via episodic future thinking: A meta-analysis

Rösch, S. A. [1,2], Stramaccia, D. F. [1], & Benoit, R. G. [1]

[1] Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany, [2] Leipzig University Hospital, Leipzig, Germany

Episodic future thinking (EFT) denotes our capacity to imagine prospective events. It has been suggested to promote farsighted decisions that entail a trade-off between short-term versus long-term gains. This meta-analysis synthesised the evidence for the impact of EFT on intertemporal choices that have monetary or health-relevant consequences. Across 174 effect sizes, from 48 articles, a three-level model yielded a medium-sized effect of g = 0.44, 95% CI [0.33, 0.55]. Notably, this analysis included a substantial number of unpublished experiments, and the effect remained significant following further adjustments for remaining publication bias. We exploited the observed heterogeneity to determine critical core components that moderate the impact of EFT. Specifically, the effect was stronger when the imagined events were positive, more vivid, and related to the delayed choice. We further obtained evidence for the contribution of the episodicity and future-orientedness of EFT. These results indicate that the impact of EFT cannot simply be accounted for by other modes of prospection (e.g., semantic future thinking). Of note, EFT had a greater impact in samples characterised by choice impulsivity (e.g., in obesity), suggesting that EFT can ameliorate maladaptive decision making. It may accordingly constitute a beneficial intervention for individuals who tend to make myopic decisions. Our analyses moreover indicated that the effect is unlikely to merely reflect demand characteristics. This meta-analysis thus highlights the potential of EFT in promoting long-term goals, a finding that extends from the laboratory to real-life decisions. All data and analysis scripts are publicly available at the Open Science Framework.

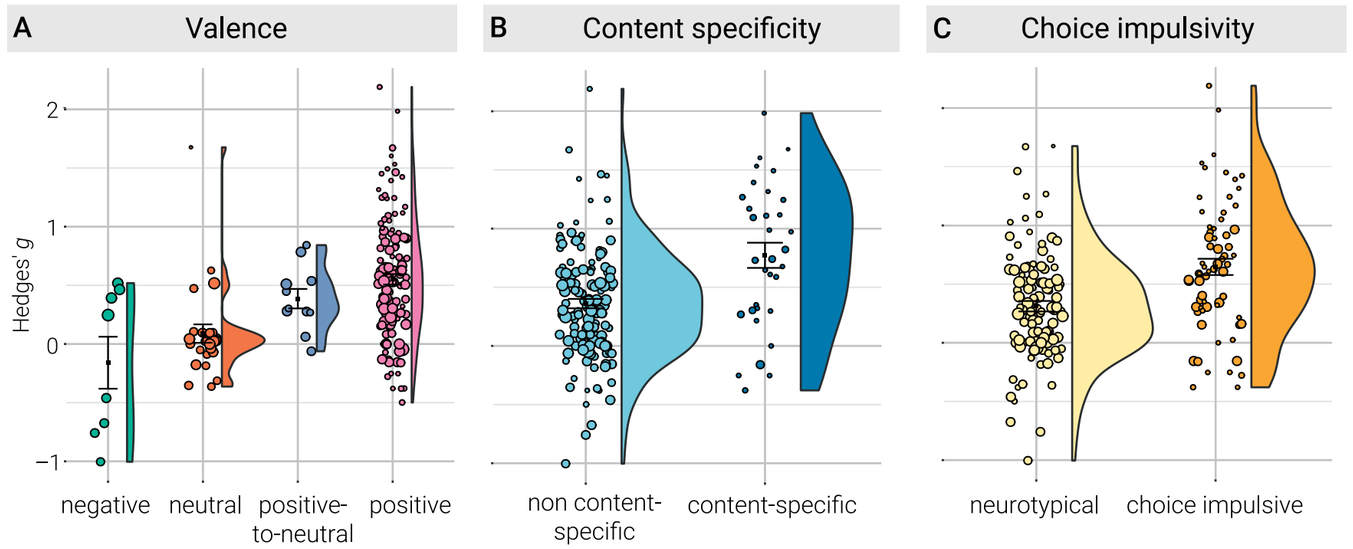


Figure 5.1.1 Selected moderator analyses. The impact of episodic future thinking on intertemporal choices was stronger, (A) when the imagined episodes conveyed a more positive affect, and (B) when they were directly related to the delayed reward. (C) Notably, the effect was stronger in individuals who tend to make more impulsive decisions in their everyday life. Each dot shows the observed effect size for a single study for the respective moderator level. Studies with larger samples (i.e., greater precision) are displayed with larger dots. Black squares indicate the mean, and whiskers the standard error. The shape illustrates the distribution of effect sizes for the respective moderator level.

5.1.2 Computational and neural mechanisms of simulation-based learning

Dabas, A.[1,2], Bruckner, R.[3], Schultz, H.[1], & Benoit, R. G.[1]

[1] Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany, [2] Humboldt-Universität zu Berlin, Berlin School of Mind and Brain, Berlin, Germany, [3] Free University of Berlin, Germany

Our ability to imagine future episodes has much in common with our ability to remember past episodes. Such episodic simulation is largely based on the same core network of brain regions, shows a parallel life-span trajectory, and exhibits similar phenomenological properties. Here, we further examine the hypothesis that we also learn from merely simulated episodes, in much the same way as we learn from actual past experiences. Using functional MRI and computational modelling, we tested whether this simulation-based learning is based on a common mechanism of reinforcement learning. To examine this hypothesis, participants made a series of choices between two people that they were personally familiar with. They then vividly imagined an interaction with the chosen person (serving as the conditioned stimuli, CS) in a presented scenario that was either pleasant (e.g., eating ice cream on a sunny day; positive unconditioned stimuli, US) or unpleasant (e.g., getting stuck in a thunderstorm; negative US). Critically, over the course of the experiment, participants acquired a preference for the person that they had imagined more frequently in a pleasant scenario. They moreover showed a positive shift in their general attitude towards that person. Notably, this simulation-based learning can best be accounted for by a Rescorla-Wagner (RW) model of reinforcement learning that is mediated via a striatal and medial-prefrontal prediction error. This study thus further highlights how mere simulations shape our real-life preferences and sheds light on the underlying computational and neural mechanisms.

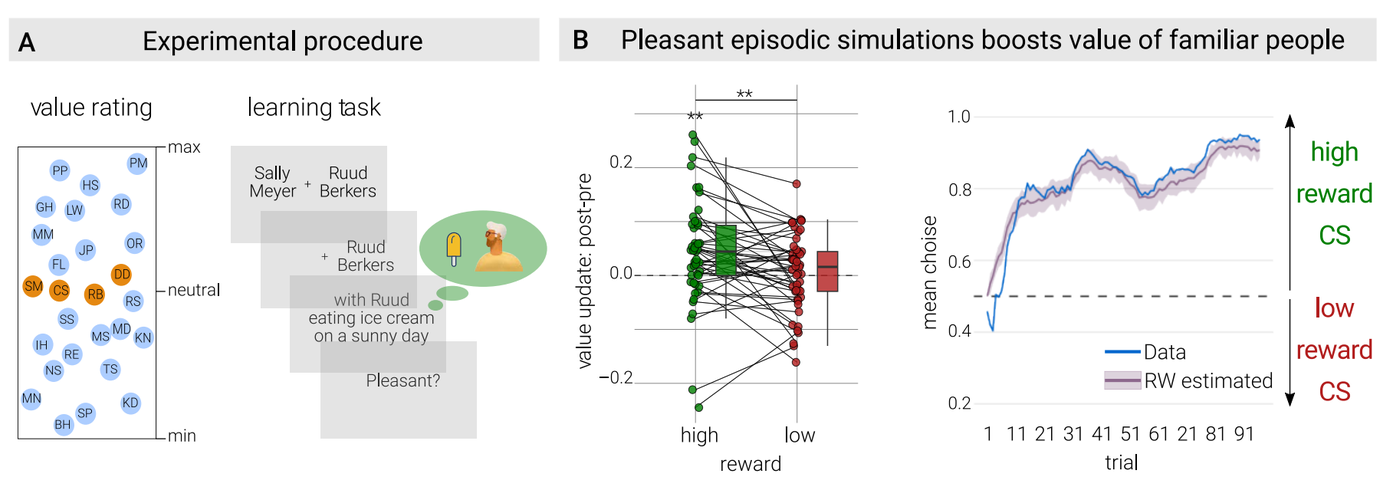
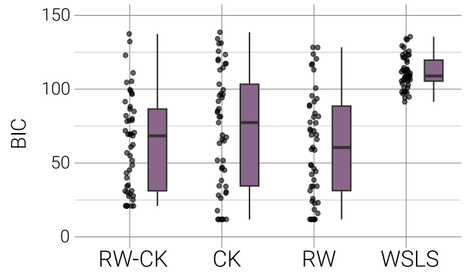
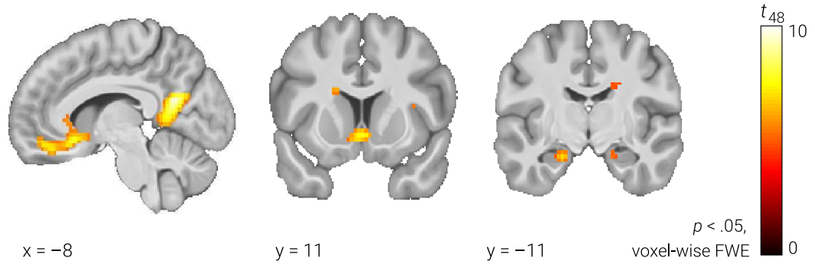


Figure 5.1.2 (A) Participants provided names of known people and rated their affective value. The four most neutral people served as the CS for the subsequent learning task. In the MRI scanner, on a given trial, participants selected one of two presented CS (i.e., they chose a person). They were then prompted to imagine an episode with the respective person in a specified scenario for 8 s. The scenarios served as the US and were either pleasant (e.g., eating ice cream on a sunny day) or unpleasant (e.g., spilling coffee on a laptop). Participants then indicated the experienced reward on a given trial by rating the pleasantness of the imagined episode. Two of the four names were imagined with a pleasant event at 0.8 probability (high-reward CS), whereas the other two names were imagined with a pleasant event at 0.3 probability (low-reward CS). Outside the scanner, participants once again rated the affective value of the known people (B). Across the session, participants acquired a preference for the high-reward CS. Moreover, consistent with our previous reports (Benoit et al., 2019; Paulus et al., 2022), they also experienced a positive shift in their general attitude towards that person.

C Rescorla-Wagner model best accounts for simulation-based learning



D Simulation-based prediction error in NAcc, mPFC, PCC and hippocampus



(C) We compared the data fit of the RW model to competing models, i.e., a choice kernel (CK), a noisy win-stay lose-shift (WSLS), and a combined RW-CK model. The BIC scores indicated that the learning could best be accounted for by the RW model. (D) Notably, the analysis of the fMRI data demonstrated that simulation-based reinforcement learning was also implemented in a similar fashion as experience-based reinforcement learning. That is, it was associated with a prediction-error signal in the medial prefrontal (mPFC) and nucleus accumbens (NAcc). In addition, we also observed involvement of the hippocampus and posterior cingulate cortex (PCC), regions that critically support the simulation of prospective episodes. The whole-brain maps were thresholded at p < .05, FWE corrected. ** p < .01.

5.1.3 The structure of experience: Examining the emergence of schematic representations in the medial prefrontal cortex

Paulus, P. C. [1,2], Williams, A. N., [1,3], Wiese, S. S. [1], & Benoit, R. G. [1]

[1] Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany, [2] University of Freiburg, Germany, [3] Nottingham Trent University, UK

Unique experiences are encoded as episodic memories in the hippocampus. In contrast, the medial prefrontal cortex (mPFC) has been argued to encode more generalised memory representations, i.e., memory schemas (Gilboa & Marlatte, 2017). These representations are thought to be extracted across multiple related experiences (Ghosh & Gilboa, 2014). Recently, we have demonstrated that the mPFC encodes such schemas of our real-life environment as well as of the people that live in it (Paulus et al., 2020). Here, we examine how schemas emerge *de novo* by immersing people in an unfamiliar environment: The character-rich TV show *The Wire*. Across two weeks, participants watched the entire first season and thereby learned the complex structure of its characters' relationships. We quantified participants' *subjective schemas* from repeated fine-grained behavioural assessments and defined the *objective relationships* between the characters by their co-occurrences. Preliminary analyses indicate that the structure of participants' subjective schemas can best be accounted for by a model that is based on the co-occurrences in the same scenes. Moreover, we use representational similarity analyses of functional MRI data to probe the neural implementation of the subjective schemas. Our preliminary analysis indicates that they are encoded in the mPFC. These findings elucidate how lifelike experiences lead to the emergence of memory schemas in the brain.

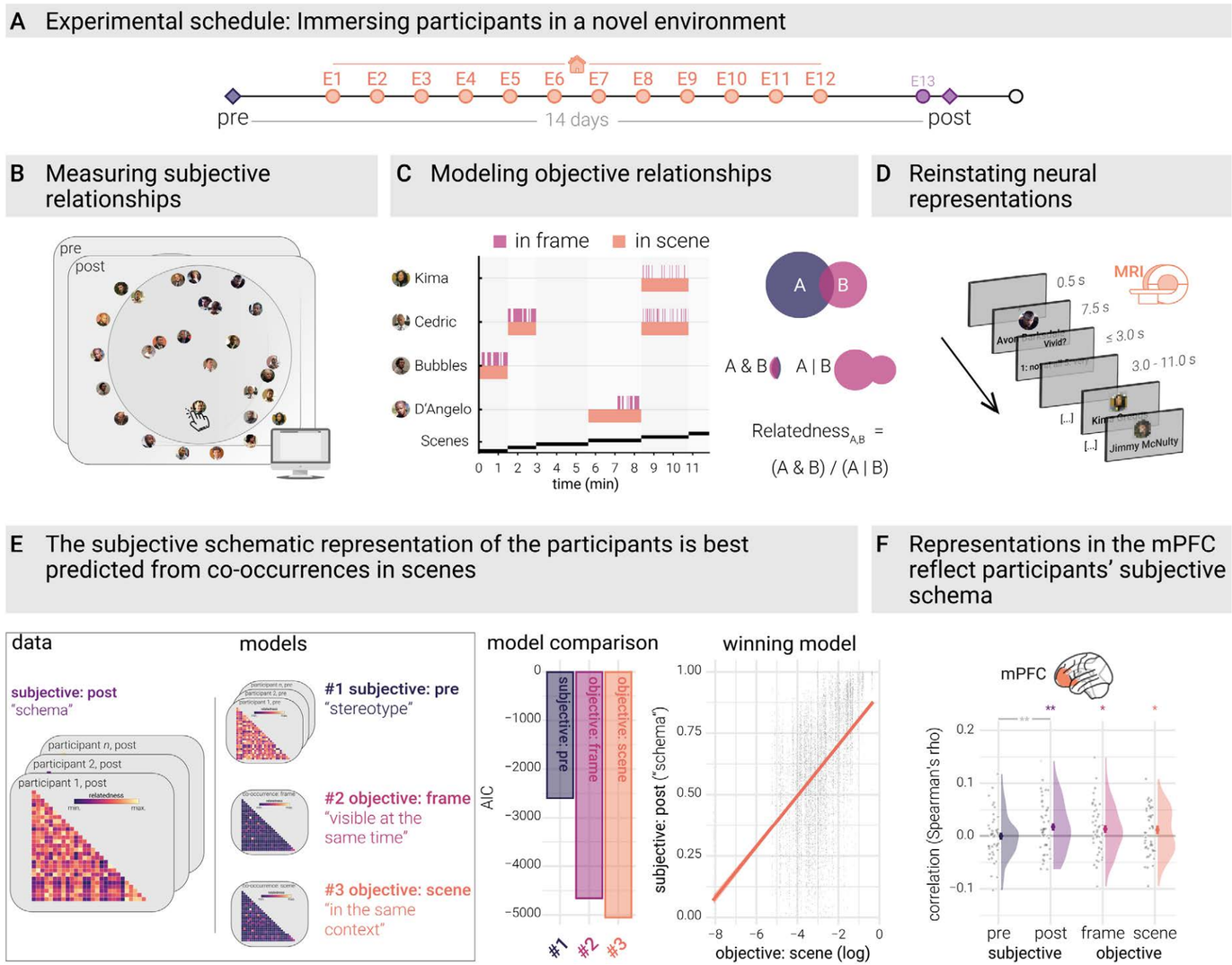


Figure 5.1.3 Lifelike experiences shape the structure of memory schemas and their neural representation in the mPFC. (A) Participants (n = 34) were exposed to the entire first season of the character rich TV show *The Wire* over the course of 14 days. (B) Before and after they watched the show, participants indicated how they subjectively associate the featuring characters with each other using the multiple arrangements task (Kriegeskorte & Mur, 2012)in which the distances reflect the dissimilarities. Such an arrangement can be obtained by multidimensional scaling (MDS. (C) We modelled the objective relationships between the characters from their co-occurrences in individual frames and in scenes. (D) In the fMRI scanner, participants reinstated each individual character's neural representation by imagining them in a typical scenario. (E) Using linear mixed effects models, we predicted participants' subjective schema (*subjective: post*) of the network of characters either from the stereotyped arrangement (*subjective: pre*) or as a function of the two *objective models*. Model comparisons revealed strongest evidence for the objective model that is based on co-occurrences of the characters in scenes. (F) The medial prefrontal cortex (mPFC) encodes neural memory representations that reflect the structure of the *subjective schema*.

5.1.4 Complementary memory representations in the prefrontal cortex and medial-temporal lobes support knowledge-guided retrieval

Schultz, H.[1], & Benoit, R. G.[1]

[1] Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany

As humans, we have the remarkable ability to form detailed episodic memories of events. Over time, we also extract commonalities across similar events. Such generalised memories constitute pre-existing knowledge that aids the encoding and retrieval of new episodic memories. Previous work indicates that pre-existing knowledge facilitates episodic retrieval through interactions of the prefrontal cortex (PFC) and medial temporal lobe (MTL). Here, we test the hypotheses that (i) pre-existing knowledge facilitates episodic retrieval (ii) via a transfer of pre-existing knowledge from the left ventrolateral (vlPFC) to the MTL. We varied the availability of pertinent knowledge during retrieval and assessed its neural representation using fMRI at 7T. On each trial, a cue prompted participants to retrieve a scene from memory (Figure 4A). The cue either predicted the scene category (i.e. house or field, knowledge condition), or not (control condition). Supporting (i), pre-existing knowledge improved episodic retrieval (Figure 4B, left panel), though it also increased knowledge-consistent memory errors (Figure 1B, right panel). The availability of pre-existing knowledge was associated with increased vlPFC activity and decreased amygdala/MTL activity (Figure 5A). To test (ii), we conducted a multivariate decoding analysis (Figure 5B-C). As predicted, for the vlPFC, the preliminary analysis yielded category information in the knowledge condition only, irrespective of retrieval success. This region thus seems to represent pre-existing knowledge that can guide episodic retrieval. By contrast, within the MTL, the parahippocampal cortex yielded category information during the successful recall of episodic memories. Notably, it also showed evidence for category information during unsuccessful retrieval, but only when the category had been provided by pre-existing knowledge. This region thus seems to represent both the outcome of the retrieval process as well as pre-existing knowledge that helps constrain the retrieval process. Together, the data highlight the complementary roles of the PFC and MTL in knowledge-guided retrieval.

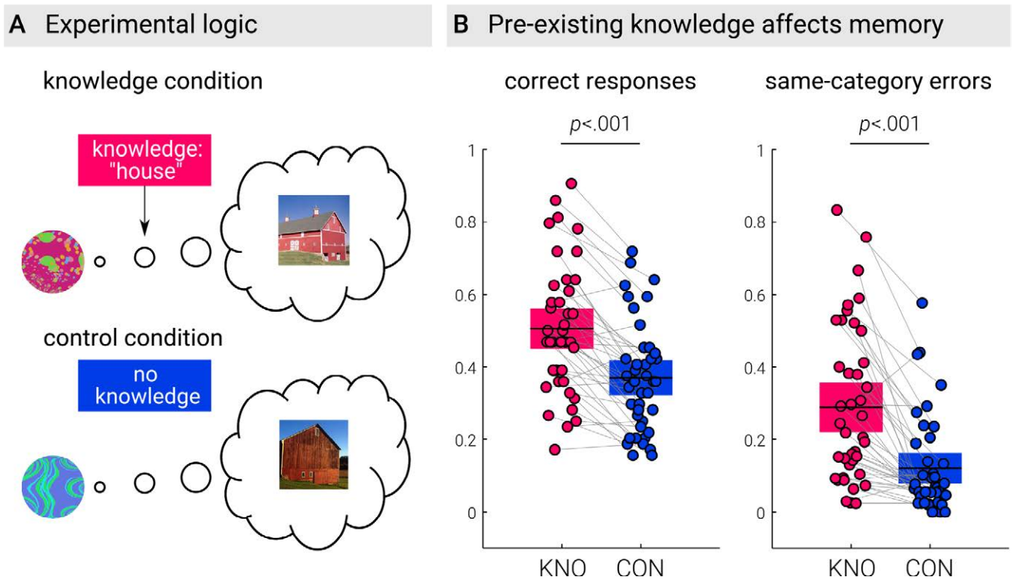


Figure 5.1.4.1 Experimental logic and behavioural results. (A) Participants saw a cue and retrieved a scene from memory. The cue predicted the scene category (house or field) in the knowledge but not the control condition. Pre-existing knowledge significantly increased (B) correct memory responses, but (C) also same-category errors (relative to all errors), i.e. participants were more likely to pick a same-category distractor in the knowledge compared to the control condition. Error boxes indicate 95% confidence interval. Scene images from Brady, Konkle, Alvarez & Oliva (2008).

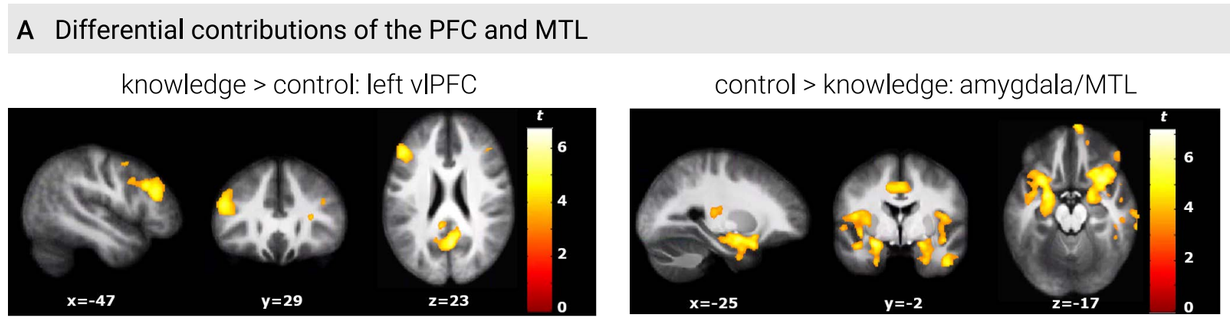


Figure 5.1.4.2 Neuroimaging results. (A) Pre-existing knowledge was associated with increased activity in the left ventrolateral PFC (vlPFC) and decreased activity in the bilateral amygdala/MTL. Display threshold p < .001 unc. (B) A linear classifier was trained to distinguish houses vs. fields in independent localiser data and tested on the retrieval data. (C) Multivariate decoding results in two regions of interest (ROIs). The bar plots depict average decision values (DVs, i.e. distance of each trial to the hyperplane) for each experimental condition: knowledge-remembered (KNO-R), knowledge-forgotten (KNO-F), control-remembered (CON-R), control-forgotten (CON-F). The vlPFC shows stronger decoding for knowledge than control trials, irrespective of memory status. In contrast, the parahippocampal cortex (PHC) shows decoding for both remembered and forgotten knowledge trials, but only for remembered control trials. Error bars denote 95% confidence intervals. Scene images from Brady, Konkle, Alvarez & Oliva (2008).

Congresses, Workshops, and Symposia

2020

- Meyer, A.-K. (May) *Climate Change of Mind – 1st Network Meeting oft he MPG Sustainability Initiatives.* Virtual Conference.

2021

- Benoit, R. G., & Lonsdorf, T. (June) *Parsing avenues for future fear conditioning research*, Psychologie & Gehirn. Virtual.

2022

- Benoit, R. G., & Schultz, H. (June) *Updates on complementary memory systems in the brain*, Psychologie & Gehirn, Freiburg, Germany.

Degrees

PhD Theses

2022

- Paulus, C.P. *Schema and value: characterizing the role of the rostral and ventral medial prefrontal cortex in episodic future thinking.* Leipzig University, Germany.

Appointments

2022

- Benoit, R. G. *Associate Professor of Psychology and Neuroscience,* University of Colorado Boulder, USA.
- Benoit, R. G. *Faculty member of the International Max Planck Research School on Cognitive NeuroImaging (IMPRS CoNI)*, Max Planck Institute for Cognitive and Brain Sciences, Leipzig, Germany.

Publications

Journal Articles

Ashton, S. M., Benoit, R. G., & Quaedflieg, C. W. E. M. (2020). The impairing effect of acute stress on suppression-induced forgetting of future fears and its moderation by working memory capacity. *Psychoneuroendocrinology*. https://doi.org/10.1016/j.psyneuen.2020.104790

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Index of Published Figures

Figure 5.1.1

Figure adapted from Rösch, S., Stramaccia, D.F., & Benoit, R.G. (2022). Promoting farsighted decisions via episodic future thinking: A meta-analysis. Journal of Experimental Psychology: General, 151(7), 1606.

5.2

Dr Falk Eippert

Max Planck Research Group Pain Perception

(commenced June 2018)

Pain is an important warning signal of impending or actual tissue damage, yet in its chronic form it is also a source of immense suffering. Importantly, the perception of pain is not a direct reflection of the strength of peripherally received noxious input but is strongly modulated by a plethora of contextual factors, such as our current expectations or our past experience of pain. This argues for a significant involvement of the central nervous system in the construction of the experience of pain.

The central aim of our research is to identify the neural building blocks involved in this process. We approach this from a predictive processing perspective that characterises perception as an active inferential process, in which the central nervous system generates predictions about the inputs it receives and adjusts these predictions in light of new sensory input. Towards this end, we use behavioural and autonomic recordings in combination with advanced neuroimaging methods at all levels of the nervous system. A special focus is placed on the spinal cord, in order to capture signals at the earliest level of central nervous system pain processing, since they are likely to exert a profound effect on processing at higher levels and the ensuing perceptual experience.

In one line of research, we are seeking to characterise pain signals at the level of the spinal cord using fMRI. For example, we are assessing the stability of such signals across time (5.2.1) and are testing whether it is possible to capture robust spinal cord responses at the level of individual participants using ultra-high field recordings (5.2.2). In another strand of research, we are developing paradigms to test core principles of predictive processing in the context of pain, using psychophysiological and electrophysiological (EEG) approaches (5.2.3). Here, we are also aiming to extend non-invasive electrophysiological assessments of neuronal responses towards the spinal cord and are thus working on optimising such data acquisition and analysis approaches (5.2.4). Taken together, our research aims to provide an integrative perspective on the processes that occur along the neural hierarchy and shape the experience of pain.

5.2.1 Reliability of task-based fMRI in the dorsal horn of the human spinal cord

Dabbagh, A.[1], Horn, U,.[1], Kaptan, M.[1], Mildner, T.[1], Mueller, R.[1], Lepsien, J.[1], Weiskopf, N.[1,2], & Eippert, F.[1]

[1] Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany, [2] Felix Bloch Institute for Solid State Physics, Leipzig University, Germany

The spinal cord is the first station of nociceptive processing within the central nervous system, as well as a target of top-down modulation and thus of considerable interest in pain research. Assessing spinal cord function non-invasively via fMRI is still a relatively young field of research however and faces many challenges. Here, we aimed to probe the limitations of task-based spinal fMRI by investigating the reliability of spinal cord BOLD responses to identical nociceptive stimulations across two consecutive days. Towards this end, we made use of a recently developed method for improved spinal fMRI data quality and recorded ratings of pain intensity, autonomic nervous system responses, and BOLD responses at 3T from 40 participants who received painful heat stimuli (Figure 5.2.1A). At the group level, we observed BOLD responses that exhibited clear spatial specificity, were highly significant at the expected location (ipsilateral dorsal horn in spinal cord segment C6; Figure 5.2.1B), but that also had slightly different non-overlapping spatial peaks within the dorsal horn across days (Figure 5.2.1C). While ratings of pain intensity and autonomic indicators of pain processing generally showed good-to-excellent test-retest reliability (Figure 5.2.1C), both beta-estimates and z-scores of task-related BOLD responses showed poor test-retest reliability across days. The reason for this is currently unclear, particularly given that split-half reliability, in our region of interest, and test-retest reliability, in a region including draining veins, were in the fair-to-good range. Taken together, these data provide encouraging insights for using fMRI to assess 'temporal snapshots' of nociceptive processing at the spinal level, but also hint at a lack of signal-stability over days that needs to be addressed with improved data acquisition and analysis techniques. Related to this work, we also assessed the reliability of spinal cord resting-state connectivity, which will be important for future projects where we aim to assess non-transient painful states and aim to characterise them with connectomic approaches.

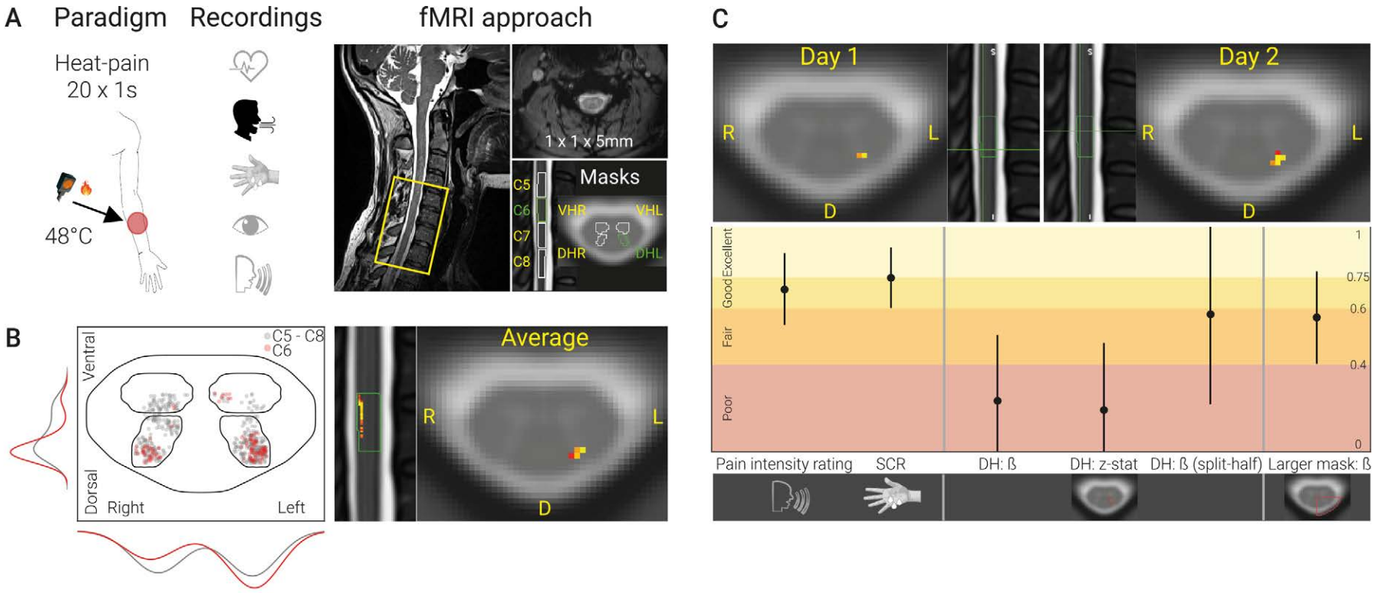


Figure 5.2.1 (A) Participants received 20 painful heat stimuli of 1s duration to their left forearm on two consecutive days. In addition to fMRI data, we acquired heart rate, respiration, skin conductance (SCR), pupil diameter, and verbal ratings. The extent of the EPI slice stack is shown in yellow (overlaid on a T2-weighted image) and an exemplary transversal EPI slice with an in-plane resolution of 1x1mm is depicted as well. Outlines depict masks of spinal segments C5 to C8, as well as grey matter masks of the 4 dorsal horns (DH: dorsal horn, VH: ventral horn), with our region of interest being the left DH in segment C6 (highlighted in green). (B) The scatter-histogram on the left descriptively shows the group-level spatial distribution of all active voxels in the grey matter of the spinal cord (at $p < .001$ uncorrected; jitter introduced for visualisation purposes) for all segments (grey) and for our segment of interest (red), where a clear trend towards the left dorsal part can be appreciated (see also kernel density estimates). On the right, group-level responses averaged across both days show a significant activation within the left DH of segment C6 (after correction via voxel-wise permutation testing at $p < 0.05$); both sagittal and transversal views are provided with activation overlaid on a template image. (C) The upper row depicts group-level BOLD responses separately for each day ($p < 0.05$ corrected): left DH activation can be observed for both days, though at different levels within segment C6 (indicated by green crosshairs). The bottom panel depicts a formal assessment of test-retest reliability via the intra-class coefficient (ICC) for different aspects of our data: i) pain intensity ratings and skin conductance responses, ii) beta-estimates and z-stats in the left DH of C6, as well as beta-estimates for split-half reliability in the same region, and iii) beta-estimates for test-retest reliability in an extended region including the veins draining the DH.

5.2.2 7T fMRI of the human spinal cord: BOLD responses on the single-subject level

Horn, U.[1], Gross-Wege, N.[2], Revina, Y.[1], Vannesjo, J.[3], Kaptan, M.[1], Dabbagh, A.[1], Trampel, R.[1], Möller, H. E.[1,] Weiskopf, N.[1,4], & Eippert, F.[1]

[1] Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany, [2] Siemens Healthcare GmbH, Erlangen, Germany, [3] Department of Physics, Norwegian University of Science and Technology, Trondheim, Norway, [4] Felix Bloch Institute for Solid State Physics, Leipzig University, Germany

The advent of ultra-high field fMRI at 7T provides new opportunities for the investigation of small-scale structures such as the spinal cord, but also poses severe technical challenges. As a consequence, custom-built coils for imaging the human spinal cord at 7T have only recently become available and no task-based fMRI studies have been published yet. Here, we aimed to assess whether it is possible to observe BOLD responses in the dorsal horn of the cervical spinal cord at the level of individual participants. Considering that data quality of spinal cord acquisitions at 7T is highly variable across participants, we first carried out a screening study ($N > 60$) in order to identify participants with adequate spinal cord data quality, who were then invited for a task-based study ($N = 16$). In all acquisitions, we employed a custom-built 24-channel coil in combination with a susceptibility-matched collar around the neck and sequence parameters optimised to prevent signal loss and distortion. We acquired high-resolution T2*-weighted images, centred on segment C6 in order to allow for a precise grey matter delineation (Figure 5.2.2A–B), that could then be overlaid on EPI data, which presented with adequate quality and only few occurrences of local signal loss (Figure 5.2.2C). We employed a paradigm consisting of nociceptive heat stimulation that was rated as clearly painful and elicited prominent changes in concurrently recorded autonomic nervous system parameters (Figure 5.2.2D–E). After using tailored preprocessing and rigorous denoising procedures, we observed BOLD responses in the expected location (ipsilateral dorsal horn) in the majority of participants, well localised to the individual grey matter (Figure 5.2.2F). In ongoing work, we are evaluating different procedures to address distortions in EPI data in order to allow for a more fine-grained response characterisation. This is a necessary step towards our goal of delineating the interplay of bottom-up and top-down factors in pain processing in different layers of the dorsal horn.

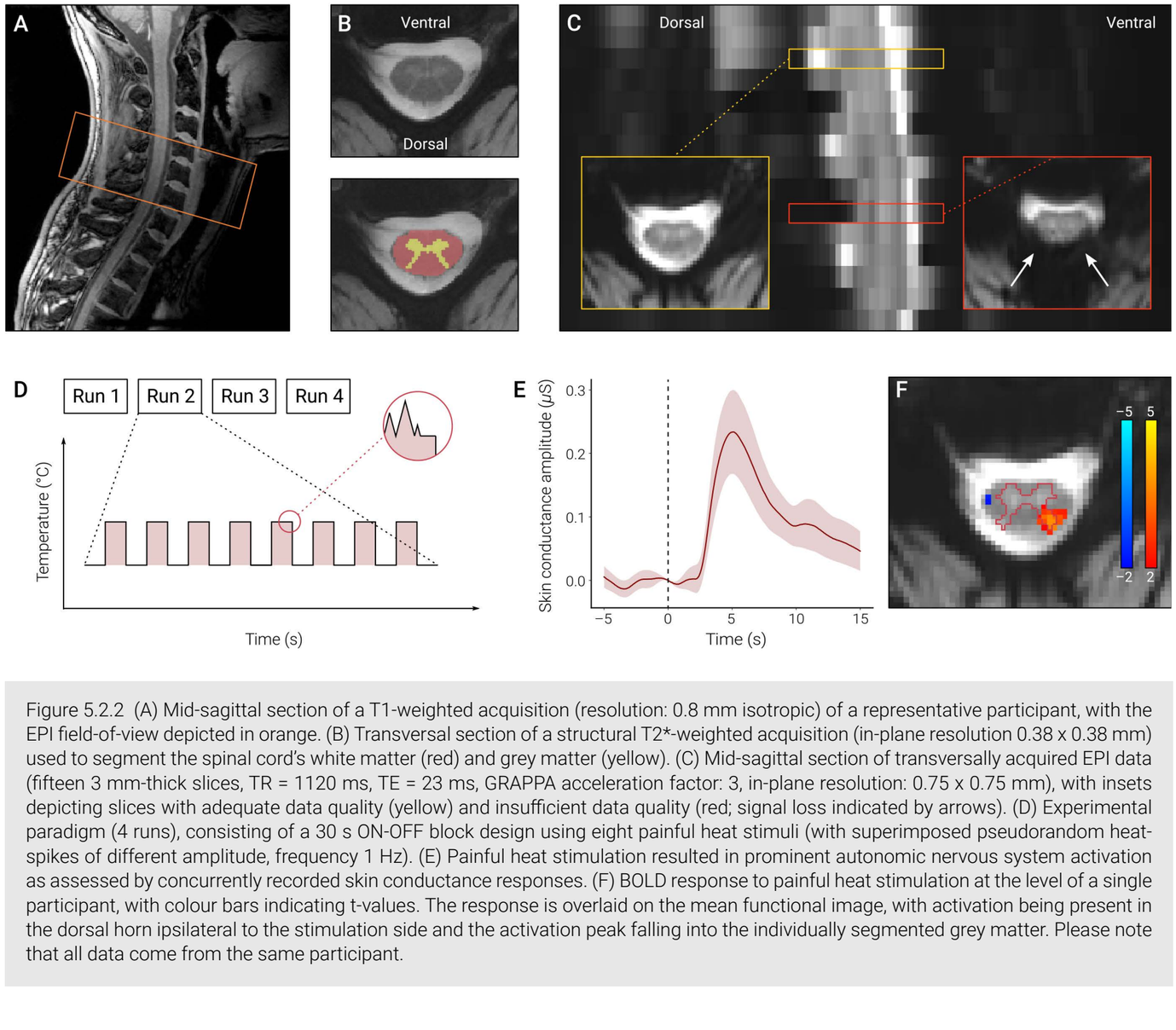


Figure 5.2.2 (A) Mid-sagittal section of a T1-weighted acquisition (resolution: 0.8 mm isotropic) of a representative participant, with the EPI field-of-view depicted in orange. (B) Transversal section of a structural T2*-weighted acquisition (in-plane resolution 0.38 x 0.38 mm) used to segment the spinal cord's white matter (red) and grey matter (yellow). (C) Mid-sagittal section of transversally acquired EPI data (fifteen 3 mm-thick slices, TR = 1120 ms, TE = 23 ms, GRAPPA acceleration factor: 3, in-plane resolution: 0.75 x 0.75 mm), with insets depicting slices with adequate data quality (yellow) and insufficient data quality (red; signal loss indicated by arrows). (D) Experimental paradigm (4 runs), consisting of a 30 s ON-OFF block design using eight painful heat stimuli (with superimposed pseudorandom heat-spikes of different amplitude, frequency 1 Hz). (E) Painful heat stimulation resulted in prominent autonomic nervous system activation as assessed by concurrently recorded skin conductance responses. (F) BOLD response to painful heat stimulation at the level of a single participant, with colour bars indicating t-values. The response is overlaid on the mean functional image, with activation being present in the dorsal horn ipsilateral to the stimulation side and the activation peak falling into the individually segmented grey matter. Please note that all data come from the same participant.

5.2.3 Expectation effects on repetition suppression in nociception

Pohle, L.M.G[1], Horn, U.[1], Nierula, B.[1], & Eippert, F.[1]

[1] Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany

The neurobiological processing and the perceptual experience of pain are not only driven by bottom-up factors, but also strongly shaped by top-down aspects, such as the expectations we hold. In this context, our research addresses the behavioural consequences of specific pain-related expectations as well as the underlying cortical mechanisms. Here, we aimed to assess the latter by asking whether expectations influence a classical cortical response pattern, namely, repetition suppression (i.e., reduced neural responses to the repeated presentation of a stimulus). It has been suggested that repetition suppression can be explained via predictive processing models, since expected repetitions elicit smaller prediction error responses. However, evidence for this is scarce in the context of pain. We made use of a CO_2-laser—that allows for a transient and highly synchronised activation of nociceptors—to create a nociceptive repetition suppression paradigm, in which we explicitly varied the frequency of repetitions (thus rendering them either expected or unexpected) and recorded autonomic nervous system responses as well as EEG data. Participants' expectations regarding the likelihood of receiving repeated painful stimuli closely followed the experimental contingency (Figure 5.2.3A). When these expectations were violated, i.e. when repeated stimuli occurred surprisingly, we observed stronger autonomic responses (Figure 5.2.3B). Crucially, direct evidence for repetition suppression was obtained both in evoked EEG responses and pain-induced gamma oscillations (Figure 5.2.3C,D). However, preliminary analyses did not provide evidence for a modulation by expectation. In ongoing work, we are assessing whether power in different frequency bands is related to the modulation of repetition suppression and are also investigating whether this might already occur in the first cortical response-component. This would point towards earlier—possibly spinal—contributions to this phenomenon.

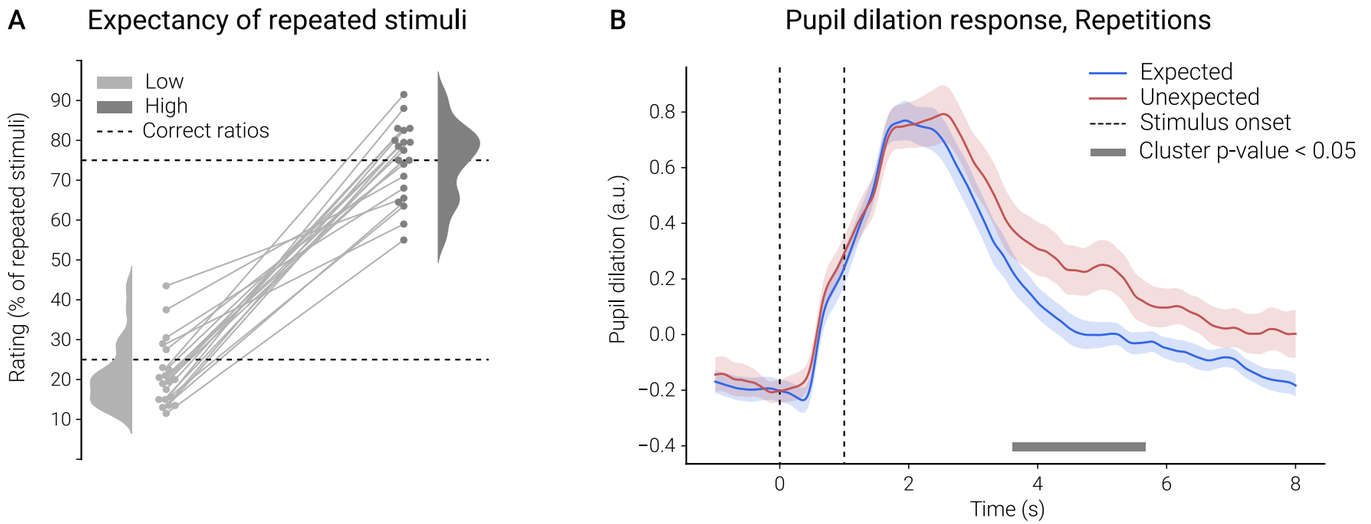
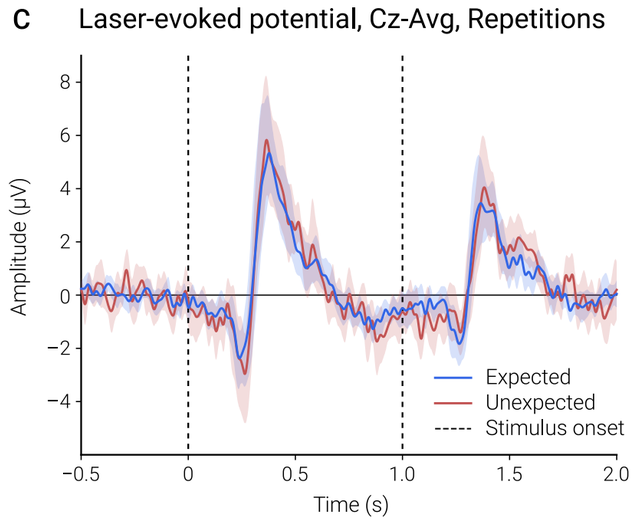
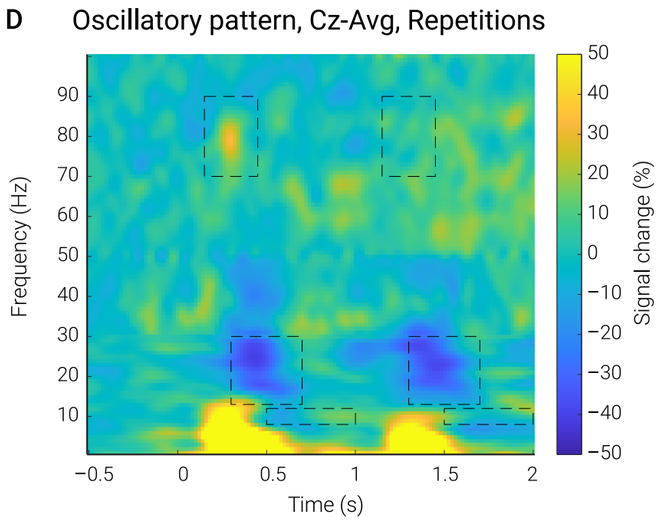


Figure 5.2.3 (A) Subjective ratings of how often participants expected repetitions in the upcoming block of trials (scale anchored at never (0) and always (100)); points depict individual responses and dashed lines indicate the actual repetition probability. (B) Group-level pupil dilation responses for expected (blue) and unexpected repetitions (red) show higher amplitudes for the unexpected condition (statistically confirmed by a cluster-based permutation test). Dashed lines indicate the occurrence of laser stimuli at 0s and 1s.





(C) Group-level average waveforms of EEG data at electrode Cz to repeated laser stimuli at 0s and 1s (dashed lines), with blue indicating expected and red indicating unexpected repetitions. The laser-evoked potential consists of a negative peak followed by a positive peak (N2P2) in response to each of the stimuli. It is clearly diminished in response to the second stimulus, showing strong repetition suppression, though without an obvious difference between the expectation conditions. (D) Group-level time-frequency representation of EEG data at electrode Cz, with regions of interest marked by dashed lines and containing stimulus induced desynchronisations in the alpha and beta band as well as synchronisation in the gamma band. A strong repetition suppression effect for gamma-band synchronisation can be observed.

5.2.4 Cardiac artefact removal in non-invasive electrophysiology of the human spinal cord

Bailey, E.[1], Nierula, B.[1], Stephani, T.[1], Nikulin, V.V.[1], Maess, B.[1], & Eippert, F.[1]

[1] Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany

The spinal cord is of fundamental importance for pain processing, but non-invasive recordings of spinal cord activity to nociceptive stimulation with high temporal resolution have not been performed yet. This is due to many technical challenges, one of which is physiological noise arising from cardiac activity: While cortical electrophysiological recordings do not typically suffer from extensive cardiac noise, this is different for spinal cord recordings (Figure 5.2.4A), where cardiac artefacts are more than 100-fold larger than somatosensory potentials of interest. We recently developed an electrophysiological approach—based on a high-density electrode-montage—that included cardiac-artefact correction and allows for a spatiotemporal characterisation of spinal cord somatosensory evoked potentials. Here, we sought to extend this approach by examining different algorithms that might reduce the impact of cardiac activity even further and render spinal cord electrophysiology a desirable technique for further research. We observed that signal space projection (SSP) techniques allow for a considerable reduction in the cardiac artefact (Figure 5.2.4B), with a denoising performance that is superior to previously employed approaches based on principal component or independent component analysis. Importantly, SSP also substantially increases the signal-to-noise ratio (SNR) of spinal cord potentials to somatosensory stimulation (Figure 5.2.4C). Taken together, this improvement in cardiac noise removal opens up the possibility to carry out non-invasive electrophysiological spinal cord recordings in scenarios with low SNR, such as when employing nociceptive stimulation.

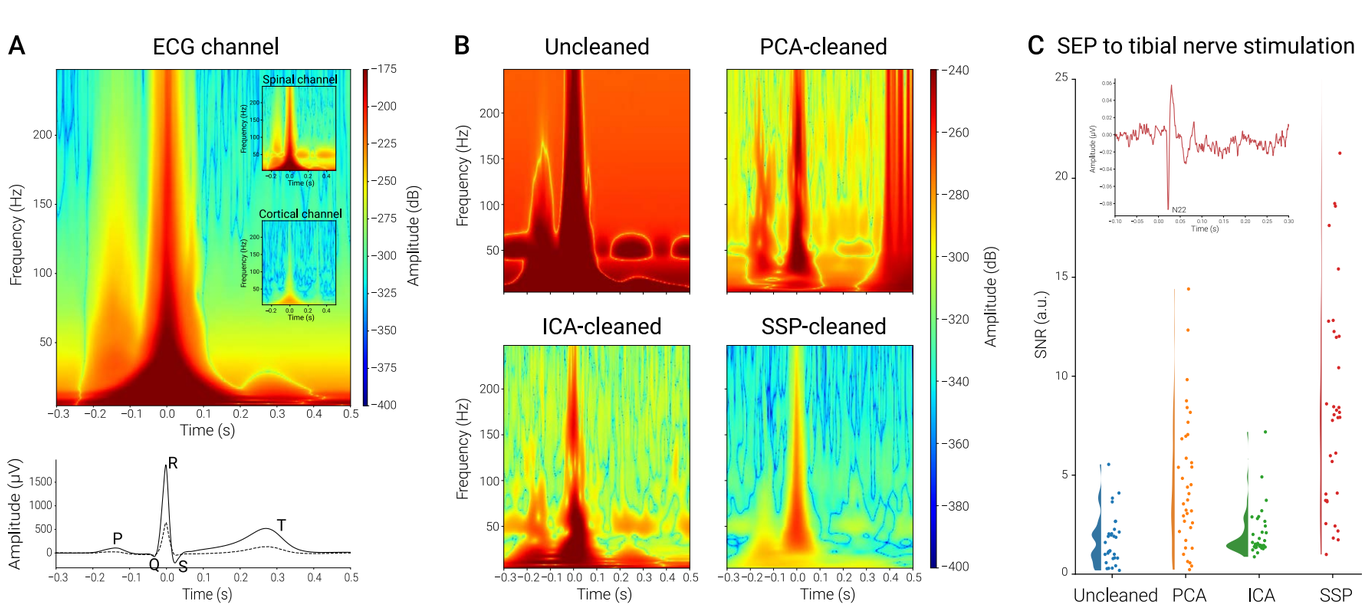


Figure 5.2.4 (A) Upper part: grand-average (N = 36) time-frequency plots demonstrating the manifestation of the heartbeat in the ECG recording channel, with insets demonstrating the corresponding effect of the heartbeat in a spinal and cortical channel of interest. Lower part: corresponding grand-average time-domain elucidation of the heartbeat in the ECG channel (solid) and the spinal channel of interest (dashed), with key components of the heartbeat highlighted by the corresponding letters. The R-peak is centred at 0s and represents the highest magnitude point in each heartbeat occurrence. (B) Grand-average time-frequency plots demonstrating the prominence of the cardiac artefact in the spinal channel of interest before and after cleaning of the cardiac artefact. The three cleaning methods (PCA, ICA,

and SSP) show varying degrees of success at reducing the magnitude of key waveforms in a typical heartbeat: SSP was more successful at reducing the amplitude associated with the QRS complex, as well as the later T-wave, which both PCA and ICA struggled to remove effectively. (C) Effects of the different cleaning methods on the signal-to-noise ratio (SNR) of the somatosensory evoked potential (SEP; stimulation of the tibial nerve at the left ankle and recording from the same lumbar spinal channel as above, i.e. centred over the first lumbar vertebra); points reflect individuals and the densities reflect the group distribution. SSP again offers the best performance as evidenced by the higher SNR (two outliers with SNR > 25 are not shown). The inset depicts the grand average SEP after cleaning of the cardiac artefact via SSP, with a clear negative peak at the expected latency of 22ms (labelled N22).

Workshops

2021

- Eippert, F., Valk, S. L., & Weiskopf,N. (July). *Career building. Expertise session II.* 10th IMPRS NeuroCom Summer School in Cognitive Neuroscience. International Max Planck Research School on Neuroscience of Communication: Function, Structure, and Plasticity (IMPRS NeuroCom), Max Planck Institute for Human Cognitive and Brain Sciences & ICN, Leipzig & London, Germany & UK. Virtual.

2022

- Revina, Y. & Eippert, F. *Perception – a predictive processing perspective.* Workshop. 11th IMPRS NeuroCom Summer School in Cognitive Neuroscience. International Max Planck Research School on Neuroscience of Communication: Function, Structure, and Plasticity (IMPRS NeuroCom), Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany.

Degrees

PhD Theses

2022

- Kaptan, M. *Neuroimaging of the human spinal cord at 3 Tesla: Investigation of acquisition and denoising strategies through resting-state functional magnetic resonance imaging.* Leipzig University, Germany.

Appointments

2021

- Revina, Y. *Equal Opportunities Officer*, Max Planck Institute for Cognitive and Brain Sciences, Leipzig, Germany.
- Eippert, F. *Deputy Ombudsperson*, Max Planck Institute for Cognitive and Brain Sciences, Leipzig, Germany.

2022

- Eippert, F. *Ombudsperson*, Max Planck Institute for Cognitive and Brain Sciences, Leipzig, Germany.
- Eippert, F. *Faculty member of the International Max Planck Research School on Cognitive NeuroImaging (IMPRS CoNI)*, Max Planck Institute for Cognitive and Brain Sciences, Leipzig, Germany.

Awards

2021

- Babayan, A., Pfeifer, F., & Revina, Y. *GOLD for Gender Equality Plan 2021–2023 of the Max Planck Institute for Human Cognitive and Brain Sciences.* Max Planck Society, Munich, Germany.

2022

- Pohle, L.-M. *Poster award*. 11th IMPRS NeuroCom Summer School in Cognitive Neuroscience. International Max Planck Research School on Neuroscience of Communication: Function, Structure, and Plasticity (IMPRS NeuroCom), Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany.
- Zhao, H. *Travel award*, IASP (International Association for the Study of Pain) World Congress of Pain.

Publications

This list also includes publications of team members of the Max Planck Research Group Pain Perception that resulted from work they carried out prior to their arrival. These articles are included as they speak to the unique qualifications of the team members.

Books & Book Chapters

Sanchez-Vives, M. V., Slater, M., & Nierula, B. (2021). Agency and responsibility while controlling movement through brain-computer interfaces for neurorehabilitation. In D. Torricelli, M. Akay, & J. L. Pons (Eds.), *Converging Clinical and Engineering Research on Neurorehabilitation IV. ICNR 2020. Biosystems & Biorobotics* (Vol. 28, pp. 557–561). Springer, Cham. https://doi.org/10.1007/978-3-030-70316-5_89

Journal Articles

Cohen-Adad, J., Alonso-Ortiz, E., Abramovic, M., Arneitz, C., Atcheson, N., Barlow, L., Barry, R. L., Barth, M., Battiston, M., Büchel, C., Budde, M., Callot, V., Combes, A. J. E., De Leener, B., Descoteaux, M., de Sousa, P. L., Dostál, M., Doyon, J., Dvorak, A., Eippert, F., Epperson, K. R., Epperson, K. S., Freund, P., Finsterbusch, J., Foias, A., Fratini, M., Fukunaga, I., Gandini Wheeler-Kingshott, C. A. M., Germani, G., Gilbert, G., Giove, F., Gros, C., Grussu, F., Hagiwara, A., Henry, P.-G., Horák, T., Hori, M., Joers, J., Kamiya, K., Karbasforoushan, H., Keřkovský, M., Khatibi, A., Kim, J.-W., Kinany, N., Kitzler, H. H., Kolind, S., Kong, Y., Kudlička, P., Kuntke, P., Kurniawan, N. D., Kusmia, S., Labounek, R., Laganà, M. M., Laule, C., Law, C. S., Lenglet, C., Leutritz, T., Liu, Y., Llufriu, S., Mackey, S., Martinez-Heras, E., Mattera, L., Nestrasil, I., O'Grady, K. P., Papinutto, N., Papp, D., Pareto, D., Parrish, T. B., Pichiecchio, A., Prados, F., Rovira, À., Ruitenberg, M. J., Samson, R. S., Savini, G., Seif, M., Seifert, A. C., Smith, A. K., Smith, S. A., Smith, Z. A., Solana, E., Suzuki, Y., Tackley, G., Tinnermann, A., Valošek, J., Van De Ville, D., Yiannakas, M. C., Weber II, K. A., Weiskopf, N., Wise, R. G., Wyss, P. O., & Xu, J. (2021). Open-access quantitative MRI data of the spinal cord and reproducibility across participants, sites and manufacturers. *Scientific Data*, *8*. https://doi.org/10.1038/s41597-021-00941-8

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5.3

Professor Dr Gesa Hartwigsen

Lise Meitner Research Group Cognition and Plasticity

(commenced January 2019)

The goal of our research group is to elucidate mechanisms of adaptive systems plasticity in neural networks for cognition. Flexible network adaptation enables efficient cognitive functioning in everyday life. Yet, how specialised networks adapt to challenges and lesions is poorly understood. In the last few years, our research has provided novel insight into generic mechanisms of adaptive network plasticity across the adult lifespan, for example, in healthy young brains (e.g., Rysop et al., 2020; Kuhnke et al., 2021), aging brains (e.g., Martin et al., 2022a; Rysop et al., 2022) and lesioned brains (e.g., Graessner et al., 2021). Our focus is on language as a key function of human cognition, but we are interested in common and distinct mechanisms of plasticity across cognitive domains (e.g., Numssen et al., 2021; Williams et al., 2022). We combine neurostimulation with neuroimaging to probe plasticity at the systems level. In collaboration with the research group Brain Networks, we established novel targeting approaches for neurostimulation that substantially increase stimulation efficiency (e.g., Weise et al., 2022 5.3.1). Applying such protocols in healthy young brains, we find that specialised nodes for cognition differ in their potential for flexible adaptation in response to stimulation-induced inhibition (5.3.2). Our research further reveals that network disorders such as dyslexia can be characterised by aberrant profiles in network recruitment and interactions (5.3.3). Using network modelling, we have identified age-related changes in the recruitment of networks during cognitive tasks (5.3.4), which allowed the disentanglement of compensation from overall cognitive decline in the aging brain. In collaboration with McGill University, we quantified the impact of brain lesions on core networks for different cognitive functions, providing new insight into hemispheric specialisation (5.3.5). In collaboration with Leipzig University, we have unravelled changes in network interactions across the time course of language recovery after stroke (5.3.6). These results support our key hypothesis that increased interactions between specialised networks and domain-general networks support recovery after stroke.

5.3.1 Optimised dosing and targeting for transcranial magnetic stimulation during conceptual processing

Kuhnke, P.[1,2], Numssen, O.[1], Voeller, J.[1], Kolbe, E.[1], Kalloch, B.[1], Weise, K.[1], & Hartwigsen, G.[1,2]

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Conceptual knowledge is central to human cognition. Previous neuroimaging studies suggest that conceptual processing relies on the joint contribution of modality-specific and multimodal brain regions. However, as neuroimaging is correlational, it remains unknown whether the interaction between modality-specific and multimodal cortices is causally relevant for conceptually-guided behaviour. To tackle this issue, we applied inhibitory transcranial magnetic stimulation (TMS) over modality-specific cortex (somatomotor, auditory, or sham), before healthy participants received TMS over multimodal cortex (inferior parietal lobe, or sham) during conceptual tasks. To optimise the coil position and intensity for each target, we performed computational simulations of the TMS-induced electrical field (e-field). Specifically, we determined the coil position that maximised the e-field strength in each target and identified the stimulation intensity

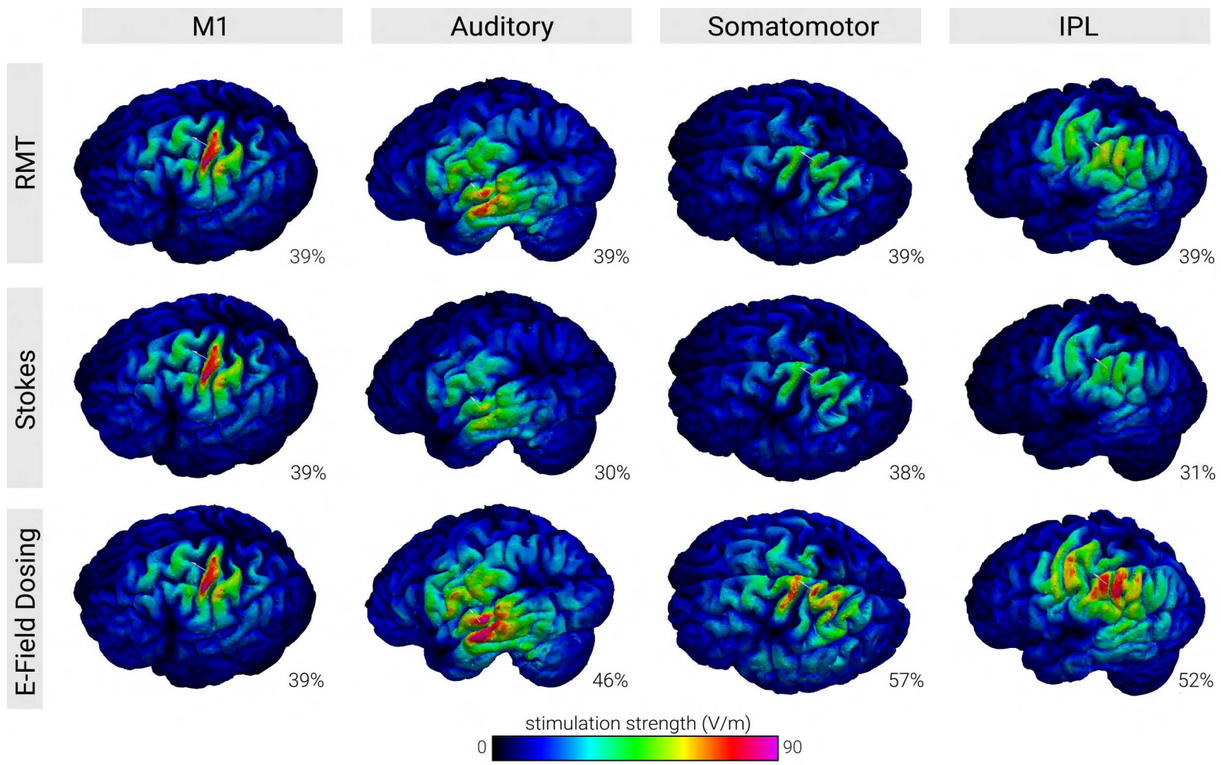
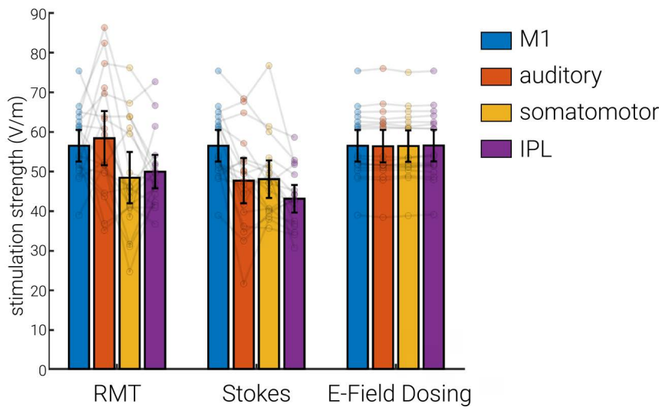


Figure 5.3.1.1 E-field-based dosing outperforms other dosing strategies on the subject level. Dosing based on resting motor threshold (RMT) alone (top row) applies the same stimulator intensity across regions (39% stimulator output in the given example), yielding highly variable cortical stimulation strengths. The so-called “Stokes” method (middle row) adjusts the intensity for distance between coil and cortex in a linear fashion, but still results in a suboptimal match between areas. Finally, e-field-based dosing (bottom row) yields the same stimulation strength for all targets, resulting in considerable adjustments of stimulation intensities for some targets due to differences in their responsiveness. M1 = primary motor cortex.



that elicited the same e-field in each target, as in the primary motor cortex at resting motor threshold. First simulation results showed that e-field-based dosing better matches the effective cortical stimulation than previous dosing approaches, both within participants (Figure 5.3.1.1) and across participants (Figure 5.3.1.2). These results indicate that e-field-based dosing may increase the stimulation efficacy and reduce both the within- and between-subject variability of TMS effects. Therefore, *a priori* e-field simulations have the potential to substantially improve TMS studies of higher cognition.

Figure 5.3.1.2 E-field-based dosing outperforms other dosing strategies on the group level. The effective stimulation strength is highly variable for dosing based on RMT (left) and the Stokes method (middle), both within and across participants. In contrast, e-field-based dosing (right) yields the same stimulation strength for the different targets within each participant, which also minimises the between-subject variability. Connected dots show individual subject data; error bars represent the 95% confidence interval. IPL = inferior parietal lobe, M1 = primary motor cortex.

5.3.2 Short-term network reorganisation in cognition after inferior parietal lobe perturbation

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The inferior parietal lobe (IPL) is an important hub of neural network function across multiple cognitive states, contributing to task-negative networks (default mode network; DMN) and task-active networks. To investigate flexible network behaviour in cognition, we combined double continuous theta burst stimulation (cTBS) with neuroimaging in both task and rest states. Thirty healthy, young volunteers participated in three measurements in which posterior IPL was inhibited using either right, left, or sham cTBS (Figure 5.3.2.1 for electrical field distribution and network overlap). This was done prior to a three-task fMRI experiment encompassing the key cognitive domains of attention, semantics, and social cog-

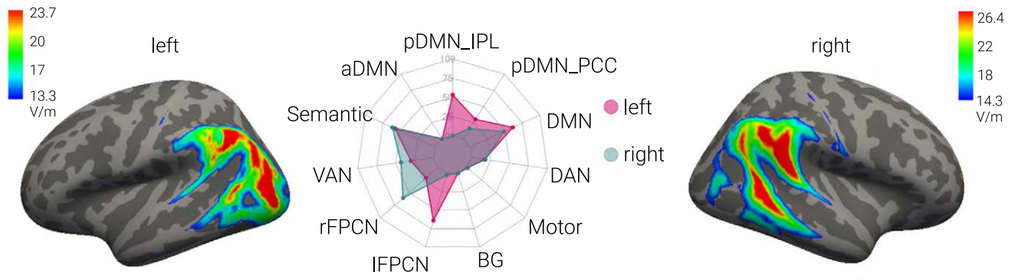

Figure 5.3.2.1 Stimulation-induced electric field coverage. The surface plots of the cortex show the left and right stimulation electric field norms, simulated using SIMNIBS, averaged across participants and thresholded at 90% of the maximum. The radar plot in the centre displays the proportions of each stimulation field that intersect with each functional connectivity network, as determined through overlapping network spatial maps with the union of all subject-specific stimulation regions of interest defined in volume space. pDMN_IPL: posterior default mode network that includes inferior parietal lobe; pDMN_PCC: posterior default mode network that includes posterior cingulate cortex; DMN: default mode network; DAN: dorsal attention network; BG: basal ganglia/subcortex network; (l/r)FPCN: left/right fronto-parietal control network; VAN: ventral attention network; aDMN: anterior default mode network.

nition. We identified 11 large-scale connectivity networks that organised during the tasks and assessed stimulation-induced changes of interactions between network pairs within each domain (Figure 5.3.2.2). Compared to sham, cTBS decreased several network interactions during social cognition, primarily from the posterior subnetwork of the DMN to task-positive networks. Stimulation increased interactions between default mode subnetworks and control networks during semantics. Only right-hemisphere stimulation influenced network connectivity during attention, with a mix of inhibition and facilitation. Collectively, our results demonstrate that beyond inducing local changes, cTBS influences large-scale network interactions in a domain-specific manner. The observed patterns suggest that the most complex cognitive task shows high responsiveness to stimulation, with more distributed changes across networks, while overall effects exhibit distinct alterations between task-active and task-negative networks.

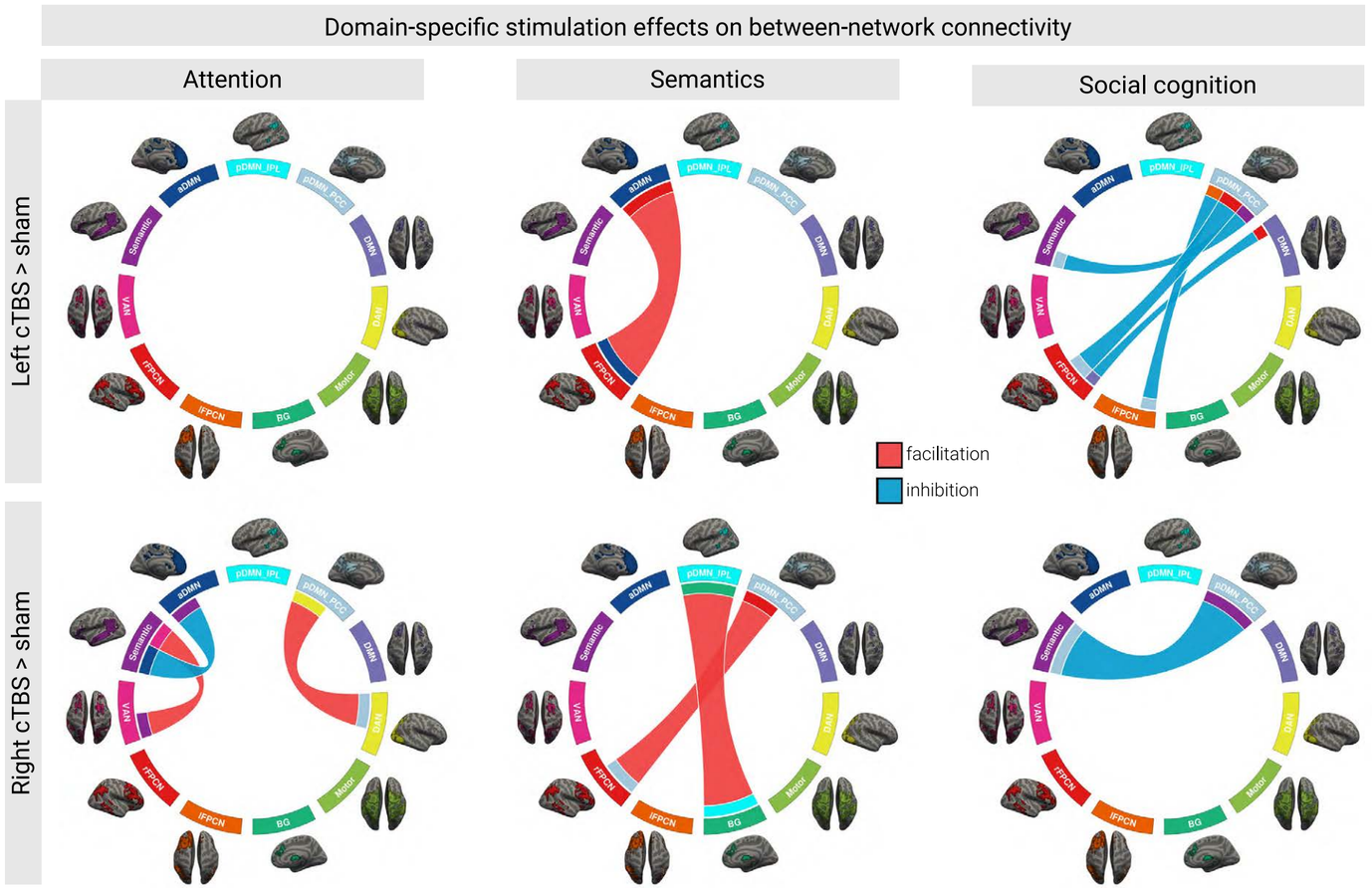

Figure 5.3.2.2 Domain-specific stimulation effects on between-network connectivity. Circular plots display significant changes in connectivity between 11 networks of interest that were derived from group-wise independent component analysis (ICA) performed on the sham task fMRI data. One-sided t-tests of the selected component spatial maps, resulting from back-projection to each subject's sham fMRI session run, were thresholded to sufficiently spatially represent each network ($p < 0.001$, uncorrected) and are displayed in each circle plot. Task-specific network connectivity was measured by correlational psychophysiological interaction (cPPI) analysis of the back-projected network time series for each task, contrasting the target and control conditions. Stimulation-induced changes were assessed within task through permutation testing between correlations for sham and either left or right stimulation ($p < 0.05$). Red and blue indicate increases and decreases in connectivity, respectively, connection widths indicate the strength of change in interaction, scaled within each plot.

5.3.3 Disrupted functional and effective connectivity underlie reading difficulties in dyslexia

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Dyslexia, a learning disability affecting reading and writing, is characterised by hypoactivation in classical reading areas, as well as compensatory activation outside the reading network. Despite years of research, the underlying changes in network interactions remain unknown. In the present study, we compared functional activation and functional and effective connectivity during word and pseudoword reading between neurotypical readers and adults with dyslexia. We found strong behavioural differences between groups and further confirm left-lateralised hypoactivation in dyslexics during word reading and bilateral hypoactivation during pseudoword reading (Figure 5.3.3.1). Functional connectivity analyses

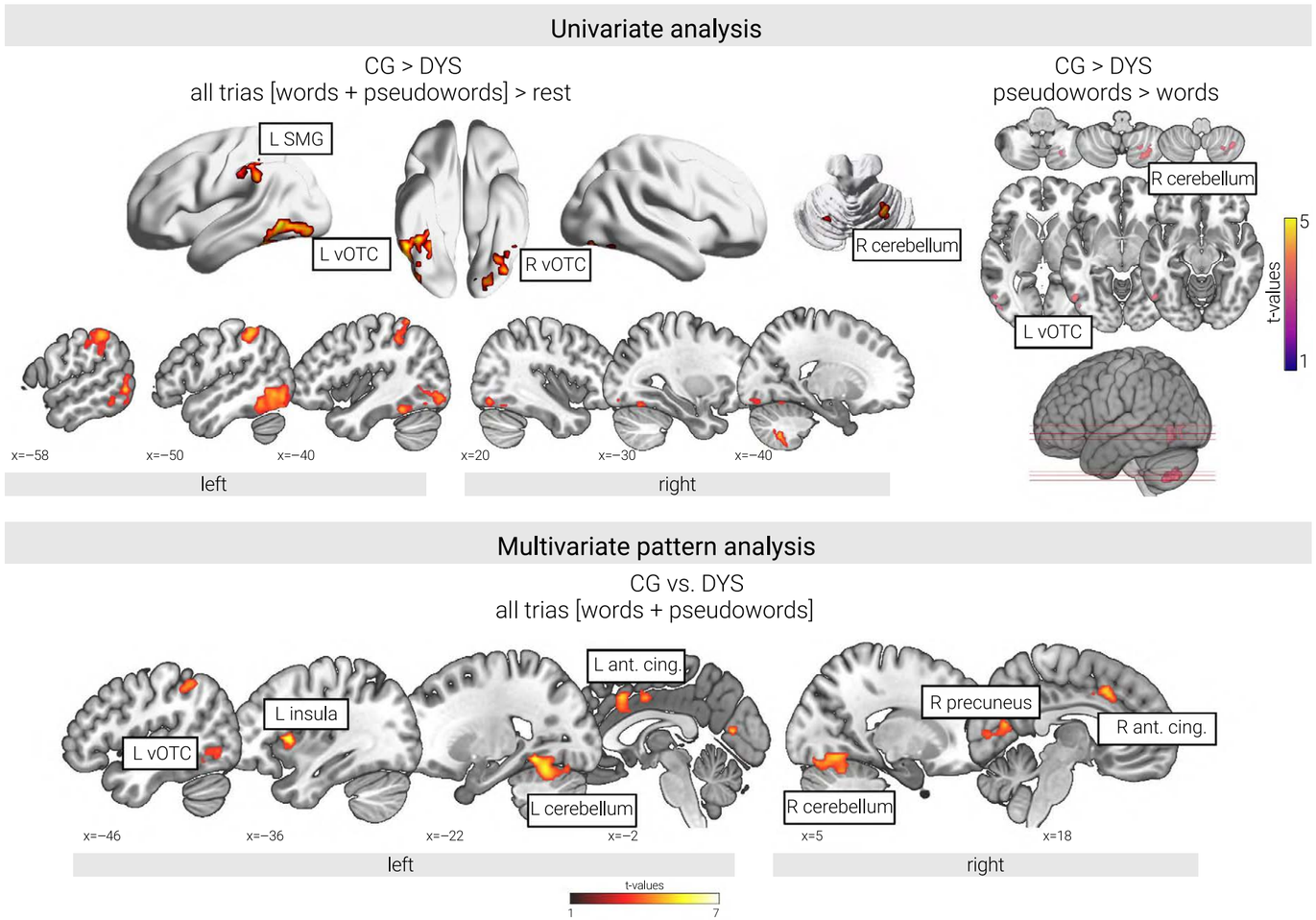

Figure 5.3.3.1 Univariate and multivariate brain contrasts showing hypoactivation in individuals with dyslexia in several regions in- and outside the classical reading network. All activation maps were thresholded at a voxel-wise $p < 0.001$ and a cluster-wise $p < 0.05$ FWE-corrected. CG: control group, DYS: adults with dyslexia, ant cing: anterior cingulate cortex, SMG: supramarginal gyrus, vOTC: ventral occipito-temporal cortex.

revealed weaker functional coupling from all reading regions in dyslexics, with the right cerebellum showing the strongest disruption. Effective connectivity analyses suggest that adults with dyslexia process words and pseudowords via a dorsal phonological decoding route and show reading-related interactions with the right cerebellum. Moreover, dyslexics had overall weaker intrinsic coupling between reading regions that varied substantially depending on word type (Figure 5.3.3.2). Furthermore, intrinsic connectivity between reading regions was linked to reading performance, suggesting that successful reading depends on stronger functional coupling. Overall, we provide the first evidence for aberrant functional and effective connectivity during reading that is linked to behavioural performance in adults with dyslexia.

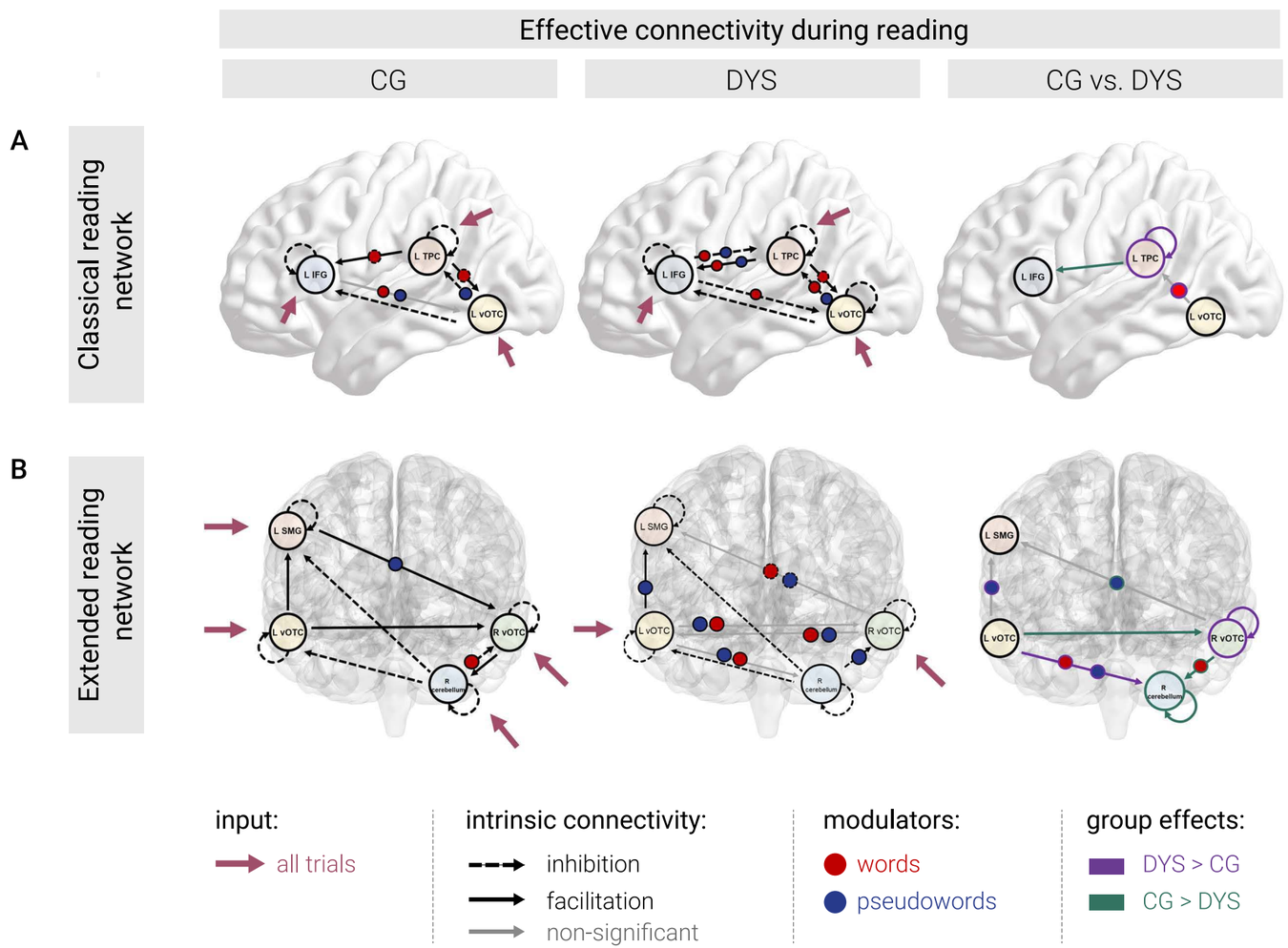

Figure 5.3.3.2 Aberrant effective connectivity in dyslexia. Differences in effective connectivity in the classical reading network (A) and the extended reading network (B) between neurotypical readers (control group, CG) and adults with dyslexia (DYS) as investigated through Dynamic Causal Modelling (DCM). We display the best model for each group, as well as a comparison DCM across groups. The Bayesian model average was thresholded to selectively retain parameters with a posterior probability > 95%. IFG: inferior frontal gyrus, SMG: supramarginal gyurs, TPC: temporo-parietal cortex, vOTC: ventral occipito-temporal cortex.

5.3.4 Age-related reorganisation of functional network architecture in semantic cognition

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Cognitive aging is associated with widespread neural reorganisation in the human brain. However, the behavioural impact of such reorganisation is not well understood. The current neuroimaging study investigated age differences in the functional network architecture during semantic retrieval in young and older adults. Combining task-based functional connectivity, graph theory, and cognitive measures of fluid and crystallised intelligence, our findings show age-accom-

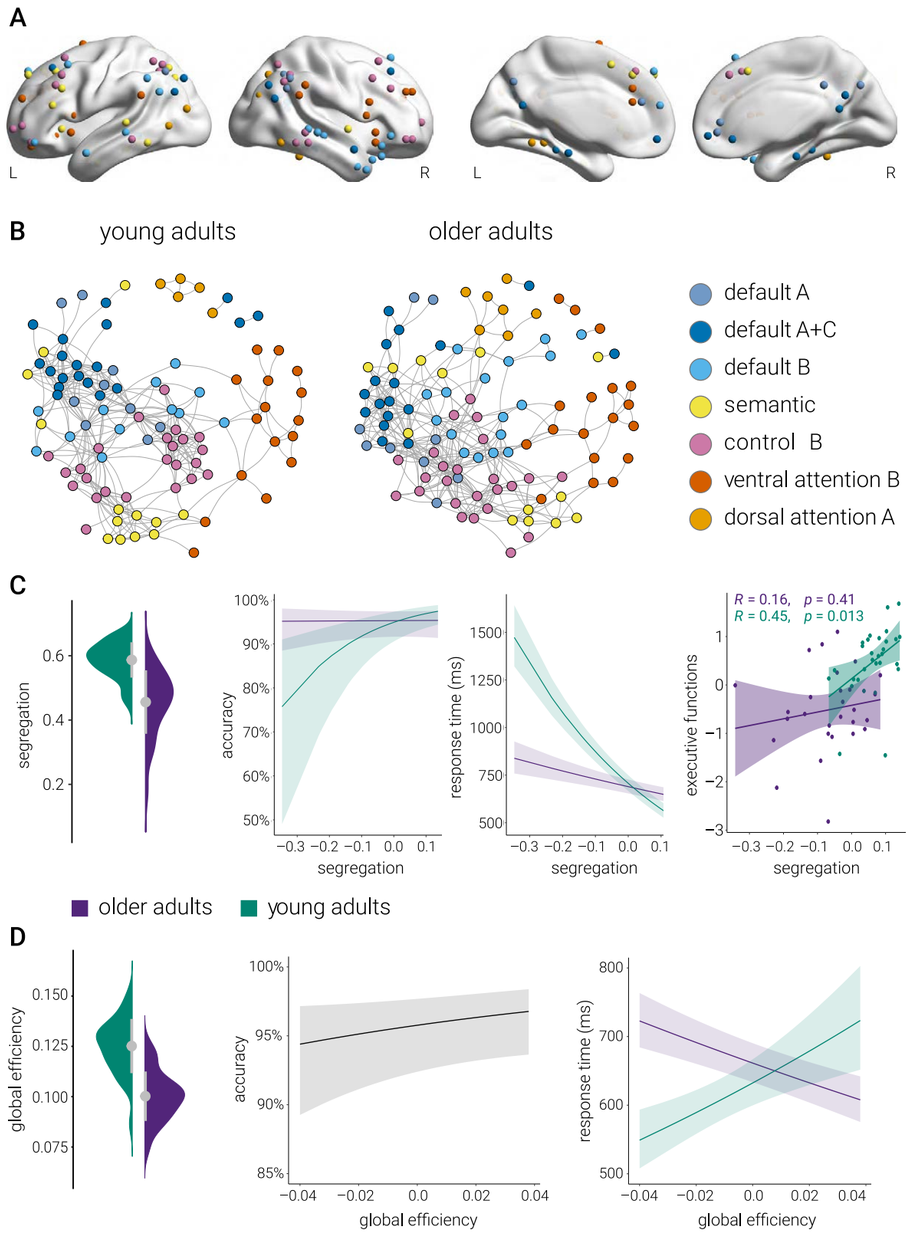

Figure 5.3.4.1 Age-related differences in whole-brain segregation and integration and their behavioural relevance. (A) For each participant, a task-related brain network graph was constructed using 121 nodes. The nodes were based on significant global and local peak maxima of the seven networks derived from an independent component analysis (ICA). (B) Spring-embedded graphs depicting age differences in the modular organisation of the brain. Graphs are based on average connectivity in each age group. Stronger segregation is reflected by higher within- and lower between-network correlations. In comparison, young adults show stronger segregation than older adults for most networks. For visualisation purposes, graphs are displayed at 5% graph density. (C) Brain-wide system segregation was higher for young adults and had distinct effects on behaviour for each age group, with young adults profiting from increasing segregation. (D) A different picture emerged for global efficiency. Global efficiency was calculated for individual orthogonal minimum spanning trees (OMST), which were based on weighted correlation matrices. The graphs of young adults showed stronger global efficiency than older adults. While increasing global efficiency was associated with better performance in both age groups, it predicted slower performance in young and faster performance in older adults. Note that segregation and global efficiency values were mean-centred for analyses with behaviour.

panied network reorganisation even when older adults have intact word retrieval abilities. Networks of older adults were characterised by reduced decoupling between systems (Figure 5.3.4.1), reduced segregation and efficiency, and a larger number of hub regions relative to young adults (Figure 5.3.4.2). Exploring the predictive utility of these age-related changes in network topology revealed high, albeit less efficient, performance for older adults whose brain graphs showed stronger dedifferentiation and reduced distinctiveness. Our results extend theoretical accounts of neurocognitive aging by revealing the compensational potential of the commonly reported pattern of network dedifferentiation when older adults rely on their prior knowledge for successful task processing. We also demonstrate the limitations of such compensatory reorganisation and show that a youth-like network architecture, in terms of balanced integration and segregation, is associated with more economical processing.

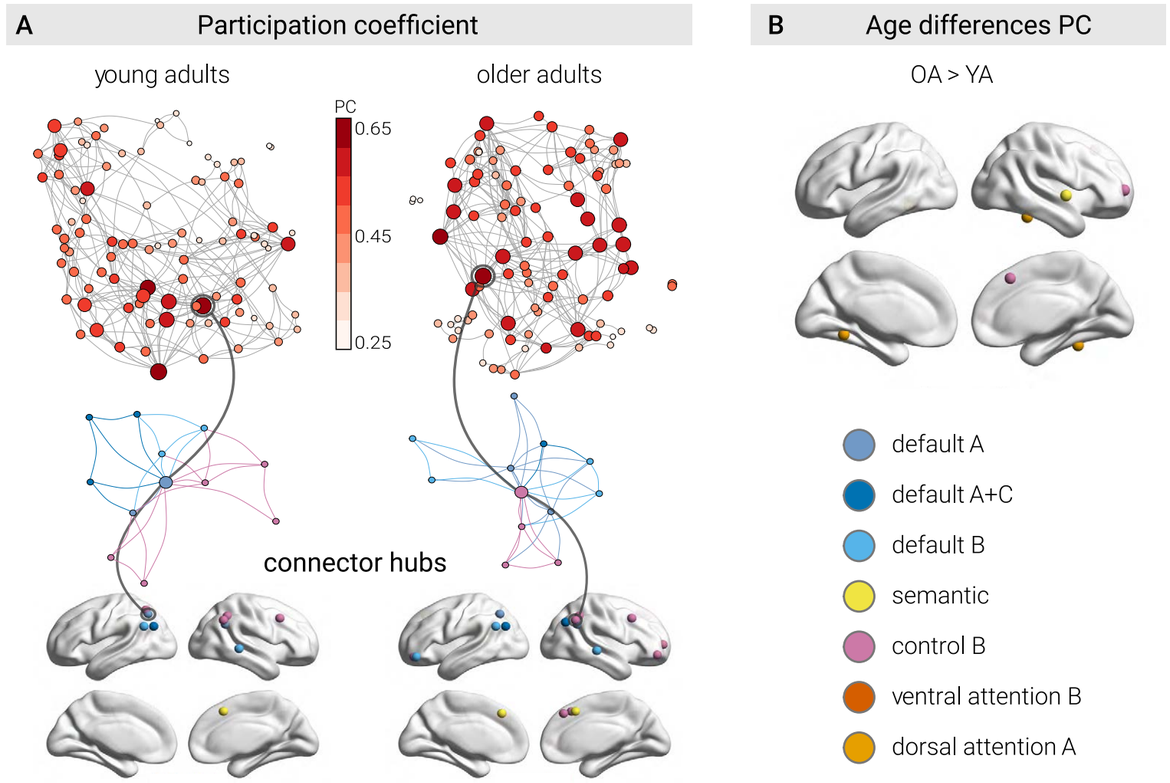

Figure 5.3.4.2 Topology of network hubs in young and older adults. (A) The normalised participation coefficient (PC) was calculated for individual orthogonal minimum spanning trees (OMST). Graphs display the PC of each node for the average OMST in each age group (top). For visualisation purposes, the strongest 5% of connections are shown. Stronger PC values are reflected by colour and node size. The higher the PC, the more a node is connected with nodes from other communities. The node with the highest PC value in each age group is extracted and displayed with its neighbouring nodes coloured by community (middle). Note that these connector hubs are connected to many different communities. Connector hubs were defined in each age group via PC values at least 1SD above the mean. In both groups, connector hubs were detected in frontal, parietal, and temporal regions (bottom). (B) A linear model with age as predictor revealed nodes with stronger PC only in older adults. The top and middle graphs were plotted using the ForceAtlas2 algorithm. The force-directed layout causes nodes of the same community to cluster together and diversely connected hubs (connector hubs) to appear in the centre of the graph.

5.3.5 Bayesian modelling dissociates key domains of human cognition in stroke patients

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[1] Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany, [2] Department of Biomedical Engineering, McConnell Brain Imaging Centre, Montreal Neurological Institute, Faculty of Medicine, McGill University, Montreal, Canada, [3] Mila - Quebec Artificial Intelligence Institute, Montreal, Canada, * shared senior authors

Stroke is the leading cause of long-term disability worldwide. It often severely impairs cognitive function. However, despite its dramatic impact on global health systems and societies at large, the neural substrates of stroke-induced impairments remain poorly understood. Most previous lesion studies focused on single cognitive domains derived from small patient cohorts with univariate analyses. We combined a novel Bayesian hierarchical modelling approach with compre-

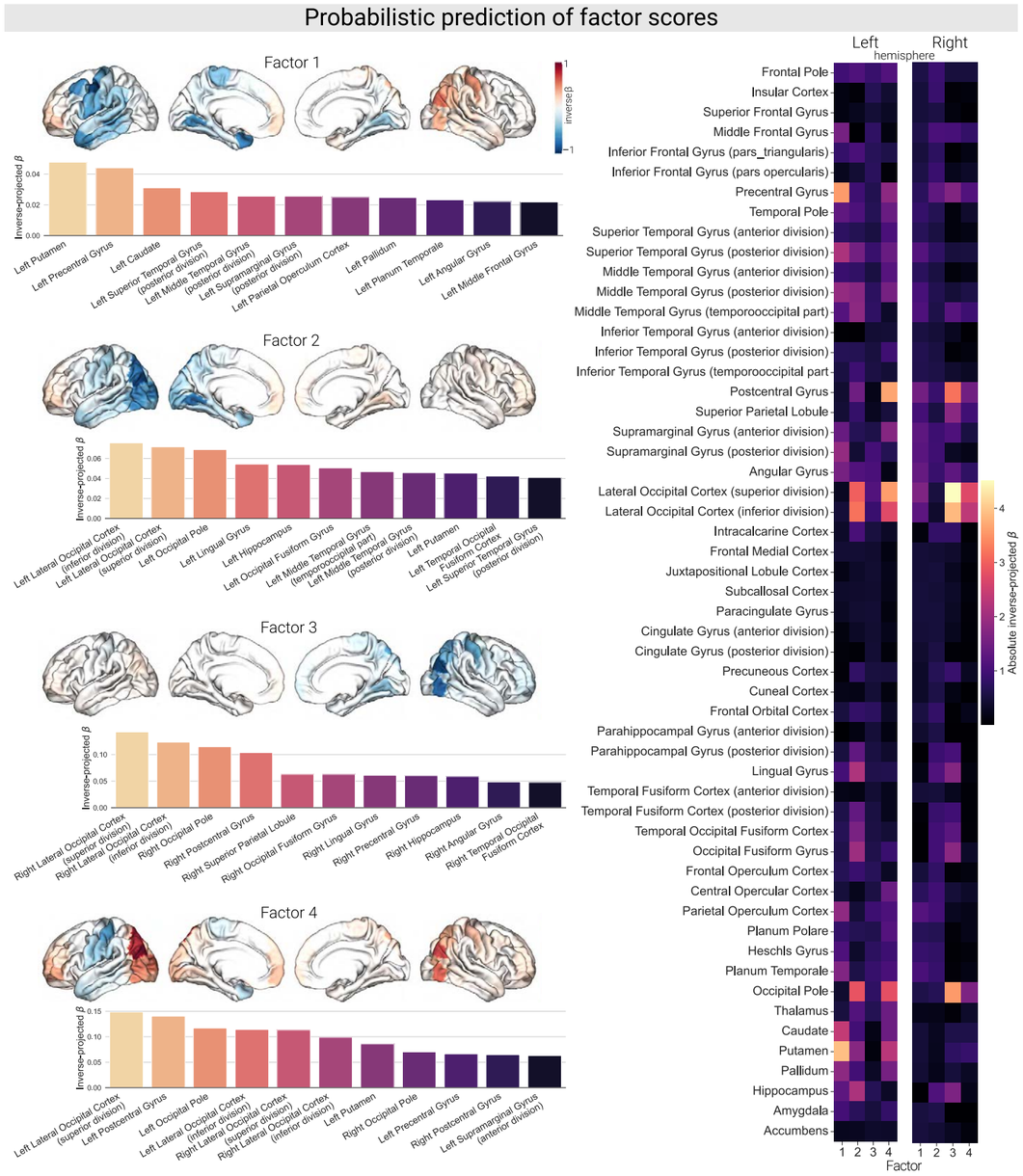

Figure 5.3.5 Stroke-induced cognitive impairments are predicted by lesions to distributed brain regions. Based on the inclusion of six neuropsychological tests, a four-factor solution was selected to represent distinct cognitive domains. Factor 1 comprises cognitive control processes, Factor 2 represents language-executive functions, Factor 3 represents mental flexibility, and Factor 4 summarises verbal memory. Left side: Lesion-deficit prediction for each factor. Coloured brains reflect associations of brain regions with lost (blue colour) or preserved (red colour) cognitive functions. Factors 1, 2, and 4 show a stronger left-hemispheric lateralisation, factor 3 is right-lateralised. Right side: 54 parcels per hemisphere were included based on the Harvard-Oxford cortical and subcortical atlas.

hensive clinical data in a sample of 1401 stroke patients to dissociate key dimensions of human cognition. Our framework predicted specific cognitive impairments based on distinct lesion atoms in distributed brain networks. Four factors distinguished unique left- and right-hemispheric contributions to cognition: cognitive control, language-executive functions, and verbal memory were mainly associated with left-hemispheric brain regions, while mental flexibility was strongly related to right-hemispheric areas (Figure 5.3.5). These results provide new insight into the causal relevance of hemispheric specialisation for human cognition and motivate process-specific lesion-centred treatment after stroke.

5.3.6. Changes in effective connectivity between language and domain-general networks contribute to language recovery after stroke

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Stroke often severely affects language function. A better understanding of post-stroke language recovery is crucial to identify reorganisation mechanisms and improve clinical interventions. Previous work suggested that early upregulation of lesion-homologous and domain-general areas contributes to recovery. However, the role of the right hemisphere remains debated. Moreover, it is unclear how changes in task-related activity are reflected at the neural network level. We

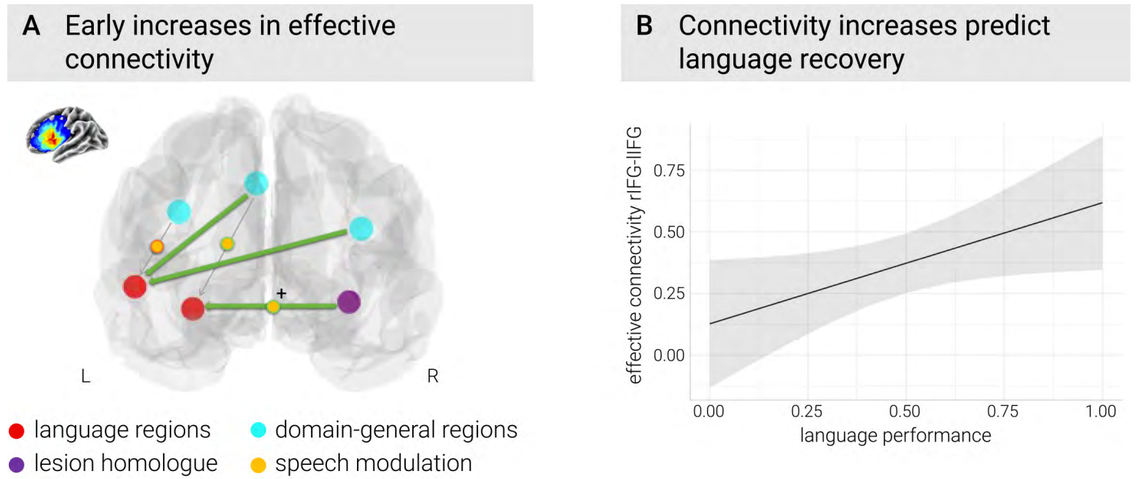

Figure 5.3.6 Changes in effective connectivity predict language recovery. Directed functional connections and their modulation by speech (yellow circles and +) were investigated during the acute, subacute, and chronic phases using Dynamic Causal Modelling and the Parametric Empirical Bayes framework. Regions-of-interest were selected based on language-related activation in a previous study, including the bilateral inferior frontal gyrus (IFG), bilateral dorsolateral prefrontal cortex, left posterior temporal lobe, and left supplementary motor area/ dorsal anterior cingulate cortex. For individual-level analysis, a full model was specified and estimated for each participant. The full model assumed full connectivity via reciprocal connections. At the group level, connection strengths of each subject were entered into a PEB model to compare the differences between patients and controls. A) Significant changes in connectivity in patients with frontal stroke during the acute phase (posterior probability > 95%). We found significantly increased facilitatory connectivity from the right IFG to the left IFG during speech processing (green arrow with yellow circle). Connectivity was also increased between domain-general and language regions (green arrows: facilitatory intrinsic connectivity, grey arrows: non-significant intrinsic connectivity, green outline: facilitation, orange outline: inhibition by speech). B) Increased connectivity from right to left IFG predicted language recovery as measured with a composite score from the Aachen Aphasia battery (AAT) in both patient groups (frontal and temporo-parietal lesions). $p < 0.05$.

examined changes in the effective connectivity between core areas of language-specific and domain-general networks after temporo-parietal and frontal stroke in the left hemisphere during speech comprehension. Two patient groups (n = 17 in each group) were investigated during the acute, subacute, and chronic phase after stroke and compared with healthy controls. First results suggest that domain-general regions exerted a facilitatory influence onto language areas during recovery. Patients with frontal stroke showed increased facilitatory connectivity from the right to the left prefrontal cortex during speech comprehension in the acute phase (Figure 5.3.6.1A). This increase in the facilitatory influence of the right on the left hemisphere correlated with better language recovery (Figure 5.3.6.1B). Collectively, our results support the notion that both lesion-homologous and domain-general areas are crucial for language recovery after stroke. Our results emphasise that an early upregulation of the lesion homologue may be adaptive after left-hemispheric stroke.

Congresses, Workshops, and Symposia

2021

- Hartwigsen, G., & Weiss-Lucas, C. (March). *Kartierung und Netzwerkplastizität von Sprachfunktionen – vom Modell zur Neuroonkologie.* Symposium at 65th Annual Meeting of the Deutsche Gesellschaft für Klinische Neurophysiologie und Funktionelle Bildgebung (DGKN), Frankfurt, Germany.

2022

- Jiang, Z. (April). *Language, communication, and brain – how do humans process language?* Workshop at Future Day "Discover the Brain". Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany.
- Hartwigsen, G., & Bergmann, T. O. (June). *Recent advances in NIBS.* Symposium at Psychologie und Gehirn, Freiburg, Germany.
- Hartwigsen, G. (June). *Computational Models in Language and Communication.* Symposium. 11th IMPRS NeuroCom Summer School in Cognitive Neuroscience. International Max Planck Research School on Neuroscience of Communication: Function, Structure, and Plasticity (IMPRS NeuroCom), Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany.
- Martin, S., & Jiang, Z. (October). *Introduction to data analysis in cognitive neuroscience.* Workshop for students from University of Amsterdam, NL. Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany.

Degrees

PhD Theses

2021

- Kuhnke, P. *The Neural Basis of Conceptual Knowledge Retrieval – Insights from fMRI and TMS in the Healthy Human Brain.* Potsdam University, Germany.
- van der Burght, C. *The central contribution of prosody to sentence processing: Evidence from behavioural and neuroimaging studies.* Leipzig University, Germany.

2022

- Chien, P.-J. *Neural bases of linguistic pitch in a tonal language: Intonation, lexical tone, and the role of language experience.* Leipzig University, Germany.
- Graessner, A. *The neural correlates of basic semantic composition.* Leipzig University, Germany.

Appointments

2021

- Hartwigsen, G. *Full Professorship for Biological Psychology*, Innsbruck, Austria (declined).
- Hartwigsen, G. Rank II, *Professorship for Cognitive Neuropsychology and Development*, Trier University, Germany.

2022

- Hartwigsen, G. *Full Professorship (W3) for Cognitive and Biological Psychology*, Leipzig University, Germany (accepted).
- Hartwigsen, G. *Board member and Deputy Spokesperson of the International Max Planck Research School on Cognitive Neuroimaging (IMPRS CoNI)*, Max Planck Institute for Cognitive and Brain Sciences, Leipzig, Germany.

Awards

2020

- Ferrante, M. *Scholarship of the German Academic Scholarship Foundation*, Bonn, Germany.
- Hartwigsen, G. *Early Career Award*. Society for the Neurobiology of Language (SNL).
- Hartwigsen, G. (as coauthor). *Poster award*. 5th International Conference on Non-invasive Brain Stimulation (NIBS), Leipzig, Germany.
- Martin, S. *Poster award*. 64th Annual Meeting of the German Society for Clinical Neurophysiology and Functional Imaging (DGKN), Germany (together with Gesa Hartwigsen).
- Turker, S. *Humboldt Research Fellowship for Postdoctoral Researchers.*

2021

- Zhizhao, J. *Scholarship of the German Academic Scholarship Foundation*, Bonn, Germany.

2022

- Hartwigsen, G. *ERC Consolidator Grant FLEXBRAIN.*

Publications

This list also includes publications of team members of the Lise Meitner Research Group Cognition and Plasticity that resulted from work they carried out prior to their arrival. These articles are included as they speak to the unique qualifications of the team members.

Books & Book Chapters

Alexandrovsky, D., Friehs, M., Grittner, J., Putze, S., Birk, M. V., Malaka, R., & Mandryk, R. L. (2021). Serious snacking: A survival analysis of how snacking mechanics affect attrition in a mobile serious game. In *Proceedings of the 2021 CHI Conference on Human Factors in Computing Systems*. New York, NY, USA: ACM. https://doi.org/10.1145/3411764.3445689

Chien, P.-J. (2022). Neural bases of linguistic pitch in a tonal language: Intonation, lexical tone, and the role of language experience. *MPI Series in Human Cognitive and Brain Sciences*: Vol. 221. Leipzig: Max Planck Institute for Human Cognitive and Brain Sciences.

Graessner, A. (2022). The neural correlates of basic semantic composition: Evidence from fMRI, lesion-behavior mapping and EEG. *MPI Series in Human Cognitive and Brain Sciences*: Vol 222. Leipzig: Max Planck Institute for Human Cognitive and Brain Sciences.

Kuhnke, P. (2021). The neural basis of conceptual knowledge retrieval: Insights from fMRI & TMS in the healthy human brain. *MPI Series in Human Cognitive and Brain Sciences*: Vol. 214. Leipzig: Max Planck Institute for Human Cognitive and Brain Sciences.

Journal Articles

Bergmann, T. O., & Hartwigsen, G. (2021). Inferring causality from noninvasive brain stimulation in cognitive neuroscience. *Journal of Cognitive Neuroscience*, *33*(2), 195–225. https://doi.org/10.1162/jocn_a_01591

Bikson, M., Hanlon, C., Woods, A., Gillick, B., Charvet, L., Lamm, C., Madeo, G., Holczer, A., Almeida, J., Antal, A., Reza Aye, M., Baeken, C., Blumberger, D., Campanella, S., Camprodon, J., Christiansen, L., Loo, C., Crinion, J., Fitzgerald, P., Gallimberti, L., Ghobadi-Azbari, P., Ghodratitoostani, I., Grabner, R., Hartwigsen, G., Hirata, A., Kirton, A., Knotkova, H., Krupitsky, E., Marangolo, P., Nakamura-Palacios, E., Potok, W., Praharaj, S., Ruff, C., Schlaug, G., Siebner, H., Stagg, C., Thielscher, A., Wenderoth, N., Yuan, T.-F., Zhang, X., & Ekhtiari, H. (2020). Guidelines for TMS/tES clinical services and research through the COVID-19 pandemic. *Brain Stimulation*, *13*(4), 1124–1149. https://doi.org/10.1016/j.brs.2020.05.010

Chapman, C., & Martin, R. C. (2022). Effects of semantic diversity and word frequency on single word processing. *Journal of Experimental Psychology: General*, *151*(5), 1035–1068. https://doi.org/10.1037/xge0001123

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Chien, P.-J., Friederici, A. D., Hartwigsen, G., & Sammler, D. (2021). Intonation processing increases task-specific fronto-temporal connectivity in tonal language speakers. *Human Brain Mapping*, *42*(1), 161–174. https://doi.org/10.1002/hbm.25214

Ekhtiari, H., Ghobadi-Azbari, P., Thielscher, A., Antal, A., Li, L. M., Shereen, A. D., Cabral-Calderin, Y., Keeser, D., Bergmann, T. O., Jamil, A., Violante, I. R., Almeida, J., Meinzer, M., Siebner, H. R., Woods, A. J., Stagg, C. J., Abend, R., Antonenko, D., Auer, T., Bächinger, M., Baeken, C., Barron, H. C., Chase, H. W., Crinion, J., Datta, A., Davis, M. H., Ebrahimi, M., Esmaeilpour, Z., Falcone, B., Fiori, V., Ghodratitoostani, I., Gilam, G., Grabner, R. H., Greenspan, J. D., Groen, G., Hartwigsen, G., Hauser, T. U., Herrmann, C. S., Juan, C.-H., Krekelberg, B., Lefebvre, S., Liew, S.-L., Madsen, K. H., Mahdavifar-Khayati, R., Malmir, N., Marangolo, P., Martin, A. K., Meeker, T. J., Ardabili, H. M., Moisa, M., Momi, D., Mulyana, B., Opitz, A., Orlov, N., Ragert, P., Ruff, C. C., Ruffini, G., Ruttorf, M., Sangchooli, A., Schellhorn, K., Schlaug, G., Sehm, B., Soleimani, G., Tavakoli, H., Thompson, B., Timmann, D., Tsuchiyagaito, A., Ulrich, M., Vosskuhl, J., Weinrich, C. A., Zare-Bidoky, M., Zhang, X., Zoefel, B., Nitsche, M. A., & Bikson, M. (2022). A checklist for assessing the methodological quality of concurrent tES-fMRI studies (ConTES checklist): A consensus study and statement. *Nature Protocols*, *17*(3), 596–617. https://doi.org/10.1038/s41596-021-00664-5

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Figure 5.3.4.1 & Figure 5.3.4.2

Figures taken from Martin, S., Williams, K. A., Saur, D., & Hartwigsen, G. (2022). Age-related reorganization of functional network architecture in semantic cognition. *Cerebral Cortex*. doi: 10.1093/cercor/bhac387.

5.4

Dr Lars Meyer

Max Planck Research Group Language Cycles

(commenced April 2019)

How Neurobiology Constrains Language (Processing) from the Inside Out

Language comprehension is mostly effortless. Yet, challenges can arise when speakers speak too fast or too slowly—or serve too much information in too little time. While we are flexible, our comprehension abilities are certainly limited.

We investigate whether inherent properties of the human brain are the culprit behind our limited verbal processing abilities. Our main focus is time: Does our preferred speech rate follow from the brain's preferred pace of information processing? How much information can we process within a given time window, and how long are the time windows that our brain uses for language processing? Might the language-processing time windows of the brain be the reason that the languages of the world have evolved to package information into sequences of discrete units, optimising the processability of human language(s)?

We combine methods from cognitive neuroscience and natural language processing. By relating neural oscillations in the magneto-/electroencephalogram to specific behavioural tasks and peripheral measures such as eye-tracking, we characterise the relevant electrophysiological time windows that determine the pace of linguistic information processing endogenously, that is, from the inside out. The workhorse of our experiments is speech or text that does not provide sufficient sensory information to inform the pace of neurocognitive sampling. This allows us to study the impact of the inherent temporal constraints that endogenous brain activity imposes on language comprehension.

The concomitant use of natural language processing enables us to quantify the size of acoustic and abstract units of information in the languages of the world. Through the use of information theory and dependency parsing, this addresses the overarching hypothesis that neurobiology is an evolutionary driving force behind the communicative effectiveness of human language.

In combination, the full circle of neurobiology, linguistic behaviour, and computational cultural science has the potential to explain the shape of human language through the processing cycles of the human brain—the language cycles.

5.4.1 Fast and slow endogenous rhythms of naturalistic reading revealed by combined eye-tracking and EEG

Henke, L.[1], Lewis, A. G.[2,3], & Meyer, L.[1,4]

[1] Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany, [2] Neurobiology of Language Department, Max Planck Institute for Psycholinguistics, Nijmegen, the Netherlands, [3] Radboud University, Donders Institute for Brain, Cognition and Behavior, Nijmegen, the Netherlands, [4] Clinic for Phoniatrics and Pedaudiology, University Hospital Münster, Germany

Neural oscillations have mostly been discussed in the context of sampling stimuli and inheriting rhythms that are physically present in those stimuli. We have proposed that oscillations may also fulfil endogenous functions, affecting processing from the inside out (Henke & Meyer, 2021; Meyer et al., 2019, 2020). In particular, oscillations may impose their temporal pace onto language processing. Studying this is challenging because speech contains physical rhythms that mask endogenous activity. To overcome this challenge, we investigated naturalistic reading, where text does not require the reader to sample at a specific rhythmic rate; any observed rhythmicity could thus be interpreted as endogenous. We analysed temporal regularities in eye movements (i.e., saccades and fixations), recorded by an eye-tracker, and linked them statistically to frequency-selective brain activity in simultaneously recorded EEG. We observed rhythmic patterns of eye movements that were synchronous with oscillatory activity in the EEG. First, word-locked saccades at 4 - 5 Hertz displayed coherence with occipital theta-band activity. Second, fixation durations fluctuated rhythmically at ~1 Hertz, in coherence with occipital delta-band activity. The faster (saccadic) rhythm may reflect active sampling of individual words, whereas the slower rhythm within the delta-band could index an endogenous chunking mechanism that serves to integrate words into larger linguistic units. We could additionally support the latter interpretation through the observa-

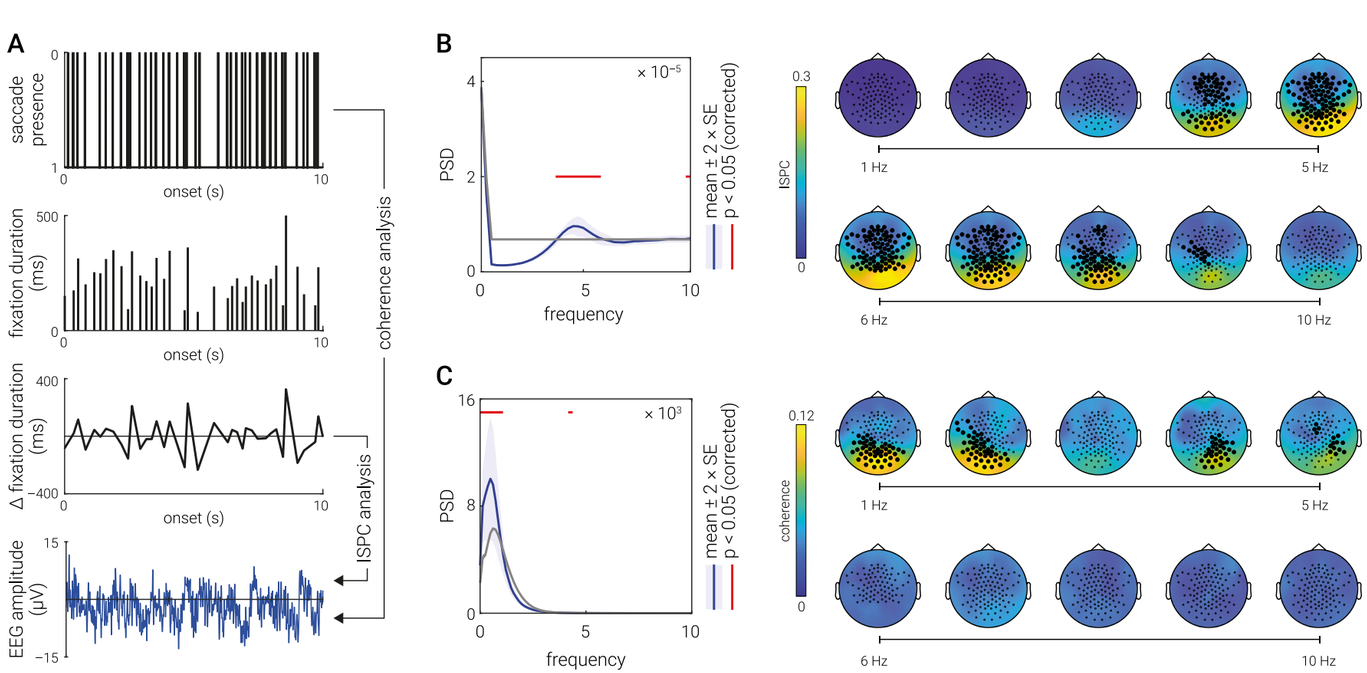

Figure 5.4.1 (A) Analysis pipeline; saccades and differenced fixation durations were paired with EEG recordings for the calculation of ISPC and coherence, respectively. (B) Left: PSD of saccades with a peak at ~5 Hz; right: ISPC showing coherence between saccades and the EEG at 5 Hz over the visual system. (C) Left: PSD of differenced fixation durations with a peak between 1–2 Hz over the visual system.

tion of phase-clustering of the EEG at sentence-final words. This suggests that readers actively align sentence endings to specific phase angles of those oscillations that subserve the formation of multi-word chunks. Since text does not provide any exogenous temporal rhythm, we suggest that rhythmic electrophysiological activity may serve as an endogenous pacemaker for language processing and in this way, shape reading into a periodic behaviour.

5.4.2 Prosodic rhythm influences subsequent sentence comprehension through sustained neural entrainment: MEG evidence

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Neural oscillations facilitate speech processing by synchronising with acoustic rhythms in speech. In particular, delta-band oscillations (< 4 Hertz) synchronise with prosodic rhythms. In four replications, we have shown behaviourally that prosodic rhythms can trigger downstream effects beyond stimulation, affecting the comprehension of upcoming visual sentences devoid of prosody (Lamekina & Meyer, 2022). To show that these effects reflect preceding entrainment of neural oscillations, that continues beyond the offset of prosody, we conducted a MEG experiment. We combined an initial prosodic rhythm with a subsequent visual target sentence. Targets were either long or short (e.g., “Max sees Tom and Karl laughs” vs. “Max sees Tom and Karl”). These were combined in a 2 × 2 design with prosodic contours that were either long or short (matching the durations of “Max sees Tom and Karl” and “Max sees Tom”, respectively). In the initial section of each trial, a contour was repeated 3 times to induce rhythmic entrainment. Subsequently, a visual target sen-

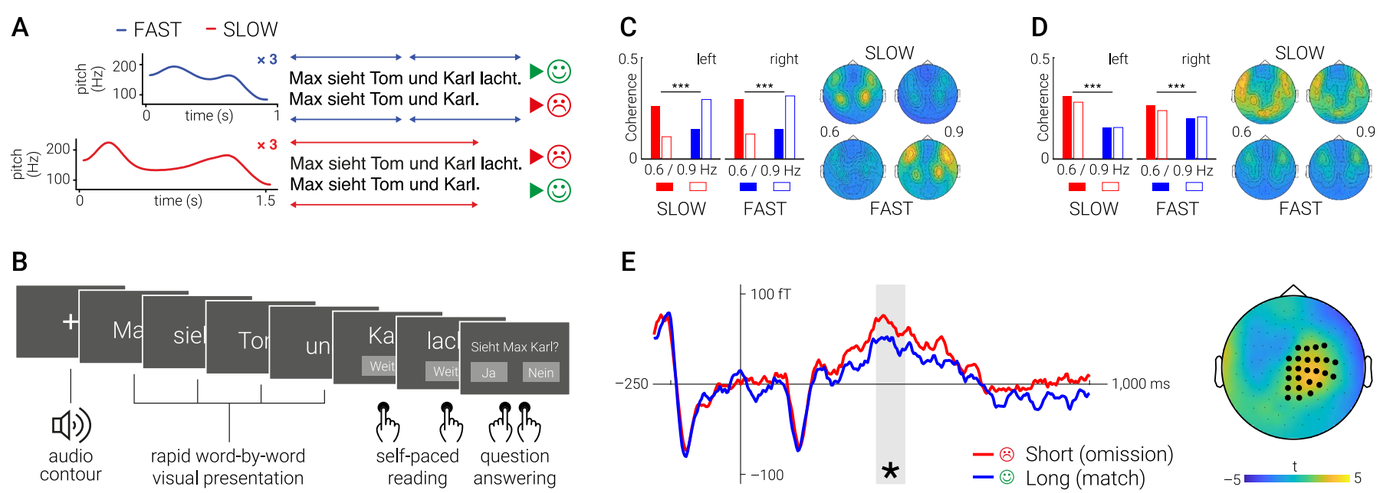

Figure 5.4.2 (A) Prosodic contour repeated 3 times to induce entrainment, followed by time-matched visual presentation of the sentence. The contour had two conditions: SLOW and FAST. Target conditions were LONG and SHORT. The combination of SLOW contour and SHORT sentence would yield an omission effect for the verb (B). Analysis of SLOW vs. FAST entrainment conditions for SHORT sentences; timepoint = onset of missing verb. Significant positive cluster in right centro-parietal area ($p < .01$, corrected) at 390 - 470 ms. (C) Pitch–brain coherence in entrainment phase. Significant differences in the whole brain: Under SLOW entrainment, coherence is stronger at 0.6 Hz, under FAST entrainment at 0.9 Hz. (D) Pitch–brain coherence (with absent contour) during target sentence. Significant differences between SLOW and FAST conditions in whole brain; differences within FAST condition.

tence was presented word by word; presentation was duration-matched to the rate of the previous stimulus. During auditory stimulation, we observed MEG coherence with prosody at the stimulation rate across sensors ($p < 0.001$, corrected). Strikingly, coherence persisted into the target section of the trial ($p < 0.001$, corrected), with a topographical shift to anterior sensors. Critically, when long contours were followed by short sentences, an ERF in the P300 - P600 time range was observed at the offset of the short sentence—likely indicating an omission response under the expectation of a long sentence. Together with our behavioural results, we conclude that a prior rhythmic prosodic context can drive sustained prosodic entrainment that affects subsequent sentence comprehension in a predictive fashion. More specifically, the stimulation frequency is conserved by brain areas associated with higher-level linguistic processing. Generally, we show that entrainment allows endogenous oscillations to exploit stimulus rhythms to serve downstream predictive functions.

5.4.3 Abstract segment boundaries block dependency processing: Evidence from neural frequency tagging and ERPs

Lo, C.-L.[1], & Meyer, L.[1,2]

[1] Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany, [2] Clinic for Phoniatrics and Pedaudiology, University Hospital Münster, Germany

To construct compositional meaning from sentences, we link single words in working memory. The resulting dependencies (NADs) can span multiple words. Both adults and children can process NADs induced from artificial grammars (AG). We demonstrate that NAD processing is restricted by the active segmentation of speech into multi-word memory

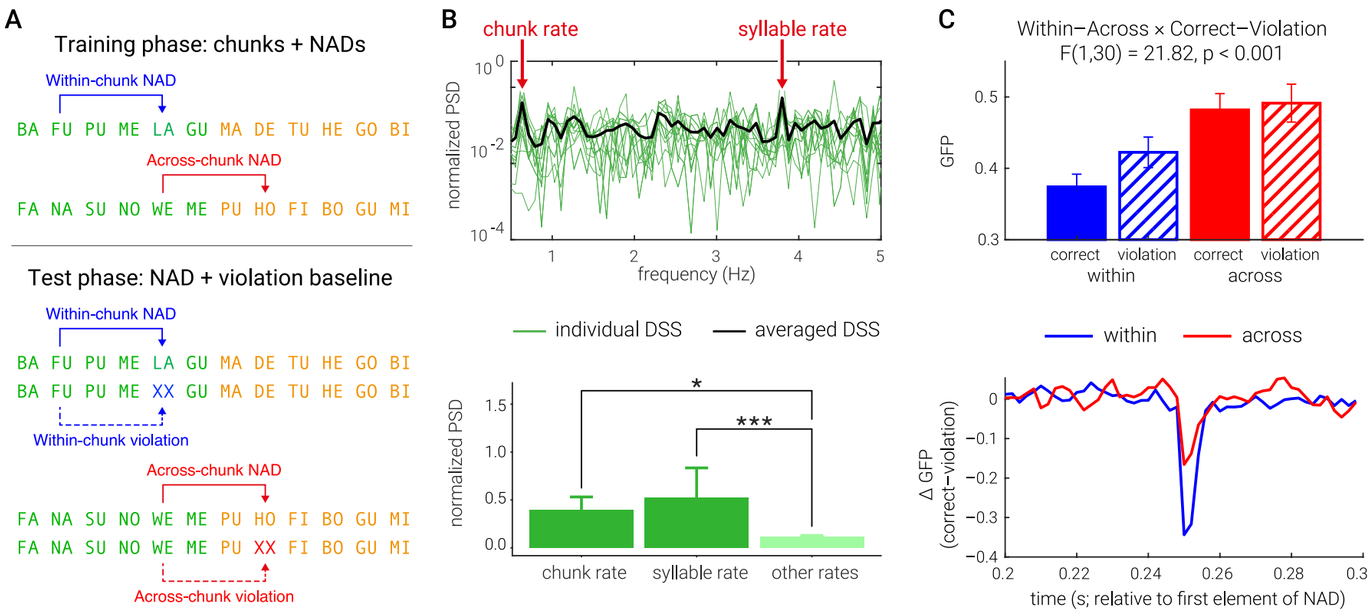

Figure 5.4.3 (A) Power spectra, learning phase. Peaks at the chunk and syllable rates are visible. (B) Significant differences in comparison between chunk rate and other rates ($p < 0.05$) and between the syllable rate and other rates ($p < 0.001$), but not the comparison between syllable and chunk rates ($p = 0.67$). (C) Example of stimuli for each condition. For both within- and across-chunk conditions, the differences of the syllables that constitute the second element of the NADs and the syllables that violate the dependency were compared. (D) GFP differences are larger in the within-chunk condition. (E) GFP across conditions.

chunks, by which our brain circumvents the temporal deterioration of memorised verbal information. During EEG acquisition, we trained subjects on NADs that would either be confined to the limits of a single memory chunk or cross the boundary between two chunks. We hypothesised that chunk boundaries would block NAD processing. During an initial learning phase, subjects listened to chunks that were delineated by a short gap and a decrease in transitional probability. Stimuli contained NADs that would span two syllables, either within or across chunks. In a subsequent test phase, subjects listened to stimuli that either contained within- or across-chunk NADs, or not. To assess chunk induction, we computed evoked power (EP) for the learning phase. To contrast NAD processing across the within- and across-chunk conditions, we analysed global field power (GFP) at the second element of the NAD, relative to an NAD violation baseline. In line with our hypothesis, we observed a peak at the chunk frequency during the learning phase, suggesting that participants learn the chunks and boundaries. Critically, GFP in the test phase indicated NAD processing in the within-chunk condition, whereas GFP was attenuated in the across-chunk condition. Hence, chunk boundaries appear to block NAD processing. Our results provide a link between the active segmentation of speech into multi-word memory chunks and the construction of compositional meaning, which may be restricted to the words of the current memory chunk.

5.4.4 Is speech rhythmic enough to be processed by neural oscillations? Corpus evidence for short-term periodicity of prosodic phrasing

Stehwien, S.[1], & Meyer, L.[1,2]

[1] Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany, [2] Clinic for Phoniatrics and Pedaudiology, University Hospital Münster, Germany

Speech is perceived as a sequence of meaningful units of various sizes, from phones to phrases. Prosody is one of the means that help the auditory system to segment speech into prosodic phrases, which correspond to meaningful multi-word units. In this speech corpus study, we studied prosodic boundaries in natural speech from the perspective of cognitive neuroscience. Our assumption was that in order to be understood, prosodic phrases must obey neurobiological constraints. In particular, electrophysiological processing has been argued to operate periodically—with one electrophysiological processing cycle being devoted to the processing of one prosodic phrase. We thus hypothesised that prosodic phrases in speech should exhibit periodicity. We assessed a large-scale corpus of radio news, which has been annotated for full intonational and intermediate phrases by human experts. We performed autocorrelation analyses on the spacing of intermediate phrase offsets, observing that sequences of 2–5 intermediate phrases were periodic at 0.8–1.6 Hertz, within their superordinate intonation phrase. Across utterances, the duration of intermediate phrases alternated with the duration of superordinate intonation phrases, indicating a dependence of prosodic time scales. While the determinants of periodicity are unknown, the results are compatible with an association between periodic electrophysiological processing mechanisms and rhythmic spacing of prosodic boundaries. We may speculate that speech provides acoustic cues that are rhythmic enough for periodic electrophysiological activity—neural oscillations—to align to. This points to a relationship between the properties of speech, as a cultural system, and neurobiology. In order for language to be comprehensible, it may have evolved to meet the processing functionalities of the brain.

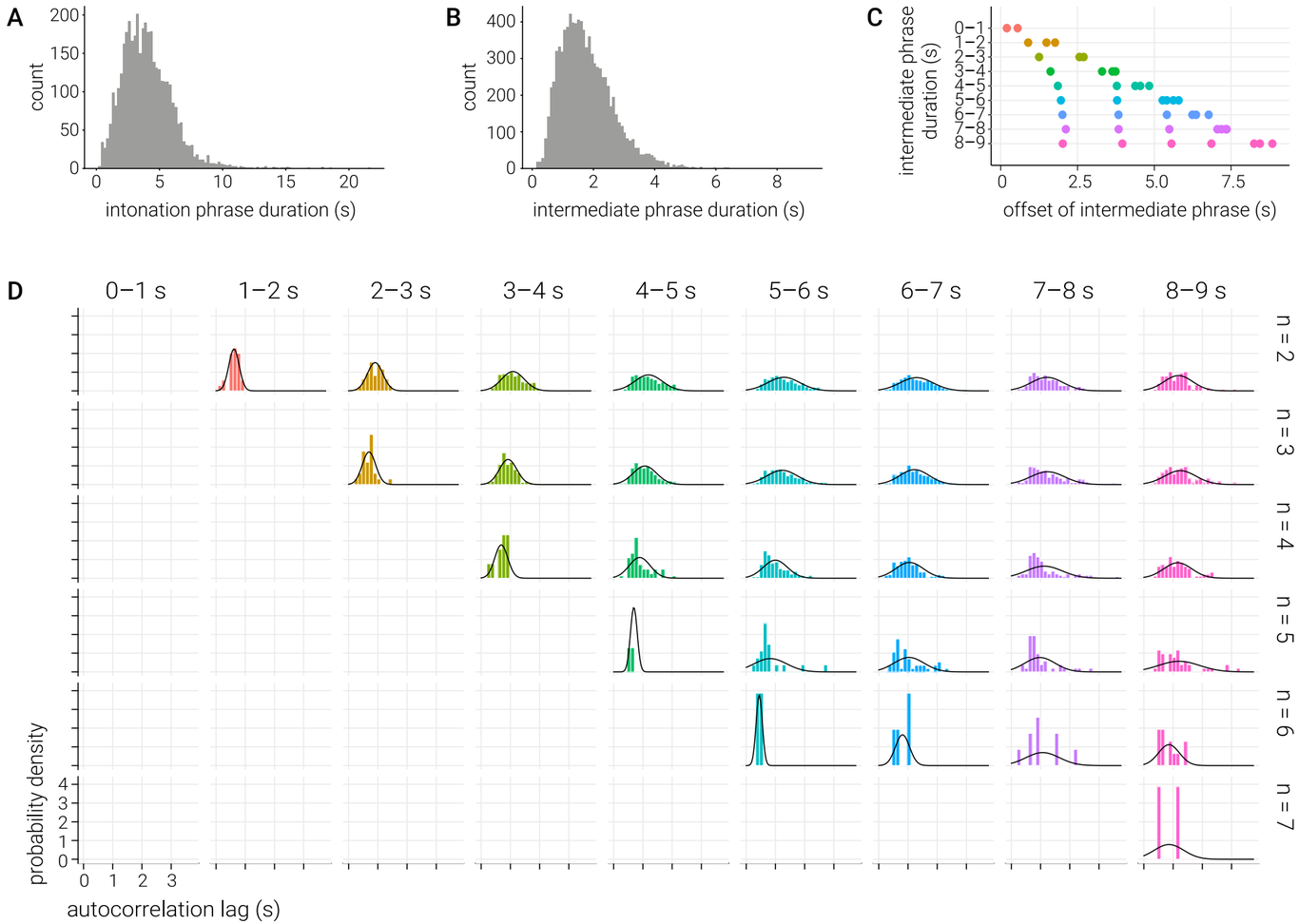

Figure 5.4.4 (A) Histogram of intonation phrase durations. (B) Histogram of intermediate phrase durations. (C) Spacing of intermediate phrase offsets split by intonation phrase duration. (D) Distribution of autocorrelation lags as a function of count of subsequent intermediate phrases (major y-axis) and intonation phrase duration (major x-axis).

Congresses, Workshops, and Symposia

2022

- Meyer, L. (February). *(Why) is Language (Not) Rhythmic? Workshop at the 44th Annual Conference of the German Linguistic Society (DGfS)*, University of Tübingen, Germany (Co-chair together with Antje Strauß).
- Meyer, L., & Nikulin, V. (June). *Promises, Practices, and Pitfalls of Current M/EEG Analysis Approaches.* Workshop. 11th IMPRS NeuroCom Summer School in Cognitive Neuroscience. International Max Planck Research School on Neuroscience of Communication: Function, Structure, and Plasticity (IMPRS NeuroCom), Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany.

Appointments

2022

- Meyer, L. *Faculty member of the International Max Planck Research School on Cognitive NeuroImaging (IMPRS CoNI)*, Max Planck Institute for Cognitive and Brain Sciences, Leipzig, Germany.

Awards

2020

- Lo, C.-W. *The SNL Graduate Student Abstract Merit Award - Honorable Mention*, The Society for the Neurobiology of Language, USA.

2021

- Lamekina, Y. *Best Poster Award.* 10th IMPRS NeuroCom Summer School in Cognitive Neuroscience. International Max Planck Research School on Neuroscience of Communication: Function, Structure, and Plasticity (IMPRS NeuroCom), Max Planck Institute for Human Cognitive and Brain Sciences & ICN, Leipzig & London, Germany & UK. Virtual.

Publications

Journal Articles

Henke, L., & Meyer, L. (2021). Endogenous oscillations time-constrain linguistic segmentation: Cycling the garden path. *Cerebral Cortex*, *31*(9), 4289–4299. https://doi.org/10.1093/cercor/bhab086

Lamekina, Y., & Meyer, L. (2022). Entrainment to speech prosody influences subsequent sentence comprehension. *Language, Cognition and Neuroscience*. https://doi.org/10.1080/23273798.2022.2107689

Lo, C., Tung, T.-Y., Ke, A. H., & Brennan, J. (2022). Hierarchy, not lexical regularity, modulates low-frequency neural synchrony during language comprehension. *Neurobiology of Language*, *3*(4), 538–555. https://doi.org/10.1162/nol_a_00077

Menn, K., Männel, C., & Meyer, L. (in press). Does electrophysiological maturation shape language acquisition? *Perspectives on Psychological Science*.

Menn, K., Michel, C., Meyer, L., Hoehl, S., & Männel, C. (2022). Natural infant-directed speech facilitates neural tracking of prosody. *NeuroImage*, *251*. https://doi.org/10.1016/j.neuroimage.2022.118991

Menn, K., Ward, E., Braukmann, R., van den Boomen, C., Buitelaar, J., Hunnius, S., & Snijders, T. M. (2022). Neural tracking in infancy predicts language development in children with and without family history of autism. *Neurobiology of Language*, *3*(3), 495–514. https://doi.org/10.1162/nol_a_00074

Meyer, L., Lakatos, P., & He, Y. (2021). Language dysfunction in schizophrenia: Assessing neural tracking to characterize the underlying disorder(s)? *Frontiers in Neuroscience*, *15*. https://doi.org/10.3389/fnins.2021.640502

Meyer, L., & Schaadt, G. (2020). Aberrant prestimulus oscillations in developmental dyslexia support an underlying attention shifting deficit. *Cerebral Cortex Communications*, *1*(1). https://doi.org/10.1093/texcom/tgaa006

Meyer, L., Sun, Y., & Martin, A. E. (2020). "Entraining" to speech, generating language? *Language, Cognition and Neuroscience*, *35*(9), 1138–1148. https://doi.org/10.1080/23273798.2020.1827155

Preprints

Zhu, J., Tian, Z., Liu, Y., Zhang, C., & Lo, C. (2022, October 23). Bootstrapping meaning through listening: Unsupervised learning of spoken sentence embeddings. *ArXiv*. https://doi.org/10.48550/arXiv.2210.12857

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Figure 5.4.4

Stehwien, S., & Meyer, L. (2022). Short-term periodicity of prosodic phrasing: Corpus-based evidence. *In Proceedings of Speech Prosody* (pp. 693-698).

5.5

Dr Charlotte Grosse Wiesmann

Minerva Fast Track Group Milestones of Early Cognitive Development

(commenced September 2019, maternity leave from 08/2021–4/2022)

Human cognition is inherently social. Preverbal infants already pay particular attention to social information and excel at predicting how other people will act. Yet, it is not before the age of 4 years that children are thought to infer what other people think or believe. This ability, referred to as Theory of Mind (ToM), is a hallmark of human social cognition. In our research group, we aim to understand the cognitive and neural developments that give rise to this milestone and its precursors in infancy. Our research indicates a behavioural and neural dissociation between mature verbal ToM, emerging in the preschool years, and nonverbal precursors of ToM in infancy, suggesting two different systems for reasoning about other agents (5.5.1). Mature ToM requires understanding that another person's perspective may differ from our own. Managing these different perspectives makes considerable demands on executive functions, which young infants are lacking. A central hypothesis of our research is that infants do not represent several perspectives, but instead, only hold a single representation of their environment, which is biased by the view of others. These biases would allow infants, despite their limited executive capacities, to consider the other's view without the need to manage several distinct perspectives. Indeed, we have found evidence for such biases in infants' behaviour and neural processing of their environment (5.5.2).

Children's executive functions improve rapidly in the preschool years, providing a basis for mature ToM. In a second line of research, we study the neural maturation underlying this cognitive leap in executive function (5.5.3) and its interaction with social cognition (5.5.4). A guiding hypothesis for this research is that executive functions are not only needed for mature social cognition, but that social cognition and emotion also modulate our executive capacities from early on in childhood. Accordingly, we find different subsystems for executive control in neutral cognitive versus emotional situations in the developing brain.

We propose that the different systems found in development persist until adulthood and provide efficient routes to understanding others and to executive control in situations of high social saliency and limited time or cognitive resources. Thus, by clarifying the cognitive structure and neural mechanisms of these developmental achievements, our research advances our understanding of the fundamental building blocks of human cognition.

5.5.1 Two systems for thinking about others' thoughts in the developing brain

Grosse Wiesmann, C.[1,2], Friederici, A. D.[1], Singer, T.[3], & Steinbeis, N.[4]

[1] Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany, [2] Institute for Psychology, Copenhagen University, Denmark, [3] Social Neuroscience Lab, Max Planck Society, [4] Faculty of Brain Sciences, UCL, UK

Human social interaction crucially relies on our ability to infer what other people think, referred to as Theory of Mind (ToM). This ability has long been argued to emerge around 4 years of age when children start passing verbal ToM tasks. This developmental dogma, however, has been questioned by nonverbal ToM tasks that preverbal infants can already pass in their first two years of life. How do infants solve these tasks, and what is the relation to later developing verbal ToM reasoning? Are there two different systems for nonverbal and verbal ToM, and when is the developmental onset of mature adult-like ToM? To address these questions, we related markers of cortical brain structure (i.e., cortical thickness and surface area) of 3- and 4-year-old children (N = 38) to their performance in infant nonverbal and traditional verbal ToM tasks. This showed that the breakthrough in verbal ToM reasoning between 3 and 4 years was associated with increased cortical surface area and thickness of the precuneus, posterior temporal, and temporoparietal brain regions, classically involved in ToM in adults (see Figure 5.5.1). Nonverbal ToM task performance, in contrast, was supported by the cortical structure of independent brain regions including the supramarginal gyrus and dorsal precuneus, which are part of the salience network and involved in social attention. This neural dissociation suggests two different systems for reasoning about others—mature verbal ToM that emerges around 4 years of age and nonverbal ToM tasks that rely on different processes that may be based on social attention.

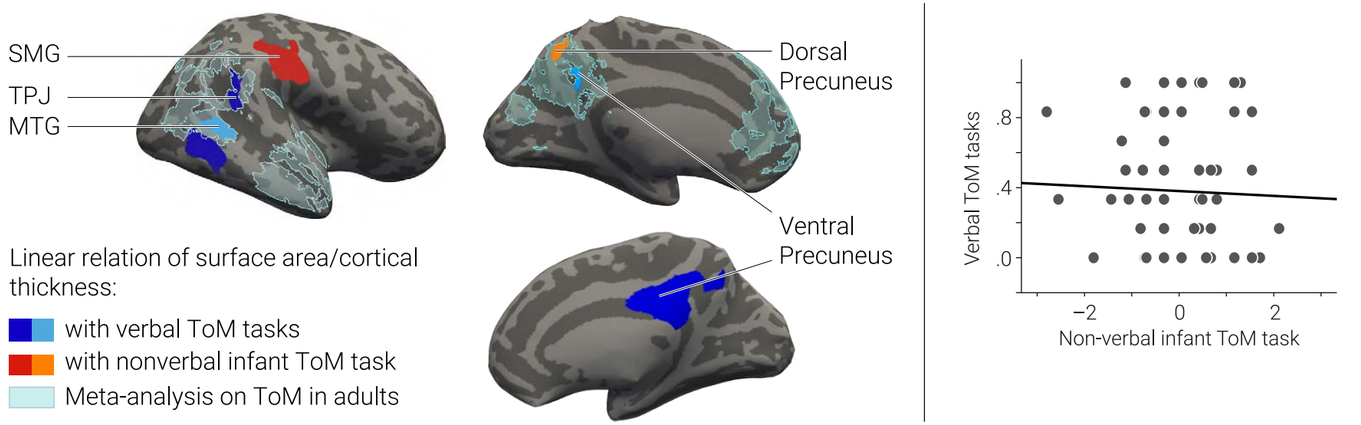


Figure 5.5.1 (A) Verbal ToM task performance of 3- to 4-year-old children (N = 38) showed a linear relation with cortical surface area (dark blue) and cortical thickness (light blue) in regions activated for ToM in adults (transparent turquoise area), i.e., the temporo-parietal junction (TPJ), posterior middle temporal gyrus (MTG), and precuneus. Nonverbal ToM task performance, in contrast, was related with cortical surface area (red) and cortical thickness (orange) in independent brain regions, i.e., the supramarginal gyrus (SMG) and dorsal precuneus. These relations were independent of age, gender, and co-developing cognitive abilities (with the exception of the dorsal precuneus effect for nonverbal ToM). The relations with verbal ToM were independent of the nonverbal ToM task and vice versa. All effects are cluster-size corrected with significance threshold $p < 0.05$ and are shown on the inflated surface of a common group template. (B) Behavioural task performance in verbal ToM showed no correlation with nonverbal ToM task performance in an overlapping sample of N = 60 children aged 3 to 4 years.

5.5.2 Infants' and adults' neural object processing is biased by the perspective of another agent

Tebbe, A. L.[1], Rothmaler, K.[1], Köster, M.[2], & Grosse Wiesmann, C.[1]

[1] Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany, [2] Institute for Psychology, University of Regensburg, Germany

From their first year of life, infants excel at predicting how other agents will act and thereby consider the other's perspective. However, it is not before the age of 4 years that children begin to reason verbally that different agents may have different perspectives. Based on the observed behavioural and neural dissociation between verbal ToM in preschool-age and nonverbal infant ToM tasks, we hypothesised that infants may not represent different perspectives, but that, instead, their own processing of their environment may be biased by the visual attention of other agents. We hypothesised that such biases may persist until adulthood as a fast route to understanding others. We therefore tested whether infants' and adults' neural object processing is biased by what other agents can see. We presented participants with an agent that was watching an object, which either moved into a tunnel (blocking the agent's view) or behind an occluder (blocking the participant's view but not the agent's, see Figure 5.5.2). The object flickered at 4 Hz, evoking neural oscillations at the same frequency (referred to as steady-state visually evoked potentials, ssVEP), thus providing a specific signature of participants' neural object processing. As predicted, both adults (N = 40) and 12- to 14-month-old infants (N = 56, both sample sizes from preregistered Bayesian sequential testing scheme) showed larger 4 Hz responses when the agent continued to see the object (occluder condition), compared to when the agent's view was blocked (tunnel condition). For adults, this effect was most pronounced while the object was disappearing but persisted after the object was fully occluded. For infants, the difference was found only after the object was fully occluded. A non-social control condition ensured that this effect was related to the agent's perspective and did not result from visual differences between the tunnel and occluder. In sum, these findings support the view that infants' and adults' object processing is biased by what other agents can see, providing a potential mechanism for nonverbal ToM success in infancy.

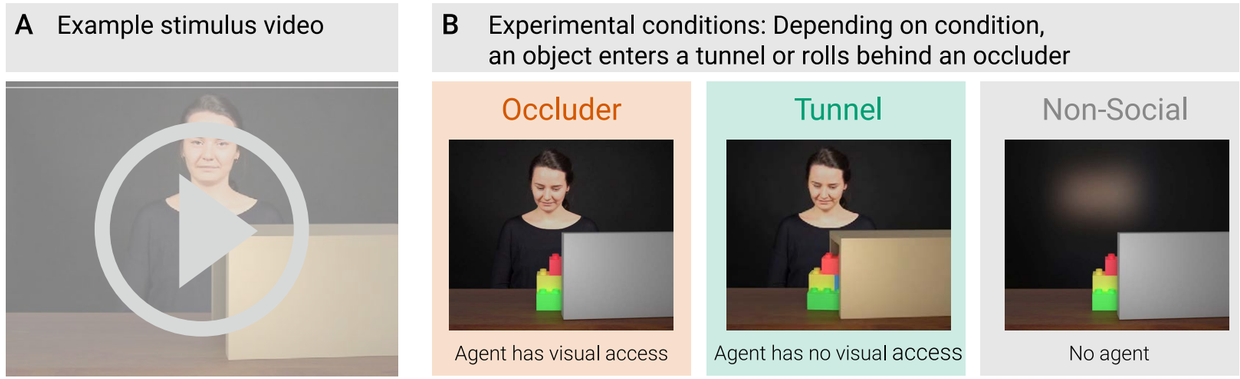
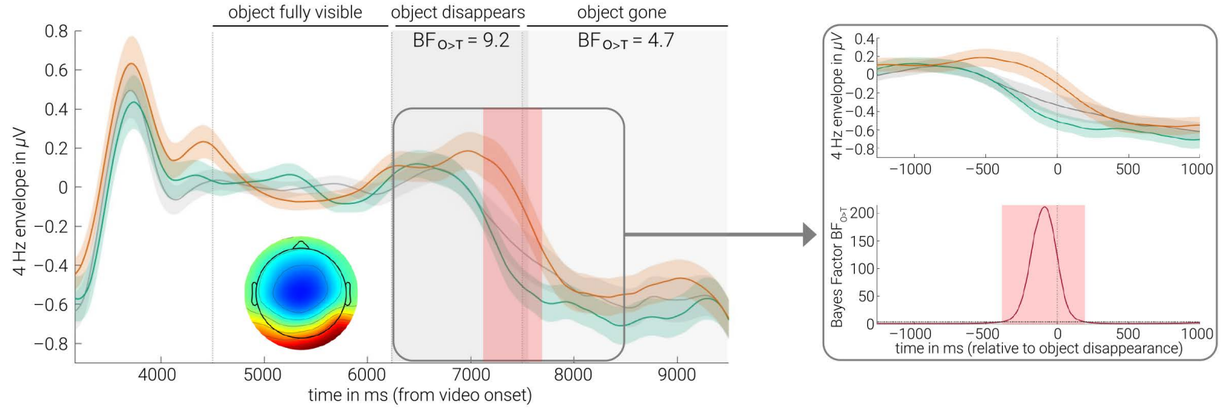
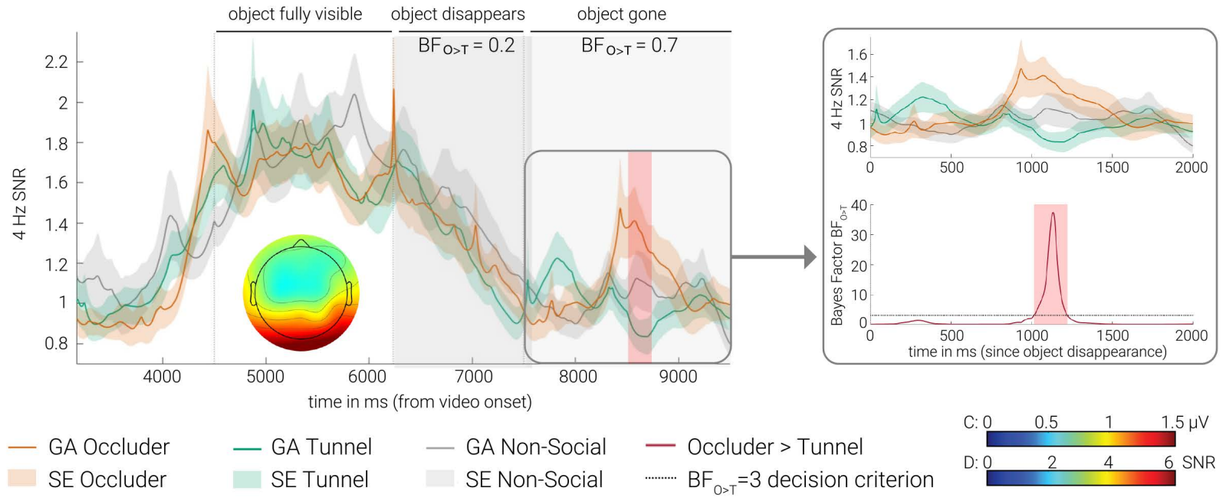


Figure 5.5.2 (A) Example of the video stimuli: An object flickering at 4 Hz enters a tunnel or occluder, depending on condition. (B) Three experimental conditions: in the occluder condition, the agent continues to see the object after its occlusion. In the tunnel condition, in contrast, the agent's view of the object is blocked. Finally, in a non-social control condition, the same scene was shown without an agent.

C Adult results: Adults showed prolonged ssVEP responses to the flickering object in the occluder condition, i.e., when the agent continued to see the object



D Infant results: 12-14-month-old infants showed increased ssVEP responses after the disappearance of the flickering object in the occluder condition, i.e., when the agent continued to see the object



(C) Adult results (N = 40): Amplitude of the 4 Hz signal envelope in response to the flickering object over the course of the trial and topography of the response while the object was fully visible. We found evidence for a larger 4 Hz response in the occluder compared to the other two conditions in two preregistered time windows (grey shaded areas) and in a preregistered dynamic analysis (red shaded area). (D) Infant results (N = 56): Signal to noise ratio (SNR) of the power at the stimulated frequency (4 Hz) compared to neighbouring frequencies in response to the flickering object over the course of the trial and topography of the response while the object was fully visible. As preregistered, SNR was used as a baseline-free measure because of systematic baseline differences between the conditions. We found evidence for a larger 4 Hz response in the occluder compared to the tunnel condition in a preregistered dynamic analysis (red shaded area).
Abbreviations: ssVEP = steady state visually evoked potential, BFO>T = Bayes factor quantifying the evidence in favour of a bigger signal in the occluder compared to the tunnel condition, SNR = signal to noise ratio, GA = Grand Average, SE = Standard Error

5.5.3 Maturational indices of the cognitive control network are associated with executive control in early childhood

Berger, P.[1], Friederici, A. D.[1], & Grosse Wiesmann, C.[1]

[1] Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany

Complex human behaviour crucially relies on our capacity to suppress immediate impulses and predominant responses. This ability, called executive control, emerges in early childhood with marked improvements between 3 and 4 years. A distinction between neutral cognitive ('cold') and emotional ('hot') contexts has been proposed. Here, we asked which

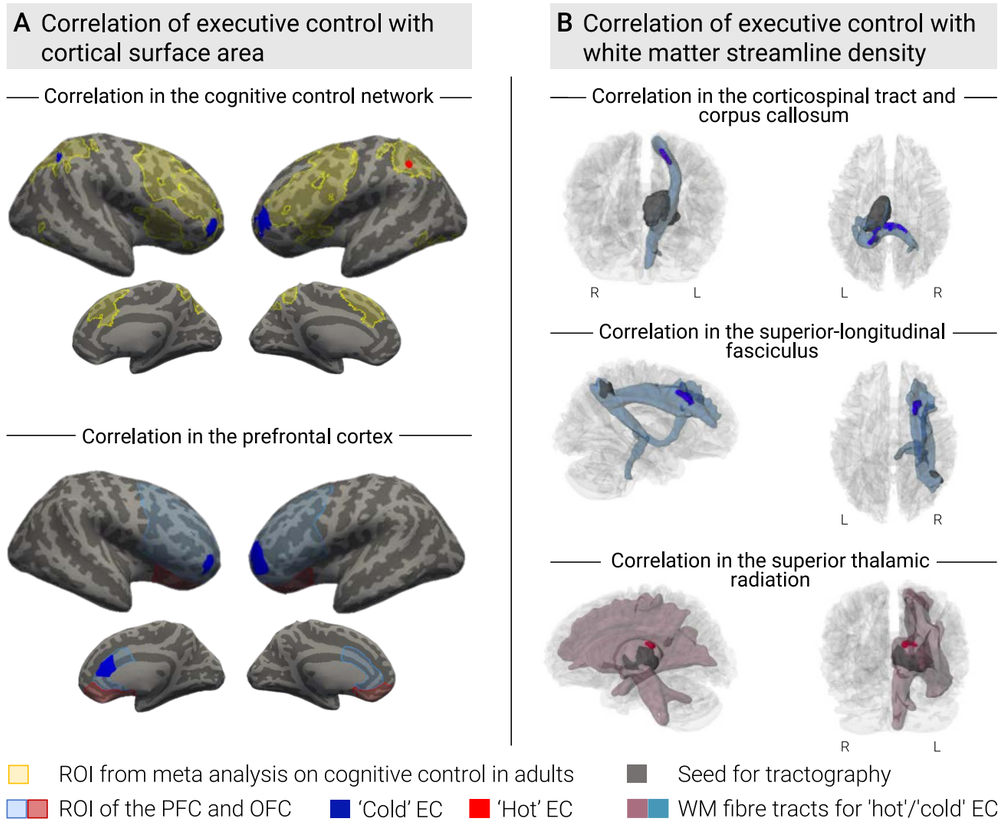


Figure 5.5.3 (A) **Top:** Linear relation of 3- to 4-year-old children's (N = 38) cortical surface area with their performance in the neutral 'cold' executive control task (dark blue, in the bilateral rostral frontal cortex (BA10) and right inferior parietal lobe) and in the emotional 'hot' executive control task (red, in the left supramarginal gyrus (SMG)) within regions activated for cognitive control in adults (transparent yellow area). These relations were independent of age and gender. The relations with the 'cold' executive control task were independent of the 'hot' executive control task and vice versa. All effects are cluster-size corrected with significance threshold $p < 0.05$ and are shown on the inflated surface of a common group template. **Bottom**: Small-volume correction within the prefrontal cortex (transparent blue area) additionally revealed a linear relation of cortical surface area with children's 'cold' executive control (dark blue) in the caudal ACC. (B) White matter fibre tracts reconstructed with probabilistic tractography seeded in the regions related with 'cold' (light blue) and 'hot' (light red) executive control (seeds in grey). Streamline density of these tracts showed a linear relation with children's 'cold' executive control performance (dark blue) in the left corticospinal tract, the forceps major, and the right superior-longitudinal fasciculus. 'Hot' executive control, in contrast, was correlated with streamline density of the right superior thalamic radiation (red). These relations were independent of age and gender and cluster-size corrected with significance threshold $p < 0.05$.
Abbreviations: EC = Executive control, PFC = Prefrontal Cortex, OFC = Orbitofrontal Cortex, WM = White Matter

brain structures support the emergence of this critical ability, and whether these differ for neutral and emotional contexts. Using a multimodal neuroimaging approach, we related behavioural performance in 3- and 4-year-olds' (N = 37) executive control, in neutral versus emotional situations, to structural indices of their grey and white matter maturation. Our results show that the cortical structure of distinct parts of the cognitive control network were associated with children's 'hot' versus 'cold' executive control (Figure 5.5.3A). Specifically, children's executive control in the neutral context was related to the cortical surface area in the lateral prefrontal cortex, anterior cingulate cortex (ACC), and the volume of the left thalamus, areas classically involved in 'cold' inhibitory control tasks in adults. In addition, probabilistic tractography revealed an association with frontoparietal and thalamocortical connections (Figure 5.5.3B). In contrast, executive control in the emotional context was related with the inferior parietal cortex, implicated in attentional control in adults, as well as the volume of the right thalamus, and its connection to motor and parietal cortices. This suggests that controlling approach-avoidance tendencies may be critical for the development of 'hot' executive control. The dissociation of brain networks associated with 'hot' versus 'cold' executive control development suggests that different subsystems support executive function in neutral cognitive versus emotional contexts.

5.5.4 Positive emotion enhances conflict processing in preschoolers

Berger, P.[1], & Grosse Wiesmann, C.[1]

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The rapid detection and resolution of conflict between opposing action tendencies is one of the crucial mechanisms of executive control. Research in adults suggests that emotions can serve as a 'relevance detector' that alerts attentional and sensory systems, leading to more efficient conflict processing. In contrast, research in children has almost exclusively stressed the impeding influence of emotion on the attentional system, based on the protracted development of performance in 'hot' executive function tasks. Do preschool children also show a facilitative effect of emotion on conflict processing? We addressed this question in children aged 2.8 to 7.0 years (N = 43, preregistered Bayesian sequential design) with a new modified colour-flanker task that involved emotional or neutral stimuli, depending on condition (Figure 5.5.4A). Our data show a robust conflict effect with higher error rates in incongruent compared to congruent trials (Figure 5.5.4B). Crucially, conflict resolution was faster in emotional compared to neutral conditions. Efficient conflict processing increased with age in the preschool period, whereas the modulatory influence of emotion was stable throughout the age range. These findings provide the first evidence that emotion can trigger efficient executive control processes from early on in life. In contrast to the predominant view in developmental psychology, this suggests that, depending on the role that emotion has in conflict processing, it may show a facilitative or impeding effect.

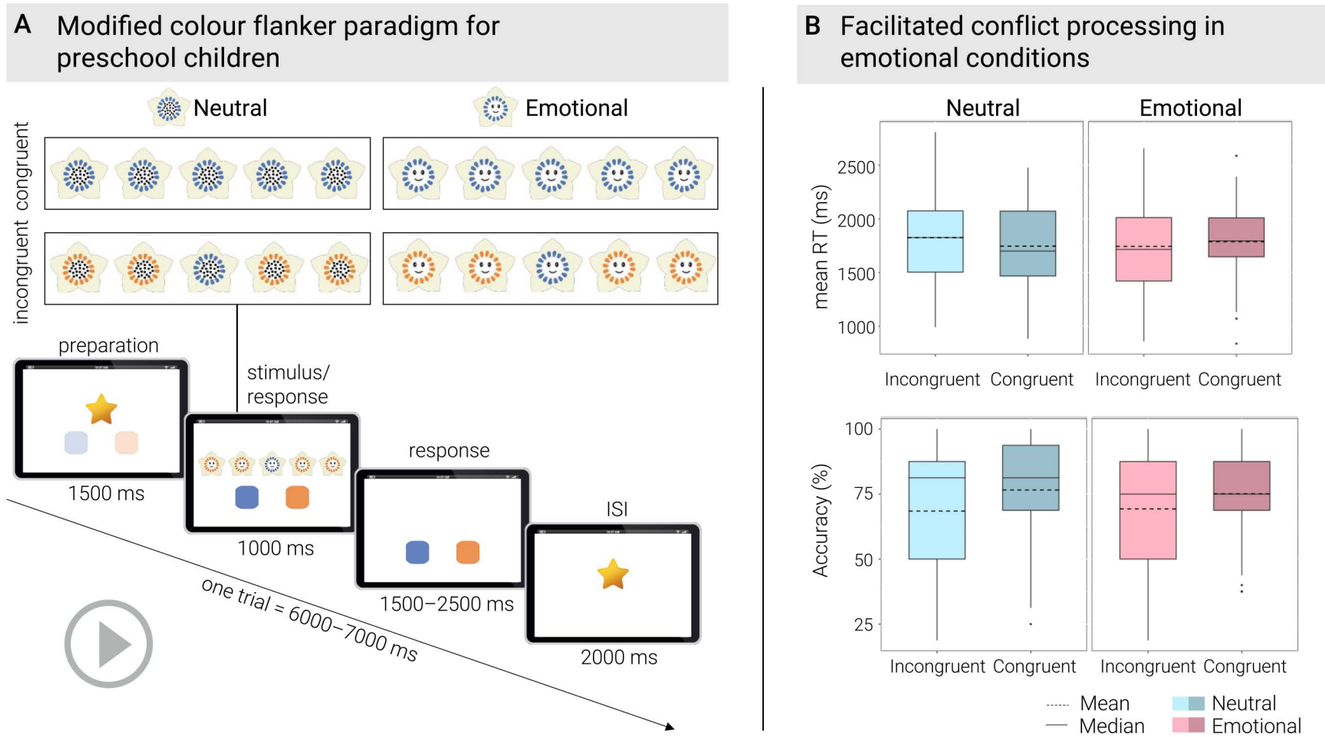

Figure 5.5.4 (A) Modified colour flanker task for preschool children (N = 43, aged 2.8 – 7.0 years). The task was designed for tablet devices with a touchscreen and was conducted online. Children's task was to indicate the colour of the middle flower via button press, while ignoring the colour of the flanking flowers (in congruent vs. incongruent conditions). The flowers either showed a face (emotional condition) or no face (neutral condition), yielding a fully crossed design of conflict and emotion. (B) Box plots depicting mean reaction times (RT, top) and accuracy data (bottom) for emotional (red) and neutral (blue) conditions, by incongruent and congruent conditions. Results show a modulation of the conflict effect by emotional context, reflected in an interaction of congruency and emotion in the RT data (top). In the accuracy data (bottom), a main effect of conflict was reflected in lower accuracy in the incongruent compared to congruent condition. The box plots indicate the median, first, and third quartile. In addition, the mean is shown as a dashed line.
Abbreviations: ISI = Interstimulus Interval, RT = Reaction Time

Congresses, Workshops, and Symposia

2021

- Grosse Wiesmann, C. (July). *Representing the world in the developing mind: From object to context.* Summer Course. Central European University, Budapest, Hungary.

2022

- Köster, M., & Grosse Wiesmann, C. (January). *Novel applications of rhythmic perceptual entrainment in infancy research.* Symposium. Budapest CEU Conference for Cognitive Development (BCCCD), Budapest, Hungary.
- Grosse Wiesmann, C. (since September). *European Society for Philosophy and Psychology (ESPP) conference (Acting Program Chair)*.

Appointments

2020

- Grosse Wiesmann, C. *Faculty member, International Max Planck Research School (IMPRS) NeuroCom*, Max Planck Society, Germany.

2022

- Grosse Wiesmann, C. *Faculty member of the International Max Planck Research School on Cognitive NeuroImaging (IMPRS CoNI)*, Max Planck Institute for Cognitive and Brain Sciences, Leipzig, Germany.

Publications

Books & Book Chapters

Grosse Wiesmann, C., & Southgate, V. (2021). Early theory of mind development: Are infants inherently altercentric? In K. Ochsner & M. Gilead (Eds.), *The neural basis of mentalizing* (pp. 49–66). Cham: Springer. https://doi.org/10.1007/978-3-030-51890-5_3

Journal Articles

Bednarski, F. M., Musholt, K., & Grosse Wiesmann, C. (2022). Do infants have agency? The importance of control for the study of early agency. *Developmental Review*, *64*. https://doi.org/10.1016/j.dr.2022.101022

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Index of Published Figures

Figure 5.5.1

Figure adapted from Grosse Wiesmann C., Friederici A. D., Singer T., & Steinbeis N. (2020). Two systems for thinking about others' thoughts in the developing brain. *Proceedings of the National Academy of Sciences, 117*(12), 6928-6935. doi: 10.1073/pnas.1916725117.

Figure 5.5.3

Figure adapted from Berger, P., Friederici, A. D., & Grosse Wiesmann, C. (2022). Maturational Indices of the Cognitive Control Network Are Associated with Inhibitory Control in Early Childhood. *Journal of Neuroscience, 42*(32), 6258–6266. doi: 10.1523/JNEUROSCI.2235-21.2022

Figure 5.5.4

Figure adapted from Berger, P., & Grosse Wiesmann, C. (2022). Positive emotion enhances conflict processing in preschoolers. *Developmental Science, 25*(5), e13199. doi: 10.1111/desc.13199

5.6

Professor Dr Martin N. Hebart

Max Planck Research Group Vision and Computational Cognition

(commenced February 2020)

The visual sense is remarkably rich. In a single glance, we can quickly identify and locate the objects and their material properties around us, easily assess whether we want to approach or avoid them, use all of this information for navigating around our world and for social interactions with others, and in many cases do this even at a distance of tens to hundreds of meters. It is not surprising that about a third of our cortex is critically involved in visual processing (Van Essen, 2003). Beyond understanding vision alone, given the richness of the incoming stimuli and how close vision is to the physical parameters of the world, visual neuroscience has been serving as a testbed for new methodological developments that are later applied in studies of other sensory and cognitive domains. Thus, studying visual processing is not only fascinating and important for understanding our brain; it serves as an important driver for methodological innovation in the cognitive and computational neurosciences.

The central aim of the Vision and Computational Cognition (ViCCo) group is to yield a detailed understanding of the content and format of our visual representations and how they change across stages of visual processing, ranging from basic vision to high-level semantics and overt behaviour. To achieve this aim, we have been taking several novel approaches. First, we have been developing key infrastructure and methods for addressing outstanding questions in vision science at a comprehensive scale, based on thousands to millions of datapoints that we make publicly available. Second, we have been using a data-driven approach for revealing interpretable representational dimensions in behaviour, brain, and artificial intelligence, thus offering a new window into mental and neural object representations. Third, we complement these data-driven approaches with theory-driven experimental studies to reveal the degree to which visual representations depend on the presentation format (Singer et al., 2021, 2022a, 2022b), be it abstract visual depictions, or the visual context in which we perceive objects.

5.6.1 The THINGS initiative: A global, multimodal data-sharing initiative for research on object recognition and object understanding

There are three central challenges to our understanding of visual representations in brain and behaviour. First, our visual input is highly complex, despite the fact that we are able to generalise from the infinity of possible images on our retina to an oftentimes precise interpretation of our external visual world. This complexity has made it very difficult to identify the principles driving our ability to recognise and understand our visual world. Second, many of the visual and semantic features in our world are intricately linked, making it difficult to determine their unique contribution to our ability to perceive. For example, animate objects tend to be rounder than inanimate objects, and food tends to be colourful and consist of many small parts. Third, it has been challenging to link results of different studies to identify the degree to which they generalise beyond the stimuli used in a given experiment, and to reveal how strongly results generalise beyond selection biases in individual datasets.

To address these challenges, we have recently developed the THINGS database (Hebart et al., 2019), a publicly available database of 1,854 object concepts sampled comprehensively from the American English language and 26,107 high-quality, manually curated natural images of these objects. THINGS aims at providing a common basis for diverse research in visual object recognition and semantic processing. A central goal of our team at MPI CBS has been to develop THINGS into a valuable research asset for object recognition and understanding. To this end, we have conducted numerous studies. First, we have collected three massive behavioural and neuroimaging datasets, consisting of 4.7 million behavioural similarity responses from thousands of online participants, as well as 12 - 14 sessions of MRI and MEG data in 3 - 4 individuals, covering up to tens of thousands of individual image presentations per participant (Hebart et al., 2022). These datasets are currently in the process of being made publicly available and, in contrast to comparable existing datasets (Chang et al., 2019; Allen et al., 2021), promise a highly detailed and multimodal picture into object representations with unprecedented semantic diversity. With these behavioural data, we have recently been able to identify core dimensions underlying our mental representation of objects (Hebart et al., 2020; see 5.8.2). To foster the power of THINGS, we have additionally collected diverse metadata, including 57 high-level categories with typicality scores, ratings along numerous basic object dimensions, and an additional 1,854 images free of copyright restrictions for visualisations (Stoinski et al., 2022). We have further developed a novel approach based on the large language model GPT-3 for automatically identifying key semantic features characterising diverse object concepts. We have demonstrated that these feature norms rivals norms created by human raters that were manually curated (Hansen and Hebart, 2022). Finally, we have collected memorability scores for all 26,107 THINGS images and have revealed the value of this dataset by demonstrating that semantic dimensions capture a surprising degree of how easily we can remember visual images (Kramer et al., 2022).

These developments have sparked interest in other researchers and teams around the world. Today, more than 15 laboratories have been contributing or are planning to contribute massive datasets based on THINGS images. To bring together these diverse datasets, we have founded the THINGS initiative (Figure 5.6.1), a platform for bringing together researchers from diverse disciplines for sharing their data publicly. By collecting massive datasets using the same image database, gaps between disciplines can be bridged for examining their similarities and differences, while providing the opportunity for multimodal investigations previously not possible.

In the coming years, we plan to continue collecting metadata for THINGS, and we aim to centrally curate and simplify the process of accessing existing datasets. We have been collecting additional large THINGS datasets in close collaboration with other teams, including the CNeuromod initiative. In the future, we will aim at a purely data-driven assessment of these individual datasets and at developing strategies for bringing them together for assessments of object recognition across data modalities and species.

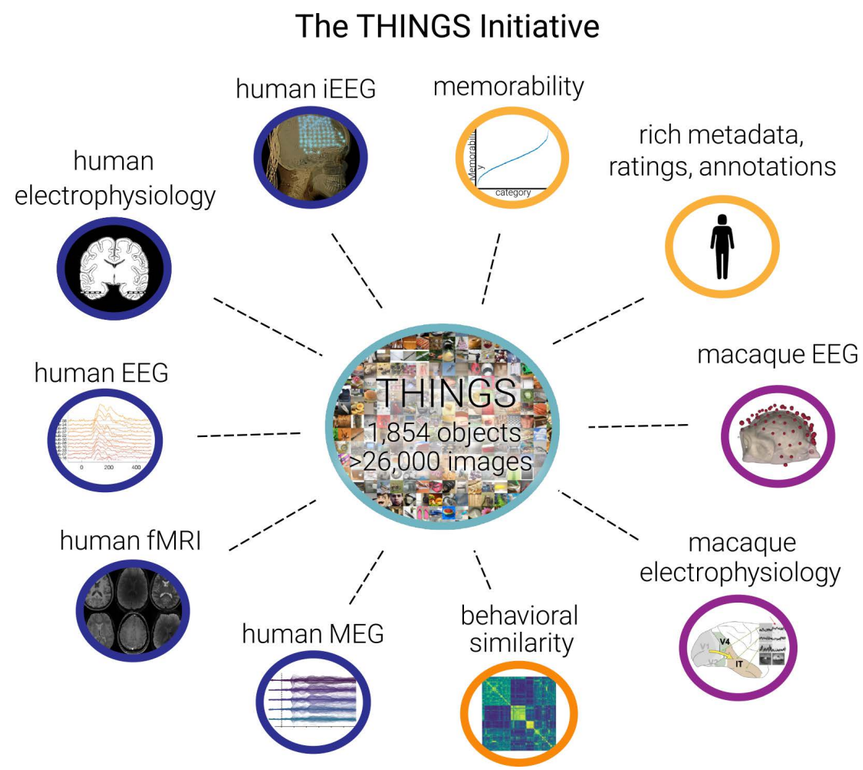

Figure 5.6.1 Our research group founded the THINGS initiative, a global initiative of more than 15 laboratories for sharing large-scale datasets, all using the same broad and well-controlled image dataset. The initiative has the purpose of strongly advancing research in object recognition and object understanding.

5.6.2 Interpretable representations in brain, behaviour, and artificial intelligence

A central goal in cognitive neuroscience is understanding the content of our representations at different processing stages: How do we structure the world around us and break it up into meaningful units, and how does our brain support this ability? For visually-perceived objects, a prominent idea in the cognitive sciences is that we break down the world into a set of core properties, or dimensions, based on which we form categories, identify similarities between objects, and structure our object knowledge more generally (Murphy, 2004). Recently, we aimed at identifying a set of core dimensions underlying our mental representation of objects, based on a large-scale assessment of object similarity. To this end, we used large-scale online crowdsourcing to collect 1.46 million similarity judgments in a triplet odd-one out task for 1,854 objects (Hebart et al., 2020). We then developed a computational model that mirrors the assumed cognitive process underlying this task. Our model performed close to the human noise ceiling, yielding 49 interpretable dimensions that reflected object properties that were both perceptual (e.g. colour, shape) and conceptual (e.g. category) and accurately reproduced human similarity judgments (Figure 5.6.2).

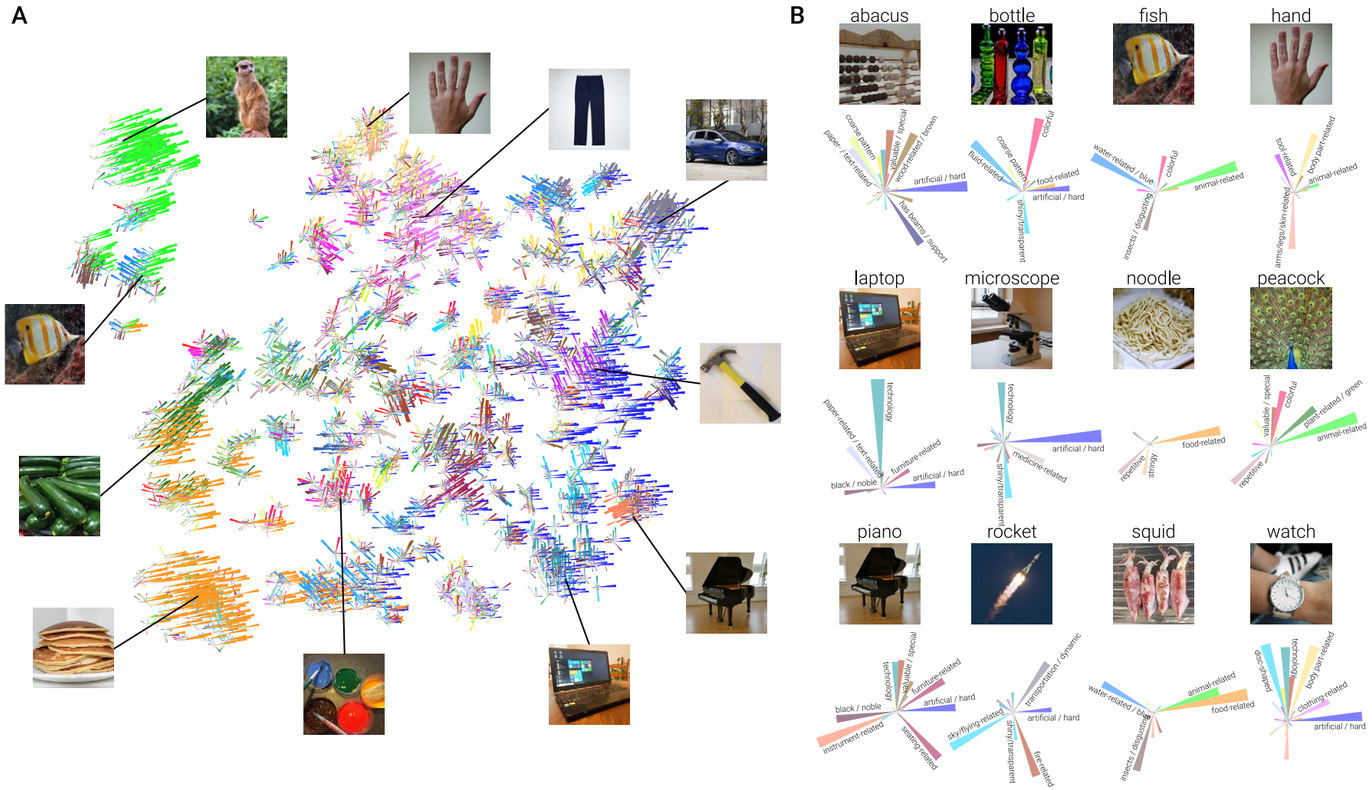

Figure 5.6.2 Visualisation of the multidimensional object space derived from 1.46 million similarity ratings on 1,854 objects. A. Our modelling approach captures human similarity judgments close to the human noise ceiling and does so with a set of 49 interpretable dimensions derived from the judgments in a data-driven fashion. Dimensions for a given object are visualised using an individual petal in a role plot, with the strength of a dimension highlighted by the length of the petal. The arrangement of objects reflects the global similarity structure between object images. B. Visualisation of individual image spectra, highlighting their interpretability and the degree to which these dimensions are expressed in individual objects.

Building on this approach, we are currently moving in several research directions. We have identified core dimensions for other domains, including: reachable spaces (Josephs et al., 2021), human social actions (Dima et al., 2022), and material properties (Schmidt et al., 2021). We have been mapping these dimensions to the human brain using fMRI (Oliver Contier) and MEG (in collaboration with Lina Teichmann and Chris Baker at NIMH), demonstrating, among others things, that behaviourally-relevant dimensions are well-reflected in brain responses even at the earliest cortical processing stages. Based on these dimensions, we have developed a new approach for predicting human similarity judgments for unseen object images (Philipp Kaniuth). We are currently applying this approach to identify core dimensions in neural network representations (Florian Mahner and Lukas Muttenthaler). We have additionally developed an approach for generating synthetic stimuli that maximally activate a brain region (Roth et al., 2021), an approach that we are continuing to develop and validate (Katja Seeliger).

Moving forward, beyond relating brain and behavioural representations, our group is taking several approaches to identify interpretable representations in brain and behaviour. As part of the recently approved ERC Starting Grant COREDIM, we aim at identifying core representational dimensions directly in individual human brain regions. This approach has recently been used to identify food selectivity in the human ventrotemporal cortex in a data-driven fashion (Khosla et al., 2022). Our aim is to move beyond a global characterisation of ventral vision and identify core representational dimensions across all processing stages, with a newly created massive structural and functional neuroimaging dataset (Maggie Mae Mell).

5.6.3 Methodological innovation

Beyond these major research lines and our theory-driven research, our team has been conducting purely methodological work, which will be described only briefly:

- We have created the now widely used toolbox THINGSvision for simplifying the extraction of activations from a wide range of artificial neural network models (Muttenthaler and Hebart, 2021).
- We have tested and broadly verified the general usefulness of feature-reweighted representational similarity analysis (RSA), yielding increased statistical power as compared to vanilla RSA, and we have created a toolbox for applying this method (Kaniuth and Hebart, 2022).
- We have developed and publicly shared a variational Bayesian method for identifying core representational dimensions and yielding more stable results, specifically for smaller datasets (Muttenthaler et al., 2022).
- We are working on novel denoising strategies for functional MRI data, promising more powerful automated denoising than existing automatic approaches (Josefine Zerbe & Oliver Contier).

Congresses, Workshops, and Symposia

2020

- Hebart, M. (April) *Virtual high-performance computing course*. Workshop. Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany.
- Hebart, M. (April) *Introduction to services of MPCDF*. International Max Planck Research School on Neuroscience of Communication: Function, Structure, and Plasticity, Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany.

Appointments

2022

- Hebart, M. *Associate Professor (W2 tenure-track to W3) of "Computational Cognitive Neuroscience and Quantitative Psychiatry"*. Justus Liebig University Gießen, Germany.
- Hebart, M. *Faculty member of the International Max Planck Research School on Cognitive NeuroImaging (IMPRS CoNI)*, Max Planck Institute for Cognitive and Brain Sciences, Leipzig, Germany.

Awards

2020

- Kaniuth, P. *Elsevier/Vision Research Travel Award*. Vision Science Society, California, USA.

2021

- Kaniuth, P. *Poster Competition Winner.* 10th IMPRS NeuroCom Summer School in Cognitive Neuroscience. International Max Planck Research School on Neuroscience of Communication: Function, Structure, and Plasticity (IMPRS NeuroCom), Max Planck Institute for Human Cognitive and Brain Sciences & ICN, Leipzig & London, Germany & UK. Virtual.

2022

- Contier, O. *Open Science Prize*. Interest Group for Open and Reproducible Research (IGOR), Division of Biological and Neuropsychology, German Psychological Society, Berlin, Germany.
- Hebart, M. *ERC Starting Grant.* European Research Council (ERC), Brussels, Belgium.
- Hebart, M. *LOEWE Start Professorship*. Hessian Ministry of Higher Education Research, Science and the Arts, Wiesbaden, Germany.

Publications

Journal Articles

Bönstrup, M., Iturrate, I., Hebart, M. N., Censor, N., & Cohen, L. G. (2020). Mechanisms of offline motor learning at a microscale of seconds in large-scale crowdsourced data. *npj Science of Learning*, *5*. https://doi.org/10.1038/s41539-020-0066-9

Grootswagers, T., Zhou, I., Robinson, A. K., Hebart, M. N., & Carlson, T. A. (2022). Human EEG recordings for 1,854 concepts presented in rapid serial visual presentation streams. *Scientific Data*, *9*(1). https://doi.org/10.1038/s41597-021-01102-7

Hansen, H., & Hebart, M. N. (2022). Semantic features of object concepts generated with GPT-3. In *Proceedings of the Annual Meeting of the Cognitive Science Society* (Vol. 44). https://escholarship.org/uc/item/44s454ng

Hebart, M. N., & Schuck, N. W. (2020). Current topics in computational cognitive neuroscience. *Neuropsychologia*, *147*. https://doi.org/10.1016/j.neuropsychologia.2020.107621

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Josephs, E. L., Hebart, M. N., & Konkle, T. (2023). Dimensions underlying human understanding of the reachable world. Cognition, 234. https://doi.org/10.1016/j.cognition.2023.105368

Kaniuth, P., & Hebart, M. N. (2022). Feature-reweighted representational similarity analysis: A method for improving the fit between computational models, brains, and behavior. *NeuroImage*, *257*. https://doi.org/10.1016/j.neuroimage.2022.119294

Le, L., Ambrogioni, L., Seeliger, K., Güçlütürk, Y., van Gerven, M., & Güçlü, U. (2022). Brain2Pix: Fully convolutional naturalistic video frame reconstruction from brain activity. *Frontiers in Neuroscience*, *16*. https://doi.org/10.3389/fnins.2022.940972

Liu, P., Chrysidou, A., Doehler, J., Hebart, M. N., Wolbers, T., & Kuehn, E. (2021). The organizational principles of de-differentiated topographic maps in somatosensory cortex. *eLife*, *10*. https://doi.org/10.7554/eLife.60090

Muttenthaler, L., & Hebart, M. N. (2021). THINGSvision: A Python toolbox for streamlining the extraction of activations from deep neural networks. *Frontiers in Neuroinformatics*, *15*. https://doi.org/10.3389/fninf.2021.679838

Muttenthaler, L., Zheng, C. Y., McClure, P., Vandermeulen, R. A., Hebart, M. N., & Pereira, F. (in press). VICE: Variational Interpretable Concept Embeddings. *Advances in Neural Information Processing Systems* 35 (NeurIPS 2022) https://doi.org/10.48550/arXiv.2205.00756

Seeliger, K., Ambrogioni, L., Güçlütürk, Y., van den Bulk, L. M., Güçlü, U., & van Gerven, M. A. J. (2021). End-to-end neural system identification with neural information flow. *PloS Computational Biology*, *17*(2). https://doi.org/10.1371/journal.pcbi.1008558

Singer, J., Cichy, R. M., & Hebart, M. N. (2022). The spatiotemporal neural dynamics of object recognition for natural images and line drawings. *The Journal of Neuroscience*. https://doi.org/10.1523/JNEUROSCI.1546-22.2022

Singer, J., Seeliger, K., Kietzmann, T. C., & Hebart, M. N. (2022). From photos to sketches-how humans and deep neural networks process objects across different levels of visual abstraction. *Journal of Vision*, *22*(2). https://doi.org/10.1167/jov.22.2.4

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Dima, D. C., Hebart, M. N., & Isik, L. (2022, September 23). A data-driven investigation of human action representations. *BioRxiv*. https://doi.org/10.1101/2022.09.22.509054

Hebart, M. N., Contier, O., Teichmann, L., Rockter, A. H., Zheng, C. Y., Kidder, A., Corriveau, A., Vaziri-Pashkam, M., & Baker, C. I. (2022, July 23). THINGS-data: A multimodal collection of large-scale datasets for investigating object representations in brain and behavior. *BioRxiv*. https://doi.org/10.1101/2022.07.22.501123

Kramer, M. A., Hebart, M. N., Baker, C. I., & Bainbridge, W. A. (2022, April 30). The features underlying the memorability of objects. *BioRxiv*. https://doi.org/10.1101/2022.04.29.490104

Schmidt, F., Hebart, M. N., Schmid, A. C., & Fleming, R. W. (2022, December 2). Core dimensions of human material perception. *PsyArXiv*. https://doi.org/10.31234/osf.io/jz8ks

Seeliger, K., Güçlü, U., Le, L., Güçlütürk, Y., & van Gerven, M. (2021, February 3). Brain2Pix: Fully convolutional naturalistic video reconstruction from brain activity. *BioRxiv*. https://doi.org/10.1101/2021.02.02.429430

Stoinski, L. M., Perkuhn, J., & Hebart, M. N. (2022, July 20). THINGS+: New norms and metadata for the THINGS database of 1,854 object concepts and 26,107 natural object images. *PsyArXiv*. https://doi.org/10.31234/osf.io/exu9f

Zheng, X. Y., Hebart, M. N., Dolan, R. J., Doeller, C. F., Cools, R., & Garvert, M. (2022, August 29). Parallel cognitive maps for short-term statistical and long-term semantic relationships in the hippocampal formation. *BioRxiv*. https://doi.org/10.1101/2022.08.29.505742

5.7

Dr Michael A. Skeide

Research Group Learning in Early Childhood

(commenced February 2020)

The overarching theoretical objective of our lab (https://skeidelab.com/) is to understand how the developing human brain generates intelligent behaviour. We aspire to discover universal principles of neurocognitive development in the first years of life. At the same time, we are interested in identifying individual, cross-cultural, and clinically relevant differences. Our two central research questions are: How does the developing brain learn to understand the senses and how does it build semantic systems?

(i) Making sense of the senses

Children do not learn, from scratch, how to decode sensory information. Instead, they are born with neural processing resources that allow them to start understanding and integrating the inputs they are flooded with. In our *ERC* Starting Grant project, we currently investigate how the developing brain learns to link visual letter strings with auditory speech to make reading possible. Recently, we also conducted a number of studies on early neural origins of developmental disorders associated with multisensory information processing difficulties, in particular dyslexia (5.9.1) (Kuhl et al., 2020) and dyscalculia (5.9.2) (Kuhl et al., 2021).

(ii) Building semantic systems

The developing brain builds mental models of the world to organize sensory experience into semantic systems. We have previously provided evidence that brain representations of visual and verbal semantic systems, of children as young as 4 years of age, are already comparable to those of adults (5.9.3) (Enge et al., 2021). In our ongoing project funded by the German Research Foundation (*DFG*), we examine how numerical semantic systems emerge in the developing brain. Our specific aim is to find out how the brain represents numerical information across different sensory formats such as visual patterns, digits, and words.

Our methodological framework builds on longitudinal observation studies and causally relevant intervention studies in early childhood. Within this framework, our repertoire ranges from single-subject to population-level designs. In our experiments, we combine brain recording techniques (MRI, EEG, NIRS) with behavioural measures (e.g., response accuracy, reaction time, cognitive assessment tools). Our analytical approaches comprise frequentist statistics, psychophysical modelling, probabilistic inference and machine learning. Furthermore, our spectrum of methods also extends to genetic and environmental association studies in a global *NIH*-funded consortium.

5.7.1 Early detection of developmental dyslexia

Kuhl, U.[1], Neef, N.[1], Kraft, I.[1], Schaadt, G.[1], Dörr, L.[1], Brauer, J.[1], Czepezauer, I.[2], Müller, B.[2], Wilcke, A.[2], Kirsten, H.[2], Emmrich, F.[2], Boltze, J.[2], Friederici, A. D.[1], & Skeide, M. A.[1]

[1] Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany, [2] Fraunhofer Institute for Cell Therapy and Immunology, Leipzig, Germany

Developmental dyslexia, a severe deficit in literacy learning, is a neurodevelopmental learning disorder. It is not clear whether existing neurobiological accounts of dyslexia capture potential predispositions to the deficit or consequences of reduced reading experience. Here, we longitudinally followed 32 children from preliterate to school age using functional and structural magnetic resonance imaging techniques. Based on standardised and age-normed reading and spelling tests administered at school age, children were classified as 16 dyslexic participants and 16 controls. This longitudinal

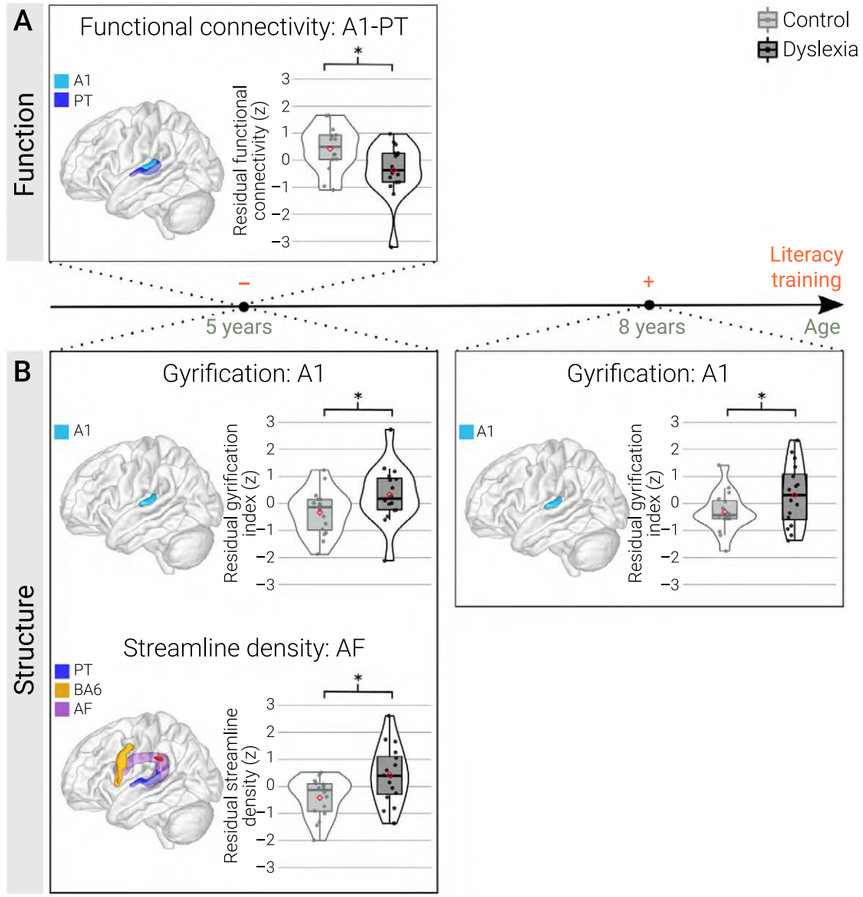


Figure 5.7.1 Neurodevelopmental differences between typical controls and children who went on to develop dyslexia. Group comparison of cortical and subcortical morphometry measures revealed significantly higher gyrification of the left primary auditory cortex in dyslexic children compared to controls, persistent across time points. Additionally, functional connectivity between left primary auditory cortex and left planum temporale was significantly lower in dyslexic children before literacy training. In terms of structural connectivity, we found significantly higher streamline density at a preliterate age for dyslexic children compared to controls in the white matter fibre tract connecting the left planum temporale with the left ventral premotor area (BA 6), i.e. the arcuate fasciculus (N = 32, 70 voxels, F (1,24) = 19.80, p = 0.0040, η^2 = 0.45). All significant statistics survived family-wise-error-correction for multiple comparison at the respective critical α levels, i.e., α = 0.0063 for comparison of surface-based measures (CT, GI, SD, CF); α = 0.0046 for comparisons of fALFF, ReHo, T1-signal, tract-wise mean MD, FA and SLD and seed-target based functional connectivity. Voxel-wise whole-brain analyses were assessed at a significance level of α < 0.05 (family-wise-error-corrected). None of the other region-of-interest or whole-brain control analyses revealed any additional statistically significant effects for any neural indices. Horizontal lines within the bars represent the group median. Vertical lines at the top and the bottom of the bars depict the standard deviation. Red diamonds denote the mean of the distribution. Grey and black dots represent individual data points. Rotated kernel density plots on each side of the bar show the probability density of the data at different values. Asterisks indicate family-wise-error-corrected differences significant at p < 0.05. A1 = primary auditory cortex; PT = planum temporale; BA 6 = Brodmann Area 6; AF = arcuate fasciculus. Figure adapted from Kuhl et al. (2020). The emergence of dyslexia in the developing brain. *NeuroImage*, 211: 116633. Source: https://doi.org/10.1016/j.neuroimage.2020.116633

design allowed us to disentangle possible neurobiological predispositions for developing dyslexia from effects of individual differences in literacy experience. In our sample, the disorder was predicted before literacy learning, based on auditory cortex gyrification and aberrant downstream connectivity within the speech processing system. These results provide evidence for the notion that dyslexia may originate from an atypical maturation of the speech network that precedes literacy instruction.

5.7.2 Early detection of developmental dyscalculia

Kuhl, U.[1], Sobotta, S.[1], & Skeide, M. A.[1]

[1] Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany

Mathematical learning deficits are defined as a neurodevelopmental disorder (dyscalculia) in the International Classification of Diseases. It is not known, however, how such deficits emerge in the course of early brain development. Here, we conducted functional and structural magnetic resonance imaging (MRI) experiments in 3- to 6-year-old children without formal mathematical learning experience. We followed this sample until the age of 7 to 9 years, identified individuals who developed deficits, and matched them to a typically developing control group using comprehensive behavioural assessments. Multivariate pattern classification distinguished future cases from controls with up to 87% accuracy based on the regional functional activity of the right posterior parietal cortex (PPC), the network-level functional activity of the right dorsolateral prefrontal cortex (DLPFC), and the effective functional and structural connectivity of these regions. Our results indicate that mathematical learning deficits originate from atypical development of a fronto-parietal network that is already detectable in early childhood, prior to formal math training.

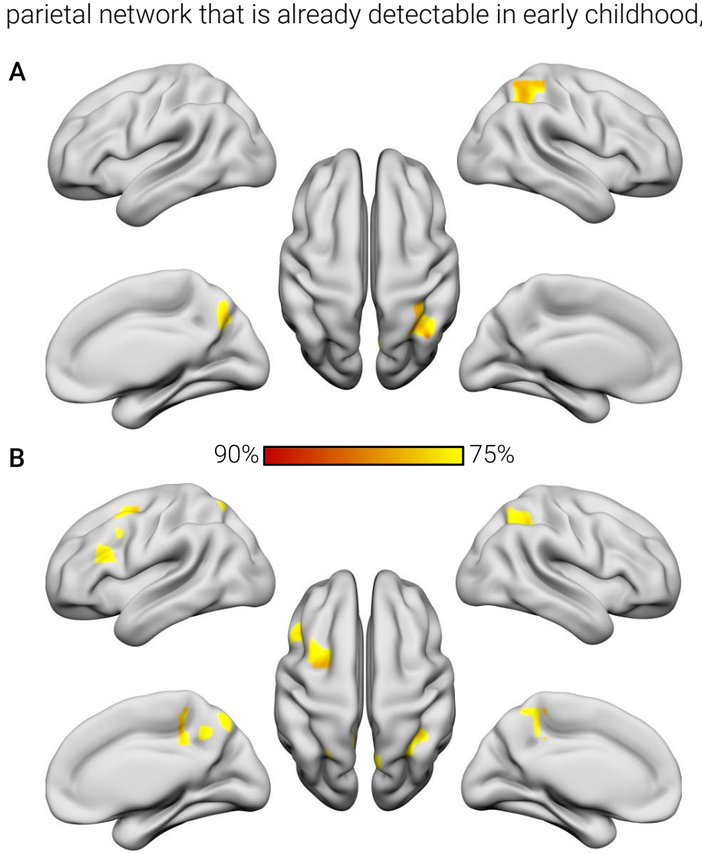
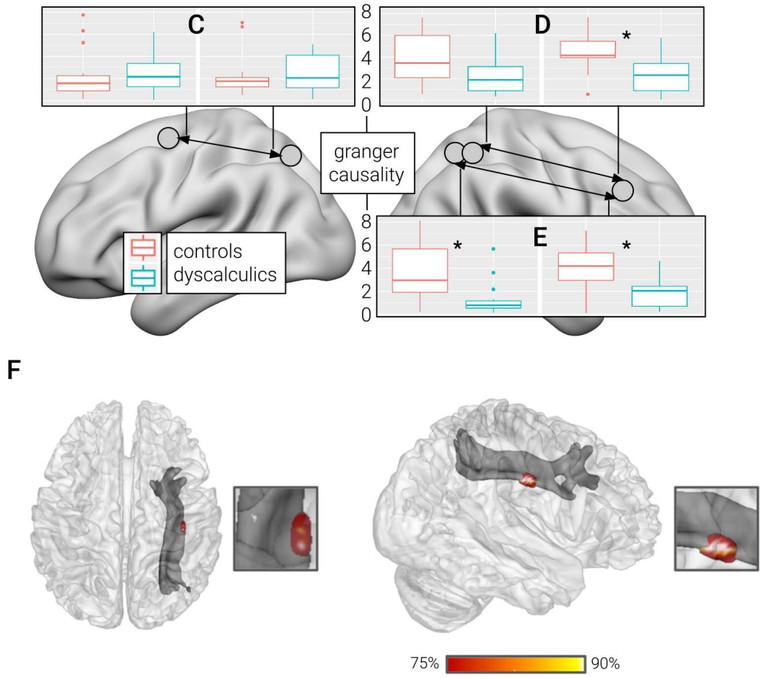


Figure 5.7.2 (A, B) Regional functional classification results. Our whole-brain classifier was able to distinguish typically developing children from children who went on to develop dyscalculia based on (A) the amplitude of low-frequency fluctuations and (B) the regional homogeneity of posterior parietal and dorsolateral prefrontal cortices (PPC and DLPFC). The colour bar indicates the peak accuracy for the classification at a threshold of $P < 0.001$ (corrected by permutation testing).



(C, D, E) Effective connectivity differences. Granger causality indices for pairs of regions of interest derived from (C) the regional homogeneity of the left PPC and the left DLPFC, (D) the amplitude of low-frequency fluctuations of the right PPC and the degree centrality of the right DLPFC, and (E) the regional homogeneity of the right PPC and the degree centrality of the right DLPFC. Compared to children who developed dyscalculia, control children showed a significantly stronger influence of the right PPC on the right DLPFC and partly also in the opposite direction. Arrows indicate the direction of the influence of one hemodynamic time series on the other. Vertical lines at the top and the bottom of the bars depict the SD. Horizontal lines within the bars represent the group median. Dots denote single cases that are more than 1.5 SDs away from the group mean. Asterisks indicate significant differences between children with dyscalculia and controls at a threshold of $P < 0.05$ (family-wise error corrected). DLPFC = dorsolateral prefrontal cortex; PPC = posterior parietal cortex. (F) Structural connectivity classification results. The classifier successfully separated cases from controls based on the streamline density of the right SLF connecting the right PPC and the right DLPFC. The colour bar indicates the peak accuracy for the classification of children with dyscalculia versus typical controls ($P < 0.001$, corrected by permutation testing). Figure adapted from Kuhl et al. (2021). Mathematical learning deficits originate in early childhood from atypical development of a fronto-parietal brain network. *PLOS Biology*, 19: e3001407.
Source: https://doi.org/10.1371/journal.pbio.3001407

5.7.3 Emergence of visual and verbal semantic systems

Enge, A.[1,2], Abdel Rahman, R.[2], & Skeide, M. A.[1]

[1] Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany, [2] Department of Psychology, Humboldt University Berlin, Germany

Our capacity to derive meaning from things that we see and words that we hear is unparalleled in other animal species and current AI systems. Despite a wealth of functional magnetic resonance imaging (fMRI) studies examining where different semantic features are processed in the adult brain, the development of these systems in children is poorly understood. Here, we conducted an extensive database search and identified 50 fMRI experiments investigating semantic world knowledge, semantic relatedness judgments, and the differentiation of visual semantic object categories in children (total N = 1,018, mean age = 10.1 years, range 4–15 years). Synthesizing the results of these experiments, we found consistent activation in the bilateral inferior frontal gyri, fusiform gyri, and supplementary motor areas, as well as in the left middle and superior temporal gyri. Within this system, we found little evidence for age-related changes across childhood and high overlap with the adult semantic system. In sum, the identification of these cortical areas provides the starting point for further research on the mechanisms by which the developing brain learns to make sense of its environment.

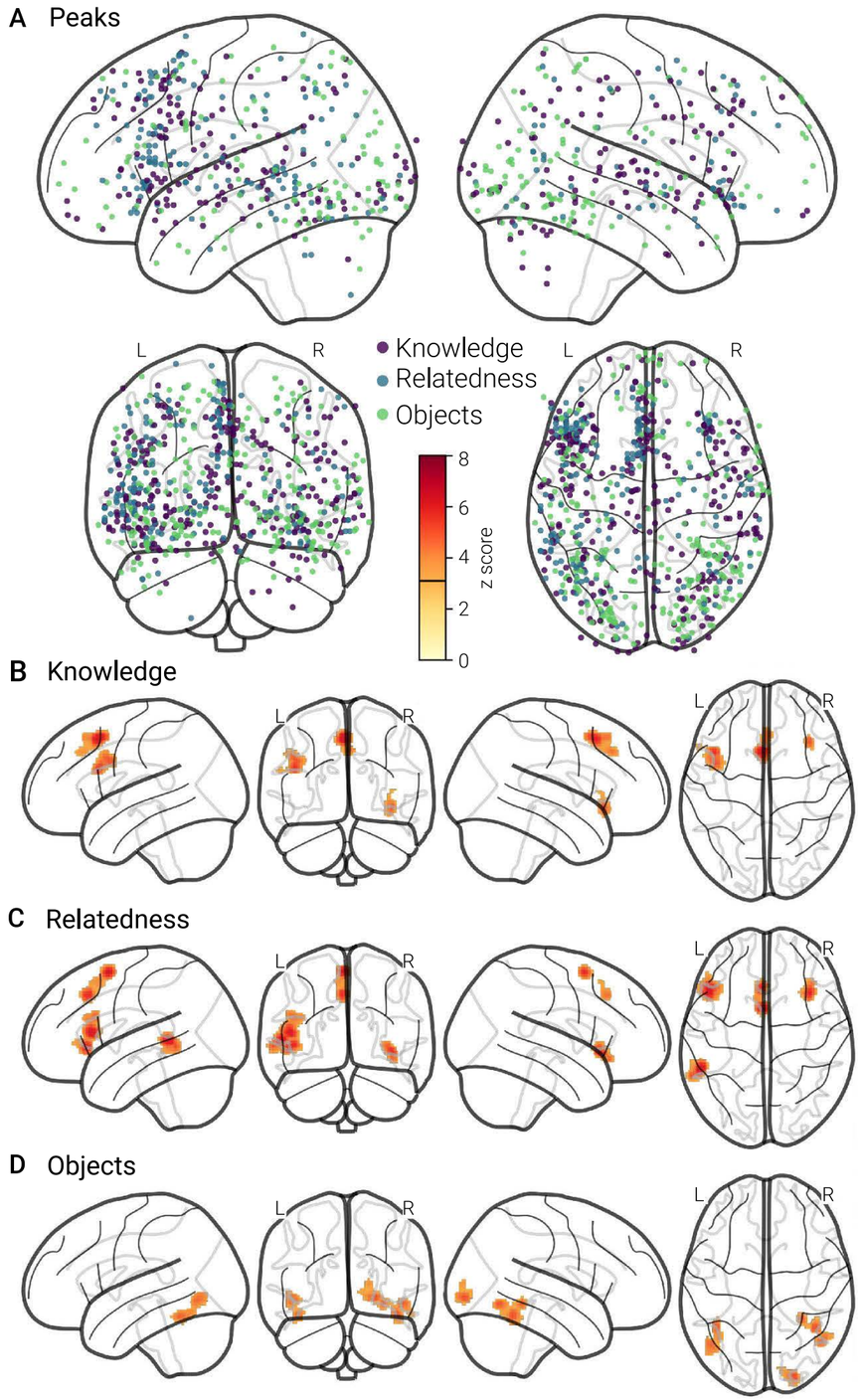


Figure 5.7.3 Semantic representations in the developing brain derived from a coordinate-based meta-analysis of the currently available fMRI experiments probing semantic cognition in children. (A) Individual hemodynamic activation peaks are shown with colour-coding representing the category of semantic task (purple: semantic world knowledge, blue: semantic relatedness judgment, green: discrimination of visual semantic object categories). (C, D, E) Activation clusters derived from activation likelihood estimation for (B) semantic knowledge experiments, (C) semantic relatedness experiments, and (D) visual semantic object category experiments. Each cluster is thresholded at $P < 0.001$ (uncorrected) at the voxel level and $P < 0.01$ (FWE-corrected) at the cluster level. Figure adapted from Enge et al. (2021). A meta-analysis of fMRI studies of semantic cognition in children. *NeuroImage*, 241: 118436.
Source: https://doi.org/10.1016/j.neuroimage.2021.118436

Master Theses

2021

- Enge, A. *Event-related potentials of the semantically informed perception of unfamiliar objects.* Humboldt University, Berlin, Germany.

Appointments

2020

- Skeide, M. A. *ERC Group Leader.* Max Planck Institute for Cognitive and Brain Sciences, Leipzig, Germany.
- Skeide, M. A. *Heisenberg Fellow,* German Research Federation (DFG). Max Planck Institute for Cognitive and Brain Sciences, Leipzig, Germany.

2022

- Skeide, M. A. *Faculty member of the International Max Planck Research School on Cognitive Neuroimaging (IMPRS CoNI)*, Max Planck Institute for Cognitive and Brain Sciences, Leipzig, Germany.

Awards

2020

- Skeide, M. A. *Science Prize, German Society for Dyslexia and Dyscalculia*, Bonn, Germany.

2021

- Enge, A. *PhD scholarship*, German Academic Scholarship Foundation, Bonn, Germany.
- Enge, A. *Best MSc degree in Psychology*, Humboldt University, Berlin, Germany.
- Skeide, M. A. *Stefan Engel Prize*, German Society for Social Pediatrics & Child Medicine, Berlin, Germany.
- Skeide, M. A. *Early Career Award*, International Mind, Brain and Education Society, Stanford, USA.

2022

- Skeide, M. A. *Early Career Award*, Society for the Neurobiology of Language, Philadelphia, USA.

Publications

Books & Book Chapters

Skeide, M. A. (Ed.). (2022). *The Cambridge handbook of dyslexia and dyscalculia*. Cambridge University Press. https://doi.org/10.1017/9781108973595

Journal Articles

Aristei, S., Knoop, C. A., Lubrich, O., Nehrlich, T., Enge, A., Stark, K., Sommer, W., & Abdel Rahman, R. (2022). Affect as anaesthetic: How emotional contexts modulate the processing of counterintuitive concepts. *Language, Cognition and Neuroscience*. https://doi.org/10.1080/23273798.2022.2085312

Eiserbeck, A., Enge, A., Rabovsky, M., & Rahman, R. A. (2022). Electrophysiological chronometry of graded consciousness during the attentional blink. *Cerebral Cortex*, *32*(6), 1244–1259. https://doi.org/10.1093/cercor/bhab289

Enge, A., Abdel Rahman, R., & Skeide, M. A. (2021). A meta-analysis of fMRI studies of semantic cognition in children. *NeuroImage*, *241*. https://doi.org/10.1016/j.neuroimage.2021.118436

Enge, A., Friederici, A. D., & Skeide, M. A. (2020). A meta-analysis of fMRI studies of language comprehension in children. *NeuroImage*, *215*. https://doi.org/10.1016/j.neuroimage.2020.116858

Kessler, R., & Heinrich, S. P. (2022). Temporal frequency dependence of the polarity inversion between upper and lower visual field in the pattern-onset steady-state visual evoked potential. *Documenta Ophthalmologica*. https://doi.org/10.1007/s10633-022-09904-9

Kuhl, U., Friederici, A. D., the LEGASCREEN Consortium, & Skeide, M. A. (2020). Early cortical surface plasticity relates to basic mathematical learning. *NeuroImage*, *204*. https://doi.org/10.1016/j.neuroimage.2019.116235

Kuhl, U., Neef, N., Kraft, I., Schaadt, G., Dörr, L., Brauer, J., Czepezauer, I., Müller, B., Wilcke, A., Kirsten, H., Emmrich, F., Boltze, J., Friederici, A. D., & Skeide, M. A. (2020). The emergence of dyslexia in the developing brain. *NeuroImage*, *211*. https://doi.org/10.1016/j.neuroimage.2020.116633

Kuhl, U., Sobotta, S., Legascreen Consortium, & Skeide, M. A. (2021). Mathematical learning deficits originate in early childhood from atypical development of a frontoparietal brain network. *PloS Biology*, *19*(9). https://doi.org/10.1371/journal.pbio.3001407

Skeide, M. A., Wehrmann, K., Emami, Z., Kirsten, H., Hartmann, A. M., Rujescu, D., & Legascreen Consortium (2020). Neurobiological origins of individual differences in mathematical ability. *PloS Biology*, *18*(10). https://doi.org/10.1371/journal.pbio.3000871

Preprints

Eiserbeck, A., Enge, A., Rabovsky, M., & Rahman, R. A. (2021, February 24). Distrust before first sight: Knowledge- and appearance-based effects of trustworthiness on the visual consciousness of faces. *BioRxiv*. https://doi.org/10.1101/2021.02.24.432562

5.8

Dr Sofie Louise Valk

Otto Hahn Group Cognitive Neurogenetics

(commenced March 2020)

Nature and nurture of human brain and cognition

The central goal of our Otto Hahn group is to investigate how heritable and environmental factors shape brain structure and function (Figure 5.8). To reach this goal, we integrate approaches from neuroscience, genetics, psychology, and data science. We use multimodal and multiscale neuroscientific datasets including in-vivo neuroimaging scans and post-mortem cell-body staining to describe and understand the principles of human brain structure and functional organization. Combined with twin modelling, transcriptomic expression, and comparative approaches enables us to probe the brains' genetic basis. Moreover, we employ longitudinal models and behavioural measurements to describe the dynamic interplay between brain structure and function at the level of the individual in both health and disease. Together, our work helps in understanding how the structure of the human brain supports human cognition.

Our group is well embedded within the Max Planck Society, with Sofie Louise Valk serving as the Institute's Scientific Staff representative at the HS Section of the society. Moreover, Sofie is a faculty member of the International Max Planck Research School on Neuroscience of Communication: Function, Structure and Plasticity (IMPRS NeuroCom) as well as the IMPRS on Cognitive Neuroimaging. Lina Schaare is the Deputy Spokesperson of the Max Planck PostdocNet while Meike Hettwer is spokesperson for the School of Cognition. Our team is involved in the local open science committee and regularly presents our work at major and specialised international conferences (e.g. Organization of Human Brain Mapping, OHBM). We also regularly communicate science to the general public, including a *TEDx* talk and an article in *Gehirn und Geist*.

Currently, Sofie Louise Valk is also a research group leader at the Institute for Neuroscience and Medicine-7 (INM-7), Brain and Behavior, Forschungszentrum Jülich (FZJ), Jülich, Germany. There the group focuses on integration of post-mortem histology and in-vivo function, whilst at the MPI we focus more strongly on genetic and multimodal cognitive neuroimaging.

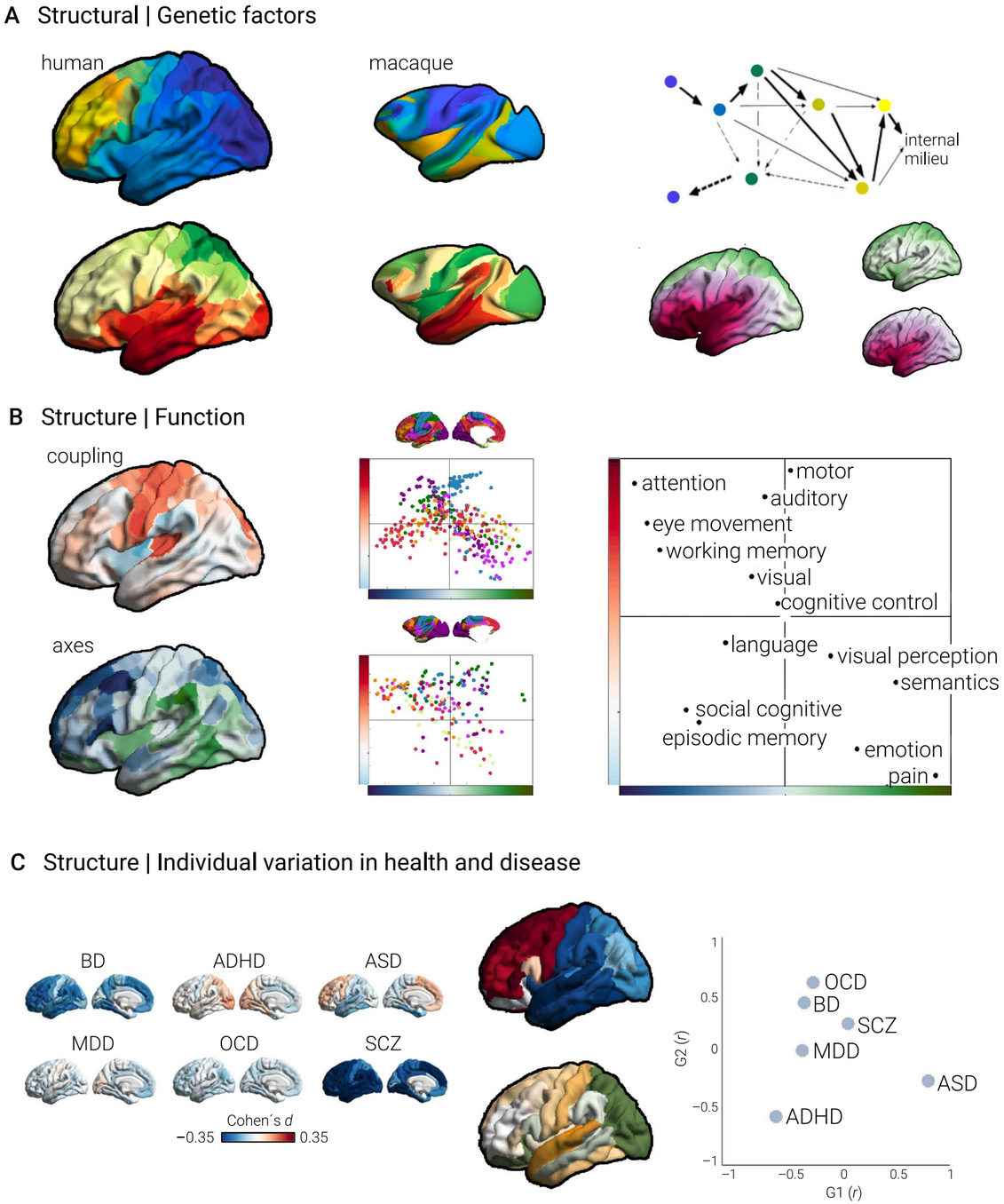


Figure 5.8.1 Overarching themes of the group. (A) Gradients of genetic correlation reflect function and development, Valk, 2020, Science Advances; (B) Heritable and evolutionary uncoupling of structure and function in transmodal areas links to abstract cognition and affect, Valk, 2022, Nature Communications; (C) Individual variation in health and disease; Transdiagnostic models of covariance, Hettwer, 2022, Nature Communications.

Heritable axes of brain organisation

To understand how brain structure supports human cognition, it is important to assess the brains' genetic and evolutionary basis, providing a biological scaffold for its functions. Such insights help to gain understanding into what extent functional processing in the brain may be under genetic control and whether similar structural topographies are evolutionary conserved in primates. This will reveal common and unique neurogenetic landscapes that constrain human cognitive functional features.

5.8.1 Shaping brain structure: Genetic and phylogenetic axes of macroscale organisation of cortical thickness

Valk, S. L. [1,2,3], Xu, T. [4], Margulies, D. S. [4,5], Kharabian Masouleh, S. [2,3], Paquola, C. [6], Goulas, A. [7], Kochunov, P. [8], Smallwood, J. [9], Yeo, B. T. T. [10,11,12,13], Bernhardt, B. C. [6], & Eickhoff, S. B. [2,3]

[1] Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany, [2] INM-7, Research Centre Jülich, Germany, [3] Institute of Systems Neuroscience, Heinrich Heine University Düsseldorf, Germany, [4] Center for the Developing Brain, New York City, USA, [5] Front lab, Institut de Cerveau et de la Moelle epiniere, Paris, France, [6] Multimodal Imaging and Connectome Analysis Lab, McConnell Brain Imaging Centre, Montreal Neurological Institute and Hospital, McGill University, Montreal, QC, Canada, [7] Institute of Computational Neuroscience, University Medical Center Hamburg-Eppendorf, Hamburg University, Germany, [8] Maryland Psychiatric Research Center, University of Maryland School of Medicine, Baltimore, MD, US, [9] Department of Psychology, Queen's University, Kingston, ON, Canada, [10] Department of Electrical and Computer Engineering, National University of Singapore, Singapore, [11] Centre for Sleep and Cognition (CSC) & Centre for Translational Magnetic Resonance Research (TMR), National University of Singapore, Singapore, [12] N.1 Institute for Health & Institute for Digital Medicine (WisDM), National University of Singapore, Singapore, [13] Martinos Center for Biomedical Imaging, Massachusetts General Hospital, Charlestown, MA, USA

The organisation of the cerebral cortex has been suggested to scaffold the organisation of human cognition. In a sample of twins (n = 1113), we determined structural covariance of cortical thickness to be arranged along both a posterior-to-anterior and an inferior-to-superior axis. Both axes were present when investigating the genetic correlation of cortical thickness, suggesting a strong genetic component in humans, and had a comparable organisation in macaques, demonstrating they are evolutionary conserved in primates. In both species, the inferior-superior dimension of cortical organisation aligned with the predictions of dual-origin theory. In humans, we found that the posterior-to-anterior axis related to a functional topography describing a continuum of functions from basic processes involved in perception and action to more abstract features of human cognition. As a whole, our study provides important insights into how functional and evolutionary patterns converge at the level of macroscale cortical structural organisation.

5.8.2 Heritability of hippocampal functional and microstructural organisation

Bayrak, Ş. [1,2,3,4], Vos de Wael, R. [5], Schaare, H. L. [1,2,3], Hettwer, M. D. [1,2,3,6], Caldairou, B. [7], Bernasconi, A. [7], Bernasconi, N. [7], Bernhardt, B. C. [5], & Valk, S. L. [1,2,3]

[1] Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany, [2] Institute of Neuroscience and Medicine, Brain & Behaviour (INM-7), Research Centre Jülich, Germany, [3] Institute of Systems Neuroscience, Medical Faculty, Heinrich Heine University Düsseldorf, Germany, [4] Department of Cognitive Neurology, Leipzig University Hospital, and Faculty of Medicine, Leipzig University, Germany, [5] Multimodal Imaging and Connectome Analysis Laboratory, McConnell Brain Imaging Centre, Montreal Neurological Institute, McGill University, Montreal, Canada, [6] Max Planck School of Cognition, Max Planck Institute of Human Cognitive and Brain Sciences, Leipzig, Germany, [7] Neuroimaging of Epilepsy Laboratory, McConnell Brain Imaging Centre, Montreal Neurological Institute, McGill University, Montreal, Canada

The hippocampus is a uniquely folded allocortical structure in the medial temporal lobe that consists of microstructurally and functionally divergent subregions: subiculum, cornu ammonis, and dentate gyrus. As a highly plastic region, the hippocampus is important for learning and memory. In parallel, it has been shown that hippocampal subregion volumes are heritable and that gene distribution profiles vary along an anterior-to-posterior axis. Leveraging the twin design of the

Human Connectome Project with microstructural imaging (T1w/T2w) and intrinsic functional connectivity (resting-state fMRI), we observed that: i) functional connectivity between hippocampus and cortex was heritable and ii) a genetic correlation between hippocampal and cortical microstructure. Moreover, both functional and microstructural organisation could be consistently captured by anterior-to-posterior and medial-to-lateral axes across individuals. However, the heritability of functional organisation, relative to microstructural organisation, was found to be reduced. This suggests that individual variation in functional organisation may be better explained by experience-driven factors. Together, this work demonstrates an interplay of stability and plasticity within the hippocampal organisation axes.

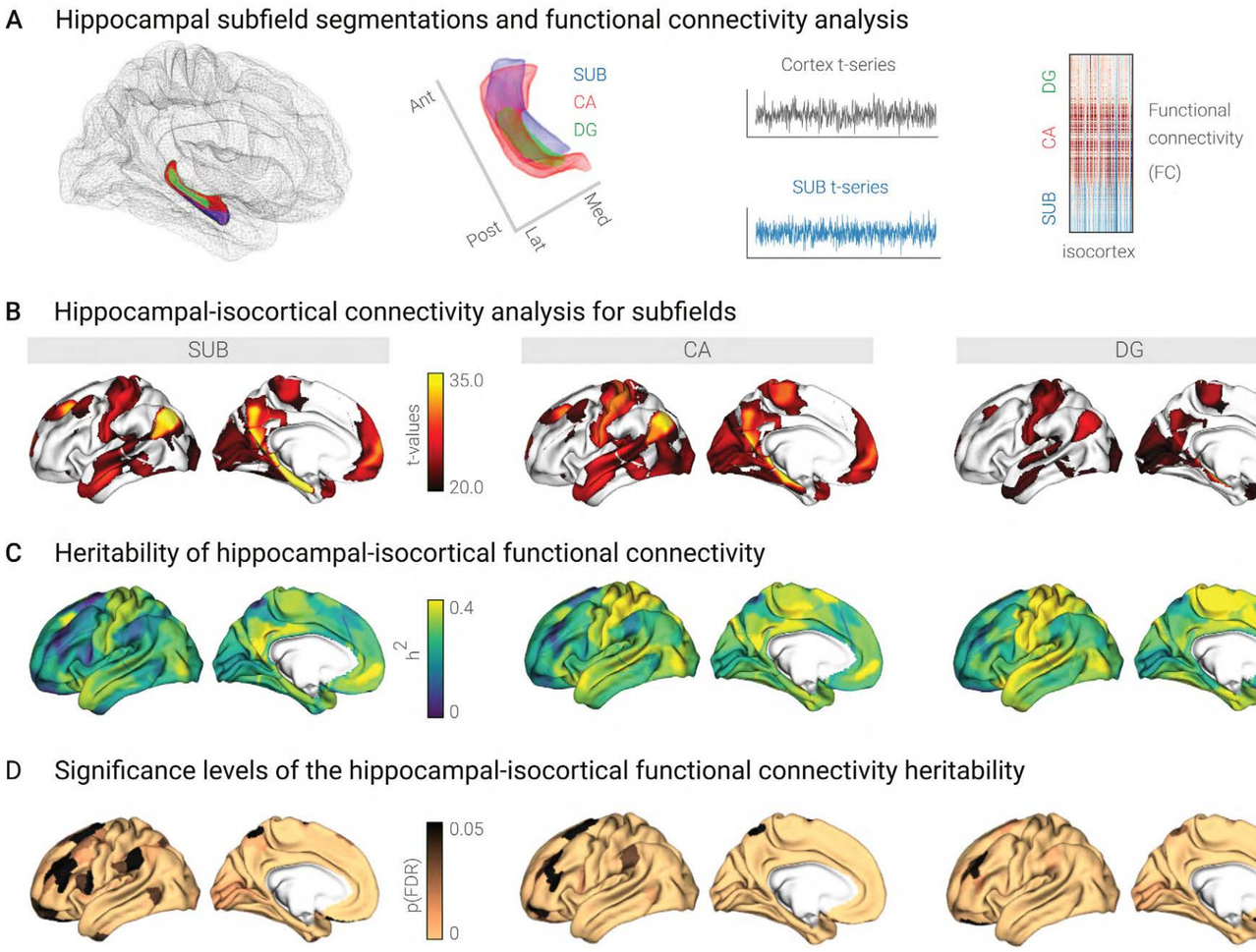


Figure 5.8.2 Hippocampal-isocortical functional connectivity and its heritability. A. Hippocampal subfield surfaces were automatically delineated using SurfPatch (Caldairou et al., 2016): subiculum (SUB, blue), CA1-3 (CA, red), and CA4-DG (DG, green). rs-fMRI time series were extracted along the individual subfields and correlated with the time series of the isocortex to obtain the functional connectivity (FC). B. Isocortex-wide FC of SUB (left), CA (middle), and DG (right). Isocortex-wide findings were thresholded at t > 20 to represent the highest connections. C. Heritability (h2) scores of the subfield-isocortical functional couplings throughout the cortex. D. Significance levels of the scores from panel C. Significance level was reported with the multiple comparison corrected p-values (p(FDR)). Copper colour denotes pFDR < 0.05 and black colour pFDR ≥ 0.05.

Structure and function

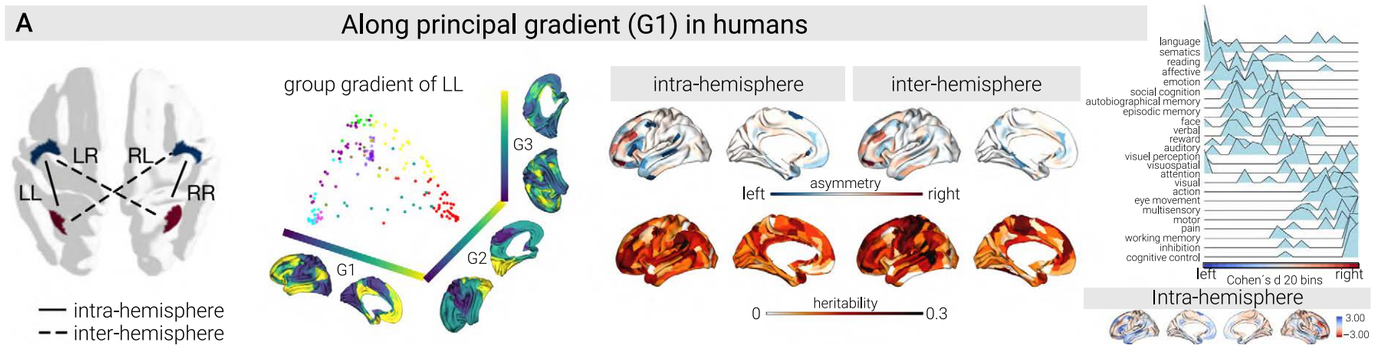
While it is important to provide insights into the genetic basis of brain organisation in order to understand how the brain scaffolds human cognition, a further step would relate brain structure to intrinsic function. In the past two-and-a-half years we have investigated the organisation of intrinsic function, its relationship to structure, and its asymmetry in the human brain. In the next years we are aiming to extend this work towards task-based designs, to probe the interplay between brain structure and cognitive function.

5.8.3 Heritability and cross-species comparisons of human cortical functional organisation asymmetry

Wan, B. [1,2,3,4], Bayrak, Ş. [1,3,4], Xu, T. [5], Schaare, H. L. [1,3,4], Bethlehem, R. A. I. [6], Bernhardt, B. C. [7], & Valk, S. L. [1,3,4,8]

[1] Max Planck Institute for Human Cognitive and Brain Sciences, Germany, [2] International Max Planck Research School on Neuroscience of Communication: Function, Structure, and Plasticity (IMPRS NeuroCom), Germany, [3] Department of Cognitive Neurology, Leipzig University Hospital, and Faculty of Medicine, Leipzig University, Germany, [4] Institute of Neuroscience and Medicine (INM-7: Brain and Behavior), Research Centre Jülich, Germany, [5] Center for the Developing Brain, Child Mind Institute, United States, [6] Department of Psychiatry, University of Cambridge, UK, [7] McConnell Brain Imaging Centre, Montréal Neurological Institute and Hospital, McGill University, QC, Canada, [8] Institute of Systems Neuroscience, Heinrich Heine University Düsseldorf, Germany

The human cerebral cortex is symmetrically organised along large-scale axes but also presents inter-hemispheric differences in structure and function. The quantified contralateral homologous difference (i.e. asymmetry) is a key feature of the left-right axis of the human brain and supports functional processes, such as language. Here, we assessed whether the asymmetry of cortical functional organisation is heritable and phylogenetically conserved between humans and macaques. Our findings indicate asymmetric organisation along an axis describing a functional trajectory from perceptual/action to abstract cognition. Whereas the language network showed leftward asymmetric organisation, the frontoparietal network showed rightward asymmetric organisation in humans. These asymmetries were heritable in humans and showed a similar spatial distribution with macaques, in the case of intra-hemispheric asymmetry of functional hierarchy. This suggests (phylo)genetic conservation. However, both language and frontoparietal networks showed a qualitatively larger asymmetry in humans relative to macaques. Overall, our findings suggest a genetic basis for asymmetry in intrinsic functional organisation, linked to higher order cognitive functions uniquely developed in humans.



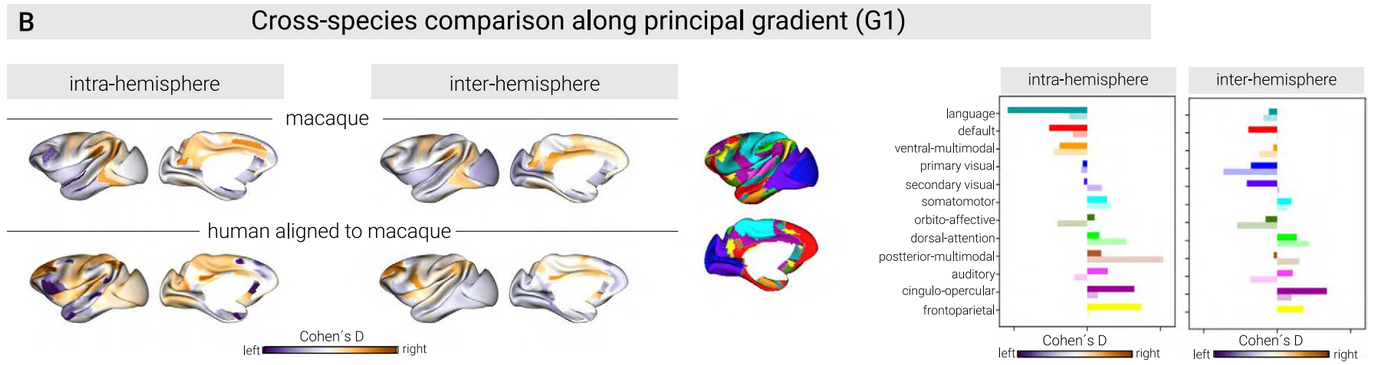


Figure 5.8.3 (Phylo)genetic asymmetry of functional gradients. (A) Asymmetry of intrinsic cortical functional organisation in humans (B) Comparing the asymmetry of cortical functional organisation between humans and macaques.

5.8.4 Genetic and phylogenetic uncoupling of structure and function in human transmodal cortex

Valk, S. L.[1,2,3], Xu, T. [4], Paquola, C. [5], Park, BY. [6,7], Bethlehem, R. A. I. [8], Vos de Wael, R. [6], Royer, J.[6], Kharabian Masouleh, S. [2], Bayrak, Ş.[1,2,3], Kochunov, P. [9], Yeo, B. T. T. [10-14], Margulies, D. [15], Smallwood, J. [16], Eickhoff, S. B. [2,3,*], & Bernhardt, B. C. [6,*]

[1] Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany, [2] Institute of Neuroscience and Medicine, Brain & Behavior (INM-7), Research Centre Jülich, Germany, [3] Institute of Systems Neuroscience, HHU Duesseldorf, Germany, [4] Center for the Developing Brain, New York City, USA, [5] Institute of Neuroscience and Medicine, Structural and functional organization of the brain (INM-1), Research Centre Jülich, Germany, [6] Multimodal Imaging and Connectome Analysis Lab, McConnell Brain Imaging Centre, Montreal Neurological Institute and Hospital, McGill University, Montreal, QC, Canada, [7] Department of Data Science, Inha University, Incheon, South Korea, [8] Department of Psychiatry, Cambridge University, UK, [9] Maryland Psychiatric Research Center, University of Maryland School of Medicine, Baltimore, MD, US, [10] Department of Electrical and Computer Engineering, National University of Singapore, Singapore, [11] Centre for Sleep and Cognition (CSC) & Centre for Translational Magnetic Resonance Research (TMR), National University of Singapore, Singapore, [12] N.1 Institute for Health & Institute for Digital Medicine (WisDM), National University of Singapore, Singapore, [13] Martinos Center for Biomedical Imaging, Massachusetts General Hospital, Charlestown, MA, USA, [14] Integrative Sciences and Engineering Programme (ISEP), National University of Singapore, Singapore, [15] Neuroanatomy and Connectivity Lab, Institut de Cerveau et de la Moelle epiniere, Paris, France, [16] Department of Psychology, Queen's University, Kingston, ON, Canada

Brain structure supports intrinsic function, scaffolding cognition and ultimately behavioural flexibility. However, it remains unclear how a static, genetically-controlled architecture supports flexible cognition and behaviour. Here, we synthesise genetic, phylogenetic, and cognitive analyses to understand how the macroscale organisation of structure-function coupling across the cortex can inform its role in cognition. In humans, structure-function coupling was highest in regions of unimodal cortex and lowest in transmodal cortex, a pattern that was mirrored by a reduced alignment with heritable connectivity profiles. Structure-function uncoupling in macaques had a similar spatial distribution, but we observed an increased coupling between structure and function in association cortices relative to humans. Meta-analysis suggested regions with the least genetic control (low heritable correspondence and different across primates) are linked to social cognition and autobiographical memory. Our findings suggest that genetic and evolutionary uncoupling of structure and function in different transmodal systems may support the emergence of complex, culturally embedded forms of cognition.

Inter-individual variability

We integrate our models of brain organisation with individual differences in behaviour in health and disease. This helps us to further pin-point the behavioural relevance of models of brain organisation, and create brain-first models of behaviour.

5.8.5 Coordinated cortical thickness alterations across six neurodevelopmental and psychiatric disorders

Hettwer, M. D. [1-4,*], Larivière, S. [5], Park, BY. [5-7], van den Heuvel, O. A. [8], Schmaal, L. [9,10], Andreassen, O. A. [11], Ching, C. R. K. [12], Hoogman, M. [13], Buitelaar, J. [14], van Rooij, D. [14], Veltman, D. J. [8], Stein, D. J. [15], Franke, B. [13], van Erp, T. G. M. [16,17], ENIGMA ADHD Working Group, ENIGMA Autism Working Group, ENIGMA Bipolar Disorder Working Group, ENIGMA Major Depression Working Group, ENIGMA OCD Working Group, ENIGMA Schizophrenia Working Group, Jahanshad, N. [12], Thompson, P. M. [12], Thomopoulos, S. I. [12], Bethlehem, R. A. I. [18,19], Bernhardt, B. C. [5], Eickhoff, S. B. [2,4], & Valk, S. L. [2-4,*]

[1] Max Planck School of Cognition, Max Planck Institute of Human Cognitive and Brain Sciences, Leipzig, Germany, [2] Institute of Neuroscience and Medicine, Brain & Behavior (INM-7), Research Centre Jülich, Germany, [3] Max Planck Institute for Cognitive and Brain Sciences, Leipzig, Germany, [4] Institute of Systems Neuroscience, Medical Faculty, HHU Düsseldorf, Germany, [5] Multimodal Imaging and Connectome Analysis Lab, McConnell Brain Imaging Centre, Montreal Neurological Instituteand Hospital, McGill University, Montreal, QC, Canada, [6] Department of Data Science, Inha University, Incheon, Republic of Korea, [7] Center for Neuroscience Imaging Research, Institute for Basic Science, Suwon, Republic of Korea, [8] Amsterdam UMC, Vrije Universiteit Amsterdam, Department of Psychiatry, Department of Anatomy & Neuroscience, Amsterdam, the Netherlands, [9] Centre for Youth Mental Health, The University of Melbourne, Parkville, Australia, [10] Orygen, Parkville, Australia, [11] NORMENT Centre, Division of Mental Health and Addiction, University of Oslo and Oslo University Hospital, Norway, [12] Imaging Genetics Center, Mark & Mary Stevens Neuroimaging and Informatics Institute, Keck School of Medicine, University of Southern California, Marina del Rey, CA, USA, [13] Departments of Psychiatry and Human Genetics, Donders Institute for Brain, Cognition and Behaviour, Radboud University Medical Center, Nijmegen, the Netherlands, [14] Department of Cognitive Neuroscience, Donders Institute for Brain, Cognition and Behaviour, Radboud University Medical Center, Nijmegen, the Netherlands, [15] South African Medical Research Council Unit on Risk & Resilience in Mental Disorders, Dept of Psychiatry & Neuroscience Institute, University of Cape Town, South Africa [16] Clinical Translational Neuroscience Laboratory, Department of Psychiatry and Human Behavior, University of California Irvine, Irvine, CA, USA, [17] Center for the Neurobiology of Learning and Memory, University of California Irvine, 309 Qureshey Research Lab, Irvine, CA, USA, [18] Autism Research Centre, Department of Psychiatry, University of Cambridge, UK, [19] Brain Mapping Unit, Department of Psychiatry, University of Cambridge, UK

Mental disorders are increasingly conceptualised as overlapping spectra sharing neurobiological alterations at multiple levels. However, whether transdiagnostic cortical alterations are organised in a biologically meaningful way across the cortex is currently unknown. Here, we studied pathological structural covariance via co-alteration networks across six mental disorders. In 12,024 patients and 18,969 controls from the ENIGMA consortium, we observed that co-alteration hubs were co-located with normative connectivity hubs and were anchored to prefrontal and temporal disease epicentres. Manifold learning revealed prefrontal-to-temporal and sensory/limbic-to-occipitoparietal transdiagnostic gradients, capturing maximally different transdiagnostic co-alteration patterns between these apices. The principal gradient aligned with a normative cortical thickness covariance gradient and established a transcriptomic link to cortico-cerebello-thalamic circuits. Moreover, transdiagnostic gradients segregated functional networks involved in basic sensory, attentional/perceptual, and domain-general cognitive processes, and distinguished between regional cytoarchitectonic profiles. Together, our findings indicate that shared illness effects are coordinated across the cortex and across diagnoses along connectomic, cytoarchitectonic, and functional dimensions.

5.8.6 Behavioural, Anatomical, and Heritable Convergence of Affect and Cognition in Superior Frontal Cortex

Kraljevic, N. *[1,2], Schaare, H. L. *[1,3], Eickhoff, S. B. [1,2], Kochunov, P. [4], Yeo, B. T. T. [5,6,7], Kharabian Masouleh, S. [1,2], & Valk, S. L., [1,2,3]

[1] Institute of Neuroscience and Medicine (INM-7: Brain and Behaviour), Research Centre Jülich, Germany, [2] Institute of Systems Neuroscience, Heinrich Heine University Düsseldorf, Germany, [3] Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany, [4] Maryland Psychiatric Research Center, University of Maryland School of Medicine, Baltimore, MD, USA, [5] Department of Electrical and Computer Engineering, Centre for Sleep and Cognition, Centre for Translational MR Research, N.1 Institute for Health and Institute for Digital Medicine, National University of Singapore, Singapore, [6] Athinoula A. Martinos Center for Biomedical Imaging, Massachusetts General Hospital, Charlestown, MA, USA, [7] NUS Graduate School for Integrative Sciences and Engineering, National University of Singapore, Singapore

Cognitive abilities and affective experience are key human traits that have an overlapping impact on behaviour and share brain structural correlates. Individual variation of cognitive and affective traits, as well as brain structure, has been shown to be partly heritable, indicating genetic factors contribute to individual variability. Here we studied phenotypic and genetic correlations of cognitive and affective traits in behaviour and brain structure (cortical thickness, surface area and subcortical volumes) in the pedigree-based Human Connectome Project sample (*N* = 1091). Both cognitive and affective trait scores were heritable and correlated. Cortical thickness in the left superior frontal cortex showed an association with both affect and cognition. Decomposing the phenotypic correlations into genetic and environmental components showed that the associations were partly accounted for by shared genetic effects between the traits. Quantitative functional decoding of the left superior frontal cortex further indicated that this region is associated with cognitive and emotional functioning at a meta-analytical level. In sum, using a multi-level approach to study the association between affect and cognition, we could illustrate the partial convergence of both in superior frontal cortical thickness.

Congresses, workshops, and symposia

2020

- Valk, S. L. *International "Gradients in Brain Organization" workshop.* Satellite for the Organization of Human Brain Mapping (OHBM) Annual Meeting in 2020 (co-organizer).
- Valk, S. L. *Diversity symposium (co-organizer)*. Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany.

2021

Co-organisation of:

- Eippert, F., Valk, S. L., & Weiskopf,N. (July). *Career building. Expertise session II.* 10th IMPRS NeuroCom Summer School in Cognitive Neuroscience. International Max Planck Research School on Neuroscience of Communication: Function, Structure, and Plasticity (IMPRS NeuroCom), Max Planck Institute for Human Cognitive and Brain Sciences & ICN, Leipzig & London, Germany & UK. Virtual.
- Valk, S. L. *Open Science Room (co-organizer).* Hackathon for the Organization of Human Brain Mapping (OHBM) Annual Meeting in 2021. Virtual.
- Valk, S. L. *Hackathon (co-organizer).* Hackathon for the Organization of Human Brain Mapping (OHBM) Annual Meeting in 2021. Virtual.
- Valk, S. L. *International "Gradients in Brain Organization" workshop (co-organizer).* Satellite for the Organization of Human Brain Mapping (OHBM) Annual Meeting in 2021. Virtual.

2022

- Valk, S. L. (June). *International "Gradients in Brain Organization" workshop (co-organizer).* Satellite for the Organization of Human Brain Mapping (OHBM) Annual Meeting in 2022.
- Valk, S. L. (June). *Surface-based modelling of brain organisation. Workshop*. 11th IMPRS NeuroCom Summer School in Cognitive Neuroscience. International Max Planck Research School on Neuroscience of Communication: Function, Structure, and Plasticity (IMPRS NeuroCom), Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany.

Degrees

PhD Theses

2022

- Bayrak, S. *The Impact of Human Brain Structure on Its Functional Connectomics in Health and Stroke Injury.* Leipzig University, Medical Faculty. Germany (co-supervision)

Appointments

2020

- Valk, S. L. *Max Planck Otto Hahn research group leader (W2)*, Max Planck Society, Germany.
- Valk, S. L. *Faculty member of the International Max Planck Research School on Neuroscience and Communication: Function, Structure, and Plasticity (IMPRS NeuroCom)*. Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany.

2021

- Valk, S. L. *Research group leader at the Institute of Neuroscience and Medicine-7 (Brain and Behavior)*, Research Center Jülich, Jülich, Germany.
- Valk, S. L. *Member, Human Sciences Section, Scientific Council of the Max Planck Society (as elected scientific staff representative of the MPI for Human Cognitive and Brain Sciences).*
- Schaare, H. L. *Postdoc representative at the Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany.*
- Schaare, H. L. *Postdoc representative, PostdocNet steering group, Max Planck Society.*

2022

- Valk, S. L. *Faculty member of the International Max Planck Research School on Cognitive Neuroscience (IMPRS CoNI).* Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany.
- Valk, S. L. *Organization for Human Brain Mapping (OHBM) council: educational chair (2022–2025).*

Awards

2021

- Schaare, H. L. *OHBM Merit award for poster.*

2022

- Manoli, E. *Scholarship of the German Academic Scholarship Foundation*, Bonn, Germany.
- Valk, S. L. *Early Career Award der Deutschen Gesellschaft für Psychophysiologie und ihre Anwendung (DGPA e.V.),* (to be handed out in 2023, due to the COVID-19 pandemic).

Publications

This list also includes publications of team members of the Otto Hahn Group Cognitive Neurogenetics that resulted from work they carried out prior to their arrival. These articles are included as they speak to the unique qualifications of the team members.

Journal Articles

Bayrak, S., de Wael, R. V., Schaare, H. L., Hettwer, M., Caldairou, B., Bernasconi, A., Bernasconi, N., Bernhardt, B. C., & Valk, S. L. (2022). Heritability of hippocampal functional and microstructural organisation. *NeuroImage*, *264*. https://doi.org/10.1016/j.neuroimage.2022.119656

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Minerva Fast Track Group Neural Codes of Intelligence

(commenced September 2022)

Human intelligence exhibits features that are unparalleled by other species or its artificial counterpart. A hallmark of human intelligence is the ability to learn quickly in face of sparse or ambiguous information in the environment and to make solid inferences that go beyond our direct experience. Humans can recognize similarity in the internal structure of two situations independent of perceptual resemblance or statistical covariation, and apply knowledge from one context to solve problems in a different one. Our research is guided by the overarching question of how the human brain processes information to enable this inferential capacity. Particularly, we are interested in (i) how the brain forms and represents abstract conceptual knowledge and (ii) how these representations are leveraged to guide new learning, reasoning, and novel problem solving. Lastly, we aim to (iii) identify properties of neural information processing that account for interindividual differences in general cognitive ability. We investigate these questions using a combination of behavioural and neuroimaging methods.

How is knowledge organized to allow its flexible use? Previous work suggests that concept learning, the ability to extract commonalities and mark distinctions across experiences to build structured knowledge, is supported by the same coding properties of the hippocampal system (e.g. place and grid cells) that form cognitive maps of the environment by integrating multiple relations in a common representational space. This representational format would be advantageous to infer relations that are not directly experienced and to generalize knowledge about one instance to nearby ones. We have shown that when learning novel categories, the hippocampus encodes the distances between exemplars as well as category boundaries in concept space akin to distances and boundaries in physical space, and that this representation emerges from a selective integration of behaviourally-relevant feature dimensions (Theves et al., 2019; Theves et al., 2020). Our recent work further indicates that the extension of category boundaries causes memory changes, that mimic the pattern of hippocampal place field distortions in response to environmental boundary extensions (Theves et

al., in prep). Furthermore, the formation of hierarchical concept representations, which structure knowledge at different level of abstraction, was supported by a hippocampal-prefrontal interplay (Theves et al., 2021). Categorization can sometimes be guided by prototypical representations – in ongoing work, we evaluate whether representations of unseen categorical prototypes can be interpolated from neural patterns of other exemplars in concept space as predicted by a metric function of its dimensions (Schäfer et al., in progress). More generally, a current theoretical view in the field is that the hippocampal-entorhinal system might support generalization by factorizing knowledge into representations of its structure and specifics, which can be flexibly recombined to map new experiences. Yet evidence for a direct link to generalization performance is still limited, and a potential contribution of these codes to the broader scope of generalization problems and human reasoning behaviours, as well as their interplay with long-term knowledge and neocortical processing, are unclear. In sum, the central objective of our newly established group is to gain a broader understanding of the neural geometry that underlies inferential leaps in learning, reasoning, and novel problem solving, and to identify representational mechanisms that shape our general cognitive abilities.

Congresses, Workshops, and Symposia

2021

- Doeller, C. F., & Theves, S. (regular). *Mind Meeting Seminar Series.* Seminar Series. Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany.

2022

- Doeller, C. F., & Theves, S. (regular). *Mind Meeting Seminar Series.* Seminar Series. Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany.

Appointments

2022

- Theves, S. *Minerva Fast Track Fellow*, Max Planck Society, Germany.
- Theves, S. *Faculty member of the International Max Planck Research School on Computational Methods in Psychiatry and Ageing Research (IMPRS COMP2PSYCH)*, Max Planck Institute for Human Development and Humboldt-Universität zu Berlin, Berlin, Germany.
- Theves, S. *Faculty member of the International Max Planck Research School on Cognitive NeuroImaging (IMPRS CoNI)*, Max Planck Institute for Cognitive and Brain Sciences, Leipzig, Germany.

Awards

2021

- Theves, S. *Otto Hahn Medal of the Max Planck Society*, Germany.
- Theves, S. *Invited participant at the 4th World Laureate Forum*, Shanghai, China.

2022

- Theves, S. *Postdoctoral Fellow Award.* Annual Meeting of the Cognitive Neuroscience Society, San Francisco, CA, USA.

Publications

Books & Book Chapters

Theves, S., Grande, X., Düzel, E., & Doeller, C. F. (in press). Pattern completion and the Medial Temporal Lobe Memory System. In *Oxford Handbook of Human Memory*. Oxford: Oxford University Press.

Journal Articles

Theves, S., Neville, D. A., Fernández, G., & Doeller, C. F. (2021). Learning and representation of hierarchical concepts in hippocampus and prefrontal cortex. *The Journal of Neuroscience, 41*(36), 7675–7686. https://doi.org/10.1523/JNEUROSCI.0657-21.2021

Theves, S., Fernández, G., & Doeller, C. F. (2020). The hippocampus maps concept space, not feature space. *The Journal of Neuroscience*, *40*(38), 7318–7325. https://doi.org/10.1523/JNEUROSCI.0494-20.2020

Theves, S., Chan, J. S., Naumer, M. J., & Kaiser, J. (2020). Improving audio-visual temporal perception through training enhances beta-band activity. *NeuroImage*, *206*. https://doi.org/10.1016/j.neuroimage.2019.116312

6.1

Professor Dr Harald E. Möller

Nuclear Magnetic Resonance

Complementing support of the Institute's magnetic resonance imaging (MRI) infrastructure, our research revolves around the development and adaptation of methods to study brain anatomy, metabolism, and function. This ranges from radiofrequency (RF) hardware to MR pulse sequences and image analysis concepts. Another focus is on contrast mechanisms that generate information concerning tissue structure and composition or physiology. This work has largely benefitted from collaborations within and outside the Institute. While some of these are mentioned along with selected projects, others include colleagues from the Paul Flechsig Institute, as well as in Cologne, Amsterdam, Maastricht, Lyon, Lund, Bristol, Purdue, USC, Duke, and Berkeley.

Custom-made RF coils remain instrumental for imaging small tissue specimens. An unexpected observation was a relevant radiation damping already present at 3 T, which needs to be considered in reference experiments for quantitative MRI. A highlight in hardware sophistication was a 64-channel receive array with integrated field camera for our Connectom scanner (Figure 6.1). Finally, extended simulations of electromagnetic fields during MRI in the presence of transcranial direct current stimulation were performed in the frequency domain.

Contrast related to neuromelanin was studied in collaboration with Segrate and Pavia (6.1.1). Besides relaxometry and quantitative susceptibility mapping (QSM), electron paramagnetic resonance (EPR) and extended X-ray absorption fine structure (EXAFS) spectroscopy were integrated, supported by colleagues at the University's Physics Faculty. Understanding orientation dependence of MRI contrast continued to be a valuable means for probing underlying mechanisms. Here, we introduced High Angular Resolution Susceptibility Imaging (HAR**S**I) as an analogue to HAR**D**I-type experiments in diffusion-weighted imaging (DWI), yielding information on fibre structure at high resolution in *post-mortem* samples (6.1.2). The acquisition of the DWI reference data benefitted from earlier established, highly segmented, multi-echo, echo-planar imaging (EPI).

Physiological information concerning deactivation was obtained from functional perfusion measurements and simultaneous recordings of the blood oxygenation level dependent (BOLD) signal (6.1.3). This was achieved by combining pseudo-continuous arterial spin labelling (pCASL) with a previously developed centre-out EPI variant (DEPICTING) that was expanded for multi-echo acquisitions. The macromolecular background in proton spectra was studied with partners from Bern at very high diffusion weighting offered by the Connectom gradients.

In applications of functional MRI (fMRI), activation patterns evoked by finger tapping in Parkinson's patients has been a joint effort with Charles University in Prague for more than a decade (6.1.4). New results show that the sensitivity can be substantially improved if region-specific activity patterns are considered. Like everywhere else, many projects have seen delays due to the COVID-19 pandemic, in particular clinical applications. We are, thus, happy about the initial results from combined MRI and positron emission tomography (PET) investigations of neurotransmitter abnormalities in Tourette syndrome, pursued jointly with Leipzig and Hannover Medical Schools.

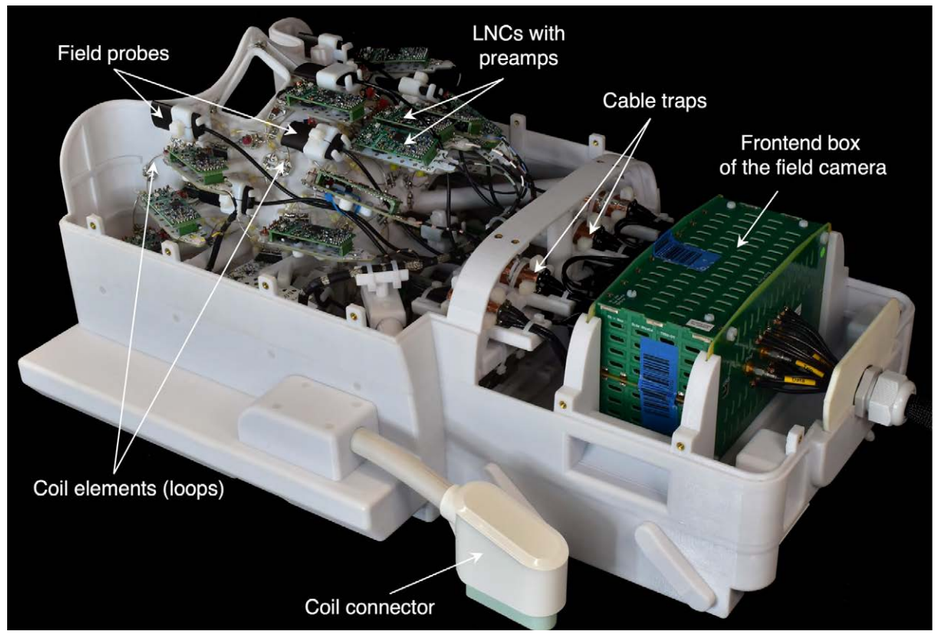

Figure 6.1 Custom-built 64-channel receive array for MRI of the human head at 3 T with 16 integrated probes for dynamic magnetic field monitoring. The coil was designed and built by Boris Keil and Mirsad Mahmutovic at Mittelhessen University of Applied Sciences, Giessen, Germany.

6.1.1 Investigation of contrast mechanisms for neuromelanin-sensitive MRI

Wallstein, N.[1], Pampel, A.[1], Pöppl, A.[2], Capucciati, A.[3], Jäger, C.[1], Monzani, E.[3], Zucca, F.A.[4], Casella, L.[3], Zecca, L.[4], & Möller, H. E.[1,2]

[1] Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany, [2] Felix Bloch Institute for Solid State Physics, Leipzig University, Germany, [3] Department of Chemistry, University of Pavia, Italy, [4] Institute of Biomedical Technologies, National Research Council of Italy, Segrate, Milan, Italy

While visualization of subcortical neuromelanin (NM) by MRI is of great interest in neurodegenerative diseases, NM-associated contrast remains elusive. Typically assumed is a paramagnetic relaxation enhancement by metals bound to NM, in particular, iron and copper. To further investigate, we performed relaxation, magnetic susceptibility ($\Delta\chi$), and EPR measurements in synthetic NM-protein conjugates with varying metal contents. The EPR spectra confirmed two iron sites in NM: a mononuclear centre demonstrating Curie behaviour and a multinuclear cluster (Figure 6.1.1). Susceptibil-

ity mapping yielded a positive shift of $\Delta\chi$, consistent with the expected magnetic moment of high-spin Fe^{3+}, up to a critical metal loading, which was inverted after this point. This suggests a preferred occupation of the mononuclear centre at low metal content, followed by increasing iron clustering. An estimate of clustered Fe^{3+} from the EPR results yielded a counterintuitive relaxivity reduction resembling a declining moment per Fe^{3+} upon increasing storage in clusters. Due to the two regimes, relaxation rates cannot predict the metal loading over the entire range and "NM-MRI" may yield invalid metal content estimates. Moreover, Fe and Cu may occupy similar sites, suggesting their involvement in the early phase of NM synthesis.

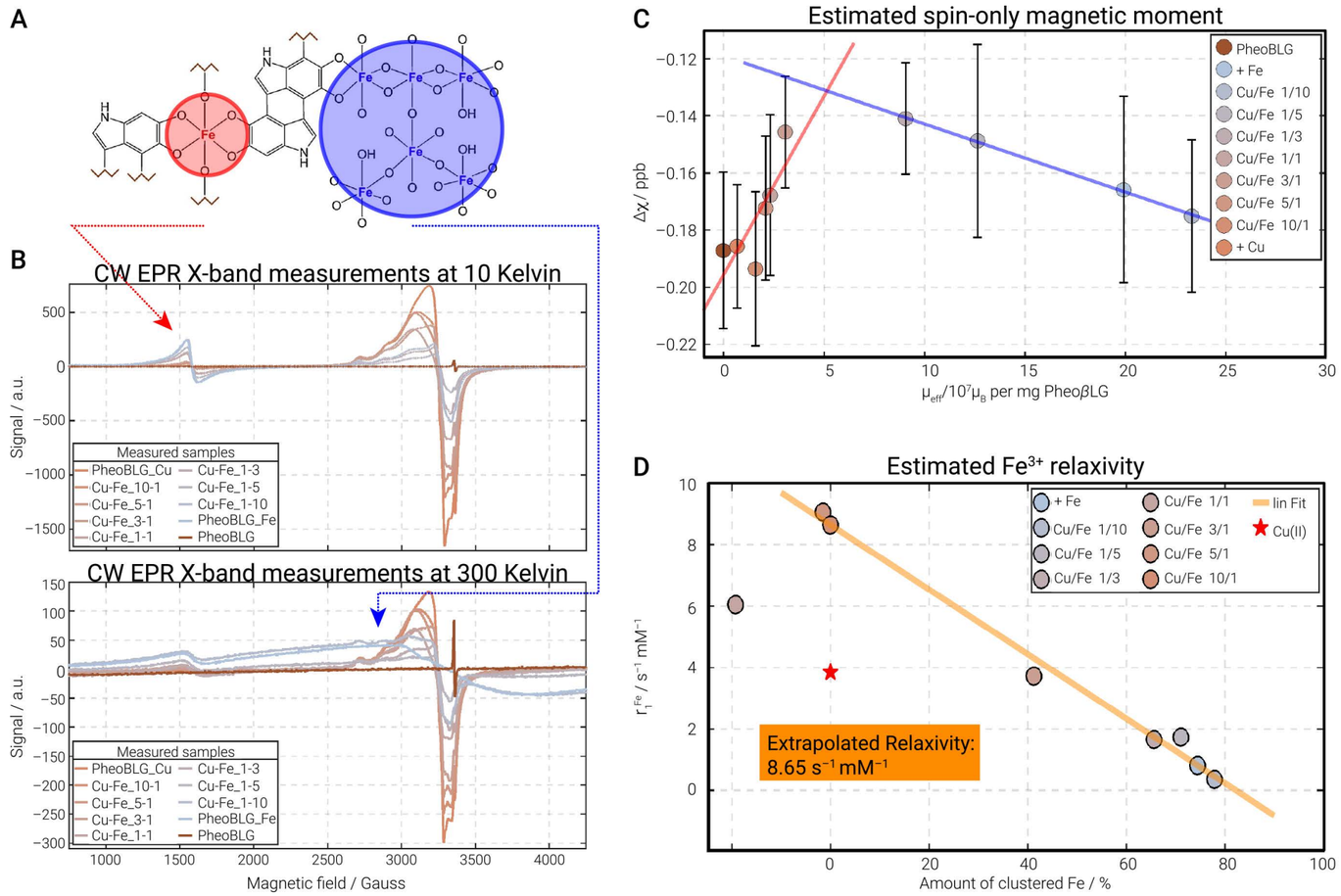

Figure 6.1.1 (A) Proposed mononuclear (red) and multinuclear (blue) iron sites in NM. (B) Besides a sharp peak of the NM free radical at g = 2.0, EPR spectra at 10 K show a Cu^{2+} signal at g_{eff} = 2.15 (hyperfine splitting) and a high-spin Fe^{3+} signal (rhombic symmetry, large zero-field splitting) at $g_{eff} \approx 4.3$, both characterised by Curie behaviour. At room temperature, another broad component was assigned to clustered Fe^{3+} in an antiferromagnetic domain. (C) Magnetic susceptibility obtained by QSM demonstrated a biphasic behaviour when plotted against the expected effective high-spin magnetic moment, according to the metal content. (D) Apparent decrease of the longitudinal relaxivity with increasing amounts of clustered Fe^{3+}.

6.1.2 High Angular Resolution *Susceptibility* Imaging (HARSI)

Gkotsoulias, D. G.[1], Müller, R.[1], Jäger, C.[1], Schlumm, T.[1], Mildner, T.[1], Eichner, C.[1], Pampel, A.[1], Jaffe, J.[2,3], Gräßle, T.[3,4], Alsleben, N.[1], Chen, J.[5]., Crockford, C.[2,3,6], Wittig, R.[2,3,6], Liu,C.[5,7], & Möller, H. E.[1]

[1] Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany, [2] Max Planck Institute for Evolutionary Anthropology, Leipzig, Germany, [3] Taï Chimpanzee Project, Centre Suisse de Recherches Scientifiques en Côte d'Ivoire, Côte Ivoire, [4] Robert Koch Institute, Epidemiology of Highly Pathogenic Microorganisms, Berlin, Germany, [5] Electrical Engineering and Computer Sciences, University of California, Berkeley, CA, USA, 6 Institute of Cognitive Sciences, CNRS UMR5229 University of Lyon, Bron, France, [7] Helen Wills Neuroscience Institute, University of California, Berkeley, CA, USA

High Angular Resolution *Diffusion* Imaging (HAR**D**I) achieves identification of intersecting fibre bundles by estimating the underlying orientation distribution function (ODF), which overcomes limitations of diffusion tensor imaging (DTI). Anisotropic properties related to white-matter microstructure are also inherent to the magnetic susceptibility, albeit resulting from an entirely different physical mechanism. While susceptibility tensor imaging (STI) has already been proposed previously, demonstrating similarities to DTI, fibre ODFs have not yet been obtained from susceptibility data. Here, we introduce High Angular Resolution *Susceptibility* Imaging (HAR**S**I) as a complementary concept to probe structural anisotropy (Figure 6.1.2). Multi-echo phase data were acquired from 61 randomly distributed orientations in a fixed chimpanzee brain. ODFs were extracted with an adapted CSA approach and achieved identification of multi-orientational fibre bundles consistent with HAR**D**I data acquired as a reference. Preliminary results suggest a higher sensitivity to secondary fibre orientations for HAR**S**I, which might yield complementary information on WM microstructure.

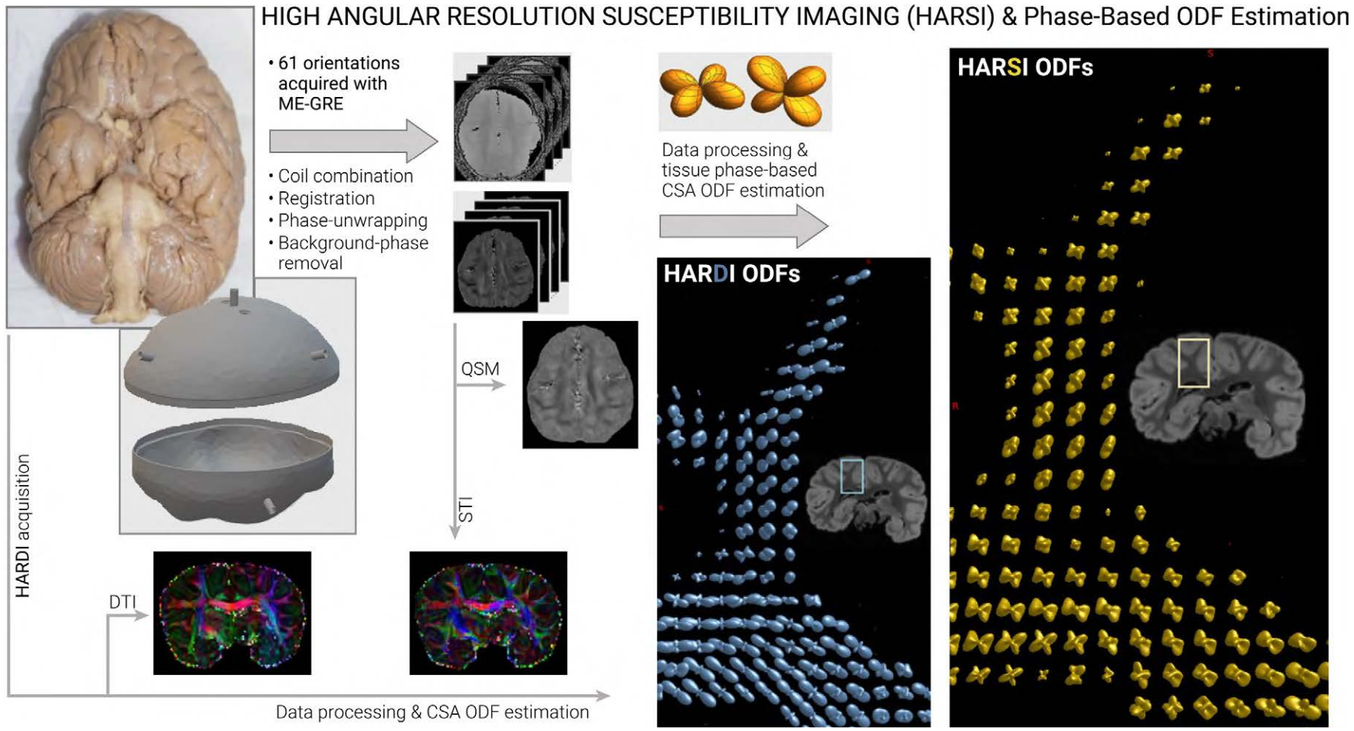

Figure 6.1.2 HAR**S**I image acquisition and processing pipeline: A fixed brain of a chimpanzee that had died of natural causes is imaged at 61 orientations inside a 3D-printed container, adapted to the individual anatomy. Following registration, an established algorithm for QSM is applied to the multidirectional data. The multi-directional phase data can be used for STI and also ODF estimation based on a constant solid angle (CSA) approach. The susceptibility results (STI, ODFs) are compared voxel-by-voxel to corresponding data from diffusion-weighted imaging.

6.1.3 Multi-echo investigations of positive and negative CBF and concomitant BOLD changes

Devi, R.[1], Lepsien, J.[1], Lorenz, K.[1], Schlumm, T.[1], Mildner, T.[1], & Möller, H. E.[1]

[1] Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany

Unlike the positive BOLD response (PBR), commonly taken as an indication of 'activation', the origin of a **negative BOLD response** (NBR), also referred to as 'deactivation', is still being debated. To gain a better understanding of its underlying mechanism we performed comprehensive measures of the NBR and its contributing cerebral blood flow (CBF) in human visual cortex, in comparison to a simultaneously induced PBR in surrounding regions. CBF measurements were obtained with pCASL and a multi-echo version of a centre-out EPI readout. It achieved very short echo and inter-echo times and simultaneous detection of CBF and the BOLD signal with improved sensitivity. Evaluations of changes of CBF and the effective transverse relaxation time, T_2^*, the coupling ratios, and their dependence on CBF at rest indicated differences between activated and deactivated regions (Figure 6.1.3). Analysis of the dynamics also revealed faster negative responses with more pronounced post-stimulus transients.

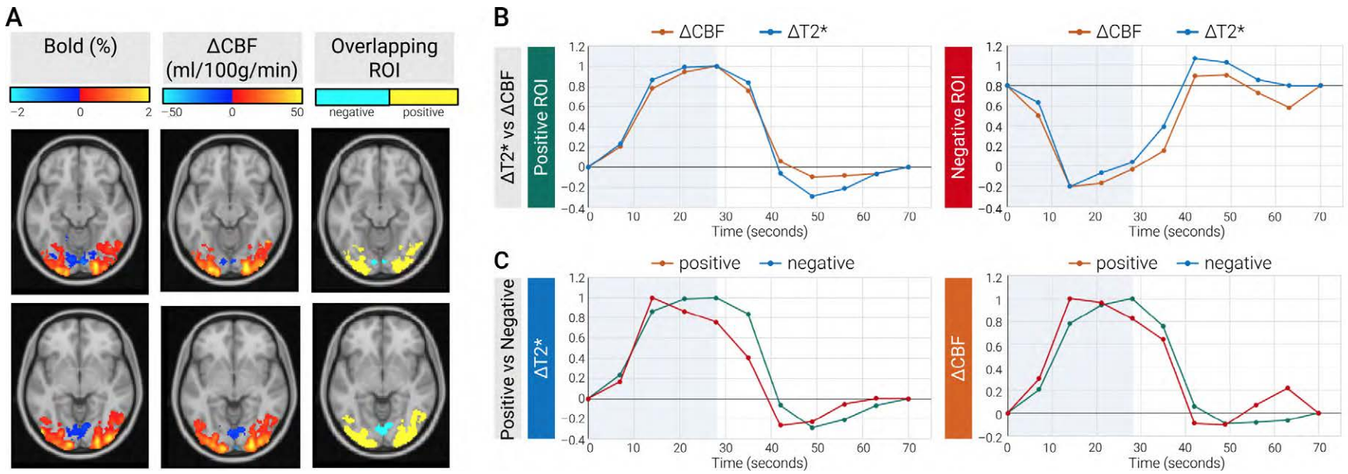

Figure 6.1.3 (A) Maps of stimulus-related BOLD and CBF changes at 3 T showing significant activation and deactivation at $p < 0.0001$ and $p < 0.01$, respectively, in two slices of the same healthy volunteer. (B) Comparison of normalised, subject-averaged ΔT_2^* vs. ΔCBF transients from 12 volunteers in the positive (left) and negative region of interest (ROI, right). Blue shaded regions indicate the duration of the task. (C) The same transients as in (B) now comparing ΔT_2^* in the positive vs. negative ROI as well as ΔCBF in the positive vs. negative ROI. Note that the transients from the negative ROI in (C) were inverted for better visualisation of temporal shifts between the ROIs.

6.1.4 Improving fMRI in Parkinson's disease by accounting for brain region-specific activity patterns

Torrecuso, R.[1], Mueller, K.[1], Holiga, Š.[1,2], Sieger, T.[3], Vymazal, J.[4], Růžička, F.[3,4], Roth, J.[3,4], Růžička, E.[3], Schroeter, M. L.[1,5], Jech, R.[3,4], & Möller, H. E.[1]

[1] Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany, [2] Roche Pharma Research and Early Development, Roche Innovation Center Basel, Switzerland, [3] Department of Neurology and Center of Clinical Neuroscience, Charles University in Prague, Czech Republic, [4] Na Homolce Hospital, Prague, Czech Republic, [5] Clinic for Cognitive Neurology, Leipzig University Hospital, Germany

In clinical fMRI, patients with Parkinson's disease (PD) performing blocks of finger-tapping and rest have been frequently investigated. Typically, such experiments assume a general linear model with a boxcar function, which may degrade the sensitivity. This is because *(i)* it inherently assumes constant activity, whereas PD patients often produce an irregular motor output, especially when off treatment. *(ii)* Different brain regions may possess different temporal signatures. Hence, a boxcar function may capture sustained activity in some regions but lose others that activate only during task initiation. To study the first limitation, we replicated earlier kinematic modelling, where the boxcar function is modulated with information on finger movements from a sensory glove. The second issue was investigated by modelling only the onsets of tapping and rest blocks. Our results suggest that different brain areas require different analysis concepts for optimised sensitivity (Figure 6.1.4). The kinematic model yielded the best performance for capturing tapping-related M1 activation, whereas the 'onset model' was superior in revealing treatment-related alterations in basal-ganglia activity.

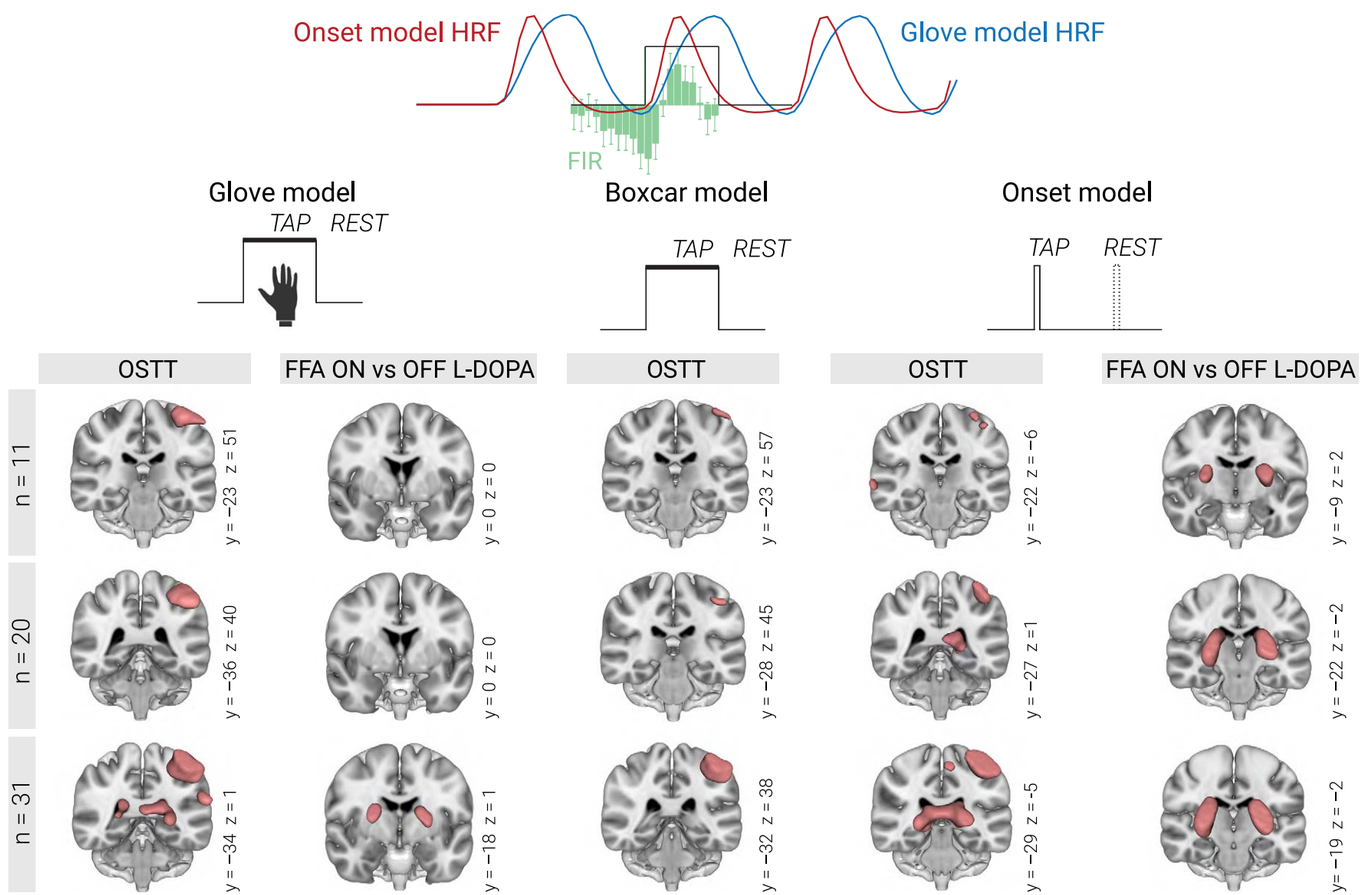

Figure 6.1.4 Activation maps for the main effect of tapping vs. rest as well as the effect of L-DOPA treatment. Data were obtained in two separate cohorts of *n* = 11 and *n* = 20 PD patients performing right-handed finger tapping (block design) as well as in the combined cohort (*n* = 31). The central column displays results from a standard analysis (boxcar function) that captures activation of the primary motor cortex (M1) but not the more subtle treatment effect. The first two columns show improved results including treatment-related subcortical activation obtained after integration of kinematic information from a sensory glove. The best sensitivity for detecting the L-DOPA effect, but not the M1 activation, was obtained upon modelling only the onsets of activation and rest periods (final two columns). Models of the different hemodynamic response functions (HRFs) and of the finite impulse response (FIR) in the putamen are shown in the top row.

Congresses, Workshops, and Symposia

2020

- Möller, H. E. (January–December). *Magnetic Resonance Methods in Brain Research.* Seminar. Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany.

2021

- Möller, H. E. (January–December). *Magnetic Resonance Methods in Brain Research.* Seminar. Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany.
- Möller, H. E. (April–December). *Leipzig Spin Resonance Colloquium.* Faculty of Physics and Earth Sciences, Leipzig University, Germany: Co-Organiser.

2022

- Möller, H. E. (January–December). *Leipzig Spin Resonance Colloquium.* Faculty of Physics and Earth Sciences, Leipzig University, Germany: Co-Organiser.
- Möller, H. E. (January–December). *Magnetic Resonance Methods in Brain Research.* Seminar. Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany.

Appointments

2022

- Möller, H. E. *Faculty member of the International Max Planck Research School on Cognitive NeuroImaging (IMPRS CoNI),* Max Planck Institute for Cognitive and Brain Sciences, Leipzig, Germany.

Degrees

PhD Theses

2021

- Gast, R. *Phase transitions between asynchronous and synchronous neural dynamics: Theoretical insight into the mechanisms behind neural oscillations in Parkinson's disease.* Leipzig University, Germany.

2022

- Molloy, E. *Behavioral, Functional, & Neurophysiological Responses to One-Week Administration of Escitalopram.* Leipzig University, Germany.
- Şimşek, K. *Extending diffusion-weighted magnetic resonance spectroscopy.* University of Bern, Switzerland.

Awards

2020

- Devi, R. *Best Trainee Abstract Reporting Award.* Current Issues in Brain Function Study Group, International Society for Magnetic Resonance in Medicine (ISMRM), Virtual Meeting.
- Devi, R. *Magna cum Laude Merit Award.* International Society for Magnetic Resonance in Medicine (ISMRM), Virtual Conference & Exhibition.
- Devi, R. *Trainee Award.* International Society for Magnetic Resonance in Medicine (ISMRM), Virtual Conference & Exhibition.

2021

- Gkotsoulias, D. *Magna cum Laude Merit Award.* International Society for Magnetic Resonance in Medicine (ISMRM), An Online Experience.

2022

- Devi, R. *Early Career Researcher Waiver.* Interpreting BOLD III: Furthering the dialogue between cellular and cognitive neuroscience, Christ Church, Oxford, UK.
- Devi, R. *Trainee Award.* International Society for Magnetic Resonance in Medicine (ISMRM), London, UK.
- Gkotsoulias, D. *Trainee Award.* International Society for Magnetic Resonance in Medicine (ISMRM), London, UK.
- Torrecuso, R. *Trainee Award.* International Society for Magnetic Resonance in Medicine (ISMRM), London, UK.
- Wallstein, N. *Trainee Award.* International Society for Magnetic Resonance in Medicine (ISMRM), London, UK.

Patents

- Müller, R., & Möller, H. E. (2020). *Vorrichtung und Verfahren zur elektrischen Anbindung von elektronischen Baugruppen mittels symmetrisch abgeschirmter Leitungen [Device and method for electrically linking assemblies by means of symmetrical screened cables].* German patent, DE 10 2014 105 800 A1.

Publications

Books & Book Chapters

Jech, R., & Mueller, K. (2022). Investigating network effects of DBS with fMRI. In A. Horn (Ed.), *Connectomic Deep Brain Stimulation* (pp. 275–301). Academic Press. https://doi.org/10.1016/B978-0-12-821861-7.00026-9

Journal Articles

Alkemade, A., Bazin, P.-L., Balesar, R., Pine, K., Kirilina, E., Möller, H. E., Trampel, R., Kros, J. M., Keuken, M. C., Bleys, R. L. A. W., Swaab, D. F., Herrler, A., Weiskopf, N., & Forstmann, B. U. (2022). A unified 3D map of microscopic architecture and MRI of the human brain. *Science Advances*, *8*(17). https://doi.org/10.1126/sciadv.abj7892

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Ballarini, T., Albrecht, F., Mueller, K., Jech, R., Diehl-Schmid, J., Fliessbach, K., Kassubek, J., Lauer, M., Fassbender, K., Schneider, A., Synofzik, M., Wiltfang, J., FTLD Consortium, Otto, M., & Schroeter, M. L. (2020). Disentangling brain functional network remodeling in corticobasal syndrome: A multimodal MRI study. *NeuroImage: Clinical*, *25*. https://doi.org/10.1016/j.nicl.2019.102112

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Eichner, C., Paquette, M., Mildner, T., Schlumm, T., Pléh, K., Samuni, L., Crockford, C., Wittig, R. M., Jäger, C., Möller, H. E., Friederici, A. D., & Anwander, A. (2020). Increased sensitivity and signal-to-noise ratio in diffusion-weighted MRI using multi-echo acquisitions. *NeuroImage*, *221*. https://doi.org/10.1016/j.neuroimage.2020.117172

Filip, P., Jech, R., Fečíková, A., Havránková, P., Růžička, F., Mueller, K., & Urgošík, D. (2022). Restoration of functional network state towards more physiological condition as the correlate of clinical effects of pallidal deep brain stimulation in dystonia. *Brain Stimulation*, *15*(5), 1269–1278. https://doi.org/10.1016/j.brs.2022.08.025

García-García, I., Kube, J., Morys, F., Schrimpf, A., Kanaan, A. S., Gaebler, M., Villringer, A., Dagher, A., Horstmann, A., & Neumann, J. (2020). Liking and left amygdala activity during food versus nonfood processing are modulated by emotional context. *Cognitive, Affective and Behavioral Neuroscience*, *20*(1), 91–102. https://doi.org/10.3758/s13415-019-00754-8

Gast, R., Gong, R., Schmidt, H., Meijer, H. G. E., & Knösche, T. R. (2021). On the role of arkypallidal and prototypical neurons for phase transitions in the external pallidum. *The Journal of Neuroscience*, *41*(31), 6673–6683. https://doi.org/10.1523/JNEUROSCI.0094-21.2021

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Gong, R., Wegscheider, M., Mühlberg, C., Gast, R., Fricke, C., Rumpf, J.-J., Nikulin, V. V., Knösche, T. R., & Classen, J. (2021). Spatiotemporal features of β-γ phase-amplitude coupling in Parkinson's disease derived from scalp EEG. *Brain*, *144*(2), 487–503. https://doi.org/10.1093/brain/awaa400

Guidi, M., Huber, L., Lampe, L., Merola, A., Ihle, K., & Möller, H. E. (2020). Cortical laminar resting-state signal fluctuations scale with the hypercapnic blood oxygenation level-dependent response. *Human Brain Mapping*, *41*(8), 2014–2027. https://doi.org/10.1002/hbm.24926

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Index of Published Figures

Figure 6.1

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Figure 6.1.1

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Figure 6.1.2

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Figure 6.1.3

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Figure 6.1.4

Torrecuso, R., Mueller, K., Holiga, Š., Urgosik, D., Vymazal, J., Sieger, T., et al. (2022). Different brain areas require different analysis models: fMRI observations in Parkinson's disease. In *Proceedings of the 31st Joint Annual Meeting of the International Society for Magnetic Resonance in Medicine (ISMRM), London, UK.*

6.2

Professor Dr Thomas R. Knösche

Dr Burkhard Maess

Brain Networks

We study mechanistic and biologically realistic models of functional and structural networks in the brain. They are designed to link physiological and anatomical knowledge with experimental data from EEG/MEG, functional MRI, diffusion MRI, and non-invasive brain stimulation, as well as with cognitive function. In the past three years, we have approached this goal from different directions. First, we developed and explored a new generation of mean field models for signal transmission in axonal bundles (6.2.1) and neural populations (6.2.2), which provide a mechanistic account of basic building blocks of brain functionality. Second, we designed new methods, based on electric field simulation, for linking transcranial magnetic stimulation with localised neuronal populations and behavioural effects (6.2.3). Currently, we are working to combine both approaches into a general modelling framework (work in progress), including the development of a general-purpose software package for assessing sensitivity and uncertainty in complex models (6.2.9). Third, we conducted several series of studies to investigate the correlative relationship between functional and structural brain signatures with cognitive functions. In particular, we studied the role of long-range structural (derived from diffusion MRI) and functional (derived from MEG) connectivity in language functionality and their improvement through training (6.2.4), MEG signatures for sound regularity (6.2.7) and auditory attention (6.2.8), and EEG biomarkers for Parkinson's disease (6.2.5). Finally, an important part of our work was dedicated to the development of novel MEG data acquisition techniques (6.2.6).

6.2.1 Modelling spike transmission in axon bundles

Schmidt, H.[1,2], Hahn, G.[1,3], Deco, G.[4], & Knösche, T. R.[1,5]

[1] Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany, [2] Institute of Computer Science, The Czech Academy of Sciences, Prague, Czech Republic, [3] evocenta GmbH, Gelsenkirchen, Germany, [4] Pompeu Fabra University, Barcelona, Spain, [5] Institute for Biomedical Engineering and Informatics, Ilmenau University of Technology, Germany

We devised a simple and efficient computational framework to model spike propagation in axonal fibre bundles. We studied the influence of fibre parameters on transmission velocities and ephaptic coupling among fibres. For brain white matter bundles, we demonstrate that ephaptic coupling increases transmission velocity (Schmidt et al., 2021), while for peripheral nerves, a slowing and synchronisation of the spikes is observed (Schmidt & Knösche, 2022). We specify how these effects depend on fibre heterogeneity and density, bundle size, and initial strength and synchronisation of spike volleys.

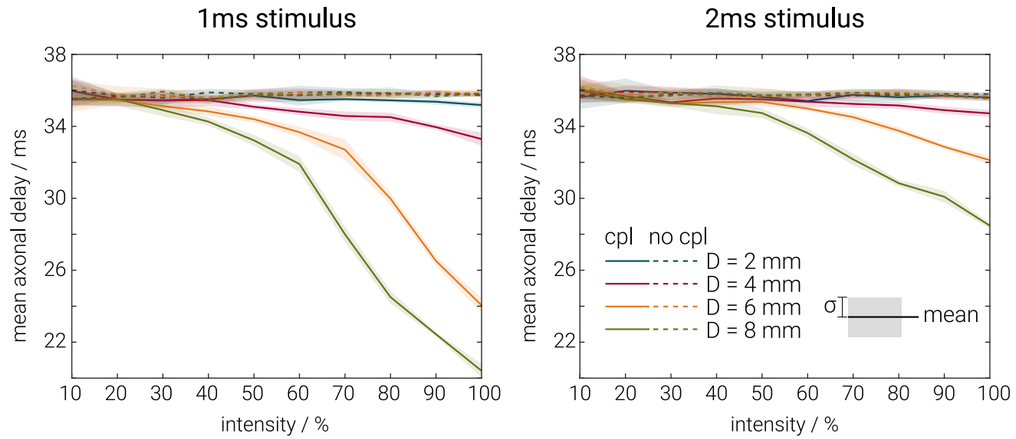

Figure 6.2.1 Mean axonal delay of a spike volley in a 10 cm long fibre bundle in the brain white matter. Intensity: percentage of axons carrying a spike. Stimulus duration (1 or 2 ms) determines the degree of synchronisation of spikes in the volley. Solid/dotted lines: with/without ephaptic coupling. Colours: diameter of fibre bundle. Adapted from Schmidt et al., 2021.

6.2.2 Next generation neural mass modelling

Gast, R.[1,2], Gong, R.[1,3], Meijer, H. G. E.[4], Schmidt, H.[1,5], & Knösche, T. R.[1,6]

[1] Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany, [2] Department of Neuroscience, Feinberg School of Medicine, Northwestern University, Chicago, IL, USA, [3] Emory Brain Health Center, Emory University, Atlanta, GA, USA, [4] Department of Applied Mathematics, Technical Medical Centre, University of Twente, Enschede, the Netherlands, [5] Institute of Computer Science, The Czech Academy of Sciences, Prague, Czech Republic, [6] Institute for Biomedical Engineering and Informatics, Ilmenau University of Technology, Germany

Neural mass models (NMMs) are simple yet biologically realistic models of the mean behaviour of neural populations. While previously heuristically derived, modern approaches allow for a rigorous derivation of NMMs from spiking neuron models (Coombes and Byrne, 2019). We (i) extended these modern approaches with short-term adaptation mechanisms (Gast et al., 2020, Gast et al., 2021a), and (ii) applied them to the study of neural synchronisation in the external pallidum under parkinsonian and control conditions (Gast et al., 2021b).

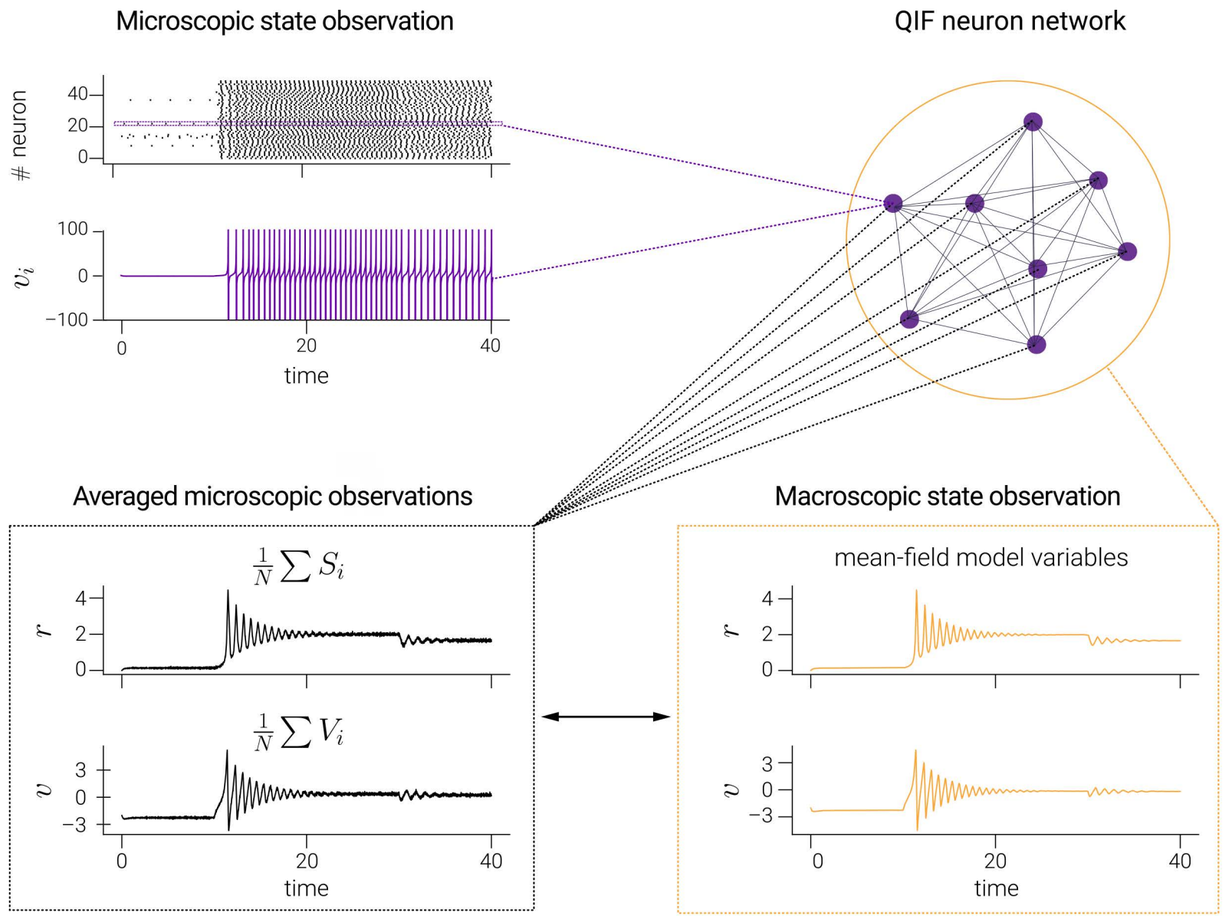

Figure 6.2.2 Mean field representation of a population of quadratic integrate-and-fire (QIF) neurons (top right), each represented by spiking (top left, upper panel) and membrane potential (top left, lower panel). The averaged microscopic states (firing rate r and membrane potential v) of the neurons (bottom left) are faithfully reproduced by the respective states of the NMM (bottom right). Adapted from Gast et al., 2020

6.2.3 Motor mapping with transcranial magnetic stimulation (TMS)

Weise, K.[1,2], Numssen, O.[3], Kalloch, B.[1], Zier, A.-L.[1,3], Thielscher, A.[4,5], Hartwigsen, G.[3], & Knösche, T. R.[1,6]

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We developed an effective strategy for the cortical mapping of TMS-induced physiological, behavioural, and brain effects. This approach is based on the voxel-wise correlation between the local TMS-induced electric field and the effect size over TMS pulses from varying coil positions/orientations and intensities. We applied this technique to locate hand muscle representations in primary motor cortex (Weise et al., 2020, Numssen et al., 2021). A detailed protocol together with a software toolbox was devised to allow easy and reliable application by other researchers (Weise et al., 2022).

Figure 6.2.3 Maps of normalised coefficient of determination (R^2 of linear regression between electric field and MEP amplitude) for different hand muscle representations (columns 1–3). Column 4 shows the hotspots in relation. The maps are scaled to maximum. Dotted line separates PMd (dorsal premotor cortex) and M1 (primary motor cortex) according to the atlas of Glasser et al., 2016. APB: musculus abductor pollicis brevis, FDI: first dorsal interosseous, ADM: musculus abductor digiti minimi. Adapted from Numssen et al., 2021.

6.2.4 The role of structural and functional long-range connectivity for processing complex syntactic structures

Wang, P.[1], Sanchez, S. M.[2], Schmidt, H.[1,3], Gallardo, G.[4], Anwander, A.[4], He, Y.[5], Yue, J.[6], Chen, L.[7], Brauer, J.[4,8], Friederici, A. D.[4], Maess, B.[1], & Knösche, T. R.[1,9]

[1] Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany, [2] Laureate Institute for Brain Research, Tulsa, OK, USA, [3] Institute of Computer Science, The Czech Academy of Sciences, Prague, Czech Republic, [4] Department of Neuropsychology, Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany, [5] Department of Psychiatry and Psychotherapy, Philipps University Marburg, Germany, [6] Laboratory for Cognitive and Social Neuroscience, Harbin Institute of Technology, China, [7] College of Chinese Language and Culture, Beijing Normal University, China, [8] Office of the Vice-President for Young Researchers and Diversity Management, Friedrich Schiller University, Jena, Germany, [9] Institute for Biomedical Engineering and Informatics, Ilmenau University of Technology, Germany

We used diffusion MRI and magnetoencephalography to study structural/functional connectivity in adult German native speakers in relation to their ability to process centre-embedded sentences and improve by training. To this end, we conducted a series of MR and MEG recordings: Starting and finishing with structural MR recording, including T1-, T2- and diffusion weighting, we invited all participants for four successive language training sessions with MEG recording within a single week. Structurally, we found multiple network motifs related to individual language performance as well as training success (Sanchez et al., 2022). Functionally, we found complexity-dependent training-induced changes in local synchronisation and long-range connectivity of Broca's area in the gamma (55–95 Hz) range (Wang et al., 2021). We also found a reduction of left temporal-parietal alpha (8–12 Hz) power that correlated with individual performance (Wang et al., 2022).

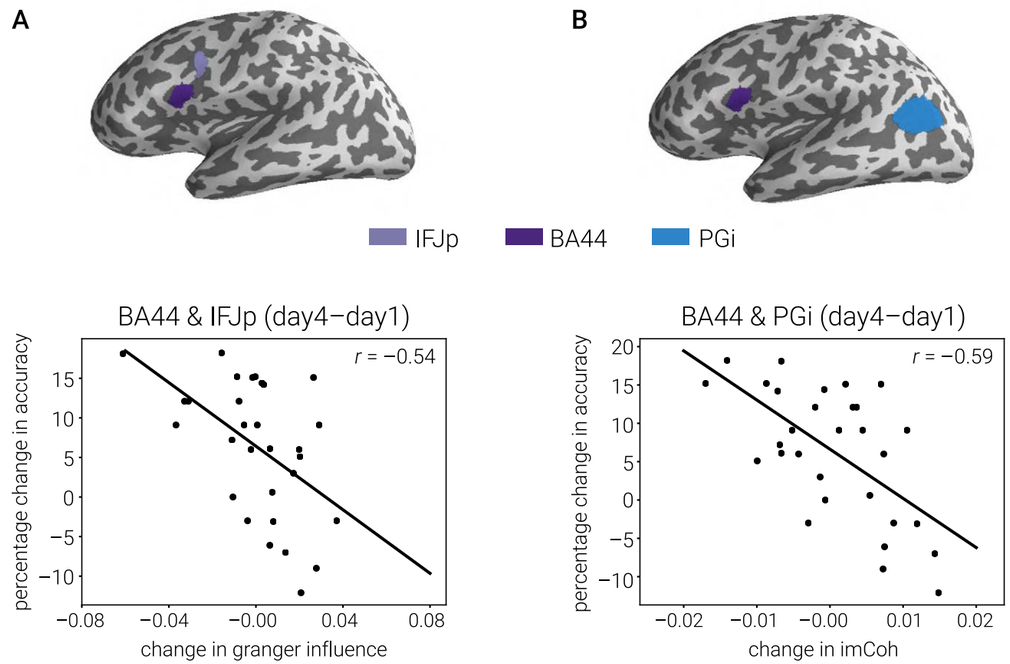

Figure 6.2.4 Correlation of training-induced changes (day 4 vs. day 1) of gamma range functional connectivity with individual performance changes in language task. Left: Granger influence between Broca's area (BA 44) and posterior inferior frontal junction (IPJp), indicating modulatory coupling of the gamma power. Right: Imaginary coherence (imCoh) between BA 44 and inferior parietal cortex (PGi) indicating tight phase coupling. Adapted from Wang et al., 2021.

6.2.5 Phase-amplitude coupling as a Parkinsonian biomarker

Gong, R.[1,2], Mühlberg, C.[2], Wegscheider, M.[2], Fricke, C.[2], Rumpf, J.-J.[2], Nikulin, V.[3], Gast, R.[1,4], Claßen, J.[5], & Knösche, T. R.[1,6]

[1] Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany, [2] Emory Brain Health Center, Emory University, Atlanta, GA, USA, [3] Neural Interactions and Dynamics Group, Department of Neurology, Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany, [4] Department of Neuroscience, Feinberg School of Medicine, Northwestern University, Chicago, IL, USA, [5] Clinic for Cognitive Neurology, Leipzig University Hospital, Germany, [6] Institute for Biomedical Engineering and Informatics, Ilmenau University of Technology, Germany

Abnormal beta-gamma phase-amplitude coupling (PAC) has been proposed as a biomarker of Parkinson's disease (PD). Yet, its relationship to motor impairment is unclear. Using EEG, we showed enhanced resting-state PAC in somato-motor cortex of PD patients (Gong et al., 2021). During movement, overall PAC enhancement in patients did not correlate with motor impairment, while a distinct PAC motif around movement onset was linked to performance. This highlights the role of dysfunctional evolution of neural dynamics during movement execution in the pathophysiology of PD bradykinesia (Gong et al., 2022).

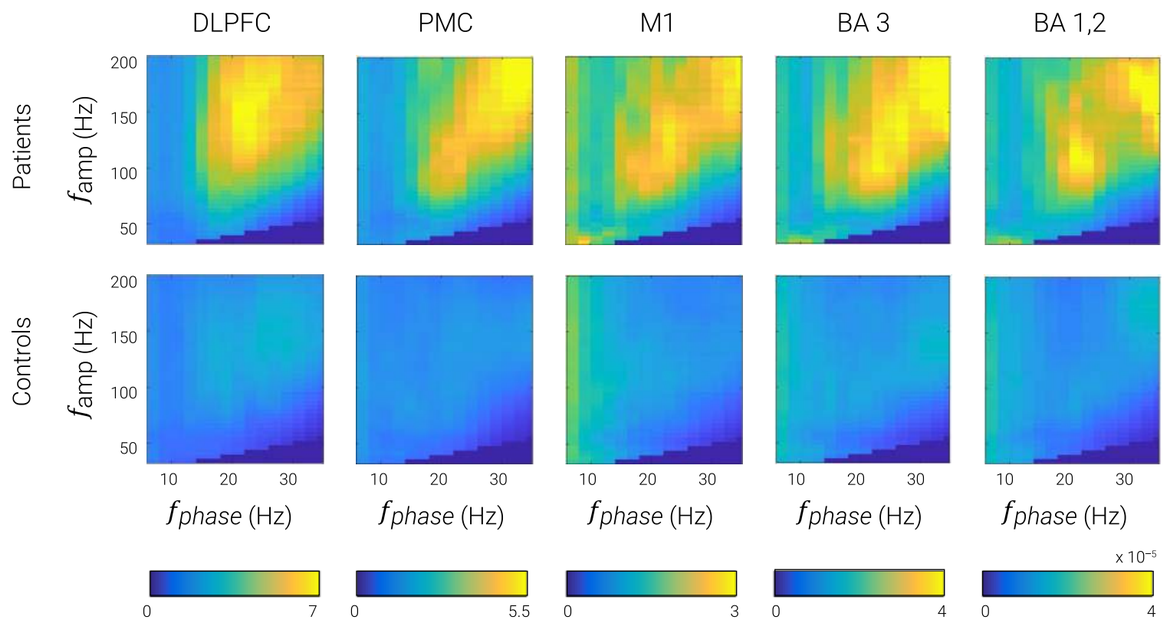

Figure 6.2.5 Phase-amplitude coupling in dorso-lateral prefrontal cortex (DLPFC), premotor cortex (PMC), primary motor cortex (M1), and Brodmann areas 1 and 2. The comodulograms show the median of the Kullback-Leibler modulation index (KL-MI) across subjects in patients and healthy controls. Adapted from Gong et al., 2021

6.2.6 Magnetic field compensation coil design for magnetoencephalography

Kutschka, H.[1,2,3], Doeller, C.[3,4,5], Haueisen, J.[2,6], & Maess, B.[1]

[1] Brain Networks Group, Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany, [2] Institute for Biomedical Engineering and Informatics, Ilmenau University of Technology, Germany, [3] Department of Psychology, Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany, [4] Kavli Institute for Systems Neuroscience, Centre for Neural Computation, The Egil and Pauline Braathen and Fred Kavli Centre for Cortical Microcircuits, Norwegian University of Science and Technology (NTNU), Trondheim, Norway, [5] Institute of Psychology, Leipzig University, Germany, [6] Hans-Berger Department of Neurology, University Hospital Jena, Germany

A set of eight coils is proposed to compensate for the remnant magnetic field within the shielding room. Each coil extends over five of the six faces of a 2x2x2 m³ cube. Each coil is designed to suppress one of the orthogonal magnetic field components of the zeroth and the first order. The effect of the walls of the shielding room, on the compensating fields, was considered during coil design using the concept of mirror sources reaching a precision of at least 0.1 %. Simulations show that this design will suppress the remnant field within a spherical target volume of 60 cm in diameter by three orders of magnitude (Kutschka et al., 2021).

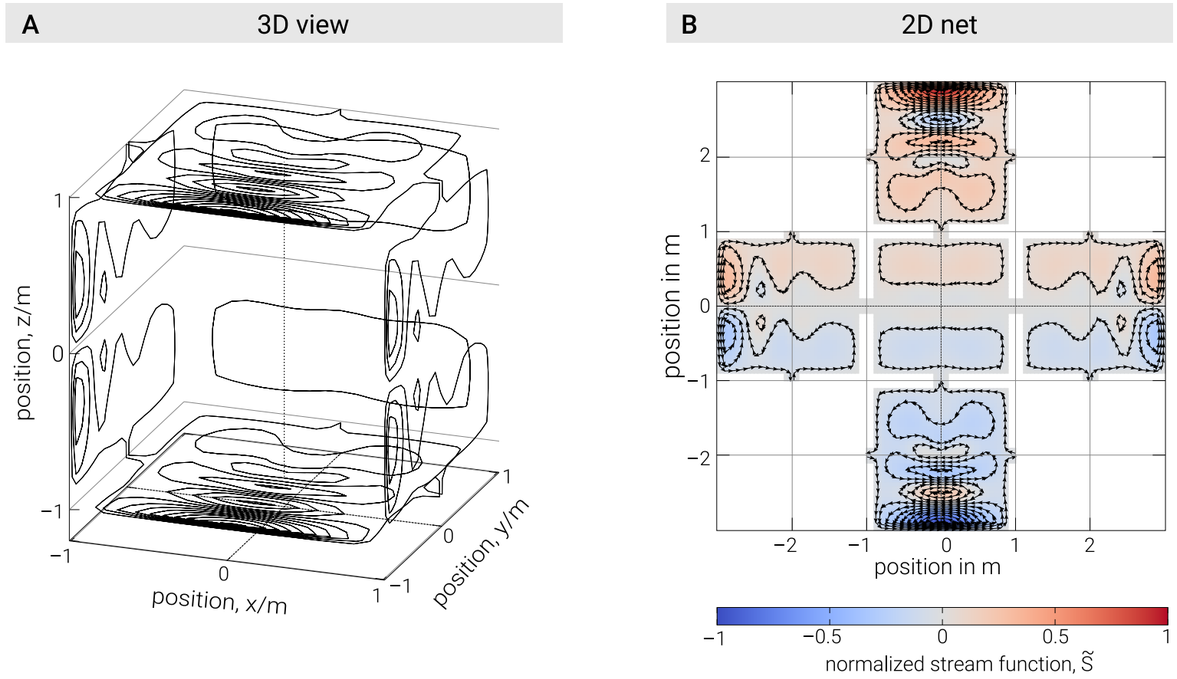

Figure 6.2.6 Wire paths of compensation coils. (A) 3D view of stream function contour lines of the vertical homogeneous field component. (B) 2D net representation of the same coil. Wire connections between stream function contours are not shown. Adapted from Kutschka et al., 2021.

6.2.7 A neural signature of regularity in sound is reduced in older adults

Herrmann, B.[1,2,3], Maess, B.[4], & Johnsrude, I. S.[5,6]

[1] Department of Psychology, Rotman Research Institute, Faculty of Arts & Science, University of Toronto, ON, Canada, [2] Rotman Research Institute, Baycrest, North York, ON, Canada, [3] Department of Psychology, University of Toronto, ON, Canada, [4] Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany, [5] School of Communication Sciences & Disorders, The University of Western Ontario, London, ON, Canada, [6] Department of Psychology & Brain and Mind Institute, The University of Western Ontario, London, ON, Canada

We investigated how age-related changes in hearing may lead to reduced performance in elderly compared to young humans. Younger and older adults listened to sequences of tones, which either contained a pattern (repeated sets) or not. Using magnetoencephalography, we showed that older adults had stronger neural responses to tone onsets and weaker responses to sound patterns in comparison to younger adults. Apparently, the sensitivity of neural populations in the auditory cortex fundamentally differs between younger and older adults (Herrmann et al., 2022).

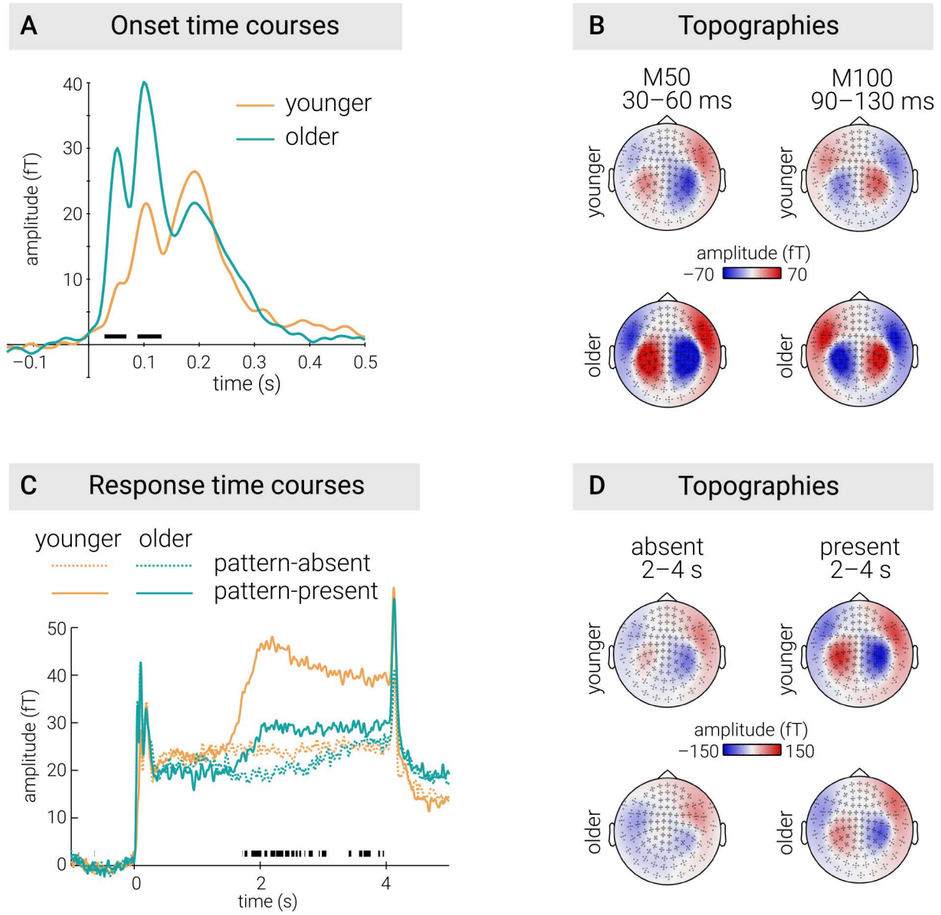

Figure 6.2.7 Top row: Evoked responses to sound onsets comparing older and younger adults. Field topographies were similar between groups, revealing that the source of activity was the same. Bottom row: Evoked responses to pattern showing the reverse effect – younger adults evoked the strongest response when patterns were present. Topographies were comparable between groups and to sound onset topographies – pointing to the same source. Adapted from Herrmann et al., 2022.

6.2.8 Task-related temporal fluctuations in auditory attention generate neural signatures that change with age

Herrmann, B.[1,2,3], Maess, B.[4], Henry, M.[5], Obleser, J.[6], & Johnsrude, I. S.[7,8]

[1] Department of Psychology, Rotman Research Institute, Faculty of Arts & Science, University of Toronto, ON, Canada, [2] Rotman Research Institute, Baycrest, North York, ON, Canada, [3] Department of Psychology, University of Toronto, ON, Canada, [4] Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany, [5] Max Planck Research Group Neural and Environmental Rhythms, Max Planck Institute for Empirical Aesthetics, Frankfurt/Main, Germany, [6] Department of Psychology, University of Lübeck, Germany, [7] School of Communication Sciences & Disorders, The University of Western Ontario, London, ON, Canada, [8] Department of Psychology & Brain and Mind Institute, The University of Western Ontario, London, ON, Canada

Electro- and magnetoencephalography were recorded from younger and older adults of both genders. Analysis focused on attention regulation as monitored by alpha oscillatory activity. We showed that alpha activity indicates when in time attention is deployed and that deployment varies with listening difficulty. Both age groups show attention regulation, while the recruited brain regions differ between groups. In younger adults, the superior parietal cortex is more involved, whereas in older adults the superior temporal cortex is more strongly activated during the task performance, but not during rest (Herrmann et al., 2022).

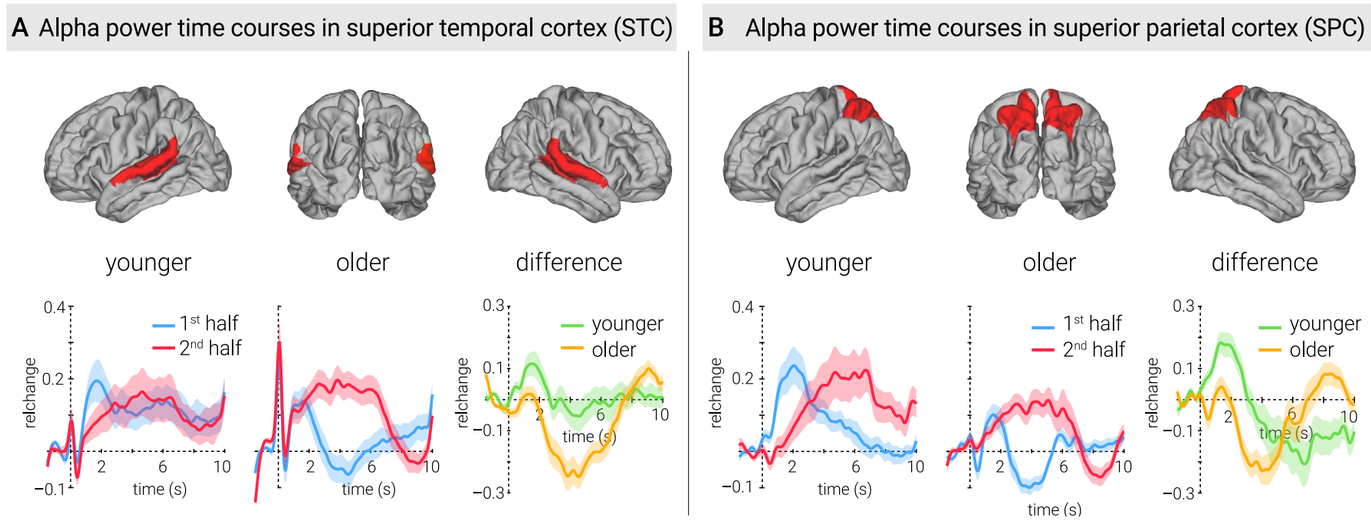

Figure 6.2.8 Alpha power time courses for two regions of interest, both age groups, and first/second halves of the experiment. Adapted from Herrmann et al., 2022.

6.2.9 Sensitivity and uncertainty analysis with generalised polynomial chaos

Weise, K.[1,2], Müller, E.[2], Poßner, L.[3], Gast, R.[1,4], & Knösche, T. R.[1,5]

[1] Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany, [2] Advanced Electromagnetics Group, Ilmenau University of Technology, Germany, [3] Institute for Electronics and Biomedical Information Technology, Leipzig University of Applied Sciences, Germany, [4] Department of Neuroscience, Feinberg School of Medicine, Northwestern University, Chicago, IL, USA, [5] Institute for Biomedical Engineering and Informatics, Ilmenau University of Technology, Germany

We developed a novel Python package for nonintrusive generalised polynomial chaos, which can be used for uncertainty and sensitivity analysis of complex models (Weise et al., 2020). We examined the state-of-the-art sampling schemes, categorised in space-filling-optimal designs such as Latin Hypercube sampling and L1-optimal sampling, and compared their empirical performance in various test and application examples against standard random sampling (Weise et al., 2022).

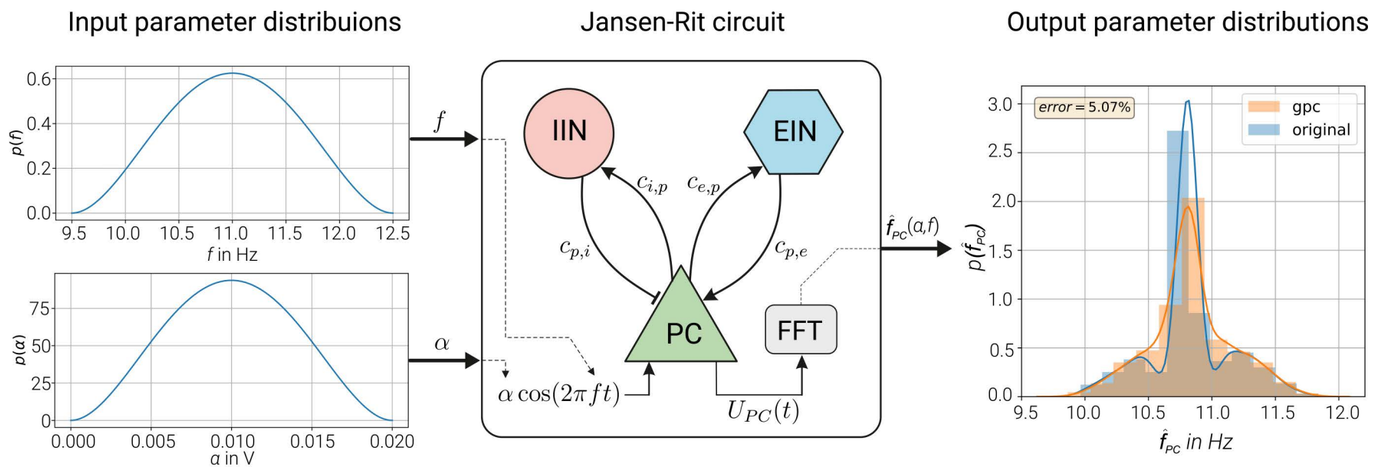

Figure 6.2.9 Example of gPC analysis of the input-output behaviour of a Jansen-Rit type neural mass model of a local cortical microcircuit. On the left the input distributions of input frequency and amplitude are seen, on the right the resulting distribution of the dominant frequency of the output, computed by simulation of the original model (blue) and the gPC (orange). Adapted from Weise et al., 2020.

Congresses, Workshops, and Symposia

2020

- Knösche, T. R., & Maess, B. (January). *Brain Networks Retreat 2020*. Retreat. Bad Kösen, Germany.
- Haueisen, J., & Knösche, T. R. (August). *9th International Summer School in Biomedical Engineering*. Erfurt, Germany.
- Schmidt, H. (August). *Multiple Scales in Mathematical Neuroscience.* Minisymposia. Dynamics Days Digital 2020. Virtual.

2021

- Pliquett, U. & Knösche, T. R. (May). *13th International Conference on Bioelectromagnetism (ICBEM)*. Virtual.
- Schmidt, H., Gast, R., & Knösche, T. R. (May). *Mean-Field Models of Spiking Neural Networks with Spike Frequency Adaptation and Synaptic Plasticity*. Workshop. SIAM Conference on Applications of Dynamical Systems (DS21). Virtual.
- Schmidt, H. & Gast, R. (August). *Recent Advances in Mean-Field Modelling of Brain Dynamics*. Minisymposia. Dynamics Days–XL, Nice, France.
- Knösche, T. R. (September). *Targeting and Readout in Non-Invasive Brain Stimulation – Motor Cortex and Beyond*. Symposium. 20th World Congress of Psychophysiology (IOP). Virtual.

2022

- Knösche, T. R. (June). *Modeling the Building Blocks of Cognition with Neural Masses*. Workshop. 11th IMPRS NeuroCom Summer School in Cognitive Neuroscience. International Max Planck Research School on Neuroscience of Communication: Function, Structure, and Plasticity (IMPRS NeuroCom), Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany.
- Knösche, T. R. (July). *White Matter, Axons, and the Role of Delays – Modeling Axonal Transmission*. Workshop. 31st Annual Computational Neuroscience Meeting (CNS*2022), Melbourne, Australia.
- Weise, K. (August). *Brain and Human Body Modeling Conference*. Conference. Hybrid format, Athinoula A. Martinos Center for Biomedical Imaging at Massachusetts General Hospital, Boston, USA.
- Haueisen, J. & Knösche, T. R. (September). *EEG/MEG Source Reconstruction*. Educational Course. 32nd International Congress of Clinical Neurophysiology (ICCN), Geneva, Switzerland.

Appointments

2022

- Knösche, T. R. *Faculty member of the International Max Planck Research School on Cognitive NeuroImaging (IMPRS CoNI)*, Max Planck Institute for Cognitive and Brain Sciences, Leipzig, Germany.
- Maess, B. *Faculty member of the International Max Planck Research School on Cognitive NeuroImaging (IMPRS CoNI)*, Max Planck Institute for Cognitive and Brain Sciences, Leipzig, Germany.

Degrees

PhD Theses

2020

- Chien, V. S. C. *Brain network dynamics in deviance response and auditory perception*. Technical University of Ilmenau, Germany.

2021

- Gast, R. *Phase transitions between asynchronous and synchronous neural dynamics: Theoretical insight into the mechanisms behind neural oscillations in Parkinson's disease*. Leipzig University, Germany.

2022

- Bialas, O. *An electroencephalographic investigation of the encoding of sound source elevation in the human cortex*. Leipzig University, Germany.
- Gong, R. *β-γ phase-amplitude coupling derived from non-invasive electroencephalogram: Insight into the pathophysiology of Parkinson's disease.* Leipzig University, Germany.

Publications

Books & Book Chapters

Knösche, T. R., & Haueisen, J. (2022). *EEG/MEG source reconstruction: Textbook for electro-and magnetoencephalography*. Cham: Springer.

Journal Articles

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Index of Published Figures

Figure 6.2.1

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Figure 6.2.2

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Figure 6.2.3

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Figure 6.2.4

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Figure 6.2.5

Adapted from Gong, R., Wegscheider, M., Mühlberg, C., Gast, R., Fricke, C., Rumpf, J.-J., et al. (2021). Spatiotemporal features of β-γ phase-amplitude coupling in Parkinson's disease derived from scalp EEG. *Brain, 144*(2), 487-503. doi:10.1093/brain/awaa400.

Figure 6.2.6

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Figure 6.2.7

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Adapted from Herrmann, B., Maess, B., Henry, M. J., Obleser, J., & Johnsrude, I. S. (2022). Neural signatures of task-related fluctuations in auditory attention change with age. *bioRxiv.* doi:10.1101/2022.04.12.487991.

Figure 6.2.9

Adapted from Weise, K., Poßner, L., Müller, E., Gast, R., & Knösche, T. R. (2020). Pygpc: A sensitivity and uncertainty analysis toolbox for Python. *SoftwareX, 11*: 100450. doi:10.1016/j.softx.2020.100450.

6.3

Dr Nico Scherf

Neural Data Science and Statistical Computing

Understanding how thought emerges from matter is one of the most exciting questions about our universe. How can a network of cells map, navigate, and understand its surroundings? What fundamental structures and dynamics give rise to a neural system's cognitive functions?

Experimental methods such as high-resolution structural and functional magnetic resonance imaging, spectroscopy, microscopy, or single-cell sequencing give us unique views into the brain's structures and processes. To validate our understanding of the underlying computational principles, we also study neural network models *in silico*. Ultimately, we will need to integrate these complementary perspectives to understand how neural systems work, and, how they fail.

Analysing such complex systems is challenging, as we have to explore, quantify, and interpret high-dimensional data with intricate dependencies. Our group develops tools that help uncover the underlying patterns. Our mission is to support data-driven neuroscience research across scales and modalities, covering everything from designing experiments to analysing and visualising the data. One of our goals is to foster collaboration and knowledge exchange. We contribute via consulting, workshops, and regular meetings.

In our collaborative, methods-oriented research, we pursue a neuroscience-inspired approach to data science (Figure 6.3). On one hand, we use artificial intelligence (AI) to build tools that help us make sense of patterns in neural data. On the other hand, we use AI agents as virtual model organisms to study fundamental principles of representation learning and to validate analytical methods. We focus on the geometrical and topological aspects of neural data to help us reveal their underlying structures. We want to contribute conceptual and computational tools to map, explore, and understand neural systems that help us improve cognitive science, AI, and clinical practice in complementary areas:

- Analysis: Mapping brain structure and function and cognitive processes across scales in health and disease, e.g. see (Mueller et al., 2020) and 6.3.1,
- Exploration: Visualising the geometry and structure of neural systems and their internal representations of information, e.g. (Waschke et al., 2021, ↗),
- Synthesis: Modelling neural structures and their development, the emerging neural representations, and the cognitive processing that operate on this substrate, e.g. (Zoraghi et al., 2021).

With funding from the BMBF, we recently established an AI research group on artificial cognitive neuroimaging, starting in 09/2022 (see 6.3.2). Since 06/2022, we have been a part of the Center for Scalable Data Analytics and Artificial Intelligence (ScaDS.AI) Dresden/Leipzig ↗, together with Nikolaus Weiskopf (Department of Neurophysics) and Christian F. Doeller (Department of Psychology) (see 6.3.3).

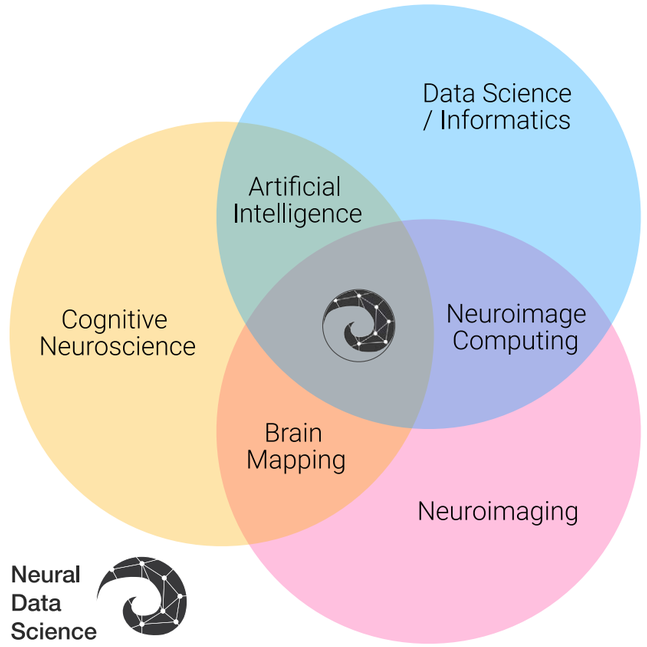

Figure 6.3 We focus our research on Neural Data Science at the interface between informatics, cognitive neuroscience, and neuroimaging.

6.3.1 Differential effects of levodopa and DBS on brain connectivity in Parkinson's disease

Mueller, K.[1], Kiakou, D.[1,2], Jech, R.[2], Holiga, S.[1], Schroeter, M. L.[1,3], & Möller, H. E.[1]

[1] Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany, [2] Department of Neurology and Center of Clinical Neuroscience, First Faculty of Medicine, Charles University and General University Hospital in Prague, Czech Republic, [3] Clinic for Cognitive Neurology, Leipzig University Hospital, Germany

In an ongoing collaboration with Robert Jech at Charles University in Prague, we study the neural correlates of medical intervention in patients with Parkinson's Disease (PD). Our future goal is to enable personalised medicine using the patient's data to refine the medical treatment. In particular, using functional MRI, we study brain activity alterations with levodopa treatment (L-DOPA) and deep brain stimulation of the subthalamic nucleus (STN DBS). Previously we found that L-DOPA treatment altered brain activity in the left and right putamen during a simple motor task (see Figure 6.3.1) (Mueller et al., 2020). In a related project we investigated treatment effects on brain connectivity with graph-based analysis of task-free functional MRI. Comparing brain connectivity between L-DOPA treatment and STN DBS, we observed a consistent connectivity increase with STN DBS between the primary motor cortex and other brain regions, particularly the thalamus and cerebellar regions (Mueller et al., 2018). Note that we have also investigated the effects on brain connectivity separately for L-DOPA treatment and STN DBS: Here, we found a major connectivity increase with levodopa in cerebellar brain regions (Jech et al., 2013) and a connectivity increase in the motor cortex with STN DBS (Mueller, Jech, & Schroeter, 2013). We are currently extending these lines of work with a much larger cohort of 94 PD patients treated with STN DBS to identify brain connectivity patterns that predict a patient's treatment state in terms of disease severity.

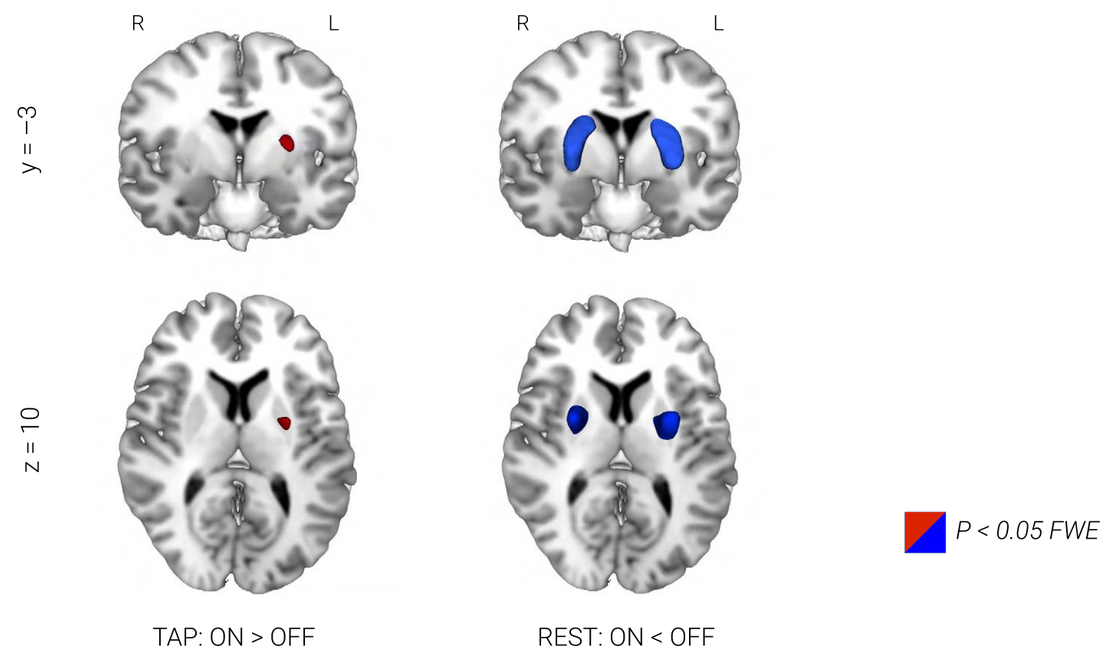

Figure 6.3.1 Brain activity change with L-DOPA treatment during finger tapping (TAP) and rest (REST) within a cohort of 32 patients with Parkinson's disease. Using an experimental design with consecutive blocks of finger tapping and rest in both treatment states with (ON) and without (OFF) L-DOPA medication, we observed a differential pattern of brain activity change in the putamen. During TAP phases, increased brain activity with L-DOPA medication (left column, colour-coded in red). During REST, putamen activity was decreased with L-DOPA (right column, colour coded in blue). See Mueller et al., 2020 for details.

6.3.2 Artificial Cognitive Neuroimaging – ACONITE

Milosevic, N.[1], Torbati, N.[1], Hofmann, S.[1], Niehaus, S.[1], & Scherf, N.[1]

[1] Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany

The goal of the research group is to establish neuroscientific methods and concepts of representation learning in AI to improve our tools for training and understanding deep neural networks. We are particularly interested in the geometric and topological properties of "cognitive maps" that arise in such networks. To this end, we want to establish AI systems as virtual model organisms on which we can systematically compare, validate, and improve models and analysis methods. Furthermore, focusing on the structure and emergence of neural representations will allow us to design more efficient, interpretable, and secure deep learning methods for applications with sparsely annotated data and for applications in which we need to understand or explain how the networks work.
Our methodological focus is on three areas: (i) the development and use of neuroscientific methods of cognitive map analysis for better interpretability in AI models, (ii) the use of AI agents as virtual model systems to explore general principles of the emergence of cognitive maps from interaction with the environment, and (iii) the application of these insights in the development of more efficient, secure, and interpretable methods in the analysis of multidimensional data (e.g., videos, volumetric or 4D imaging).

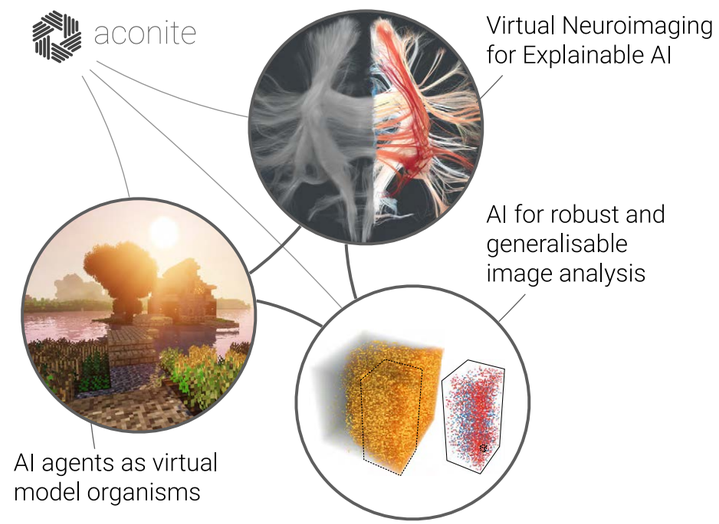

Figure 6.3.2 Within the ACONITE project, we will focus on three main projects: (i) using conceptual and analytical tools from cognitive neuroimaging to study and explain AI systems, (ii) using AI agents as virtual model organisms, and (iii) translating our insights to improve AI-based image analysis.

6.3.3 ScaDS.AI

Beylier, C.[1,2], Beltran-Velandia, F.[1,2], Singla, K.[1,2], Weiskopf, N.[1], Doeller, C. F.[1], & Scherf, N.[1]

[1] Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany, [2] Center for Scalable Data Analytics and Artificial Intelligence ScaDS.AI Dresden/ Leipzig, Germany

Since the beginning of AI research, neuroscience has been one of the most important and heavily debated influences in designing models and concepts. As part of the Center for Scalable Data Analytics and Artificial Intelligence Dresden/ Leipzig, we want to establish and develop the topic of neuroscience-inspired AI. Our research (in collaboration with Christian F. Doeller and Nikolaus Weiskopf) explores two directions: (i) connecting deep neural networks and cognitive neuroscience models and (ii) using deep neural networks as tools to analyse cognitive neuroimaging data.

(i) Neuroscience-inspired AI: Unravelling Neural Geometry and Representation Learning in Humans and Machines. We will use deep neural networks as models and discovery tools in various cognitive neuroscience fields (such as learning, memory, navigation, decision-making, vision, and knowledge acquisition). As a starting point, we will establish Deep Reinforcement Learning systems as a model to study the emerging neural representations with varying environments and task settings and test our findings in concurrent neuroimaging studies. Finally, we will translate the conceptual findings and computational tools into practical AI applications and contribute to improved interpretability of neural networks and label-efficient multi-modal learning.

(ii) AI for deep functional neuroanatomy: Analysing large-scale ND neuroimaging data to understand the brain as a complex system. One of our primary goals is to quantify plasticity in the brain from large-scale imaging data by focusing on AI methods that can quantify changes in structure and function. Our data is at least 4D or 5D (fMRI 3D + t (+ samples), MPM MRI 3D + channels (+ time or + samples), 3D light-sheet microscopy (+ time or + samples)). At the same time, we have comparably few labelled data points. Furthermore, the patterns of interest in neuroimaging often intrinsically live on manifolds (such as cortical layers or surfaces) or networks (functional and structural connectivity between brain regions). In this project, we will focus on developing and applying self-supervised Deep Learning to process and quantify multi-modal, multi-dimensional neuroimaging data and on geometric deep learning for mapping the structural and functional patterns across the human brain.

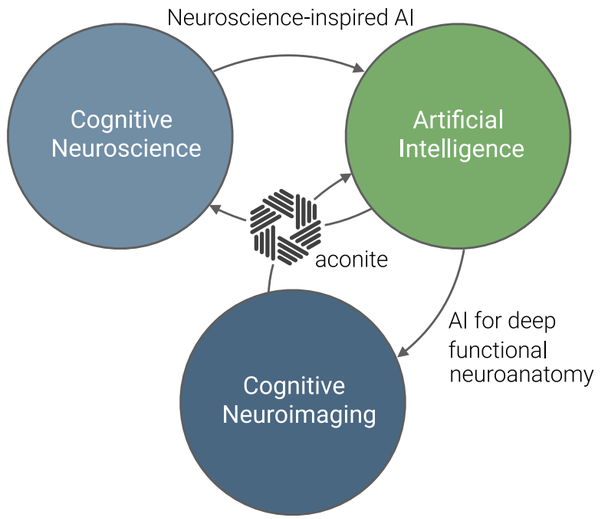

Figure 6.3.3 Our research within ScaDS.AI, at the interface between neuroscience and AI, focuses on two main topics: (i) deep neural networks as computational models in cognitive neuroscience and (ii) deep neural networks as tools for analysis and discovery in cognitive neuroscience. The ACONITE project (6.3.2) will complement this research by using cognitive neuroscience and neuroimaging insights to improve AI systems.

Congresses, Workshops, and Symposia

2021

- Scherf, N., & Bazin, P. (November). *Nighres Tutorial and Mini-Brainhack.* Workshop. Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany.

2022

- Scherf, N. (June). *A gentle introduction to Deep Learning.* Workshop. 11th IMPRS NeuroCom Summer School in Cognitive Neuroscience. International Max Planck Research School on Neuroscience of Communication: Function, Structure, and Pasticity (IMPRS NeuroCom), Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany.
- Scherf, N. (July). *8th International Summer School on AI and Big Data – AI in Medicine/Life Science session.* Center for Scalable Data Analytics and Artificial Intelligence (ScaDS.AI), Leipzig, Germany, Co-organiser.
- Scherf, N., & Krieghoff, V. (August). *Introduction to (G)LMMs*. Workshop. Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany, Co-organiser.

Appointments

2020

- Scherf, N. *Faculty member of the International Max Planck Research School on Neuroscience of Communication: Function, Structure, and Plasticity (IMPRS NeuroCom)*, Max Planck Institute for Cognitive and Brain Sciences, Leipzig, Germany.

2021

- Scherf, N. *Group leader position,* Max Planck Institute for Human Cognitve and Brain Sciences, Leipzig, Germany.

2022

- Scherf, N. *Faculty member of the International Max Planck Research School on Cognitive NeuroImaging (IMPRS CoNI)*, Max Planck Institute for Cognitive and Brain Sciences, Leipzig, Germany.

Publications

Note: This list also includes publications of members of the research team of the Methods and Development Group Neural Data Science and Statistical Computing that were published prior to their arrival. These articles are included as they are highly relevant to our research topics and speak to the unique qualifications of the team members.

Books & Book Chapters

Jech, R., & Mueller, K. (2022). Investigating network effects of DBS with fMRI. In A. Horn (Ed.), *Connectomic Deep Brain Stimulation* (pp. 275–301). Academic Press. https://doi.org/10.1016/B978-0-12-821861-7.00026-9

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Index of Published Figures

Figure 6.3.1

Modified from Mueller, K., Urgošík, D., Ballarini, T., Holiga, Š., Möller, H. E., Růžička, F., Roth, J., Vymazal, J., Schroeter, M. L., Růžička, E., & Jech, R. (2020). Differential effects of deep brain stimulation and levodopa on brain activity in Parkinson's disease. *Brain Communications, 2*(1), fcaa005. https://doi.org/10.1093/braincomms/fcaa005

Figure 6.3.2

Modified from Project sketch. Submitted to DLR PT: Deutsches Zentrum für Luft- und Raumfahrt e. V. (DLR)

6.4

Dr Davide Chiarugi

Computing and Databases Services

Workflow Management Systems for the Cloud-HPC Continuum

The research activity of the IT & Database group regards mainly the design and implementation of methods and software to support data processing and analysis workflows that can run on hybrid Local-Cloud-HPC environments. In this way, data-intensive computations can be executed seamlessly in a Cloud-HPC Continuum context thus optimizing the usage of the available resources and, in fact, reducing the time and overall computational power requested.

In fact, the demand of computational power for data processing and analysis has increased massively in the last few years mainly due to extensive usage of Machine Learning /Artificial Intelligence approaches in different domains (e.g. image analysis) that needs to be trained with a considerable quantity of data. More in general, the typical scenario of data-intensive scientific studies includes data processing and analysis workflows that are composed by a complex series of interdependent steps. Workflow Management Systems (WMS) are therefore necessary to manage and automatise the data dependencies, the scheduling in the execution environment, and other aspects of the workflow such as, e.g., fault tolerance.

A very useful feature of many WMS is their portability with respect to the different computational environments so that the same workflow (as a whole) can be executed in a local, smaller environment, on a powerful HPC, or on a cloud-based system such as AWS. It is worth noticing, though, that data analysis workflows are generally composed by heterogeneous steps, each requiring a different environment for the optimal execution. In some cases, only a few steps require extensive computational power while others can be executed on a less powerful machine. The cost of accessing HPC resources, which will not be used to the maximum for the entire workflow execution, may not be advantageous compared to a more prolonged execution in cloud environments. In specific cases, therefore, it might be better to use an HPC

environment rather than a cloud, and vice versa. However, the optimal solution would be to combine the two executions by matching the environment suitable to the hardware needs of each single workflow step.

Devising a WMS that could handle the workflow execution on two (or more) different environments is an extremely difficult task due to the heterogeneity of the computational systems. The literature indeed reports only on a few WMS embedding this feature.

One of the most promising WMS platforms aiming at the seamless integration of different computational environments is represented by StreamFlow (Figure 6.4.1 and Figure 6.4.2), a novel WMS explicitly designed by the Alpha Research Group at the University of Turin that implements effectively the hybrid workflow paradigm. The IT & Database Group is cooperating with the Alpha group to optimize the specification of StreamFlow and to build specific analysis workflows to support the effective usage of the available computational resources, especially for tasks of interest for our Institute such as (ML-driven) image analysis and pattern recognition.

A significant part of this cooperation is occurring in the context of the European High Performance Computing Joint Undertaking (EuroHPC JU), a joint initiative between the EU European countries and private partners to develop a World Class Supercomputing Ecosystem in Europe.

Deploy anything

Manage complex multi-agent environments, ensuring co-scheduling and orchestration of heterogeneous applications

Reuse your code

Leverage containers to run the same code on different architectures, ensuring portability and numerical stability to your application

Run anywhere

Seamlessly bind each step of your workflow to the best suitable architecture, without worrying about shared data volumes

Figure 6.4.1 Main features of StreamFlow

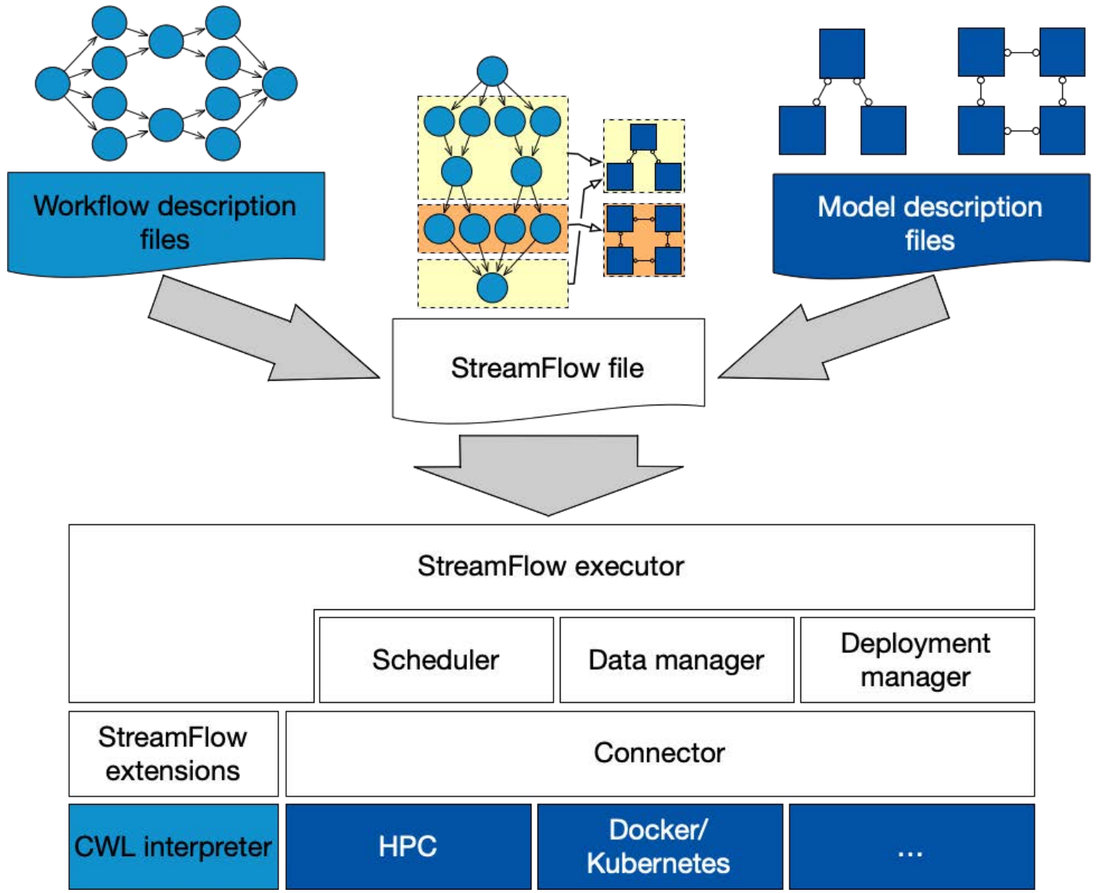

Figure 6.4.2 StreamFlow framework's logical stack

Publications

Note: This list also includes publications of members of the research team of the Methods and Development Group Computing and Databases Services that were published prior to their arrival. These articles are included as they are highly relevant to our research topics and speak to the unique qualifications of the team members.

Journal Articles

Alvarez-Guaita, A., Patel, S., Lim, K., Haider, A., Dong, L., Conway, O. J., Ma, M. K. L., Chiarugi, D., Saudek, V., O'Rahilly, S., & Savage, D. B. (2021). Phenotypic characterization of Adig null mice suggests roles for adipogenin in the regulation of fat mass accrual and leptin secretion. *Cell Reports*, *34*(10). https://doi.org/10.1016/j.celrep.2021.108810

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D'Amore, S., Sano, H., Chappell, D. D. G., Chiarugi, D., Baker, O., Page, K., Ramaswami, U., Johannesdottir, F., Cox, T. M., Deegan, P., Poole, K. E., Cox, T. M., Platt, F. M., Banka, S., Chakrapani, A., Deegan, P. B., Geberhiwot, T., Hughes, D. A., Jones, S., Lachmann, R. H., Santra, S., Sharma, R., & Vellodi, A. (2022). Radiographic cortical thickness index predicts fragility fracture in Gaucher disease. *Radiology.* https://doi.org/10.1148/radiol.212779

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7.1

Professor Dr Julia Sacher

Minerva Research Group EGG (Emotions & neuroimaGinG) Lab

This former Minerva Research Group has successfully transitioned into the Cognitive Neuroendocrinology Group, bridging the MPI CBS, the Department of Endocrinology, the Department of Nuclear Medicine and the Clinic for Cognitive Neurology. By obtaining 1.2 million EUR from the MPG for the Brain HATCH (Human Cognition Hormones) Project during a competitive internal and external review process, we aim to map the human brain during hormonal transition periods.

Brain HATCH (Human **C**ognition **H**ormones**) Project**

Mapping the human brain during hormonal transitions

Sex steroid hormones are powerful modulators of the human brain in development. The effects of reproductive hormone change on brain structure and cognitive function throughout the adult life-span lifespan, however, remain poorly understood for two main reasons: first, current knowledge on the plastic nature of the brain predominantly focuses on early development. Whereas examples for neuroplasticity beyond infancy have existed for some time, a better understanding of the different regulators that modulate and underlie neural plasticity during adulthood has only emerged recently. Second, we are still lacking a mechanistic understanding of specific neurochemical targets of sex-steroid action in the human brain. Addressing this gap requires the integration of different quantitative in-vivo neuroimaging techniques. Such interdisciplinary methods have recently become available, e.g. with the development of novel PET-compounds for neuroinflammatory biomarkers and the possibility for synthesis and application of such compounds in the joint MR-PET hybrid scanner in collaboration of the MPI CBS with the University Clinic of Leipzig. We need a systematic integration of hormonal profiles, behavioural, inflammatory, metabolic and multimodal neuroimaging measures, as well as longitudinal data-acquisition and hormonal challenge/depletion paradigms to go beyond correlational findings. Here, we present a collaborative approach implementing techniques from the fields of cognitive neuroscience, endocrinology,

neurophysics and molecular neuroimaging to address this gap and (1) **discover the basic scientific mechanisms underlying risk for accelerated cognitive aging**, and (2) **identify potential tipping points for timely intervention.**

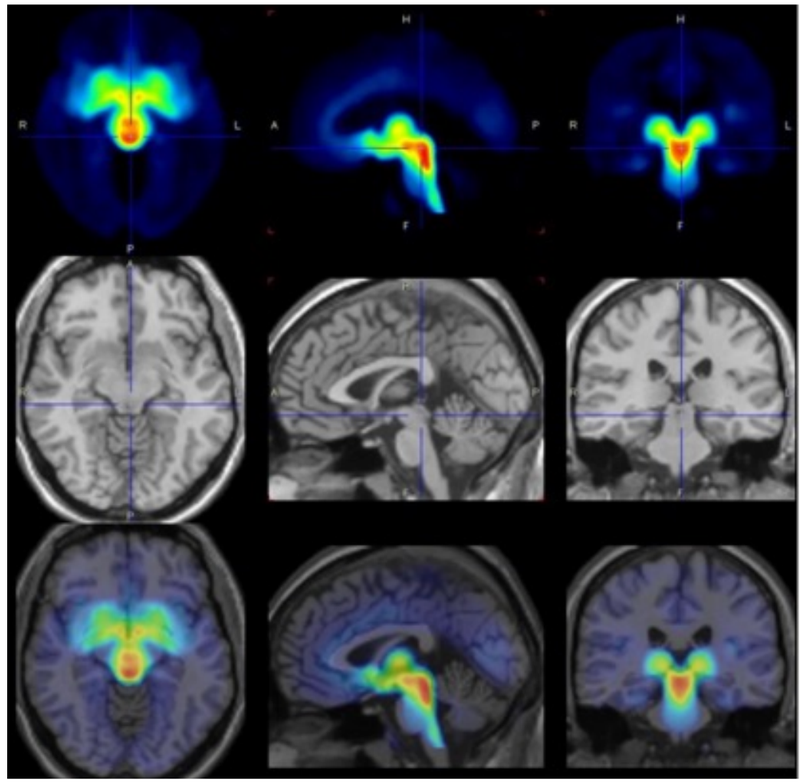

Figure 7.1 **Molecular neuroimaging of serotonin transporter binding.** Serotonin transporter (5-HTT) expression patterns by radiotracer 11C-DASB binding obtained by dynamic positron emission tomography (PET) in living human brain across the menstrual cycle in coronal, sagittal and axial view (top panel) and structural Magnetic Resonance Imaging (MRI) scan in same individual (core panel) are displayed in overlay (bottom panel). We are the first to use this quantitative in-vivo method in a longitudinal design in patients and healthy women across the menstrual cycle.

Appointments

2022

- Sacher, J. *W2 Professorship.* Professor for Cognitive Neuroendocrinology, Leipzig University Hospital, Germany.
- Sacher, J. *Faculty member of the International Max Planck Research School on Cognitive NeuroImaging (IMPRS CoNI)*, Max Planck Institute for Cognitive and Brain Sciences, Leipzig, Germany.

Degrees

PhD Theses

2022

- Molloy, E. Behavioral, functional, and neurophysiological response to one week administration of escitalopram. Leipzig University, Germany.
- Zsido, R.G. *Ovarian hormones shape brain structure, function, and chemistry: A neuropsychiatric framework for female brain health (submitted)*, Leipzig University, Germany.

MD Theses

2022

- Heinrich, M. *Oestradiol moderates the association of visceral fat on brain structure and cognitive function in woman.* Leipzig University, Germany.

Publications

Books & Book Chapters

Zsido, R., & Sacher, J. (2021). Time to rethink the default settings in neuroscience: Hormonal transition periods as natural experiments and why sex matters. In U. Weber (Ed.), *Fundamental questions: Gender dimensions in Max Planck research projects* (pp. 27–42). Baden-Baden: Nomos. https://doi.org/10.5771/9783748924869-27

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Wikman, A., Sacher, J., Bixo, M., Hirschberg, A. L., Kopp Kallner, H., Epperson, C. N., Comasco, E., & Sundström Poromaa, I. (2022). Prevalence and correlates of current suicidal ideation in women with premenstrual dysphoric disorder. *BMC Women's Health*, *22*(1). https://doi.org/10.1186/s12905-022-01612-5

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7.2

Professor Dr Veronika Engert

Max Planck Research Group Social Stress and Family Health

The World Health Organization claims that stress is one of the major health risks of the 21st century, and indeed, every second sick call is due to stress. It is specifically the human tendency to mount a stress response for psychosocial reasons that leads to chronic stress exposure, and eventually, stress-related disease in modern societies. In the Social Stress and Family Health Research Group, we investigate stress and its health sequelae in the social context.

A central research topic concerns the transmission of stress, both emotionally and physically, from one individual to another. After showing that such “stress resonance” is stronger in both emotionally and spatially close relationships among adults, we currently study the phenomenon in parent-child dyads. With the integral importance of the parent-child bond for child health, behaviour, well-being, and development, and high rates of chronic stress in families, we suggest that stress resonance in the family system has implications for children’s daily life outcomes.

Another research topic of the group concerns factors that can protect the individual from the adverse effects of stress. This line of research focuses, for example, on inter-individual differences in resilience and related constructs. Recent work in this context examined whether resilience and the Big Five personality traits predict the emotional and cortisol stress response in the early months of the Covid-19 pandemic (7.2.1).

Reduced vulnerability to stressful experiences can also be achieved by means of mental training interventions. Here, we studied the efficacy of techniques targeting social abilities, such as empathy, compassion, and theory of mind, in buffering the chronic, everyday stress load (7.2.2). Another study then explored whether stress reduction, as a consequence of mental training, is mediated by changes in levels of the neuropeptide and social hormone oxytocin (7.2.3).

Data in our group are collected using advanced methods of social neuroscience, including functional magnetic resonance imaging and functional near-infrared spectroscopy. These data are combined with peripheral physiological biomarkers such as cortisol, pro-inflammatory cytokines, and cardiovascular activity, as well as with self-report questionnaires, and semi-structured narrative interviews.

7.2.1 Resilience and personality as predictors of the biological stress load during the first wave of the Covid-19 pandemic in Germany

Engert, V.[1,2], Blasberg, J.U.[1], Köhne, S.[1], Strauss, B.[1], Rosendahl, J.[1]

[1] Institute of Psychosocial Medicine, Psychotherapy and Psychooncology, Jena University Hospital, Friedrich Schiller University, Jena, Germany, [2] Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany

With the outbreak of the Covid-19 pandemic, the already severe stress load across the world potentiated, increasing the risk for the development of stress-associated mental and physical disease. Focusing on the early stages of the pandemic, we asked whether resilience and the Big Five personality traits (extraversion, neuroticism, extraversion, openness, agreeableness and conscientiousness) could predict the biological stress response to the first lockdown in Germany. Using a prospective, longitudinal, observational study design, 80 adult volunteers first completed an internet-based survey (T0). Importantly, this happened *prior to* the first Covid-19-related fatality in Germany (T0). The survey was repeated during the first lockdown period (T1), as well as during the subsequent contact restriction period (T2). As biological markers of chronic stress load, hair strands for the assessment of systemic cortisol and cortisone levels were collected at T2. We found that higher levels of neuroticism—the tendency to respond with negative emotions to threat, frustration, or loss—predicted higher levels of hair cortisol, cortisone, and subjective stress. Higher extraversion—the tendency to be sociable, assertive, active, and positive—predicted higher hair cortisone levels. There were no effects of resilience on either subjective or physiological stress markers. This study provides longitudinal evidence that the personality traits of neuroticism and extraversion predict the accumulation of biological stress during a prolonged stressful period such as the Covid-19 pandemic. Higher neuroticism has traditionally been viewed as a risk factor for worse health outcomes. However, extraverted individuals were thought to be protected. We conclude that we cannot simply generalise the response to a pandemic from pre-pandemic knowledge. While neurotic individuals may suffer due to their general emotional lability, extraverted individuals may be the most susceptible to social stress posed by the pandemic and social isolation measures. To minimise the stress burden caused by the current and potential future pandemics, individualised stress management programs need to be developed and offered in a lockdown-friendly format.

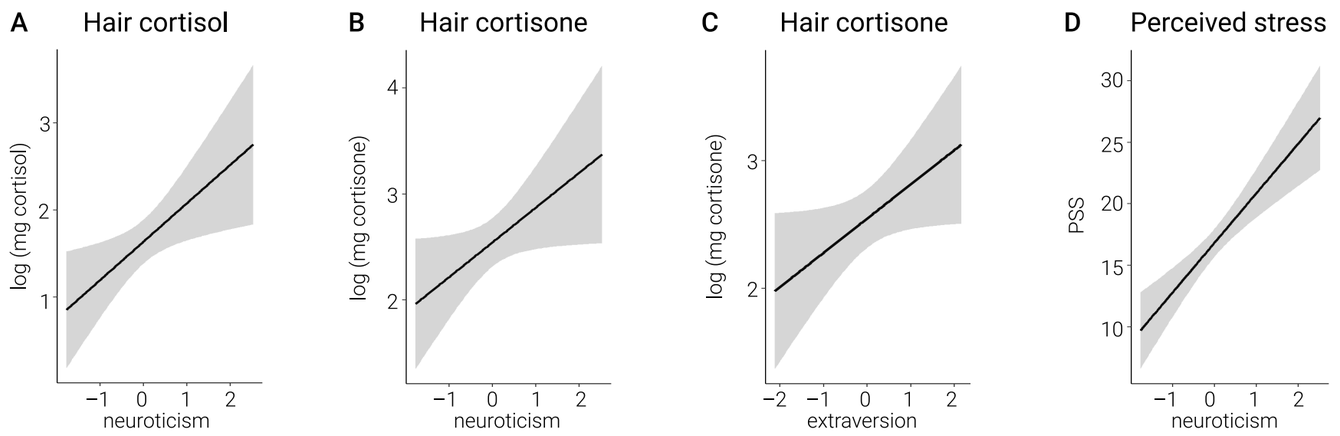

Figure 7.2.1 Estimated effects (and SD) of neuroticism and extraversion on (A) hair cortisol, (B, C) hair cortisone and (D) subjective stress scores (measured using the Perceived Stress Scale; PSS). Higher scores in neuroticism predicted higher stress across all markers, suggesting increasing physiological and subjective strain with increasing neuroticism. Extraversion had a significant effect on hair cortisone, such that higher levels of extraversion predicted higher levels of hair cortisone.

7.2.2 Contemplative mental training reduces hair glucocorticoid levels in a randomised clinical trial

Puhlmann, L.M.C.[1,2], Vrtička, P.[2,3], Linz, R.[2], Stalder, T.[4], Kirschbaum, C.[5], Engert, V.[2,6,*], & Singer, T.[7,*]

[1] Leibniz Institute for Resilience Research, Mainz, Germany, [2] Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany, [3] Department of Psychology, University of Essex, Colchester, UK, [4] Department of Clinical Psychology, University of Siegen, Siegen, [5] Department of Biological Psychology, Technische Universität Dresden, [6] Institute of Psychosocial Medicine, Psychotherapy and Psychooncology, Jena University Hospital, Germany, [7] Social Neuroscience Lab, Max Planck Society, Berlin, Germany, * joint last authors

In this study we investigate the effect of regular contemplative mental training on hormonal and subjective-psychological indices of long-term stress. An open-label efficacy trial comprising three distinct 3-month long modules targeting attentional processes, socioaffective, or sociocognitive abilities through secularised meditation practices was conducted in a sample of healthy adults. Participants underwent the training for either 3 months, 9 months, or they were assigned to a retest control cohort. Indices of chronic stress were collected at four time points: pretraining and after 3, 6, and 9 months. Our main outcome measures were hair cortisol (HC) and cortisone (HE) concentrations as well as self-reported long-term stress. Data on hair-based glucocorticoids were available from *n*= 227 participants, and subjective-psychological stress data from *n*= 326 participants. Results from three independent training cohorts (TC1, TC2, TC3) revealed consistent decreases in levels of HC and HE over the first three months (in TC3) to 6 months (in TC1 and TC2) of training. There was no further reduction at the final 9-month mark. HC training effects increased with individual practice frequency. Effects on both HC and HE were independent of training content and change in self-reported chronic stress. These results suggest a reduction of long-term cortisol exposure as one possible mechanism through which meditation-based mental training may exert positive health effects.

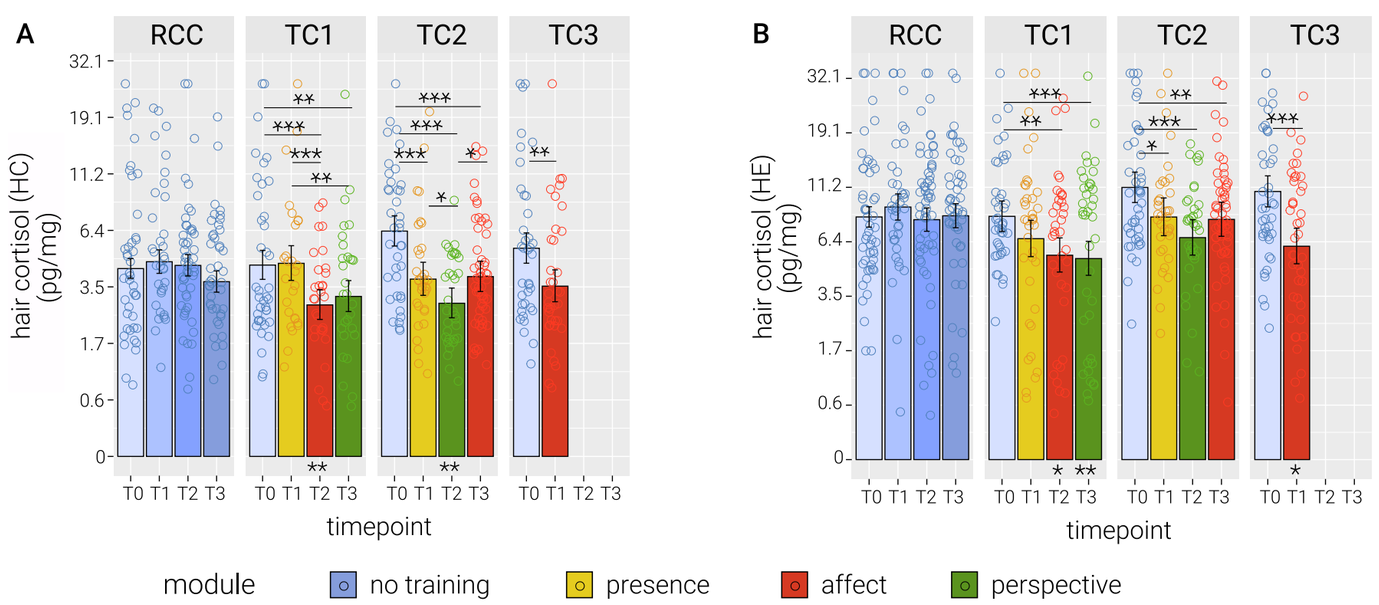

Figure 7.2.2 Levels of (A) hair cortisol (HC) and (B) hair cortisone (HE) as a function of training cohort and time-point show stable reduction after six months of mental training, irrespective of the type of practice. No further reduction is found at the final 9-month mark. Note natural log scale on the y-axis. Error bars represent +/-1 SE; each circle represents one raw data point. Asterisks below bars indicate comparison with the retest control cohort (RCC) at the matched time point. *Significant at p ≤ .05. **Significant at p ≤ .01. ***Significant at p ≤ .001.

7.2.3 Plasma oxytocin is modulated by mental training, but does not mediate its stress-buffering effect.

Hoehne, K.[1], Vrtička, P.[2,3], Engert, V.[1,3,*], & Singer, T.[4,*]

[1] Institute of Psychosocial Medicine, Psychotherapy and Psychooncology, Jena University Hospital, Germany, [2] Department of Psychology, University of Essex, Colchester, UK, [3] Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany, [4] Social Neuroscience Lab, Max Planck Society, Berlin, Germany,
* joint last authors

Oxytocin is involved in social processing and stress regulation. Due to these roles, it has been suggested that the neuropeptide mediates stress-reduction after socio-affective, compassion-based mental training. In the current study, we tested this hypothesis in the context of the ReSource Project. In this 9-month longitudinal mental training study, participants practiced three different types of meditation-based mental training, targeting either attentional (Presence Module), socio-affective or socio-cognitive abilities (Affect and Perspective Modules). In detail, we examined whether training-induced changes in plasma oxytocin levels in 313 participants were linked to training-induced changes in cortisol and subjective-psychological stress reactivity. We found that, independent of mental training, stress triggered the acute release of plasma oxytocin. Training effects on oxytocin were present, however, they were not specific to stress reactivity but rather showed in *overall* oxytocin release (before, during, and after stress exposure). In comparison to no training, the 3-months compassion-based Affect training decreased overall oxytocin levels in the context of psychosocial stress. However, these training-induced changes in overall oxytocin were unrelated to cortisol and subjective stress reactivity. Based on the theory of oxytocin as an allostatic hormone with anticipatory properties by Quintana and Guastella's (2020), we interpret training-induced changes in overall oxytocin levels as alterations in the anticipated emotional relevance of a stressful event. Following the 3-months training of socio-affective skills, stressful situations may lose their emotional saliency. We conclude that changes in peripheral oxytocin release do not mediate stress reduction after mental training. We encourage the investigation of an allostatic concept of oxytocin in future research.

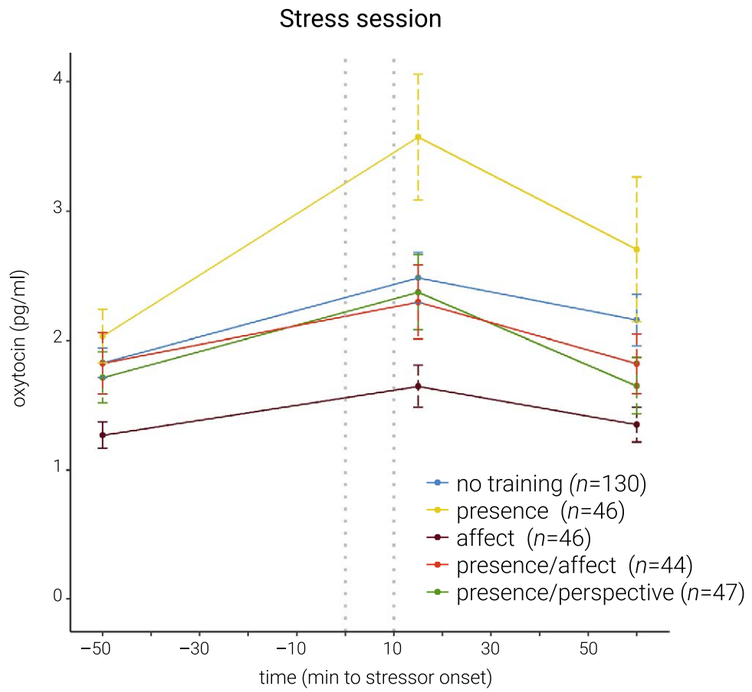

Figure 7.2.3 Means of plasma oxytocin levels (raw data) in the different mental training groups during psychosocial stress. Error bars represent the standard errors of the mean.

Congresses, Workshops, and Symposia

2020

- Engert, V. (January). *Stressregulierung im sozialen Kontext: Entwicklung, Interaktion und Resistenz.* Colloquium. Department of Clinical Psychology, Friedrich Schiller University Jena, Germany.
- Engert, V. (January). *Vulnerability and strength through social factors.* Invited talk at Open Academy of Medicine, Venice, Italy.

2021

- Engert, V. (January). *Stress regulatioin in the social context: Empathic stress and empathic processes in stress reduction.* Invited talk at Cluster of Excellence "Centre for the Advanced Study of Collective Behavior", University of Konstanz, Konstanz, Germany.
- Engert, V. (January). *Stress regulation in the social context: Empathic stress and empathic processes in stress reduction.* Colloquium Department of General Psychology, Friedrich-Schiller-University, Jena, Germany.
- Engert, V. (September). *Using ecological momentary assessment to track how contemplative mental training is implemented into everyday life.* Talk at 51st Annual Conference of the International Society of Psychoneuroendocrinology, online meeting.
- Engert, V. (September). *Mentales Training für Herz, Geist und Körper: Ergebnisse aus dem ReSource Projekt.* Workshop given at Benediktushof – Zentrum für Meditation und Achtsamkeit, Holzkirchen, Germany.

2022

- Puhlmann, L. (March). *Measuring and analyzing digital biomarkers of mental health.* Workshop given at Hendler Lab, Ichilov Hospital and Tel Aviv University, Tel Aviv, Israel.
- Puhlmann, L. (April). DynaMORE open methods workshop series. Mainz, Germany. Virtual.
- Puhlmann, L. (May). DynaMORE methods workshop series. Mainz, Germany. Virtual.
- Engert, V. (June). *Influence of distinct contemplative mental training elements on daily life stress, thoughts, and affect.* 47th Talk at Psychologie und Gehirn, Freiburg, Germany.

Degrees

PhD Theses

2020

- Linz, R. *Investigating mind-brain-body interactions within the multi-systemic phenomenon of stress*. Humboldt-Universität zu Berlin, Germany.

2022

- Puhlmann, L. *From mind to body: effects of contemplative mental training on biomarkers of stress related disease risk.* Leipzig University, Germany.

Appointments

2022

- Puhlmann, L. *Research fellow in the EU Horizon 2020 Project 'Dynamic Modelling of Resilience' (DynaMORE)*, Leibniz Institute for Resilience Research, Research Group Kalisch, Mainz, Germany.

Awards

2020

- Puhlmann, L. *ISPNE Best Early Career Abstract Award.* Virtual.

2021

- Puhlmann, L. *LIR Young Investigator Award.* Mainz, Germany.

2022

- Puhlmann, L. *Early-Career Scientist Short Talk Award* at 8th International Resilience Symposium on Resilience Research. Mainz, Germany.

Publications

Books & Book Chapters

Linz, R. (2020). Investigating mind-brain-body interactions within the multi-systemic phenomenon of stress. *MPI Series in Human Cognitive and Brain Sciences: Vol. 209*. Leipzig: Max Planck Institute for Human Cognitive and Brain Sciences.

Journal Articles

Blasberg, J. U., Kanske, P., Böckler, A., Trautwein, F.-M., Singer, T., & Engert, V. (2022). Associations of social processing abilities with psychosocial stress sensitivity. *Comprehensive Psychoneuroendocrinology*, *12*. https://doi.org/10.1016/j.cpnec.2022.100159

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8.1

IMPRS on Neuroscience of Communication: Function, Structure, and Plasticity

INTERNATIONAL MAX PLANCK RESEARCH SCHOOL

The International Max Planck Research School on Neuroscience of Communication: Function, Structure, and Plasticity (IMPRS NeuroCom) is an interdisciplinary PhD programme. The school is based at the MPI CBS and Leipzig University (LU) and also involves the Max Planck Institute for Evolutionary Anthropology (MPI EVA), also in Leipzig, and the Institute of Cognitive Neuroscience (ICN) at UCL in the UK. The IMPRS NeuroCom is funded by the Max Planck Society, the MPI CBS, and the LU. The school was founded in 2009 and will be phased out in June 2023. In the past years, we received more than 370 applications per year, from which we selected 15 – 20 outstanding doctoral researchers annually. The graduate school has strengthened the already-existent, close working relationship between the participating institutions. The final cohort of IMRPS NeuroCom doctoral researchers started in autumn 2021. We will ensure that each doctoral researcher can complete the teaching curriculum by June 2023.

Doctoral researchers and projects

We differentiate the following project stages: Orientation: Doctoral researcher has recently started the PhD project and is in the process of finding a PhD topic; Progressed: Doctoral researcher is planning/running studies and writing papers; Final: Doctoral researcher is writing up the thesis; Submitted: Doctoral researcher has submitted the thesis at University and is waiting for the defense, Completed: Doctoral researchers who successfully defended their thesis between 2020–2022. Left the program: Doctoral researchers who left the program without defending their thesis.

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Module I: Language and Communication

Student	Project	Project Stage
Adamson, Helyne	Understanding mechanisms of brain plasticity using multimodal imaging to assess brain structure changes during L2 learning	left the programme during 2020–2022
Dr Cheung, Ka-Ming (Vincent)	The neurocognitive basis of musical expectancy and pleasure: A computational modelling approach	completed
Dr Chien, Pei-Ju	Neural bases of linguistic pitch in a tonal language: Intonation, lexical tone, and the role of language experience	completed
Ferrante, Matteo	Probing the functional relevance of pre-SMA and aIFG for controlled semantic processing with transcranial magnetic stimulation	progressed
Girlich Sarah	First language acquisition: How children learn verbs in German.	progressed
Dr Graessner, Astrid	The neural correlates of basic semantic composition	completed
Gugnowska, Katarzyna	Neural bases of interpersonal coordinated behaviour during music performance	progressed
Hellbernd, Nele	Intentions in prosody: expression, comprehension and neural bases	final
Henke, Lena	Electrophysiological time constraints on segmentation	progressed
Klein, Cheslie Celine	The neural basis of syntax acquisition during early childhood	progressed
Kohler, Natalie	Neural bases of musical joint action: The role of familiarity	final
Krause, Carina-Denise	Wer macht was mit wem? – Die differenziellen Rollen von Kanonizität, Rekursion und phonologisch-verbalem Arbeitsgedächtnis beim Verstehen komplexer Syntax	final

Student	Project	Project Stage
Lamekina, Yulia	The influence of prosodic entrainment on speech comprehension	progressed
Jiang, Zhizhao	Changes in effective connectivity of the language and domain-general network after left temporo-parietal and frontal stroke	progressed
Jing, Ying	Modeling the Effects of Transcranial Magnetic Stimulation on Cognitive Functions	progressed
Maran, Matteo	The implementation of the syntactic Merge mechanism in the cortical language network: causal neuronal indexes of grammatical category access and hierarchization	final
Menn, Katharina	The emergence of rhythmic auditory sampling and linguistic knowledge in early childhood: A naturalistic approach	progressed
Papitto, Giorgio	The involvement of Broca's area in the neural networks for language and action	progressed
Pyatigorskaya, Elena	Spatio-temporal neural correlates of unconscious syntactic processing in human adult brain	progressed
Dr Qi, Ting	The brain structure during language development. Neural correlates of sentence comprehension in preschool children.	completed
Ringer, Hanna	Perceptual learning of random acoustic patterns	progressed
Roho, Inès	Relation of vocal production and white matter connectivity in the chimpanzee brain	progressed
Rysop, Anna	Modulating neural network dynamics of speech comprehension: The role of the angular gyrus	final
Schroën, Joëlle	The chronometry of semantic processing in the brain	progressed
Dr Stuckenberg (née Erfort), Maria Victoria	Preceding visual information modulates auditory information processing: A crossmodal prediction view	completed
Titone, Lorenzo	Neural oscillations in language processing: Tracking and predicting	progressed
Trettenbrein, Patrick	Modality (in-)dependence of syntactic processing	progressed
Wei, Xuehue	The language connectome: plasticity in second language acquisition	progressed
Winkler, Marina	Nested dependency processing in infants and adults	final

Module II: Cognitive and Affective Neuroscience

Student	Project	Project Stage
Asgeirsdottir, Unnur Andrea	Neural mechanisms underlying reasoning abilities	orientation
Barnaveli, Irina	Cognitive spaces in action representation	progressed
Bednarski (née Teichmann), Florian	Minimal agency	final
Deilmann, Felix	Integrating knowledge about structure and reward contingencies for generalization and inference	progressed

Student	Project	Project Stage
Elnagar, Salma	The effect of prior knowledge on new learning	progressed
Eperon, Alex	Structured knowledge for efficient inference: investigating abstract action representation in the brain	progressed
Gallistl, Mathilde	Examination of social processes and physiological stress resonance in dyads	progressed
Kaniuth, Philipp	Identifying core dimensions underlying human object recognition	progressed
Karew, Artem	Development of grid cells and their effect on cognition in children	left the programme during 2020–2022
Dr Langeloh, Miriam	Why do infants imitate selectively? Neural correlates of infants‘ action understanding in the head-touch paradigm”	completed
Lewis, Carolin	Hormonal and pharmacological modulators of female and male decision-making processes	final
Dr Linz, Roman	Investigating mind-brain-body interactions within the multisystemic phenomenon of stress	completed
Meyer, Ann-Kristin	Tracking the impact of memory suppression on individual memory representations	final
Dr Molloy, Eoin	Responses to one-week administration of escitalopram	completed
Nitsch, Alexander	Coding principles for memory and value-based decision making	progressed
Dr Oligschläger, Sabine	Gradients of connectivity distance in the primate cerebral cortex	completed
O’Malley, Bonnie	Psychosocial stress and stress resonance: investigation, review & intervention	progressed
Dr Paulus, Philipp	Schema and value: characterizing the role of the rostral and ventral medial prefrontal cortex in episodic future thinking	completed
Dr Puhlmann, Lara	From mind to body: effects of contemplative mental training on biomarkers of stress-related disease risk	completed
Reisner, Volker	Spatial mapping in the human brain	progressed
Schäfer, Theo	Spatial coding principles for concept structures in the medial temporal lobe	progressed
Schüler, Clara	Self and other in the developing brain	progressed
Stoffregen, Hanna	Emergence of generalized reward representations	left the programme during 2020–2022
Tebbe, Anna-Lena	Neural correlates of the development of perspective taking	progressed
Yang, Chen	Development of implicit and explicit Theory-of-Mind in early childhood: cultural differences and neural basis	orientation
Zsido, Rachel	Ovarian hormones shape brain structure, function, and chemistry: A neuropsychiatric framework for female brain health	submitted, waiting for defense

Module III: Basic and Clinical Neuroscience

Student	Project	Project Stage
Açıl, Dorukhan	When do youth generalize representations of parents to peers: the role of maltreatment and attachment	progressed
Dr Baczkowski, Blazej	Inferring risk in the absence of threat: on the interaction of Pavlovian threat memory with pre-existing knowledge of environmental structure	completed
Bailey, Emma	Noninvasive electrophysiology of the human spinal cord	progressed
Belger, Julia	Application of virtual reality for the assessment of unilateral spatial neglect: the immersive virtual road-crossing task (iVRoad)	progressed
Dr Bialas, Ole	An Electroencephalographic investigation of the encoding of sound source elevation in the human cortex	completed
Dr Bloechl-Sevinchan, Maria	Situating determinant of mental health and wellbeing during ageing within a lifespan perspective	completed
Bracher, Angelika	Too much in synch? Investigating co-regulation in child-caregiver dyads with maltreatment experience	progressed
Braga, Alessandro	Predictive processes in the auditory cortex	progressed
Chen, Xiuhui	Pathophysiology and neural correlates of symptoms in patients with stroke affecting the somatosensory system	progressed
Dabbagh, Alice	Imaging the spinal cord: Pain processing and beyond	progressed
Elmalem, Michael	Idiographic AI: high-dimensional single-subject invasive mapping of the human brain	progressed
Gippert, Magdalena	Neural mechanisms of linked movements	progressed
Dr Gong, Ruxue	β-γ phase-amplitude coupling derived from non-invasive electroencephalogram – insight into the pathophysiology of Parkinsons´s disease	completed
Grigoryan, Khosrov	Neural correlates of brain-computer interface-based post-stroke motor rehabilitation	progressed
Herzog, Nadine	Working memory gating in obesity	final
Hofmann, Simon	Explainable deep learning methods for cognitive neuroscience	progressed
Kandia, Dimitra-Maria	Effects of early music experience on language development	progressed
Kapralov, Nikolai	Understanding and optimizing the efficacy of neurofeedback based on electrophysiological recordings	progressed
Dr Kaptan, Merve	Neuroimaging of the human spinal cord at 3 Tesla: Investigation of acquisition and denoising strategies through resting-state functional magnetic resonance imaging	completed
Lee, Harin	Cross-cultural music perception	progressed
Manoli, Katerina	he role of the cerebellum in Theory of Mind: structure, function, and development	orientation

Student	Project	Project Stage
Morozova, Maria	Microstructure informed tractography – ground truth and evaluation of assumptions	progressed
Pohle, Lisa-Marie Gertje	Predictions of pain and pain relief	progressed
Reinfeld, Pia	Explainable Artificial Intelligence (XAI) methods to study Body-Brain Interactions	orientation
Roesch, Sarah	Efficacy and underlying mechanisms of near-infrared spectroscopy-based neurofeedback for binge-eating disorder	progressed
Ruthig, Philip	Comparative microanatomy of mammalian auditory brain areas	final
Dr Schaare, Herma Lina	Neurocognition of vascular risk factors	completed
Schulz, Charlotte	Effects of child maltreatment on adolescent brain structure and function	final
Dr Shih, Pei-Cheng	Bilateral upper-limb coordination in aging and stroke	completed
Stephani, Tilmann	On the organization of neural response variability: Probing somatosensory excitability dynamics with oscillatory brain states and stimulus-evoked potentials	submitted, waiting for defense
Tu, Hsing-Fen	Attentional control in early development	submitted, waiting for defense
Uhlig, Marie	Brain changes after psychosocial stress and their relation to other stress markers	final
Vartanian, Meghedi	Effects of microbiome-changing interventions on mood decision-making and the gut-brain axis in obesity	progressed
Waltmann, Maria	Shared and differential mechanisms of maladaptive decision-making in binge eating disorder and obesity	final
Wan, Bin	Organization of brain asymmetry	final
Zhao, Hongyan	Non-invasive investigation of excitability changes in the human spinal cord	progressed

Module IV: Neuroimaging Physics and Signal Processing

Student	Project	Project Stage
Beltran, Ferney	Modelling the olfactory system using spiking neural networks with synaptic dynamics to study drifting in electronic noses	progressed
Beylier, Charlotte	Analysis of representations in machine learning models	progressed
Brammerloh, Malte	Biophysical modeling of iron-induced MRI relaxation in the human substantia nigra	final
Dr Chien, Shih-Cheng	Brain network dynamics in deviance response and auditory perception	completed
Damm, Juliane	Towards a comprehensive microstructural human connectome: combining ultra-high resolution qMRI with advanced DWI in-vivo	orientation

Student	Project	Project Stage
Devi, Ratnamanjuri	Magnetic resonance investigations of physiological effects related to functional inhibition	final
Dr Gast, Richard	Phase transitions between asynchronous and synchronous neural dynamics – theoretical insight into the mechanisms behind neural oscillations in Parkinson's Disease	completed
Gkotsoulias, Dimitrios G.	Pathophysiology of Tourette syndrome - multimodal characterization of metabolic alterations	progressed
Haenelt, Daniel	Submillimeter fMRI - which MR sequence yields the best results?	final
Iporre Rivas, Ariel	Geometric deep learning framework for ischemic stroke brain diagnosis and analysis of risks of cognitive impairment	progressed
Dr Jamshidi Idaj, Mina	New machine learning methods for modeling nonlinear interactions in neural data	completed
Dr Kalloch, Benjamin	Towards individualized transcranial electric stimulation therapy through computer simulation	completed
Movahedian Attar, Fakhereh	Identification and characterisation of short cortico-cortical association fibres (U-fibres) using diffusion MRI	final
Podranski, Kornelius	Improved processing of high-resolution multi parameter maps	progressed
Rose, Daniel	Informing neural mass models with MRI-based in-vivo histology	left the Institute during 2020–2022
Schmidt, Jochen	In vivo high-resolution quantitative T2 mapping at high-field strength	progressed
Torrecuso, Renzo	Advanced image processing concepts for characterizing movement disorders and for cross-disorder comparisons	progressed
Vakulchiakova, Lenka	Mapping of myelination using quantitative MRI	final
Wallstein, Niklas	MR investigations of water relaxation mechanisms in brain tissue - influence of metal ions and myelin	progressed
Dr Waschke, Johannes	Trajectory data analysis in biomedical application	completed
Zarubin, Georgy	Development of a tACS-EEG closed loop system in order to understand and utilize the neuromodulatory role of tACS	final
Zoraghi, Mahsa	Integration of multi-resolution multi-modal data	progressed

Faculty

Module I: Language and Communication

Professor A. D. Friederici (since 2009), MPI CBS, Dept of Neuropsychology

Professor G. Hartwigsen (since 2016), LU and MPI CBS, LMRG "Cognition and Plasticity"

Professor J. Jescheniak (since 2009), LU, Dept of Cognitive Psychology

Professor C. Maennel (2019–2020), MPI CBS, Dept of Neuropsychology, RG "Early Language Acquisition"

Dr L. Meyer (since 2018), MPI CBS, MPRG "Language Cycles"

PD Dr D. Sammler (2013–2020), MPI CBS, Dept of Neuropsychology

Professor D. Saur (since 2016), LU, Dept of Neurology, Language and Aphasia Lab

Professor E. Schroeger (since 2009), LU, Dept of Cognitive and Biological Psychology

Module II: Cognitive and Affective Neuroscience

Dr R. G. Benoit (since 2016), MPI CBS, MPRG "Adaptive Memory"

Professor C. F. Doeller (since 2018), MPI CBS, Dept of Psychology

Professor V. Engert (since 2016), MPI CBS, RG Social Stress and Family Health & Friedrich-Schiller University Jena, Institute of Psychosocial Medicine and Psychotherapy

Dr M. Garvert (2018–2021), MPI CBS, Dept of Psychology

Dr C. Grosse Wiesmann (since 2021), MPI CBS, Minerva fast-track group "Milestones of Early Cognitive Development"

Professor D. Haun (2016–2020), MPI EVA, Dept of Comparative Cultural Psychology

Professor M. N. Hebart (since 2019), MPI CBS, MPRG "Vision and Computational Cognition" & Justus-Liebig University, Giessen

Professor K. Musholt (since 2018), LU, Dept of Philosophy

PD Dr J. Sacher (since 2016), MPI CBS, Minerva Research Group - EGG (Emotions & neuroimaGinG)-Laboratory

Professor M.L. Schroeter (since 2012), LU, Day Clinic of Cognitive Neurology, and MPI CBS, Dept of Neurology

PD Dr M.A. Skeide (since 2019), MPI CBS, Dept of Neuropsychology, RG "Learning in Early Childhood"

Module III: Basic and Clinical Neuroscience

Professor I. Bechmann (since 2012), LU, Institute for Anatomy

Professor J. Classen (since 2012), LU, Dept of Neurology, RG Motor and Plasticity

Module III: Basic and Clinical Neuroscience

Dr F. Eippert (since 2018), MPI CBS, MPRG "Pain Perception"

PD Dr S. Geyer (since 2009), MPI CBS, Dept of Neurophysics, RG "Anatomical Analysis of the Organization of the Human and Non-Human Primate Brain"

Professor M. Morawski (2020), LU, Paul-Flechsig-Institute for Brain Research

Professor H. Obrig (since 2009), LU, Day Clinic for Cognitive Neurology, and MPI CBS, Dept of Neurology

Professor P. Ragert (since 2016), LU, Dept of Movement Neuroscience

Dr S. L. Valk (since 2020), MPI CBS, OHG "Cognitive Neurogenetics"

Professor M. Schönwiesner (since 2016), LU, Dept of General Zoology and Neurobiology

Professor A. Villringer (since 2009), MPI CBS, Dept of Neurology

Professor K. von Klitzing (2009-2021), LU, Clinic and Polyclinic of Children and Youth Psychiatry

PD Dr V. Witte (since 2018), MPI CBS, Dept of Neurology

Module IV: Neuroimaging Physics and Signal Processing

Professor M. Bogdan (since 2012), LU, Dept of Computer Engineering

Professor J. Haase (since 2009), LU, Dept of Magnetic Resonance of Complex Quantum Solids

Professor M. Hlawitschka (since 2012), Leipzig University of Applied Sciences, Faculty for Computer Science and Media

Dr E. Kirilina (since 2018), MPI CBS, Dept of Neurophysics, RG MRI Biophysics

Professor T. R. Knösche (since 2009), MPI CBS, "Brain Networks" Unit

Dr B. Maess (since 2009), MPI CBS, "Brain Networks" Unit

Professor H. E. Möller (since 2009), MPI CBS, "Nuclear Magnetic Resonance" Unit

Professor K. Mueller (since 2009), MPI CBS, "Methods and Development Group Neural Data Science and Statistical Computing"

Dr V. Nikulin (since 2017), MPI CBS, Dept of Neurology, RG "Neural Interactions and Dynamics"

Dr N. Scherf (since 2021), MPI CBS, "Methods and Development Group Neural Data Science and Statistical Computing"

Professor G. Scheuermann (since 2009), LU, Dept of Image Processing

Professor R. Valiullin (since 2018), LU, Felix Bloch Institute für Solid State Physics

Professor N. Weiskopf (since 2015), MPI CBS, Dept of Neurophysics

Please note: MPRG = Max Planck Research Group, LMRG = Lise Meitner Research Group, OHG = Otto Hahn Group, RG = Research Group

Structure of the Graduate School

The International Max Planck Research School on Neuroscience of Communication: Function, Structure, and Plasticity (IMPRS NeuroCom) focuses on the functional, structural, and neural plasticity foundations of the neuroscience of human communication, through an integrative and interdisciplinary approach. The overriding goal of this programme is to train doctoral researchers in the multidisciplinary aspects of cognition, psychology, neuroscience, computer science, and neurophysics. The school offers an innovative, interdisciplinary, and international research environment.

Besides introducing behavioural methodology, the programme draws on powerful modern neuroimaging techniques such as functional and structural magnetic resonance imaging (MRI), electroencephalography (EEG), magnetoencephalography (MEG), near-infrared spectroscopy (NIRS), and transcranial magnetic stimulation (TMS). The breadth of these tools works toward our aim of understanding the brain in all its complexity and functionality. There is a strong interaction between doctoral projects focusing on neuroscientific methodologies and those focusing on cognitive science, which is supported by the school's infrastructure and facilities.

Research Topics

Research projects and teaching are assigned to four modules:

1. Language and Communication
2. Cognitive and Affective Neuroscience
3. Basic and Clinical Neuroscience
4. Neuroimaging Physics and Signal Processing

Fundamental knowledge covering all four modules is imparted in the form of lecture series, courses, and seminars. This provides a comprehensive foundation for conducting doctoral research in neuroscience, and opens up horizons for potential interdisciplinary approaches. The curriculum not only includes lectures, courses, and seminars, but also colloquia, an annual summer school, and an exchange program in the final year.

Admission to the School

Doctoral researchers with a variety of professional backgrounds were recruited. In the context of the annual recruitment periods, we receive about 370 applications, of which, about 7% are admitted to the graduate school. This rate illustrates that admission to the school is highly competitive. Doctoral researchers, who hold a PhD position with one of the faculty members, could also apply to IMPRS NeuroCom throughout the year. As with all candidates, students entering via this route had to pass an admission interview, attended by at least three faculty members.

Supervision of Students

At the beginning of the PhD (during the first three months), each doctoral researcher is asked to set up a Thesis Advisory Committee (TAC). The TAC is composed of at least one supervisor from the relevant module and two advisors. The supervisor provides the main scientific support for the thesis. The function of the advisors is to support the PhD project by providing academic counselling and advice. Once the TAC is assigned, IMPRS doctoral researchers and their TAC have to sign a supervision agreement based on a template provided by IMPRS NeuroCom. The supervision agreement aims

to ensure that doctoral researchers meet the requirements of their doctoral projects and the requirements of their supervisors. It also guarantees continuous support and advice of the doctoral researcher by the supervisor(s) and advisors.

The TAC and the doctoral researchers are required to meet on a regular (at least annual) basis. The basis of each TAC meeting is a written report, including a timeline and filling in a standardised feedback form. It is each doctoral researcher's duty to take care that the TAC meeting takes place (on time) and that the meeting requirements are fulfilled.

Teaching Curriculum

Lecture Series

The PhD curriculum combines opportunities for outstanding research with excellent teaching to ensure that doctoral researchers are highly qualified for a successful career in relevant areas of Neuroscience. Courses held in 2019–2022 included basic and advanced lecture series on 'Foundations of Neuroscience', 'Clinical Neuroscience', 'Physics of Neuroimaging', 'Electroencephalography and Magnetoencephalography', 'Language and Communication', 'Neuroplasticity', 'Social, Cognitive, and Affective Neuroscience', and 'General Linear Mixed Models'. Lecture series were conducted by members of the IMPRS faculty from all involved institutions in Leipzig as well as by external guest speakers. In addition, several scientific courses on 'Matlab' and 'R' took place. As a result of the pandemic, from March 2020 onwards, IMPRS lectures were offered as online lectures on Zoom. This format was well received by the doctoral researchers, and we took it as a possibility to open our teaching program to a broader public. As soon as the pandemic situation allowed, we moved from virtual-only classes to hybrid classes. This gave us the possibility to allow doctoral researchers to attend on-site or virtual, depending on their individual situation and preferences. A detailed overview of the previous curricular activities can be found at the online archive.

IMPRS NeuroCom Summer School

As a special highlight of our graduate program, IMPRS NeuroCom offers an annual Summer School. Every third year this event is hosted by our partner institute, the Institute of Cognitive Neuroscience at UCL. During the other years the Summer School takes place in Leipzig at MPI CBS. Due to the pandemic, the summer school 2020, which was planned to take place at ICN in London had to be moved to 2021. Finally, we decided to hold the event online under the lead of scientists from ICN, especially Professor Patrick Haggard and Professor Antonia Hamilton.

As a result of all the uncertainty in past years related to planning large events and the strong motivation to offer the IMPRS students an in-person event, we decided to hold the summer school in 2022 as a hybrid event. IMPRS NeuroCom students were given the possibility to attend onsite while external students could join virtually on Zoom. The umbrella topic of this summer school, which took place from the 27th – 29th of June 2022 at MPI CBS in Leipzig, was 'Computational Neuroscience'. Theoretical input through lectures was offered, taught by internationally renowned speakers, as well as hands-on workshops on related topics. Where possible, doctoral researchers were provided many opportunities for direct exchange with the speakers, for example, during a panel discussion or the 'meet the speakers' lunch, which were offered for each session. In addition, early career scientists had the chance to present their research in the form of posters during an online poster session. The latest program was rounded off by several hands-on workshops, social activities, and the award of the poster prize.

Transferable Skills Training

Based on the suggestions and recommendations received from the students and their Thesis Advisory Committees via feedback forms, we offered several transferable skills courses, such as Good Scientific Practice, Career Development, Time- and Project Management, Scientific Writing, and Presentation Skills as part of our PhD curriculum. As we could of course only offer a selection of potential courses, we were glad that our doctoral researchers had the possibility to attend additional and complementary courses at Research Academy Leipzig, the umbrella organisation of all graduate schools at Leipzig University. In addition, they could join courses offered by the Planck Academy. Furthermore, international students were encouraged and financially supported to participate in German language courses.

To continuously improve all types of training and teaching that we offer, each event is evaluated by the students. A detailed overview of our past training activities, including schedules of the lecture series, can be found in the archive on our website.

Coordination Team

Former Spokesperson

Professor Arno Villringer
(2013 – May 2020)

Director, Department of Neurology
Email: villringer@cbs.mpg.de

Spokesperson

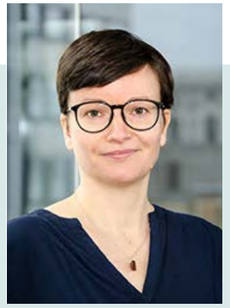
Professor Nikolaus Weiskopf
(since May 2020)

Director, Department of Neurophysics
Email: weiskopf@cbs.mpg.de

Coordinator

Dr Veronika Krieghoff
(since October 2015)

Email: vkrieghoff@cbs.mpg.de



Assistant

Susann Glasewald
(since January 2017)

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8.2

Max Planck School of Cognition

In the international competition for the highest calibre doctoral candidates, several German research institutions are in very good standing. However, some of the leading US and UK universities still have advantages, due to their considerably larger faculties and regular entry of PhD candidates from the Bachelor level. In response to that, the president of the Max Planck Society, Martin Stratmann, suggested creating **nationwide joint schools.** Such schools would integrate leading experts across Germany in certain fields, from Max Planck institutes, universities, and other non-university research institutions. Together with the former Federal Research Minister, Johanna Wanka, and the former President of the German Rectors' Conference, Horst Hippler, the concept was further developed and a competitive call was initiated for the foundation of three pilot Schools for a five-year pilot phase (initially until September 2023 and later extended until September 2025). During the pilot phase, the three Schools are **funded by the German Federal Ministry of Education and Research (BMBF), the Max Planck Society, the Fraunhofer Society, as well as other participating institutes**. Arno Villringer was the leading principal investigator for the proposed Max Planck School of Cognition (MPSCog). He formed the School's faculty and presented the proposal, which was selected as one of the three pilot Schools. The coordination team of MPSCog started setting the foundation of the program for the first cohort of doctoral candidates, who joined in 2019. Since then, MPSCog has taken a new cohort of doctoral candidates yearly. More recently, in **September 2022**, the **first clinician scientists** joined MPSCog under the clinician scientist track.

MPSCog is an **interdisciplinary four-year doctoral program** that offers exceptionally bright candidates the opportunity to acquire a multi-faceted understanding of the different methods and approaches used in the rapidly evolving field of cognition. Candidates come from backgrounds such as psychology, cognitive (neuro)science, philosophy, neurobiology, and computer science. The program is characterised by a passion to better understand both human and animal cognition as well as "mental phenomena" potentially occurring in non-biological systems and agents (artificial intelligence). The program not only offers an attractive alternative to the traditional single-discipline approach but also offers a **flexible, candidate-centred learning approach** during the first year. Candidates have access to a cluster of highly visible and internationally known faculty members from diverse scientific backgrounds.

Max Planck School of Cognition's goals

MPSCog bundles world-leading researchers from 16 different universities (including UCL, which is an international partner of the School) and 14 non-university research institutions (Figure 8.2.1). The School has three primary aims: **1) Prepare the next generation of leading international cognition researchers** by recruiting talented young scientists and providing them with an outstanding education in the theoretical concepts and methods of the rapidly evolving field of cognition, **2) Develop a new "scientific language" of cognition and intelligence** through discussion, evaluation and integration of concepts of cognition from fields such as cognitive neuroscience, philosophy, and artificial intelligence, **3) Train future generations of clinician scientists** with an interest in the fields of psychiatry and/or neurology. Clinician scientist candidates will be able to uniquely translate questions from the clinical setting into a laboratory research setting. In the long-term future, MPSCog expects to **contribute to innovations for the human health system and society at large.**

Figure 8.2.1 Geographical distribution of the Max Planck School of Cognition's partners.

Moreover, given the collaborative nature of the MPSCog, this program has fostered scientific communication and collaborations among faculty members from different scientific backgrounds. Such collaborations will **actively elevate cognitive research in Germany,** in line with other leading institutes abroad.

Model life-cycle of a doctoral candidate

MPSCog offers a four-year doctoral program (Figure 8.2.2). Candidates can enter one of **two tracks** that run in parallel to each other. The **regular doctoral track** has been in place since the inception of MPSCog while the **clinician scientist track** was established in September 2022. Both tracks begin with an orientation phase (first year) followed by the doctoral research phase (second-fourth years). The MPSCog regular doctoral track allows applicants to enter with bachelor's (the "fast-track" route) and/or master's degrees. The clinician scientist track requires applicants to have successfully completed their medical studies. Candidates are admitted into the doctoral program after a preliminary match with one faculty member is accomplished during the selection phase.

1. First year (orientation phase)

The **first year** of the program **is similar** for both the **regular doctoral candidates** and the **clinician scientist candidates**. That is, candidates from both tracks complete laboratory rotations and attend lectures, the latter consisting of e-learning and classroom teaching. The **laboratory rotations** aim to equip candidates with the necessary interdisciplinary knowledge and hands-on research experience via three rotations (on average) in partnering laboratories. Moreover, the rotations will aid candidates in making an informed decision about the focus of their doctoral work, as well as confirming the provisional match with the doctoral supervisor(s) for the following three years.

Overall, during the first year, the emphasis is on course work. Candidates attend online courses (after an individually tailored curriculum) during which the fundamentals of cognition are covered. In addition, candidates attend **Cognition Academies** (i.e., classroom weeks) in which these topics are presented in greater detail by international experts in the field. There are three such academies in the first year, each lasting approximately two weeks.

Fast-track candidates

Doctoral candidates entering the MPSCog program with a bachelor's degree (the 'fast-track' route) will need to obtain a master's degree before entering the doctoral phase of the MPSCog program. Therefore, in parallel to MPSCog, fast-track candidates are enrolled in one of the partner master's programs; either the **Berlin School of Mind and Brain** at *Humboldt-Universität zu Berlin* or the **Master Cognitive Neuroscience Berlin** at the *Free University of Berlin*. In the first year of the MPSCog doctoral program, fast-track candidates are asked to fulfill all requirements from one of the master's programs and from the orientation year of MPSCog. Both programs coordinate to ensure that their core elements (e.g., e-learning and lab rotations) are recognised, which facilitates the candidates' ability to attend the master's program and the orientation phase of the MPSCog. After successfully completing the master's program and orientation phase of the MPSCog, these candidates can then move to the doctoral research phase.

Clinician scientist candidates

In 2022, MPSCog established the clinician-scientist track. This newly established track offers candidates the opportunity for cutting-edge training in cognitive neuroscience research while pursuing their clinical residency training at university clinics in fields such as psychiatry and neurology. The first cohort of clinician scientist candidates started in September 2022, together with the regular fourth cohort of MPSCog candidates. Like the regular cohort of candidates, the clinician scientist candidates can also choose the laboratories where they would like to do their rotations from across the associated MPSCog partners.

2. Second to fourth year (doctoral research phase)

The second year marks the beginning of the doctoral phase, during which doctoral candidates can **focus on their research work for three years** (i.e., they do not have to attend e-learning courses nor complete further lab rotations). They are, however, still required to attend two Cognition Academies in the second and in the third years and one Academy in the fourth year. The candidates are provided with the opportunity and necessary funding to organise advanced courses, including transferable skills, for one week of each Academy. In this way, candidates are given autonomy to shape their own education on in-depth topics that they would like to explore together.

Figure 8.2.2 Synopsis of the four-year doctoral program offered by the Max Planck School of Cognition. Clinician scientists will dedicate one year of their doctoral phase (second to fourth years) to clinical training (often combined with clinical research) at a German university clinic.

During the doctoral research phase, the clinician scientist candidates will pursue their clinical residency training at university clinics, in fields such as psychiatry and neurology, while doing cutting-edge training in cognitive neuroscience research. The “clinical period” takes one year and flexibility is granted depending on how that period is distributed across the three years of the doctoral phase.

Admission to MPSCog

MPSCog accepts international bachelor’s or master’s students from a variety of areas such as artificial intelligence, biology, (cognitive) neuroscience, genetics, linguistics, mathematics, neurobiology, neuroimaging, neurology, neurophysics, philosophy, physics, psychiatry, psychology, and medicine. Since the onset of the MPSCog, the number of applications has more than tripled (from 173 in 2018 to 562 in 2022) and the acceptance rate is currently 4-5%.

Figure 8.2.3 First, second, and third cohorts of doctoral candidates attending the July 2022 Cognition Academy, Dresden.

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Doctoral Candidates

The **first cohort** of doctoral candidates joined MPSCog in **September 2019**. Since then, MPSCog has taken a **new cohort of doctoral candidates yearly**. More recently, in **September 2022**, the **first clinician scientists** joined MPSCog under the clinician scientist track.

First Cohort (started in 2019)

Doctoral candidates	Project title	Supervisor and institution
Hassan Bassam	The role of functional brain connectivity in emotion regulation in autism spectrum disorder: a graph theory approach	Isabel Dziobek, *Humboldt-Universität zu Berlin* & Daniel S. Margulies, *University of Paris*, France
Pattarawat Chormai	Explaining and understanding artificial neural networks through high-level concepts	Klaus-Robert Müller *Technische Universität Berlin*
Oliver Contier	Revealing fine-grained neural representations of objects using large-scale functional neuroimaging	Martin Hebart & Christian F. Doeller *Max Planck Institute for Human Cognitive and Brain Sciences*, Leipzig
Nina Coy	Is the oddball just an odd-one out? The predictive value of rule-violating information in human auditory process-ing	Erich Schröger *Leipzig University*
Moritz Dörfler	Deep learning in philosophy of cognitive science	Michael Pauen, *Humboldt-Universität zu Berlin*, & Arno Villringer, *Max Planck Institute for Human Cognitive and Brain Sciences*, Leipzig
Antonin Fourcade	Multimodal affective computing in naturalistic settings	Arno Villringer *Max Planck Institute for Human Cognitive and Brain Sciences*, Leipzig
Bojana Grujičić	Explaining the brain using deep neural networks – A philosophy of science perspective	Michael Pauen *Humboldt-Universität zu Berlin*
Karla Matić	How rich is visual awareness? Testing the empirical assumptions of the overflow argument	John-Dylan Haynes *Charité – Berlin University of Medicine*
Pietro Nickl*	The social dynamics of cultural evolution online	Ralph Hertwig *Max Planck Institute for Human Development*, Berlin
Leonardo Pettini	Bridging short-term and long-term memory	Christian F. Doeller, *Max Planck Institute for Human Cognitive and Brain Sciences*, Leipzig & John-Dylan Haynes, *Charité – Berlin University of Medicine*
Carolin Scholl **	n.a.	
Caedyn Stinson	Cognitive mechanisms of social sampling from memory	Ralph Hertwig *Max Planck Institute for Human Development*, Berlin

Doctoral candidates	Project title	Supervisor and institution
Rebekka Tenderra	Interindividual differences in cognitive map formation	Stephanie Theves & Christian F. Doeller *Max Planck Institute for Human Cognitive and Brain Sciences*, Leipzig

* Candidate who entered the doctoral programme with a bachelor degree. This candidate will perform all academic requirements from MPSCog first year and simultaneously finish his master at the *Berlin School of Mind and Brain, Humboldt-Universität zu Berlin.*

** Left the programme in 2020 to join a position in industry.

Second Cohort (started in 2020)

Doctoral candidates	Project title	Supervisor and institution
Tamer Ajaj	The role of moral compromises and wilful ignorance in the design of AI systems	Iyad Rahwan *Max Planck Institute for Human Development,* Berlin
Maria Azanova	Mind-body interactions in decision-making	Vadim Nikulin & Arno Villringer *Max Planck Institute for Human Cognitive and Brain Sciences,* Leipzig
Maria Badanova*	Mindfulness-based stress reduction: Outcomes, moderators and mechanisms of change	Isabel Dziobek *Humboldt-Universität zu Berlin*
Clara N. Bersch	The psychological and societal impacts of AI advisory systems and their implications for AI design	Iyad Rahwan *Max Planck Institute for Human Development,* Berlin
Giacomo Bignardi	On the etiology of aesthetic sensitivity	Simon E. Fisher, *Max Planck Institute for Psycholinguistics,* Nijmegen, the Netherlands, & Fredrik Ullén, *Max Planck Institute for Empirical Aesthetics,* Frankfurt/Main
J. Karolis Degutis	Spatial and temporal dynamics of visual working memory maintenance	John-Dylan Haynes *Charité – Berlin University of Medicine*
Susanne Haridi	How does human cognition scale? The adaptive computational and memory complexity of human cognition	Klaus Scheffler & Eric Schulz *Max Planck Institute for Biological Cybernetics,* Tübingen
Meike Hettwer	How brain organization shapes vulnerability and resilience in mental health	Simon B. Eickhoff, *Heinrich-Heine-Universität Düsseldorf & Forschungszentrum Jülich*, & Sofie L. Valk, *Max Planck Institute for Human Cognitive and Brain Sciences*, Leipzig
Janis S. Keck	Neural manifold learning	Jürgen Jost, *Max Planck Institute for Mathematics in the Sciences,* Leipzig, & Christian F. Doeller, *Max Planck Institute for Human Cognitive and Brain Sciences*, Leipzig
Johannes J. Mohn	Investigating early-life cognitive development in environmental context	Christine Heim *Charité – Berlin University of Medicine*

Doctoral candidates	Project title	Supervisor and institution
Surabhi S. Nath*	Human and machine creativity	Peter Dayan, *Max Planck Institute for Biological Cybernetics,* Tübingen
C. Ofure A. Okoh	Identification and characterization of gene variants associated with stress and trauma-induced psychiatric disorders, by use of enhancer screening tools and cellular models based on pluripotent stem cells	Elisabeth Binder *Max Planck Institute of Psychiatry,* Munich
Fabian M. Renz	Replay induced representation changes	Nicolas Schuck, *Max Planck Institute for Human Development,* Berlin, & Christian F. Doeller, *Max Planck Institute for Human Cognitive and Brain Sciences,* Leipzig
Jennifer Sander	The influence of individual differences in the quality of social interaction on concept acquisition within the first three years of life	Caroline Rowland *Max Planck Institute for Psycholinguistics, Nijmegen,* the Netherlands
M. Hashim Satti	Effect of anxiety on learning under uncertainty and varying levels of threat	Hauke Heekeren *Free University of Berlin*
Robert Scholz	Principles of neural network organization that enable the emergence of complex functions in spatially defined regions of the brain	Erich Schröger, *Leipzig University,* & Daniel S. Margulies, *University of Paris,* France
John Tuff	The action control system in the avian brain	Onur Güntürkün *Ruhr-Universität Bochum*

* Candidates who entered the doctoral programme with a bachelor degree. These candidates will perform all academic requirements from MPSCog first year and simultaneously finish their master at the *Berlin School of Mind and Brain, Humboldt-Universität zu Berlin.*

Third Cohort (started in 2021)

Doctoral candidates	Project title	Supervisor and institution
Rena Bayramova	Replay strategies for hierarchical planning	Christian F. Doeller *Max Planck Institute for Human Cognitive and Brain Sciences,* Leipzig
Jorik D. Elberse	The glymphatic system as the molecular foundation of sleep-mediated neuroprotection against Alzheimer's disease	Simon Eickhoff *Heinrich-Heine-Universität Düsseldorf & Forschungszentrum Jülich*
Lioba Enk	Respiratory modulation of brain activity and its contribution to somatosensory perception	Arno Villringer *Max Planck Institute for Human Cognitive and Brain Sciences,* Leipzig
Ole Goltermann	Pushing the boundaries of neuroimaging techniques in pain and pain expectation	Christian Büchel *Universitätsklinikum Hamburg-Eppendorf*
Max A. B. Hinrichs	Replay and social decision-making	Christian F. Doeller *Max Planck Institute for Human Cognitive and Brain Sciences,* Leipzig

Doctoral candidates	Project title	Supervisor and institution
Sophie Holtz	The songsystem of the Seba's short tailed bat, Carollia perspicillata: Studying behavioural and neurobiological foundations of vocal production in bats	Constance Scharff *Free University of Berlin*
Fabian Kamp	Neural dynamics of adaptive cognition	Ulman Lindenberger *Max Planck Institute for Human Development,* Berlin
Yuliya Kovalchuk	Use-dependent neuroplasticity in the female genital cortex	Christine Heim *Charité – Berlin University of Medicine*
Debottam Kundu	Communication and phase synchronization in the mice brain	Jürgen Jost, *Max Planck Institute for Mathematics in the Sciences,* Leipzig, & Peter Dayan, *Max Planck Institute for Biological Cybernetics,* Tübingen
Jialin Li	Neural and computational mechanisms of pain-related learning processing	Onur Güntürkün, *Ruhr-Universität Bochum*, & Ulrike Bingel, *Universitätsklinikum Essen*
Marie-Helen Link*	n.a.	
Yulia Nurislamova	Brain networks and their role in visual cognition	Rosanne Rademaker, *Ernst Strüngmann Institute for Neuroscience,* Frankfurt/Main, & Christian F. Doeller, *Max Planck Institute for Human Cognitive and Brain Sciences,* Leipzig
Konstantin Offer	Deliberate ignorance as a strategic device in social interactions	Ralph Hertwig *Max Planck Institute for Human Development,* Berlin
Alina E. C. Panzel	Cognitive and affective modulations of pain in healthy individuals and patients with chronic pain	Christian Büchel *Universitätsklinikum Hamburg-Eppendorf*
Bianca Serio	Principles of brain organization	Simon Eickhoff, *Heinrich-Heine-Universität Düsseldorf & Forschungszentrum Jülich,* & Sofie L. Valk, *Max Planck Institute for Human Cognitive and Brain Sciences,* Leipzig
Alexandrina Vasilichi	A computational and physiological modelling account of interoceptive processing and brain-body interactions	Peter Dayan, *Max Planck Institute for Biological Cybernetics,* & Micah Allen, *Aarhus University,* Denmark
Chih Yeh	Bilingualism in the developing brain	Caroline Rowland *Max Planck Institute for Psycholinguistics,* Nijmegen, the Netherlands

* Left the programme in 2022 to join a position in industry.

Fourth Cohort (started in 2022)

Doctoral candidates	Project title	First lab rotation
Asli Akdeniz-Karatay	Clinician scientist track	Arno Villringer *Max Planck Institute for Human Cognitive and Brain Sciences*, Leipzig
Anne Felsenheimer		Isabel Dziobek *Humboldt-Universität zu Berlin*
Benjamin Hänisch		Andreas Fallgatter *Universitätsklinikum Tübingen*
Leon D. Lotter		Simon B. Eickhoff *Heinrich-Heine-Universität Düsseldorf & Forschungszentrum Jülich*
Anastasiia Asmolova*	Regular doctoral track	Bachelor candidate at *Free University of Berlin**
Valeria Baragona		Erich Schröger *Universität Leipzig*
Berfin Bastug		Jürgen Jost *Max Planck Institute for Mathematics in the Sciences*, Leipzig
Thomas Graham		Ralph Hertwig & Bernhard Spitzer *Max Planck Institute for Human Development*, Berlin
Joshua N. Hindmarsh		Christine Heim *Charité – Berlin University of Medicine*
Abhay Koushik		Arno Villringer *Max Planck Institute for Human Cognitive and Brain Sciences*, Leipzig
Tiantian Li*		Bachelor candidate at *Free University of Berlin**
Marie M. G. Michael		Daniel B. M. Haun *Max Planck Institute for Evolutionary Anthropology*, Leipzig
Alexander Y. Platt		Patrick Haggard *UCL*, UK
Eva-Madeleine Schmidt		Isabel Dziobek *Humboldt-Universität zu Berlin*
Marianna E. Schmidt		Nikolaus Weiskopf *Max Planck Institute for Human Cognitive and Brain Sciences*, Leipzig
Viktor Studenyak		Klaus-Robert Müller *Technische Universität Berlin*
Annika Werwach		Christine Heim *Charité – Berlin University of Medicine*
Deniz Yilmaz		Peter Falkai *Ludwig-Maximilians-Universität Munich*
Leonardo Zeine Mendes de Souza		David Poeppel *Ernst Strüngmann Forum for Neuroscience*, Frankfurt/Main

* Candidates who entered the doctoral programme with a bachelor degree. These candidate will perform all academic requirements from MPSCog first year and simultaneously finish their masters at *Free University of Berlin*.

Note. Candidates of the fourth cohort were only admitted into the doctoral programme after a preliminary match with one faculty member was accomplished. The laboratory rotations in the first year aid candidates in confirming the provisional match with the doctoral supervisor(s) for the following three years.

Faculty Members

The initial proposal of MPSCog and its founding faculty members was developed during the original School proposal by Arno Villringer. All 44 members are world-renowned scientists with diverse scientific backgrounds and yet overlapping research interests. The MPSCog faculty members at the Max Planck Institute for Human Cognitive and Brain Sciences are presented below. Information on the remaining 40 MPSCog faculty members, and their respective academic institutions, can be found here.

Professor Christian F. Doeller, Department of Psychology

Professor Angela D. Friederici, Department of Neuropsychology

Professor Arno Villringer, Department of Neurology

Professor Nikolaus Weiskopf, Department of Neurophysics

Coordination Team

The coordination team (Figure 8.2.4.) and the logistic hub of MPSCog are situated at the Max Planck Institute for Human Cognitive and Brain Sciences. Overall, the coordination team supports the candidates and fellows so that they can fully dedicate themselves to their coursework and research.

Figure 8.2.4 The MPSCog coordination team: Arno Villringer (speaker), Nicole Lorenz, Ewa Koper, Matthias Bolz, Natacha Mendes, and Mario Fischer (from right to left, missing: Tomoko Koda)

8.3

IMPRS on Cognitive NeuroImaging

INTERNATIONAL MAX PLANCK RESEARCH SCHOOL

The International Max Planck Research School (IMPRS) on Cognitive NeuroImaging provides world-class training for doctoral researchers and aims to nurture the next generation of scientists in the highly interdisciplinary and fast-paced fields of human neuroscience, particularly cognitive neuroscience and neuroimaging. The research field spans a wide range, from applications in various fields of human neuroscience and cognition to the development of novel methods in neuroimaging, computational neuroscience, and artificial intelligence. To cover this broad spectrum and provide top scientific quality, the IMPRS on Cognitive NeuroImaging integrates international excellence through a partnership of the Max Planck Institute for Human Cognitive and Brain Sciences (MPI CBS) and Leipzig University (LU). These two main partners are joined by additional faculty from the associated partners TU Dresden (TUD) and UCL (UCL).

The IMPRS on Cognitive NeuroImaging is the PhD program succeeding the IMPRS on Neuroscience of Communication. The studies of the first cohort will start in fall 2023. We are currently in the process of recruiting applicants for this cohort and aim to select 20 – 25 candidates to start the new program.

Faculty

The founding IMPRS faculty consists of the directors of MPI CBS, the independent W2 research group leaders at MPI CBS, as well as four Early Career Researchers (ECR) from MPI CBS. Additionally, renowned LU professors with proven PhD training records related to the scope of the graduate school were invited to become founding members of the faculty of the IMPRS on Cognitive NeuroImaging. Furthermore, selected scientists from our associated partners TUD and UCL are included in the faculty. The IMPRS aims to admit further ECR faculty at a later stage. Members of the IMPRS faculty participate in: the recruitment process of new IMPRS doctoral researchers, Thesis Advisory Committees (TAC), the biannual summer school of the IMPRS on Cognitive NeuroImaging, and teaching the core curriculum.

The school also aims to create a positive, nurturing, and excellent supervision culture. Accordingly, the IMPRS on Cognitive NeuroImaging will offer professional development of supervisors and mentoring opportunities, especially for ECR faculty members. Firstly, each ECR faculty member has the possibility to be assigned to a mentor (experienced senior Faculty, ideally from a partner institution) who will offer general support, and who will be approachable for consultation in challenging supervision situations. Secondly, IMPRS will offer a monthly supervisors' lunch. During such lunches a typical challenging supervision situation will be addressed and discussed among peers.

Module I: Cognitive Neuroscience

Dr R. G. Benoit, MPI CBS, MPRG "Adaptive Memory"

Professor C. F. Doeller, MPI CBS, Dept of Psychology

Professor A. D. Friederici, MPI CBS, Dept of Neuropsychology

Professor T. Goschke, TU Dresden,Institute for General Psychology

Dr C. Grosse Wiesmann, MPI CBS, Minerva fast-track group "Milestones of Early Cognitive Development"

Professor P. Haggard, Institute of Cognitive Neuroscience, UCL, UK

Professor M. N. Hebart, MPI CBS, MPRG "Vision and Computational Cognition" & Justus-Liebig University, Giessen

Professor S.-C. Li, TU Dresden, Institute of Educational and Developmental Psychology

Dr L. Meyer, MPI CBS, MPRG "Language Cycles"

Professor M. Schönwiesner, LU, Dept of General Zoology and Neurobiology

Professor E. Schroeger, LU, Dept of Cognitive and Biological Psychology

PD Dr M.A. Skeide, MPI CBS, Dept of Neuropsychology, RG "Learning in Early Childhood"

Dr S. Theves, MPI CBS, Minerva Fast Track Group Neural Codes of Intelligence

Dr S. L. Valk, MPI CBS, OHG "Cognitive Neurogenetics"

Module II: Clinical and Translational Neuroscience

Professor I. Bechmann, LU, Institute for Anatomy

Professor J. Classen, LU, Dept of Neurology, RG Motor and Plasticity

Dr F. Eippert, MPI CBS, MPRG "Pain Perception"

Professor G. Hartwigsen, LU and MPI CBS, LMRG „Cognition and Plasticity"

Professor P. Kanske, TU Dresden, Institute of Clinical Psychology and Psychotherapy

Module II: Clinical and Translational Neuroscience

Professor M. Morawski, LU, Paul-Flechsig-Institute for Brain Research

Professor H. Obrig, LU, Day Clinic for Cognitive Neurology, and MPI CBS, Dept of Neurology

PD Dr J. Sacher, MPI CBS, Minerva Research Group - EGG (Emotions & neuroimaGinG)-Laboratory

Professor D. Saur, LU, Dept of Neurology, Language and Aphasia Lab

Professor M. L. Schroeter, LU, Day Clinic of Cognitive Neurology, and MPI CBS, Dept of Neurology

Professor K. von Kriegstein, TU Dresden, Institute for General Psychology, Biopsychology, and Methods of Psychology

Professor A. Villringer, MPI CBS, Dept of Neurology

Module III: Development of Neuroimaging and Modeling Methods

Professor M. Bogdan, LU, Dept of Computer Engineering

Professor S. Kiebel, TU Dresden, Institute for General Psychology, Biopsychology, and Methods of Psychology

Dr E. Kirilina, MPI CBS, Dept of Neurophysics, RG MRI Biophysics

Professor T. R. Knösche, MPI CBS, Brain Networks Unit

Dr B. Maess, MPI CBS, Brain Networks Unit

Professor H. E. Möller, MPI CBS, Nuclear Magnetic Resonance Unit

Dr N. Scherf, MPI CBS, Methods and Development Group Neural Data Science and Statistical Computing

Professor G. Scheuermann, LU, Dept of Image Processing

Professor R. Valiullin, LU, Felix Bloch Institute für Solid State Physics

Professor N. Weiskopf, MPI CBS, Dept of Neurophysics

Please note: LMRG = Lise Meitner Research Group, MPRG = Max Planck Research Group, OHG = Otto Hahn Group, RG = Research Group

Table 8.3.1 Members of the faculty of the IMPRS on Cognitive NeuroImaging

Structure of the Graduate School

The IMPRS on Cognitive NeuroImaging covers the highly interdisciplinary and fast-paced fields of cognitive neuroscience, clinical and translational neuroscience, and neuroimaging. The school comprises three modules for training and research: 1) Cognitive Neuroscience, 2) Clinical and Translational Neuroscience, and 3) Development of Neuroimaging and Modelling Methods. Each faculty member is assigned to one module based on their research profile.

Research Topics

Doctoral researchers will be exposed to cutting-edge research in training and projects. The field of cognitive neuroimaging is highly interdisciplinary and rapidly developing. The IMPRS on Cognitive NeuroImaging is one of the very few graduate schools covering the field comprehensively, particularly considering neuroscientific applications and methods alike. The school capitalises on the unique position of the MPI CBS and its partners to offer excellent training and opportunities for cutting-edge research projects.

Doctoral researchers will benefit from a unique infrastructure enabling all types of cognitive neuroimaging experiments. The IMPRS on Cognitive NeuroImaging covers all major imaging and neurostimulation methods and their appropriate use. This includes: magnetic resonance imaging (MRI) (including access to one of only four Connectom MRI systems worldwide for diffusion imaging), electroencephalography (EEG), magnetoencephalography (MEG), positron emission tomography (PET)-MRI, near-infrared spectroscopy (NIRS), transcranial magnetic stimulation (TMS), and direct current stimulation (tDCS). On top of this, the school offers high performance computing facilities for computational modelling and data analysis.

Teaching and Supervision

The IMPRS on Cognitive NeuroImaging aims to offer its students a cutting-edge educational program qualifying them for an excellent research career in cognitive neuroimaging. Therefore, the school offers a wide range of theoretical and methodological training opportunities in this rapidly evolving field of research. In addition to basic courses, the school will offer advanced courses tailored towards the interest and needs of doctoral researchers for the PhD project.

Lectures will be complemented by practical exercises, summer schools, retreats, and workshops. The IMPRS on Cognitive NeuroImaging will also offer hybrid teaching, which allows both doctoral researchers and faculty to work and contribute remotely and to participate from all partner sites. In addition, course content will be digitised to increase the flexibility for doctoral researchers to conduct their thesis work, participate in lab visits, and learn/revise according to their preferences or needs. A major focus of the IMPRS on Cognitive NeuroImaging curriculum is the flipped classroom concept to increase students' engagement and problem-solving abilities. The school also aims to integrate novel training technology, such as virtual and embedded learning tools.

Importantly, the school strives for diversity in the doctoral researcher cohorts (concerning gender, internationality, and scientific/personal background). In order to achieve this, we emphasise equal opportunities in all respects. Individual development plans (IDP) for each doctoral researcher will take diverse academic backgrounds into account and help to adapt the training to each individual student's needs.

Each IMPRS doctoral researcher will be supervised by a Thesis Advisory Committee (TAC) composed of 1 - 2 supervisor(s) and two additional advisors. TAC members are mainly IMPRS faculty members, but may also include one external

TAC member. The doctoral researchers and supervisor(s) decide jointly on the advisors. Once the TAC is assigned, the doctoral researcher and their TAC sign a supervision agreement, documenting expectations and obligations for all parties. The TAC meets at least once a year.

Admission to the School

Candidates for the IMPRS on Cognitive NeuroImaging will be recruited on an annual basis through an international call for applications. Candidates are expected to hold an excellent master's degree (or equivalent) in a wide spectrum of potential disciplines, such as cognitive neuroscience, computational neuroscience, translational neuroscience, clinical neuroscience, psychology, medicine, neurobiology, computer science, engineering, mathematics, physics, neuroimaging, biochemistry, or related fields. The study program should include an extensive original research project and a written thesis in one of those disciplines. Candidates are evaluated through a 3-phase process (pre-evaluation by the coordinator, evaluation by faculty, admission interviews). In addition, doctoral researchers who already have a PhD position with one of the faculty members can join the IMPRS on Cognitive NeuroImaging throughout the year. As with all candidates, doctoral researchers entering via this route have to pass an admission interview, attended by at least three faculty members (including one board member). In total, the IMPRS expects to admit between 20 and 25 doctoral researchers per year.

More details about the graduate program can be found on the school's website.

Coordination Team

Spokesperson
Professor Nikolaus Weiskopf

Director, Department of Neurophysics
Email: weiskopf@cbs.mpg.de

Coordinator
Dr Veronika Krieghoff

Email: vkrieghoff@cbs.mpg.de

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LISTS OF EMPLOYEES

DEPARTMENT OF NEUROPSYCHOLOGY

Director: Professor Dr Dr h.c. Angela D. Friederici

Research Group Leaders

Dr Claudia Männel (14) (*)

Group Leaders

Dr Emiliano Zaccarella

Scientific Researchers and Postdocs

Dr Alfred Anwander (35)
Dr Yannick Becker (12)
Dr Philipp Berger (14) (*)
Dr Luyao Chen (*)
Dr Cornelius Eichner (87)
Dr Guillermo A. Gallardo Diez (*)
Dr Tomás Barato Goucha (*)
Dr Thomas C. Gunter
Dr Cody McCants (in cooperation with Newcastle University, UK) (*)
Dr Michael Paquette (14)
Dr Daniela Sammler (14) (*)
Dr Gesa Schaadt (14) (*)
Dr Michael A. Skeide (**)
Dr Stan (Constantijn Laurens) van der Burght (*)

Doctoral Candidates

Helyne Adamson (*)
Vincent Ka Ming Cheung (Dr rer. nat. since 2021) (*)
Pei-Ju Chien (Dr rer. nat. since 2022) (*)
Gisela Govaart (16)
Cheslie Klein
Matteo Maran
Giorgio Papitto (14)
Mariella Paul (16) (Dr rer. nat. since 2022) (*)
Elena Pyatigorskaya
Ting Qi (Dr rer. nat. since 2020) (*)
Inés Roho
Joëlle Schroën
Matthias Schwendemann (Dr phil. since 2023) (*)
Patrick Trettenbrein
Stan (Constantijn Laurens) van der Burght (Dr rer. nat. since 2021) (*)
Xuehu Wei (14)

Personal Assistants

Anne Dornfeld (maternity cover) (*)
Margund Greiner
Nicole Lorenz (maternity cover) (**) (shared position with Max Planck School of Cognition)
Melanie Trümper

Technical and Administrative Assistants

Ulrike Barth
Heike Boethel
Katja Friedrich de Guzmán
Martina Dietrich (14)
Maren Grigutsch
Sven Gutekunst
Cornelia Henschel (*)
Kristiane Klein
Katrin Ina Koch
Christina Ruegen (*)
Michael Vollmann (14) (**)

Guest researchers

Dr Luyao Chen (College of Chinese Language and Culture Beijing Normal University, Beijing, China)
Professor Dr Torrey Loucks (*) (University of Alberta, Canada)

DEPARTMENT OF NEUROPSYCHOLOGY

Director: Professor Dr Dr h.c. Angela D. Friederici

Meghan Puglia (*) (University of Virginia, USA)

Jessica Ramos-Sanchez (*) (Radboud University, Donders Institute for Brain, Cognition, and Behaviour, Nijmegen, the Netherlands)

Vanessa Ruiz-Stovel (*) (Jardines Universidad Mexico)

Professor Dr Annett Schirmer (University of Hongkong)

Swetlana Schuster (*) (University Oxford, UK)

Anna Tendera (*) (University of Alberta, Canada)

Dr Guido Seddone (*) (Universitá di Parma, Italy)

Ivonne Weyers (*) (University of Osnabrueck, Germany)

Research Associates

Professor Dr Gustavo Deco (*) – Theoretical and Computational Group, Universitat Pompeu Fabra/ICREA, Barcelona, Spain

Dr Manuela Friedrich – Department of Psychology, Humboldt-University Berlin, Germany

Professor Dr Hyeon-Ae Jeon – Department of Brain & Cognitive Sciences, Daegu Gyeongbuk Institute of Science & Technology (DGIST), South Korea

Professor Dr Stefan Koelsch (*) – Department of Biological and Medical Psychology, Faculty of Psychology, University in Bergen, Norway

Professor Dr Claudia Männel – Department of Audiology and Phoniatrics, Charité – Berlin University of Medicine, Germany

PD Dr Daniela Sammler (*) – Research Group Neurocognition of Music and Language, Max Planck Institute for Empirical Aesthetics, Frankfurt/Main, Germany

Former Researchers and PostDocs

Dr Philipp Berger – Frühe Hilfe Leipzig e.V. Zentrum für kindliche Entwicklung, Leipzig, Germany

Professor Dr Claudia Männel – Department of Audiology and Phoniatrics, Charité – Berlin University of Medicine, Germany

PD Dr Daniela Sammler –Research Group Neurocognition of Music and Language, Max Planck Institute for Empirical Aesthetics, Frankfurt/Main, Germany

Professor Dr Gesa Schaadt – Department of Education and Psychology, Free University of Berlin, Germany

Dr Luyao Chen – College of Chinese Language and Culture Beijing Normal University, Beijing, China

Dr Guillermo A. Gallardo Diez – Pagoda, Barcelona, Spain

Dr Cody McCants – Newcastle University, UK

Dr Stan (Constantijn Laurens) van der Burght – Psychology of Language Department, Max Planck Institute for Psycholinguistics, the Netherlands

Former PhD Students

Helyne Adamson – VineForecast, Göttingen, Germany

Vincent Ka Ming Cheung – Music Dynaformics Lab, Sony Computer Science Laboratories, Inc. (SonyCSL), Tokyo, Japan

Pei-Ju Chien – job-seeking

Mariella Paul – Faculty of Biology and Psychology, The University of Göttingen, Germany

Ting Qi – Department of Neurology, University of California, San Francisco, CA, USA

Matthias Schwendemann – Herder Institute, Leipzig University, Germany

(12) Fyssen Foundation, France
(14) German Research Foundation (DFG)
(16) Graduate School of Mind and Brain, Humboldt University Berlin, Germany/funded by German Research Foundation (DFG)
(35) European Union, ERC Advanced Grant, funded by European Research Council
(87) Inter-institutional research project "Hominoid Brain Connectomics", Coop. with MPI EVA

(*) Left the institute during 2020–2022
(**) Left the department during 2020–2022

DEPARTMENT OF NEUROLOGY

Director: Professor Dr Arno Villringer

Research Group Leader

Professor Dr Vadim Nikulin

Professor Dr Julia Sacher (**) (until July 2022 Minerva Research Group, since August 2022 group leader in cooperation with Leipzig University – reports independently, Research Report)

Group Leaders

Professor Dr Thomas H. Fritz

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Professor Dr Annette Horstmann (*) (17, 48) (in cooperation with University of Helsinki)

Professor Dr Hellmuth Obrig (in cooperation with Leipzig University)

Professor Patrick Ragert, PhD (in cooperation with Leipzig University)

Professor Dr Dr Matthias L. Schroeter (74) (in cooperation with Leipzig University)

PD Dr Bernhard Sehm

PD Dr Veronica Witte (**) (48) (in cooperation with Leipzig University)

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Dr Anahit Babayan

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Susan Prejawa (17, 48) (*) (in cooperation with Leipzig University)

Sandra Zurborg, PhD

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Ramona Menger

Maria-Josephine Paerisch (*)

Kirsten Scharr (49) (*)

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Sylvia Stasch

Annett Wiedemann

Senior Researchers and Postdocs

Dr Zeynep Akbal

Dr Nazife Ayyildiz

Dr Ekaterina Chekha

Dr Christopher Gundlach (in cooperation with Leipzig University)

Dr Samyogita Hardikar

Dr Lieneke Janssen (in cooperation with Leipzig University)

Dr Marie-Theres Meemken (in cooperation with Leipzig University)

Dr Till Nierhaus (*)

Dr Maryna Polyakova (11) (19) (in cooperation with Leipzig University)

Doctoral Candidates (at Leipzig University, unless specified differently)

Ismet Zeynep Akbal (with University of Potsdam, Dr phil. since 2022)

Esra Al (*) (at Charité – Berlin University of Medicine, Dr phil. since 2022)

Anastassia Asmolova

Maria Azanova (95)

Blazej Baczkowski (*) (Dr rer. nat. since 2021)

Tommaso Ballarini (*) (Dr rer. nat. since 2020)

Seyma Bayrak

DEPARTMENT OF NEUROLOGY

Director: Professor Dr Arno Villringer

Julia Belger (30, 19)

Frauke Beyer (48) (*) (Dr rer. med. since 2020)

Maria Bloechl-Sevinchan (in cooperation with Münster University, Dr rer. nat. since 2021)

Elena Cesnaite (*)

Xiuhui Chen (at Charité – Berlin University of Medicine)

Yonghao Chen

Miray Erbey (16)

Aimee Arely Flores (at Charité – Berlin University of Medicine & Einstein Center for Neuroscience Berlin & Bernstein Center for Computational Neuroscience)

Carina Forster (in cooperation with Charité – Berlin University of Medicine & Einstein Center for Neuroscience Berlin & Bernstein Center for Computational Neuroscience)

Antonin Fourcade (95) (Max Planck School of Cognition)

Moritz Gerster (at Charité – Berlin University of Medicine)

Magdalena Gippert

Khosrov Alexander Grigoryan (19)

Martin Grund (*) (Dr rer. nat. since 2022)

Hendrik Hartmann (30,48) (in cooperation with University of Helsinki)

Nadine Herzog (19, 30)

Simon Hofmann (30,19) (at Technical University, Berlin)

Fivos Iliopoulos (at Charité – Berlin University of Medicine & LIFE International Max Planck Research School, Berlin)

Mina Jamshidi Idaji (19) (*) (Dr Ing. since 2022, at Technical University, Berlin)

Anna-Thekla Jaeger (23)

Benjamin Kalloch (19) (**) (Dr rer. nat. since 2021)

Nikolai Kapralov (95)

Dimitra-Maria Kandia (19) (*)

Rouven Kenville (*) (Dr rer. med. since 2021)

Felix Klotzsche (11)

Natalie Kohler (*)

Jana Kube (17) (*) (Dr rer. nat. since 2021)

Deniz Kumral (*) (Dr rer. medic. since 2021, at Charité – Berlin University of Medicine)

Carolin Lewis (at University of Tübingen)

Tom Maudrich (*) (Dr rer. med. since 2021) (at Sports Faculty, Leipzig University)

Evelyn Medawar (16) (*)

Marie-Theres Meemken (*) (Dr rer. med. since 2020)

Eóin Molloy (*) (Dr rer. nat. since 2022)

Max Archibald Montgomery (at University of Ghent)

Toni Muffel (55) (*)

Madeleine Ordnung (23) (*)

Eleni Panagoulas (at Charité – Berlin University of Medicine in cooperation with Berlin School of Mind and Brain)

Katja Paul (76) (*) (PhD since 2022) (at University of Groningen, NL)

Daniéle Pino

Maria Poessel (48) (*) (Dr rer. nat. since 2022)

Josefin Roebbig (*)

Firat Sansal (16) (*)

Lina Schaare (19, 49) (**) (Dr rer. med. since 2020)

Lydia Schneider (**) (MPG Stiftungsgelder)

Pei-Cheng Shih (19) (*) (Dr rer. med. since 2021)

Tilman Stephani (19)

Paul Steinfath (19)

Alina Studenova

Ronja Thieleking (14)

Hsing-Fen Tu (19, 83) (*)

Marie Uhlig (19)

Cornelia van Scherpenberg (16) (*) (Dr rer. med. since 2022)

Meghedi Vartanian (19) (in cooperation with Leipzig University)

Maria Waltmann (30, 19)

Juliane Weicker (*) (Dr rer. nat. since 2021) (in cooperation with Leipzig University)

DEPARTMENT OF NEUROLOGY

Director: Professor Dr Arno Villringer

Kathleen Wiencke (48)
Juanli Zhang (67)
Georgi Zarubin (19) (*)
Rachel Zsido (19)

MD Students (at Medical Faculty of Leipzig University, unless specified differently)

Nathalie Beinhölzl
Josef Bormann (*) (Dr med. since 2021)
Nora Breuer
Luise Claaß (*)
Lina Eisenberg
Konrad Endres
Maria Felber
Leila Gajieva
Johanna Girbardt
Annegret Glathe
Linda Grasser
Matthias Heinrich (*) (Dr med. since 2022)
Stella Kunzendorf (*) (Dr med. since 2022, at Charité – Berlin University of Medicine)
Laurenz Lammer
Mathis Lammert
Lerato Maleka (*) (Dr med. since 2020)
Diaa Masri
Larissa Pauli (*) (Dr med. since 2022)
Claudia Predel
Franziska Rausch (*) (Dr med. since 2021)
Dr Janis Reinelt (*) (Dr med. since 2021)
Jana Schurig (neé Grothe)
Seidel-Marzi, Oliver (*) (Dr med. since 2021)
Kevin Thomas (*) (Dr med. since 2020)
Emmy Töws
Sten Hannes Voigtländer
Charlotte Wiegank
Jonas Witt
Matthias Wagner

Guest Researchers

Dr Pierre-Louis Bazin – University of Amsterdam, the Netherlands
Dr Frauke Beyer – Leipzig University, Germany
Dr Maria Bloechl-Sevinchan – University of Münster, Germany
Dr Christopher Gundlach – Leipzig University, Germany
Dr Martin Grund – VDI/VDE Innovation + Technik GmbH, Leipzig, Germany
Dr Lydia Hellrung – University Hospital Zurich, Switzerland
Dr Rouven Kenville – Leipzig University, Germany
Dr Elisabeth Kaminski – Leipzig University, Germany
Dr Tom Maudrich – Leipzig University, Germany
Professor Hadas Okon-Singer – University of Haifa, Israel
Professor Smadar Ovada-Caro – University of Haifa, Israel
Dr Birol Taskin – Charité – Berlin University of Medicine, Germany

Research Associates

Dr Lorenz Deserno – Psychiatry and Ageing Research, Max Planck UCL Centre for Computational, London, UK
Professor Dr Bogdan Draganski – Centre Hospitalier Universitaire Vaudois (CHUV), University of Lausanne, Switzerland
Professor Andreas Melzer (*) – Innovation Center Computer Assisted Surgery (ICCAS), Leipzig University, Germany
Professor Dr Hellmuth Obrig – Clinic of Cognitive Neurology, Leipzig University Hospital, Germany
Professor Michael Pauen – Berlin School of Mind and Brain, Humboldt University Berlin
Professor Patrick Ragert – Institute for General Kinesiology and Exercise Sciences, Faculty of Sport Science, Leipzig University, Germany

DEPARTMENT OF NEUROLOGY

Director: Professor Dr Arno Villringer

Professor Dr Florian Schlagenhauf (*) – Department of Psychiatry and Psychotherapy (CCM), Charité – Berlin University of Medicine, Germany

Christopher Steele, PhD – Department of Psychology Concordia University, Montreal, Canada

Clinic of Cognitive Neurology, Leipzig University Hospital

Professor Dr Hellmuth Obrig

Professor Dr Julia Sacher

Dr Annerose Engel

Dr Sabine Herzig

Danièle Pino

Frank Regenbrecht

Professor Dr Dr Matthias L. Schroeter

Dr Juliane Weicker

PD Dr Veronica Witte

Former Researchers and Postdocs

Mehmet Mert Akbal – Visual artist in cognitive neuroscience

Professor Dr Stefan Haufe – Charité – Berlin University of Medicine, Germany

Professor Dr Annette Horstmann – University of Helsinki, Finland

Professor Dr Jane Neumann – University Jena, Germany

Dr Tilmann A. Klein – Otto von Guericke University Magdeburg, Germany

Dr Ulrike Lachmann – Max Planck School of Cognition

Dr Natacha Mendes – Max Planck School of Cognition

Professor Dr Claudia Maennel – Charité – Berlin University of Medicine, Germany

Mauricio J. D. Martins – PhD, University of Vienna, Austria

Dr Till Nierhaus – Free University Berlin, Germany

Dr Smadar Ovadia-Caro – University of Haifa, Israel

Professor Dr Gesa Schaadt – Free University of Berlin, Germany

Former PhD Students

Dr Esra Al (*) – PostDoc, Columbia University, US

Dr Blazej Baczkowsk – PostDoc, University of Hamburg, Germany

Dr Tommaso Ballarini – Sidekick Health, Berlin, Germany

Dr Frauke Beyer – PostDoc, University of Bordeaux, France

Dr Maria Bloechl-SevinchanPostDoc, Charité – Berlin University of Medicine, Germany

Elena Cesnaite – PostDoc, University of Münster, Germany

Dr Martin Grund (*) VDI/VDE Innovation + Technik GmbH, Leipzig, Germany

Dr Nicole Hudl – Group leader, Technical University of Chemnitz, Germany

Dr Mina Jamshidi Idaij – PostDoc, Technical University of Berlin, Germany

Dr Benjamin Kalloch PostDoc – Methods and Development Group Brain Networks, Max Planck Institute of Human Cognitive and Brain Sciences, Leipzig, Germany

Dimitra Kandia – Charité – Berlin University of Medicine, Germany

Dr Rouven Kenville – PostDoc, Leipzig University, Germany

Dr Jana Kube – Thiem-Research GmbH, Cottbus, Germany

Dr Deniz Kumral – PostDoc, Albert Ludwigs University Freiburg, Germany

Lilian Yee Teng Lee – Postdoc, (in cooperation with Leipzig University)

Dr Tom Maudrich – PostDoc, Leipzig University, Germany

Dr Marie-Theres Meemken – PostDoc, Leipzig University, Germany

Evelyn Medawar – PostDoc, Aicura medical GmbH, Berlin, Germany

Dr Eóin Molloy – PostDoc, German Center for Neurodegenerative Diseases (DZNE), Magdeburg, Germany

Toni Muffel – Recovery Cat, Berlin, Germany

Madeleine Ordnung – Leipzig University, Germany

Katja Isabel Paul – University of Groningen, the Netherlands

DEPARTMENT OF NEUROLOGY

Director: Professor Dr Arno Villringer

Dr Maria Poessel

Dr Janis Reinelt – Aicura medical GmbH, Berlin, Germany

Josefin Roebbig – Leipzig University, Germany

Firat Sansal

Dr Lina Schaare – PostDoc, Otto Hahn Group Cognitive Neurogenetics, Max Planck Institute of Human Cognitive and Brain Sciences, Leipzig, Germany

Dr Cornelia v. Scherpenberg – VDI/VDE Innovation + Technik GmbH, Munich, Germany

Dr Pei-Cheng Shih – PostDoc, National Yang Ming Chaio Tung University, Taipei, Taiwan

Hsing-Fen Tu – Uppsala University, Sweden

Dr Juliane Weicker – PostDoc, Leipzig University, Germany

Georgy Zarubin – Leipzig University, Germany

(11) Federal Ministry of Education and Research (BMBF), Germany
(14) German Research Foundation (DFG)
(16) Berlin School of Mind and Brain, Humboldt University Berlin, Germany/funded by Germany Research Foundation (DFG)
(17) Integrated Research and Treatment Center (IFB) AdiposityDiseases, Leipzig University Hospital, Germany
(19) IMPRS NeuroCom, Leipzig, Germany
(22) Leipzig Research Center for Civilization Diseases (LIFE) funded by European Union and State of Saxony
(23) MaxNetAging Research School, Germany
(30) Leipzig University, Germany
(47) FAZIT Foundation, Germany
(48) CRC Obesity Mechanism, Leipzig University, Germany
(49) Branco Weiss Foundation, Germany
(55) IMPRS LIFE Max Planck Institute for Human Development, Berlin, Germany
(67) Charité – Berlin University of Medicine, Germany
(71) German Center for Neurodegenerative Diseases Magdeburg
(72) University of Magdeburg
(73) McGill University, Toronto, Canada
(74) Michael J. Fox Foundation
(75) Bundesinstitut für Sportwissenschaft
(76) Ubbo Emmius Foundation, University of Groningen, the Netherlands
(80) Studienstiftung des deutschen Volkes
(81) Konrad Adenauer Foundation
(83) Musikkindergarten e.V. Berlin
(85) Foundation of Max Planck Society

(*) Left the Institute during 2020–2022
(**) Left the department during 2020–2022

DEPARTMENT OF NEUROPHYSICS

Director: Professor Dr Nikolaus Weiskopf

Research Group Leader

PD Dr Stefan Geyer

Dr Evgeniya Kirilina

Senior Researchers and Postdocs

Dr Denis Chaimow

Luke J. Edwards, PhD (77) (78)

Dr Saskia Helbling (8)(*)

Dr Mikhail Kozlov

Dr Tobias Leutritz (78) (*)

Dr Ilona Lipp (87)

Dr Shubhajit Paul (11) (77) (*)

Kerrin J. Pine, PhD (11) (77) (78)

Dr Tilo Reinert

Dr Patrick Scheibe (77) (78)

Dr Robert Trampel (joint position, shared with NMR group)

Doctoral Candidates

Fakhereh Movahedian Attar

David Malte Brammerloh

Juliane Damm (14)

Jonas Karolis Degutis (95) (in cooperation with Charité – Berlin University of Medicine, Germany)

Daniel Haehnelt

Maria Morozova

Kornelius Podranski

Daniel Rose (*) (joint position, shared with Brain Networks group)

Jochen Schmidt

Marianna Schmidt (95)

Lenka Vaculčiaková (*)

Mahsa Zoraghi

Personal and Technical Assistants

Angela Muehlberg

Aline Peter

Dr Carsten Jaeger

Anna Jauch (87)

Simon Jung (14)

Domenica Klank

Enrico Reimer

Elisabeth Wladimirow (*)

Research Associates

Professor Dr Patrick Freund – Spinal Cord Injury Centre, Research, Balgrist University Hospital, University of Zurich, Switzerland

PD Dr Gunther Helms – Faculty of Medicine, Department of Clinical Sciences, Lund University, Sweden

Dr Romy Lorenz – Sir Henry Welcome Postdoctoral Fellow, University of Cambridge, UK

Dr Siawoosh Mohammadi –Institute of Systems Neuroscience, University Clinic Hamburg, Germany

Dr Maryam Seif – Spinal Cord Injury Centre, Research, Balgrist University Hospital, University of Zurich, Switzerland

Guest Researchers

Dr Pierre-Louis Bazin – Integrative Model-based Cognitive Neuroscience Research Unit, University of Amsterdam, the Netherlands

Dr Peter McColgan – UCL, UK

Dr Nicholas Groß-Weege – Siemens Healthineers, Erlangen, Germany

Professor Dr Dr Markus Morawski – Leipzig University, Germany

Professor Dr Benjamin Stahl – Medical School Berlin, Germany

DEPARTMENT OF NEUROPHYSICS

Director: Professor Dr Nikolaus Weiskopf

Former Researchers and Postdocs

Dr Saskia Helbling – The Ernst Strüngmann Institute (ESI) for Neuroscience, Frankfurt/M., Germany

Dr Tobias Leutritz – Institute for Medical Teaching and Educational Research, University Hospital Würzburg, Julius Maximilians University of Würzburg, Germany

Dr Shubhajit Paul – Biomedical Engineering Department, King's College London, UK

Dr Nico Scherf – Methods and Development Group Neural Data Science and Statistical Computing, Max Planck Institute for Human Cognitive and Brain Science, Leipzig, Germany

Former PhD Students

Julia Huck – Concordia University Montréal, Canada

Stephanie Schindler – Leipzig University Hospital, Germany

(8) European Union 7th Framework Programme
(11) Federal Ministry of Education and Research (BMBF), Germany
(14) German Research Foundation
(40) Pontius Foundation, Germany
(77) ERC Consolidator Grant
(78) EU H2020
(87) Inter-institutional research project "Hominoid Brain Connectomics", Coop. with MPI EVA
(95) MPSCog, Leipzig, Germany

(*) Left the Institute during 2020–2022

DEPARTMENT OF PSYCHOLOGY

Director: Professor Dr Christian F. Doeller

Research Group Leaders

Dr Mona Garvert (*)

Senior Researchers and Postdocs

Dr Blazej Baczkowski (*)
Dr Marcia Bécu (DoellerLab at Kavli Institute, Trondheim) (77)
Dr Jacob Bellmund (*)
Dr Johanna Bergmann
Dr Tora Bonnevie (DoellerLab at Kavli Institute, Trondheim) (77)
Dr Qiaoli Huang (1)
Dr Joshua B. Julian (DoellerLab at Kavli Institute, Trondheim) (*) (77)
Dr Misun Kim (*)
Dr Hermann Kutschka (née Sonntag)
Dr Nicholas Menghi
Dr Matthias Nau (DoellerLab at Kavli Institute, Trondheim) (*) (77)
Dr Tobias Navarro Schröder (DoellerLab at Kavli Institute, Trondheim) (*) (77)
Dr Daniel Reznik
Dr Stephanie Theves (**)
Dr Simone Viganò (in cooperation with University of Trento)

Doctoral Candidates

Irina Barnaveli
Rena Bayramova
Anna Naomi de Haas (PhD since 2021) (*) (88)
Felix Deilmann
Salma Elnagar
Alexander Eperon (in cooperation with University of Trento)
Markus Frey (DoellerLab at Kavli Institute, Trondheim) (*) (77)
Anna-Maria Grob (in cooperation with University of Hamburg)
Max Hinrichs (95)
Moritz Jäckels (DoellerLab at Kavli Institute, Trondheim) (77)
Sein Jeung (in cooperation with Technical University of Berlin)
Artem Karew (*)
Janis Keck (95) (in cooperation with the MPI for Mathematics in the Sciences, Leipzig)
Dörte Kuhrt (DoellerLab at Kavli Institute, Trondheim) (77)
Matthias Nau (DoellerLab at Kavli Institute, Trondheim) (PhD since 2020) (*) (77)
Alexander Nitsch
Loes Ottink (in cooperation with Donders Institute, Radboud University, Nijmegen) (PhD since 2022) (*) (89)
Leonardo Pettini (95) (in cooperation with Charité – Berlin University of Medicine)
Ignacio Polti (DoellerLab at Kavli Institute, Trondheim) (77)
Volker Reisner
Fabian Renz (95) (in cooperation with MPI for Human Development, Berlin)
Theo A. J. Schäfer
Ingrid Framås Syversen (DoellerLab at Kavli Institute, Trondheim) (PhD since 2021) (*) (77)
Rebekka Tenderra (95)
Stephanie Theves (PhD since 2020) (**)
Aleksei Zabolotnii (Orientation scholarship holder)

MD Students

Markus Badwal (in cooperation with Leipzig University)

Personal and Technical Assistants

Anja Hanisch
Michaela Rittmeyer (maternity cover) (*)
Susanne Starke

Ronny Borries (joint position, shared with Brain Networks Group + MPRG Pain Perception)
Kerstin Schumer (née Träger)
Merethe Andresen (DoellerLab at Kavli Institute, Trondheim)

DEPARTMENT OF PSYCHOLOGY

Director: Professor Dr Christian F. Doeller

Kevin Aspaas Eriksen (DoellerLab at Kavli Institute, Trondheim) (*) (90)

Stian Jensen Framvik (DoellerLab at Kavli Institute, Trondheim) (*) (91)

Ivan Krasovec (DoellerLab at Kavli Institute, Trondheim)

Visiting Research Fellows & Guest Researchers

Professor Dr Roberto Bottini – CIMeC - Center for Mind/Brain Sciences, University of Trento, Mattarello (TN), Italy

Dr Casper Kerrén – Max Planck Institute for Human Development, Berlin, Germany

Dr Matthias Nau – National Institute of Health (NIH), Bethesda, Maryland, USA

Javier Ortiz-Tudela, Ph.D. – Goethe University, Frankfurt am Main, Germany

Dr Marit Petzka – Max Planck Institute for Human Development, Berlin, Germany

Professor Dr Kiran Varanasi – HTWK Leipzig, Deutschland

Dr Simone Viganò – CIMeC - Center for Mind/Brain Sciences, University of Trento, Mattarello (TN), Italy

Research Associates

Professor Dr Roberto Bottini – CIMeC - Center for Mind/Brain Sciences, University of Trento, Mattarello (TN), Italy

Former Researchers and Postdocs

Dr Blazej Baczkowski – Faculty of Psychology and Human Movement Science, University of Hamburg, Germany (Schwabe lab)

Dr Jacob L. S. Bellmund – Agentur für Innovation in der Cybersicherheit GmbH Halle, Germany

Dr Mona M. Garvert – Leopoldina, Halle, Germany; AYA Technologies Limited, London, England

Dr Joshua B. Julian – Postdoctoral Research Associate, Princeton Neuroscience Institute, US (Tank/Brody labs)

Dr Misun Kim – Postdoctoral Research Associate, UCL Queen Square Institute of Neurology, UK (Burgess lab)

Dr Matthias Nau – Postdoctoral Research Associate, National Institute of Health (NIH), Bethesda, Maryland, US (Baker lab)

Dr Tobias Navarro Schröder – Associate Professor, Kavli Institute for Systems Neuroscience, Trondheim, Norway

Dr Stephanie Theves – Minerva Fast Track Group Leader, Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany

Former PhD Students

Anna Naomi de Haas – Consultant at Hezelburcht Subsidieadviesbureau, the Netherlands

Ingrid Framås Syversen – MR physicists, Oslo University Hospital, Oslo, Norway

Markus Frey – Postdoctoral Research Associate, Université de Génève, Geneva, Switzerland (Mathis lab)

Artem Karew – UX Conception & Design, toom Baumarkt, Cologne, Germany

Matthias Nau – National Institute of Mental Health, Bethesda, US

Loes Ottink – Noldus Information Technology, Wageningen, the Netherlands

Former Visiting Research Fellows & Guest Researchers

Dr David Neville (*) – Donders Institute for Brain, Cognition and Behavior, RU Nijmegen, the Netherlands; Nostos Genomics, Berlin

(1) Alexander von Humboldt Foundation, Germany
(77) ERC Consolidator Grant
(88) NWO MaGW Research Talent Grant
(89) ZonMw (the Netherlands Organisation for Health Research and Development)
(90) Samarbeidsorganet Helse Midt-Norge, Stjørdal, Norway
(91) Romanian – EEA Grants 2014–2021
(95) MPSCog, Leipzig, Germany

(*) Left the institute during 2020–2022
(**) Left the department during 2020–2022

MAX PLANCK RESEARCH GROUP ADAPTIVE MEMORY

Head: Dr Roland G. Benoit

Postdocs

Dr Heidrun Schultz

Dr Angharad Williams (*)

Doctoral Candidates

Aroma Dabas (in cooperation with the Free University Berlin)

Ann-Kristin Meyer (19) (in cooperation with the Leipzig University)

Philipp C. Paulus (19) (*) (Dr rer. nat. since 2022) (in cooperation with the Leipzig University)

Sarah Rösch (19) (*) (in cooperation with the Leipzig University)

Hanna Stoffregen (19) (*) (in cooperation with the Leipzig University)

Scientific Staff

Seyma Bayrak (**)

Mark Lauckner (in cooperation with the Leipzig University)

Technical and Scientific Assistants

Martina Dietrich (**)

Mewes Muhs (*)

Guest Researchers

Ruud Berkers, PhD

Davide Stramaccia, PhD

Roxanne Eisenbeis (*)

Former Postdocs

Ruud Berkers, PhD

Davide Stramaccia, PhD

Zijian Zhu, PhD (DAAD)

(19) IMPRS NeuroCom, Leipzig, Germany

(*) Left the Institute during 2020–2022
(**) Left the group during 2020–2022

MAX PLANCK RESEARCH GROUP PAIN PERCEPTION

Head: Dr Falk Eippert

Postdocs

Dr Ulrike Horn (92)
Dr Birgit Nierula
Dr Yulia Revina (92)

Doctoral Candidates

Emma Bailey (19, 92)
Alice Dabbagh (19)
Merve Kaptan (19, *) (Dr rer. nat. since 2022)
Lisa-Marie Pohle (19, 92)
Hongyan Zhao (19)

Technical Assistant

Ronny Borries (joint position, shared with Brain Networks Group + Dept of Psychology)
Melanie Freund
Janek Haschke (*)

Guest Researchers

Dr Johanna Vannesjo

Guest

Haschke Janek – Gastwissenschaftler, University Clinic (Leipzig, Germany)
Kaptan Merve – Gastwissenschaftlerin, Stanford University (Stanford, USA)
Vannesjo Johanna – Gastwissenschaftlerin, NTNU, (Trondheim, Norway)

(19) IMPRS NeuroCom, Leipzig, Germany
(92) ERC Starting Grant

(*) Left the Institute during 2020–2022

LISE MEITNER RESEARCH GROUP COGNITION AND PLASTICITY

Head: Professor Dr Gesa Hartwigsen

Postdocs

Curtiss Chapman, PhD (*)
Dr Maximilian Friehs (14)
Dr Philipp Kuhnke (*) (in cooperation with Leipzig University)
Dr Sabrina Turker (in cooperation with Humboldt Foundation)
Dr Kathleen Williams

Doctoral Candidates

Matteo Ferrante (in cooperation with Studienstiftung des Deutschen Volkes)
Astrid Graessner (*) (Dr rer. nat. since 2022)
Zhizhao Jiang (in cooperation with Studienstiftung des Deutschen Volkes)
Dr Philipp Kuhnke (*) (Dr rer. nat. since 2021)
Sandra Martin (in cooperation with Studienstiftung des Deutschen Volkes & Leipzig University)
Laura Nieberlein
Ole Numssen (14)
Anna Rysop (14) (*)

Technical Assistant

Kenny Seidel

Guest Researchers

Dr Manuela Macedonia (Johannes Kepler University Linz, Austria)
Dr Jens Kreitewolf (University of Lübeck, Germany)
Prof Dr Jonas Obleser (University of Lübeck, Germany)
Lea-Marie Schmitt (*) (in cooperation with the University of Lübeck, Germany)

Former Postdocs

Dr Jana Klaus – Experimental Psychology Department, Utrecht University, the Netherlands

(14) German Research Foundation

(*) Left the institute during 2020–2022

MAX PLANCK RESEARCH GROUP LANGUAGE CYCLES

Head: Dr Lars Meyer

Postdocs

Maja Linke
Chia-Wen Lo
Sabrina Stehwien (*)

Doctoral Candidates

Lena Henke
Yulia Lamekina
Jordi Martorell
Katharina Menn
Lorenzo Titone

(*) Left the Institute during 2020–2022

MINERVA FAST TRACK GROUP MILESTONES OF EARLY COGNITIVE DEVELOPMENT

Head: Dr Charlotte Grosse Wiesmann

Postdocs

Dr Katrin Rothmaler

Doctoral Candidates

Florian Bednarski (19) (in cooperation with Leipzig University)
Cheslie Klein (19) (in collaboration with Neuropsychology)
Clara Schüler (19)
Marie Luise Speiger (14)
Anna-Lena Tebbe (19)
Chen Yang (19)

Technical Assistant

Martina Dietrich (14)

Guest Researchers

Esra Hasan

Ehemalige Gäste

Kathrine Habdank, Wissenschaftlerin, University of Copenhagen, Kollaboration

(14) German Research Foundation (DFG)
(19) IMPRS NeuroCom, Leipzig, Germany

(*) Left the institute during 2020–2022

MAX PLANCK RESEARCH GROUP VISION AND COMPUTATIONAL COGNITION

Head: Professor Dr Martin N. Hebart

Postdocs

Dr Katja Seeliger (legal name: Katja Müller) (PhD since 1/2021)
Dr Maggie Mae Mell

Doctoral Candidates

Oliver Contier (95)
Patxi Elosegi (*)
Philipp Kaniuth
Florian Mahner
Lukas Muttenthaler (co-supervised with Klaus-Robert Müller, TU Berlin) (99)
Johannes Roth
Johannes Singer (co-supervised with Radoslaw Cichy, FU Berlin) (98)
Laura Stoinski (Orientation scholarship holder)

Visiting Research Fellows & Guest Researchers

Patxi Elosegi – Basque Center on Cognition, Brain and Language (BCBL), Donostia, Gipuzkoa, Spain
Marie St. Laurent – Université de Montréal, Canada

Former PhD Students

Patxi Elosegi – Basque Center on Cognition, Brain and Language (BCBL), Donostia, Gipuzkoa, Spain

Former visiting Research Fellows & Guest Researchers

Carmen Amme – Institute of Cognitive Science, Osnabrück University, Germany
Shu Fujimori – University of Electro-Communications, Tokyo, Japan
Alireza Karami – Center for Mind/Brain Sciences (CIMeC), University of Trento, Italy
Philip Sulewski – Institute of Cognitive Science, Osnabrück University, Germany

(95) MPSCog, Leipzig, Germany
(98) Free University of Berlin, Germany
(99) Technische Universität Berlin, Germany

(*) Left the Institute during 2020–2022

RESEARCH GROUP LEARNING IN EARLY CHILDHOOD

Head: Dr Michael A. Skeide (14)

Scientific Researchers and Postdocs

Shreya Kapoor (*) (14)
Dr Roman Kessler (14)
Anne-Sophie Kieslinger (35)

Doctoral Candidates

Alexander Enge (80)

Guest Researchers

Zahra Emami (University of Toronto, Canada)
Dr Ulrike Kuhl (Bielefeld University, Germany)

Technical Assistants

Michael Vollmann (35)

(14) German Research Foundation (DFG)
(35) European Union, Starting Grant, funded by European Research Council
(80) Studienstiftung des deutschen Volkes (PhD Fellowship)

* Left the Institute during 2020–2022

OTTO HAHN GROUP COGNITIVE NEUROGENETICS

Head: Dr Sofie Louise Valk

Postdocs

Dr H. Lina Schaare

Doctoral Candidates

Bianca Serio, PhD candidate School of Cognition, in cooperation with Forschungszentrum Juelich.

Ekatherina Manoli, PhD candidate, IMPRS, funded through Studienstiftung des Deutsches Volkes

Benjamin Haenisch, Dr Med candidate, in cooperation with Forschungszentrum Juelich.

Neville Magielse, PhD candidate, via Helmholtz International Brain Analysis and Learning Laboratory (HIBALL), in cooperation with Forschungszentrum Juelich.

Svenja Kuechenhoff, PhD candidate, via Helmholtz International Brain Analysis and Learning Laboratory (HIBALL), in cooperation with Forschungszentrum Juelich.

Amin Saberi, PhD candidate, via Helmholtz International Brain Analysis and Learning Laboratory (HIBALL), in cooperation with Forschungszentrum Juelich.

Meike Hettwer, PhD candidate via School of Cognition, in cooperation with Forschungszentrum Juelich.

Seyma Bayrak, PhD candidate

Bin Wan, PhD candidate, IMPRS

Guest researchers

Giacomo Bignari – PhD candidate School of Cognition, currently PhD candidate at Max Planck Institute for Language, Nijmegen.

Yun Shuang Fan – funded through State-Sponsored Scholarship for joint PhD students

Anton Jakovcic – University of Zagreb, Erasmus Plus program

Dr Richard Bethlehem – in collaboration with University of Cambridge

MINERVA FAST TRACK GROUP NEURAL CODES OF INTELLIGENCE

Head: Dr Stephanie Theves

Postdocs

Dr Ksenija Slivac

Doctoral Candidates

Unnur Andrea Ásgeirsdóttir

Rebekka Tenderra

(19) IMPRS NeuroCom, Leipzig, Germany

(*) Left the institute during 2020–2022

NUCLEAR MAGNETIC RESONANCE

Head: Professor Dr Harald E. Möller

Senior Researchers and Postdocs

Anna Bujanow
Dr Isabell Katzmann
Dr Lorenz Lemcke (*)
Dr Jöran Lepsien
Dr Toralf Mildner
Professor Dr Karsten Mueller (**)
Dr Stefan Olthoff (*)
Dr habil. André Pampel
Dr Robert Trampel (joint position, shared with Dept of Neurophysics)
Dr Joseph R. Whittaker (*)
Anke Ziegaus (*)

Doctoral Candidates

Ratnamanjuri Devi
Richard Gast (80) (*) (Dr rer. nat. since 2021) (joint position, shared with Brain Networks group)
Dimitrios Gkotsoulias (78)
Renzo Torrecuso
Niklas Wallstein

Secretarial and Technical Staff

Nancy Muschall
Mandy Jochemko
Roland Müller
Torsten Schlumm
Manuela Hofmann
Anke Kummer
Nicole Pampus
Simone Wipper

Visiting Research Fellows and Guest Researchers

Chaoyang Jin (in collaboration with NDSSC group) – Northeastern University, Shenyang, China
Professor G. Allan Johnson, PhD – Center for In Vivo Microscopy, Duke University Medical Center, Durham, NC, USA
Professor Dr Boris Keil – Department of Life Science Engineering, Institute of Medical Physics and Radiation Protection, Mittelhessen University of Applied Science, Giessen, Germany
Professor Dr Roland Kreis – Magnetic Resonance Methodology, Institute of Diagnostic and Interventional Neuroradiology, University of Bern, Switzerland
Professor Chunlei Liu, PhD – Electrical Engineering and Computer Sciences & Helen Wills Neuroscience Institute, University of California, Berkeley, CA, USA
Dr Falk Lüsebrink-Rindsland – Workgroup Medicine and Digitalization – MedDigit, Department of Neurology, Institute of Cognitive Neurology and Dementia Research, Medical Faculty, Otto von Guericke University Magdeburg, Germany
Mirsad Mahmutovic – Department of Life Science Engineering, Institute of Medical Physics and Radiation Protection, Mittelhessen University of Applied Science, Giessen, Germany
Dr Kadir Şimşek – School of Psychology, Cardiff University Brain Research Imaging Centre, Cardiff University, Wales, UK
Professor Dr Luigi Zecca – Institute of Biomedical Technologies, National Research Council of Italy, Segrate, Milan, Italy

Former Researchers and Postdocs

Dr Lorenz Lemcke – Clinic for Neurology, Sana Hospitals Leipziger Land, Borna, Germany
Dr Stefan Olthoff – Department of Diagnostic & Interventional Radiology, Leipzig Heart Center, Helios Kliniken Group, Leipzig, Germany
Dr Joseph R. Whittaker – Capital One Europe Plc, Nottingham, UK
Anke Ziegaus – Clinic for Radiotherapy and Radiooncology, St. Georg Hospital gGmbH, Leipzig, Germany

Former Doctoral Researcher

Dr Richard Gast – Department of Neuroscience, Feinberg School of Medicine, Northwestern University, Chicago, IL, USA

(78) EU H2020
(80) Studienstiftung des deutschen Volkes

(*) Left the Institute during 2020–2022
(**) Left the group during 2020–2022

BRAIN NETWORKS

Heads: Professor Dr Thomas R. Knösche, Dr Burkhard Maess

Senior Researchers and Postdocs

Dr Benjamin Kalloch (14) – (in cooperation with Ilmenau University of Technology)

Dr Helmut Schmidt (14) (*)

Dr Peng Wang (*)

Dr Konstantin Weise (14) – in cooperation with Ilmenau University of Technology, Germany, and Aarhus University Hospital, Denmark)

Doctoral Candidates

Ole Bialas (69) (*) (Dr rer. nat. since 2022) (in cooperation with Leipzig University)

Vincent Chien (*) (Dr-Ing. since 2020) (in cooperation with Leipzig University)

Richard Gast (80) (*) (Dr rer. nat. since 2021) (joint position, shared with NMR group)

Ruxue Gong (14) (*) (Dr rer. nat. since 2022) (in cooperation with University Hospital Leipzig)

Ying Jing (97) (in cooperation with Hangzhou Normal University, China)

Daniel Rose (*) (joint position, shared with Dept of Neurophysics)

Lab Rotation MPSCog

Carolin Scholl (95)

Secretarial and Technical Staff

Nancy Muschall

Ronny Borries (joint position, shared with Dept of Psychology + MPRG Pain Perception)

Yvonne Wolff-Rosier

Visiting Research Fellows and Guest Researchers

Dr Vincent Chien – Neuroscience Research Center, Taipei Medical University, Taiwan

Professor Dr Joseph Claßen – Clinic for Cognitive Neurology, Leipzig University Hospital, Germany

Lingyun Gu – Southeast University, Nanjing, Jiangsu, China

Professor Dr Jens Haueisen – Biomedical Engineering Group, Department of Computer Science and Automation, Institute of Biomedical Engineering and Informatics, Ilmenau University of Technology, Germany

Dr Björn Herrmann – Department of Psychology, Rotman Research Institute, Faculty of Arts & Science, University of Toronto, ON, Canada

Dr Hermann Kutschka (née Sonntag) – Biomedical Engineering Group, Department of Computer Science and Automation, Institute of Biomedical Engineering and Informatics, Ilmenau University of Technology, Germany

Sergey Makarov, PhD – Athinoula A. Martinos Center for Biomedical Imaging, Charlestown, MA, USA

Aaron Miller – Samu Taulu (MEG) Group, Institute for Learning and Brain Sciences, University of Washington, Seattle, WA, USA

PD Dr Daniela Sammler – Research Group Neurocognition of Music and Language, Max Planck Institute for Empirical Aesthetics, Frankfurt/Main, Germany

Stella M. Sánchez, PhD – Laureate Institute for Brain Research, Tulsa, OK, USA

Professor Dr Axel Thielscher – Danish Research Centre for Magnetic Resonance, Copenhagen University Hospital Hvidovre, Denmark, and Department of Health Technology, Technical University of Denmark, Kongens Lyngby, Denmark

Dr Peng Wang – Institute of Psychology, University of Greifswald, Germany

Dr Hiroki Watanabe – Center for Information and Neural Networks, National Institute of Information and Communications Technology (NICT), Tokyo, Japan

BRAIN NETWORKS

Heads: Professor Dr Thomas R. Knösche, Dr Burkhard Maess

Former Senior Researchers and Postdocs

Dr Helmut Schmidt – Institute of Computer Science, The Czech Acadamy of Sciences, Prague, Czech Republic

Dr Peng Wang – Institute of Psychology, University of Greifswald, Germany

Former Doctoral Researchers

Dr Ole Bialas – Department of Biomedical Engineering, University of Rochester, NY, USA

Dr Vincent Chien – Neuroscience Research Center, Taipei Medical University, Taiwan

Dr Richard Gast – Department of Neuroscience, Feinberg School of Medicine, Northwestern University, Chicago, IL, USA

Dr Ruxue Gong – Emory Brain Health Center, Emory University, Atlanta, GA, USA

Daniel Rose – unknown

(14) German Research Foundation (DFG)
(69) Stiftung der deutschen Wirtschaft (sdw) gGmbH, Berlin, Germany
(80) Studienstiftung des deutschen Volkes
(95) MPSCog, Leipzig, Germany
(97) China Scholarship Council (CSC)

(*) Left the Institute during 2020–2022

NEURAL DATA SCIENCE AND STATISTICAL COMPUTING

Head: Dr Nico Scherf

Senior Researchers and Postdocs

Simon Hofmann (11)

Professor Dr Karsten Mueller

Doctoral Candidates

Ferney Beltrán Velandia (96) (in cooperation with Leipzig University)

Charlotte Beylier (96) (in cooperation with Leipzig University)

Dimitra Kiakou (in cooperation with Charles University Prague, Czech Republic)

Nikola Milosevic (11)

Gesine Müller (in cooperation with Georg August University of Göttingen)

Sebastian Niehaus (in cooperation with TU Dresden)

Kajal Singla (96) (in cooperation with Leipzig University)

Nahid Torbati (11)

Assistant

Nancy Muschall

Visiting Research Fellows and Guest Researchers

Full Professor Dr Vladimir K. Dubovoy – Department of Mathematics and Computer Science, Karazin National University, Kharkiv, Ukraine

Ing. Tereza Duspivová – Center for Interventional Therapy of Movement Disorders, Department of Neurology, 1st Faculty of Medicine and General University Hospital, Charles University Prague, Czech Republic

Chaoyang Jin (in collaboration with NMR group) – Northeastern University, Shenyang, China

Dr Birol Taskin – Department of Neurology, Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, and MindBrainBody Institute, Berlin School of Mind and Brain, Charité – Berlin University of Medicine and Humboldt University Berlin, Germany

(11) Federal Ministry of Education and Research (BMBF), Germany
(96) Center for Scalable Data Analytics and Artificial Intelligence (ScaDS.AI), Dresden/Leipzig, Germany

COMPUTING AND DATABASES SERVICES

Head: Dr Davide Chiarugi

Heads

Dr Davide Chiarugi (IT & DB)
Professor Dr Mathias Goldau (DB) (*)
Dr Helmut Hayd (IT) (*)

Secretarial and Technical Staff

Nancy Muschall (IT & DB)
Khaled Bahlawan (IT)
Stefan Bunde (DB) (84)
Frank Burkhardt (IT)
Heiko Korsawe (IT)
Hagen Lipka (IT) (*)
Elke Maess (DB)
Stephan Moeller (IT)
Sebastian Neumann (IT) (*)
Karin B. Rudisch (DB)
Markus Then (IT)
Alexander Tyapkov (DB) (84) (*)

Former Heads

Professor Dr Mathias Goldau – Faculty of Digital Transformation, Leipzig University of Applied Sciences (HTWK), Germany
Dr Helmut Hayd – Early retirement

Former Technical Staff

Hagen Lipka – unknown
Sebastian Neumann – unknown
Alexander Tyapkov– Freelance Software Developer, Germany

(84) Castellum Project / Max Planck Society, Germany

(*) Left the Institute during 2020–2022

MINERVARESEARCHGROUPEGG(EMOTIONS&NEUROIMAGING)LAB

Head: Professor Dr Julia Sacher (**)

Doctoral Candidates

Carolin A. Lewis (in cooperation with University of Tübingen)
Dr Eóin Molloy (*) (PhD since 2022)
Rachel Zsido (19) (PhD thesis submitted 2022)

MD Students in cooperation with Leipzig University

Nathalie Beinhölzl
Matthias Heinrich (*) (MD since 2022)

Technical and administrative assistants

Ulrike Scharrer (*)
Gegana Zheleva (*)

Guest researcher

Professor Dr Veronika Engert – University Clinic Jena, Germany
Professor Dr Gesa Schaadt – Free University of Berlin, Germany
Dr Esmeralda Hildago-Lopez – University of Salzburg, Germany
Dr Daniela Stanikova – University Clinic Leipzig, Germany

(19) IMPRS NeuroCom, Leipzig, Germany

(*) Left the Institute during 2020–2022
(**) Left the group during 2020–2022

MAX PLANCK RESEARCH GROUP SOCIAL STRESS AND FAMILY HEALTH

Head: Professor Dr Veronika Engert

Senior Researchers and Postdocs

Dr Roman Linz (since 2022)
Dr Lara Puhlmann (since 2022)
Dr Katrin Preckel (since 2021)

Doctoral Candidates

Bonnie O'Malley (80)
Mathilde Gallistl

Personal and Technical Assistants

Elisabeth Murzik
Henrik Grunert

Research Associates

Professor Dr Philipp Kanske – Professur für Klinische Psychologie und behaviorale Neurowissenschaft, TU Dresden, Germany

Guest Researchers

Professor Dr Anne Böckler – Institut für Psychologie, Julius-Maximilians-Universität Würzburg, Germany
Christiane Wesarg – University of Amsterdam, the Netherlands
Professor Dr Pascal Vrticka – Department of Psychology, University of Essex, UK

(80) Studienstiftung des deutschen Volkes (PhD Fellowship)

(*) Left the Institute during 2020–2022
(**) Left the group during 2020–2022