Annual Report 2002

Max Planck Institute of Cognitive NeuroScience Leipzig

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The year 2002 was characterized not only by exciting research and results but also by a remarkable number of academic degrees awarded to our junior researchers. A total number of 3 habilitations and 12 doctoral degrees were given to members of our institute including the youngest ever recipient of a doctorate within the Max Planck Society. One of our recently habilitated staff members, Christoph Herrmann, has already been offered a Professorship in Psychology at the University of Magdeburg.

The institute further established its excellent scientific relations with the Max Planck Institute for Psychological Research in Munich, with which a number of successful projects both on the neural basis of action and action control and on the perception of meaningful gestures are under way. Together with the Max Planck Institute for Evolutionary Anthropology, we also launched scientific cooperations in two areas: together with the group of Svante Pääbo, we started a project on the genetic basis of language and, together with Bernhard Comrie, we organized an international workshop on Universals of Semantic Roles, thereby initiating a dialogue between linguists, psychologists and neuroscientists on the neural correlates underlying the processing of structurally different languages.

At a conceptual and administrative level we have fostered our efforts in institutionalizing the fruitful cooperation with the Max Planck Institute for Psychological Research. We believe that a joint enterprise between this institute and ours will result in a scientifically most effective center with a research focus on human brain and behavioral sciences within the Max Planck Society.

Angela D. Friederici
D. Yves von Cramon

Leipzig, February 2003

TABLE OF CONTENTS

PREFACE

1	ORGANIZATION OF THE INSTITUTE		9
2	RESEARCH		17
	2.1	NEUROCOGNITION OF LANGUAGE PROCESSING	17
	2.2	NEUROCOGNITION OF LANGUAGE LEARNING	41
	2.3	NEUROCOGNITION OF MUSIC	49
	2.4	NEUROCOGNITION OF PROSODY	55
	2.5	CLINICAL AND EXPERIMENTAL NEUROPSYCHOLOGY	63
	2.6	FUNCTIONAL NEUROANATOMY OF THE FRONTAL LOBE	81
	2.7	SIGNAL AND IMAGE PROCESSING	101
	2.8	NUCLEAR MAGNETIC RESONANCE	115
	2.9	MATHEMATICAL METHODS IN FMRI	127
	2.10	MEG AND EEG: SIGNAL ANALYSIS AND MODELING	133
3	OTHER ACTIVITIES		151
4	DEGREES AND AWARDS		163
5	PUBLICATIONS		165
6	INDEX OF NAMES		205

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NEUROCOGNITION OF LANGUAGE PROCESSING 2.1

The three-phase *neurocognitive model of language processing* by Friederici (2002) which focuses on the cortical functions of the left hemisphere was extended with respect to three different aspects. First, together with the Neurocognition of Prosody Group the lateralization of different language functions in the left and the right hemisphere and their interhemispheric interplay was specified in a so-called Dynamic Dual Pathway View (Friederici & Alter, to appear, 2.1.1).

Second, the function of the basal ganglia and their interaction with cortical structures during language processing are investigated (2.4.6).

Third, the second phase of the three-phase model was respecified with respect to thematic processes which take place in parallel with syntactic processes in a so-called Argument Dependency Model (Bornkessel & Schlesewsky, 2.1.2).

Syntactic and semantic processes. Empirical evidence for the Argument Dependency Model is provided in 2.1.3. The influence of focus structure on syntactic processes is discussed in 2.1.4, and the interplay between focus structure and prosody in 2.1.5. The neuronal network of sentence level syntactic processes and the functional connectivity of its parts is presented in 2.1.6. The brain activation supporting the selection of grammatical gender is discussed in 2.1.7. Processing of grammatical gender as measured by ERP appears to vary as function of instruction, see 2.1.8.

Processing words. The neural basis of auditory word processing was investigated and specified using fMRI, see 2.1.9. Another fMRI study compared the neural network for phonological processing involved in comprehension and production, see 2.1.10. The crucial segmental and suprasegmental phonological information for word processing in tone languages was examined in 2.1.11. Semantic priming in a cross-modal (auditory-visual) and in a within-modal (visual-visual) fragment priming experiment reveals that the use of semantic information diverges early during word recognition, see 2.1.12. The processing of compounds and the special status of the elements linking two constituents was investigated in 2.1.13. Moreover, the network of brain regions involved in working memory for semantic concepts independent of aspects of verbal memory was identified, see 2.1.14.

Processing Sign Language and Gestures. A new area of research was entered into over the past year. In an fMRI study the neural network supporting the comprehension in German Sign Language is presented in 2.1.15. A study investigating the processing of conceptual and structural relations in action recognition measured by means of ERPs reveals that conceptual mismatches result in an N400 and structural mismatches in a P600, very similar to components observed in language processing, see 2.1.16. Two additional studies, using EEG and MEG respectively, examined the processing of symbolic hand postures. The EEG study reports an anteriorly distributed N300 followed by an N400 for the processing of meaningful hand postures, 2.1.17. The MEG study, using current source density estimations indicates activation in the region of BA 6/BA 45 in the right hemisphere for the processing of meaningful hand postures, 2.1.18.

Finally, a basic study relevant for all studies dealing with auditory language stimuli and musical stimuli concerned the inter-individual variability of the functional neuroanatomy of Heschl's gyrus, in 2.1.19.

2.1.1 Lateralization of auditory language functions: The dual pathway view

Friederici, A.D. & Alter, K.

Spoken language comprehension requires the coordination of different subprocesses in time. After the initial acoustic analysis the system has to extract segmental information such as phonemes, syntactic elements and lexical-semantic elements as well as suprasegmental information such as accentuation and intonational phrases, i.e., prosody. According to the dynamic dual pathway model of auditory language comprehension, syntactic and semantic information are primarily processed in a left hemisphere temporo-frontal pathway including separate circuits for syntactic and semantic information whereas prosodic information is processed in a right hemisphere temporo-frontal pathway. The circuit supporting on-line syntactic processes involve the anterior portion of the superior temporal gyrus and the inferior frontal gyrus (frontal operculum and BA 44), while the circuit subserving semantic processes involve the mid portion of the superior temporal gyrus and the posterior portion of the superior and middle temporal

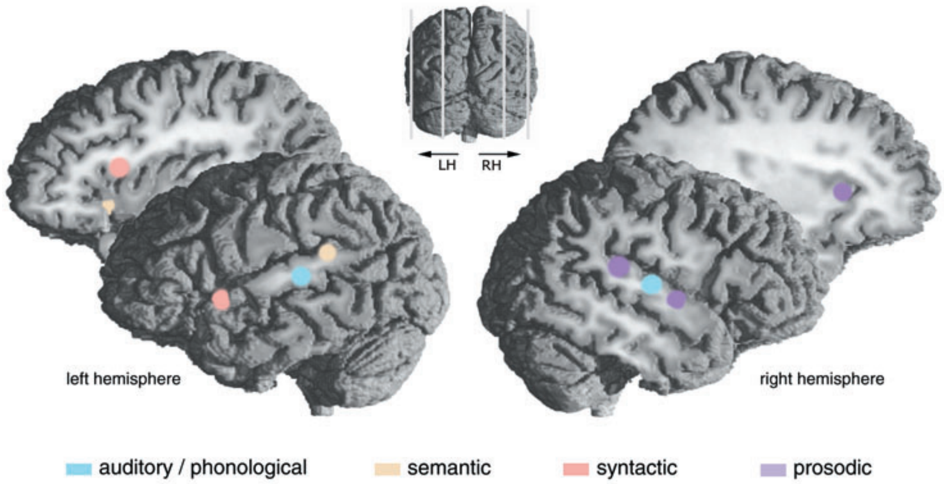

Figure 1.

gyrus and BA 45/47 in the inferior frontal gyrus. The right hemispheric pathway also recruits the superior temporal gyrus and the frontal operculum. The relative lateralization of these functions occurs as a result of stimulus properties and processing demands. The observed interaction between syntactic and prosodic information during auditory sentence comprehension is attributed to dynamic interaction between the two hemispheres.

2.1.2 The Argument Dependency Model: A neurocognitive approach to incremental interpretation

Bornkessel, I.[1] & Schlesewsky, M.[2]

[1] *Max Planck Institute of Cognitive Neuroscience*
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In order for a sentence to be interpretable, the linguistic input must be assigned an internal structure. In particular, it has been claimed that a central aspect of such a structuring consists of establishing a hierarchical relation between sentential arguments (Frisch & Schlesewsky, 2001; Bornkessel et al., 2002), which may then be mapped onto the specific representation of the event denoted by the verb. Within the framework of a recently proposed model of argument processing, the Argument Dependency Model (ADM; Bornkessel, 2002), it is assumed that the language processing system relies upon two alternative means of creating such hierarchical dependencies, namely (a) a thematic processing subsystem and (b) a syntactic processing subsystem. Which of these two pathways is chosen during the processing of a sentence is determined by the degree of morphological informativeness of the arguments, i.e., while unambiguously case marked arguments are hierarchized thematically, syntactic hierarchizing applies to case ambiguous arguments (Bornkessel et al., 2002).

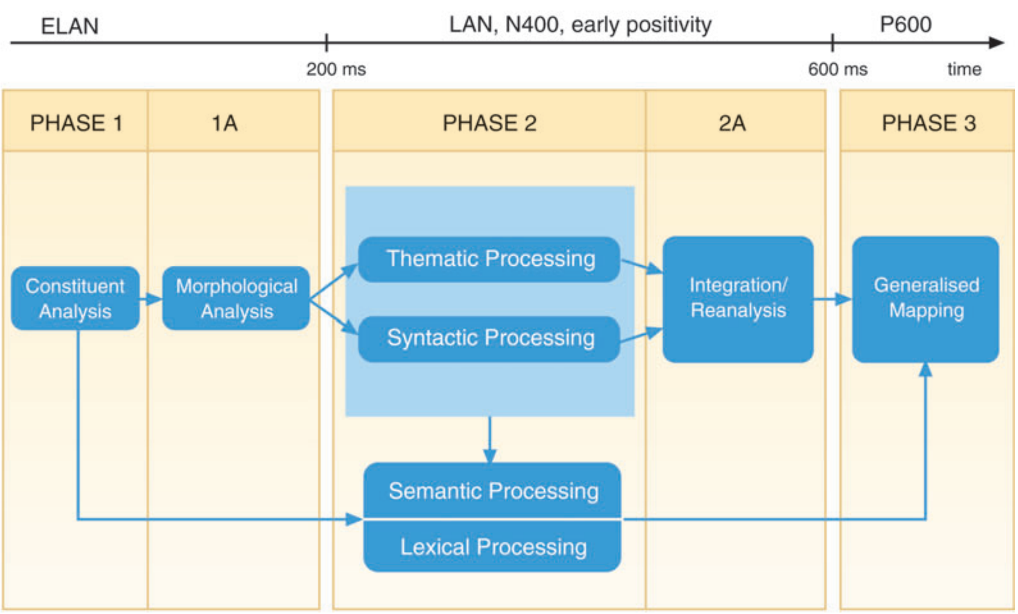

Figure 2. The processing architecture of the Argument Dependency Model (Bornkessel, 2002).

The processing architecture of the ADM is shown in Figure 2. As in Friederici's (2002) neurocognitive model of language comprehension, language processing is essentially divided into three phases. Within phase 1, very basic processes of constituent structuring based on word category information apply. Phase 2 is the locus of the hierarchical processing mechanisms giving rise to the thematic and the syntactic processing pathways. Crucially, although plausibility/world knowledge information and lexeme specific (in particular: verb specific) information is also processed in this time range, these information types do not influence the hierarchization process. Where the outputs of the thematic and the syntactic processing pathways are integrated with one another in phase 2a, a 'generalized mapping' of all information types takes place in phase 3.
The ADM confirms the assumption that the language processing system endeavours to maximize incremental interpretation, although this maximization clearly underlies certain architectonic restrictions. The identification of two processing pathways which determine the relation between arguments depending on their morphological informativeness leads to a number of cross-linguistic predictions which may contribute substantially to a new, neurocognitively based, typological classification of different languages.

2.1.3 Experimental evidence in support of the Argument Dependency Model

Bornkessel, I.[1], Schlesewsky, M.[2] & Friederici, A.D.[1]

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Where experimental evidence for the most important architectonic assumption of the Argument Dependency Model (ADM), namely the distinction between a thematic and a syntactic processing pathway during phase 2 of comprehension, was reported in Bornkessel et al. (2002), further studies support the internal structure of phase 2 as postulated within the model.
Firstly, both the syntactic and the thematic pathway were shown to operate independently of verb-specific information even in sentences in which the verb precedes its arguments (Bornkessel, 2002). Thus, the processing of an object-experiencer verb led neither to a preference for object-initiality (syntactic pathway; cf. Figure 3) nor for dative-initiality (thematic pathway). These results show that, at least within phase 2 of processing, the two relational processing subsystems operate on the basis of universal preference strategies applying to the structuring of hierarchical information, rather than on sentence- or lexeme-specific information.
Secondly, the thematic hierarchization process operates independently of plausibility/ world-knowledge information, i.e., it draws upon only a very limited set of information types such as morphological case marking and animacy (Bornkessel, 2002). Where the well-known N400-P600 pattern in sentences with two identically case marked arguments, in which the N400 has been shown to be a reflex of thematic hierarchization problems, is reduced to a P600 effect in sentences with two identically case marked arguments that differ in animacy (Frisch & Schlesewsky, 2001), the biphasic pattern is unaffected by manipulations of the plausibility of the Agent-Patient relation between two identically case-marked arguments. Since an N400 modulation did, however, obtain in the

grammatical control sentences, it appears that plausibility/world knowledge information and relational information as a part of the thematic processing pathway are processed within the same time window (i.e., within phase 2 of processing), but with a hierarchical priority system such that the hierarchization process proceeds independently of world knowledge information.

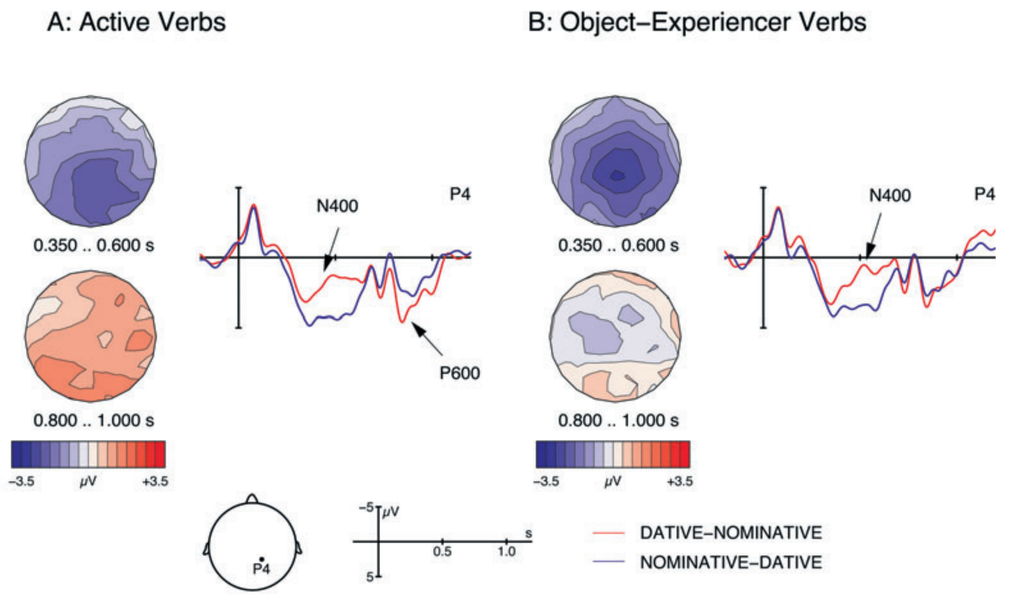

Figure 3: Grand average ERPs for ambiguous dative-initial vs. ambiguous nominative-initial sentences of the form Adverb-Verb-NP1-NP2 with active (A) and object-experiencer verbs (B) at the position of NP2. The topographical maps indicate the distribution of the voltage differences between dative- and nominative-initial structures.

2.1.4 Information structure licences syntax: An ERP correlate of focus processing

Bornkessel, I.[1], Schlesewsky, M.[2] & Friederici, A.D.[1]

[1] *Max Planck Institute of Cognitive Neuroscience*

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The question of how contextual factors may influence syntactic processes in sentence comprehension is central to an understanding of language architecture. The present study examines how context modulates early syntactic integration processes in *unambiguous* sentences.

Unambiguously marked clause medial word order variations in German ('scrambling') give rise to processing difficulties, which, in ERP measures, are reflected in a centrally-distributed negativity between 300 and 450 ms post-onset of the non-canonically positioned NP (e.g., *den Sänger* in 1; cf. Rösler et al., 1998; Bornkessel et al., 2002; Schlesewsky et al., in press a).

(1) *Vielleicht hat <u>den Sänger</u> der Geiger gelobt.*
perhaps has the-ACC singer the-NOM violinist praised

The present study examined whether the 'scrambling negativity' may be influenced by the information structural status of the scrambled element. Participants read question-answer pairs, in which the question was either neutral ("What happened?") or established the first NP of the ensuing answer as a topic (given) or a focus (new) constituent. Answer sentences were presented in a phrase-by-phrase manner and were either subject-initial (canonical) or object-initial (scrambled).

In a neutral context, scrambled NPs gave rise to a centrally distributed negativity between 300 and 500 ms post-onset of the phrase (thus replicating previous results), which was not reduced for scrambled NPs that were topics (cf. Figure 4). By contrast, scrambled NPs that were focused gave rise to a broadly distributed positivity between 300 and 500 ms post onset of the phrase in comparison to the (neutral) canonical control condition (cf. Figure 4; Schlesewsky et al., in press b). A comparable positivity was also observable for focused initial subjects (cf. Figure 4) and focused second NPs (irrespective of their case marking).

The general appearance of a distinct ERP pattern for focused arguments indicates that constituents which are expressly focused by the context are processed differently from other constituents, most likely on account of the explicit expectations that the context generates with regard to these constituents. Secondly, since, for scrambled focus constituents, the 'focus positivity' superceded the negativity generally observed for scrambled arguments, we may conclude that information structural considerations derived from the context may influence even early phases of structural integration by licensing non-canonical word orders.

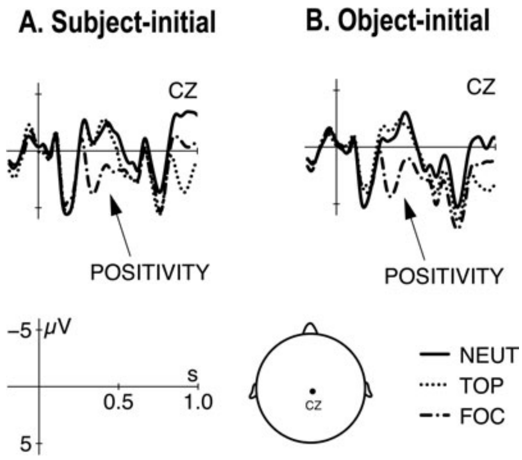

Figure 4. Grand average ERPs for subject- (A) and object-initial sentences (B) at the position of the first NP in a neutral context (NEUT), a focusing context (FOC) and a topic context (TOP).

Prosody and focus structure during reading: The brain knows the difference

2.1.5

Stolterfoht, B., Friederici, A.D. & Alter, K.

Whereas it is a well-known phenomenon that a prosodic representation is built during silent reading (e.g., Slowiaczek & Clifton, 1980; Van Orden et al., 1988; Fodor, 1998), only a few studies have investigated the interplay of prosodic representation and focus structure in sentence processing (e.g., Birch & Clifton, 1995). This could be a result of the fact that it is difficult to find sentence types in which focus structure can be separated from prosodic structure. One rare example is the case of contrastive ellipsis:

default assignment

(1) [Am Freitag hat der Onkel den **VA**ter gesehen ....]$_{F}$

contrastive object, no focus particle (**ON**) → change of focus

(2a) Am Freitag hat der Onkel [den **VA**ter]$_{KF}$ gesehen, und nicht den Neffen.

On Friday, the uncle$_{nom}$ *saw the father*$_{acc}$*, and not the nephew*$_{acc}$*.*

contrastive subject, no focus particle (**SN**) → change of focus and prosody

(2b) Am Freitag hat [der **ON**kel]$_{KF}$ den Vater gesehen, und nicht der Neffe.

On Friday, the uncle$_{nom}$ *saw the father*$_{acc}$*, and not the nephew*$_{nom}$*.*

*control***:** *contrastive object, with focus particle* (**OF**) → no change

(2c) Am Freitag hat der Onkel *nur* [den **VA**ter]$_{KF}$ gesehen, und nicht den Neffen.

*control***:** *contrastive subject, with focus particle* (**SF**) → no change

(2d) Am Freitag hat nur [der **ON**kel]$_{KF}$ den Vater gesehen, und nicht der Neffe.

For a sentence like (1), we assume that the sentence processor assigns wide focus associated with sentence accent on the object (focus structure is indicated by brackets, sentence accent by bold capitals). We will call this the *default assignment* of prosodic structure and focus structure. If this sentence continues with a contrastive ellipsis, in (2a), the processor has to change the *focus structure*: *wide focus → narrow contrastive focus*. In (2b), a change of *focus structure and prosodic structure* is necessary: *wide focus → narrow contrastive focus, accent object → accent subject.* In the control sentences (2c) and (2d), there is *no need* for a prosodic or focus structural revision. The focus particle *nur* ('only') assigns narrow focus and accent independently.

We analyzed three different comparisons:

PROSODY (ON-SN): In both sentence types, a focus structural revision takes place, but only in (2b) was an additional prosodic change necessary. We found a widely distributed negativity (450 to 650 ms), which we interpret as the correlate of prosodic processing.

FOCUS (ON-OF): Sentence type (2a) in contrast to the control sentence (2c) requires a focus structural change. This process is reflected in a positive component (550 to 750 ms).

CONTROL (OF-SF): For both control sentences (2c) and (2d), no revision process was necessary. As predicted, we found no significant effect in the relevant time windows. Our results show that prosodic and focus structural processes can be differentiated in the ERP pattern by their polarity.

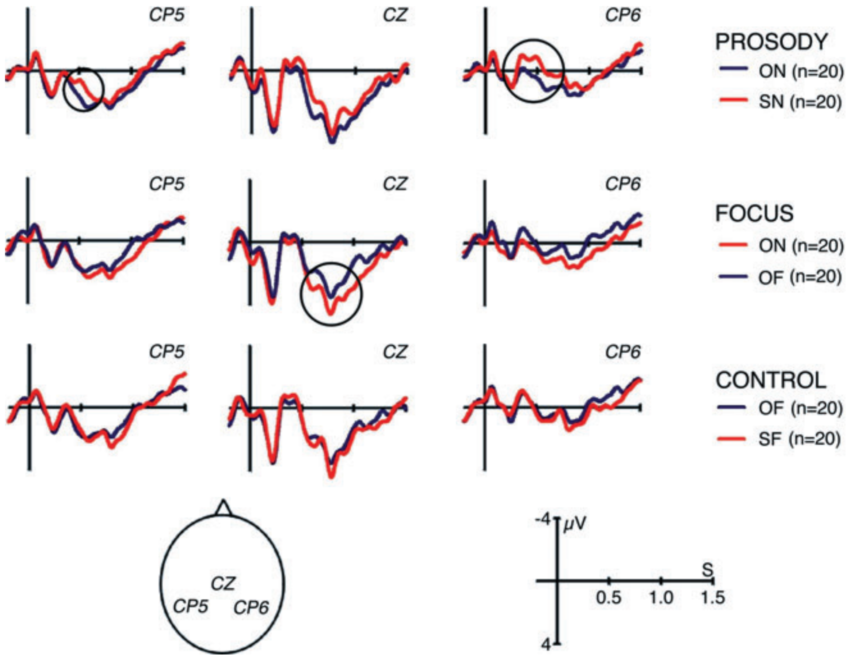

Figure 5. Grand average ERPs on the last phrase of the sentences for three different comparisons: PROSODY, FOCUS and CONTROL.

2.1.6 Functional connectivity of Broca's area during processing of sentences of varying syntactic complexity. Evidence for a modulatory involvement of the basal ganglia

Fiebach, C.J., von Cramon, D.Y. & Friederici, A.D.

In the present study, we set out to investigate the functional connectivity of Broca's area during sentence processing. We used a data set from an experiment in which participants processed grammatical sentences of varying structural complexity as well as ungrammatical sentences (Fiebach et al., submitted; see Fiebach et al., Annual Report 2001, 2.1.3). In this experiment, we observed that activity in the inferior tip of the pars opercularis (BA 44) of the left inferior frontal gyrus covaried with syntactic complexity in a parametric design. In order to investigate the functional connectivity of Broca's area, we used the time series of the voxel with greatest activity in this region as a regressor for a general linear model. The peak voxel and time series was determined individually for each participant in order to account for individual variability of anatomical and functional organization.

The area showing the strongest correlation with Broca's area was the left fronto-opercular region (Figure 6A). This result reflects the correlation of the peak voxel of this area with itself and the immediately surrounding structures. Correlated activity with Broca's area was also found in the right frontal operculum and in posterior cortices (cuneus, lateral occipital cortex bilaterally, posterior fusiform gyri, cerebellum). Finally, correlated activity was found in the basal ganglia and in the thalamus (Figure 6B). Although present bilaterally, this subcortical involvement appeared to be stronger in the left than in the right hemisphere. This finding is in line with recent reports showing that patients with disturbed basal ganglia functions exhibit highly specific problems with syntactic processing. In particular, it was demonstrated that these patients showed no ERP reflections of late syntactic integration processes, whereas early syntactic structure building processes were unaffected (Friederici et al., 1999; Friederici et al., in press; Frisch et al., in press; Annual Report 2000, 2.5.12). However, the present result dissociates from the observation that activation in the basal ganglia was not modulated by syntactic complexity or grammaticality (Fiebach et al., submitted; Annual Report 2001, 2.1.3).

We conclude that the present findings support an involvement of basal ganglia in syntactic processing (Ullman, 2001), as suggested also by anatomical studies demonstrating strong recurrent interconnections between frontal areas and the subcortical structures just described (Alexander et al., 1986). However, our results indicate that the function of the basal ganglia and thalamus is not identical to the role which the involved cortical regions play during syntactic processing. We propose that our data support the assumption of an indirect, modulatory involvement of the basal ganglia in sentence processing.

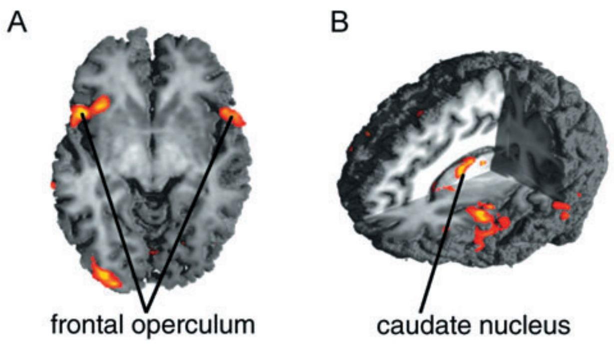

Figure 6. Brain areas showing correlated activation with Broca's area. Statistical parametric maps are thresholded at z>3.09.

2.1.7 The neural correlates of grammatical gender selection during language production

Heim, S.[1], *Opitz, B.*[1,2] & *Friederici, A.D.*[1]

[1] *Max Planck Institute of Cognitive Neuroscience*
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The number of imaging studies on language production is relatively small. In particular, there is only little and contradictory evidence for the neural systems underlying syntactic processing during production. In a picture naming experiment, Levelt et al. (1998) did not observe any inferior frontal activation with MEG, whereas Indefrey et al. (2001)

reported activation in BA 44 and in the posteriorly adjacent Rolandic operculum in a PET study of overt production. However, this activation is also correlated with the amount of articulation required in the experimental conditions. Moreover, the Rolandic operculum has been shown to be involved in articulatory processes in a number of studies (e.g., Dronkers, 1996). Thus, it remains questionable whether the activation reported by Indefrey et al. (2001) really reflects syntactic processing.

We therefore conducted an event-related fMRI experiment with 12 subjects (mean age: 24.3 years; 6 females; TR= 2 s, TE= 10 ms, FOV 19.2 cm, 12 sagittal slices 3 mm/1 mm in the left hemisphere) including four conditions, (1) null events (NULL); (2) saying "jaja" in response to a smiley (BASE); (3) naming a picture (NAME); (4) producing the definite determiner of a picture name (GEN). Only in condition GEN, subjects had access to gender information (van Berkum, 1997). The following contrasts were calculated, reflecting activation to the corresponding processes: BASE–NULL (articulation), NAME–BASE (lexical access), and GEN–NAME (gender selection). While articulation and lexical access resulted in activation patterns consistent with the literature, gender selection selectively evoked activation in the superior portion of BA 44 reaching into the inferior frontal sulcus (Figure 7). This result is in line with data from other studies (Heim et al., submitted; Miceli et al., 2002) in which subjects silently produced the definite determiner of a noun in order to perform a gender judgement task. It can be concluded that the superior portion of BA 44 in Broca's area is crucial for the selection of grammatical gender information during language production.

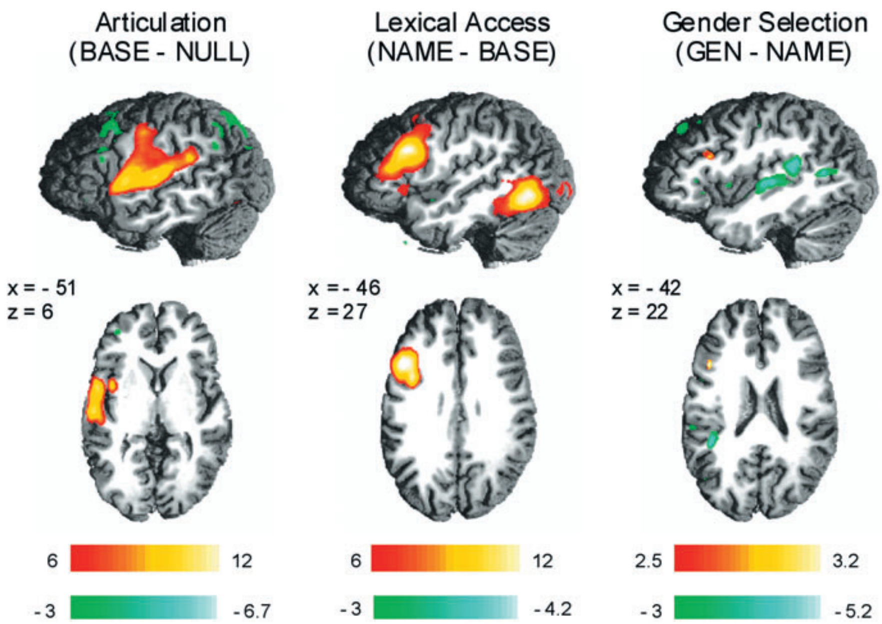

Figure 7. Activations in the contrasts reflecting articulation, lexical access, and gender selection (left to right).

Grammatical gender processing: Modulation of ERP components as a function of instruction

2.1.8

Hofmann, J. & Kotz, S.A.

Previous event-related potential (ERP) studies investigated grammatical gender violation processing at the sentence level. Gunter et al. (2000) showed a left anterior negativity (LAN) and a P600 for the violation condition in comparison to the agreement condition. We were interested in the processing of gender at the word level. We explored the processing of feminine, masculine and neuter German nouns in two visual gender decision tasks using ERPs; (A) Is the noun's syntactic gender feminine or not? (B) Is the noun's syntactic gender masculine or not? The ERPs were recorded from 64 electrodes. While an early negativity for feminine nouns was found in both tasks, a reduced N400 and a higher amplitude of the P3 showed an instruction dependent pattern. Feminine nouns showed a reduced N400 and a higher P3 in task (A) as compared to masculine and neuter nouns. In task (B) the masculine nouns showed a reduced N400 in contrast to the feminine and neuter nouns and a higher P3 as compared to the neuter nouns (see Figure 8). We interpret the early negativity as possibly reflecting the processing of strong phonological cues in feminine nouns (70% ended with an -e), which were not present in the other gender types. The reduced N400 might indicate less semantic processing of the gender type that is in focus. The higher P3 might reflect task dependent target detection. One can conclude that the N400 is modulated by instruction.

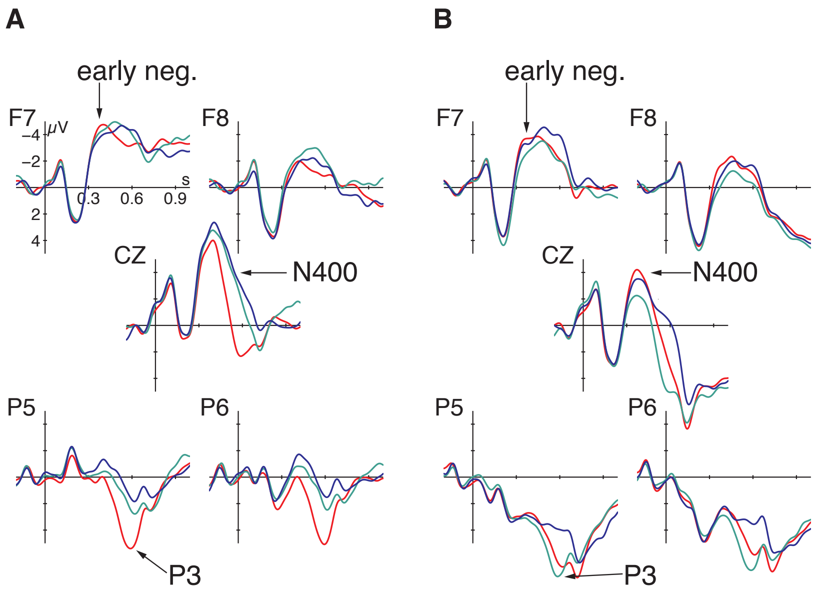

Figure 8. Grand average ERPs for feminine (red), masculine (green) and neuter (blue) nouns in (A) the feminine gender decision and (B) the masculine gender decision task displayed at selected electrodesites.

2.1.9 Neural correlates of lexicality and word frequency in the auditory lexical decision task

Fiebach, C.J. & Friederici, A.D.

Using a visual lexical decision task (i.e., word-pseudoword discrimination), we have demonstrated that words elicited greater activity than pseudowords in basal occipital and temporal cortical areas (Fiebach et al., 2002). Furthermore, we could demonstrate in the same study that rare words elicit greater activity than frequent words particularly in the inferior frontal gyrus of the left hemisphere (word frequency effect). We concluded that basal temporal brain areas are involved into direct access to stored word representations from orthography, a conclusion that is in line with recent reports attributing left fusiform areas to visual word form processing (Cohen et al., 2000; Dehaene et al., 2002). The inferior frontal lobe, in contrast, contributes to more controlled aspects of word recognition, supporting mechanisms such as grapheme-to-phoneme conversion (e.g., Fiez et al., 1999; Fiebach et al., 2002).

Here we replicated the above-described study in the auditory modality using the same stimulus material and the same task (i.e., an auditory lexical decision task). When compared to pseudo word processing, processing of real words elicited stronger activity in the ascending posterior segment of the parallel sulcus and the surrounding angular gyrus, as well as in the posterior inferior temporal lobe (Figure 9). As the posterior-inferior temporal activity is also observable for lexicality in the visual domain, we conclude that this area is related to modality-independent aspects of word recognition. The angular gyrus, in contrast, appears to be specifically involved in auditory lexical decisions. We therefore suggest tentatively that the angular gyrus is likely to be involved in processes analogous to those implemented in the fusiform gyrus for visual word processing. Thus, we propose the hypothesis that the angular gyrus holds a representation of the auditory or phonological form of the word.

The analysis of word frequency revealed increased activation for low frequency words in the most anterior portion of the inferior frontal gyrus (BA 47; Figure 10). Thus, as expected, areas involved in grapheme-to-phoneme conversion during visual word processing (such as BA 44 superior) are not activated when the input is already available in phonological form. In contrast, more anterior inferior frontal areas are activated for

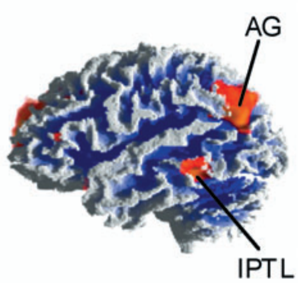

Figure 9. Activity for words as compared to pseudowords in the angular gyrus (AG) and inferior-posterior temporal lobe (IPTL). Medial frontal activity is observable but not discussed here. Statistical parametric maps are thresholded at z>3.09.

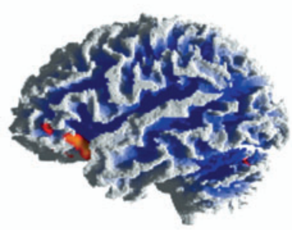

Figure 10. Greater activity for low frequency words as compared to high frequency words in the orbital portion of the inferior frontal gyrus (BA 47). Statistical parametric maps are thresholded at z>3.09.

low frequency words independent of the input modality. This result supports our previous proposal that these areas are involved in controlled access to the lexical-semantic system (Fiebach et al., 2002).

A common neural network for phonological processing in production and comprehension

2.1.10

Heim, S.[1], *Opitz, B.*[1,2] & *Friederici, A.D.*[1]

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Imaging studies of phonological processing during language comprehension consistently reveal activation of a left fronto-temporal network, including the posterior superior temporal gyrus (pSTG) and the superior portion of BA 44 in the inferior frontal gyrus (IFG) (Burton et al., 2000; Démonet et al., 1992; Zatorre et al., 1992, 1996). Studies of phonological processing during production, however, do not yield a consistent picture with respect to left IFG activation (Levelt et al., 1998: no frontal activation; Lurito et al., 2000: BA 44; Price et al., 1997: BA 46). This discrepancy may be due to the different tasks used in the comprehension (phoneme decisions) and production (naming, rhyming, generation) experiments.

We therefore conducted an event-related fMRI experiment (TR= 1 s, TE= 10 ms, FOV 19.2 cm, 12 axial slices 6 mm/2 mm) using the same kind of task as in the comprehension studies which were also administered in electrophysiological studies in the domain of production (e.g., van Turennout et al., 1997; 1998). Eight right-handed subjects (mean age: 26.4 years, 3 females) performed the following tasks in response to pictures of real objects: (1) decision on the initial phoneme of the picture name: /b/ or not? (PHON1);

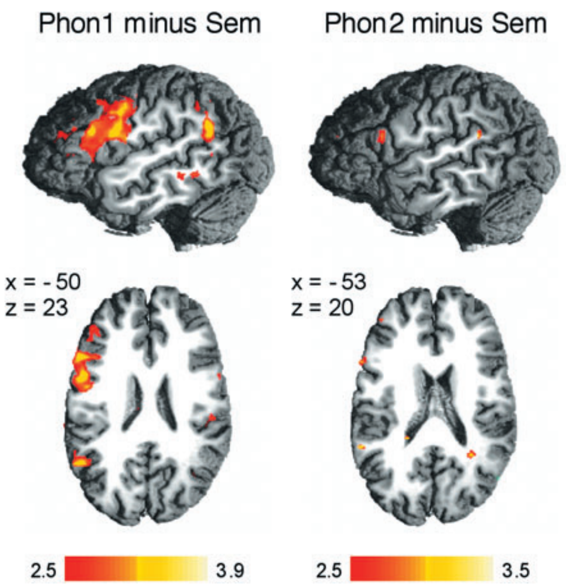

Figure 11. Activations in the experimental contrasts reflecting phonological processing (PHON1–SEM and PHON2–SEM).

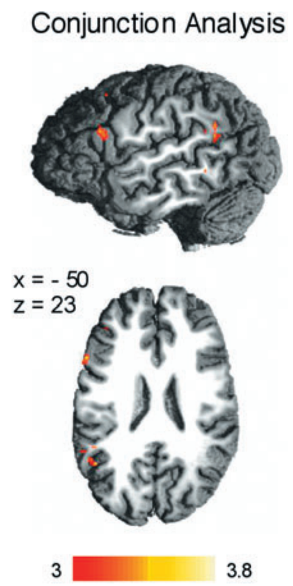

Figure 12. Activations in the conjunction analysis.

(2) decision on the initial phoneme of the picture name: vowel or not? (PHON2); (3) semantic decision: natural or man-made object? (SEM); (4) target detection (BASE); in addition, null events were included. The contrasts PHON1–SEM and PHON2–SEM as well as the conjunction analysis of both contrasts revealed activation in the left hemisphere in the superior portion of BA 44 and in the pSTG (Figures 11 and 12). Thus, the activation found here for production is identical to that reported in the comprehension studies. It can be concluded that phonological processing in language production and comprehension relies on the same neural network in the left hemisphere.

2.1.11 ERP correlates for the processing of segmental and suprasegmental information in Cantonese

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[2] *Chinese University of Hong Kong, China*

Tone languages such as Cantonese express semantic meaning via segmental and suprasegmental information. The term segmental information refers to the consonants and vowels that constitute words. Suprasegmental information refers to the tone in which a string of consonants and vowels is spoken. In Cantonese, tone distinguishes between different meanings of the same segmental information. For example, the meaning of the syllable 'ma' can either be 'mother' or 'horse' depending on whether it is spoken with a high level or low rising tone.
The present study should determine whether segmental and suprasegmental information are of similar importance for semantic processing in Cantonese. Cantonese listeners heard sentences and decided via button press whether or not a sentence was semantically correct. Semantically incorrect sentences contained a word that differed from the semantically expected word (e.g., 'ma' with a low falling tone) in the segmental information (e.g., 'mou' with a low falling tone), in the suprasegmental information (e.g., 'ma' with a high level tone) or in both segmental and suprasegmental information (e.g., 'sau' with a high rising tone).

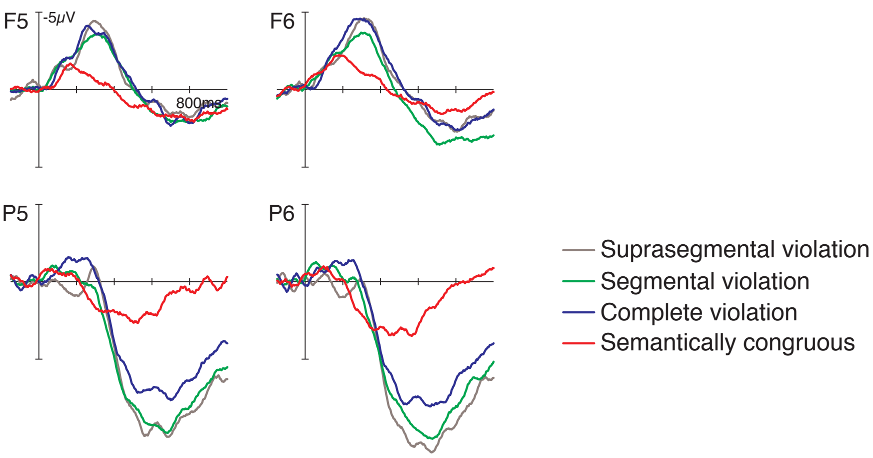

Figure 13. ERPs to semantically congruous and incongruous words elicited in Cantonese listeners.

The event related potential (ERP) revealed an early negativity between 200 and 400 ms and a late positivity between 400 and 1000 ms following word onset, which were larger for semantically incongruous as compared to congruous words (see Figure 13). While the early effect did not differentiate between the three violation conditions, the late positivity was smaller for the complete violation than for the segmental and the suprasegmental violation. The latter two conditions did not differ. The present data suggest an equivalent role of segmental and suprasegmental information in Cantonese. Furthermore, a later re-analysis process seems to differ for words that constitute a complete semantic violation as compared to semantically incongruous words that bear some similarity to the expected, semantically congruous word.

ERP correlates of semantically based word fragment priming

2.1.12

Friedrich, C.K., Fiehler, K., Gunter, T.C. & Kotz, S.A.

In previous studies we showed that form-based word fragment priming evokes a P350 deflection in the ERP (see for instance Annual Report 2001). In this paradigm prime-target pairs are presented that share form information (e.g., *Tai-Taifun* [Engl.: typhoon]) or not (e.g., *Tai-Flamme* [Engl.: flame]). Primes are either letter strings (within-modal priming) or parts of spoken words (cross-modal priming). They are immediately followed by visual targets. The P350 was found to be reduced for matching targets in both types of form priming. Thus, it was interpreted as reflecting activation in a modality-independent mental lexicon.

The present study investigated the correlation of the P350 to semantic processes in a within-modality and in a cross-modality experiment. The same primes as in the previous experiments were used. Half of the targets were associatively related to the matching targets of the previous experiments (e.g., *Sturm* [Engl: storm] was chosen for *Taifun*). Thus, the resulting prime-target pairs were semantically related (e.g., *Tai-Sturm* [Engl.: storm]). Half of the targets were completely unrelated to the prime (e.g., *Tai–Hektar* [Engl: hectare]).

The P350 was enhanced for unrelated as compared to semantically related targets in both experiments (see Figure 14A and B), confirming that this ERP deflection can be related not only to word from activation, but also to semantic activation. However, for

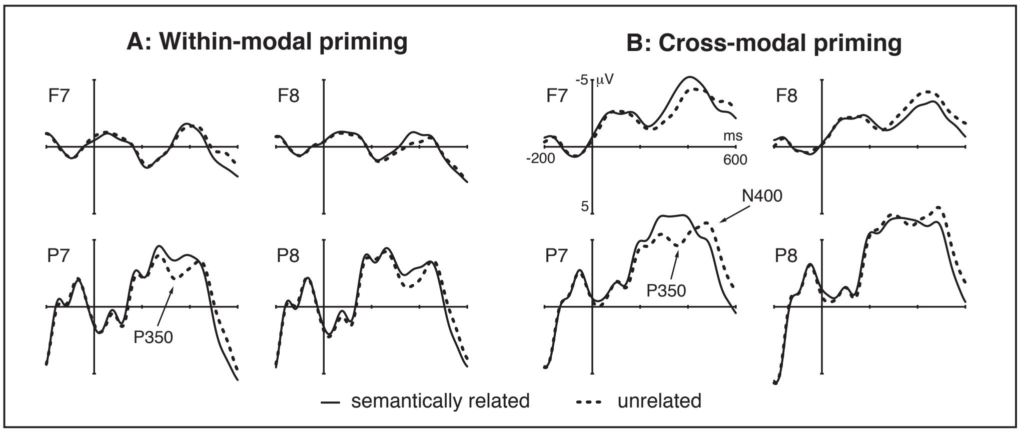

Figure 14. ERPs for selected electrodes elicited by targets in the within-modality experiment (A) and in the cross-modality experiment (B).

cross-modal priming the P350 effect was overlapped by an N400 effect (see Figure 14B) which was absent for within-modal priming (see Figure 14A). This suggests that the use of semantic information diverges during early stages of written and spoken word recognition.

2.1.13 The processing of German noun compounds: Linking elements are not processed online as plural morphemes

Köster, D., Gunter, T.C. & Wagner, S.

Psycholinguistic models of compound processing assume either that linking elements (e.g., -en- in "Autorenrechte") are plural morphemes of the preceding constituent (Clahsen, 1999) or that they simply link constituents obeying phonological functions (Gawlitzek-Maiwald, 1994). In previous experiments we demonstrated the access of morphosyntactic representations of each compound constituent, using event-related potentials (ERP), by a gender incongruity with a preceding determiner. If linking elements are, indeed, plural morphemes they should elicit, as another morphosyntactic feature, a left-anterior negativity (LAN) if incongruent with a preceding numeral. In order to manipulate the abstract number agreement relation the presence and the absence of linking element has to be considered as both are indicative for plural and singular, respectively.
The ERP was measured while subjects were presented with a numeral ("ein" or "zwei") acoustically followed by a two-constituent compound whereby each constituent might

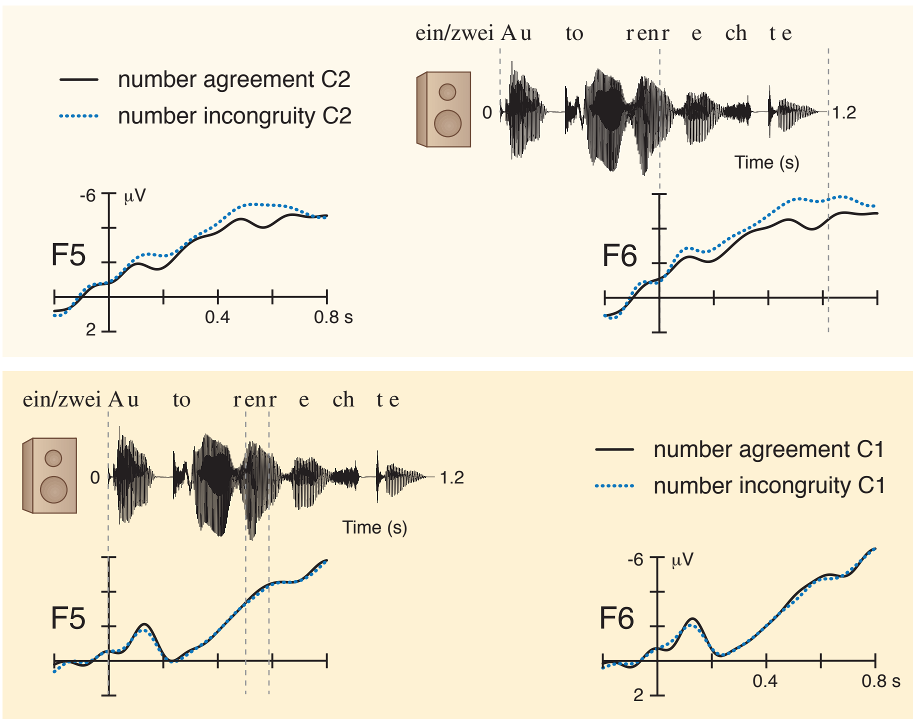

Figure 15. The ERP effect in response to number incongruity shown at the frontal electrodes F5 (left) and F6 (right). Top: A bilateral negativity time-locked to the onset of last constituents (C2) is observed at frontal electrodes only. Bottom: The number incongruity of initial constituents (C1) does not give rise to any ERP effect.

disagree with the numeral in number independently of one another. Half of the constituents were used in the singular form and the other half in the plural form. All compound words were acceptable word of the German language.
The number violation of the last constituent, irrespective of the form, yielded a bilateral frontal negativity indicating the detection of a number mismatch (Figure 15 upper panel). The number violation of the first constituent, irrespective of the form, did not give rise to any effect (Figure 15 lower panel). If linking elements are no plural morphemes as indicated by the latter result, the agreement and the violation conditions are incorrectly coded for the supposed plural forms (for the first constituent). After recoding of plural forms, a sustained negativity was observed in response to the number violation of the first constituent. This indicates that the first constituents of compound words are always processed as singular instances irrespective of the presences of a linking element.
These results show that linking elements are not processed online as plural morphemes of the first constituent. However, plural suffixes at the end of compound words are processed as such morphemes. Therefore, we argue that each constituent is accessed from the lexicon as a minimal morphosyntactic representation including all its invariable features (e.g., gender) but the analysis and assignment of variable, inflectional features (e.g., number) is only done after the last compound constituent is accessed.

2.1.14 The neural network underlying comprehension in German Sign Language: Processing discourse structures

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[2] Centre for Functional Imaging Studies, Edinburgh, United Kingdom
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Sign languages have been shown to employ all the criteria defined for natural languages. They have naturally developed in deaf communities of the deaf, their vocabulary is subject to constant changes and they employ the same linguistic units and levels (i.e., phonological, syntactic and semantic) that we find in the grammars of spoken languages. However, one important aspect of sign languages is that they rely more on discourse structures than most of the spoken languages seem to do. Although it is very common to investigate single word or sentence processing in the auditory and/or visual modality in spoken languages, this would be a rather unnatural way of exploring the processing of studying signed languages. Following this line of reasoning, we set out an fMRI-study that aimed to identify the brain regions mediating the comprehension of German Sign Language (DGS; Deutsche Gebärdensprache) by delivering 6 congenitally deaf volunteers with dialogue sequences that consisted of 4 sentences, each mimicking a possible every-day conversation between two signers.
Figure 16 shows left and right brain areas including frontal and temporo-occipital cortex for one congenitally deaf participant during the processing of sign-language communication. This result can be taken as primary evidence that secondary and tertiary sensory (vision and motor) cortices constitute a network which represents sign language comprehension. Obviously the visuo-spatial and motion related aspects of sign languages

account for the involvement of premotor and higher visual circuits. Activation in the posterior temporal parietal junction area apparently reflects the processing of linguistic information available in the sentences presented.

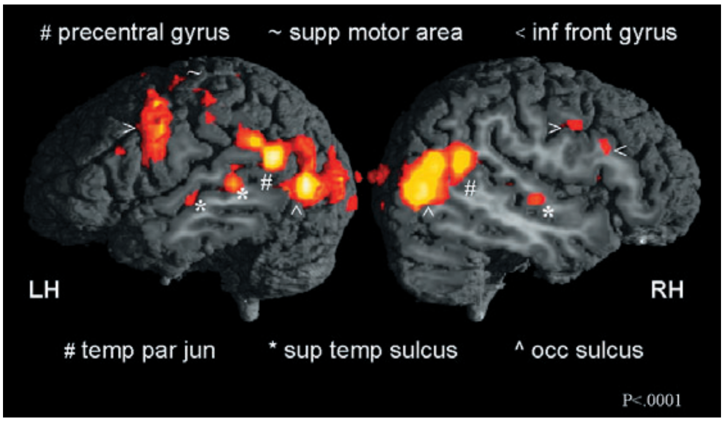

Figure 16. Main activation foci obtained whilst one individual participant processed sign language communication.

2.1.15 Conceptual and structural relations in action comprehension

Bach, P.[1], Gunter, T.C.[2], Knoblich, G.[1], Prinz, W.[1] & Friederici, A.D.[2]

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[2] Max Planck Institute of Cognitive Neuroscience

Everyday actions can be applied to a multitude of objects by millions of actors and may even be mediated by different tools. Thus, the understanding of an action is a combinatorial problem. It can only be solved when knowledge about the different entities involved is related to one another. We provide evidence that at least two types of information are used to establish these relations.
27 subjects were presented with still frames of objects and still frames of actions directed at these objects. Their EEG was measured while they judged these combinations in respect to whether they contained a mismatch or not (cf. Figure 17). Two types of mismatch were possible. Conceptual mismatches were present when the action was not appropriate to the meaning of the target object (Figure 17, middle panel). Structural mismatches were present if the structural features of action and target object were not corresponding (i.e., different orientation of screwdriver and screw, cf. Figure 17, right panel).
Different effects were associated with both types of mismatch (Figure 18). Conceptual mismatches elicited the N400-component (Figure 18, middle panel), which is related to conceptual/semantic processes in a vast number of tasks. It was followed by a small positivity. Structural mismatches evoked a negative effect in a similar time range as the N400, which, however, was clearly lateralized to the left (Figure 18, right panel). This effect probably reflects the detection of a structural mismatch or structural feature matching per se. It was followed by a long-lasting positive effect widely distributed over posterior electrodes (i.e., P600).
The present study clearly shows that the brain processes related to structural and conceptual relations between the constituent entities of a perceived action are different.

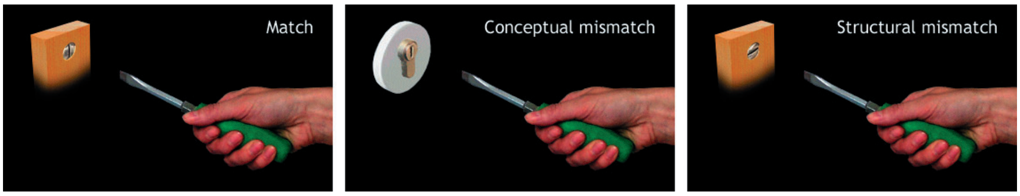

Figure 17. Examples for the stimuli used in the experiment.

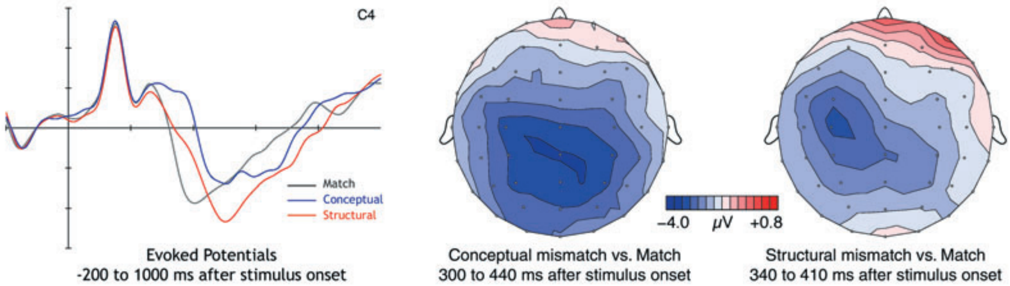

Figure 18. Evoked potentials and scalp distributions for both types of mismatch.

Communicating hands: ERPs elicited by meaningful symbolic hand postures

2.1.16

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Face-to-face communication relies on visual and auditory cues. The auditory stream has the highest informational content and is therefore investigated in most language research. Visual information (i.e., gestures), however, also plays an important, though less explored role in normal communication. Gestures, for instance, can assist the processing of auditory information through disambiguation. Hand postures can be used symbolically and can carry a clear cut meaning as in the example of the 'thumbs-up' gesture. Such meaningful hand postures, or 'emblems', are very intriguing communicative tools because a very complex/abstract message can be transferred with the use of a single gesture. Note that the use of emblems has a different linguistic status as the hand postures used in sign language which can also reflect syntactic and morphological information. Thus, although (re)presented by hands, emblems typically have an abstract meaning similar to that of words. Meaningful and meaningless hand postures were presented to subjects who had to carry out a discrimination task during which electrical brain responses were measured. Both sets of hand postures were matched as closely as possible. The ERPs elicited by meaningful hand postures showed an anteriorly distributed N300 and a centro-posteriorly distributed N400 component. The N300 might reflect processes related to activation of image based representations. The N400, is related to meaning processes. The scalp-distribution of the N400 which is more posterior than usually reported in picture processing, suggests that the meaningful hand postures employed have an abstract semantic representation comparable to words in language processing.

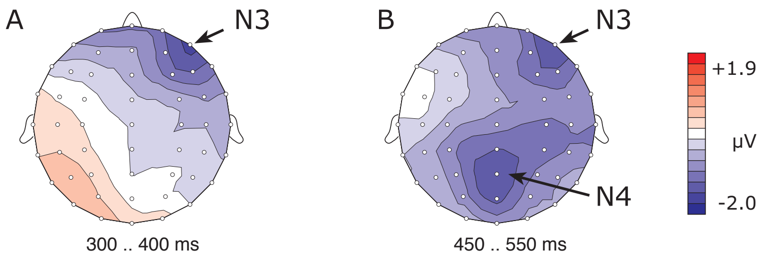

Figure 19. The ERP-data as found for the meaningful vs. meaningless hand-postures.
Figure 19A shows the Regions of Interest (ROI) used for the scalp distribution analysis and the scalp distribution of the N3 and N4 component here shown as a difference between meaningful and meaningless.

2.1.17 Recognition of meaningful and meaningless hand postures

Nakamura, A.[1], Maess, B.[1], Gunter, T.C.[1], Knösche, T.R.[1], Bach, P.[2] & Friederici, A.D.[1]

[1] *Max Planck Institute of Cognitive Neuroscience*
[2] *Max Planck Institute for Psychological Research, Munich*

Hand postures play an important role for human communication, so some hand postures have strong symbolic meanings. The objective of this study is to disclose a spatio-temporal profile of human brain mechanisms for hand posture recognition. We selected 11 meaningful and 11 meaningless hand postures according to a psychological questionnaire filled out by 47 German volunteers. Visual stimuli are digitized gray-scale photos of those hand postures taken from 6 subjects. The task was to judge the meaningfulness of the hand postures. Visual event-related magnetic fields were measured

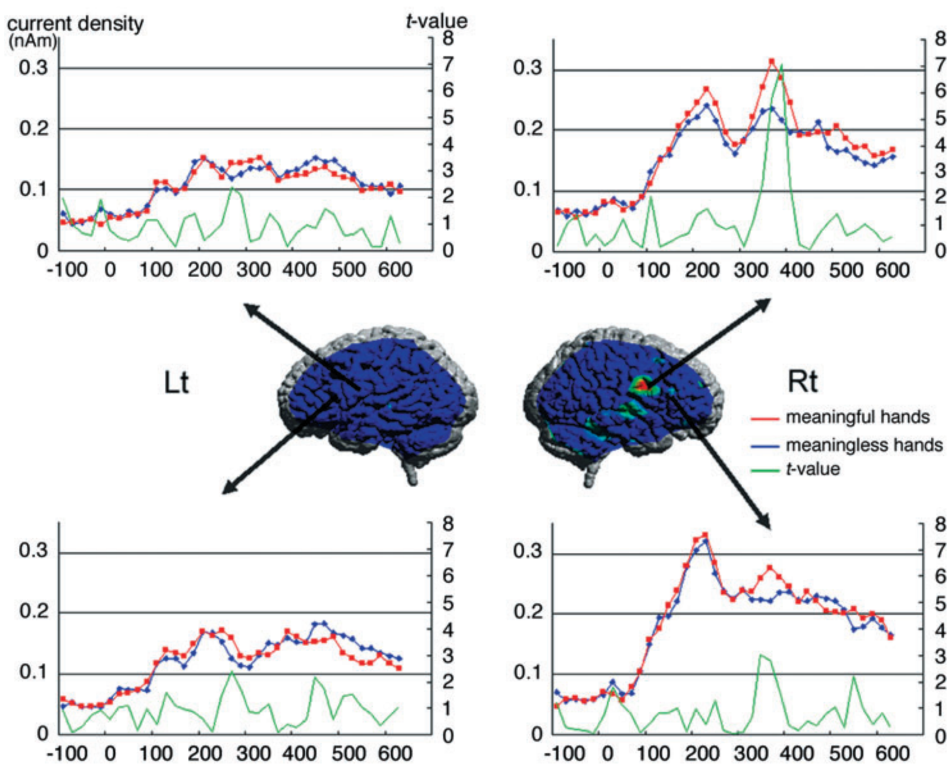

Figure 20. *t*-map of the condition differences and temporal profiles of the current density in the right ventral BA 6 and BA 45, and their counter parts in the left hemisphere.

from 20 volunteers. Data was analyzed by combining current density estimation, spatial normalization and statistical parametric mapping. The averaged current density maps and statistic analyses showed no significant condition differences until 360 ms after stimulus onset. Both meaningful and meaningless postures increased the current density around the primary visual cortices (latencies around 100 ms), bilateral inferior occipitotemporal cortices (~160 ms), the left occipito-parietal cortex (~200 ms), and the right sensory-motor area for the hand representation (~340 ms). Statistically significant condition differences were found in the latencies from 360 to 400 ms. The meaningful postures elicited larger activities than the meaningless in the ventral BA 6. Time courses of the current density in the right ventral BA 6, BA 45, and their counter part in the left hemisphere, clearly showed right hemispheric predominance (Figure 20). Those activated regions should cooperate during hand posture recognition. Especially, the right BA 6 is considered to be important for semantic processing.

Working memory for semantic concepts: An event-related fMRI study

2.1.18

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[2] *Department of Psychology, University of California, San Diego*
[3] *Department of Psychology, University of Michigan, Ann Arbor*

The contribution of frontal and temporal brain regions to conceptual-semantic processes during the retention interval of a working memory task was investigated using event-related fMRI. Participants maintained emergent (novel) semantic concepts derived during the encoding of a verbal memory set to eventually compare to a test probe (e.g., when encoding the word triplet 'banana-well-peeled' the concept 'peeled banana' is maintained and the color 'white' is such an emergent property). Participants could not predict the specific target word immediately, but rather had to maintain emergent concept(s) over a retention interval (7.5 s) until the target probe appeared. In a phonological control task, participants rehearsed unrelated word triplets (to be compared to a test probe) and in a baseline task (not requiring working memory involvement) they made judgments about the physical properties of letter strings.

Phonological rehearsal of unrelated words activated areas classically associated with articulatory rehearsal (left inferior frontal cortex, ventral premotor cortex, SMA, cerebellum; Figure 21A). In the delay interval of the semantic working memory task, an even more extended area of the left inferior frontal lobe exhibited increased activity, also covering more anterior IFG areas, the posterior inferior frontal sulcus, and the middle frontal gyrus. Specific increases in activation were observed in left superior frontal gyrus and in the posterior left middle and inferior temporal cortex (Figure 21B). We propose that a network of superior frontal, ventro-lateral frontal and posterior-inferior temporal brain areas cooperate in the retrieval (and possibly maintenance) of emergent semantic concepts in the conceptual combination task. These brain areas provide a functional-neuroanatomical basis for semantic working memory.

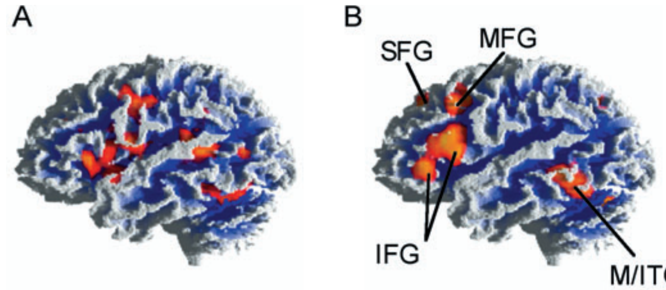

Figure 21. (A) Activation elicited by phonological rehearsal of verbal material in working memory, as compared to the physical baseline task. (B) Increased activation for semantic working memory as compared to the phonological working memory task in the inferior frontal gyrus (IFG), the middle (MFG) and superior frontal gyrus (SFG) and in the posterior inferior temporal lobe (M/ITG). Statistical parametric maps are thresholded at z>3.09 and rendered onto a white-matter segmented template brain.

2.1.19 Is it tonotopy after all?

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In this functional MRI study the frequency-dependent localization of acoustically evoked BOLD responses within the human auditory cortex was investigated. A blocked design was employed, consisting of periods of tonal stimulation (random frequency modulations with center frequencies 0.25, 0.5, 4.0, and 8.0 kHz) and resting periods during which only the ambient scanner noise was audible. Multiple frequency dependent activation

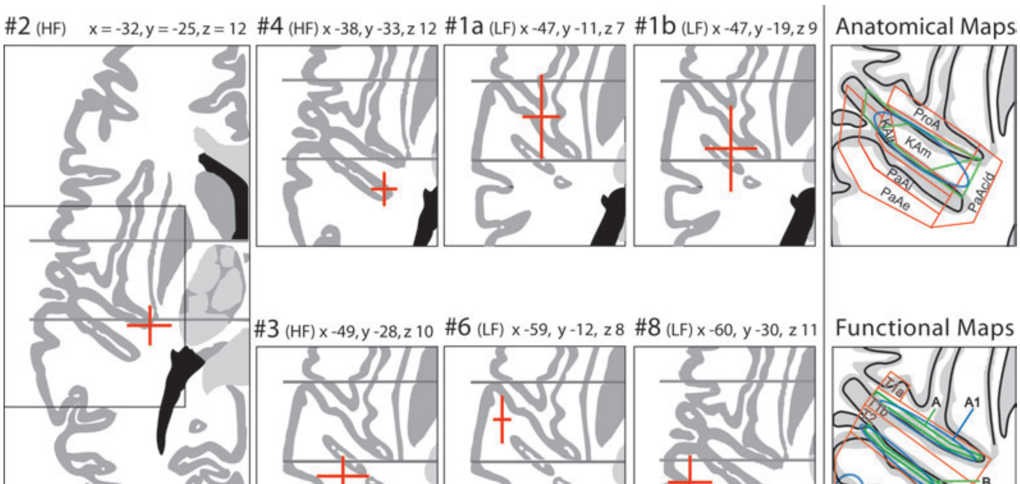

Figure 22. The locations of seven frequency dependent foci are shown on schematic outlines of the cortex based on the Talairach atlas (Talairach & Tournoux, 1988). The crossbars indicate the mean location and the 95% confidence area of the respective foci. The header of each image gives the number of the depicted focus (adopted from Talavage et al., 2000) followed by the frequency dependence (HF or LF) and the Talairach coordinates. Note the large fronto-occipital variance for foci #1a and #1b, which is due to the anatomical variability of HG across the subjects. The location of foci #2 and #4 showed the least variability. In order to facilitate comparison with results of other studies, the two rightmost subfigures show fractions of relevant anatomical (Galaburda & Sanides, 1980; Rivier & Clarke, 1997; Morosan et al., 2001) and functional maps (Scheich *et al.*, 1998; Hashimoto *et al.*, 2000; Di Salle *et al.*, 2001) overlaid on schematic drawings of HG and the surrounding cortex.

sites were reliably demonstrated on the surface of the auditory cortex (Figure 22). The individual gyral pattern of the superior temporal plane (STP), especially the anatomy of Heschl's gyrus, was found to be the major source of inter-individual variability. Considering this variability by tracking the frequency responsiveness to the four stimulus frequencies along individual Heschl's gyri (Figure 23) yielded medio-lateral gradients of responsiveness to high frequencies medially and low frequencies laterally (Figure 24). It is, however, argued that, with regard to the results of electrophysiological and cytoarchitectonical studies in humans and in non-human primates, the multiple frequency-dependent activation sites found in the present study as well as in other recent fMRI investigations are no direct indication of tonotopic organization of cyto-architectonical areas. An alternative interpretation is that the activation sites correspond to different cortical fields, the topological organization of which cannot be resolved with the current spatial resolution of fMRI. In this notion, the detected frequency selectivity of different cortical areas arises from an excess of neurons engaged in the processing of different acoustic features, which are associated with different frequency bands. Differences in the response properties of medial compared to lateral and frontal compared to occipital portions of HG strongly support this notion.

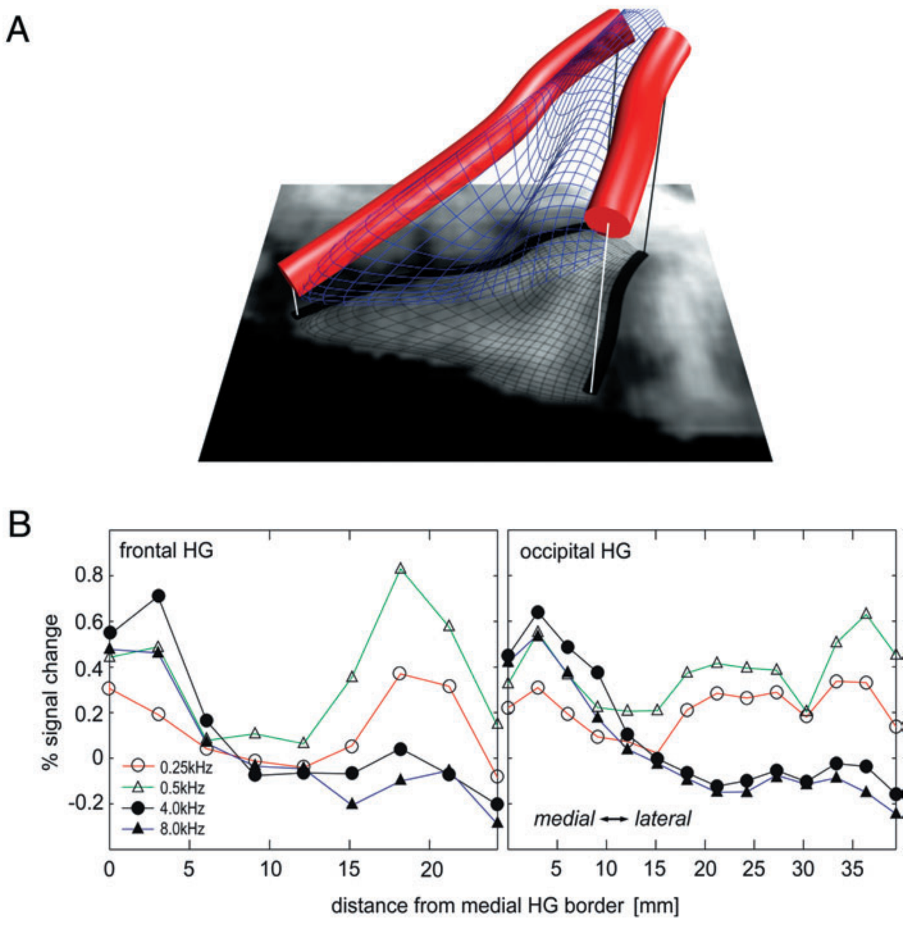

Figure 23. Tubular regions of interest (ROI) used to extract individual frequency profiles along Heschl's gyri. (**A**) Two tubular ROIs were manually aligned with the frontal and occipital walls of Heschl's gyrus. (**B**) The relative activation strength of voxels in the four frequency conditions analyzed from medial to lateral along the regions indicated in (A) at the frontal and occipital wall of HG.

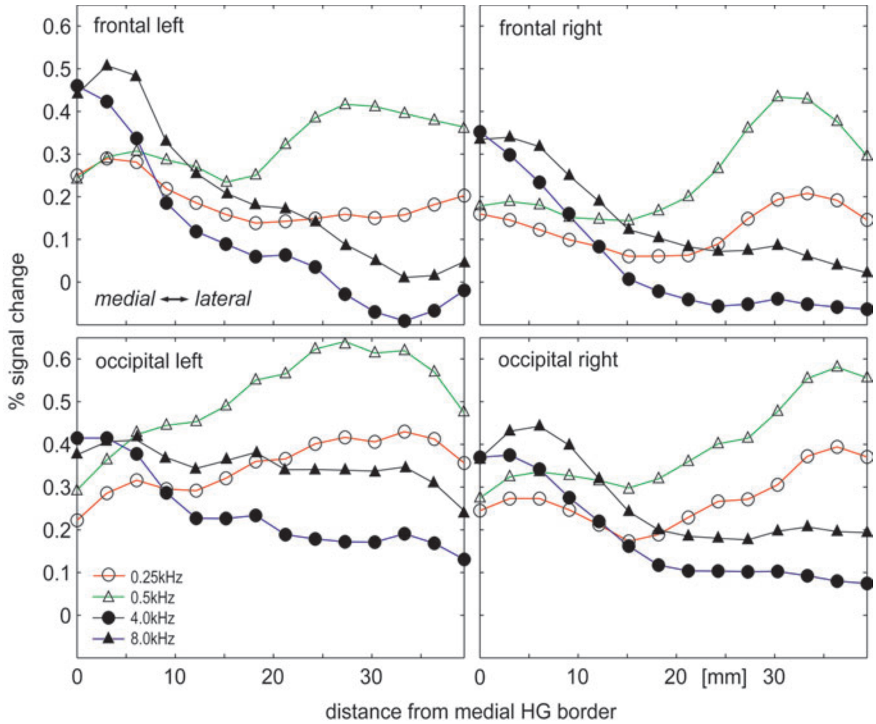

Figure 24. Averaged frequency profiles for the frontal and occipital walls of the left and right Heschl's gyri (frequencies indicated in the graph). The strength of activation caused by high-frequency stimulation decreases from medial to lateral in the four domains analyzed. Low-frequency stimulation caused maximum activation in the lateral third of the medio-lateral HG extension. Note the differences between the frontal and the occipital frequency profiles as well as between the medial and the lateral HG portions.

First and second language learning are in the focus of this research group.

Basic language learning processes and their neural underpinning was investigated in an fMRI study on artificial language learning, see 2.2.1.

Second language learning. An fMRI study on the processing of semantically and syntactically incorrect as well as correct German sentences was conducted with a group of Russian native speakers identifying the neural network recruited during sentence comprehension, see 2.2.2. Using ERPs one study investigated the processing of semantically and syntactically ambiguous words in sentence context in German native speakers learning English, see 2.2.3. The effect of learners' proficiency on translating ambiguities was in the focus of another ERP experiment, see 2.2.4.

First language learning. The infants' ability to process syllable duration in 2 months-old normal infants was reported in the Annual Report 2001. Here a study is presented indicating that infants from families with risk for Specific Language Impairment (SLI) already differ in their ERP pattern from those of normals at the age of 2 months, see 2.2.5. The processing of two syllable items was investigated in 4 months old infants, suggesting that these are already sensitive to first versus second syllable stress patterns, see 2.2.6.

2.2.1 The neuronal correlates of rule-based and similarity-based learning

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Language learning is one of the mysteries of human cognition. One important view on learning, gaining considerable interest over the past years, proposes two distinct processes. According to this view, individuals either learn item-specific information on the basis of superficial similarity to some exemplar or learn by abstracting a representation of the underlying rules. Recent neuroimaging studies have highlighted the importance of the hippocampus and the prefrontal cortex, in rule-learning and language processing. However, the posited importance of hippocampal-prefrontal interaction remains to be empirically tested. In the present study we used functional magnetic resonance imaging to examine in detail this interaction by assessing learning-related changes in hemodynamic activity during artificial language acquisition. One aspect that has received little attention in previous studies is the potential difference between artificial grammars (AG) of the Reber-type used to study language abilities in infants and adults and natural language. In the present work we investigate the neural basis of AG learning by emphasizing language-like rules.
Subjects (n=21, 12 male) with profound knowledge of a miniature artifical grammar system called BROCANTO (see Annual Report 2001) acquired in a previous experiment took part in this study. During MR scanning they were presented with a slightly modified version. For one group the superficial similarity was changed by introducing a new

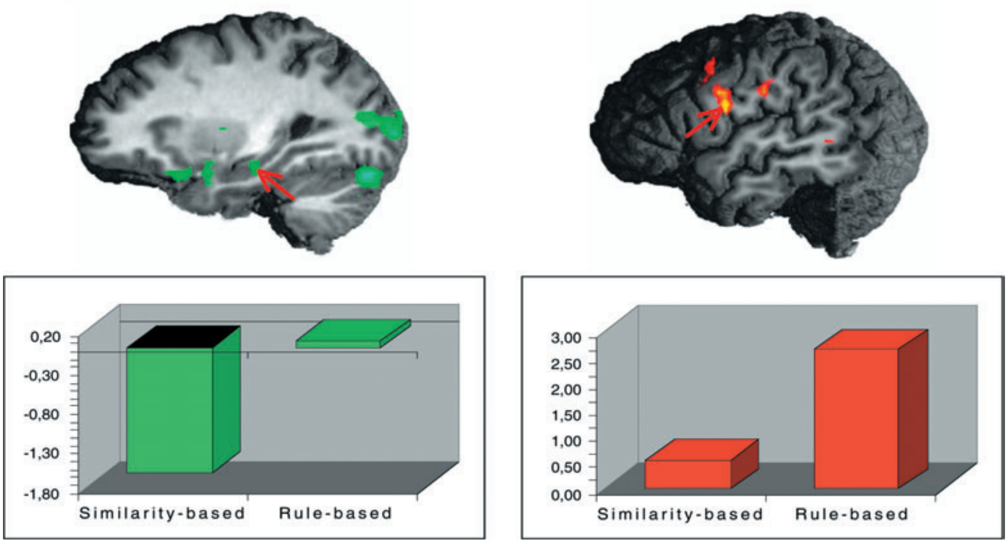

Figure 1. Brain regions in which a significant Condition by Time interaction was observed. Sagittal section at x=-26 mm (left panel) and x=-48 mm exihibit brain areas with changes of activity during learning relative to recurring control. Decreased activity in left anterior hippocampus (left panel, indicated by an arrow) was noted for similarity-based learning only (bottom left). Regions demonstrating increased activity during learning included the left precentral gyrus (right panel) and was predominant for rule-based learning (bottom right).

word order without changing the underlying rules (WORD condition). For the other half the new word order implied also a new grammatical rule. This latter condition led to a significant decrease in grammaticality judgment immediately after the change with subsequent learning of the new rule. In the WORD condition increasing performance was observerd throughout the entire session.
Increased proficiency in artificial grammar use resulted in a gradual decrease of left anterior hippocampal activity in the WORD condition only. In contrast, a gradual increase of activity in the left inferior precentral gyrus was observed solely for the RULE condition (Figure 1). The current findings agree well with previous studies demonstrating that changes in superficial features of an AG modulated activation in the left anterior hippocampus whereas bilateral anterior prefrontal cortices were selectively engaged following abstract rule change. These results point to a differentiation between similarity-based learning and rule-abstraction during language acquisition with similarity-based learning playing a non-obligatory role during the initial phase and rule-based abstracting during a later phase.

2.2.2 Cerebral representation of syntactic and semantic processing in bilinguals

Rüschemeyer, S.A., Fiebach, C.J., Hahne, A. & Friederici, A.D.

The present study set out to investigate differences in the cerebral representation of language processing in bilinguals. Previous electrophysiological studies (Hahne, 2001; Hahne & Friederici, 2001) showed a modulation of classical, language-related ERP-components in bilingual speakers. Specifically, semantically violated sentences brought on a reduced negative peak at approximately 400 ms (N400) in non-native speakers in comparison to native speakers. Furthermore, syntactic violations, which elicited an early (ELAN, ca. 180 ms) and a late (P600, ca. 600 ms) component in native speakers, elicited only a reduced late component in non-natives. Based on the fact that differences between native and non-native speakers were evident at the electrophysiological level, we used event-related functional magnetic resonance imaging to examine the role of specific cerebral structures in processing semantic and syntactic violations. In this study the same stimuli used in the previously mentioned ERP studies were presented to (1) a group of native German speakers, and (2) a group of non-native, fluent speakers of German (participants were native speakers of Russian). The hemodynamic response was recorded while participants listened to stimuli consisting of correctly spoken, semantically incorrect and syntactically incorrect sentences.

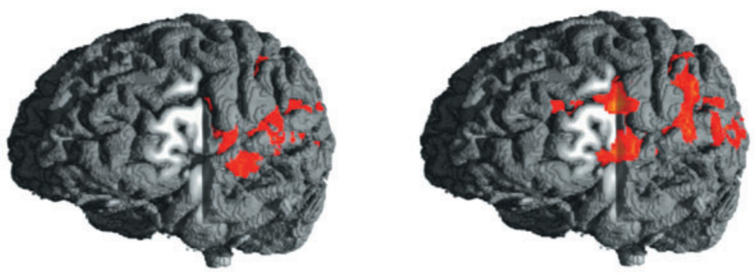

Figure 2. Upon hearing a syntactic violation L1 speakers (left) show increased levels of activation primarily along the STG. L2 speakers (right) show more increased activation along the IFS and less STG activation.

The results show that native and non-native speakers utilize different cerebral structures to deal with incorrect sentences presented in the auditory modality. Specifically, L1 speakers show increased activation predominantly in temporal cortex, whereas L2 speakers employ additional frontal and parietal cortices not significantly activated in L1 speakers. Across conditions, L1 speakers showed a greater increase in activation in the posterior superior temporal gyrus (STG), an area which has been implicated in the processing of lexical semantic information (Binder, 2000; Hickok & Poeppel, 2000; Price, 2000). L2 speakers show increased levels of activation in mid STG regions, lateral to Heschl's Gyrus, however in the posterior regions seen activated in L1 speakers, L2 speakers do not show increased levels of activation. In none of the three critical conditions do L1 speakers show a main effect of increased activation in frontal cortex classically associated with language processing (Broca's Area). L2 speakers, on the other hand, do show activation here, and along the length of the inferior frontal sulcus (IFS). We interpret this result as a reflection of the increased effort involved in comprehending a second language.

2.2.3 Lexical ambiguity in the L2: How autonomous is meaning access and use of semantic and syntactic context cues? — An event-related brain potential (ERP) study

Elston-Güttler, K., Hahne, A. & Friederici, A.D.

Little (neuro)cognitive research has been conducted on L2 processing of words in sentence context that are semantically ambiguous (same-class: *bank*) or syntactically ambiguous (mixed-class: *trip*). We explored the nature of homonym meaning access and use of dominance and/or sentence context cues in an English semantic priming lexical decision experiment presented with stimulus-onset asynchronies (SOAs) of 200, 500, and 800 ms to 48 advanced, late learners of English (German = L1). Reaction times (RTs) and event-related potentials (ERPs) were measured on targets (e.g., STUMBLE) that were preceded by homonym or unrelated primes (i.e., *They looked forward to the fun* **trip** [unrelated: **program**]). Targets reflected the contextually appropriate or inappropriate meaning for dominant and subordinate meanings of same- and mixed-class ambiguity types. At the 200 ms and 500 ms SOAs, overall RT and ERP N400 priming effects were observed for both same- and mixed-class ambiguity types (see left and middle parts of Figure 3a and 3b) with no dominance, contextual appropriacy, or ambiguity type effects, indicating pure multiple access. The 800 ms SOA again showed overall RT and N400 priming, but also an early attenuated negativity at about 100 ms (possibly linked to detection of syntactic anomalies) for the related targets of mixed-class, contextually appropriate meanings only (see right part of Figure 3a and 3b). The results indicate that L2 learners are capable of native-like multiple access at very short SOAs, but that subsequently they do not effectively use dominance or purely semantic sentence context to inhibit inappropriate meanings. The early negativity for mixed-class ambiguities at the 800 ms SOA, however, indicates that, when given enough time to process semantic *and* syntactic context cues, learners indeed use context in L2 lexical ambiguity resolution.

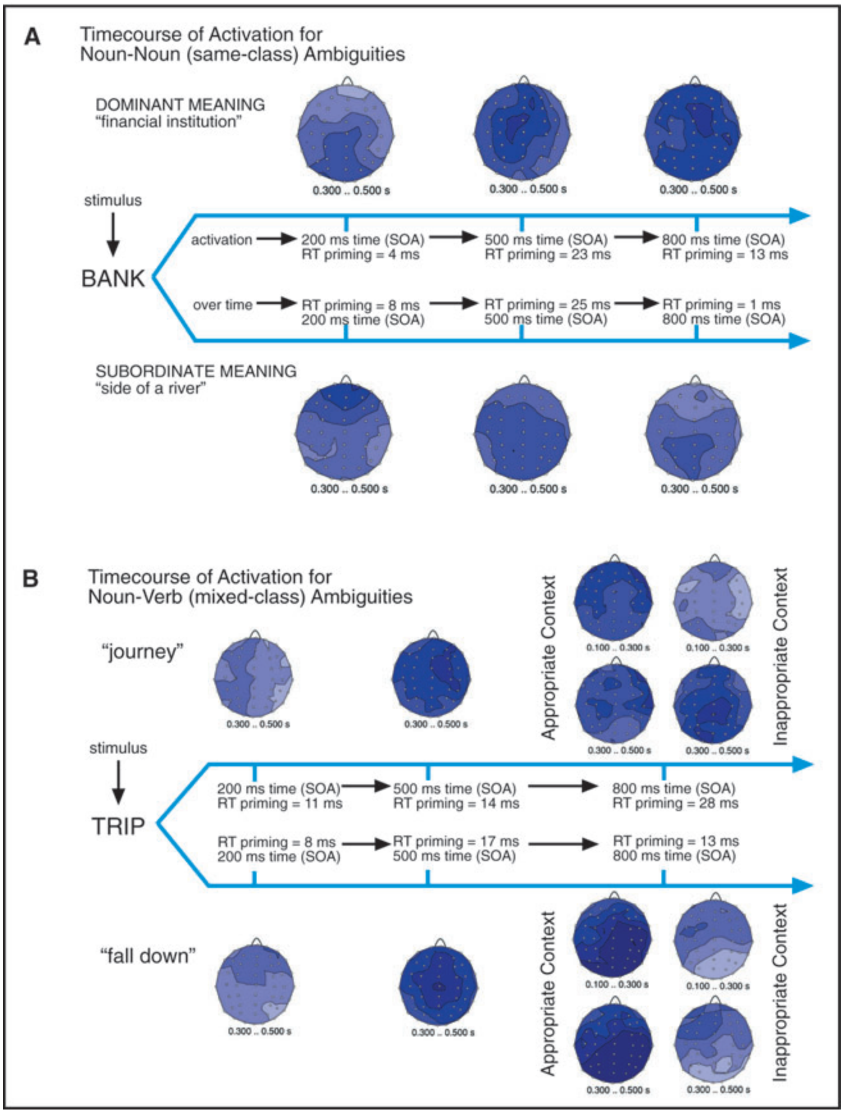

Figure 3.

Are L2 learners in control? Language proficiency effects on the processing of L1 translated ambiguities in the L2

2.2.4

Elston-Güttler, K. & Kotz, S.A.

A previously unexplored type of intralingual ambiguity that tests how "controlled" an L2 learner has become in L2 processing is when a word is a homonym in the L1 and hence has two distinct translations in the L2. For example, German *Kiefer* can be translated as either *pine* or *jaw* in English. We predicted that less proficient L2 learners would be more likely to activate irrelevant cross-language meaning relations even when one of the English words is encountered in context. This would result in stronger cross-language mediated priming (i.e., an attenuated N400) of the target *jaw* after encounter of *pine* in a sentence context for low proficiency learners than for high proficiency learners. We conducted an English semantic priming lexical decision ERP experiment presented with a stimulus-onset asynchrony (SOA) of 200 ms to 34 learners of English (L1 = German) divided into high and low proficiency groups (17 each) based on testing and an extensive language questionnaire. ERPs were measured on targets (e.g., *jaw*) that were preceded by translated homonym or unrelated primes (i.e., *The beautiful table was made of solid* **pine** [unrelated: **oak**]). The results indeed show a significant group difference, but not in the N400 time window. Rather, the low proficiency group showed an early (100 to 250 ms), left frontal interference effect with an attenuated negativity for *unrelated* targets (see Figure 4), while the higher proficiency group showed no significant cross-language effects at all. The early negativity appears to be a form-related interference caused by activation of the German homonym (and may suggest an inhibitory relationship between L2 translations), while the absence of any N400 priming may suggest that this cross-language effect does not involve semantic access. High proficiency learners, in contrast, appear not to activate irrelevant L1 word forms in L2 processing in sentence context.

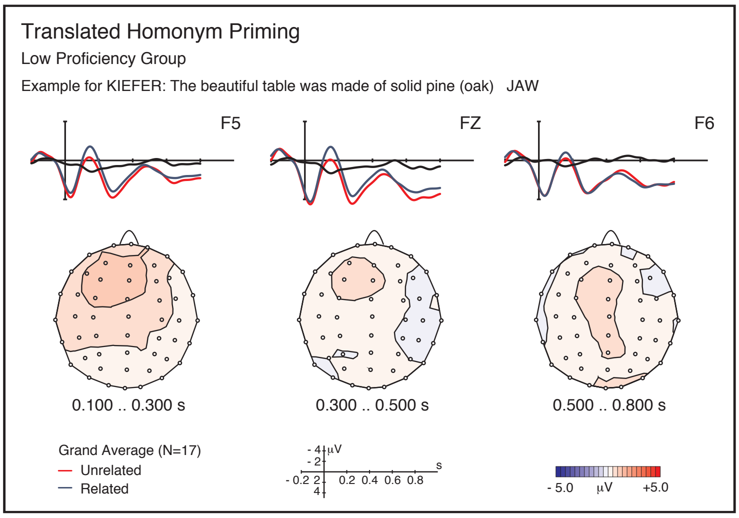

Figure 4.

2.2.5 Electrophysiological evidence for delayed stimulus processing in infants with a risk for SLI

Friedrich, M., Weber, C. & Friederici, A.D.

Several studies have found that children with specific language impairments (SLI) process auditory information more slowly than children with normal language development.

Using the ERP technique, we investigated whether an auditory stimulus discrimination deficit in SLI children, assumed to be based on lower speed of information processing, develops later during the infant's first years of life, or whether, as a primary deficit, is already present in early infancy.

8-week-old infants with and without a family history of SLI were tested in a passive oddball paradigm with CV-syllables as stimuli and with vowel duration as phonemic contrast. During two experimental runs, long and short syllables were used as either standard or deviant stimulus. For investigating the mismatch response, we compared each syllable as standard in one experimental run to itself as deviant in the other one.

The main feature of the ERP pattern in 8-week-old infants is a slow positive wave. In infants with a risk for SLI, this positivity generally has a higher amplitude than in infants without a risk. For the *short syllable*, the latency of the positive wave is delayed in the at-risk group compared to the not-at-risk group. This can be observed for both standard and deviant syllables. It suggests that 8-week-old infants with a risk for SLI are already delayed in processing short auditory information. For the *long syllable* the ERP response does not show a group latency effect when presented as standard, but only when presented as deviant. This difference indicates that, although the temporal processing of a frequently occurring long standard stimulus does not differ between infants with and without a risk for SLI, processing of the same stimulus as an occasionally occurring stimulus change is delayed in at-risk infants. Thus it appears that temporal processing of auditory stimuli is already affected in infants at risk for SLI in the first 2 months of life.

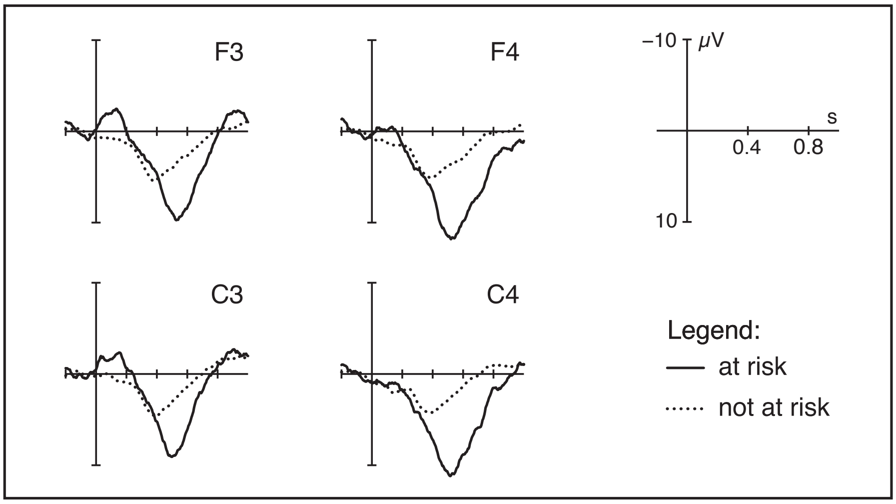

Figure 5. Difference waves (deviant minus standard) for the long syllable in 8-week-old infants with and without a risk for SLI. The long lasting positivity in the at risk group is caused by the fact that for the long syllable the response is only delayed on the deviant but not on the standard.

2.2.6 Processing of varying stress patterns in 4-month-old infants: Electrophysiological evidence

Weber, C., Hahne, A., Friedrich, M. & Friederici, A.D.

One of the crucial problems for the language learning child is how to segment the incoming speech stream into lexical entities. In this study we used an MMN paradigm to examine whether German infants at the age of 4 months would show any preference for the more frequent trocheeic stress pattern of their target language. 22 infants (11 female) participated in the study. Two experimental runs in a passive oddball paradigm were created (standard: p=5/6, deviant: p=1/6):

(1) CONDITION TROCHEE: the frequently occurring iambic CVCV item /baba:/ was occasionally replaced by the trocheeic deviant CVCV item /ba:ba/ and

(2) CONDITION IAMB: the trocheeic CVCV item /ba:ba/ functioned as the standard whereas the iambic CVCV item /baba:/ took the deviant position.

During each experimental run 600 trials were presented with a fixed ISI (offset to onset) of 855 ms. The order of the two runs was counterbalanced across the infants. Stimuli were presented via a loudspeaker with an intensity of 64 dBSPL while infants were sitting in a safety seat.
Figure 6 displays grand-average difference waves for 13 infants showing MMN in condition TROCHEE. A significant MMN effect was seen at about the same latency as in adults, i.e., starting at 160 ms after change onset. When re-referenced to the vertical eye electrode, polarity reversal at the mastoids was observed. Interestingly, these infants did not show any significant effects when the deviant was the iambic item. In the latter case, no effect at the mastoids was observed either.

Contrary to adults, infants at the age of 4 months do not show equal discrimination abilities for trocheeic and iambic two syllable items. Rather, an asymmetrical effect was observed demonstrating that a stable preference for the trocheeic stress pattern is not established yet. This latter effect could be an indication for a possible bias towards a certain stress pattern. Whether it is inborn or the result of sheer learning needs to be specified in future studies.

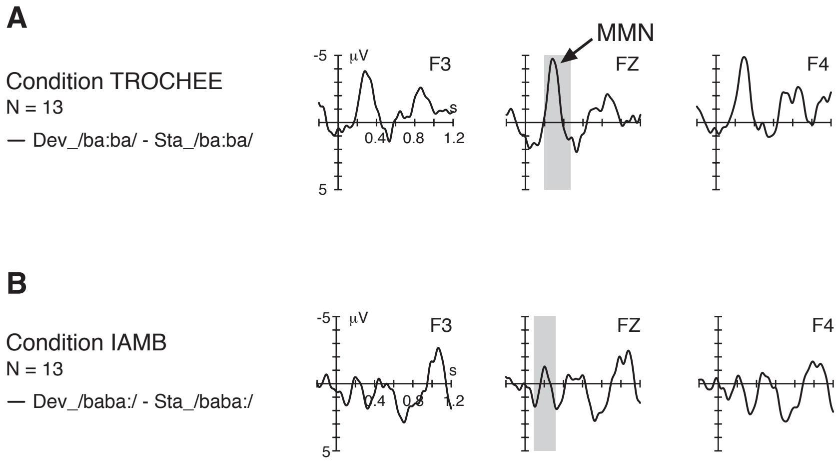

Figure 6. Difference waves (deviant minus standard) in 4-month-old infants showing MMN in individual average. 6A: Difference waves in 4-month-old infants showing individual MMN for condition TROCHEE (N=13). 6B: Difference waves in 4-month-old infants showing individual MMN for condition IAMB (N=9).

During the last year, our music group had two main foci: First, we intensified the cooperation with our prosody group. Prosody is probably the closest link between language and music, and the mechanisms underlying the processing of "musical features of speech" are still only poorly understood. One project discovered that the detection of phrase boundaries in language and music is reflected in a very similar electrophysiological effect, the Closure Positive Shift (CPS). In cooperation with our language group, another project continued our investigations of the similarities and differences between cognitive processes underlying the perception of music and language. The project approaches this issue by comparing phrase processing using familiar idioms and musical melodies in order to shed light on contextual effects at different processing stages in language and in music. The results comprise intriguing findings about the correlates of perceptual and semantic information processing in both music and language.

Within another research focus the music group took advantage of previously developed experimental paradigms to further investigate music processing and to tackle clinically relevant questions. One study investigated auditory processing under different levels of propofol anesthesia, focusing on influences of anesthesia on ERAN, MMN, and P1. The projects sheds light on the nature of these ERP effects, whilst on the other hand elucidating the clinically relevant issue of cognitive function under anesthesia. One finding is that the amplitudes of ERAN and MMN are similarly reduced as a function of increasing propofol sedation, whereas the P1 amplitude remains fairly stable until deep sedation – indicating that sensory memory operations and processes of music-syntactic analysis are affected by propofol sedation, while primary auditory processes remain mainly unaffected.

Another project investigated music processing in cochlear implant users. While many cochlear implant users enjoy success regarding speech understanding, most of them are still frustrated by their inability to accurately hear music. Moreover, the ability for an accurate differentiation of pitch information is crucial for the understanding and production of a tone language. The results indicate that the cognitive operations underlying the processing of music-syntactic information are remarkably similar between cochlear implant users and controls.

2.3.1 An electrophysiological marker for phrasing in music

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For auditory speech perception, Steinhauer et al. (1999) found that each recognized phrase boundary was indicated by a positive shift of some hundred milliseconds duration and with a centro-parietal distribution, called Closure Positive Shift (CPS). This ERP study demonstrates that a similar component exists which indicates the detection of phrase boundaries in music. 17 healthy right-handed German speaking undergraduate piano students participated. 21 melodies were specially composed for the experiment. Each melodic piece was created in three very similar versions, which had a different phrase structure (see Figure 1).

Figure 1. Example for stimuli. The first phrase is identical for all three versions. The second part contains one phrase for version A, 2 phrases (following the same musical idea) for version B and a single phrase, created by filling up the pause in version B by one or several notes, for version C.

64 channels of EEG were measured. Triggers were set at the onset of the second phrase boundary in version B and at equivalent positions in versions A and C. The results show a significant fronto-central positive wave peaking at about 650 ms. The amplitude of this component could be modulated by the "clarity of the phrasing" in the stimuli (as revealed by independent rating) and the mental state of the subjects (tired/alert). Figure 2 shows the mean square over all channels and the topographic distribution of the component.

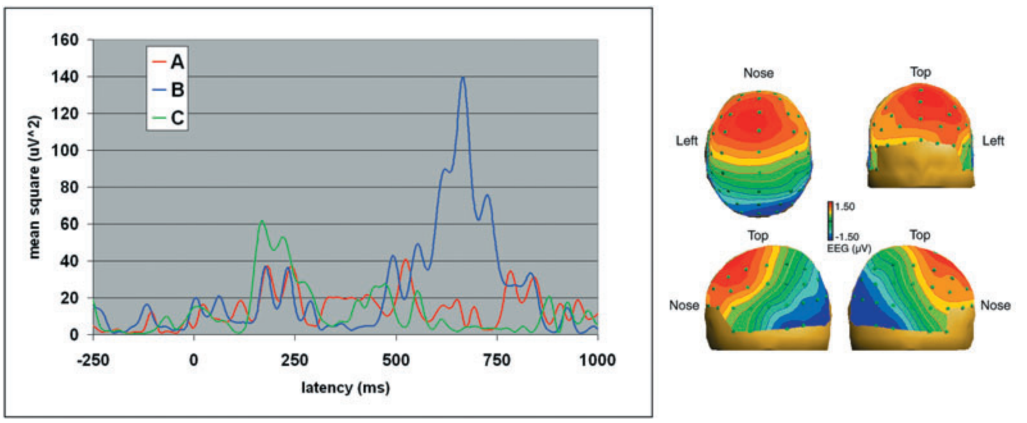

Figure 2. Left: Mean square of all channels for all stimuli. Right: Topographic distribution for condition B at 630 ms.

The component is interpreted a marker for the processing of the phrase boundary, similar to the Closure Positive Shift in language processing (Steinhauer et al. 1999). However, the distribution of the effect is fronto-central, rather than centro-parietal as found in language processing, indicating a different generator structure.

2.3.2 Expecting the expected: An ERP study on the perception of music and language

Schmidt, B.H., Gunter, T.C. & Kotz, S.A.

There is an ongoing debate whether or not music and language share similar cognitive processes. One major underlying reason for this debate is that in comparison to music, language shows a well described subdivision of processes from phonological up to phrase processing. It is therefore important to define a compatible experimental question for both domains.

Therefore, familiar idioms and melodies were utilized to test contextual effects at different processing stages in language and in music. Correct idiomatic language phrases were contrasted with phrases containing a violation at the end of the phrase (literal and semantically incongruous). Similarly, correct familiar melodies were contrasted at phrase endings with a counterpoint or a harmonic shift. In a rating study, we normed the degree of familiarity for both kinds of stimuli to differentiate between high and low familiar language and music stimuli.

ERP data for both the language and music condition show a negative deflection during the first 300 ms as a result of unexpected phrase endings. The onset latency of the early component varied as a function of expectancy. Following this early common negativity, the violation of musical context resulted in a long lasting negative shift, whereas in language, violations elicited a N400. The negative shift was most prominent for the

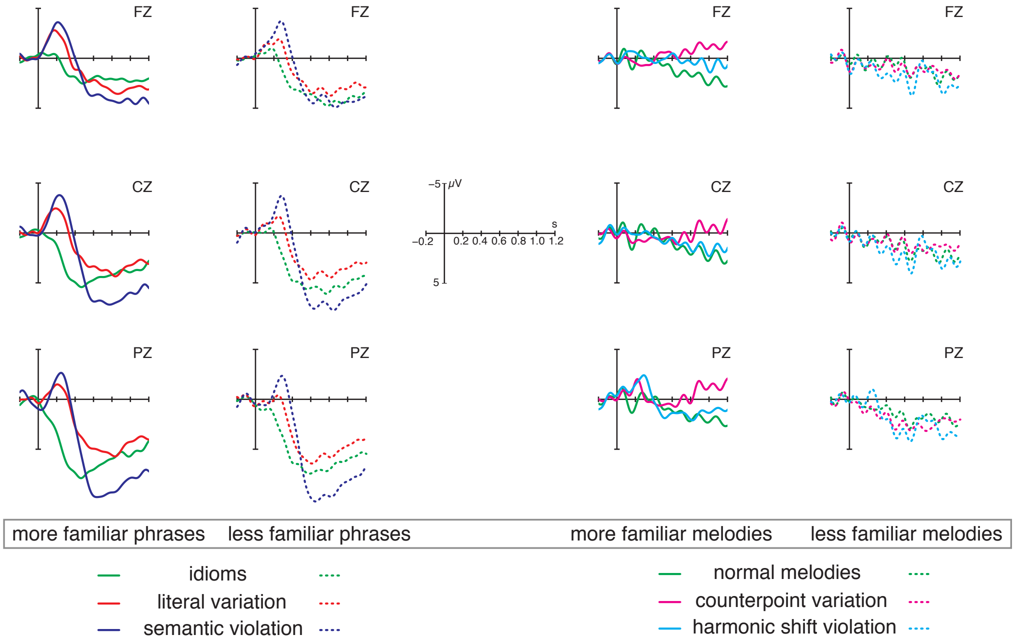

Figure 3 shows - from the left to the right - grand averages for more familiar stimuli in the language condition, followed by ERPs for less familiar language phrases; displayed on the right side the ERPs for more familiar melodies, followed by less familiar melodic phrases.

counterpoint condition for more familiar melodies, and varied as a function of familiarity. We propose that this component reflects the effort to integrate a probable continuation of a familiar melody. However, the N400 in the language study varied as a function of both familiarity and semantic violation.

We suggest that the early negative component might reflect a perceptual process connected to phonological as well as singleton selection modulated by expectancy, whereas the later potentials might reflect modality specific reactions to music and language violations.

2.3.3 The effect of propofol anaesthesia on MMN, ERAN, and P1

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[1] *Department of Anaesthesiology and Intensive Care Therapy, University of Leipzig*
[2] *Department of Psychology, University of Würzburg*
[3] *Max Planck Institute of Cognitive Neuroscience*
[4] *Department of Psychology, University of Leipzig*

We investigated the effect of increasing propofol anaesthesia on the auditory event related potential in surgical patients (n=18). An auditory oddball paradigm was used to elicit the MMN and the ERAN. ERPs were recorded during four levels of anaesthesia, adjusted with target controlled infusion of propofol: awake state (target plasma concentration of propofol: 0.0 µg/ml), light sedation (0.5 µg/ml), deep sedation (1.5 µg/ml) and unconsciousness (2.5 – 3.5 µg/ml). Simultaneously, the depth of propofol anaesthesia was assessed using a processed parameter of the EEG (i.e., the bispectral index, BIS).

Both experimental paradigms elicited distinct ERP effects during the awake state (BIS mean value 95.4 ± 2.95). Frequency-deviants compared with standard tones elicited a MMN and harmonically inappropriate chords elicited an ERAN. Propofol sedation resulted in a progressively decrease in amplitudes and an increase of latencies with a similar pattern for MMN and ERAN. Both components were still detectable during light (BIS mean 87.6 ± 7.45) as well as deep sedation (BIS mean 72.1 ± 7.11), but were abolished during unconsciousness (BIS mean 50.4 ± 6.74) (Figure 4). When comparing irregularity detection (as reflected in the MMN) with sensory encoding (as reflected in

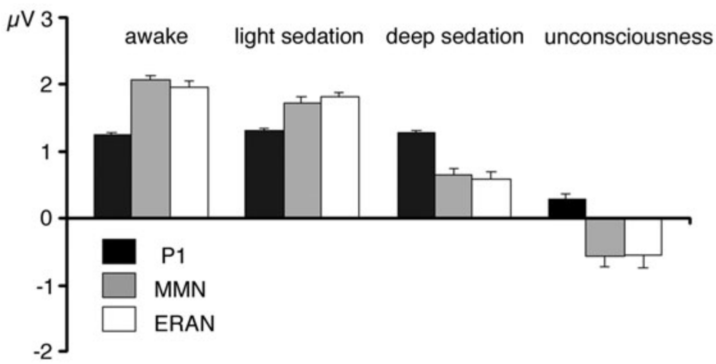


Figure 4. Mean amplitudes from three frontal electrodes of P1, MMN and ERAN during the awake state, light sedation, deep sedation and drug induced unconsciousness.

the P1) of the acoustic input we found that, in contrast to the MMN and the ERAN, the amplitude of the P1 was unchanged by sedative doses of propofol, but markedly decreased during drug induced unconsciousness (Figure 4).
Our results indicate an ongoing physical and syntactic irregularity detection up to BIS values around 70, and suggest a greater sensitivity of auditory irregularity detection to sedative propofol concentrations compared to auditory sensory encoding.

Music processing in cochlea implant users

2.3.4

[1] *Max Planck Institute of Cognitive Neuroscience*
[2] *University of Heidelberg*

Koelsch, S.[1], *Wittfoth, M.*[1,2], *Wolf, A.*[1] & *Hahne, A.*[1]

The present study compared the processing of music-syntactic irregularities between cochlear implant (CI) users and matched controls. As advances are made in CI technology and the number of CI recipients increases, demand is rising for implant systems that better meet their hearing needs. We used a musical paradigm that we developed in previous studies: Musical chord sequences were presented which infrequently contained functionally inappropriate chords. In both controls and CI users, functionally inappropriate chords elicited early (around 200 ms) and late (around 500 ms) negative electric brain responses (ERAN and N5, Figure 5). In both groups, amplitudes of effects depended on the degree of functional inappropriateness, indicating that participants of both groups had a cognitive representation of musical regularities described by music theory. The effects elicited in CI users were distinctly smaller than in controls, reflecting that the amount of sensory information received through a CI is smaller compared to an intact natural cochlea. However, because ERAN and N5 were elicited in both groups, the present results indicate that, despite the limited input provided by a CI, the cognitive

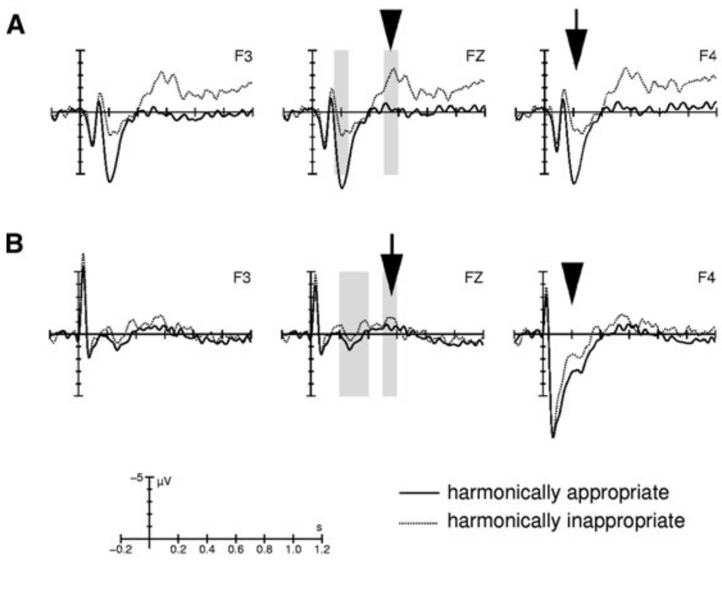


Figure 5. Grand-average ERP-waveforms elicited by chords at the fifth position, separately for controls (A) and CI users (B). In both groups, harmonically inappropriate chords elicited an ERAN (long arrow), and an N5 (short arrow).

operations processing both music-syntactic and physical information are remarkably similar between CI users and controls. This finding suggests that CI users have, even after an extended period of hearing loss, still an (implicit) representation of regularities of the major-minor tonal system, and that the mechanisms that process musical information fast and accurately according to this representation are intact in CI users. Thus, attempts to improve accuracy of music perception in CI users by modifying their processors can (at least in Western cultures) still rely on an intact (implicit) representation of the regularities underlying major-minor tonal music in CI users.

In the year 2002, the major interest of the Independent Junior Research Group 'Neurocognition of Prosody' lay in a considerably extended exploration of prosodic processing. An important part of our research is presently sponsored by third party fundings from the German Research Foundation and the Human Frontier Science Program. In addition, our group benefits from multiple well established cooperation projects with the University of Leipzig, the University of Edinburgh, and the CNRS/ Marseille.

Our research focused on three major topics:

1) The investigation of the syntax-prosody interface including the influence of the Information Structure (IS) using event related brain potentials (ERP)
2) The segregation of an incoming sound stream at several levels of the prosodic hierarchy using ERPs
3) Disentangling prosodic and syntactic pathways during speech processing in comparison to the processing to affective prosody using functional Magnetic Resonance Imaging (fMRI)

In detail, we therefore extended our work on the processing of IS and prosodically prominent accent information in the speech stream. Our understanding regarding the influence of contextual information on the perception of question-answer pairs (2.4.1) and corrections (2.4.2) has increased very much through this.
In addition, we conducted ERP-studies on the influence of subvocal prosody and the processing of locally induced influences by IS during reading (2.1.5).
We were also interested in the investigation of morpho-syntactic properties and their related morpho-phonological realizations with regard to a syntactico-semantic feature special to Germanic languages – the auditory processing of particle verbs (2.4.3).
Taken together, we are now convinced that a simple view on the syntax-prosody interface is insufficient and that semantic properties have to be considered as well when one wants to completely understand sentence and utterance processing.

Second, our research concerned with the processing of phrasal domains extended to musical phrase units (2.3.1) and to syllable boundaries. Particularly the latter has been examined extensively, including noise-vocoded material in order to gain more transparency on the interaction between the frequency spectrum, the amplitude envelope and temporal properties of incoming speech (2.4.4). The influence of speaker's voice information and biological gender stereotypes has also been examined (2.4.5).
Thirdly, we are furthermore seeking to disentangle syntactic and prosodic processing (2.1.14). The former findings published in Meyer et al. (2002) on the processing of filtered delexicalized speech with regard to syntactic and prosodic processing are only

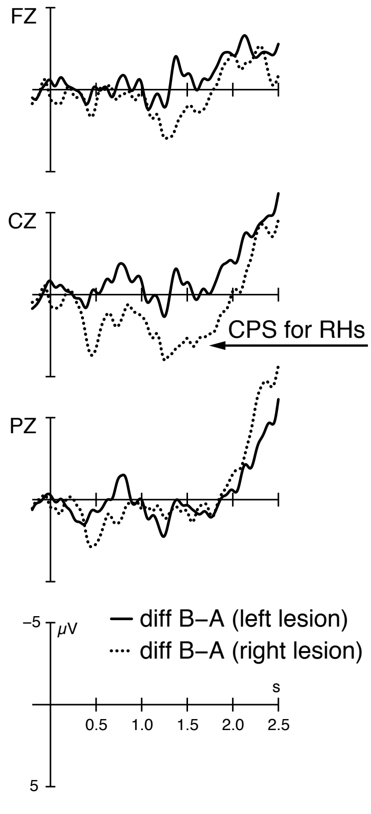
partly congruent with the findings on the processing of affective prosody. Our in-house cooperation project (2.4.6) therefore also consisted of further studies.
Last but not least, our presently running localization studies employing fMRI on primary auditory processing are concerned with the identification of a cortical network responsible for speech processing under anaesthesia (2.4.7).

Finally, first results of those studies are currently being mapped onto a neuropsychological model regarding the contribution of the left vs. right hemisphere to language processing (2.1.1).

2.4.1 Perception of IPh boundaries in unilateral lesioned patients

Hruska, C., Kotz, S.A., Friederici, A.D., Alter, K. & von Cramon, D.Y.

As previous studies of normal subject and different ages have shown, the perception of intonational phrase boundaries (IPhs) induces a positive shift (CPS) in the ERP. The question about the nature of the closure positive shift is still a matter of debate. One interpretation is that the perception of different prosodic features is correlated to the IPhs. Linguistic based theories discuss the processing of prosodic information interfacing with linguistic aspects, e.g., syntactic structure is processed in left hemisphere regions, whereas the right hemisphere maintains emotional and subordinative aspects of speech. To examinate this distinction a study with unilateral left and right lesioned patients was conducted. In an ERP experiment auditory sentence material was presented to both patient groups (examples of speech data: intransitive: "Peter verspricht Anna zu arbeiten" and transitive: "Peter verspricht|$_{\mathrm{Iph}}$ Anna zu entlasten").



The ERP results show temporally restricted (CZ: 1200 to 1300 ms) response to the IPh boundary in the transitive condition for the LH group, while the ERPs of RH group clearly display the processing of prosodic cues at the IPh position for the transitive condition in an extended time window (CZ: 1200 to 1700 ms). Thus, patients with left hemisphere lesions might have problems to integrate linguistic based prosodic features into speech within an appropriate time.

Figure 1. Difference waves of transitive - intransitive condition for both patient groups illustrates a small positivity in the LH group at the IPh boundary, while the RH group clearly shows an extend effect.

How superfluous and underspecified focus accents can bother our brains

2.4.2

Toepel, U. & Alter, K.

The contribution of information structure (IS) is currently being explored with regard to prosodic processing. Additionally, the role of tasks in experimental settings is being discussed controversially. In the two experiments presented here, dialogue conversation was investigated with event-related brain potentials (ERPs). The stimulus material in both studies consisted of sentences conveying new information accents (NF) vs. contrastive accents (CF), always embedded in a preceding context. Non-matching prosodic patterns were created by combining the context of one condition with the critical sentence of the other condition. Both studies diverged only with regard to instruction. In the first study, participants were asked to perform in a probe detection task, whereas in the second they had to judge the prosodic appropriateness of a sentence to its preceding context. Electroencephalographic data were recorded while subjects listened to the dialogues that were either coherent with respect to expected and provided focus accents or not.
Results indicate that the Closure Positive Shift (Steinhauer, Friederici & Alter [1999]; Hruska & Alter [2001]) as a perceptual correlate of IS-induced accents can again be replicated when matching prosodic patterns have to be processed. However, when the prosodic pattern implied by information structure is being violated, varying task demands modify the electrophysiological reaction. When the participants have to answer a content question, ERPs show an enhanced negativity in parietal regions when context implies a narrow focus interpretation, but the sentence constituent is contrastively accented and hence, overspecified (see Figure 2). On the other hand, negativity in the prosodic judgment task is increased at frontal and central sites for constituents that convey new information accents when context leads to anticipation of a contrastive accent, hence in the case of underspecification (see Figure 3). These results indicate that not only the difference between given vs. new information is processed online. Moreover, even the more subtle divergence of information prosodically marked new vs. contrastive modulates recognition in discourse comprehension.

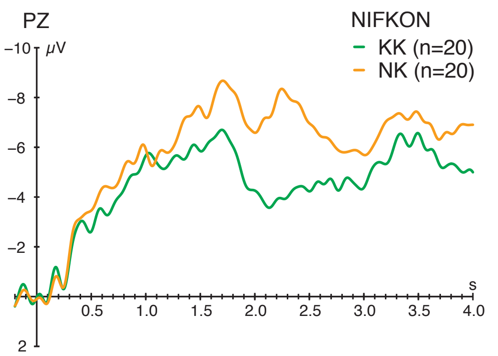


Figure 2. ERPs to contrastive pitch accents in either appropriate IS (green line) or inadequate context (orange line).

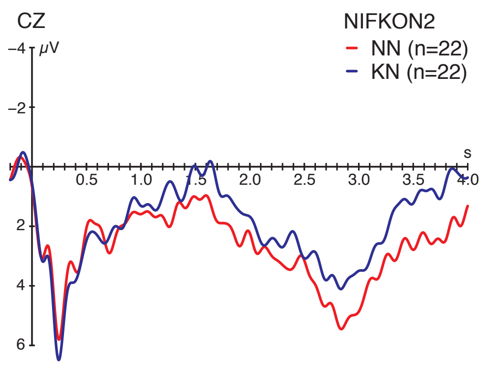


Figure 3. ERPs to new information pitch accents in an appropriate context (red line) or inadequate one (blue line).

2.4.3 Influence of prosody on sentences' structure building in German: ERPs evidence in the auditory domain

Isel, F., Alter, K. & Friederici, A.D.

The present study investigated whether prosody influences processes of syntactic structure building. Previous ERP-studies conducted in the auditory domain revealed that an incorrect intonation phrase in a temporarily ambiguous syntactic structure can *misguide* the parsing system resulting in an incorrect initial syntactic structure. In contrast, in the visual domain, Urban and Friederici (1999) showed that ambiguous German verb forms such as *Er lächelte* (he smiled) vs. *Er lächelte x an* (he smiled at x) are activated in parallel, not affecting the processing of the immediate syntactic structure. Our goal in the present study was to investigate in the auditory modality whether prosodic information contained in the ambiguous verb forms employed by Urban and Friederici can inform the parsing system about the verb's argument structure. Comparing the processing of the same materials in two modalities will allow us to estimate to what extent syntactic parsing and lexical integration are affected by either sensory modality and/or by prosody. We registrated event-related brain potentials (ERPs) while German listeners were processing (1) correct, (2) syntactically incorrect, or (3) syntactically and prosodically incorrect German sentences. The critical item was the verb's particle, which was either syntactically and prosodically congruent, or syntactically and/or prosodically incongruent with the preceding verb. Similar to the visual domain, processes of lexical integration in the auditory modality elicited a N400 component as well as a late positivity (latency: 1000 ms), indicating that lexical integration is not affected by modality (auditory vs. visual) nor by prosody. In contrast, unlike in the visual domain, an early left anterior negativity (ELAN) was found for the processing of syntactic phrase structure violations in the auditory modality. Finally, doubly syntactically and prosodically anomalous sentences elicited an early anterior negativity in both the left

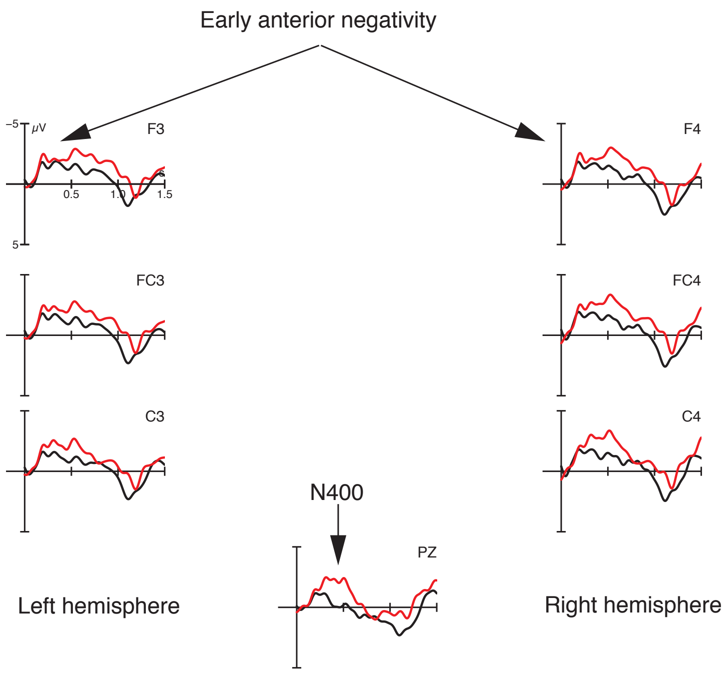


Figure 4. Grand average ERPs for correct (black) and incorrect (red) conditions.

and the right hemispheres (see Figure 4), suggesting that early syntactic processes are affected by prosody. Taken together, our data converge with previous evidence to demonstrate that prosody plays a crucial role in the processes of syntactic structure building during an early stage of processing.

2.4.4 The neural processing of syllables vs. level identical noise and the influence of task requirements

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[3] *Siemens Audiological Engineering Group, Erlangen*

One general aim in the wide field of speech research is to extract temporal acoustic factors which could serve as important cues for the understanding of meaningful units in speech. So far, it is not known which one of the different acoustic information items is most important for auditory stream segregation. Several studies have investigated the acceptability of amplitude envelope information which was extracted from the speech signal with different filtering methods. They have shown that temporal envelope information with reduced spectral information is sufficient for the listeners to recognize their native language. Our study aimed to compare the processing of envelope information presented as speech or non-speech stimuli in order to investigate the importance of speech specific neuronal processes.

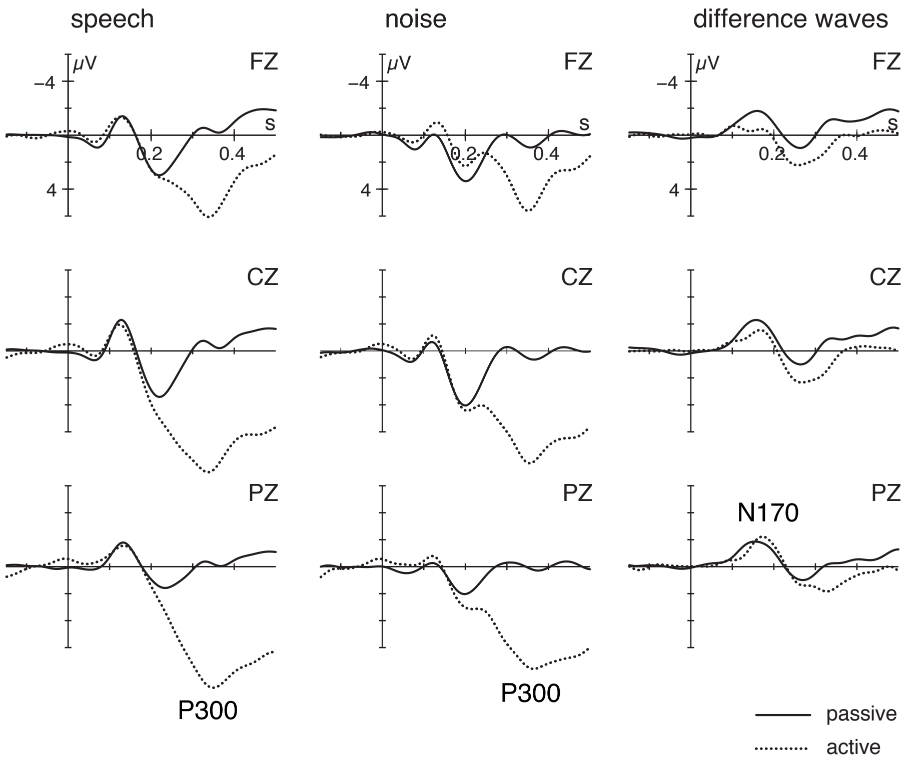

Figure 5. Responses in passive (solid line) and active (dotted line) presentation of speech and noise and difference waves for speech minus noise at central electrodes.

To measure brain activity during the auditory presentation of speech and non-speech stimuli we recorded event-related potentials (ERPs) in healthy adults. The speech stimuli we used consisted of different consonant-vowel syllables (CV). Non-speech stimuli were produced by taking the general envelope of the syllables to generate level identical noise. With this method, kinematic signals are normalized in time and amplitude, allowing us to observe the difference in processing of the underlying spectral cues. The speech and non-speech stimuli were presented in passive and active listening conditions. In summary, we found a significant difference in processing between speech and level-identical noise. The ERPs to speech-stimuli are enhanced in contrast to the ERPs to noise stimuli. The difference waves of syllable and noise-evoked potentials reveal a specific component (N170), which was independent of attention. The results present evidence for an early electrophysiological correlate of distinct neural processing of speech and noise stimuli. It has been demonstrated that this type of noise stimuli seems to be a useful tool for studying the envelope information in speech processing.

2.4.5 Talker's voice and biological gender stereotypes – An ERP investigation

Lattner, S. & Friederici, A.D.

The present study investigated the influence of implicit speaker information in sentence interpretation. We auditorily presented sentences that comprised of either stereotypically male or stereotypically female self-referent utterances. In the congruent conditions (C), these utterances were produced by speakers whose gender matched the sentence content; e.g., a female speaker uttering 'I like to wear skirts.'.
In the incongruent condition (I), stereotypically male utterances were produced by female speakers and vice versa; e.g., male voice uttering 'I like to wear lipstick.'.
The event-related brain potentials of 32 listeners (16 male) exhibited a late positivity (P600) for the incongruent condition. No significant differences were observed between male and female listeners. In the absence of any ERP effect in the earlier time range, we conclude that the access of the semantic information as such is independent of the speaker's voice, but that speaker properties, semantic content and stereotypical knowledge are integrated in a later processing stage. The P600, typically assumed to reflect a difficulty in the structural reanalysis or repair, may also reflect a process of re-integration of semantic meaning and stereotypical beliefs (Osterhout et al., 1997). The present study confirms this notion and extends it to the domain of the talker's voice.

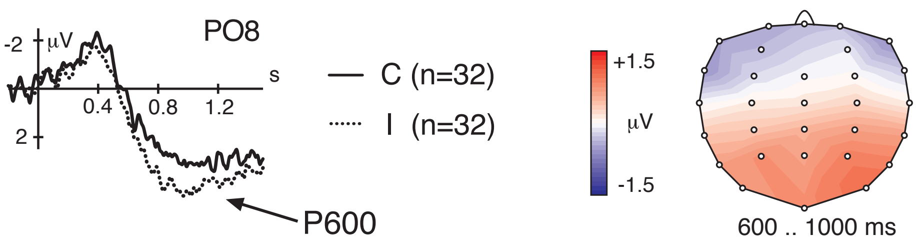

Figure 6. Brain potentials event-locked to the presentation of the sentence final words. The ERP map depicts the difference of incongruent-congruent conditions in the brain activation, averaged from 600 to 1000 ms. It indicates the posterior distribution of the P600 effect.

On the lateralization of emotional prosody: Effects of blocked versus event-related designs

2.4.6

Kotz, S.A.[1], Meyer, M.[2], Besson, M.[3] & Friederici, A.D.[1]

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[2] FIS, University of Edinburgh, United Kingdom
[3] Centre de la Recherche National (CNRS), Marseilles, France

Previous fMRI data of our group (Kotz et al., in press) indicate that the processing of emotional prosody engages a bilateral, but left-accentuated network of fronto-temporal cortical structures, while subcortical activation (e.g., basal ganglia) is symmetrical in both hemispheres. Other imaging evidence (e.g., George et al., 1996; Buchanan et al., 2000), however, shows mainly right hemisphere activation for emotional prosody. One difference between these studies was the design. While Kotz et al. used an event-related design, George et al., and Buchanan et al., used a blocked design. Thus, the question remains whether methodological factors influence lateralization of a function. The current fMRI experiment investigated brain activation related to emotional prosody by comparing a block of lexicalized and a block of delexicalized (low-pass filtered) sentences with positive, neutral and negative emotional prosody. Subjects judged the prosodic contour of a sentence on a five-point scale. The results clearly show that the perception of emotional prosody correlates with bilateral activation (fronto-temporal and subcortical), but that accentuation of the left versus right hemisphere varies as a function of fMRI design. Right hemisphere accentuation only occurred in a blocked, but not an event-related design.

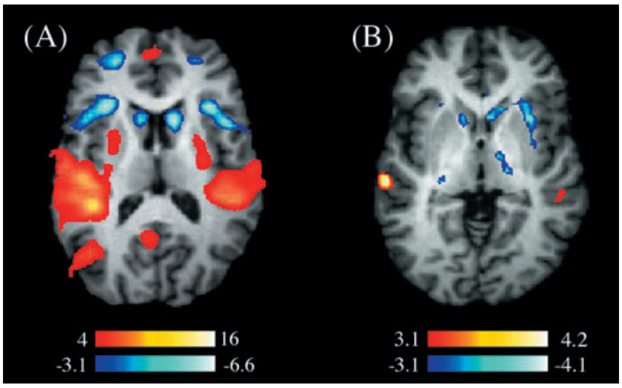

Figure 7. Displayed are in an axial view the activation of the condition effect for the event-related design (A) and the blocked design (B). The condition effect reflects a contrast between lexicalized (red) and delexicalized (blue) speech across all three prosodic contours (positive, neutral and negative).

2.4.7 Language processing and anaesthesia: An fMRI investigation of cognitive processing during induction and maintenance of propofol anaesthesia

Heinke, W.[1], Fiebach, C.J.[2], Meyer, M.[3], Schwarzbauer, C.[4], Olthoff, D.[1] & Alter, K.[2]

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[3] *Centre for Functional Imaging Studies, Institute for Adaptive and Neural Computation, University of Edinburgh, UK*
[4] *MRC Cognition and Brain Sciences Unit, Cambridge, UK*

We investigated the effect of propofol anaesthesia on brain activation during cognitive processing in a language task. Participants (n=12) heard normal sentences and sentences made up of pseudowords in a random sequence. Their task was to decide whether the sentence was wellformed or not. The experiment consisted of three blocks. In the first block, participants were awake. At the beginning of the second block, propofol infusion was commenced. This caused a slow transition from responsiveness to loss of responsiveness (indicated by missing behavioural responses to the task) observed for every participant during the second block. During the third block, anaesthesia was maintained and participants did not regain consciousness before the end of the experiment. Blood samples were taken during the experiment from each subject in order to determine the propofol plasma concentrations.
As expected, the fMRI results show the activation of typical language networks for conscious language processing. Activated were superior and middle temporal areas bilaterally and inferior frontal brain regions (Figure 8). During induction of anaesthesia (second block), after subjects lost consciousness, activity in frontal and temporal areas was significantly reduced. However, temporal activity was still detectable in the auditory cortex (Figure 9). In contrast, during the third block (maintenance of anaesthesia), no significant activity in areas involved in auditory or language processing was observable any more. This was probably the result of a further increase in propofol plasma concentration. Our findings indicate a gradual collapse of the activated language processing network caused by propofol. Areas mediating "higher" cognitive processes were first affected, whereas the primary and secondary sensory areas appear to be more resistant to the drug effect.

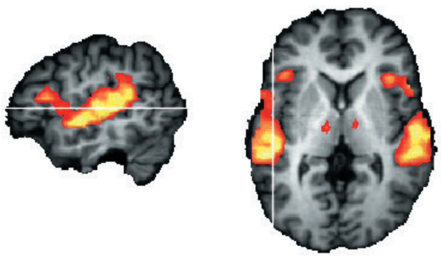

Figure 8. Brain regions showing functional activation induced by the language processing task during the awake state. The averaged z-maps were thresholded at z=3.1.

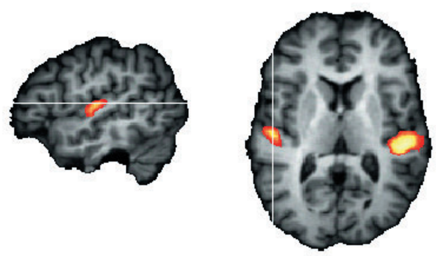

Figure 9. Residual temporal activation during block 2 after subjects lost their responsiveness.

Higher-order brain functions in patients with diffuse and focal brain lesions are the main focus of the CNPS group. One major challenge characterizes this research line: The patient as the main character appears in the first place as an individual, grouping and group averaging of patient data are much more intriguing as compared to studies with normal controls. General conclusions concerning a neuropsychological model are more questionable, unless based on a considerable amount of comparable patient data. Hence, the excellent cooperation of so many patients is our treasure; the close interaction between the Day-Care Clinic of Cognitive Neurology at the University of Leipzig and the Max Planck Institute is the platform to generate specific hypothesis and projects.
In 2002, the Day-Care Clinic treated 195 patients. 120 (61%) of the current patients participated in clinical research projects. Moreover, 109 former patients were taking part in actual studies. Our database now consists of a pool of more than 817 patients with brain injuries of various etiologies. Each patient is characterized by a detailed analysis of medical history, neuropsychological and linguistic profiles.
During the last year clinical and experimental research in this field centered around three major topics: (1) the functional and morphometric characterization of cerebral microangiopathy and its relation to the cognitive state; (2) lexical and semantic processing in patients with aphasia and basal ganglia lesions; and (3) spatial attention and interhemispheric transfer in various patients groups. Functional MRI, Brain morphometry, Near-Infrared-Spectroscopy (NIRS), Event-Related brain Potentials (ERP) and behavioral studies were the applied tools to accomplish a better understanding of the 'pathological state'.
The introduction of MR morphometry and the correlation with neuropsychological findings in cognitively impaired patients opened a new field of clinical research. Our study of patients with cerebral microangiopathy demonstrated that the cortical thickness is a relevant parameter to determine the progression of the disease. Moreover, functional near-infrared spectroscopy (fNIRS) showed a reduced and delayed haemodynamic response in patients with cerebral microangiopathy during performance of a Stroop-task. An fMRI protocol to assess a 3D cerebral autoregulation map showed that patients with cerebral microangiopathy are characterized by a significantly reduced cerebral vasoreactivity as compared to age-matched healthy controls.

The role of certain contributors within the language network was addressed in a series of linguistic projects: In an ERP study, the left anterior temporal lobe was identified as essential in initial phonological processing. Moreover, patients with anterior lesions showed a temporal deficit in verb as opposed to noun processing. No evidence was found for basal ganglia involvement in procedural aspects of language processing. Patients with basal ganglia lesions and with Parkinson's disease were included in this study.

The projects of the Experimental Neuropsychology workgroup (Prof. Pollmann) were focused on aspects of spatial attention and interhemispheric transfer. In two experiments with splenial lesion patients, we found parallel deficits in the detection of visual and auditory targets when target detection was complicated by distracting stimuli. Recent diffusion tensor imaging data suggest that the splenium carries fibers which connect neurons in the temporoparietal junction (TPJ) areas. This leads us to interpret our findings in that an intact splenium supports the detection of stimuli at unattended locations because it transfers attentional signals which alert the organism to the presence of potentially relevant stimuli. Previous patient and imaging studies had hinted at a prominent function of the TPJ area in target detection in the visual domain. In an event-related functional magnetic resonance imaging (fMRI) study of auditory spatial cueing we could show that the TPJ area is also involved in target detection in the auditory domain.
Further event-related fMRI studies of visuospatial cueing demonstrated the importance of the cortex lining the intraparietal cortex in linking perception and action, as well as lateralization effects in the occipital cortex.
Finally, we report a behavioral study on normal participants which was carried out to investigate learning-dependent changes in interhemispheric resource sharing, which was carried out as a prelude to future patient and imaging studies on interhemispheric resource sharing.

2.5.1 Loss of cortical thickness in cerebral small vessel disease: A morphometric analysis

Preul, C., Lohmann, G., Hund-Georgiadis, M. & von Cramon, D.Y.

Current pathophysiological concepts on the etiology of cerebral small vessel disease (CSVD) predominantly focus on changes in the white matter that occur on the basis of chronic hypoperfusion. The role of the grey matter in the pathophysiology of CSVD remains unclear, in particular the question whether changes of cortical thickness occur primarily in the course of the disease or evolve as a result of white matter pathology. This study investigates the significance of cortical thickness reduction and particularly addresses regional differences within the brain.
Morphometry was applied to 3D MR-images of 23 patients and 23 normal subjects. Overall volumes of the grey matter as well as regional cortical thickness in frontal, central and temporal gyri were assessed (Figure 1). According to structural abnormalities in the MR image, CVSD was classified into mild, moderate or severe.
Cortical thickness was significantly reduced in patients with CSVD, while overall brain volumes did not differ significantly between groups. The most prominent loss of cortical

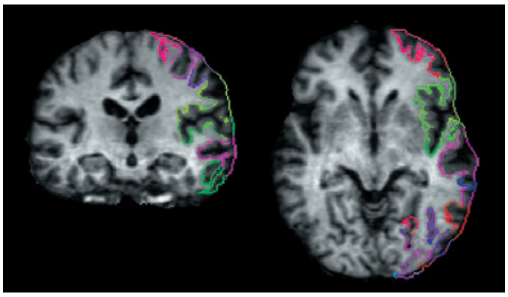

Figure 1. Sulcal basins delineate the border between white and grey matter as the basis for the calculation of regional cortical thickness. This hemisphere-wise segmentation procedure does not include medial parts of the brain to avoid miscalculation due to periventricular white matter changes in CSVD.

thickness was found in patients with severe CSVD (Figure 2) without any significant regional distribution. External brain atrophy as defined by loss of cortical thickness and internal brain atrophy estimated by the Cella-media-index showed a strong positive correlation. In sum, our morphometric data show that cortical thickness is an important indicator of the severity of CSVD.

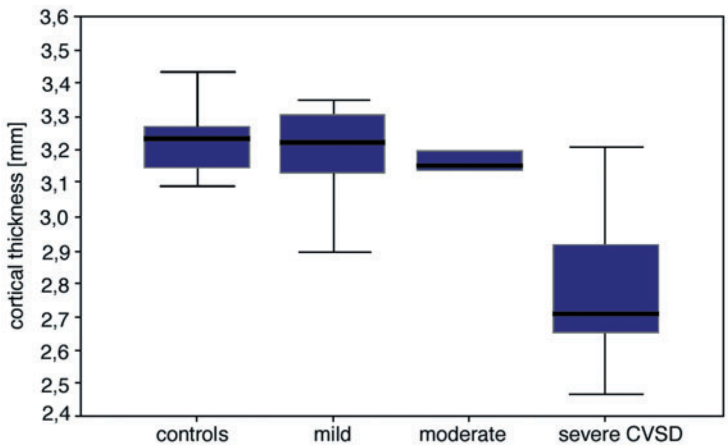

Figure 2. Reduction of cortical thickness in patients versus controls.

2.5.2 The hemodynamic response is reduced in cerebral microangiopathy during a Stroop-task

Schroeter, M.L., Kruggel, F. & von Cramon, D.Y.

Recent studies reported that vasomotor reactivity is reduced in the frontal cortex (Terborg, 2000) and that neuropsychological deficits are correlated with functional imaging parameters (Sabri, 1998, 1999) in cerebral microangiopathy. Therefore, we investigated brain activation by measuring the hemodynamic response (changes of oxy- and deoxy-hemoglobin [Hb]) with functional near-infrared spectroscopy in 9 patients with microangiopathy and 14 age-matched healthy controls during performance of a Stroop-task and visual stimulation with a checkerboard. Optodes were placed bilaterally at the

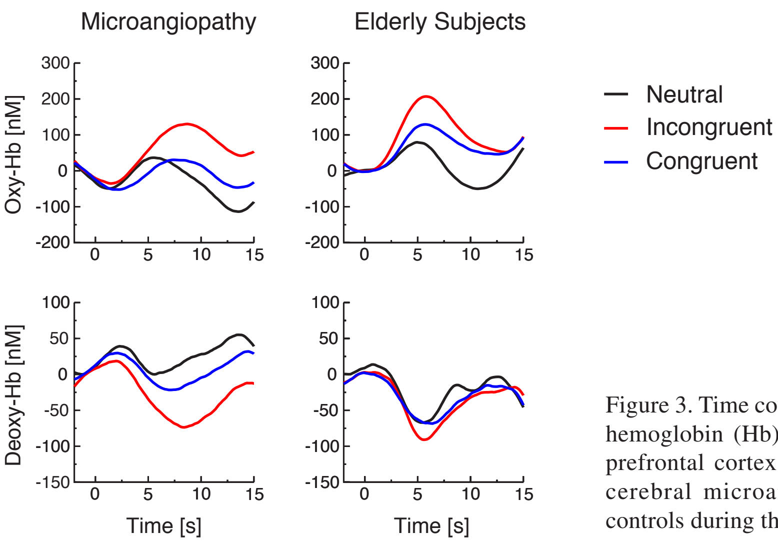

Figure 3. Time courses of oxy- and deoxy-hemoglobin (Hb) in the left dorsolateral prefrontal cortex (FC3) of patients with cerebral microangiopathy and elderly controls during the Stroop task.

lateral prefrontal (Stroop-task) and visual cortex (visual stimulation). Reaction time was longer in patients with microangiopathy than in age-matched healthy controls during the Stroop-task. As illustrated in Figure 3, incongruent trials led to a stronger hemodynamic response than neutral trials due to interference reduction. The hemodynamic response (oxy- and deoxy-Hb) was reduced and delayed in the lateral prefrontal cortex of patients with microangiopathy during the Stroop-task. Further, concentration of oxy-Hb increased less in patients with microangiopathy than in healthy controls during visual stimulation, whereas there was no difference in deoxy-Hb. In summary, the hemodynamic response is reduced and delayed in patients with cerebral microangiopathy particularly in the dorsolateral prefrontal cortex. Thus, our data support the hypothesis of a specific frontal deficit in this disease.

2.5.3 Determination of cerebrovascular reactivity by means of fMRI signal changes in cerebral microangiopathy: A correlation with morphological abnormalities

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[3] FC Donders Centre for Cognitive Neuroimaging, Nijmegen, The Netherlands

A reduced cerebrovascular reactivity (CR) is a risk factor and important progressor of cerebrovascular disease. In this study, we implemented a protocol to assess CR by means of functional MRI (fMRI) using hyperventilation.

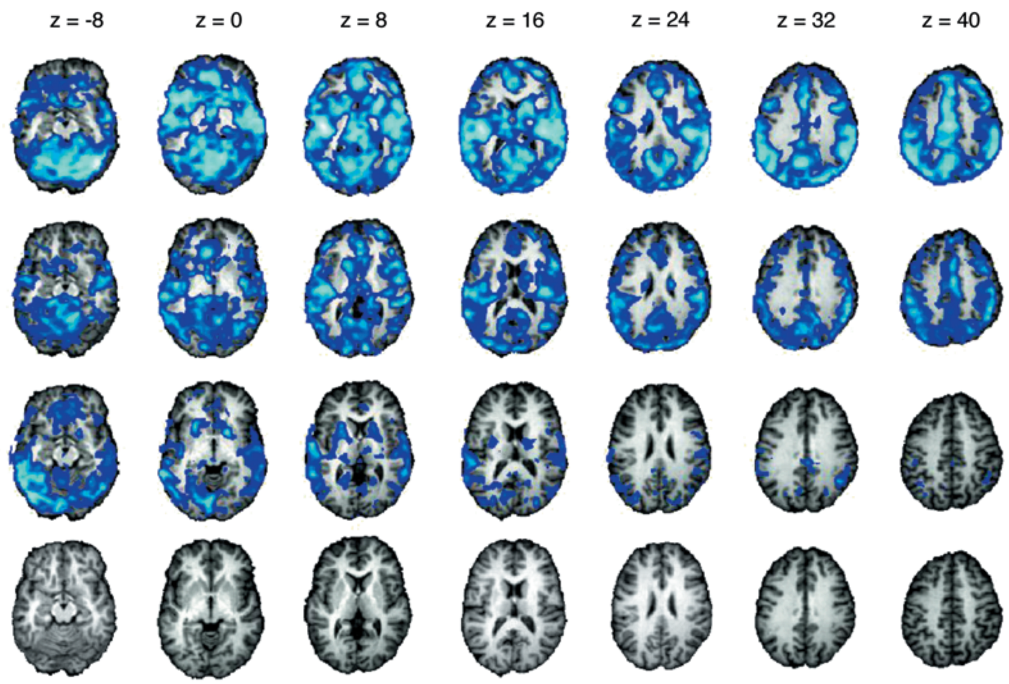

Figure 4. Averaged vasoreactivity maps (z<-5) acquired as the response to hyperventilation for the different study groups. The z-values reflect the position of the slices in the Talairach coordinate system.
1st row: young controls, 2nd row: elderly controls, 3rd row: patients with cerebral microangiopathy, 4th row: anatomical reference images.

In 5 patients with cerebral microangioapthy (CM/lacunar infarction and white matter degeneration), 6 healthy elderly subjects (age matched control), and 6 young healthy subjects, the CR in response to hyperventilation was evaluated by fMRI using gradient echo Echo-Planar Imaging. The percentage signal change normalized by endtidal CO_2 value was measured in various brain regions.
Patients with CM showed significant qualitative and quantitative differences as compared to controls. The volume of grey matter showing a significant CR was significantly reduced in patients: by 40% in comparison to the age matched elderly control group and by 60% when compared with the young controls. The CR impairment was most pronounced in frontal cortices with a drastically reduced magnitude of the MR signal change in the patients. A strong relation was evident between the fMRI based CR reduction in patients with CM and the individual severity of structural MR abnormalities. This study demonstrates that fMRI based signal changes in response to hyperventilation can reliably reflect cerebral autoregulation.

2.5.4 How does ischemia affect neural activation? A combined BOLD and perfusion study of major cerebral artery stenosis

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Stenosis of major cranial arteries is associated with a reduced vasomotor reserve without necessarily producing functional deficits. The present study aimed to examine by means of fMRI BOLD signal changes whether and how the hemodynamic responses to neural brain activation are modified under chronic ischemia due to major arterial stenosis.
FMRI motor mapping was studied in two female patients with unilateral high-grade stenosis of the middle cerebral artery (MCAS). Both patients solely exhibited transient neurological symptoms such as facial paresis and short repetitive episodes of speech arrest prior to the diagnosis of the MCAS. Severity of cortical ischemia was assessed by means of MR perfusion measurements. Functional patient data were compared to activation patterns of six age-matched healthy control subjects.
The functional activation patterns in both patients significantly differed from those of healthy controls. In both patients, unilateral finger tapping was associated with a significant co-activation of the ipsilateral primary motor hand area (M1) and premotor cortices, when the hand contralateral to the stenosis was performing the task (Figure 5). Motor performance was fully intact. The mean transit time for the primary motor cortex was significantly delayed on the ischemic side in both patients in the brain perfusion study.
Our data suggest that impaired hemodynamics due to unilateral cranial artery stenosis is compensated for by the co-recruitment of ipsilateral primary motor and premotor cortices. This strategy can be regarded as a neuronal reserve mechanism to preserve function in the presence of hemodynamic compromise due to chronic ischemia.

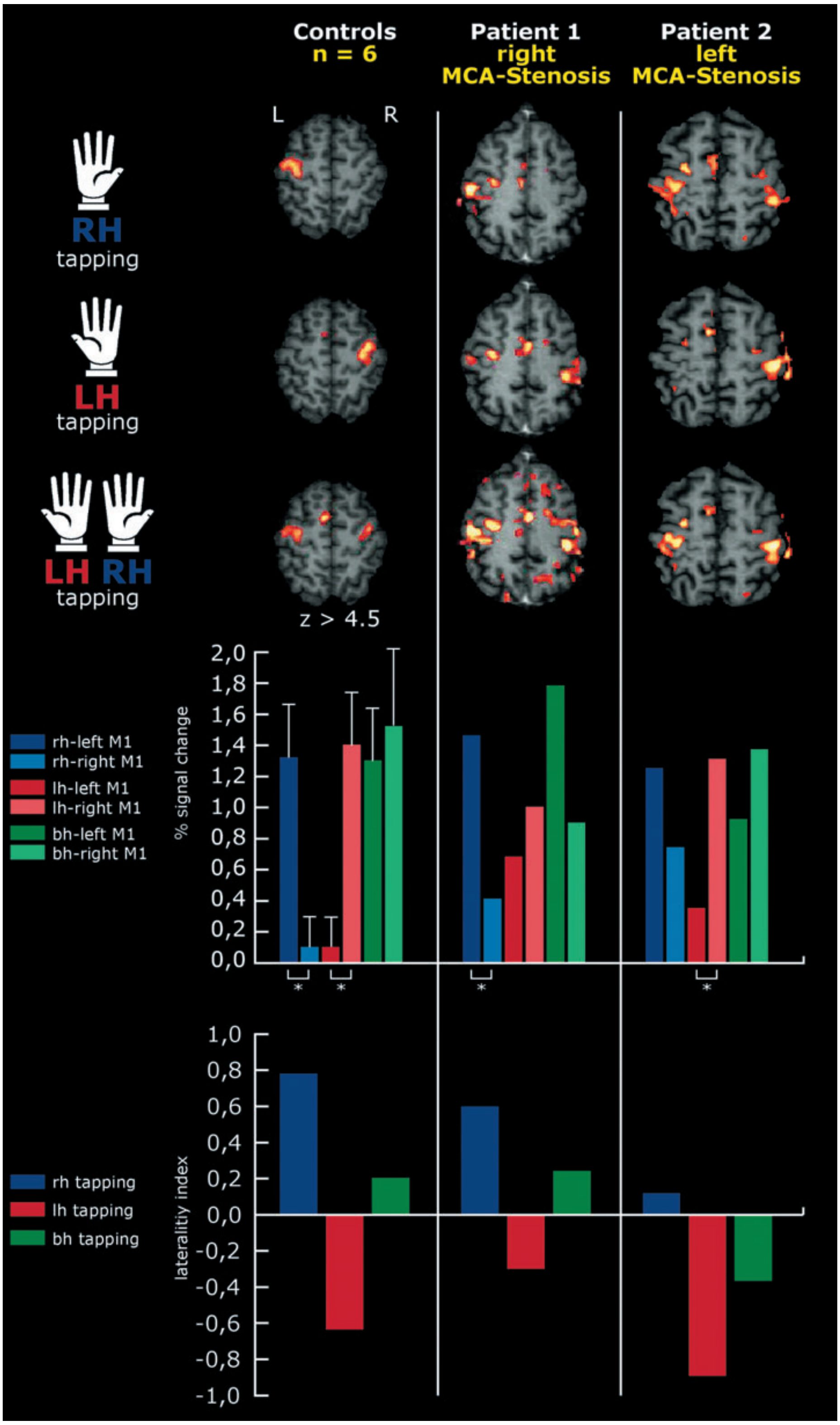

Figure 5. *Top*: Functional activation patterns of left hand, right hand and bilateral finger tapping for the two patients with high grade MCA stenosis and the control group.
Middle graph: The magnitude of the MR signal changes in the primary motor cortex (M1) of both hemispheres is displayed in the bar charts for the different conditions.
Buttom graph: Hemispheric laterality indices for the different tasks (range ±1: positive indices indicate left hemisphere dominance, negative indices show right hemisphere dominance). The expected crossed activation patterns were replaced by a more bilateral involvement of the motor network in the patients, when the hand contralateral to the stenosis was tapping.

Language related brain potentials and anterior temporal lobe lesions: Lexical and semantic processes

2.5.5

*Kotz, S.A.,
Hofmann, J.,
von Cramon, D.Y. &
Friederici, A.D.*

Currently there has been a renewed debate on the role of the left anterior temporal lobe in speech perception. While some recent PET evidence (Scott et al., 2000) indicates that this brain region is involved in speech intelligibility, others have claimed that the anterior temporal lobe is engaged in syntactic processing (Donkers et al., 1994; Meyer et al., 2000; Friederici et al., in press). One question that remains is whether speech intelligibility implies the recognition of lexical-semantic and syntactic information at the sentence level or even at the word level, as we were able to show activation of the anterior temporal lobe during word and pseudoword processing in an fMRI experiment (Kotz et al., in press). To further investigate this matter we tested a group of patients with left anterior temporal lesions (N=11) and as a control group patients with extended right anterior temporal lesions (N=8) in an auditory word list lexical primed decision task, which allows to process words and pseudowords in a speech stream. Patients with left anterior temporal lobe lesions showed no lexical N400 effect, but a delayed and reduced N400 semantic priming effect. Patients with right anterior temporal lobe lesions showed a small lexical N400 effect, but almost no N400 priming effect. These results indicate that the left anterior temporal lobe might play a role in initial phonological processes during word recognition (i.e., to identify whether a word follows the phonological rules of a language), but only indirectly in semantic priming (see also McNellis & Blumstein, 2001).

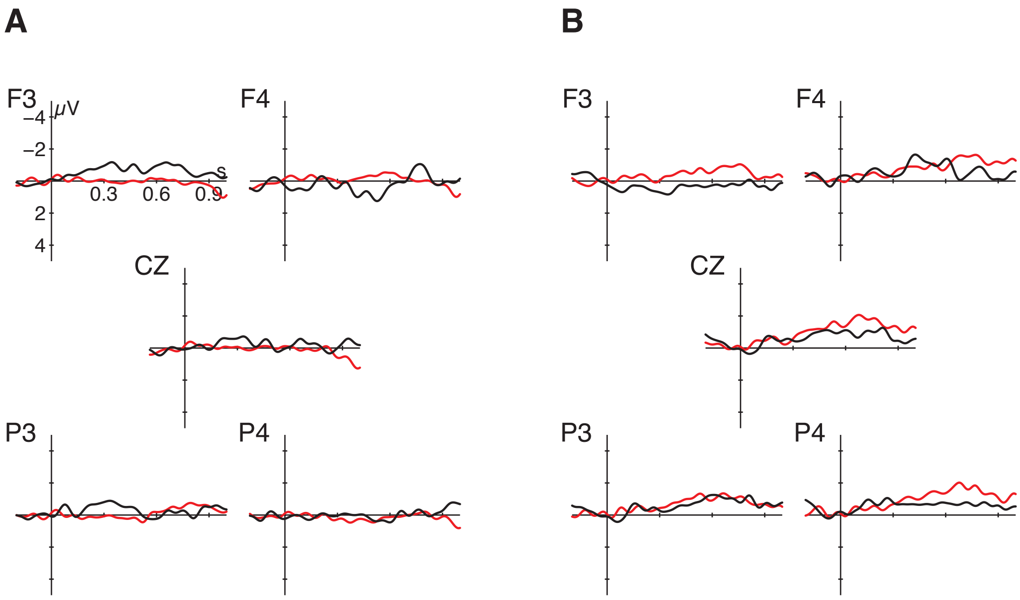

Figure 6. Displayed are difference waves of the lexical N400 effect (A) and the semantic N400 priming effect (B) at selected electrode-sites. Lines in red reflect both the lexical N400 effect and the semantic N400 priming effect for the patients with left anterior temporal lesions and the lines in black the same effects for the patients with right anterior temporal lesions.

2.5.6 Semantic differentiation of nouns and verbs: Evidence from aphasic patients with left anterior and left posterior temporal lesions

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The dissociation of nouns and verbs has been discussed as highly controversial in both patient studies and imaging studies. While some patient (see Gainotti et al., 1995 for an overview) and imaging studies (e.g., Damasio et al., 1993) report a distinction of verbs and nouns, other data is less clear about the differentiation between the two word types.

We approached the differentiation of nouns and verbs with a classical lesion approach. To test the patients' capability to select an appropriate target (either noun or verb) we visually presented sentence fragments on a computer screen. After a brief period a sequence of either six nouns or verbs (distracters and target) was presented in parallel. The subject's task was to select a fitting noun or verb for the sentence fragment by pressing one of six response buttons that matched the correct target. Eight aphasic patients with left anterior lesions and six aphasic patients with posterior temporal lesions participated in the experiment. None of the patients suffered from hemi neglect, dementia or amnesia. In addition, age-, gender-, and education-matched controls were tested.

Preliminary behavioral results show that controls semantically differentiate nouns and verbs in a similar way. On the other hand, while aphasic patients with anterior lesions respond faster to nouns than verbs, they show a similarly low pattern of correct responses to both word types. Aphasic patients with posterior temporal lesions show comparably slow and reduced correct responses to both word types. Thus, the current data indicate that when nouns and verbs have to be semantically differentiated both patient groups show a comparable deficit for nouns and verbs in terms of percentage correct. However, aphasic patients with left anterior lesions seem to have more trouble selecting a context fitting verb as compared to a noun in time. This might suggest a selective temporal deficit for verb information in aphasic patients with left anterior lesions, but an undifferentiated slow down for verbs and nouns in aphasic patients with left posterior temporal lesions.

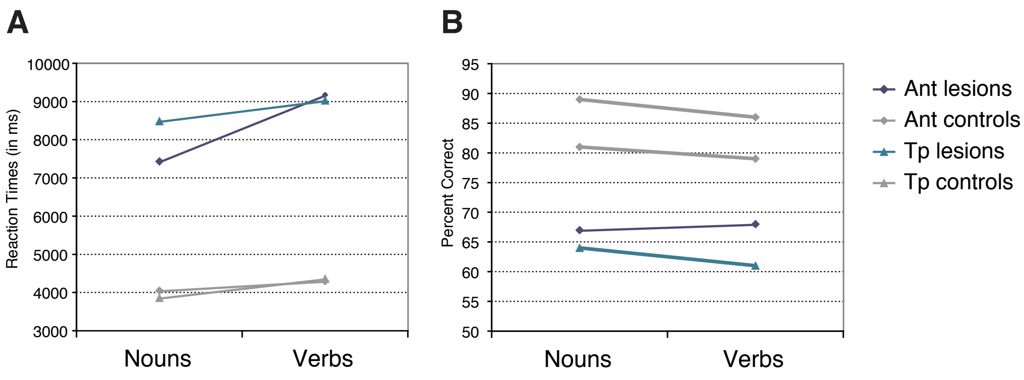

Figure 7a displays reaction times for aphasic patients with left anterior lesions (blue) and left posterior temporal lesions (green) and their respective age-matched controls (grey). Figure 7b shows the percent correct in the same set up.

Grammatical gender processing in left anterior and posterior STG patients

2.5.7

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Hofmann, J.[1], Marschhauser, A.[1,2], von Cramon, D.Y.[1,2] & Kotz, S.A.[1]

Investigations with patients give evidence that grammatical gender processing is affected as a focus of lesion site. In German there are three gender assignment types (phonological, morphological and semantic type), which might be affected differently in particular lesion groups. Behavioral performance was investigated in patients with posterior superior temporal gyrus (STG) lesions (n=4), patients with left anterior lesions (n=4) and age-, gender- and education-matched controls (n=4; n=4). Stimulus pairs were presented visually and sequentially. Subjects were asked to decide whether the first word indexing the gender ("weiblich" – feminine, "männlich" – masculine, "sächlich" – neuter) matches the second word's gender (nouns of all grammatical genders). Overall, patients always show significantly lower percentage correct in comparison to controls. Anterior patients show significantly less correct responses to the phonological type in comparison to the morphological and the semantic type (see Figure 8). Tendentially STG patients show less correct responses to the morphological in comparison to the semantic type (see Figure 9). Thus one can speculate that left anterior regions are involved in the processing of phonological gender information and the posterior STG is involved in the processing of lexical derivational-morphological gender information.

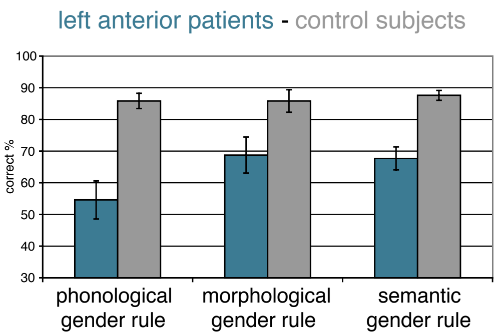

Figure 8. Percent correct for left anterior patients (dark green) and control subjects (grey).

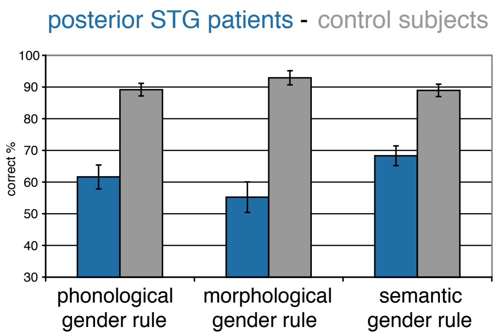

Figure 9. Percent correct for posterior STG patients (blue) and control subjects (grey).

Regularity revisited: Verb production in patients with basal ganglia lesions or degeneration

2.5.8

Kotz, S.A., von Cramon, D.Y. & Friederici, A.D.

The role of the basal ganglia in language processing and in syntactic processing in particular has been discussed controversially for years. While some studies argue no role of the basal ganglia in language processing (Nadeau & Crossen, 1997) others assume a role in language production (e.g., Alexander et al., 1987). The latter argument was tested by Ullman et al. (1997), who claim that the processing of syntactic rules involves a frontal/basal-ganglia 'procedural' system. Comparing the morphosyntactic past-tense production of irregular and regular verb forms in anterior aphasics and in Parkinson's patients (PD) the authors report that both patient groups produce more errors with regular rule-based verb forms than lexically based irregular verb forms. Previous evidence from event-related brain potential studies (see for an overview Kotz et al., 2002), however, indicates that PD patients as well as patients with focal lesions of the basal ganglia do not show a selective deficit for automatic syntactic processes in language perception studies. We thus set out to test patients with basal ganglia lesions and PD patients in a verb production paradigm comparable to Ullman et al. (1997) to find out whether the discrepancies in the reported data result from a specific production deficit. Eleven patients with circumscribed basal ganglia lesions and five PD patients as well as a respective number of age-matched controls participated in the experiment. Percent error data reveal that both patient groups do not show a deficit for regular past-tense verb production as compared to their respective age-matched controls. Rather, both patient groups show a greater deficit for irregular verb forms. We take these results as further evidence that the basal ganglia are not a necessary structure to modulate rule-based or automatic syntactic processes during either language perception or production.

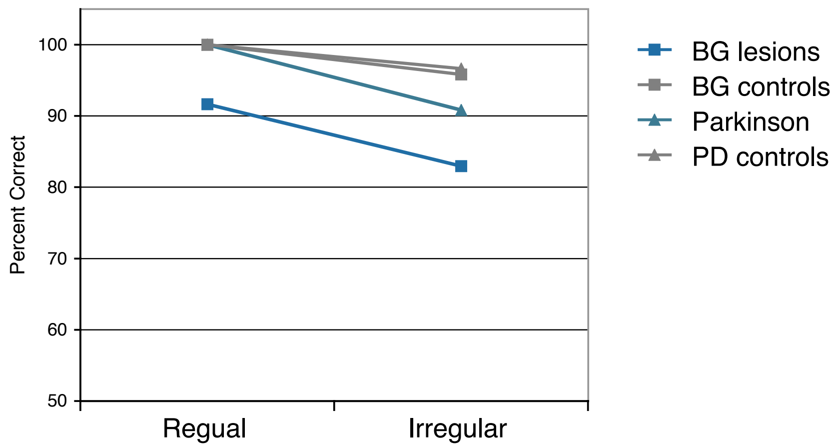

Figure 10. Displayed are the Percent Correct for regular and irregular past tense verb production in Parkinson patients (PD; green), basal ganglia lesion patients (BG; blue) and their age-matched controls (both grey, but see symbol match with respective patient group).

2.5.9 Task switching in Parkinson's disease: The impact of external and internal cueing

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Neuropsychological research has shown that cognitive set shifting is often impaired in patients with Parkinson's disease (PD). The present study addresses the question whether task switching deficits in PD depend on the nature of the cue, i.e., whether the task is preceded by an external task cue or whether performance of the task has to be initiated internally. Patients with PD and healthy controls (n=16 per group) were asked to classify one-figure numbers, either as odd/even (task A) or as smaller/greater 5 (task B). Internal task cuing was induced by the "alternating runs" schema, involving a regular, predictable task order (AABB). Additionally, task-specific graphic symbols were provided as external cues, either with a long (900 ms) or short (100 ms) cue-stimulus interval (CSI). After several blocks with both external and internal cueing, the order of tasks changed to random, and participants received only external cues. Reaction time increases after this change serve as an index for previous use of the internal cue. In controls, the reaction time increase was larger in the short CSI condition than in the long CSI condition. Thus, healthy participants made use of the internal cue if the external cue was not informative, as it appeared only shortly before the task. PD patients, in contrast, did not show enhanced use of the external cue in the short CSI condition. Our data suggest that PD patients are impaired in the flexible use of internal cues, thereby confirming the hypothesis of a specific deficit in self-initiated task switching.

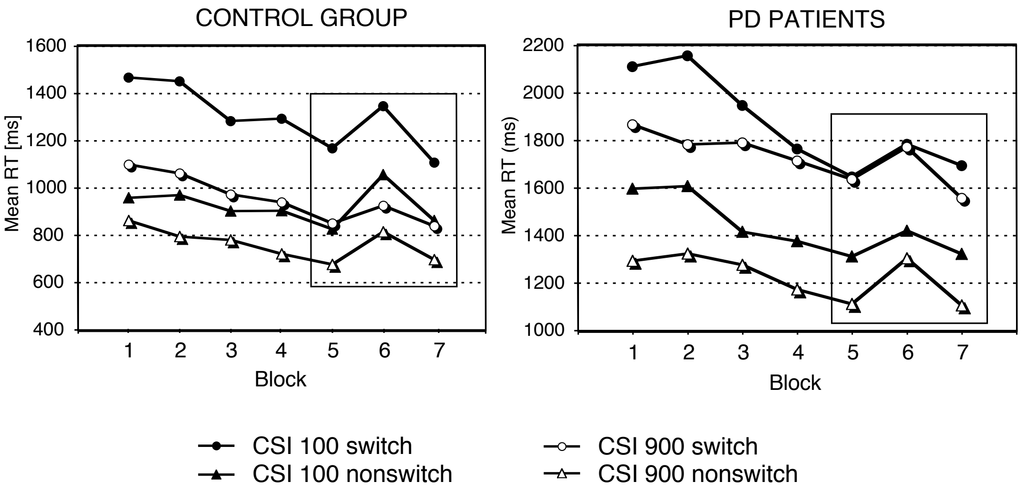

Figure 11.

Spatial hearing in patients with acquired brain lesions affecting primary auditory cortex

2.5.10

Grube, M.[1,2], von Cramon, D.Y.[1,3] & Rübsamen, R.[2]

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The principle role of primary auditory cortex (PAC) in spatial hearing is not yet known, as previous studies yielded controversial results. In animals, cortical single units with panoramic response characteristics and peak responses located in the contralateral hemifield were recorded, while in behavioral studies with brain-lesioned animals the apparent contribution of PAC to spatial hearing depended on the nature of the task. The two prevailing hypotheses on auditory space perception suggest dominant representations of the contralateral hemifields or a general right-hemisphere dominance. However, the evidence mainly stems from lateralization, i.e., headphone experiments, or from studies in patients with lesions of higher, i.e., supramodal parietal cortical areas. In this study, we specifically aimed at the functional significance of PAC in sound localization. The ability to spatially segregate auditory events was investigated in patients with acquired brain lesions affecting left or right Heschl's Gyrus (HG, the PAC anatomical correlate), in that HG was either directly damaged or deprived of its afferents. Minimal audible angles (MAA) in the horizontal plane were measured for low and high-frequency noise bursts as a function of reference direction. We applied an adaptive three-alternative forced-choice paradigm proven suitable for working with naive subjects and patients. The patients' direction discrimination thresholds critically depended on the site of lesion. Compared to data from naive control subjects, spatial resolution was severely impaired in patients with lesions affecting right HG (Figure12). Thresholds were elevated for reference directions in both hemifields, with the deficit being more pronounced for low-frequency than for high-frequency stimuli. The performance of patients with left-hemispheric lesions tended to be poorer in the right hemifield rather than in the left, if it was impaired at all (not shown). The results of our study support the assumption that, corresponding well to the generally accepted functional specialization in human space perception, a right hemisphere dominance in spatial hearing is already established at PAC level. At the same time, our findings yielded evidence for the existence of dominant contralateral representations of auditory space in human PAC.

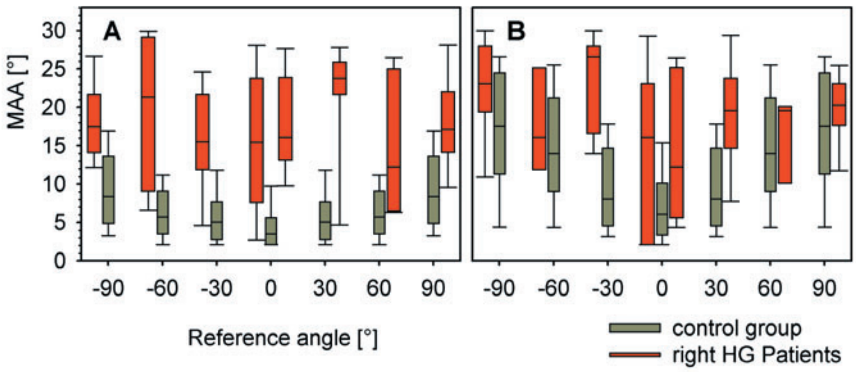

Figure12. Minimal audible angles (MAA) in patients with lesions affecting right Heschl's Gyrus (red) & control group (grey) as a function of reference direction (negative numbers: left, positive: right) for **A** low (0.25 to 1.2 kHz), **B** high-frequency (2 to 8 kHz) noise bursts.

2.5.11 Splenial fibres: An integral part of the attentional (target detection) network?

Pollmann, S.[1], Maertens, M.[1,2] & von Cramon, D.Y.[1,2]

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[2] Max Planck Institute of Cognitive Neuroscience

Patients with splenial and pre-splenial lesions of the corpus callosum as well as healthy controls were tested for their ability to detect visual and auditory targets. While healthy controls and pre-splenial patients exhibited a normal right ear advantage in the dichotic listening of CV-syllables, patients with splenial lesions showed an almost complete suppression of left ear targets. The same splenial patients also had higher costs following invalid cues in the spatial cueing paradigm whereas patients with pre-splenial lesions and healthy controls performed at normal levels. Our interpretation of the results is based on two lines of research: (1) Human post mortem degeneration studies and diffusion tensor imaging indicate that fibers in the splenium project to cortical areas at the temporo-parietal junction (TPJ). (2) The results from lesion and imaging studies suggest the TPJ-cortex to be involved in the detection of targets with behavioral relevance. In an event-related fMRI-study of dichotic listening we identified an area in the posterior segment of the right superior temporal gyrus in which correct target detections elicited a signal increase compared to correct rejection of target presence. We therefore interpret our findings as converging evidence for the disruption of signals originating in the temporo-parietal junction area, which normally alert the system to the presence of behaviorally relevant stimuli. After splenial lesions, these signals may not reach the contralateral hemisphere, leading to deficits in target detection, especially under distracting conditions.

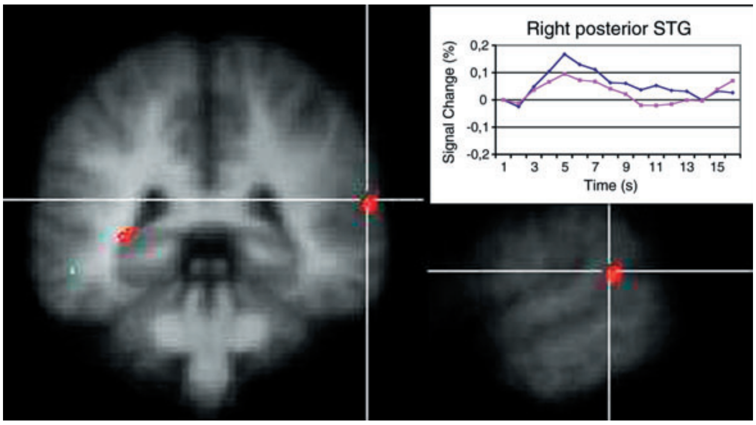

Figure 13. Localization and time courses of activations in the right superior temporal gyrus elicited by contrasting right (blue) versus left (magenta) ear target detections in subjects with a right ear advantage.

Covert reorienting in auditory spatial attention

2.5.12

Lepsien, J.[1,2] & Pollmann, S.[2]

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Most evidence of the functional neuroanatomy of spatial attention originates from investigations of the visual domain. As indicated by behavioral studies, it is also possible to spatially shift auditory attention in a comparable way. As a continuation of former experiments, the present study aimed at imaging the neuronal correlates of covert auditory reorienting, which describes processes necessary after misallocation of attentional resources.

We modified a Posner cueing paradigm for covert exogenous shifts for the use in fMRI, using *kunstkopf*-stimuli for spatial stimulation, to evoke effects of initial facilitation and inhibition of return (Posner & Cohen, 1984).

The interaction of SOA (75 ms, 900 ms) and cueing validity (valid, invalid) revealed activity related to covert reorienting mainly in the right superior temporal gyrus, matching the temporo-parietal junction area (TPJ) (see Figure 14). This area is currently discussed

as important for attentional realignment in order to detect behavioral relevant stimuli, especially when they are salient and unexpected.
The present results extend the known properties of TPJ to exogenous auditory reorienting. As indicated by distribution of percent signal change and additional contrasts, this holds not only for counteracting the attentional capture following an invalid cue, but also for counteracting the effects of inhibition of return.

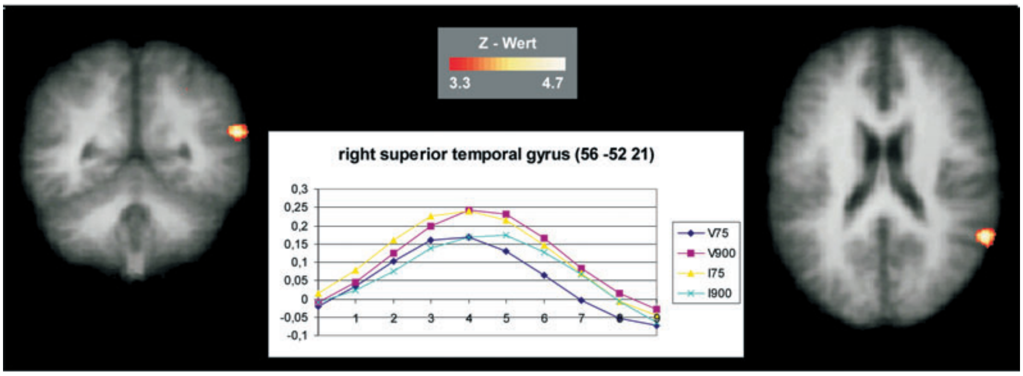

Figure 14. Activation in the right TPJ-area and timecourses for all conditions over 9 s from cue onset.

2.5.13 Differences in target detection and localization tasks in visuospatial orienting

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The present study aimed to investigate the influence of altered response-requirements on the neural networks previously identified for covert reorienting and inhibition of return (IOR) (Lepsien & Pollmann, 2002). Covert reorienting describes processes necessary after misallocation of attentional resources, and was found to be mainly supported by prefrontal areas. IOR is characterized as delayed detection of stimuli at previously cued locations (Posner & Cohen, 1984), and was accompanied by activations in oculomotor areas. The same exogenous cueing paradigm was applied in an event-related fMRI study, but with the task changed from target detection to target localization, and the response mode changed from simple reaction to choice reaction.

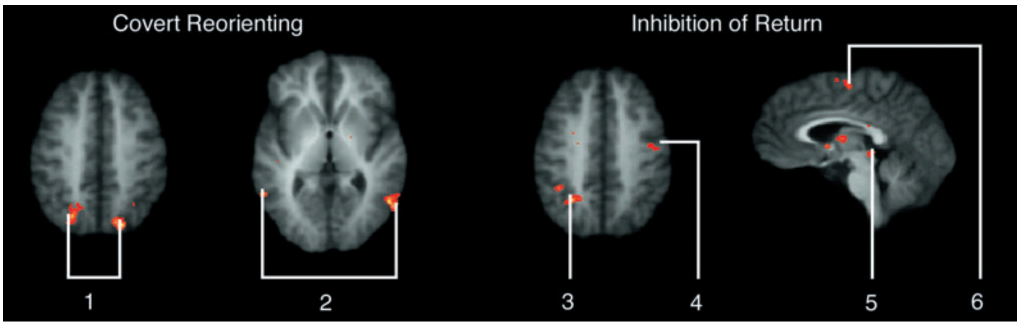

Figure 15. Signal increases following covert reorienting and inhibition of return in the [1] superior parietal lobule/intraparietal sulcus, [2] middle temporal gyrus, [3] superior parietal lobule/anterior intraparietal and postcentral sulci, [4] precentral gyrus, [5] superior colliculi, [6] and medial frontal gyrus; z>3.09.

Covert reorienting with target localization revealed activations located primarily in the bilateral superior parietal lobule, along the intraparietal sulci. Additional activation was found in the bilateral middle temporal gyri. IOR was accompanied by increased activity in the left medial frontal and right precentral gyri (supplementary and inferior frontal eye-fields), as well as the superior colliculi, again emphasizing its close link to the oculomotor system. Additional IOR-related activity was found in the left superior parietal lobule, covering the anterior intraparietal and postcentral sulci (see Figure 15).
Together, the present findings underline the role of parietal cortex as a mediator between perception and action, and reflect the increased demands in visual-spatial and response selection with target localization.

2.5.14 Left and right occipital cortices differ in their response to lateral cueing

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For a long time it has been assumed that the hemispheres differ in their capacity to respond to stimuli in ipsilateral hemispace. The preponderance of neglect after right-hemispheric lesions, e.g., has been thought to mirror mainly contralateral attending in the left hemisphere, compared to a more even distribution of attention between contra and ipsilateral hemispace in the right hemisphere.

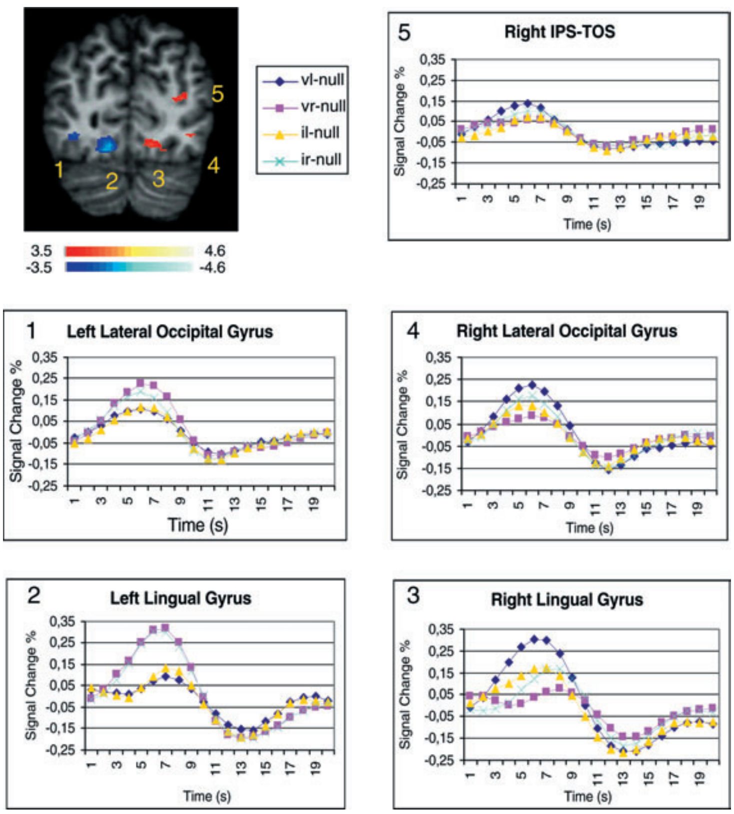

Figure 16. Cue and target-related activation in occipital cortex. V(I): valid (invalid) cue, L(R): Cue presentation in left (right) visual hemifield, Null: null event.

In the present study, we investigated cue and target-related laterality effects with event-related fMRI. Both left and right occipital areas responded maximally when both cue and target were presented in the contralateral visual hemifield (VF), and minimally when cue and target were presented in the ipsilateral VF (Figure 16). However, whereas signal increases in right ventromedial and lateral occipital cortex were intermediate in those trials in which the cue appeared in the VF contralateral to the target (invalid cue trials; Figure 16, 3 to 4), signal strength in left occipital cortex was almost identical for valid and invalid cues, i.e., high for RVF-targets, and low for LVF-targets, independent of the VF of the cue (Figure 16, 1 to 2). These data support theories which postulate a greater ability of the right hemisphere for bilateral processing. However, these laterality effects were observed earlier in the visual pathway than previously thought, leading to the question of whether the hemispheric differences observed in occipital cortex are generated in the activated areas or are the effect of reentrant processes from more anterior areas, potentially in parietal cortex.

2.5.15 Processing efficiency, not computational complexity, causes the bilateral distribution advantage

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Interhemispheric resource sharing facilitates performance in some tasks, but not in others. Typically, a bilateral distribution advantage (BDA) is observed in categorical matching tasks, whereas it is absent in physical shape comparisons. It has been proposed that the computational complexity of a task, i.e., the number of processing steps involved, determines whether processing benefits from bilateral compared to unilateral stimulus

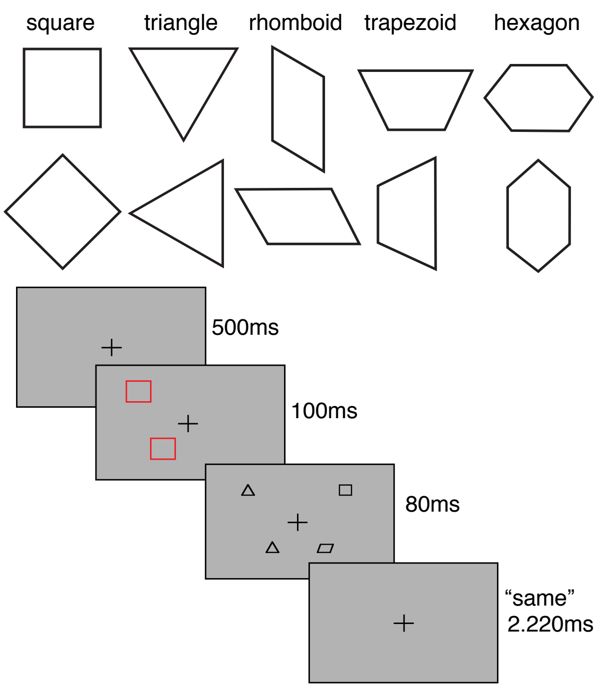

Figure 17. Elements of the geometrical shape categories (top) and trial design (bottom).

presentation. Alternatively, we consider inefficient processing at a single processing step in the hemisphere of input sufficient to produce a BDA. In a series of six geometrical figure matching experiments, processing efficiency and task complexity were contrasted as potential accounts for the BDA. The number of processing steps were determined by the matching task while processing efficiency was varied by learning. Initially, a BDA was observed for physical as well as for categorical matching of geometrical figures. In subsequent training sessions, the BDA disappeared first in the physical, and later on in the category-identity task. This result pattern strongly supports the processing efficiency account of the BDA.

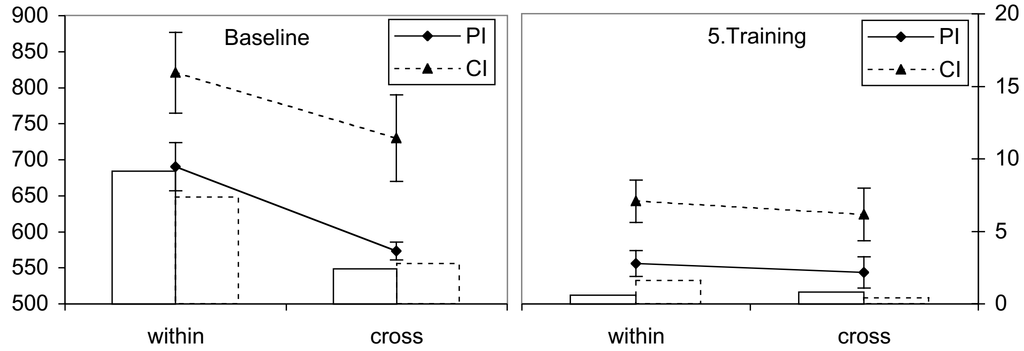

Figure 18. Mean reaction times [ms] and SE (left ordinate, line graphs) as well as mean error rates [%] (right ordinate, bar graphs) as a function of hemifield and task for matches in the baseline (left) and in the final (right) training session, dotted bars – CI task, straight bar – PI task.

Long before the development of sophisticated models of cognitive psychology on one hand and the invention of sensitive neuroimaging methods on the other, Pavlov stated in 1949 that the endeavor to localize cerebral cortical functions were merely attempts to "fit the system of abstract concepts of modern psychology into the material structure of the brain". Fifty years later, this endeavor is still going strong. We carefully devise tasks based on cognitive theories in order to identify and isolate brain regions or networks of brain regions associated with particular, seemingly well-defined subprocesses of these tasks. And, we now have available a variety of neuropsychological methods for getting a glimpse into the active brain. Besides the prevalent functional magnetic resonance imaging (fMRI) – whose methodology is continuously improved and refined – the group employs event-related potentials (ERPs) and functional near-infrared spectroscopy (fNIRS). Converging evidence for the imaging results is sought in lesion studies, reported in section 2.5.

In last year's research classical tasks testing executive functions once more played an important role. The fNIRS studies employed a Stroop paradigm, task switching was investigated behaviorally and in imaging studies, and a study on working memory added to our understanding of rehearsal. The studies on error processing illustrate how behavioral and ERP studies shed light on the influence of instructions, feedback and reward on performance monitoring. Decision making under uncertainty was a new, related topic . As in previous years, we also conducted studies on the role of the premotor cortex during sequential processes and on higher level cognition, such as language comprehension in context and evaluative processes.

Interestingly, some recent fMRI results have taught us to adjust the strategy of going from concepts in cognitive theory to functional neuroanatomy. Two important developments can be identified. First, it becomes more and more apparent that some brain areas are engaged in a multitude of different tasks for which our usual cognitive task analysis does not readily provide a common subcomponent. One important example is the frontomedian cortex (BAs 9, 10), which has been linked to higher level cognitive processes such as inferencing, Theory-of-Mind and evaluation. Now we know that this region also plays a role during sequential behavior, during working memory tasks, or when inhibiting simple finger movements. A parsimonious account of these activations requires going beyond a purely cognitive conceptualization into a more general realm. Second, subcortical structures related to more basal processes not restricted to executive functions have proven to be involved during task performance. In two studies, the involvement of reward-processing structures, such as the Nucleus Accumbens, the dopaminergic midbrain area and the dorsal thalamic system, has been shown with fMRI. Thus, it is necessary to add hypotheses on motivational and emotional by-products of task performance, and to specify the interactions between "hard" cognition and "soft" factors influencing human behavior. Moreover, these studies demonstrate the necessity of integrating the findings from cognitive neuroscience with the knowledge from other fields such as animal research and functional neuroanatomy.

2.6.1 Age-dependency of the hemodynamic response and cytochrome-c-oxidase as measured by functional near-infrared spectroscopy

*Schroeter, M.L.,
Zysset, S.,
Kruggel, F. &
von Cramon, D.Y.*

Aging reduces cerebral blood flow in association cortices during rest, and decreases the activity of cytochrome-c-oxidase (Cyt-Ox). However, the influence of age on functional brain activation is still controversial. The aim of our study was to examine age-dependency of brain activation in primary and association cortices. Therefore, changes of oxy-, deoxy-, total hemoglobin, hemoglobin difference (sum and difference of oxy- and deoxy-hemoglobin, respectively), as well as changes in the redox state of Cyt-Ox were measured by functional near-infrared spectroscopy. Optodes were placed at the lateral prefrontal and motor cortex during an event-related Stroop interference task, and in the visual cortex during stimulation with a checkerboard paradigm. Data revealed three effects of aging on brain activation: (1) Elderly and young subjects used the lateral prefrontal cortex to cope with interference during the Stroop task. In young subjects, the vascular response was higher during incongruent than neutral trials in the entire examined lateral prefrontal cortex. However, in the elderly, all lateral prefrontal regions showed a hemodynamic response but not necessarily a specific interference effect. (2) As illustrated in Figure 1, the hemodynamic response was reduced in elderly subjects in the lateral prefrontal association cortex, but obviously not in the motor and visual cortex. (3) Age reduced the increase of Cyt-Ox during visual activation, and led to a higher interference effect of Cyt-Ox in the elderly during the Stroop task (Figure 1). Our findings suggest that aging decreases the hemodynamic response in the frontal association cortex during functional activation, omitting primary cortices, and alters Cyt-Ox in both primary and association cortices.

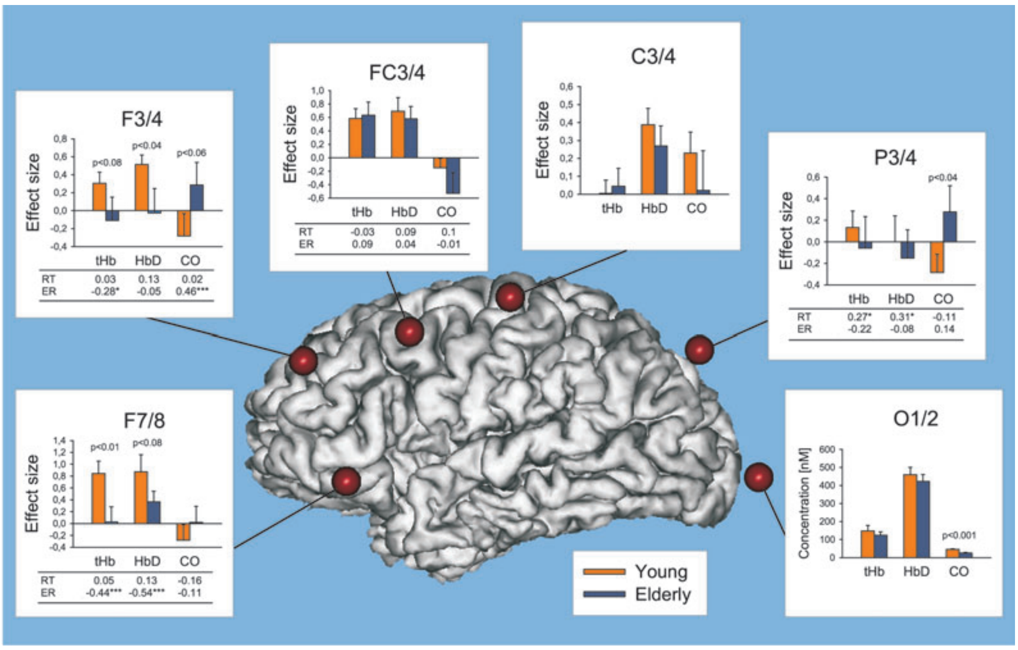

Figure 1. Effect sizes (incongruent–neutral/$SD_{neutral}$) of regional cerebral blood volume (total hemoglobin, tHb), flow (hemoglobin difference, HbD), and cytochrome-c-oxidase (CO) compared between young and elderly subjects during the Stroop task. At O1/2, changes during visual stimulation are shown. Correlation coefficients are reported between hemodynamic (tHb/HbD/CO) and behavioral effect sizes (reaction time [RT], and error rate in percent [ER]).

Shortening intertrial intervals in event-related cognitive studies with near-infrared spectroscopy

2.6.2

Schroeter, M.L., Zysset, S., Kruggel, F. & von Cramon, D.Y.

Reducing the length of the intertrial interval (ITI) seems to be a precondition for further cognitive event-related experiments with functional near-infrared spectroscopy (fNIRS), because it may increase statistical power. Therefore, this study investigated whether the ITI may be reduced from 12, 6, 4 to at least 2 s. Brain activation was examined with a NIRO-300 spectrometer at the lateral prefrontal cortex (LPFC) in 17 healthy subjects during a randomized event-related color-word matching Stroop task. Overlap of the hemodynamic response was corrected by subtracting averaged time courses of non-events from time courses during neutral and incongruent trials of the Stroop task. Corrected data (Figure 2) revealed that the concentration of deoxy-hemoglobin (Hb) decreased significantly more strongly during incongruent than neutral trials at the left LPFC due to coping with interference. Only for an ITI of 4 s we did not find an interference effect, presumably due to optimal behavioral performance (smallest effect size of reaction time at this ITI length). Decreasing the length of the ITI reduced the amplitude of oxy- and total Hb, but not of deoxy-Hb (Figure 3). Thus, event-related cognitive fNIRS experiments may be performed with an ITI as short as 2 s. With randomized experimental designs fNIRS can now be used to explore an entire new range of cognitive neuroscience paradigms and questions.

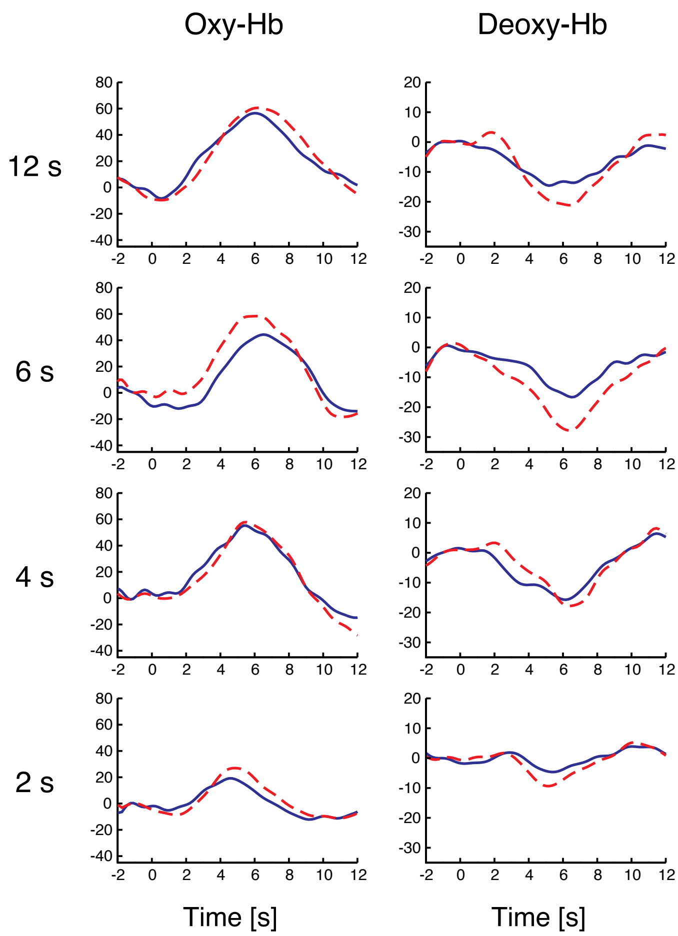

Figure 2. Concentration changes of oxy- and deoxy-hemoglobin (Hb) during the color-word matching Stroop task in the left dorsolateral prefrontal cortex. Beginning of the Stroop task at 0 s. Changes are given in nM.

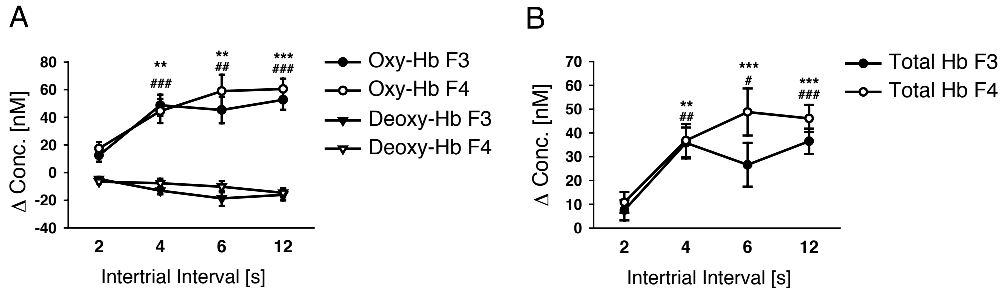

Figure 3. Concentration (conc.) changes of A. oxy-, deoxy-, and B. total hemoglobin (Hb) in relation to the several intertrial intervals. Significance values in comparison with 2 s intertrial interval.

2.6.3 Comparing different cue types in task switching

Forstmann, B.[1], *Brass, M.*[1], *Koch, I.*[2] & *von Cramon, D.Y.*[1]

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Performance in task switching is often investigated with cueing paradigms, in which external cues indicate the upcoming task. We assume that an external cue directly triggers the relevant task set without requiring endogenous control because it facilitates the memory retrieval of task-specific stimulus-response rules.
In order to explore these cue-related memory processes, we developed a new paradigm with two different external cue types (Figure 4A). While "task cues" are explicitly associated with the upcoming task, "transition cues" provide information about repeating or switching the task. Consequently, subjects, being confronted with a transition cue, have to internally activate the relevant task rule lacking any explicit information about the relevant task. To accomplish this, a comparative process between the N-1 task rule with the rule currently to be activated, has to be made. Since cue type was pseudo-randomly presented, the subjects were coerced to actively maintain the previous task rule in both conditions. Therefore, memory load cannot account for any cue type effects. This was further corroborated in two subsequent behavioral experiments where the cue type was blocked.
The results reveal prolonged reaction times for the transition cues as well as larger switch costs (Figure 4B). We suggest that these cue type effects reflect the internal activation of the relevant task-set. Furthermore, we propose that these processes are essential components of endogenous control which can be investigated with this paradigm.

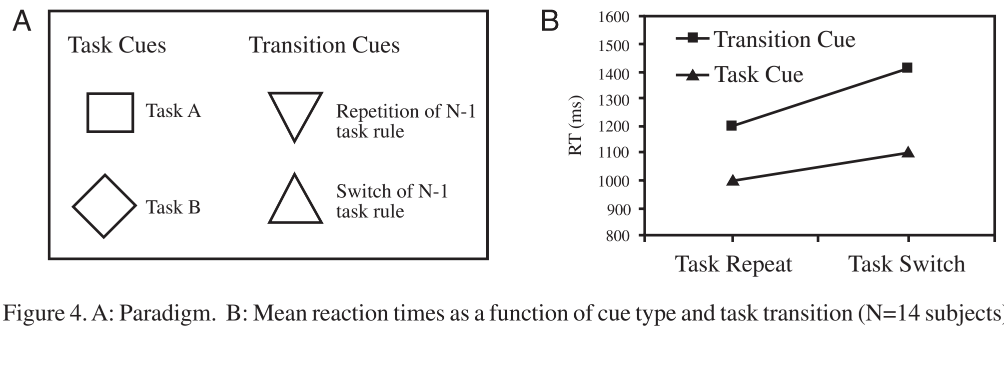

Figure 4. A: Paradigm. B: Mean reaction times as a function of cue type and task transition (N=14 subjects).

Neuronal mechanisms of conflict-triggered inhibition of distracting perceptual dimensions in task switching

2.6.4

Gruber, O.[1,2], Karch, S.[1], Goschke, T.[3] & von Cramon, D.Y.[2]

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[2]Max Planck Institute of Cognitive Neuroscience
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Adaptive human behavior requires a context-sensitive balance between flexible adjustments of cognitive sets in response to changing task demands and stable maintenance of cognitive sets in the face of distraction. We assume that control processes that promote maintenance of a current intention by suppressing distracting information are specifically triggered by the presence of response conflicts. An fMRI study was conducted to assess the neural correlates of such a "conflict-triggered inhibition" in a combined task switching and working memory paradigm in which abstract objects had to be classified or to be remembered according to either color or shape. Incongruency of the irrelevant stimulus dimension led to reliable activation of the medial frontal cortex adjacent to the anterior cingulate cortex (Figure 5). Due to the fact that during shape tasks most of the stimuli had a neutral color (white), the rare occurrence of red or blue color produced a mismatch-like effect with prolonged reaction times and enhanced activity in a network of inferior frontal, parietal and occipito-temporal brain areas (Figure 6A). These regions were also involved in the mnemonic processing of shapes (Figure 6B). Hence, we assume that these activations represent enhanced top-down attentional control processes directed to the task-relevant shape. These processes may be triggered by new (and potentially distracting) sensory information that could be relevant for adaptive behavior. Further analyses will determine the functional connectivity between the activated brain regions in order to assess the dynamic interactions of bottom-up and top-down processes involved in this task-switching paradigm.

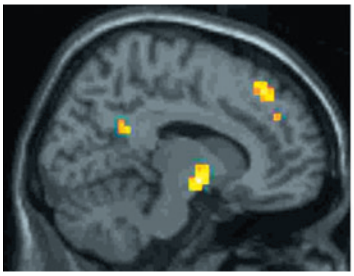

Figure 5. Medial frontal cortex activation evoked by incongruent colors.

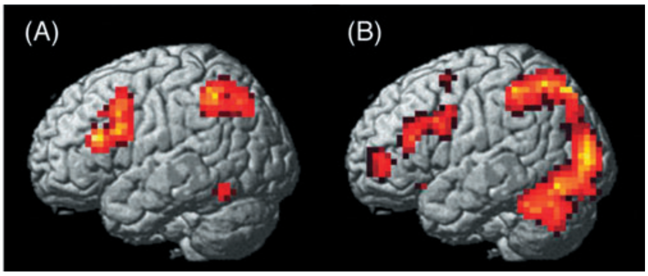

Figure 6. Inferior frontal, parietal and occipito-temporal cortex activations evoked by rarely occurring, potentially distracting colors (A) and associated with working memory for shapes (B).

2.6.5 Decomposing components of task preparation with functional MRI

Brass, M. & von Cramon, D.Y.

It is widely acknowledged that the prefrontal cortex plays a major role for the coordination of goal directed behavior. One crucial aspect regarding this coordinative function is our ability to prepare specific task situations before the actual task comes up. Imagine for example you are driving down a road and there is a traffic sign which signals that a traffic light will appear behind the corner. People are obviously able to use this sign to prepare the upcoming task without knowing whether the traffic light will be red or green. Experimentally, task preparation is investigated with a cueing version of the so called task-switching paradigm. In this paradigm participants are required to alternate between two different tasks. Because the task-rules change between the tasks, participants permanently have to adjust to the relevant task-set. In a previous study we could demonstrate that task-preparation involves the fronto-lateral cortex and the preSMA. In the present study we tried to address the question whether this activation was related to cue-encoding or preparation of the relevant task. In our paradigm participants got two task-cues with a preparation interval in between before the target was presented. These task-cues could indicate the same or a different task. In addition, catch trials were presented in which the target appeared after the first cue to ensure that subjects indeed attended to the first cue. We predicted that if both cues indicate the same task, participants only prepare once, while they should prepare twice if the second cue indicates a different task. The second experimental manipulation was related to the question of which specific processes are reflected by cue-related activation. By assigning two cues to each task one can compare a switch of cues without a switch of cue-meaning (two different cues that indicate the same task) with a switch of cues and cue-meaning (two cues that indicate different tasks). While the coding of the cue is required in both conditions, participants are only required to prepare the task twice in the condition in which the cue-meaning changed. Our fMRI data show a stronger fronto-lateral activation in the condition in which the cue-meaning changed compared to the condition in which only the task-cue changed (Figure 7). These results suggest that the fronto-lateral cortex is involved in preparation related processes that go beyond the simple encoding of the cue.

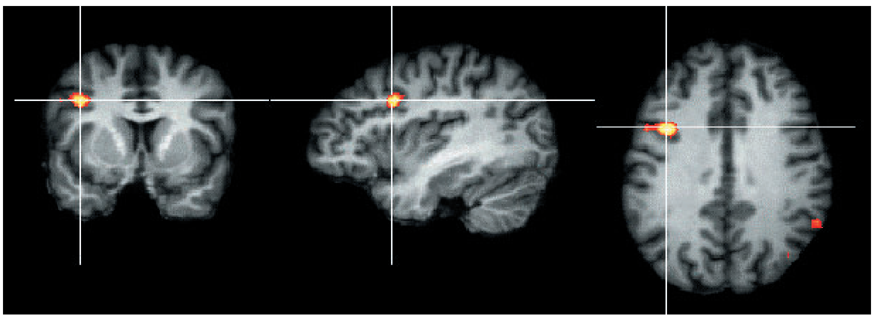

Figure 7. Cortical activation in the left fronto-lateral cortex for the comparison of meaning-switch and cue-switch

2.6.6

Manipulation of sequential verbal information in working memory causes neuronal interference effects similar to the effects of articulatory suppression

Gruber, O.[1,2], *Kittel, S.*[2] & *von Cramon, D.Y.*[2]

[1] *Department of Psychiatry, University of Ulm*
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Manipulation of sequential information held in working memory always requires simultaneous maintenance of parts of the same information. Recent fMRI studies have demonstrated that two different brain systems subserve verbal working memory maintenance according to whether speech mechanisms are available to assist memory performance or whether they are needed for other processes such as concurrent articulations. In the present fMRI study, we investigated whether previous studies of the neural correlates of manipulation of information in working memory could have been confounded by interference effects, which would make the assumption of pure insertion (i.e., that the neuronal mechanisms of memory maintenance during concurrent manipulation are identical to those in the absence of additional processes) inapplicable. Direct comparisons between verbal working memory tasks differing in memory load, manipulation demands and the presence or absence of interference due to articulatory suppression permitted more precise conclusions about the neural correlates of manipulation processes in working memory. In fact, we found that manipulation demands produced interference effects on brain activation associated with verbal working memory in a similar way as articulatory suppression does. Direct comparisons between the manipulation and the articulatory suppression conditions revealed additional bilateral activations along the posterior part of the superior frontal sulcus, along the intraparietal sulcus and in the precuneus, i.e., these activations could be attributed more specifically to manipulation processes involved in the sequential reordering of verbal information in working memory. As shown in Figure 8, manipulation of information in working memory relied to a greater part on the same neuronal resources, i.e., brain systems, that can also subserve pure memory maintenance functions during [1] rehearsal of verbal information (Broca's area and left premotor cortex), [2] non-articulatory maintenance of phonological information (bilateral anterior-prefrontal and inferior-parietal brain regions) and [3] visuospatial working memory (bilateral posterior-superior-prefrontal and intraparietal cortex).

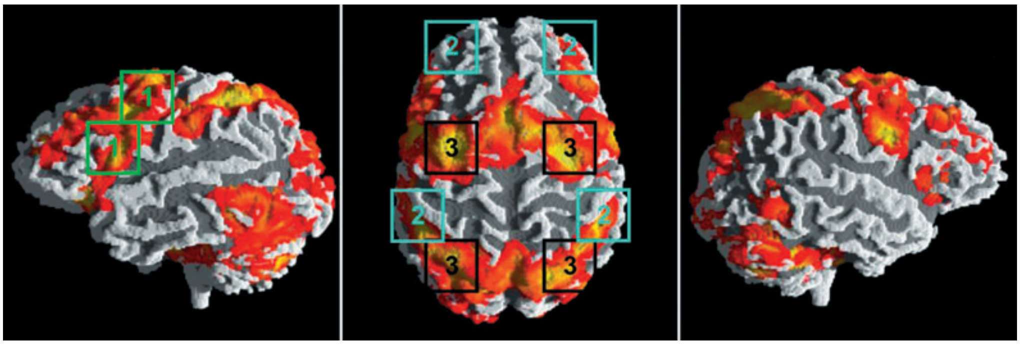

Figure 8. Brain activations associated both with manipulation of verbal information in working memory and with [1] articulatory maintenance or [2] non-articulatory maintenance of verbal information or [3] maintenance of visuospatial information.

2.6.7 Error processing based on external feedback I – An fMRI study on mistakes due to high uncertainty

Ullsperger, M. & von Cramon, D.Y.

Goal-directed behavior as well as skill acquisition require continuous performance monitoring. Good performance is reinforced, deviations from the goals, e.g., errors, call for remedial actions and adjustments of the used cognitive strategies. While action slips resulting from premature responses can be internally detected by the acting person (cf. Fiehler et al., 2.6.9), mistakes due to insufficient knowledge are recognized by their consequences – external feedbacks. Negative feedback as well as self-detected errors elicit negative event-related brain potentials probably generated in the CMA.

In a first fMRI study we investigated brain activity related to negative and positive feedback in a dynamically adaptive motion prediction task. In this task, in which participants had to extrapolate the motion of two balls presented on the screen, difficulty was dynamically adapted such that error rates were around 36%. This guaranteed high uncertainty of the participants about whether they were correct or incorrect. Whereas positive feedback raised hemodynamic activity in the ventral striatum (nucleus accumbens), negative feedback activated the CMA, the anterior pre-SMA, the inferior anterior insula, and the dorsal thalamic system (habenular complex, cf. Figure 9).

These findings underline the involvement of the posterior frontomedian wall in performance monitoring. Moreover, a link of error processing to reward-related processes becomes more obvious. To further characterize the differential roles of the brain structures found to be active during error processing based on external feedback, a follow-up study was performed (cf. Ullsperger & von Cramon, 2.6.8).

A posteriori analyses of reaction times and difficulty suggested that on trials followed by erroneous responses difficulty and uncertainty/response conflict were higher.

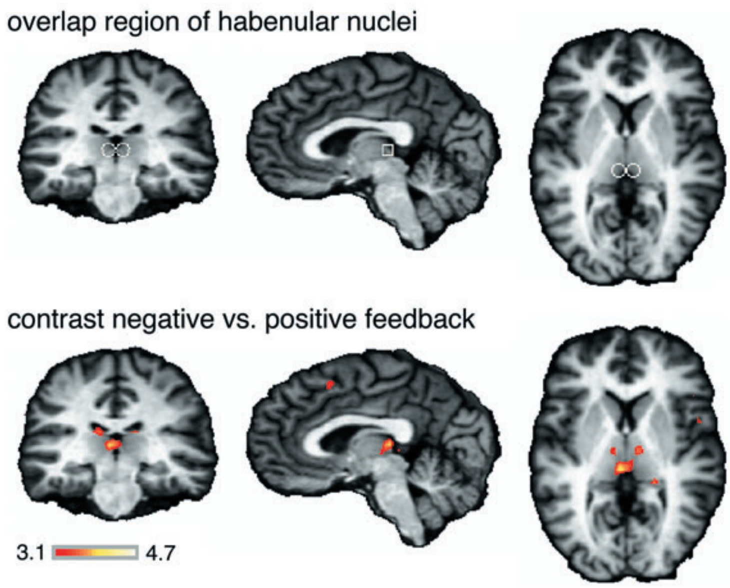

Figure 9. Upper row: Spatial overlap region of habenular nuclei in all participants. Lower row: Hemodynamic activations revealed by contrasting negative vs. positive feedback.

Error processing based on external feedback II – The role of uncertainty for differential activations of frontomedian structures and the habenular complex

2.6.8

Ullsperger, M. & von Cramon, D.Y.

In a first fMRI study we described the network which is active when error detection has to rely on external feedback in situations of high uncertainty (cf. Ullsperger & von Cramon, 2.6.7). A posteriori analyses of reaction times and difficulty suggested that on trials followed by erroneous responses difficulty and uncertainty/response conflict were higher. Therefore, the contrast aiming at the investigation of feedback processing was confounded with a variation of uncertainty during (= response conflict) and after the response. This uncertainty is resolved with feedback processing. The nature of the fMRI signal did not allow disentanglement of uncertainty/conflict-related from feedback-related activity in the first experiment.

In a follow up study, the influence of uncertainty and response conflict was disentangled from negative feedback processing by introducing non-informative stimuli which were sometimes presented instead of feedbacks. On those trials, no feedback-related activity should occur while uncertainty should be the same as in trials with informative feedbacks. On Figure 10 the main results are depicted. The ventral striatum was active only on correct trials with informative (positive) feedback, which is consistent with previous reports from neuroimaging as well as the animal literature. The CMA was mostly engaged when errors were followed by negative feedback, but not if feedback was uninformative. This suggests that the CMA is involved in error detection by use of external feedback rather than in processing response conflict or uncertainty. The pre-SMA was activated by all errors irrespective of the feedback, reflecting an effect of uncertainty. This subregional dissociation at the frontomedian wall fits an analogous dissociation which

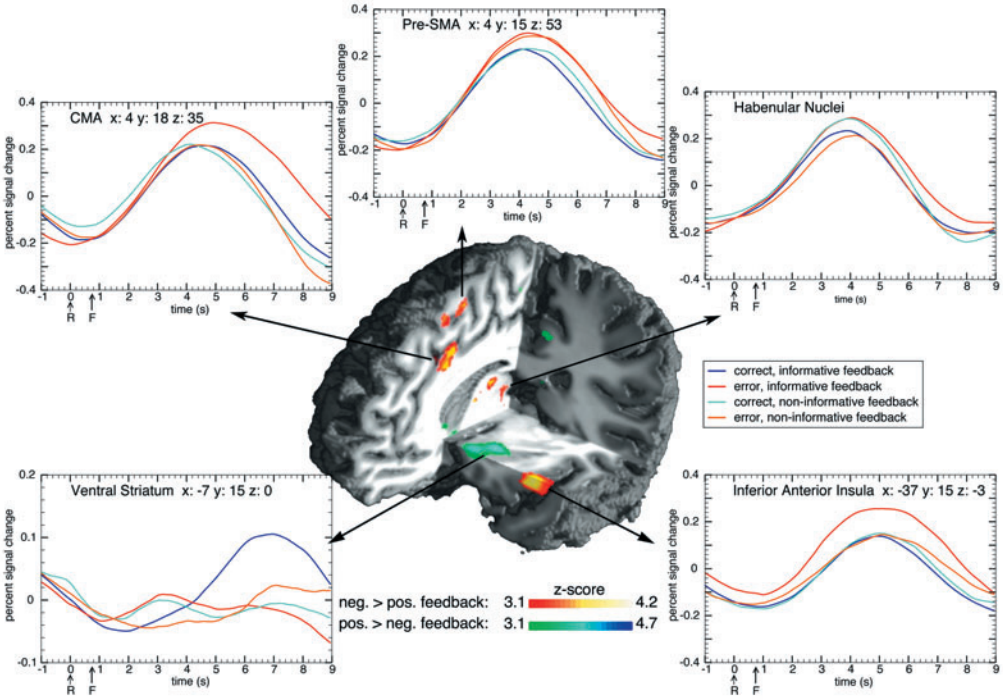

Figure 10. Hemodynamic activations revealed by contrasting negative vs. positive informative feedback. Timecourses of the hemodynamic response to all four conditions for five regions of interest.
Note: R = response, F = feedback stimulus.

we reported in studies investigating self-detected errors (e.g., Fiehler et al., 2.6.9). Finally, the habenular complex reacted in a complex manner. Studies in animals revealed that the habenular complex inhibits the dopaminergic midbrain nuclei. The current findings are consistent with this and suggest that the dorsal thalamic system is involved in integrating reward prediction and actual occurrence of rewards.

2.6.9 Neural mechanisms of error correction

Fiehler, K., Ullsperger, M. & von Cramon, D.Y.

Detecting and correcting errors represents an important domain of performance monitoring. ERP studies revealed a component, the error-related negativity (ERN), that peaked about 100 ms after the onset of an incorrect response and seems to be an objective indicator of error-monitoring. The relationship between the ERN and remedial actions is still rather unclear. Based on recent fMRI findings, we expected differences of the correlates of error processing depending on the presence of corrective behavior. A modified speeded flankers task was performed by two groups: one which had the possibility to correct its behavior (CI) and a second group where corrective behavior was not instructed (CN).

Typical effects of incompatibility were found in both groups: increased reaction times and higher error rates for incompatible trials, suggesting that response conflict was higher during incompatible trials than during compatible ones. Consistent with previous findings, subjects were faster on incompatible errors than on incompatible hits which indicates a premature response behavior based on the bias by the flanker arrows.

Figure 11 illustrates the response-locked ERPs at one midline electrode (FCz) and the isopotential maps for incompatible trials for both groups separately. The ERN was clearly observed for error trials, showed a fronto-central distribution, and peaked around 60 ms after response onset. The amplitude of the ERN was significantly larger in the CI group compared to the CN group. In contrast to previous findings, the ERN seems to be associated with error-correction and error-compensation processes. The ERN was

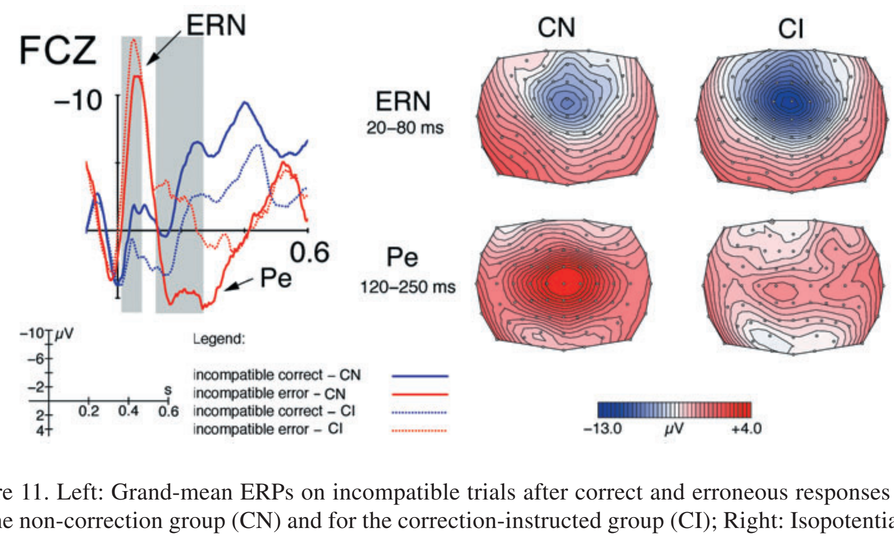

Figure 11. Left: Grand-mean ERPs on incompatible trials after correct and erroneous responses at FCz for the non-correction group (CN) and for the correction-instructed group (CI); Right: Isopotential maps of the error-related negativity (ERN) and the error positivity (Pe) interpolated over two time windows: 20 to 80 ms (upper row) and 120 to 250 ms (lower row) for both groups separately.

followed by a positive deflection, the Pe, that peaked in the 150 to 250 ms postresponse range and also differed significantly between the two groups. A possible interpretation might be that the reduced Pe in the CI group is due to lower subjective significance of an error caused by the corrective behavior.

Predicting events of varying probability: Uncertainty investigated by functional magnetic resonance imaging (fMRI)

2.6.10

Volz, K.G., Schubotz, R.I. & von Cramon, D.Y.

Many everyday life predictions rely on the experience and memory of event frequencies, i.e., natural samplings. We used functional magnetic resonance imaging (fMRI) to investigate the neural substrates of prediction under varying uncertainty. We employed a natural sampling approach, i.e., information about contingencies was provided in a cumulative manner. On the basis of preceding stimulus cues, participants predicted events that occurred with probabilities ranging from p=.6 to p=1.0. The study focused particularly on a comparison with other types of externally attributed uncertainty, such as guessing, and on the frontomedian cortex, which is known to be engaged in many types of decisions under uncertainty.
In contrast to certain predictions in a control task, predictions under uncertainty elicited activations within a posterior frontomedian area (mesial Brodmann Area 8m, BA 8m) and within a set of subcortical areas which are known to subserve dopaminergic modulations (Figure 12, left and middle panel). The parametric analysis revealed that activation within the mesial BA 8m significantly increased with increasing uncertainty (Figure 12, right panel). Results indicate that frequency-based prediction uncertainty elicits frontomedian activations that resemble those induced in long-term stimulus-response adaptation processes such as hypothesis testing, as in contrast to those engaged in short-term error processing such as guessing.

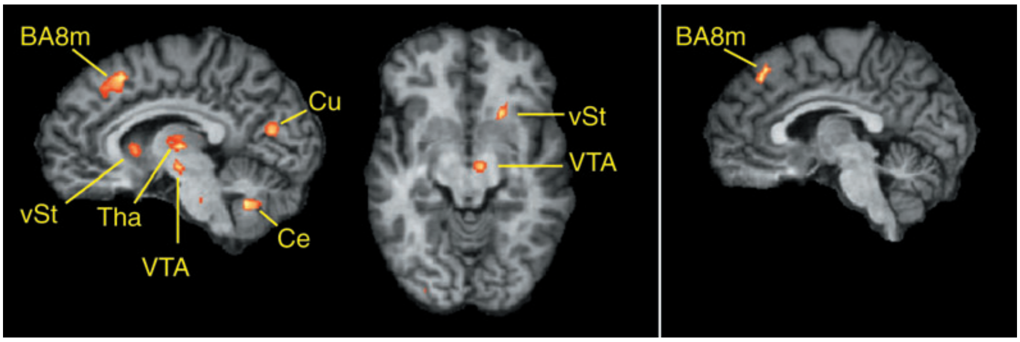

Figure 12. Left and middle panel: Main task effect (Z>3.09) for externally attributed prediction uncertainty versus control condition. Group averaged activations are shown on sagital (x=8) and axial (z=-6) slices of an individual brain normalized and aligned to the Talairach stereotactic space. Right panel: Parametric effect of externally attributed prediction uncertainty shown on a sagital (x=4) slice. Abbreviations: BA8m, mesial Brodmann Area 8; vSt:, ventral striatum; Tha, Thalamus; VTA, ventral tegmental area; Cu, Cuneus; Ce, Cerebellum.

2.6.11 Why I am unsure? Internal and external causes of uncertainty are dissociated by functional magnetic resonance imaging (fMRI)

Volz, K.G., Schubotz, R.I. & von Cramon, D.Y.

Everyday life coping strategies that are employed to overcome uncertainty always depend on the perceived cause of uncertainty. Psychological models differentiate between externally attributed uncertainty (EU, that can not be eliminated by learning) and internally attributed uncertainty (IU, that can be eliminated by learning). We used functional magnetic resonance imaging (fMRI) to investigate whether these types of uncertainty differ on the brain level. We expected that correlates of uncertainty should be the same, whereas correlates of IU should engage areas related to learning and memory. Participants had to predict events of type IU that were learned to differing degrees before the experimental session. As in a preceding study that investigated uncertainty of the EU-type, effects of IU were analyzed using the mean prediction error as a regressor. These parametric analyses revealed the mesial Brodmann Area 8 within the posterior frontal cortex as a common cortical substrate of prediction uncertainty, no matter for which reason uncertainty emerged (Figure 13, lower panel). In addition to this common activation, however, we found other areas to be differently engaged in either IU or EU predictions. While increasing EU yielded additional activation within a dopaminergic subcortical network (see 2.6.10), increasing IU elicited activation within the medial frontal gyrus and the intraparietal sulcus, i.e., within areas that underlie mnemonic processes (Figure 13, upper panel). These findings indicate that the variation between coping strategies that are employed in the face of uncertain predictions is also reflected on the brain level.

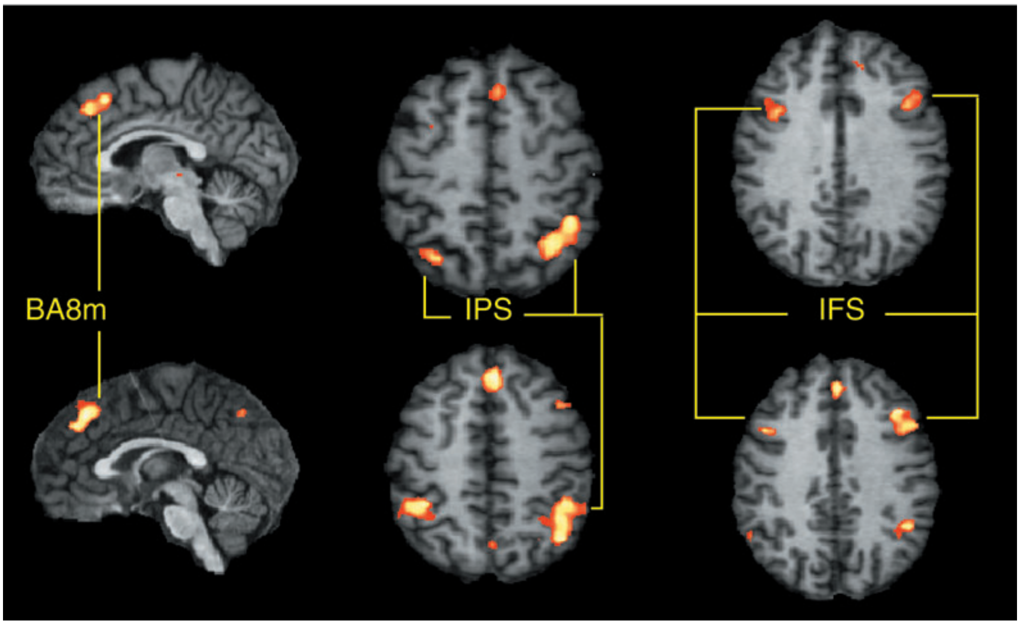

Figure 13. Upper panel: Main task effect ($Z>3.09$) for internally attributed prediction uncertainty versus control condition. Group averaged activations are shown on sagital (x=4) and axial (z=32/47) slices of an individual brain normalized and aligned to the Talairach stereotactic space. Lower panel: Parametric effects of internally attributed prediction uncertainty shown on sagital (x=1) and axial (z=35/38) slices. Abbreviations: BA8m, mesial Brodmann Area 8; IPS, intraparietal sulcus; IFS, inferior frontal sulcus.

Errors in a serial reaction task: Types of sequential violations investigated with fMRI

2.6.12

Schubotz, R.I., von Cramon, D.Y. & Zysset, S.

The processing of sequential information is mediated by both lateral and medial premotor cortices. Previous findings suggest that sequential events are transformed into a predictive model within the lateral premotor cortex, whereas the medial premotor cortex, particularly the pre-supplementary motor area, is more involved in the anticipation and selection of sequential events on the basis of this model. In order to investigate this assumption, we analyzed fMRI brain correlates of sequential deviants in a serial reaction task (Figure 14, lower panel).

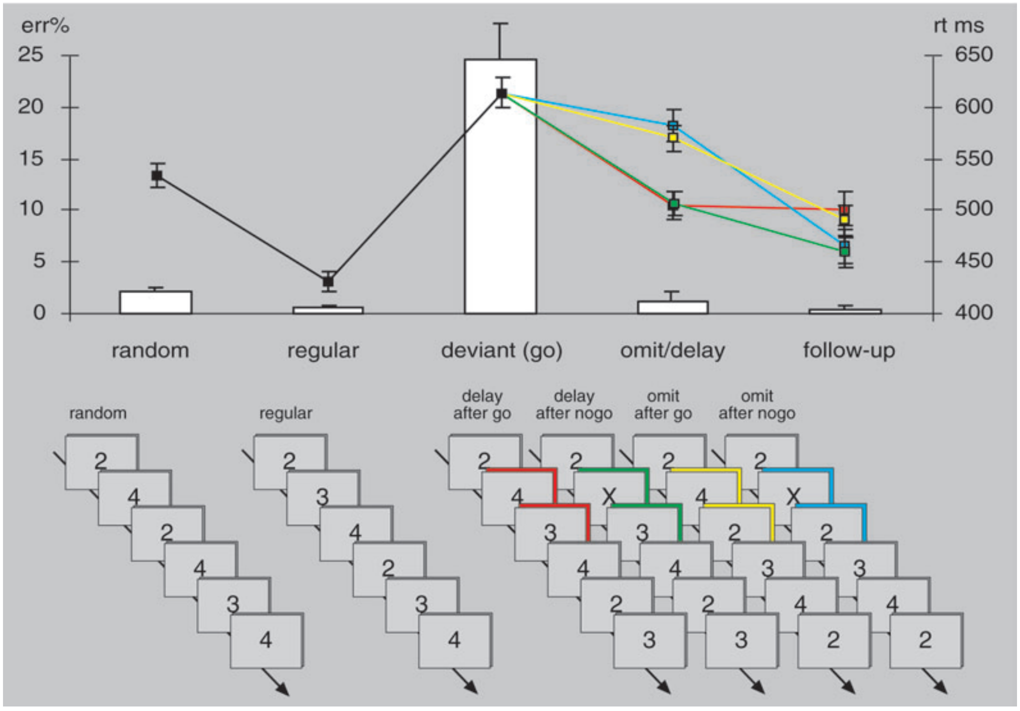

Figure 14. Task (lower panel) and behavioral findings (upper panel).

In a first step, regular and random sequences were compared to test whether medial premotor areas are more activated by the former, and lateral areas by the latter. In a second step we investigated serial reorientation, i.e., the requirement to switch shortly from internally guided to externally guided sequential production. To this end, deviants were introduced in the regular sequences that required either the omission or the delay of a prepared response, preceded by either a go or a no-go response. Deviants were expected to draw particularly on the lateral premotor areas as they required a short-term switch from memory-based to sensory-based production. Behaviorally, we expected (a) longer reaction times to *random* sequences as compared to *regular* sequences; (b) *omissions* to induce higher response costs than *delays* because responses that were prepared on the basis of an internal model had to be entirely abandoned; (c) higher response costs after *go-trials* than after *nogo-trials*, as the performance of a deviant response should interfere with the established internal model.

The behavioral data was found to confirm our three reaction time hypotheses (Figure 14, upper panel). FMRI results showed that lateral premotor networks increased activation whenever the subject was more dependent on sensory guidance, that is, in random sequences as in contrast to regular sequences, and in serial reorientation phases following the sequential deviants, as in contrast to random sequences (Figure 15, lower panel).

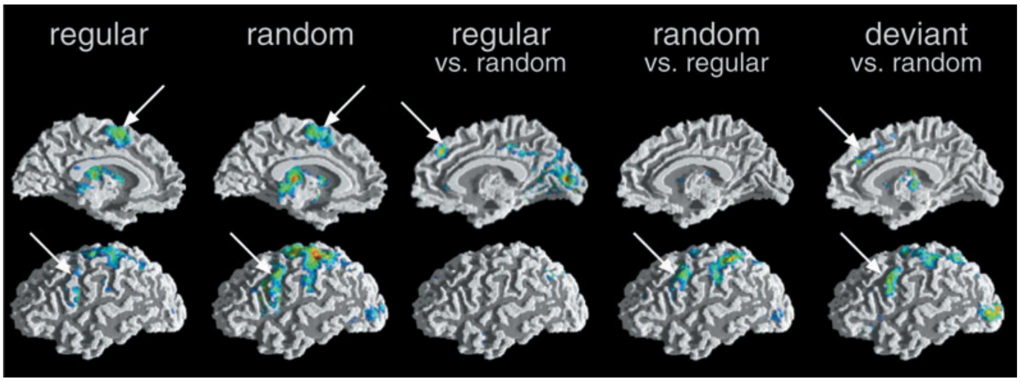

Figure 15: Brain activations in regular, random, and deviant sequences.

In contrast, frontomedian activations were boosted whenever stimuli were predictable on the basis of a sequential representation (regular vs. random, Figure 15, upper panel). However, these activations were located anteriorly to the pre-supplemetary motor area. In addition, anterior cingulate areas showed up for sequential deviants. Together, findings confirm that medial and lateral premotor cortices are functionally dissociated for memory-based and sensory-based sequential behaviors.

2.6.13 Why don't we imitate all the time?

Brass, M., Derrfuss, J. & von Cramon, D.Y.

There is converging evidence from different fields of neuroscience that the mere observation of an action leads to a tendency to imitate that action. In line with this assumption we could show in a previous neuropsychological study that patients with prefrontal lesions have problems inhibiting imitative response tendencies. It was assumed that such tendencies are based on a direct matching of the observed action onto an internal motor representation. However, if this assumption holds true, one has to postulate a mechanism which allows us to overcome imitative response tendencies and to avoid confusion between internally generated and externally triggered motor representations. The aim of the present study was to directly test this hypothesis in a choice reaction task. By comparing conditions in which participants were required to execute an action while observing another person executing the same (congruent) or a different (incongruent) action (see Figure 16) we could show that executing incongruent actions activates two cortical regions (see Figure 17) which are usually not related to interference control. Rather, the temporo-parietal junction and the anterior fronto-median cortex are required to relate the observed action to one's own body configuration and enable us to enforce our own intentions against the imitative response tendency. Since both brain regions were also found to be related to 'theory of mind' we suggest that the body-related distinction between the self-perspective and a third person perspective might be the common underlying processes.

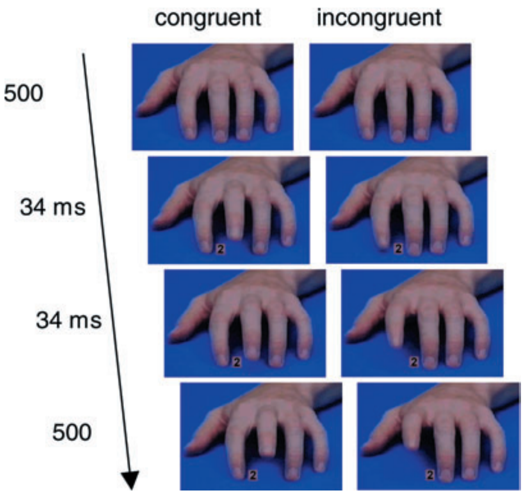

Figure 16. Experimental paradigm.

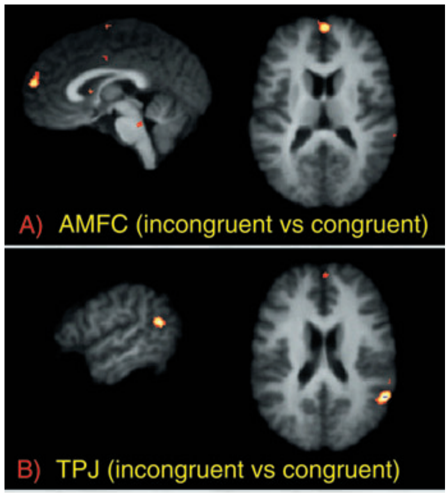

Figure 17. Cortical activation in the temporo-parietal junction and the anterior median frontal cortex for the comparison of incongruent and congruent trials.

The functional neuroanatomy of story comprehension: The contribution of the right hemisphere

2.6.14

Ferstl, E.C.[1], *Rinck, M.*[2] & *von Cramon, D.Y.*[1]

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Language processing in context differs in fundamental ways from word and sentence comprehension. Thus, it has been proposed that during text comprehension the right hemisphere is more involved than during word and sentence comprehension. In the experiment we investigated the interplay between the two hemispheres during auditory text comprehension. Twenty participants were scanned at 3 T while listening to 32 narrative texts. The length of the stories varied from 30 to 60 s. In a first analysis, we used the general linear model to identify those brain regions that were specifically engaged during the last portion of the stories, i.e., those regions that became more involved when a discourse model had been accumulated. As expected, we found an extended bilateral network. This network included the perisylvian cortex of the left hemisphere and its right-sided homologue areas. Additional regions - also activated bilaterally - were the anterior temporal lobes, the temporo-parietal junction and anterior and posterior medial regions. For a more differentiated interpretation of this possibly unspecific network, we calculated correlations between the timecourses of different voxels. Figure 18 shows correlation maps for two distinct peaks in the left inferior frontal cortex. The associated regions remain distinct, and, for both peaks, the most highly correlated ones are their right sided homologues. These results confirm that there are functionally separable sub-networks. Furthermore, the right hemisphere does play an important role during text comprehension but its contribution seems to be closely linked to that of the left hemisphere.

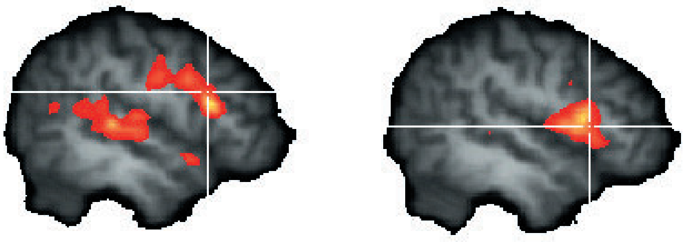

Figure 18. Correlation maps for two peaks of activation in the left prefrontal cortex. The z-maps are group averages of contrast images obtained by using the timecourse in the target voxel as a regressor in the general linear model. The z-maps are thresholded at Z>4.0. For the target voxel in the inferior frontal sulcus (a), there is significant correlation with its right-sided homologue, but also with regions in the anterior and posterior temporal gyrus. For the target voxel in the inferior frontal gyrus (BA 44), only the homologue area shows a significant correlation.

2.6.15 Making sense of nonsense: Task induced coherence processes during text comprehension

Siebörger, F. & Ferstl, E.C.

A central process for text comprehension is the establishment of coherence. Functional imaging studies revealed activation in the fronto-median wall (FMC, medial BA 9/10) during the processing of coherent texts compared to incoherent ones (e.g., Ferstl & von Cramon, 2001). To test the hypothesis that this finding reflects a domain independent, non-automatic process rather than stimulus properties we set up a task aimed at eliciting FMC activation by *incoherent* trials: Participants are asked to listen to 30 coherent and 90 incoherent sentence pairs and to judge the perceived strength of coherence on a 4 point scale (pragmatical relationship graded from 'directly evident' to 'unimaginable') instead of using a simple 'coherent' vs. 'incoherent' dichotomy. By this manipulation we expect to induce a "search for coherence" even for incoherent trials, which in turn activates the FMC. To test the feasibility of this rather unusual task we conducted a behavioral pre-test (N=20) whose results are presented here.
As expected, most of the coherent sentence pairs were rated as strongly related (Figure 19A). Moreover, the results show that the participants indeed used their creativity: 61% of the

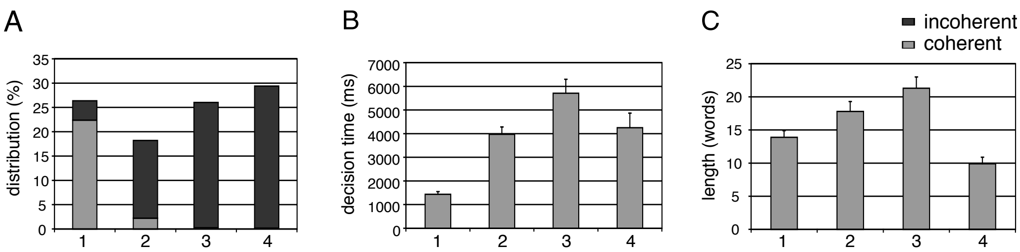

Figure 19. For each answer category (1 = 'coherence directly evident' to 4 = '...unimaginable') the relative distribution of coherent and incoherent trials (A), the decision time (B) and the length of the explanatory statement (C) is plotted.

incoherent trials were rated as somewhat related and the decision times for those trials were significantly prolonged (Figure 19B). Additionally, we asked the participants to write explanatory statements after they made their rating on some trials. The length of the explanations, taken as a rough indicator of the complexity of the argumentative chain, revealed an increase from high to a low coherence (Figure 19C). Taken together, the results of the pre-test showed that participants performed the task as intended and that they were able to apply goal directed inference processes.

Functional specialization within the anterior medial prefrontal cortex: An fMRI study

2.6.16

Zysset, S.[1], *Huber, O.*[2], *Samson, A.*[2], *Ferstl, E.C.*[1] & *von Cramon, D.Y.*[2]

[1] *Max Planck Institute of Cognitive Neuroscience*
[2] *Department of Psychology, University of Fribourg/Switzerland*

The present study investigates the involvement of the dorsal and ventral anterior medial prefrontal cortex (aMPFC) in evaluative judgment by using fMRI with spin-echo echo-planar-imaging. Previous studies have shown that the aMPFC is involved in evaluative judgment and self-referential processes. Specifically, different sections of the aMPFC are differentially influenced by attention demanding processes. Whereas the dorsal section is supposed to be involved in self-referential processes, the ventral section, a region mainly involved in emotional and affective processing, is assumed to be attenuated during attention demanding processes. Processes involved in evaluative judgment are attention-demanding, self-referential and activate regions in the dorsal and ventral section of the aMPFC.

The present findings showed that evaluative judgment not only activates the dorsal aMPFC, but that the activation extends into the ventral aMPFC. Thus, the ventral section seems to be involved both in attention demanding processes and evaluative judgment. This does not exclude the possibility that a factor like the subjective significance of the content of a sentence is relevant, which in everyday life is often confounded with formal self-reference.

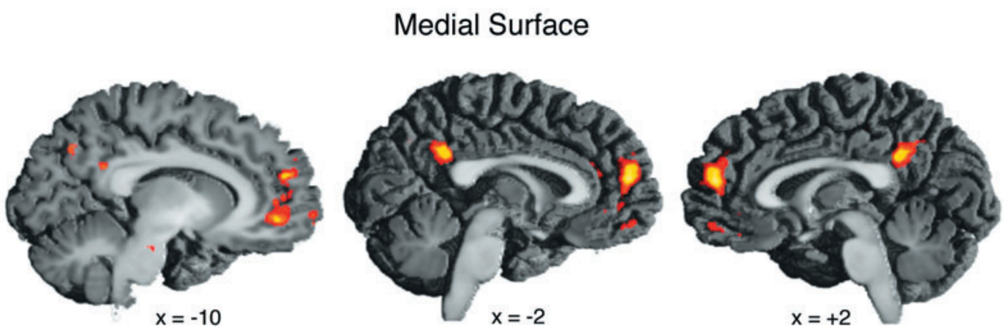

Figure 20. Averaged activation maps of the contrast evaluative judgment vs semantic memory retrieval mapped on to the reference brain. The z-value were thresholded at z=3.1 (p=0.001).

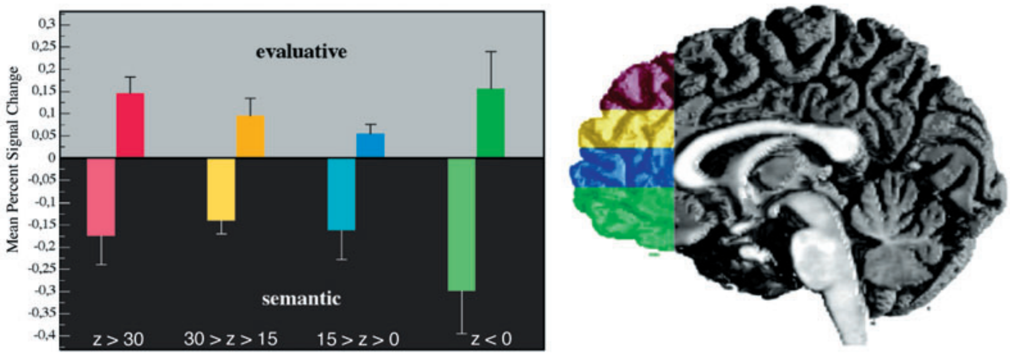

Figure 21. The 4 arbitrary sections of the anterior medial prefrontal cortex (aMPFC) are color shaded (right). Mean percent signal change (and standard error) for the semantic memory retrieval and evaluative judgment condition (left) for the 4 arbitrary sections are shown, colored according to the 4 sections.

2.6.17 Subjective relevance of errors modulates the ERN and post-error strategy adjustments

Ullsperger, M. & Szymanowski, F.

Action slips due to premature responses are commonly detected by the acting individual and followed by remedial actions such as immediate corrections and post-error strategy adjustments (e.g., the prolongation of reaction times in subsequent trials – post-error slowing). The error-detection process is accompanied by event-related potentials (ERPs), the error-related negativity (ERN) and error positivity (P_E).

It is conceivable that if the goal of a task is of low relevance for the individual, less or no remedial actions are necessary in case of an error. It would therefore be economical to reduce error-detection efforts when errors are of low subjective relevance.

In order to investigate the influence of error relevance on the remedial actions and electrophysiological correlates of error processing we measured behavioral and ERP data in 19 young healthy participants (mean age 24.1 years) while they performed two blocks of a speeded flanker task. By use of a monetary bonus system in one block response speed was encouraged whereas in a second block maximal accuracy was reinforced. Block order was counterbalanced across participants.

In the accuracy condition error rates were significantly lower and reaction times significantly longer as compared to speed instruction. Whereas sequence effects of trial compatibility (i.e., of response conflict) were not influenced by the speed/accuracy manipulation, the post-error slowing effect was only present during the accuracy condition (Figure 22). This finding reflects that detected errors trigger post-error strategy adjustments only when they are sufficiently relevant to the subject.

As can be seen in Figure 23, the ERN amplitude is significantly larger in the accuracy condition. This finding suggests that the error detection system is more active when errors are relevant and therefore require remedial actions. In contrast to the ERN, the P_E has a lower amplitude when accuracy was instructed, and its maximum is lateralized to the left side (Figure 24). It can only be speculated that this topographical shift reflects a change in later steps error processing into a less automatic mode.

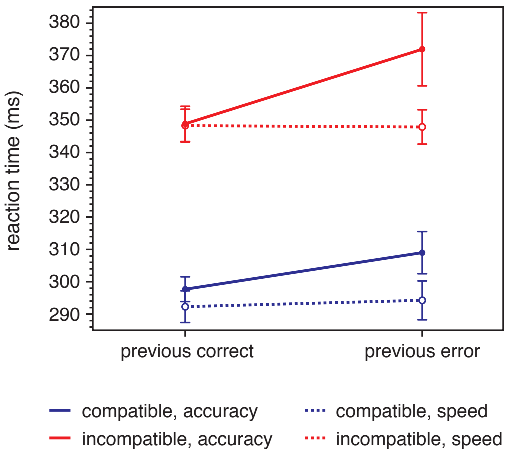

Figure 22. Sequence effects of preceding response type on the reaction times on compatible (blue) and incompatible (red) correct trials for accuracy (solid line) and speed (dotted line) conditions.

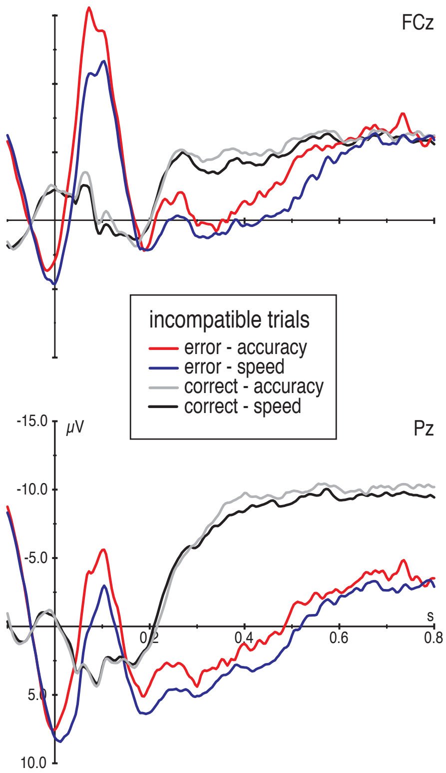

Figure 23. Grand mean ERP waveforms at FCz and Pz for incompatible correct (accuracy: grey, speed: black) and erroneous (accuracy: red, speed: blue) trials.

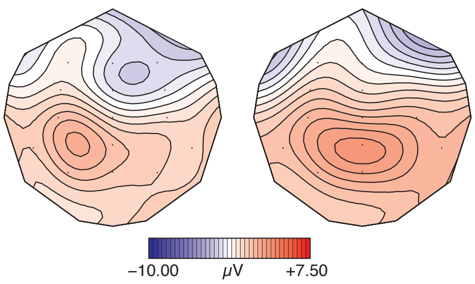

Figure 24. Scalp potential distribution of the ERPs to incompatible errors in the time range 380 to 500 ms for accuracy (left) and speed (right) instructions.

Is it the ACC after all?

2.6.18

Zysset, S., Wendling, K. & von Cramon, D.Y.

We reviewed 103 fMRI studies published between 1998 and 2002 reporting activations in the anterior cingulate cortex (ACC). The ACC (BA 24) lies in the cingulate gyrus limited dorsally by the cingulate sulcus and posteriorely by the vertical line of the anterior commissure. Anteriorely, it curves around the genu of the corpus callosum and merges with BA 25. Whereas BA 24 is pro-isocortex, the surrounding regions are cytoarchitectonically different cortices like isocortex in BA 6/8/9/10 or a transitional type of isocortex in BA 32. The ACC is assumed to support a wide variety of functions, from basic emotional processing to cognitive functions such as decision making.

All Talairach coordinates reported were mapped onto a reference brain. X-coordinates were set to +/-1 so that all activations lay within one single slice. Figure 25 shows that there is a considerable variation in the locations of so called ACC activations and are not limited to the regionally distinct area of the cingulate gyrus. It becomes obvious that the majority of the activations is not located in BA 24 but mainly in the paracingulate cortex (BA 32) and in the medial prefrontal cortex (BA 6/8/9). Activations in the right hemisphere appear to center more in the posterior part of fronto-median cortex whereas for the left hemisphere, the locations are more evenly distributed. This corresponds with the greater variability of the morphological features in the left hemisphere. In conclusion, we argue that one should be more cautious when attributing regions in the fronto-median cortex to ACC.

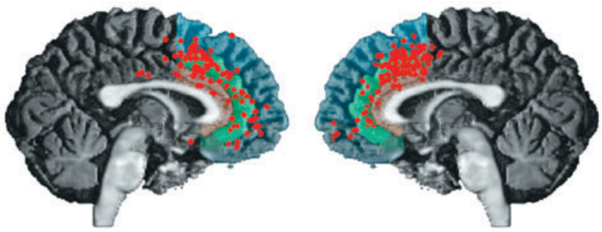

Figure 25. All 231 single activations plotted onto the left or right medial surface of an individual anatomical image. The three cytoarchitectonically different areas are color shaded. X-values from the Talairach coordinate system were changed to +/-1 in order to represent all activations within one single slice.

Cognitive processes in humans are usually studied by stimulation experiments. Responses are recorded by methods, such as functional MRI, EEG, MEG, SPECT and PET, which characterize different aspects of the underlying cognitive process. Because these different methods yield complementary information about the anatomical, metabolical, and neuropsychological state of the brain, an integrated data evaluation is highly desirable and will lead to results not achievable with a single modality.

The working group on Signal and Image Processing (SIP) focuses on the following aims: to develop and install new algorithms to improve the information yielded by these experiments, to combine results from different modalities, to achieve a precise anatomical description and quantification of the functional activity and to build structural and functional models of the brain. These long-term aims were mapped in 2002 onto two main project lines, *segmentation of anatomical and pathological MR images* and *deformation based morphometry.*

One of the long-term research goals in segmenting anatomical and pathological images is to obtain quantitative descriptors for brain structure and to test their use in the description of pathological processes. Section 2.7.1-2.7.8 describes approaches for characterizing cortex shape and growth, describing diffuse and focal brain lesions, and quantifying gender and age effects as well as the pathological changes in Alzheimer's disease.

Methods for representing variation and detecting group difference in shape can be collectively referred to as approaches for deformation-based morphometry. Here, we summarize approaches for the advanced analysis of deformation fields to detect and quantify structural changes (2.7.9) and promote their use in clinical applications (sections 2.7.10 and 2.7.11). Most of the methodological development resulted from the SimBio project. This multi-national project funded by the European Union (IST-V project 10378) aims at the implementation of a generic software environment for bio-numerical simulation. More complete information about the status of this project may be obtained from the project website (*http://www.simbio.de*). In particular, the clinical applications will be carried over to another EU funded project (GEMMS) which started recently. Focus of the GEMMS project is to provide Grid-computing in medical simulation services.
Locally, we were able to continue our collaboration with the Department of Psychiatry at the University Clinic in Leipzig, which focuses on detecting macroscopic changes in magnetic resonance images (MRI) of patients with mild cognitive deficits. Also, the fruitful scientific collaboration with the Department of Maxillo-Facial Surgery, focusing on the description of structural changes during treatment of in-borne skull deformations, and with the Department of Neurosurgery, analyzing the biomechanical consequences

of surgical intervention on brain morphology, was continued. The collaboration with these two departments is carried further within the GEMSS project.

A former member of our group, Prof. Dr. Tianzi Jiang, successfully installed a new workgroup on Medical Image Analysis with the National Laboratory of Pattern Recognition at the Chinese Academy of Science. A closer collaboration between both groups started this year by exchange of a Ph.D. student, Mr. Faguo Yang.

2.7.1 Determinants of cortex shape and growth

Hübsch, T., Tittgemeyer, M. & von Cramon, D.Y.

At the macroscopic level, the cortex shape is highly convoluted. The reason for its specific fissuring and folding is still under research. Numerous hypotheses were proposed that emphasize different causal and descriptive aspects of cortex growth and shape like cell tension and wiring between strong interconnected areas or differential cell growth as a mechanical forming process. They take place on an underlying parameter space in which fissuring and folding can happen. This parameter space consists of geometrical, physical, cellular, genetic and neuronal determinants. All of these parameters are potentially responsible for the unique cortex folding structure as we macroscopically observe it. Geometric parameters like symmetry, compactness, geodesic distance, enclosed volume of cortex segments, gyrification index, cortex thickness, curvature or other shape properties are used to describe the cortical appearance. Physics based parameters like axon length, signal velocity, power dissipation etc. can lead to an understanding of minimum energy as a forming parameter of cortex shape and growth. Cellular based parameters like cell density, cell architecture, cell differentiation, cell tension or cell migration in different cortex layers are driving forces which may have genetic roots. Genetic parameters of cortex growth and shape may be determined through cortex development diseases like polygyria or microgyria in which the folding and fissuring of the cortex is abnormal. Neuronal parameters optimize, for example, necessary thalamocortical, corticocortical, intergyral, lobal and other connections in the brain ensuring optimal component placement and a low network diameter between neurones.

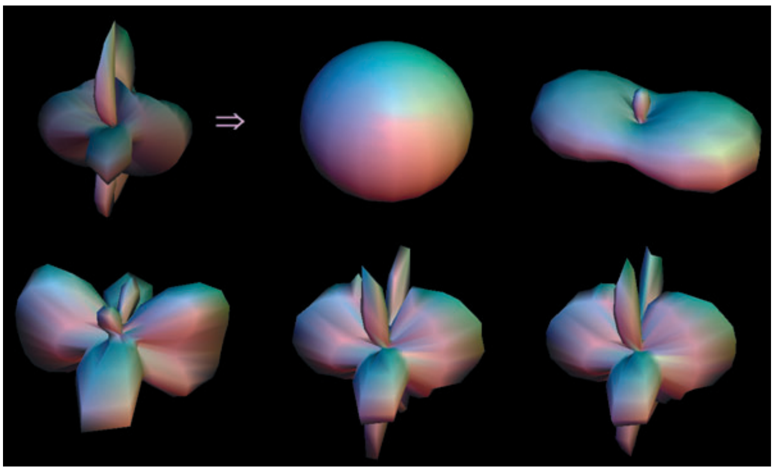

Figure 1. Approximation of an analytical function (upper row, left) by spherical harmonics using 1, 2, 4, and 14 basis functions.

Starting with geometric parameters, we use spherical harmonic functions (Figure 1) to investigate shape determinants quantitatively. We need to parameterize the surface of different cortex segments and analyze the frequency spectrum given by the spherical harmonic approximation. This analytical approximation can then be used to classify and analyze interindividual differences in cortex segments as well as provide hints about the gyrification mechanism.

2.7.2 White matter lesion segmentation

Yang, F. & Kruggel, F.

White matter lesions are common pathological findings in the brain, which are caused by head trauma, neuro-degenerative diseases or micro-vessel diseases (e.g., caused by hypertension or diabetes). Properties of the lesions related with cognitive impairment. We developed a new model-based algorithm to automatically segment such lesions. They are detected as outliers of white matter intensity distribution, which is modelled by a Gaussian distribution. The algorithm uses prior tissue (CSF, grey matter, white matter) distribution information to estimate the white matter model parameters (the mean value and the standard deviation). A tissue probability map was constructed using 48 normal brains (Figure 2). It is constructed in three steps: (1) non-brain tissues are removed from the head image volume; (2) the brain volumes are mapped to a single reference brain using a linear elastic registration method; (3) each brain volume is segmented using a fuzzy c-mean method and then averaged to obtain the tissue probability map. A head volume dataset containing white matter lesions is registered to this reference. Then, the transformed brain volume is also segmented using the fuzzy c-mean method. We can obtain the model parameters and training data used to segment the original head volumes by combining the probability map and the transformed segmented brain volume. According to the model parameters, we calculate a measure indicating whether a voxel belongs to a lesion (Figure 3). Our lesion segmentation algorithm is based on only T_1-weighted images. Experimental results demonstrate our approach is robust against noise and accurate, while at the same time being fully automatic.

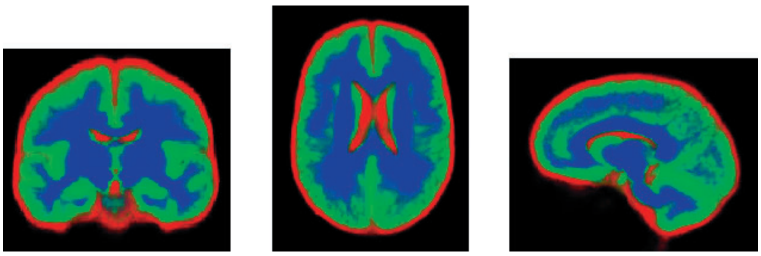

Figure 2. Tissue Probability Map. Red color: CSF; Green color: Grey matter; Blue color: White matter.

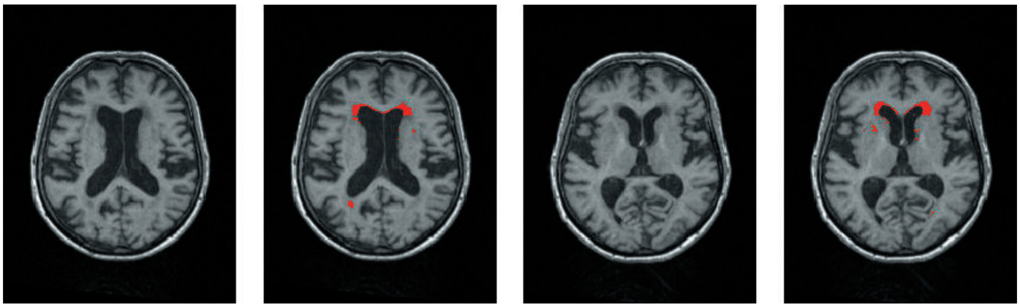

Figure 3. Labelled lesions. (a), (c) Original image slices; (b), (d) Labelled lesions.

2.7.3 Descriptors for focal lesions as revealed by MR tomography

Chalopin, C. & Kruggel, F.

Focal brain lesions (e.g., due to head trauma, intracerebral hemorrhages and cerebral infarcts) are usually revealed by MR tomography. We are interested here in developing automatic methods for lesion characterization, especially to study their evolution in time. A preliminary step includes the automatic segmentation of unilateral lesions. The method consists of comparing the local intensity statistics between a brain subregion and the corresponding contralateral subregion for the T_1- and T_2-weighted images. The deviance of the signal statistics was evaluated using a Hotelling T^2 test, the test score converted to a z-score and compiled in a "lesion probability map" (LPM). Unilateral lesions - represented by high z-scores because the contralateral brain region is generally healthy - are finally segmented by a simple thresholding of the LPM. Focal lesions are often heterogeneous, i.e., consist of completely and partially damaged areas. We propose therefore some features for the characterization of lesion damage. A global descriptor, called the *damage index D*, is the mean intensity within the lesion. We developed also

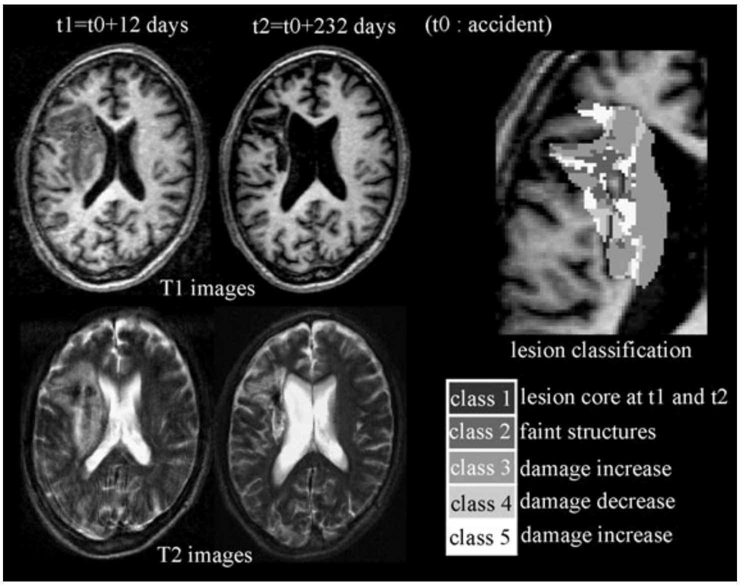

Figure 4. Characterization of focal lesion damage from MR images in time series data sets. The lesion is automatically segmented at time points t1 and t2. Then, the voxels within the lesion mask are clustered into different classes of homogeneous properties. In this example, most of them belong to the classes which are typical for a damage increase (classes 3 and 5).

an approach for clustering the voxels which belong to the lesion, according to intensities in the T_1- and T_2-weighted images, as well as the intensity changes with time. The damaged voxels of 9 patients were classified and 5 different classes have been obtained which interpretation is given in the picture. Results of such analysis are depicted on the following brain (Figure 4). The first scan shows a fresh lesion (acquired 12 days after the accident), while the lesion in the second scan (acquired 8 months later) is completely damaged. The variation of the damage index is large $\Delta D=D(t2)-D(t1)=+48$ (it is in the range [-9,+18] for the other 8 cases). Classified voxels mostly belong to class 3 and 5, which is typical for damage increase. Both results correlate the medical history of the patient and the visualization of the images.

Fast affine scaling of MR brain images with lesions

2.7.4

Jänicke, H., Khoromskaia, V., Tittgemeyer, M. & Kruggel, F.

In studies of patients with focal brain lesions, it is useful to have computer aided means to compare lesions from different subjects. By overlapping lesions from groups of subjects with similar clinical findings one may detect certain brain areas that are responsible for providing a specific ability. The task consists therefore of matching the images to some chosen reference brain image or to an accepted standard brain template. Most registration methods operate well on peeled brain images without considerably large pathological areas. For subjects with extensive brain lesions, it is necessary to include a skull-based reference. We developed an automatic fast affine scaling method of pathological MR images using skull measurements. Both sample and template images are first segmented. On the basis of these segmented images we constructed a functional which takes into account volumetric and shape characteristics of both images. The functional is minimized with respect to the parameters of an affine scaling. To find the minimum of the functional, we used a cost–effective seven point stencil, which approximates the functional by a paraboloid and yields the result in a few minutes. In this way, we register images linearly, but including shape features of both MR images. This allows comparing MR images of different subjects with extensive brain lesions as well as localizing lesions with respect to a template brain image. We analyzed results by processing the MR images for a group of subjects with lateral frontal focal lesions. Damaged areas were segmented automatically using the algorithm described previously. MR images of all subjects were scaled with respect to a chosen template brain image. An overlay of the scaled lesion masks allows a comparison of the corresponding lesion areas (Figure 5).

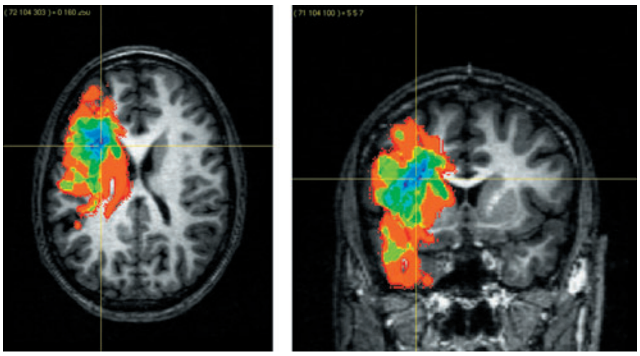

Figure 5. A scaled lesion mask for a group of subjects with lateral frontal focal lesions overlaid on the template image.

2.7.5 A software tool for three-dimensional texture analysis of MRI brain datasets

Lorenz, D., Kovalev, V.A., & Kruggel, F.

Our previous studies have demonstrated that 3D texture analysis of MRI brain datasets provides useful neurobiological information. The approach is based on extended, multi-sort co-occurrence matrices that contain a detailed description of spatial brain image structure (Kovalev et al., 2001, *IEEE Transactions on Medical Imaging, 20,* 424-433). In this work, 3D texture analysis methods are implemented as a software package which includes all facilities to calculate general, six-dimensional co-occurrence matrices and their specific sub-matrices, to normalize and store them in form of standard Vista files, to compute integral features such as energy, homogeneity, entropy, and contrast, and to perform a Principal Component Analysis on these textural brain descriptors. Figure 6 shows how the software tool can be used to quantify age-related differences of MRI brain texture. The sample consists of 55 healthy subjects, which are conditionally subdivided in two gender-matched groups: young (n=33, 16-26 years) and aged (n=22, 49-70 years) subjects. Textural differences associated with age detected with the help of integral features and principal components of co-occurrence descriptors are shown in Figure 7.

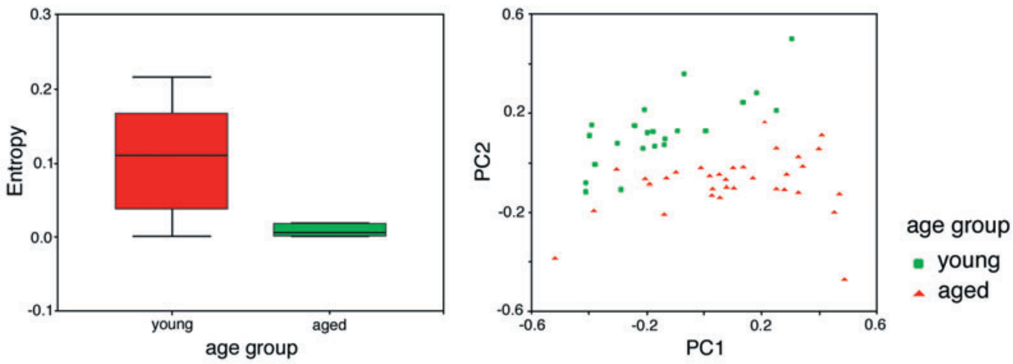

Figure 6. Age-related differences of MRI-T_1 brain image texture when comparing young (n=33, 16-26 years) and aged (n=22, 49-70 years) subjects: Box and whiskers plots of integral entropy feature (left) and subject scattering with the first two principal components of brain texture descriptors (right).

2.7.6 Gender and age effects in structural brain asymmetry as measured by MRI texture analysis

Kovalev, V.A. & Kruggel, F.

Effects of gender and age on structural brain asymmetry were studied by 3D texture analysis in 380 adults. Asymmetry is measured as dissimilarity of complex 3D grey-scale image patterns in the left and right cerebral hemispheres as revealed by anatomical T_1-weighted MRI datasets. The Talairach and Tournoux parcellation system was applied to study the asymmetry on four levels: the whole cerebrum, nine coronal sections, twelve axial sections, and boxes resulting from both coronal and axial subdivisions. The analysis revealed that the brain asymmetry increases significantly in the anterior-posterior direction starting from coronal slice 5 onwards (Figure 7). Male brains were found to be more asymmetric than female. This effect is noticeable in all sections in the anterior-posterior direction and in the majority of corono-axial blocks (Figure 8). The asymmetry increases significantly with age in the inferior prefrontal region and decreases with age in the occipital region (Figure 7 and 8, right column). The texture-based method reported here is sensitive, simple to reproduce, robust, and unbiased in the sense that segmentation of brain compartments and spatial transformations are not necessary. Thus, it may play a role as another tool for digital morphometry in Neuroscience.

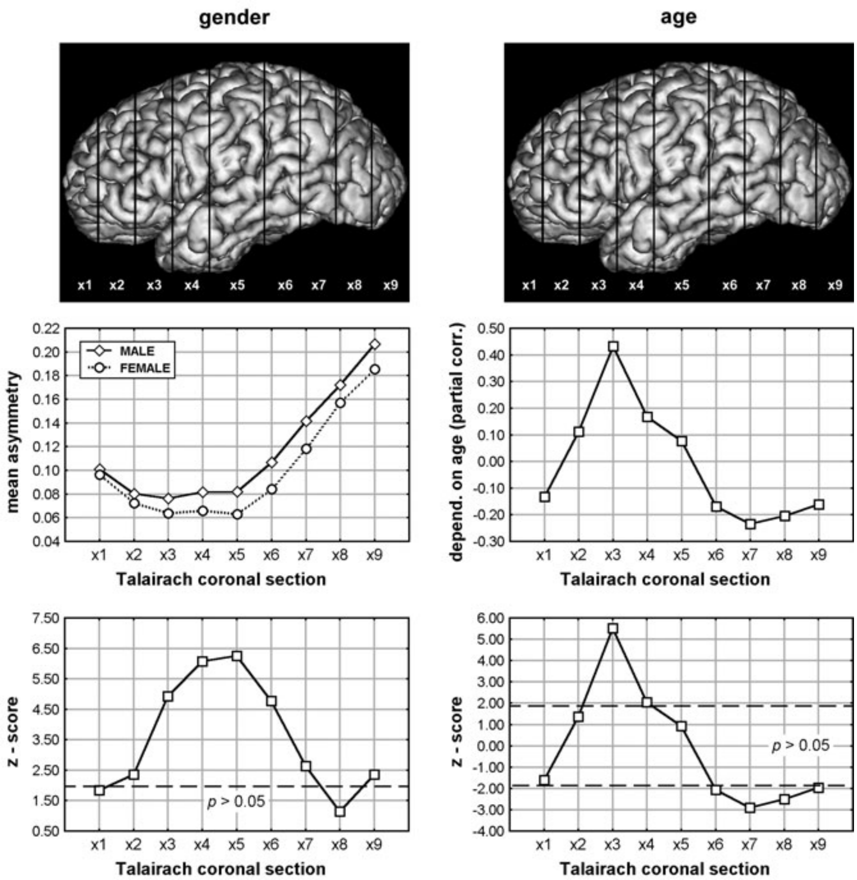

Figure 7. Interhemispheric asymmetry differences in Talairach coronal sections associated with gender (left column, n=290, 145 males, age range 18-32 years) and asymmetry changes with age (right column, n=152, 76 males, age range 18-70 years). *Upper row:* An example of Talairach brain subdivisions into nine coronal sections. *Middle row:* Mean values of interhemispheric asymmetry in each coronal section for male and female subjects (left plot) and partial correlation of the asymmetry with age provided by a multivariate linear model (right plot). *Bottom row:* The significance of asymmetry differences (z-score values $|z|>1.96$ correspond to significance levels p<0.05).

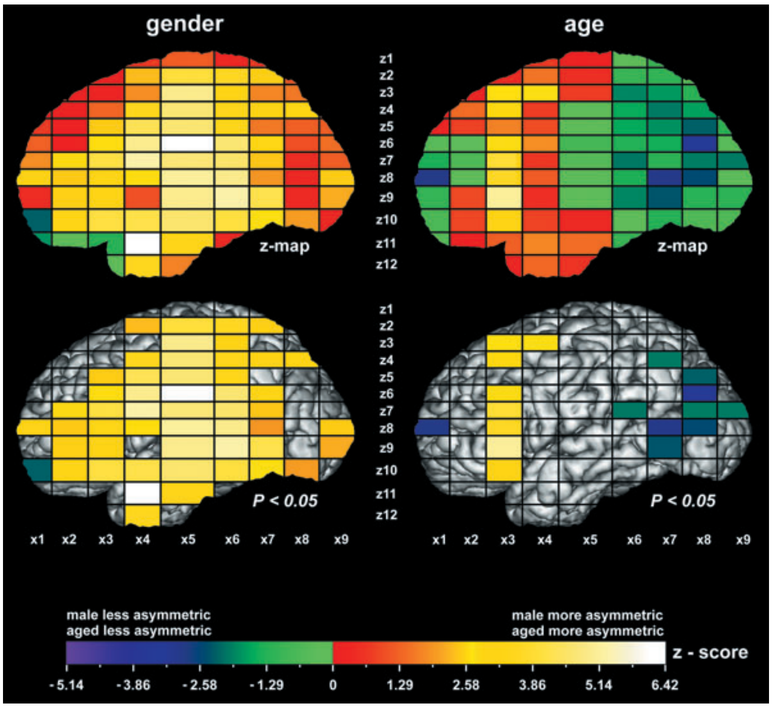

Figure 8. Significance of interhemispheric asymmetry differences in Talairach box-shaped corono-axial sections associated with gender (left column, n=290, 145 males, age range 18-32 years) and significance of asymmetry changes with age (right column, n=152, 76 males, age range 18-70 years). *Upper row:* z-score maps representing significance scores in color-coded scale provided on the bottom. *Middle row:* Same maps with regions where the asymmetry differences are significant ($|z| > 1.96$, $p<0.05$).

2.7.7 Quantitative comparison of pathological changes in Alzheimer's disease with neuromorphometric methods and high resolution MR-tomography

Föhlisch, F.[1], *Kruggel, F.*[1,2], *Brückner, M.K.*[2], *Arendt, T.*[2] & *Tittgemeyer, M.*[1]

[1] *Max Planck Institute of Cognitive Neuroscience*
[2] *Paul Flechsig Institute for Brain Research, Leipzig*

Alzheimer's disease induces macroscopic, neuronal changes which may be revealed by MRI tomography or histological staining methods and quantified by computer-based image analysis procedures. A combined evaluation of both techniques by image analysis procedures may yield a deeper understanding of the validity and precision of MR-based morphometric measures. Questions are in particular: (1) How much do volumetric measures correspond? (2) Is there a correspondence between MRI based cortical parcellation and myoarchitectural borders? (3) Does the amount of grey matter atrophy in crowns differ from the atrophy in fundi of selected gyri? (4) How much do pathological findings (e.g., lesions, diffuse white matter hypo-intensities, enlarged VRS) in the white matter compare? (5) Is it possible to extend results to in vivo examinations?

For this purpose twelve brains from patients with Alzheimer's disease and patients which ceased from non-neurological disease are examined. An image processing procedure is set up to allow comparison of histological and MR data while measuring distinct structures of interest. Given alternative algorithms are compared so as to optimize the

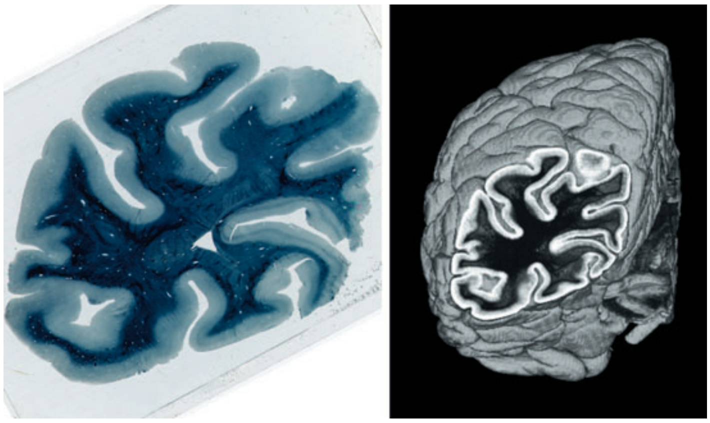

Figure 9. Histological slice (left) at the level of occipital lobe and high-resolution 3D MR data set (right), that has been cut at the same slice position where the histological slice was taken.

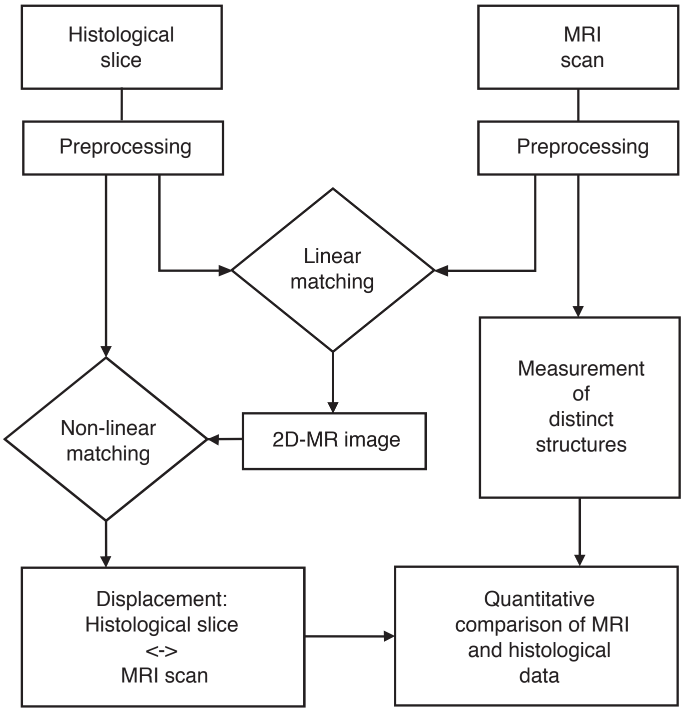

Figure 10. Sketch of the processing protocol.

processing chain. The information gained is evaluated statistically. So far, two isolated left brain hemispheres (fixed in formalin) were scanned using a high-resolution T_1-weighted 3D MDEFT protocol (matrix 256x512x512, voxel size 0.375 mm x 0.375 mm x 0.25 mm, scanning time 8 h). After scanning, each hemisphere was cut in slices with a thickness of 50 µm, stained and digitized. An example of such stained slice and the corresponding MR data set is depicted in Figure 9. Image analysis consisted of the following steps: (1) correction of B_1-field inhomogeneities in the MR data while segmenting data using an unsupervised classificator, (2) extraction of white (WM) and grey (GM) matter, (3) non-linear 2D-3D-registration of each histological slice onto the respective MR data set, (4) computation of the GM and WM surface as well as the neocortical thickness, (5) segmentation of basal ganglia and subthalamic nuclei, (6) segmentation into crown and fundus regions based on surface curvature, (7) volumetry of compartments (GM, WM).

2.7.8 Neurobiology and prognosis of mild cognitive deficits in the elderly

Hensel, A.[1], Wolf, H.[1,2], Kruggel, F.[1,2], Riedel-Heller, S.G.[3], Arendt, T.[4] & Gertz, H.J.[1]

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[3] Research Department of Evaluation and Epidemiology, University Clinic, Leipzig
[4] Paul Flechsig Institute for Brain Research, Leipzig

In an ongoing longitudinal study we investigate possible predictors for the change of cognitive function in non-demented elderly (73-87 years) and for the two alternative progression types of questionable dementia (crossover to dementia, stability). We investigate whether volumetric brain measures are significantly associated with changes in cognitive function and whether they are suitable to improve the predictive accuracy achieved by dementia screening tests and by clinical rating scales. In 2002, the first follow-up was completed. Out of 74 non-demented probands at baseline, 68 probands were followed-up (37 controls, 31 questionable dementia). At both timepoints all probands were examined using dementia screening tests (MMSE, SIDAM). The level of cognitive function was rated using the Clinical Dementia Rating (CDR). Volumetric MRI were recorded from all participants at baseline. Global brain compartments (grey and white matter, internal and external cerebrospinal fluid compartments) were segmented automatically. The corpus callosum and the hippocampus were outlined manually. The majority of probands remained stable in cognitive function (N=49). Ten probands declined, nine probands improved. We found dementia screening tests to be unsuitable for predicting the annual rate of cognitive change, when used as a single predictor variable. The combination of screening tests with the CDR sum score resulted in a significant model explaining 22% of the variance. Among brain imaging data, global brain volume (Figure 11) and grey matter volume were the best predictors of the annual rate of cognitive change and improved the proportion of explained variance to 28%. The hippocampal volume, corpus callosum area as well as cerebrospinal fluid compartment volumes lacked association to the change of cognitive function.

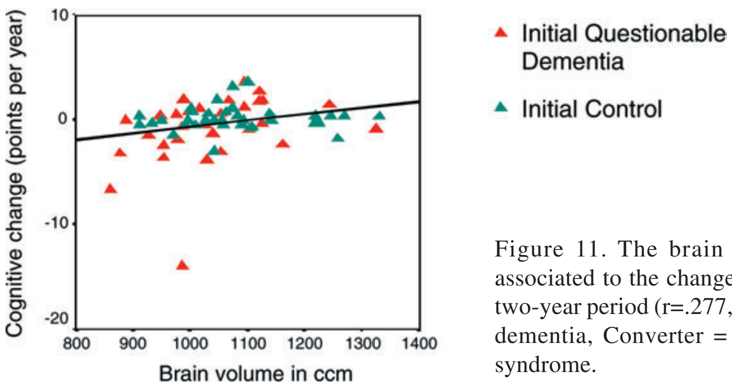

Figure 11. The brain volume was signi-ficantly associated to the change of cognitive function over a two-year period (r=.277, p=0.012) QD = Questionable dementia, Converter = development of a dementia syndrome.

Brain deformation analysis

2.7.9

Tittgemeyer, M., Wollny, G., Chalopin, C. & Kruggel, F.

Image registration algorithms create deformation transformations (maps) that indicate 3D patterns of anatomic differences between any pair of subjects as well as along time-series' of subject examinations. These deformation maps are usually high-dimensional, large and therefore, hard to interpret. In analyzing such transformations we are interested in both statistical parameters indicating significant deformation and in a simplified description of the deformation field.

By defining probability distributions on the space of deformation transformations which drive the anatomy of different subjects into correspondence, statistical parameters of these distributions can be estimated from databased anatomic data to determine the magnitude and directional bias of anatomic variation. Encoding of local variation can then be used to assess the severity of structural variants outside of the normal range, which, in brain data, may be a sign of disease. So far, we have implemented two methods based on the work of Chung et. al, 2001 (*NeuroImage, 14*, 595-606). Both methods do not require segmentation of a priori regions of interest. The first algorithm consists of calculating the Jacobian of the deformation field as a first order approximation to detect volumetric changes. Embedded in a statistical analysis of the deformation maps that are calculated between several subjects, we can extract significant local volume differences. The second method employs a Hotelling's T^2 statistic on a deformation field to robustly extract differential features, not subject to discretization errors or noise amplification in differentiation.

To get a simplified but sufficient description of a deformation transformation between examined time points contraction mapping is used to detect critical points, e.g., repellors (indicating local growth), and attractors (local shrinking) in these vector fields (Figure 12). Results are visualized to improve the understanding of the monitored disease process;

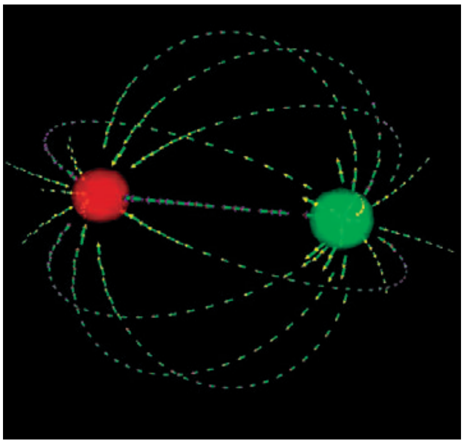

Figure 12. Sketch to illustrate the definition of a critical points in a vector field. The field vectors (shown as arrows) are repelled form one point (source) and attracted to another (sink).

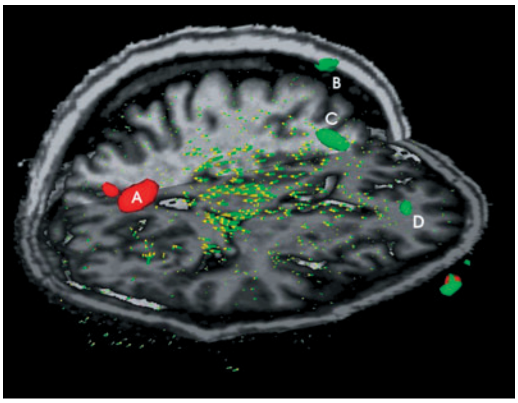

Figure 13. Shape difference of a patient's brain between two examined time points. Besides the attractor in the lesion area (A), repellors in the left frontal CSF compartment (B), the left frontal lobe (C), and the right frontal lobe (D) are visible. They indicate areas that are enlarged after the shift of the brain in the direction of the lesion.

a case example is displayed in Figure 13. The patient was scanned 2 days and 8 month after a cerebral bleeding. The spatial pattern of shape differences in the chronic disease stage is described by the displacement field obtained after non-rigid registration of the underlying MR images. The direction of tissue shift and the foci of shape change are enhanced by its critical points.

2.7.10 Analysis and simulation of midfacial distraction osteogenesis

Wollny, G.[1], Hierl, T.[2], Fingberg, J.[3] & Kruggel, F.[1]

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[3] C&C Research Laboratories, NEC Europe Ltd., St. Augustin

Using a rigid external distraction system for midfacial distraction osteogenesis is a novel method to correct the underdevelopment of the midface, surpassing traditional orthognathic surgical approaches for these patients. In complex malformations operation planning is based on CT images, followed by a modified midfacial osteotomy. Finally, the midface is slowly advanced by a halo-borne distraction device (RED system, Figure 14) until a satisfactory correction of midfacial deficiency is achieved. While striking aesthetic improvements are obvious, the analysis of the three-dimensional bony changes of the skull is important to get a better understanding of the effects of the distractor onto the whole skull, and thus, to improve therapy planning. We developed an image processing chain to analyze shape changes of the skull based on pre-and post-operative CT scans of the patients. First, rigid registration is used to remove positional differences between the images. Then, non-rigid registration based on fluid dynamics is employed to quantify the changes. Finally, the skull is segmented from the images, and changes of the skull shape are mapped on a surface mesh (Figure 15).
To achieve an optimal intervention result, pre-operative planning is crucial and has to be repeated for each patient due to the individual specifics of the in-born deformation. Tools for computing pre-operative simulations based on the Finite Element Method (FEM) were developed in collaboration with NEC in the framework of the SimBio project. Currently, only simulations involving the halo frame at low spatial resolutions are possible. It is planned to enhance these tools within the framework of the GEMSS project. Here, a GRID enabled computing environment will provide HPC resources needed to run simulations with high resolution meshes that are necessary to represent the midface structures with sufficient detail.

Figure 14. From left to right: A twelve year old boy suffering from bilateral cleft lip and palate with severe midfacial deficiency, pre-operative status; the RED system applied to a model skull; post-operative status one year after therapy.

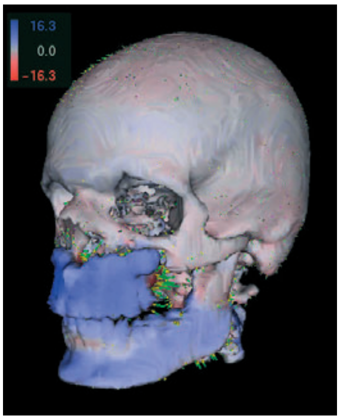

Figure 15. Visualization of a midfacial distraction after an almost complete osteomy. A color scheme is applied to indicate the magnitude and direction of shape change. Blue indicates a shift in surface normal direction (here in frontal direction). Color saturation reflects the magnitude of shape change.

Dynamic of brain deformation during and after surgical intervention

2.7.11

Tittgemeyer, M.[1], *Preul, C.*[1], *Lindner, D.*[2] & *Trantakis, C.*[2]

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Drastic structural changes in brain morphology occur during surgical intervention. In a collaborative study with the Department of Neurosurgery (NCH), University Clinic of Leipzig, we apply morphometric routines to investigate the dynamic of such changes.

A first investigation focuses on the time-dependency of brain shift, the relation between the extent of tumor removal and brain deformation, and the localization of both distinct anatomical and functional brain structures. To follow a tumor removal for instance, MR datasets were acquired by an 0.5 T OpenMR Signa SPi scanner at different stages during the intervention. Non-linear registration of the first vs. subsequent 3D T_1 data sets yield displacement fields that describe the intra-operative tissue deformation, i.e., the brain shift (Figure 16). Hypothetically, the shift follows gravity (its magnitude increase with consecutive tumor removal), with the major shift found at the rim of the tumor. Specific brain structures (e.g., the falx cerebri, the corpus calosum, and the corona radiata) limit the extent of the displacement. First results indicate that a significant brain shift occurs very early during the surgical procedure. After removal of 20% to 30% of the tumor volume an extent of 80% to 85% of the finally measured maximum of the brain shift was observed. This indicates a significant risk of surgical morbidity already at the beginning of the tumor removal. Intraoperative 3D iMRI and deformation field analysis based on a non-linear registration offer a method to capture the global as well as the circumscribed brainshift.

Another study is underway to quantify structural reconfiguration after treatment of hydrocephalus – in particular to assess information about the dynamics of ventricular reconfiguration after endoscopic ventriculostomy of the third ventricle. By subsequent MR-images the dynamics of the reconfiguration mechanism can be monitored with a deformation field analysis based on non-linear image registration. The usefulness of such analysis for surgical intervention evaluation can be demonstrated by the following case study: A 26-year-old patient with symptoms of hydrocephalus due to aqueductal stenosis underwent endoscopic ventriculostomy to ensure sufficient CSF-drainage bypassing the occluded aqueduct (Figure 17, left). 3D T_1 volume datasets were obtained prior to surgery and twice during the postoperative course. Offline analysis of individual scan data (initial linear registration, intensity adjustment and final non-linear registration of pre- to post-operative MR images) yielded 3D displacement fields describing the postoperative structural change. Extensive changes in terms of reconfiguration could be deduced in all parts of the lateral ventricles with accentuation of the middle and posterior parts in the early postoperative course. Pons and mesencephalic structures were withdrawn from the clivus; the floor of the third ventricle was elevated. In summary, the plane of the ventricular roof moved about 9 mm in average towards a normal position, ventricular floor, pons, and mesencephalon ascended about 4 mm on average. These findings give evidence for the mechanisms of brain reconfiguration after endoscopic intracranial pressure relief (Figure 17, right).

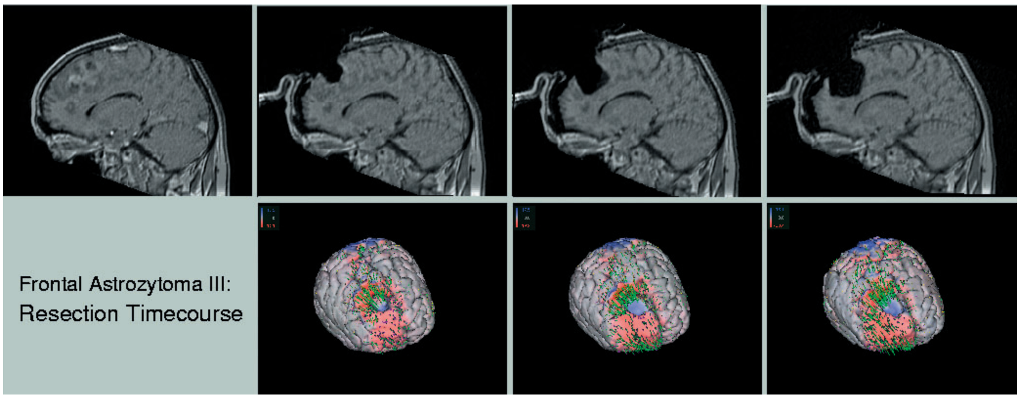

Figure 16. Repeated 3D volume datasets were acquired initially (T_0, left) and at different subsequent time points for resection control until complete tumor removal (upper line). The corresponding vector field analysis shows an increase of brain displacement with surgical progress (below).

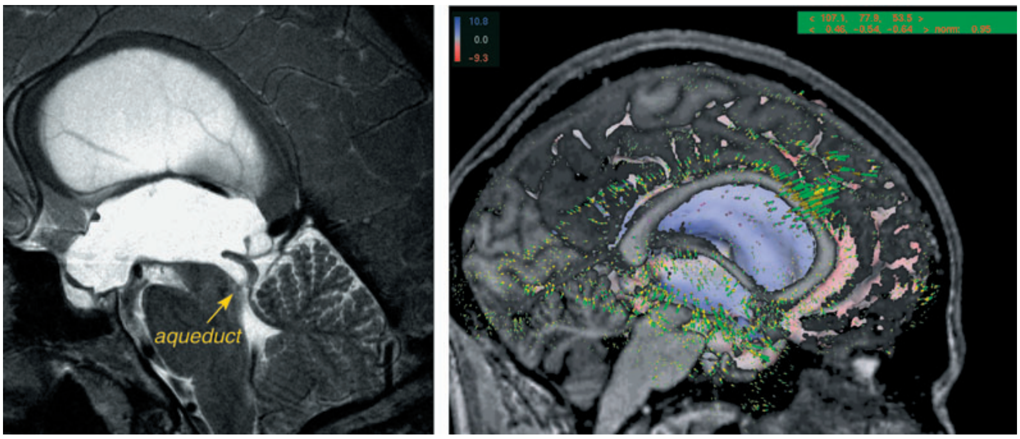

Figure 17. Midsagittal T_2 MR image of a patient suffering from non-communicating hydrocephalus (left). Visualization of brain shape change due to endoscopic ventriculostomy of the third ventricle (right).

In the year 2002, the NMR group has continued to pursue research in previous core areas. A source of substantial benefit has been collaborative work with external laboratories in Bethesda, Boston, Cambridge, Leipzig, Nijmegen, Osnabrück, and Tel Aviv, which was, quite naturally, particularly fruitful with our previous colleagues and visitors. On the hardware end, there has been valuable progress in terms of custom-designed RF coil technology for general fMRI experiments (2.8.1) as well as approaches to multinuclear imaging (2.8.2). Software developments aimed to improve the sometimes burdensome sequence programming and portability among different scanners (2.8.3). There has also been methodological progress in utilizing low-frequency BOLD signal fluctuations for investigating functional connectivity of different brain regions (2.8.4). A major focus of research was again devoted to projects related to perfusion and diffusion in the central nervous system. Refinements of arterial spin labeling using separate coils for labeling and imaging included an additional magnetic field gradient coil for adiabatic inversion at the neck (2.8.5) and have, for the first time, permitted functional perfusion studies applying a motor paradigm (2.8.6). Tackling the problem of motion artifacts in diffusion-weighted imaging has yielded steady progress with online motion compensation (2.8.7) and utilizing two-dimensional navigator techniques (2.8.8). This promises to lead to improved stability for high-resolution white-matter fiber tracking. Diffusion effects were also exploited for detecting a transient cortical cell swelling related to neuronal activation (2.8.9). A project that was more recently initiated aims at tissue characterization by magnetization transfer contrast (2.8.10) while anatomically adapted spectroscopy is being developed for metabolic investigations (2.8.11).

While the above progress has generally been encouraging, a considerable amount of effort during summer was enforced by an unforeseeable quench of the NMR magnet. Full operation without a penalty in quality was, however, possible after one month of downtime. Finally, the year's end has brought major changes to the institute's infrastructure due the installation of a second high-field scanner, which is scheduled to be taken into operation in January 2003.

2.8.1 Customized helmet quadrature transmit/receive coil for MRI at 3 T

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[3] *Interdisziplinäres Zentrum für Klinische Forschung (IZKF), University of Leipzig*

Experiments with our first helmet coil (see Annual Report 2000, Section 2.9.4) for magnetic resonance imaging (MRI) demonstrate that the sensitivity of a surface coil is attainable in superior human brain (e.g., location of the motor cortex). To improve the sensitivity with respect to deeper regions, we redesigned our coil to reduce the B_1 gradient along the z-axis.

The new helmet coil has perfect rotational symmetry (Figure 1). The design is based on two crossed, coplanar dual-loop coils arranged perpendicular to the z-axis and sharing a common circular base in the xy-plane. The circular base contains four distributed capacitors defining four points at halfway between them. At these points the radiofrequency (RF) is fed from the two pairs of spokes with two capacitors at halfway for wavelength shortening. The symmetric arrangement allows independent RF feeding into this structure to obtain a high degree of circularly polarized RF B_1 field. To reduce losses associated with the electric field generated by the coil and thereby improve the signal-to-noise ratio (SNR), a tune/match network was used to fit the unbalanced voltage from the transmitter to the balanced load of the coil. With the help of quarter-wavelength baluns in connection with parallel resonance circuits, waves on the outer jacket of the cable to the hybrid are suppressed. In axial slices, the flip-angle variation is less than 15% in plane. Along the z-axis, there is a moderate gradient, about half of that of the old helmet. First experiments on volunteers show that the new helmet permits investigations of the entire brain with good tissue contrast (Figure 2). The SNR is improved by up to a factor of 1.7 with respect to the standard birdcage head coil.

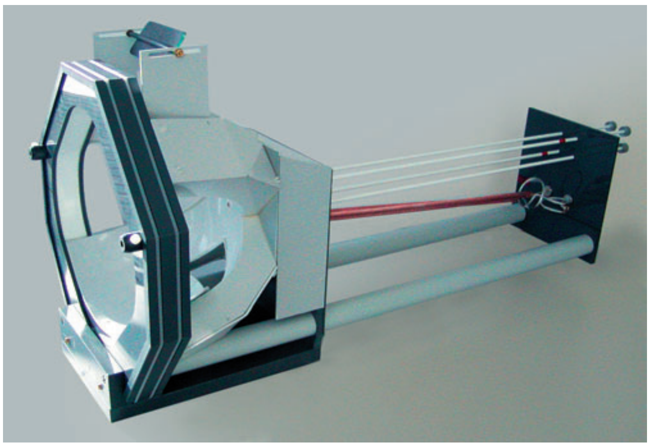

Figure 1. Dome-like shape of the new helmet coil (26 cm inner diameter, 20 cm height).

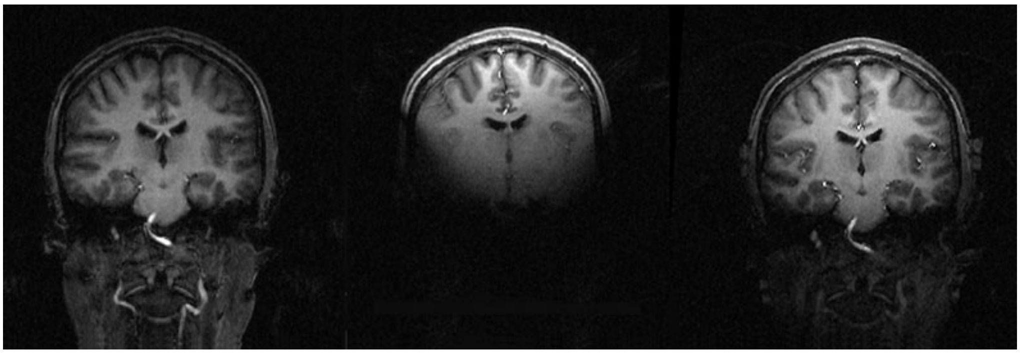

Figure 2. Coronal MDEFT images of the human head (matrix 256×256, field-of-view 25.6 cm, slice thickness 5 mm) acquired with the standard birdcage head coil (left), the old helmet coil (middle), and the new coil (right).

Coil design for ^{17}O-decoupled proton imaging of human brain

2.8.2

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[2] *FC Donders Center for Cognitive Neuroimaging, Nijmegen, The Netherlands*
[3] *School of Chemistry, Tel Aviv University, Israel*

Jochimsen, T.H.[1], *Driesel, W.*[1], *Norris, D.G.*[2] & *Navon, G.*[3]

In the previous Annual Report (Section 2.9.3), a double-tuned helmet coil was presented that permits ^{17}O decoupling and imaging at the ^{1}H resonance. However, for the purpose of proton imaging of oxygen-17 (PRIMO) in the human brain, two obstacles remained: (1) The radiofrequency (RF) power required to generate a sufficient decoupling field (400 µT found in vitro) is too large to be covered by conventional amplifiers. (2) The signal-to-noise ratio (SNR) seems insufficient for detection of the subtle T_2 changes originating from ^{17}O-^{1}H scalar coupling and ^{17}O quadrupolar relaxation (detection limit of 2 to 3% vs. < 1% changes in vivo). Alternative surface coil designs were thus considered to reduce the volume for decoupling and increase the SNR at the proton resonance. Results from experiments to determine the maximum coil size for full decoupling with an RF amplifier with a maximum continuous-wave (CW) output of 200 W are shown in Figure 3. Spectra were acquired from a water phantom containing 1% $H_2{}^{17}O$ with pulse durations of 0.1 ms for two surface coils (3 windings) and 0.5 ms for a Helmholtz coil. A pulse duration of 0.1 ms is equivalent to a 90° pulse at the field strength for full decoupling (i.e., the peak position indicates the power for full decoupling). The power limit for CW mode of the transmitter is approximately 15 dB. As expected, the smallest coil (2 cm diameter) produces the maximum decoupling field at a given power attenuation. Its 90° peak falls within an acceptable range; hence, full decoupling is achieved. By contrast, only insufficient decoupling was obtained with the other coils. The experiments indicate that full ^{17}O decoupling as a prerequisite for applying the PRIMO technique is limited to small volumes of < 3 cm^3. Studies of the whole human brain are therefore currently impossible with conventional equipment.

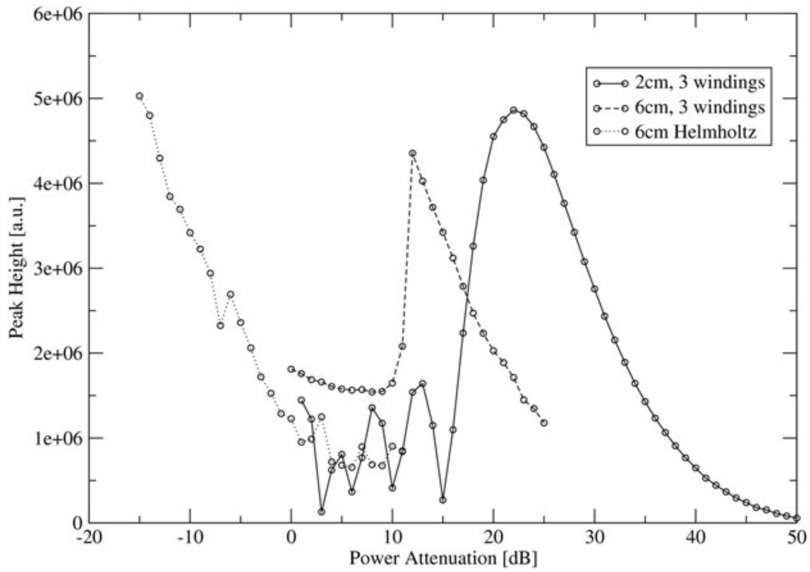

Figure 3. ^{17}O signal height as a function of the RF power (expressed as the attenuation compared to the maximum pulse power of the amplifier of 2 kW) for different coils. The data set of the Helmholtz coil was shifted on the power axis to compensate for the different pulse duration.

2.8.3 ODIN – Object-oriented development interface for NMR

Jochimsen, T.H. & von Mengershausen, M.

"ODIN" is a software package that combines solutions to common programming tasks in nuclear magnetic resonance (NMR) to support the implementation of new sequences, data reconstruction, and evaluation. For performance reasons, it is written in the C++ programming language for the UNIX/Linux environment. The object-oriented design improves code reusability and flexibility while adapting the software to applications.

A main component of the package is an object-oriented framework for implementing NMR sequences. This library possesses an interface that describes typical elements of a sequence, such as radiofrequency (RF) pulses, gradient pulses, or acquisition windows, in terms of their physical parameters, thus allowing hardware-independent sequence programming. The hardware-dependent implementation is then handled exclusively by the library. Due to the object-oriented design, it may be easily ported to different spectrometer hardware without the need to rewrite implementations (Figure 4). A module for the generation and simulation of RF pulses is another part of the software. It handles a range of pulses from simple one-dimensional to segmented two-dimensional pulses in a uniform manner. The graphical user interface "Pulsar" allows interactive pulse design and monitoring of the corresponding excitation profile. The generated pulses are easily integrated into the sequence description framework as additional objects. For NMR data evaluation, some useful freeware libraries already exist. To include such functionality, a C++ class was written, which includes an array defined by the Blitz++ library. This library offers many features for multidimensional array handling. To integrate other libraries, one has to write an interface for the Blitz++ arrays, which is often not more than copying one array into another. In ODIN, this has already been done for the libraries of FFTW. Furthermore, some useful functions for image

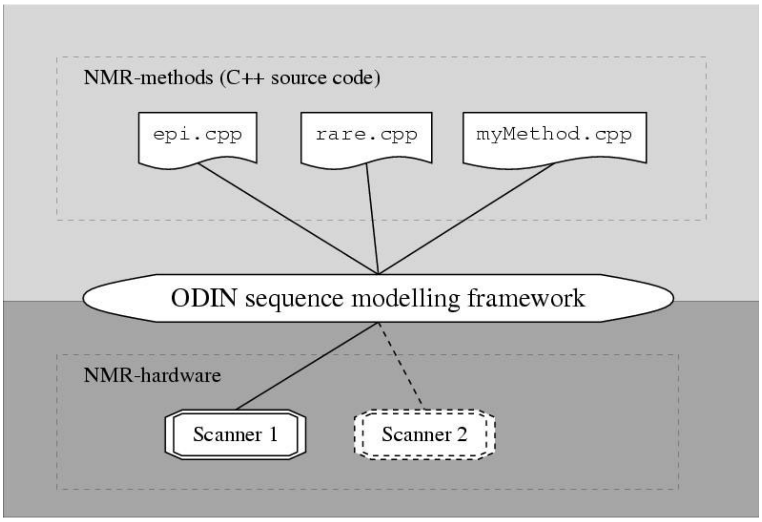

Figure 4. Different software layers for sequence design.

reconstruction are included, such as phase correction for echo planar imaging or partial Fourier reconstruction. Such functions demonstrate the clarity of source code written with object-oriented libraries, which essentially reduces time for debugging.

2.8.4 Signal stability and resting-state BOLD signal fluctuations

Görke, U.[1], *Becker, R.*[2], *Müller, K.*[1], *Norris, D.G.*[3], *Möller, H.E.*[1] & *Schwarzbauer, C.*[4]

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[2] *Institute of Cognitive Science, University of Osnabrück*
[3] *FC Donders Center for Cognitive Neuroimaging, Nijmegen, The Netherlands*
[4] *MRC Cognition and Brain Sciences Unit, University of Cambridge, United Kingdom*

Spatiotemporal correlations of low-frequency blood oxygen level dependent (BOLD) signal fluctuations in the resting state are assumed to probe functional connectivity between brain regions (see Annual Report 2001, Section 2.9.6). In such experiments, signal instabilities may cause erroneous interregional correlations, which vary spatially. Investigations of the statistical significance of resting-state BOLD signal fluctuations relative to the noise level demonstrate that partial voluming with cerebrospinal fluid (CSF) is the main source of false correlations. Additionally, motion, physiological noise, and spectrometer instabilities potentially produce signal spikes in the acquired echo planar imaging (EPI) time series. Figure 5 presents *t*-maps of a data set without and with suppression of such signal spikes. While only expected interregional correlation between the motor cortices are found in Figure 5B, additional correlations are present as artifacts in Figure 5A. Comparison between two- and three-dimensional EPI revealed that signal instabilities of the refocused transverse magnetization is the principle source of erroneous interregional correlations of EPI time series. In a study of functional connectivities of the basal ganglia in four volunteers, strong spatiotemporal correlations were found between the thalami and the putamen while the globus pallidus showed less correlations with other brain regions.

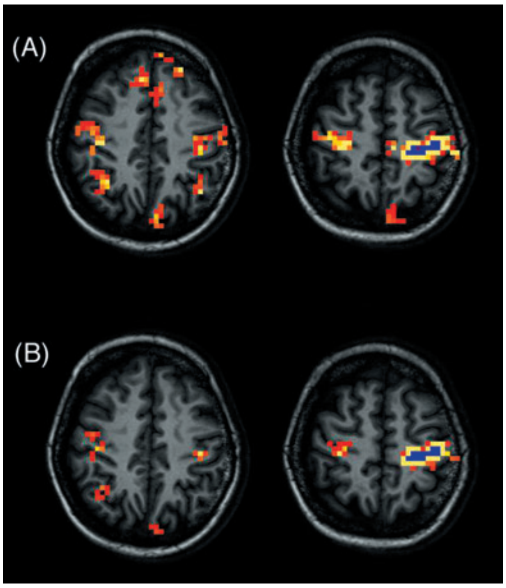

Figure 5. t-Maps of spatiotemporal correlations of the time courses seed regions marked in blue with all other brain voxels. The yellow-to-red color scale corresponds to $9.0<t<12.0$. Statistical analysis was performed without (A) and with (B) suppression of signal spikes in the time course.

2.8.5 Continuous arterial spin labeling using a local magnetic field gradient coil

Trampel, R.[1], Mildner, T.[1], Görke, U.[1], Driesel, W.[1] & Norris, D.G.[2]

[1] Max Planck Institute of Cognitive Neuroscience
[2] FC Donders Center for Cognitive Neuroimaging, Nijmegen, The Netherlands

Perfusion imaging using magnetically labeled water as an endogenous tracer is capable of measuring regional cerebral blood flow. Continuous arterial spin labeling (CASL) can be achieved by radiofrequency (RF) irradiation in the presence of a magnetic field gradient along the carotid artery, which results in an adiabatic inversion of the flowing spins. A first development was the use of separate labeling and imaging coils (see Annual Report 2001, Section 2.9.2), which facilitates multi-slice perfusion imaging. Of the numerous perfusion techniques available, CASL enjoys a high sensitivity; however, for functional imaging, the temporal resolution is poor due to the need for labeling periods of several seconds prior to image acquisition. If labeling could also be performed during image acquisition, the temporal resolution might be dramatically improved, enabling steady-state, multi-slice functional perfusion studies of the brain. This requires imaging and labeling experiments to occur completely independently of each other.

In the present work, independence of the labeling and imaging gradients is achieved by means of a separate local magnetic field gradient coil combined with an RF single-loop surface coil for adiabatic inversion as shown in Figure 6. Figure 7 shows multi-slice perfusion maps, which were obtained by a total of 140 repetitions with and without spin labeling in an alternating fashion. The local gradient and RF coils were placed over the right carotid artery of the subject. The locally induced gradient does not disturb spin-echo echo planar imaging provided a minimum distance between the gradient module and the imaging coil (helmet coil; see Annual Report 2000, Section 2.9.4) is maintained.

Figure 6. Circular RF surface coil (copper) combined with a local magnetic field gradient coil (yellow/green windings).

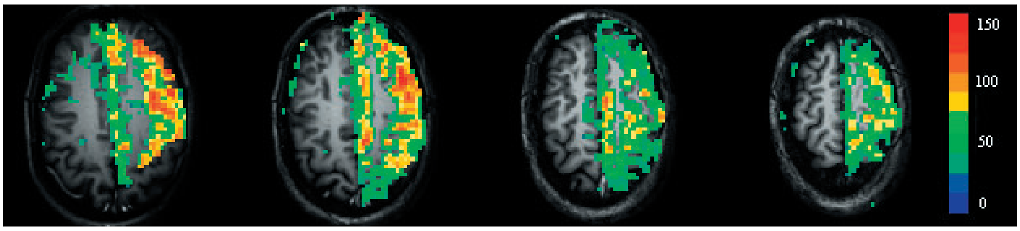

Figure 7. Quantitative perfusion maps (in ml/min/100 g) obtained by arterial spin labeling in a healthy subject. The observed range is consistent with physiology.

2.8.6 Multislice functional perfusion imaging using arterial spin labeling

Mildner, T.[1], Trampel, R.[1], Möller, H.E.[1], Wiggins, C.J.[2] & Norris, D.G.[3]

[1] *Max Planck Institute of Cognitive Neuroscience*
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[3] *FC Donders Center for Cognitive Neuroimaging, Nijmegen, The Netherlands*

Advantages of perfusion-based functional imaging as compared to the widely used blood oxygenation level dependent (BOLD) contrast include a potentially better localized area of activation and the feasibility of quantification. Functional perfusion imaging in humans with continuous arterial spin labeling (CASL) was performed for the first time with separate coils for labeling and imaging. This facilitates multi-slice perfusion imaging and eliminates the need to account for magnetization-transfer induced signal losses (see Annual Report 2001, Section 2.9.2). A helmet resonator (see Annual Report 2000, Section 2.9.4) and spin-echo echo planar imaging were used for imaging. A circular surface coil (6 cm diameter) was employed for CASL, which was achieved by radiofrequency irradiation in the presence of a magnetic field gradient along carotid artery leading to adiabatic inversion of the moving arterial water magnetization. The temporal resolution of CASL is inherently poor due to the need for labeling periods of several seconds. Therefore, labeling was applied during all repetitions of the functional run, increasing the temporal resolution and the sensitivity by factors of 2 and $\sqrt{2}$, respectively, while maintaining the capability to quantify blood flow changes. A long post-label delay of 2 s was used to minimize transit-time effects and to suppress intravascular signal contributions.

Figure 8 shows combined anatomical and functional images of a subject who performed a finger tapping task with the left hand. The labeling coil was placed over the right common carotid artery. The omega-shaped area of the primary motor cortex (Broca's knee) was activated in all subjects. Maximum signal changes varied among subjects between –0.5% and –.1%. Estimations of absolute perfusion changes yielded regional blood-flow increases upon finger tapping between 60 ml/min/100 g and 130 ml/min/100 g.

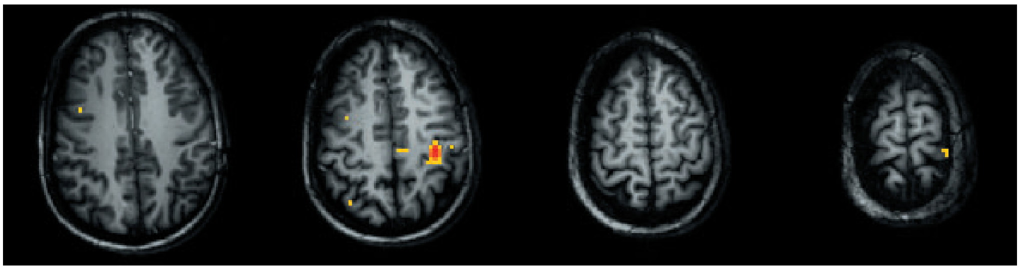

Figure 8. Anatomical MDEFT images of a subject performing a finger-tapping task with the left hand. The overlaid colored map of z-scores (threshold -3.09 corresponding to p=0.001) was obtained by evaluation of seven cycles of finger tapping and rest (each 30 s). The repetition time was 6 s and the labeling pulse duration was 3 s.

2.8.7 Diffusion-weighted imaging with online motion correction

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[2] FC Donders Center for Cognitive Neuroimaging, Nijmegen, The Netherlands

Diffusion-weighted (dw) imaging has become a powerful tool for the early detection of pathologies such as infarcts. Equally important, the acquisition of the full diffusion tensor permits in vivo fiber tracking. On the other hand, the sensitization to small molecular displacements (order of 10 µm) due to the Brownian motion by appropriate pulsed magnetic field gradients makes diffusion experiments susceptible to bulk subject motion. Motion during the diffusion-weighting part of the imaging sequence may modify the phase of the magnetization and, hence, produce image artifacts.

In this work, motion correction was applied to dw segmented echo planar imaging (EPI) and fast low angle shot (FLASH). Two orthogonal navigator echoes were acquired and zeroth- and first-order phase corrections applied online in less than 8 ms between dw preparation and data acquisition. The zeroth-order phase correction was realized by pulsing the system's B_0-coil and the first-order error corrected with appropriate magnetic field gradient pulses. Diffusion-weighted images of the brain were obtained from healthy volunteers. To avoid non-rigid body motion, ECG-triggered acquisition was applied at 380 ms after the R-wave. With both sequences, true online correction ensured that no irreversible signal loss occured in the imaging experiment. Segmented EPI images obtained with online motion correction showed a remarkably high image quality, while those acquired without correction were severely degraded by artifacts (Figure 9). Artifact-

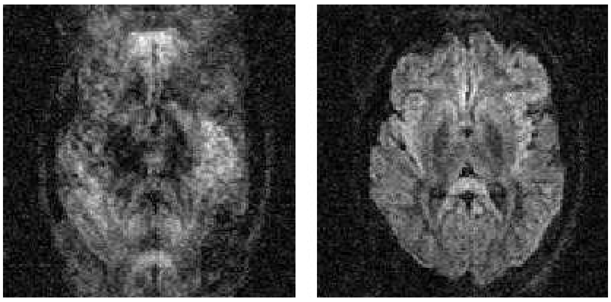

Figure 9. Segmented dw EPI images of the normal human brain acquired without (left) and with (right) online motion correction (echo time 85 ms, repetition time 4 s, matrix 128×128, 8 segments, *b*-value 800 s/mm^2).

free images were also obtained with dw FLASH; however, diffusion contrast was superimposed by residual longitudinal magnetization due to T_1 relaxation during image acquisition in this case.

2D navigators for diffusion-weighted imaging

2.8.8

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von Mengershausen, M.[1], Norris, D.G.[2] & Driesel, W.[1]

Diffusion-weighted (dw) methods of proton magnetic resonance imaging (MRI) are sensitive to the Brownian motion (i.e., self diffusion) of water molecules. During in vivo MRI of the human brain, typical distances of such motion are of the order of micrometers. This effect can be utilized to generate image contrast depending on the structural environment of the water molecules, for example, in diffusion-tensor imaging. However, as a major error source, unwanted subject movements exceed self-diffusion effects by several orders of magnitude. Such movements cause phase errors, which lead to signal decay and, depending on the imaging technique, to severe image artifacts. An approach to overcome motion artifacts is to register phase errors by so-called navigator echoes and correct them either online or during post processing. Specifically, the displacement and phase of the navigator echo maximum in *k*-space are measured (Figure 10).

In this work, navigators were implemented into a dw RARE ("rapid acquisition with relaxation enhancement") sequence with online motion correction. A first correction approach based on two orthogonal navigators, which read out *k*-space lines at k_x=0 and k_y=0, was found to be limited by a poor signal-to-noise in cases of motion-induced shifts of the signal maximum to the periphery of *k*-space. Consequently, false estimations of the echo maximum and, hence, improper corrections and artifacts may be obtained. By contrast, a single two-dimensional (2D) navigator, which may be compared to echo planar imaging. This approach provides sufficient *k*-space coverage for reliable detection of the echo maximum. Bulk head movements are thus more robustly detected, leading to improved stability of the online motion correction.

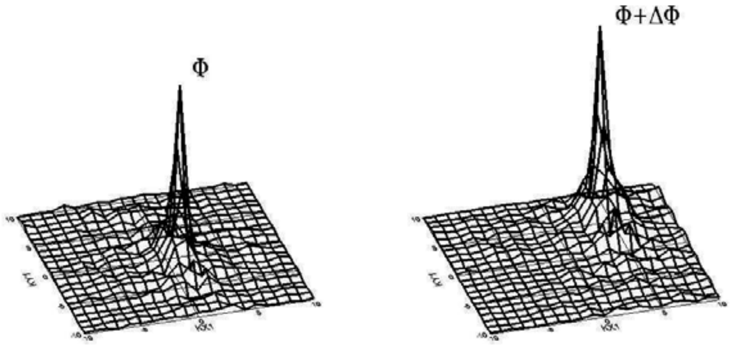

Figure 10. Undisturbed echo signal in k-space with its maximum at $[k_x,k_y] = [0,0]$ and phase Φ (left). Movements during dw MRI produce a displacement of the echo due to head rotation and a phase offset $\Delta\Phi$ due to head translation (right).

2.8.9 Detecting neuronal activation by transient ADC changes in a stimulated-echo sequence

Görke, U. & Möller, H.E.

Compared to the conventional blood oxygen level dependent (BOLD) contrast, which exploits the vascular response, detection of transient cortical cell swelling by diffusion-weighted (dw) imaging as suggested by Le Bihan et al. promises to be a more direct and better localized method to probe neuronal activation. In our study, transient ADC changes were detected with the dw primary and stimulated echoes of a three-pulse sequence (α=90°) at 3 T. For extracting ADC maps, b values of 250 and 1459 s/mm^2 were adjusted by using different diffusion times for both echoes, which are collected quasi-simultaneously. Hence, it is expected that the method is more robust against physiological noise and signal variations caused by head movements. The ADC is obtained from the ratio of the intensities of the stimulated and primary echo, which additionally depends weakly on T_1 relaxation. Potential variations in T_2 relaxation and proton density are suppressed. Significant changes of the apparent diffusion coefficient were found for three of four subjects in the visual cortex upon presentation of a strong visual stimulus. The paradigm consisted of 24 blocks of 40 s stimulus (rotating red *L*s) followed by 40 s of fixation. The high diffusion weighting was applied to suppress intravascular contributions to signal changes. In Figure 11, the surface rendering of averaged ADC changes in three volunteers is displayed. A small region of activation showing negative correlation (i.e., corresponding to a decreased ADC in the extracellular space) was found in the visual cortex.

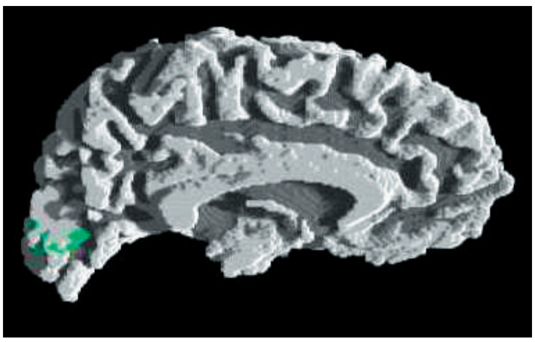

Figure 11. Surface-rendered average of the relative ADC change in three subjects upon visual stimulation (significance level: z<–3.1).

Tissue characterization by magnetization-transfer contrast imaging

2.8.10

*Wetzel, T. &
Möller, H.E.*

Magnetization transfer (MT) occurs if spins in two distinct environments exchange their magnetization via cross-relaxation or chemical exchange. In a two-pool tissue model, protons are assumed to exist in a highly mobile liquid state associated with water (free pool) or in semisolid macromolecular sites of restricted motion, such as proteins or membranes (restricted pool). In attempts to isolate MT effects, acquisitions are often performed with and without saturation of the restricted pool and MT ratio images (MTR images) are computed. Such MTR images are quantitative in a sense that they are reproducable and comparable among subjects. In the current project MT contrast was generated in a fast low-angle shot (FLASH; α 50°, repetition time 250 ms, echo time 9 ms, matrix 256×256, field-of-view 25 cm, slice thickness 5 mm) imaging sequence (Figure 12). Efficient saturation of the restricted pool was achieved by applying amplitude-modulated binomial pulse sequences (1-$\underline{3}$-3-$\underline{1}$) for each phase step. Each of these sequences comprises four 11.25°/33.75°/33.75°/11.25° rectangular pulses with a width of 200 μs and a center distance of 550 μs.

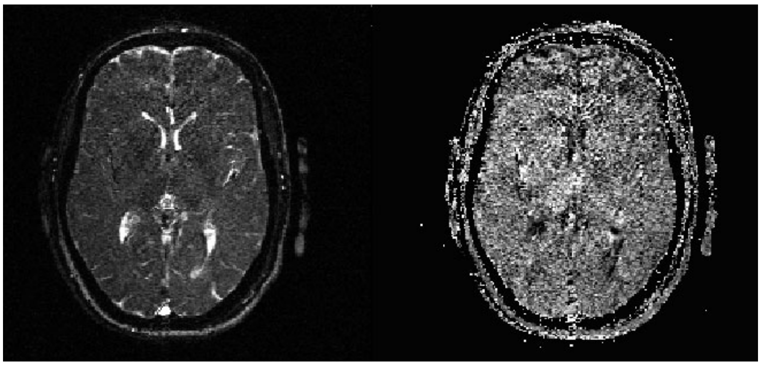

Figure 12. MT-weighted gradient-echo image (left) and computed MTR map (right).

Proton spectroscopy using segmented 2D spatially selective pulses

2.8.11

[1] *Interdisziplinäres Zentrum für Klinische Forschung (IZKF), University of Leipzig*
[2] *Max Planck Institute of Cognitive Neuroscience*

Körber, M.[1], *Riemer, T.*[1], *Jochimsen, T.H.*[2] & *Möller, H.E.*[2]

Spectroscopic experiments adapted to well-defined anatomical structures would be of great advantage over commonly-used methods based on rectangular voxels. In this pilot study, two-dimensional (2D) radiofrequency (RF) pulses were used to excite a disk-shaped volume (15 mm diameter, 10 mm height). In principle, arbitrary 2D shapes may be selected using the program "Pulsar" (see Section 2.8.3). To achieve sufficient spatial resolution, typical pulse durations of 10 to 20 ms are required leading to a bandwidth that is too low for spectroscopy. This problem can be tackled by segmented traversing through excitation *k*-space. The simple use of a shorter pulse (e.g., 2 instead of 16 ms duration yields an eightfold increase in bandwidth) results in poor localization indicated by a spiral artifact throughout the brain (Figure 13A). However, phase-sensitive addition of eight segments permits selection of a well-defined disk (Figure 13B). The observed off-resonance volume selectivity of this pin-wheel excitation scheme is acceptable for the ^{1}H chemical-shift range of the abundantly observed brain metabolites (Figures 13C, D). A in vivo spectrum acquired with the 2D pulse (Figure 14) shows well-resolved signals of *N*-acetyl-aspartate (NAA), (phospho)creatine (Cr), cholines (Cho), and myo-inositol (Myoin) with peak-area ratios identical to those of a control experiment with a standard single-voxel technique (point-resolved spectroscopy, PRESS). An additional broad lipid signal indicates residual contamination from subcutaneous fat dictated by the point-spread function. This artifact may be eliminated using standard techniques for outer-volume suppression.

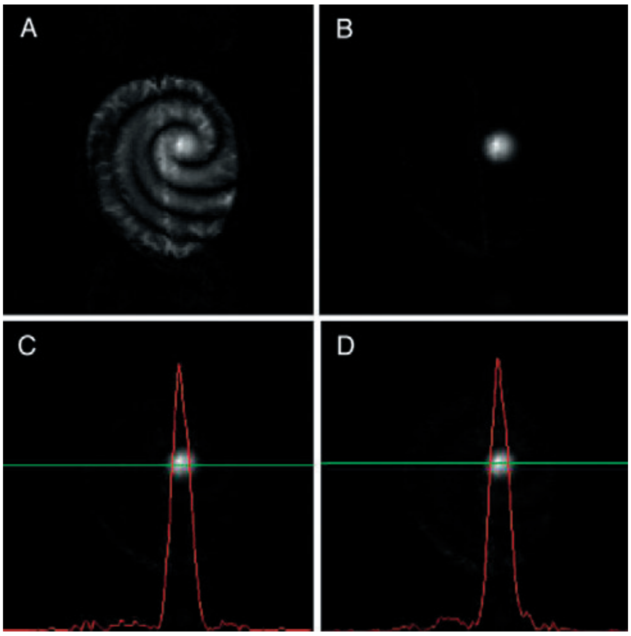

Figure 13. Axial images of the human brain obtained by echo planar imaging with a disk-shaped excitation profile: (A) first segment on resonance of the ^{1}H water frequency; (B) sum of eight segments; (C, D) off-resonance volume selectivity corresponding to excitation profiles for the methyl groups of Cr (C) and lipids (D).

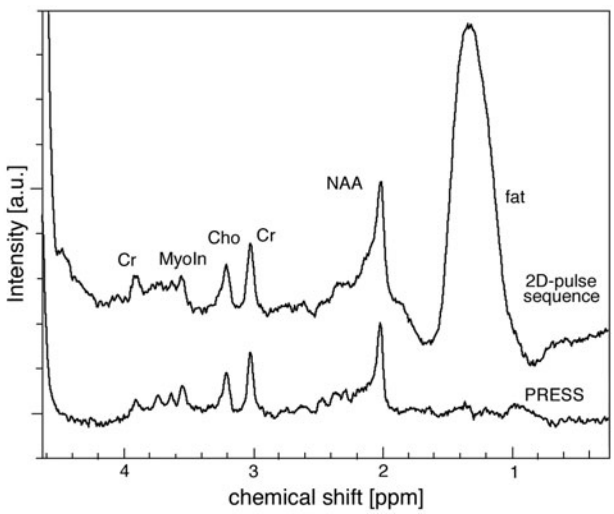

Figure 14. Proton spectra of normal human white matter obtained with a 2D excitation pulse (top) and a control experiment utilizing PRESS (bottom) with comparable voxel sizes and positions.

The working group "Mathematical Methods in fMRI" focuses on the development of new methods for the evaluation of magnetic resonance data.

As in recent years, a major aspect of our work was the improvement of our software package 'Lipsia' (Leipzig Image Processing and Statistical Analysis). Lipsia is the in-house software for the analysis of functional magnetic resonance data. During the past year, we have ported Lipsia from SGI/Irix to the Linux environment. At the same time, a number of algorithmic improvements were made. As a result, the processing time is now considerably faster than it was a year ago. The processing of an fMRI data set from the raw data to the statistical parametric map takes now less than 10 min.

Other methodological work aimed to investigate the temporal behavior of the BOLD response. We performed a study of the temporal consistency of the hemodynamic response in which four test subjects were asked to participate in the same experiment several times. We then checked the consistency of their BOLD responses from one experiment to the next. The most important result was that temporal dynamics of the BOLD response is very stable at the peak activations within one subject. However, between subjects the temporal dynamics is quite variable.

Because of the importance of an improved anatomical localization, wavelet-based methods were applied to fMRI data. In contrast to the standard fMRI data evaluation using a monoresolution Gaussian filter, wavelet-based methods are suitable for increasing the signal-to-noise ratio (SNR) without diminishing the signal. The spatial extent of the activations nearly remains unchanged that admits an improved assignment of the activations to anatomical regions. We have now developed an approach that allows us to combine the general linear model with wavelets.

A third focus of our work was the development of a set of morphometric tools for gray/white matter segmentations and cortical thickness. The most important aspects of this methodology are the ease of use and computational efficiency, but also the fact that it works even in the presence of brain diseases. Data sets of patients with pathological abnormalities are particularly difficult to process, and so this methodology is a major step forward.

Future work will be directed towards integrating the various aspects of our work. In particular, we plan to unite the spectral analysis methods that we developed in previous years with our new wavelet approach. Bayesian methods for the analysis of fMRI data are becoming increasingly popular worldwide, and we will certainly participate in this emerging field. Finally, a major aspect of our future work will be directed towards integrating our methods for the analysis of anatomical data with our fMRI analysis tools. We hope that a combination of both will lead to new insights into the anatomical understanding of fMRI activations.

2.9.1 Optimizing Lipsia – Leipzig Image Processing and Statistical Inference Algorithms

Arnold, T., Müller, K. & Lohmann, G.

Lipsia is the in-house software package for the analysis of anatomical and functional MRI data. It covers all steps, including preprocessing and registration, statistical evaluation and visualization. During the last year, Lipsia was ported from the currently used SGI mainframe to Linux PCs. To achieve outstanding performance on PCs central parts of the software had to be optimized.
As a main result, the computation time of the complete evaluation chain from raw data to statistical maps was reduced to below 10 min per subject on standard PCs and laptops. The execution time of the statistical part, i.e., the computation of the general linear model, across various types of Linux PCs compared to the SGI mainframe is shown in Figure 1. After an optimization based on the latest research on AEOS (automated empirical optimization of software) even PCs with only a moderate clock speed outperform the mainframe by a factor of 5 to 10. High-speed PCs even reach a speed-up of more than 30.

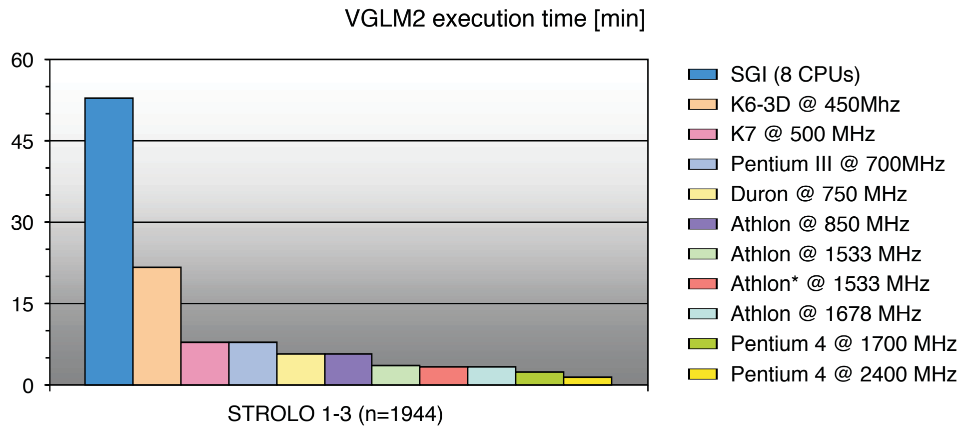

Figure 1. Computation time per subject (1944 scans) of the general linear model after the optimization of the core numerical routines measured on different Linux PCs compared to the SGI mainframe. Note that the mainframe uses 8 CPUs in parallel for computation whereas each PC can only make use of one CPU.

Other processing steps were re-implemented using more up-to-date algorithms. Examples are the slice time correction of functional data, which is now based on fast B-spline interpolation, and the non-linear registration of anatomical data using bi-directional demon matching. With the new, optimized Lipsia for Linux PCs it is now possible to evaluate a multi-subject fMRI study within only a few hours on standard hardware.

Wavelet statistics of functional MRI data and the general linear model

2.9.2

Müller, K., Lohmann, G., Zysset, S. & von Cramon, D.Y.

To improve the signal-to-noise ratio (SNR) of fMRI data, an approach was developed that combines wavelet-based methods with the general linear model. Contrast images can be investigated using methods of multiresolution analysis. Generally, the correlation between the wavelet coefficients of a signal will be small even if the signal itself is highly autocorrelated. This is also called whitening property. Thus, the errors in the wavelet domain can be assumed to be independent and identically distributed, and Gaussian. In conjunction with the orthogonality of the wavelet decomposition, contrast images can be processed using a statistical approach for thresholding of the wavelet coefficients.

In contrast to a monoresolution filter, the application of the wavelet method improves the SNR and shows a set of clearly dissociable activations. No relevant decrease of the local maxima could be observed. Wavelet-based methods increase the SNR without diminishing the signal amplitude, while preserving the spatial resolution of the image. The anatomical localization is strongly improved.

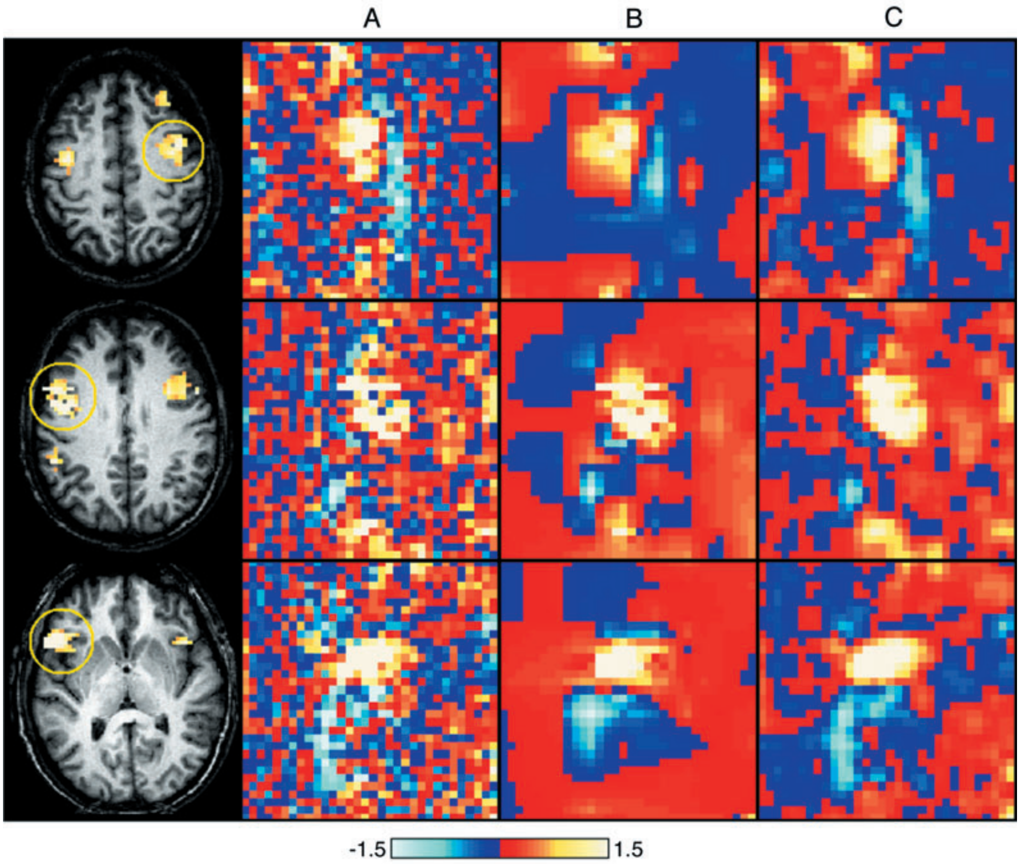

Figure 2. Several axial slices and zoomed contrast images of a single subject obtained (A) without any spatial filtering, (B) using the wavelet-based approach, and (C) applying a spatial Gaussian filter. Both the wavelet and the Gaussian filter lead to reduced noise. However, the wavelet-based method depends on the variance of the signal and, therefore, leads to a stronger improvement of the SNR compared with Gaussian filtering.

The combination of wavelet-based methods with the general linear model allows the treatment of event-related hemodynamic responses evoked by different sorts of stimuli. There is no constraint that requires long blocks of stimulation. From a practical point of view, the method is easy to integrate into fMRI data processing, because the general linear model is well established for statistical evaluation.

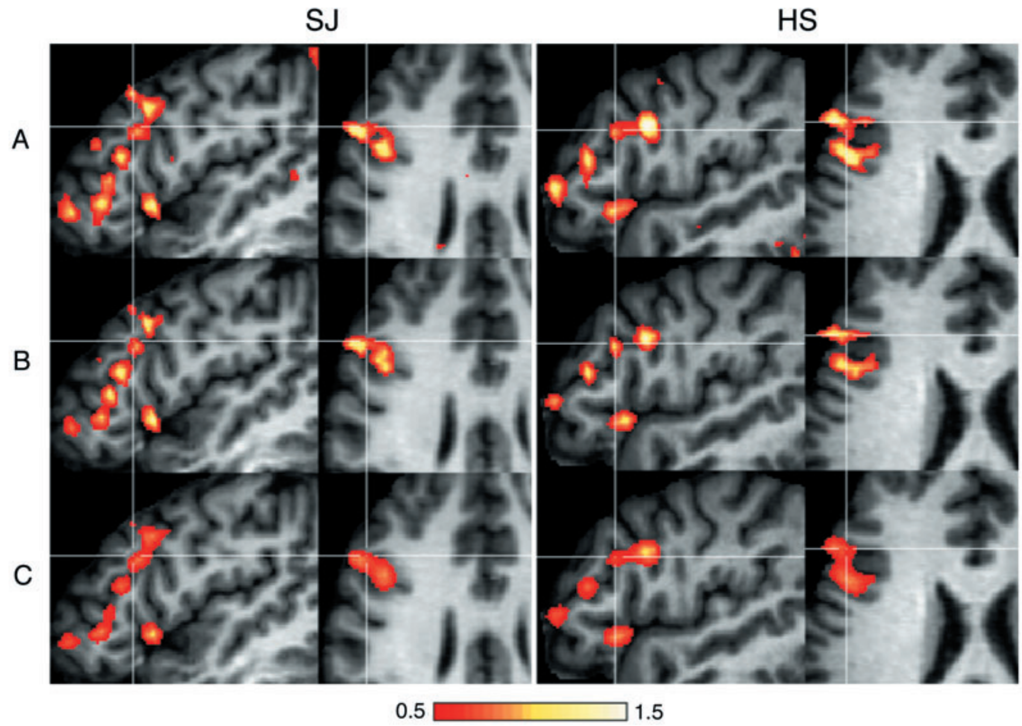

Figure 3. Axial and sagittal slices of two subjects through the left lateral prefrontal cortex. The maps show contrast images obtained (A) without any spatial filtering, (B) using the wavelet-based approach, and (C) applying a spatial Gaussian filter. Using the wavelet filter (B), the signal-to-noise ratio increased, and activations were even more dissociable than in the original unfiltered data. In contrast, the application of the Gaussian filter (C) leads to reduced contrast values in all activations.

2.9.3 Within-subject variability of BOLD response dynamics

Neumann, J., Lohmann, G., Zysset, S. & von Cramon, D.Y.

Temporal variations of the BOLD response as observed in fMRI experiments have been of longstanding interest to the fMRI research community. In this work we investigated the temporal variability of BOLD responses from 4 subjects performing a color-word matching Stroop task in 9 experimental sessions. Five parameters describing the temporal behavior of the BOLD response, including time-to-peak and time-to-onset, were estimated and analyzed with respect to their stability across repeated sessions. Among these five parameters, time-to-peak showed the most stable temporal behavior for all subjects and experimental conditions.

For the main contrast between experimental conditions, we identified five cortical regions that were activated in all individual sessions of all subjects, including left and right intraparietal and inferior precentral sulci and the presupplementary motor area. For voxels within these regions we found the temporal variation of the estimated BOLD response parameters to be very small. The standard deviation of the estimates when averaged across all repeated sessions was usually well below 500 ms. The within-subject variability is thus much smaller than the variability between subjects, which is typically found in the range of a few seconds.

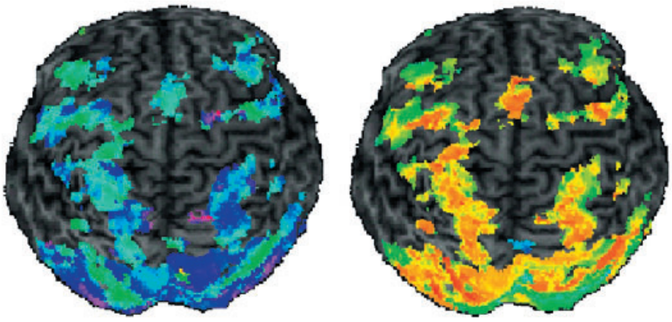

Figure 4. Intersection flat maps showing mean (left) and standard deviation (right) of time-to-onset for one subject after averaging across all sessions. Only voxels with significant activation are shown. Values are seen in a range between 0.1 (red/yellow) and 3.3 (blue). Although the mean values of time-to-peak vary between cortical regions in a range of about 3 seconds, standard deviations in activated cortical regions are mostly below 500 ms.

2.9.4 Morphometric analysis methods using high-resolution MR imaging data

Lohmann, G., Preul, C., Hund-Georgiadis, M. & von Cramon, D.Y.

Automated methods for segmenting and measuring compartments of the human brain provide important tools for studying various aspects of brain disorders. We have developed a set of automated morphometric methods for segmenting the gray and white matter compartment of the human brain including a method for regionalized cortical thickness estimation using high-resolution magnetic resonance imaging data. We are particularly concerned with in vivo imaging data of patients with pathological disorders such as cortical atrophies.

A number of difficult problems must be dealt with in the development of automated morphometric methods. First, the resulting segmentation should be topologically correct, i.e., it must not contain anatomically implausible holes or tunnels. Second, it must be robust against scanner inhomogeneities, so that nonlinear fluctations in image contrast and brightness should not influence the final result. And finally, the procedure must produce accurate segmentations, even in the presence of pathological disorders such as cortical atrophies.

The basic idea in our white matter segmentation is to exploit the fact that the brain's white matter is covered by layers of gray matter which can be iteratively eroded until the white matter surface appears. The erosion process is carefully controlled so that topological and anatomical constraints can be enforced. For the segmentation of gray matter, the erosion process is reversed and a controlled dilation is applied until the gray matter/CSF boundary is reached. For cortical thickness estimation, the "buried cortices" problem is particularly relevant. Buried cortices are cortical sheets within the same sulcal bed that belong to opposite sulcal walls. Due to the poor spatial resolution of MR imaging, it is difficult to differentiate between such cortices. Our method is capable of dealing with this problem.

We implemented the entire processing chain within the Linux/C environment. The computation time is very short: on a 1500 MHz processor, the entire processing chain takes less than 5 min per data set. The accuracy of the procedure was independently assessed by two experts.

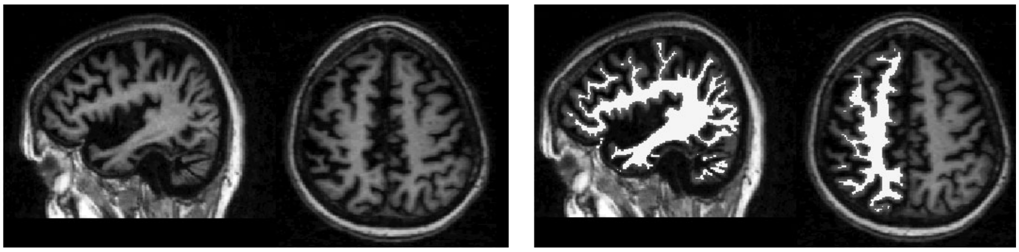

Figure 5. The left image shows an MR image of a patient with a severe cortical atrophy. Note that the white matter compartment of some gyral stalks are almost invisible. Our white matter segmentation is however capable of a correct segmentation as it obeys anatomical constraints.

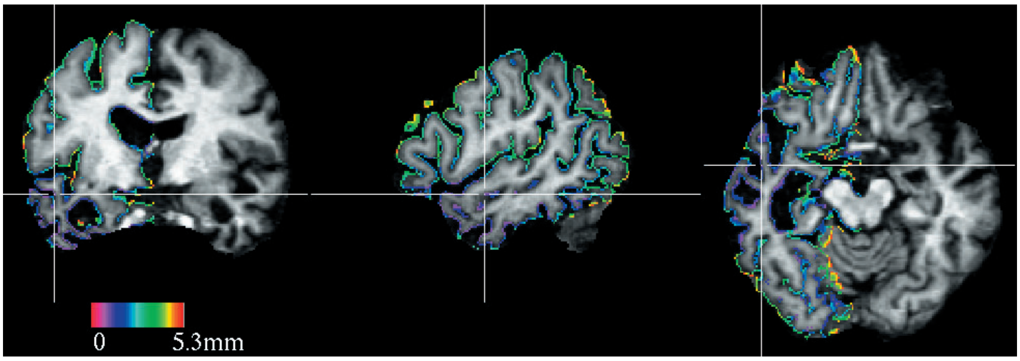

Figure 6. Result of the cortical thickness estimation. The thickness is color-coded and superimposed onto voxels that belong to the outer cortical surface. This data set shows an atrophy of the temporal lobe.

This year we have continued conducting psychological experiments as well as developing our methodological tools. Research on music perception was further deepened by establishing a joint project with the Biomag Lab, University of Jena, on processing of phrase structures investigated with EEG and MEG (2.3.1). The paper 2.10.1 aimed to investigate how the N400 component is altered in respect to amplitude and activated brain areas when subjects were solving different tasks while auditorily perceiving sentences. Finally, an auditory study using rhythmic tone pattern was conducted for a tuned analysis of the sources of the magnetic mismatch negativity equivalent (2.10.2). Although parts of oscillatory brain activity also contribute to known ERP/ERF components, the paper (2.10.3) could only find evidence for correlations within either domain (time and frequency), however no correlation between spectral band and ERP components.
Recognition of meaningful and meaningless hand-postures was investigated by means of EEG (2.1.16) and MEG (2.1.17). A study on auditory-visual integration processes demonstrated that attentional processing of bimodal stimuli led to an increase in evoked γ-band-activity whereas the corresponding ERP remained unchanged compared to unimodal and unattended stimuli (2.10.4).
Visual awareness, attention and working memory were correlated with spectral activity in three experiments on visual perception (2.10.5, 2.10.6 and 2.10.7).

In collaboration with physicians from NRZ (Neurologische Rehabilitationszentrum, Bennewitz, Michels Kliniken) a setup for monitoring motoric rehabilitation by means of MEG was established and is now used in a long term studies 2.10.8 and 2.10.9. Another study with unmedicated schizophrenic patients revealed their impaired processing capabilities during target detections tasks (2.10.10).

All methodological developments aim to improve accuracy and reliability of source localizations. Anisotropic conductivity profiles can now be included in FEM volume conductor models (2.10.11). Influence of these more realistic volumes to the forward modeling (2.10.12) and inverse modeling (2.10.13, 2.10.14) is discussed thoroughly. Options and limitations of the promising combination of fMRI based localizations with MEG determined temporal activities were revealed in a recently published article 2.10.15. A statistical analysis of current density distributions of a group of subjects was introduced in analogy to the SPM method used in PET and fMRI (2.10.16).

Within the framework of the project on phrase structures in music Christiane Neuhaus from Friedrich-Schiller-University of Jena is working as guest researcher within our group. Jens Molski left the group in March and since then Frank Burkhardt has been responsible for our computers.

2.10.1 Task effects on the amplitude and sources of the magnetic N400m response

Sivonen, P.H., Maess, B., Pilz, K. & Friederici, A.D.

We studied the influence of task on the magnetic N400m and the time course of underlying sources. Task demands were varied through the stimulus material as well as response requirement. Correct, semantically incorrect, or syntactically incorrect sentences were used in the experiment. In three tasks participants listened to all types of sentences while either (1) concentrating on their meaning (no overt response), (2) judging their correctness (semantic and syntactic), or (3) judging only semantic correctness. In the task (4) only semantically incorrect and correct sentences were presented and participants judged their correctness. The N400m-effect was significant during 400 to 600 ms in all tasks, whereas task effect was observed in the earlier time window of 400 to 500 ms. The N400m was larger when stimulus material was complex, i.e., included both syntactic and semantic violations (task 1) and when task demands were higher due to both complex stimulus material and judgment task (tasks 2 and 3) than in the task where only semantic violations occurred (task 4). Distributed source modeling revealed active sources between 400 and 600 ms around middle temporal gyrus and anterior and inferior temporal areas in both hemispheres. In task 2 activation started bilaterally and in task 3 earlier in the left hemisphere and was larger than in other two tasks in which right hemisphere activation preceded the left. Smallest and shortest lasting activation was observed in task 4, which had simpler stimulus set. Thus, the present study supports earlier findings which have located processing of semantically violated sentences in middle and anterior temporal areas, and, further, shows that task demands are reflected as an increase of the N400m amplitude and differences in the modeled sources.

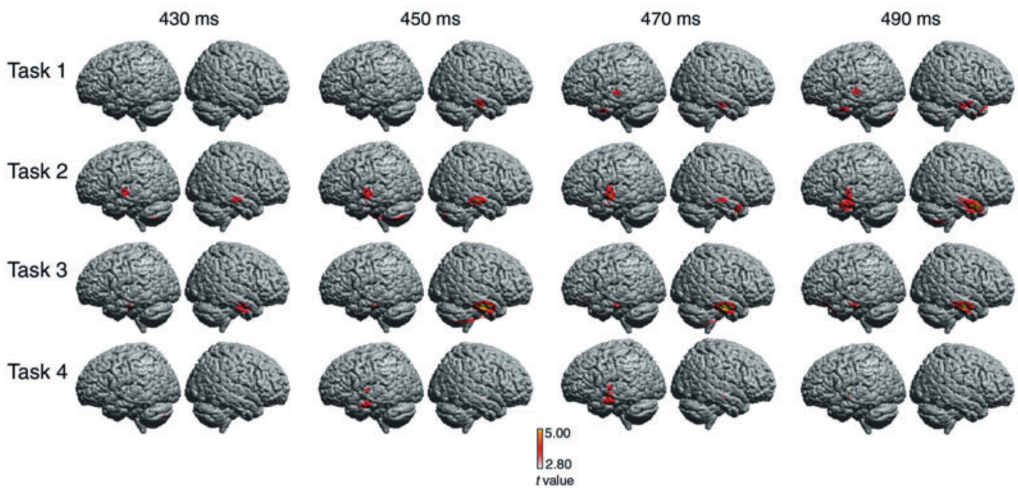

Figure 1. Significantly different activation (*t* values over 2.8) between correct and semantically incorrect sentence final words averaged over all participants and displayed onto cortical surface of a standard head model at four time points between 430 and 490 ms.

Cortical representation of tone-pause pattern in unattended auditory stimuli

2.10.2

Schauer, M., Maess, B. & Friederici, A.D.

The comprehension of speech and music depends upon a listener's ability to extract temporal patterns from the ongoing acoustic input. The mismatch negativity (MMN) is known to be evoked when varying the stimulus property after repetitive presentations of this stimulus. Variations of basic physical features like frequency, loudness and duration were tested thoroughly. More complex stimuli like words are described by all but time varying parameters interpretable in extreme as temporal on-off sequences. As an intermediate step in this study, four different tone-pause pattern were presented as stimuli. Every stimulus consists of two longer (150 ms) and two shorter (50 ms) sinusoidal tones of the equal pitch (750 Hz) and loudness (40 dB HL) which are separated by pauses of 50 ms. The different stimuli were presented in the way known as roving standard. According to earlier experiments the repetitions shall establish a memory trace. When a violation of the preceding sequence is perceived the stimulus related mismatch activity (MMN) is expected after the point of uniqueness (vertical dotted lines). The MMN could be detected at about 200 ms for stimulus transitions with early points of uniqueness and at about 500 ms for stimulus transitions with late points of uniqueness. The corresponding later differences between the conditions first and repeated presentation were identified as P3m. Additionally, significant differences were found at 750 ms after the stimulus onset. The appearance of the MMNs and later deflections gives some evidence that the time range of unconscious stimulus integration must be extended beyond the known value of 250 ms since the used stimuli (550 ms in length) were analyzed as a whole. The source localization of the mentioned activities by the MEG technique will assign the deflections to appropriate brain areas. The figure displays the grand average probe dipole strength in the auditory cortex (individual Heschl G.). 0 means short and 1 the longer tone inside the stimulus structure. R denotes repeated and F first presentations.

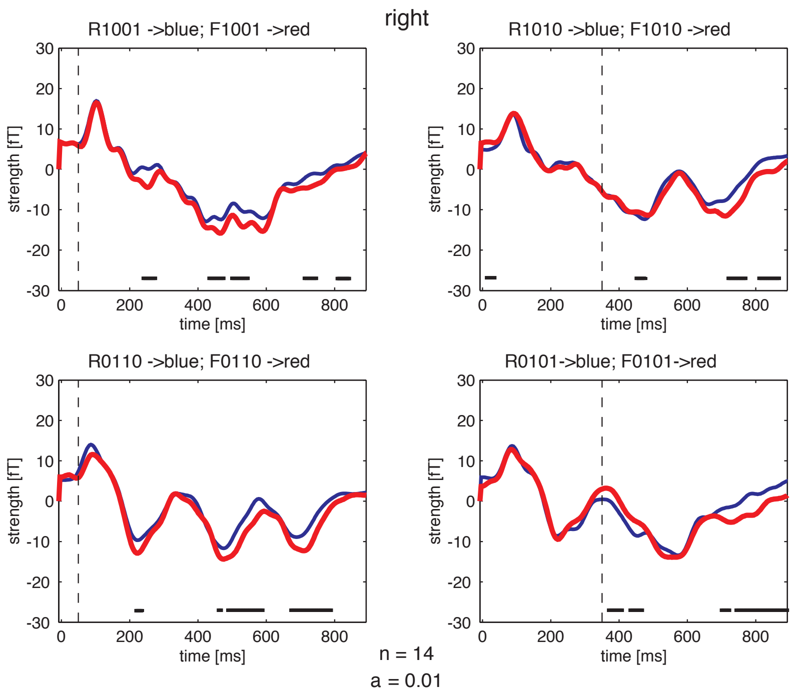

Figure 2.

2.10.3 Temporal correlations between auditory evoked responses and triggered oscillations: Evidence from a data set of 99 subjects

Hanisch, M.[1], Senkowski, D.[1], Herrmann, C.S.[1], Grigutsch, M.[1] & Gallinat, J.[2]

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[2] *Free University Berlin, Psychiatric Clinic*

Recent studies suggested that event-related potentials (ERPs) are closely related to a resetting of oscillatory processes in the EEG. Here we report evidence that evoked oscillatory activities and ERPs reveal correlations at different latencies within each other, but not between them.

We analyzed oscillations as well as ERPs in midline frontal, central, and parietal electrodes, focusing on the target stimuli in an auditory oddball paradigm. The auditory evoked P1, N1, and P3 showed respective oscillatory activations in the evoked Gamma-band, evoked Theta-band, and evoked Delta-band (Figure 3). This indicates that prominent ERP components are particularly generated by different cortical generators which are active in different frequency ranges, at the same latency. However, correlations between different latencies were only significant across frequency bands and across ERP components. E.g., the amplitude of the P1-component correlated significantly with the amplitude of the late P300-component. In addition, early Gamma-band responses correlated significantly with late Delta-band responses. No significant correlations between ERP components and triggered oscillatory processes were found for different latencies. We concluded that the lack of correlations between oscillatory processes and ERPs at different time latencies is explained by a complex superposition of different oscillatory processes, generating the ERP responses.

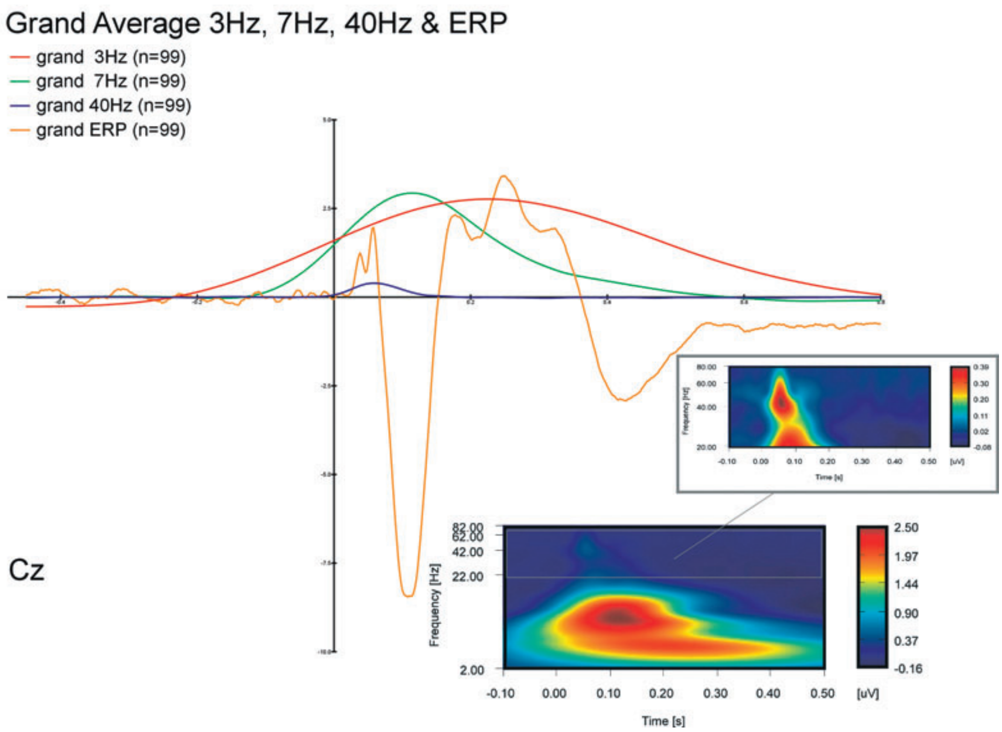

Figure 3. Grand average over 99 subjects for oscillations (3 Hz, 7 Hz, 40 Hz) and event related potentials. Time-frequency-plots (2 to 80 Hz and 20 to 80 Hz).

Early attentional binding mechanisms in multisensory integration

2.10.4

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[2] Duke University, Center for Cognitive Neuroscience, Durham, NC, USA
[3] Otto-von-Guericke-University Magdeburg, Institute of Psychology, Department of Biological Psychology

Integrative binding of different sensory inputs allow us to perceive separate features of objects coherently. Several studies have indicated that fast oscillatory responses in the EEG Gamma-band (30 to 80 Hz) play a crucial role in temporal binding. Thus far, no study has investigated the relationship between Gamma-band activity and attentional multisensory processing. Here we present a study exploring activity in the EEG-Gamma-band with relation to spatial attention and multisensory (auditory-visual) integration. Streams of auditory, visual, and audio-visual stimuli were rapidly presented to the left and right hemispaces, while subjects attended to a designated side to detect occasional deviant target stimuli (either auditory or visual). The focus of the analysis here is on the oscillatory responses to the non-target stimuli. Evoked Gamma-band activity was observed beginning at ~ 50 ms poststimulus for both the unisensory auditory and multisensory audio-visual stimuli. More interestingly, for the multisensory stimuli, we observed in this very early latency a higher Gamma-band activity for the attended relative

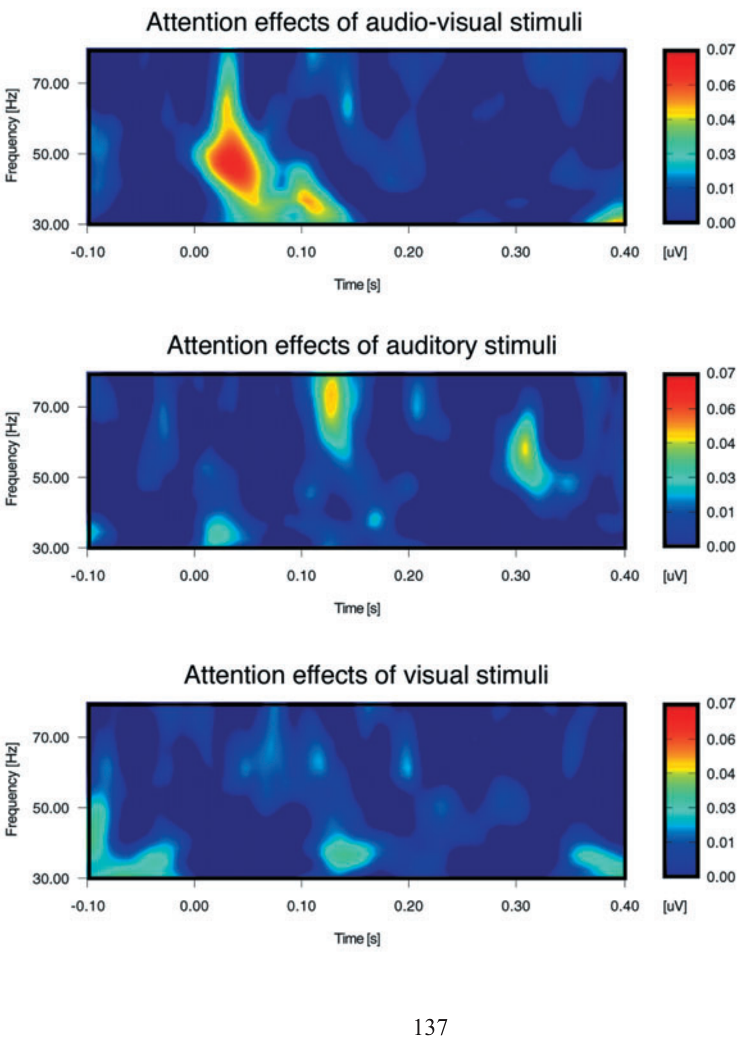

Figure 4.

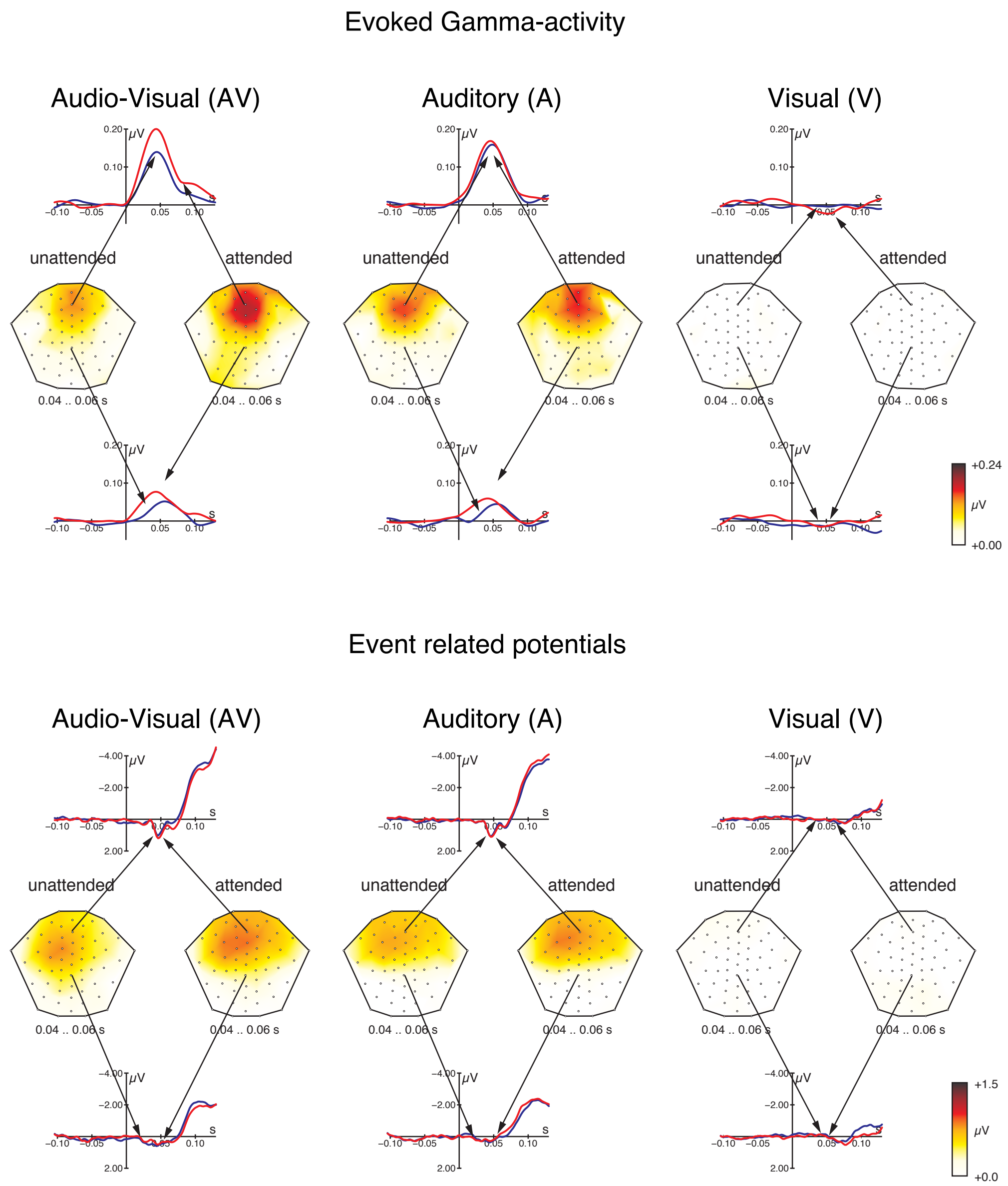

Figure 5.

to unattended condition, an effect which was strongest over medial frontal areas (see Figure 4 and 5). No corresponding attention effect was found for the unisensory stimuli. In addition, these early-latency effects showed up only in the evoked Gamma-band response and not in the event related potentials. Relative to the Gamma-band activity of the combined unisensory stimuli, Gamma-band activity of attended multisensory stimuli tended to increase, while Gamma-band activity of unattended stimuli tended to decrease, providing further data on the relationship between multisensory integration processes and early neuronal activity.

MEG alpha activity decrease reflects destabilization of multistable percepts

2.10.5

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Herrmann, C.S.[1] & Strüber, D.[2]

Multistable stimuli offer the possibility to investigate visual awareness, since they evoke spontaneous alternations between different perceptual interpretations of the same stimulus. This allows dissociation of perceptual and stimulus-driven mechanisms. In this study, we applied an ambiguous motion paradigm and compared endogenous reversals of perceived motion direction with exogenous reversals. Endogenous reversals happen when subjects view ambiguous stimuli (cf. Figure 6, A1 and A2 alternate) that allow two interpretations of motion direction, i.e., horizontal and vertical. Exogenous reversal can be forced by switching stimulation from showing HL and HR alternatively (horizontal movement, cf. Figure 6) and showing VT and VB alternatively (vertical motion, cf. Figure 6). Whole-head MEG was recorded and alpha activity was analyzed with a wavelet transform. The alpha activity showed different time courses for endogenous and exogenous reversals. In the exogenous stimulation alpha activity decreased sharply at the time of reversal and seems to reflect the sudden change from one percept to the other. However, in the endogenous condition, alpha activity slowly decreased until finally the change of perception occurred. We interpret this decrease to reflect the process of destabilization of the current percept. The findings therefore support the notion that alpha activity is associated with visual awareness.

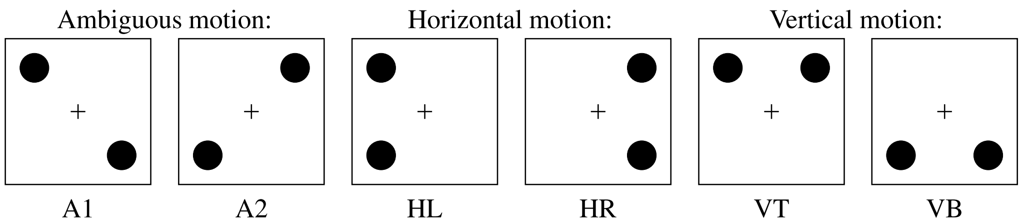

Figure 6. Ambiguous motion perception was induced by alternating the two stimuli A1 and A2. The unambiguous horizontal motion was generated by an alternating presentation of the two stimuli horizontal-left (HL) and horizontal-right (HR). Alternation of vertical-top (VT) and vertical- bottom (VB) produces unambiguous vertical motion. '+' served as fixation mark.

Bottom-up processes capture attention in visual feature binding

2.10.6

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[3] Otto von Guericke University of Magdeburg

Senkowski, D.[1], Röttger, S.[2], Grimm, S.[2] & Herrmann, C.S.[1,3]

Linking together and integrating separate features of a single object in the correct combination is one of the most important functions of visual binding. It is a long standing debate whether visual binding is affected by an automatic bottom-up process, or whether binding processes require top-down modulated selective attention. We ran two EEG experiments employing Kanizsa figures to investigate the temporal order of binding and attention. Visual search displays, either including or not including a Kanizsa figure among distractor stimuli, were used as cueing masks for a subsequent choice-reaction task. Subjects were instructed to look at the center of the screen (indicated by a fixation cross) and to indicate the pointing direction of a target triangle by pressing the right button (when the triangle pointed to the right) or the left button (when the triangle pointed to the left). We found faster reaction times and larger posterior N1 amplitudes for validly cued trials (target presentation inside a Kanizsa figure) as compared to invalidly cued trials (target presentation outside a Kanizsa figure) in both experiments (see Figure 7). This indicates that illusory Kanizsa figures in our experiments may automatically capture visual spatial attention. We conclude that binding can occur during early bottom-up processes, thereby capturing attention.

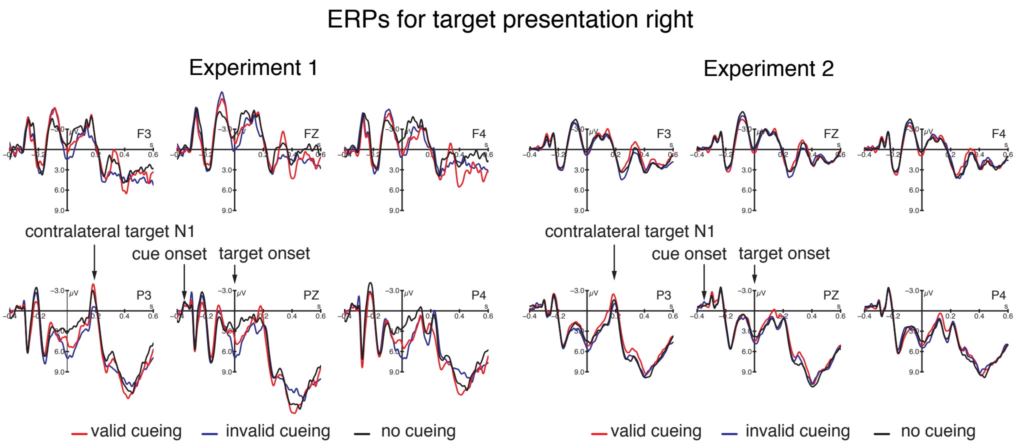

Figure 7. Event-related potentials from experiment one and two. Validly cued trials showed higher contralateral N1 amplitudes in a time range of about 180 ms after target onset than invalidly cued trials in both experiments. This may indicate that Kanizsa figures lead to an automatic visual spatial attention shift.

2.10.7 Event-related potentials and oscillations index feature binding mechanisms in different working memory processes

Busch, N.A., Herrmann, C.S. & Senkowski, D.

Previous studies demonstrated that in visual perception object features are first processed separately and have to be bound together to form an object representation. In visual working memory, however, objects seem to be stored as integrated representations rather than as separate features. Most of that work has been done in behavioral studies. Behavioral measures, however, examine the combined effect of multiple systems and processes. Therefore, electrophysiological measures are better suited to examine different subprocesses of working memory like encoding, retention, and retrieval.
We studied visual working memory in a delayed-matching-to-sample task (S1 – S2 paradigm) varying both the amount of objects (object load) and their relevant features (feature load). We found the P3 elicited by the S1 stimulus and induced alpha activity in the retention interval to be modulated by object load but not by feature load. In contrast, the behavioral data as well as the P3 elicited by the S2 stimulus were also modulated by feature load.

P3 amplitude has been discussed as an index of memory load in some ERP studies because it has been found to decrease with memory set size. Increased alpha activity during the delay interval of a working memory task has been proposed to reflect the inhibition of posterior visual areas that prevents interference with items held in memory. This alpha activity has been shown to increase with memory set size.
The results thus suggest that encoding and retrieval in visual working memory operate on integrated object representations with no need for additional feature binding. Retrieval and matching processes, on the other hand, seem to require additional resources for feature binding.

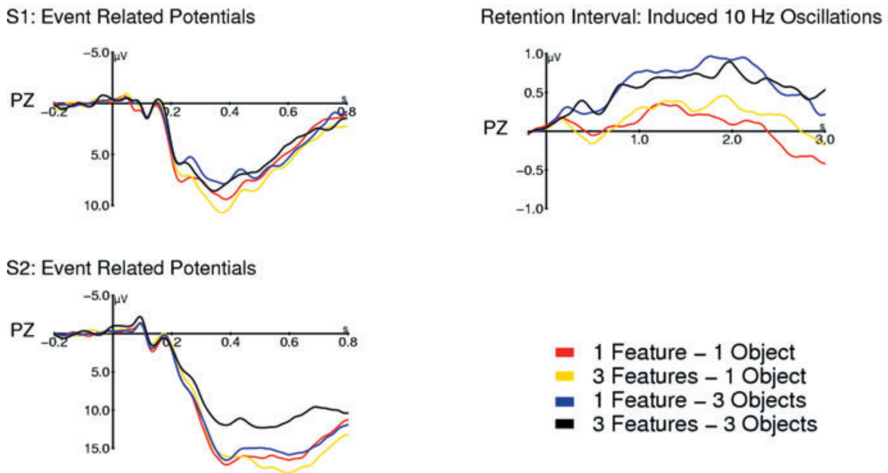

Figure 8. Grand average event related potentials during presentation of the S1 and S2 stimulus and induced 10 Hz oscillations during the retention interval. Amplitude of the P3 elicited by the S1 stimulus and induced alpha activity in the retention interval is modulated by object load but not by feature load. In contrast P3 amplitude elicited by the S2 shows an interaction with feature load.

The influence of electromyography or movement trigger on the magnetoencephalographic motor fields

2.10.8

Schauer, M.[1], Waldmann, G.[2] & Woldag, H.[2]

[1] Max Planck Institute of Cognitive Neuroscience
[2] NRZ - Neurological Rehabilitation Center, Leipzig

The early motor field (MF) and the first motor evoked field (MEF 1) serves as the event-related fields to localize equivalent current dipoles in the context of neurorehabilitative clinical studies. Common trigger events are electromyography (EMG) onset and onset of the movement's physical beginning (PB). The impact of these two trigger events on the analysis of MEF 1 and MF is yet to be clarified. The selection of the appropriate trigger becomes essentially in case of patient studies with restricted number of epochs. Furthermore, there is some evidence that the MEF 1 is more strongly coupled to the movement onset while the MF is stronger related to the EMG onset. To determine the influence of the trigger type the MF and the MEF 1 were estimated in both conditions EMG and PB. The data were recorded from 15 healthy right handed subjects. Their right distal arm and hand were fixed into a splint with a joint at the wrist, so that the hand could perform extension and flexion in the horizontal direction guided by a visual cue with an interval of 5 to 10 s (random). The movement's physical beginning was recorded by the goniometer. The EMG was recorded by surface electrodes from extensor carpi radialis and flexor carpi radialis muscles of both arms. The measurement was performed in four blocks lasting 15 min each and allowed up to 419 averaged movements per direction. EMG and movement onset were determined automatically. The mean time delay between EMG and movement onset in the extension was 85 ± 49 ms and in the flexion 107 ± 58 ms across all subjects. The equivalent current dipole strengths were estimated at MF and MEF 1 moments and were compared in both conditions. The MF strength was significantly larger in the EMG-condition as in the PB-condition ($p<0.05$). The MEF1 strengths did not differ significantly between both conditions. The result supports the postulation that the MF reflects the final cortico-spinal outflow (motor command). The EMG trigger is the better choice for the MF estimation in weak isotonic wrist movements.

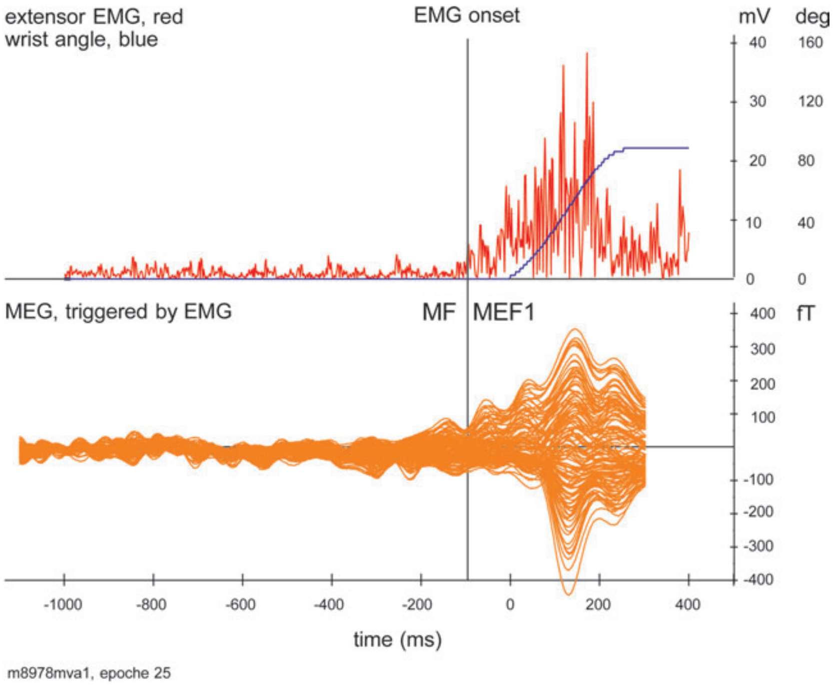

Figure 9. Upper figure: The red line displays the rectified EMG signal of the extensor carpi radialis muscle. Lower figure: The black denotes the field strength of the 148 MEG sensors.

2.10.9 Movement related cortical magnetic fields in self induced wrist movement under a physiotherapeutic intervention

Waldmann, G.[1], Woldag, H.[1], Knösche, T.R.[2] & Hummelsheim, H.[1]

[1] NRZ Neurological Rehabilitation Center Leipzig
[2] Max Planck Institute of Cognitive Neuroscience

In the knowledge from predominantly experimental studies with animals about the sensorimotor coupling and its prerequisite for motor learning, neurorehabilitative investigations of the sensorimotor system are of increasing interest. Repetition of a simple hand movement in the wrist is an evaluated therapeutic approach known as repetitive sensorimotor training (RST). Distinct investigations of functional changes of motor and sensor activity and the visualization of the concerted neuronal actions in motor learning under RST with the new non-invasive imaging methods are required to reveal any therapeutically influences. In magnetoencephalography (MEG) self paced movement related neuromagnetic fields consist of a slow pre-movement readiness field (RF, 1 to 0,5 s prior to movement onset), a motor field (MF, about the time of electromyography (EMG) onset of the active muscle) and several motor evoked fields (MEF), of which the MEF I (the first after EMG onset) is the largest and most robust signal. Seven healthy subjects were investigated in MEG performing an active right wrist movement about 60 min. Over the intervention time we found an increase of the dipole power in the RF, the MF and no change in dipole power in the MEF I. The investigation results reflect an isolated influence of RST on the activation in motor areas during a self induced performances (see Figure 10).

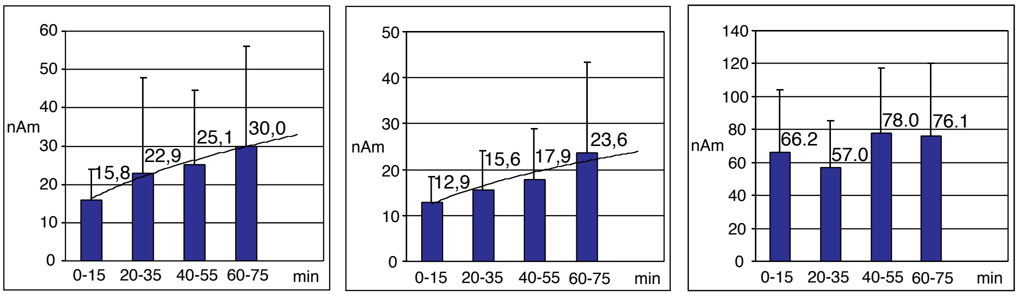

Figure 10. Activity of different cortical regions over 4 blocks in one session of repetitive sensorimotor training. LEFT: RF mean power in dipole position 35, 2, 73 in mm in the nose-ear-coordinate-system corresponding to the region of the supplementary motor. Between dipole power in block 1 and block 4 a significant difference exists (p=0.03). MIDDLE: MF mean power in dipole position 17, 30, 93 in mm corresponding to the region of the primary motor area. Between dipole power in block 1 and block 4 a significant difference exists (p=0.03). RIGHT: MEF I mean power in dipole position 3, 19, 85 in corresponding to the region of the proprioceptional afferences, Brodmann area 3a. Between dipole power in block 1 and block 4 no significant difference exists (p>0.1).

2.10.10 Reduced evoked gamma activity and P300 amplitude in medication-free patients with schizophrenia indicates impaired network processing

Senkowski, D.[1], Herrmann, C.S.[1,2], Winterer, G.[3], Busch, N.A.[2] & Gallinat, J.[4]

[1] *Max Planck Institute of Cognitive Neuroscience*
[2] *Otto-von-Guericke-University Magdeburg, Institute of Psychology, Department of Biological Psychology*
[3] *Clinical Brain Disorders Branch, National Institute of Mental Health, National Institutes of Health, Bethesda, Maryland, USA*
[4] *Free University Berlin, Department of Psychiatry*

Integration of sensory information by cortical network binding seems to be crucially involved in target detection. ERP and EEG studies in patients with schizophrenia further indicated a disordered network binding in this decease. EEG gamma activity, as an indicator of cortical binding processes, was recently found to be decreased in medicated patients with schizophrenia (Haig et al., 2000, *Clin Neurophysiol, 111,* 1461-1468).

However, findings like this could be confounded by the influence of medical treatment. To prevent this confoundation, we examined EEG gamma activity and ERPs in 15 unmedicated patients with schizophrenia and 15 healthy age and gender matched control subjects in an auditory oddball paradigm. Thereby, reduced posterior target P3 amplitudes were found for patients with schizophrenia as compared to healthy control subjects, indicating a disturbed attentional target processing. In addition, patients with schizophrenia showed a reduced evoked gamma-band response (at around 40 Hz) in a later time interval between 220 to 350 ms. This effect was observed over frontal scalp areas (see Figure 11). Evoked gamma-band responses in an earlier time interval between 40 to 60 ms did not differ between patients and healthy controls. However, since fast oscillatory activations have been shown to play an important role in cortical networks, we hypothezise that the reduced late anterior gamma activity reflects a disturbed network processing of targets in patients with schizophrenia.

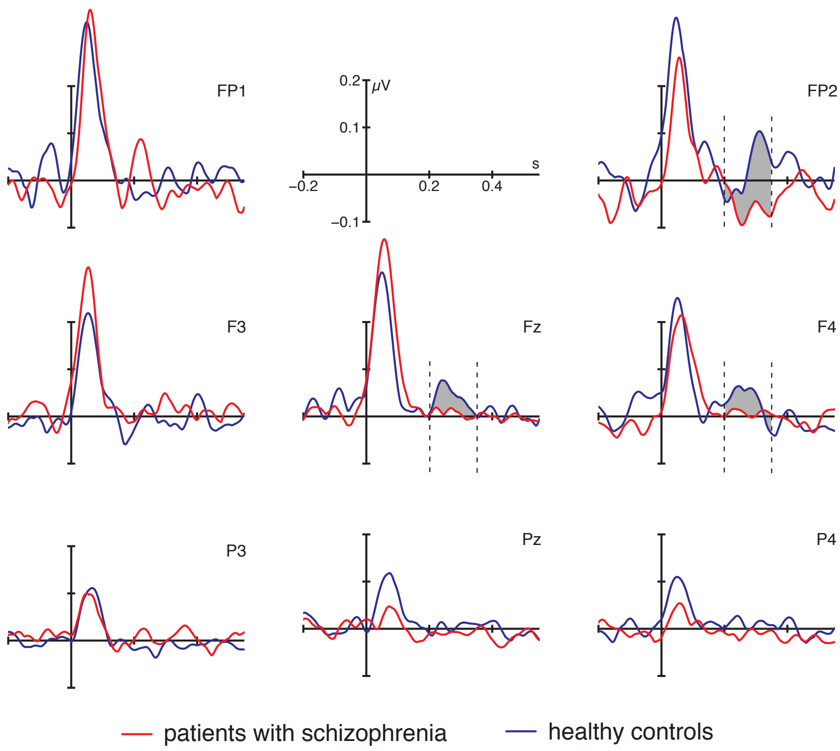

Figure 11. Evoked EEG gamma activity averaged across 15 unmedicated schizophrenics (blue line) and 15 healthy control subjects. A significantly reduced gamma activity was found for the patients with schizophrenia over anterior right scalp regions in a time range between 220 to 350 ms. No differences were found for an earlier time range of about 70 ms.

Integration of conductivity anisotropy in high resolution finite element head models

2.10.11

Wolters, C.H.[1,2], Anwander, A.[2], Koch, M.[3] & Svensén, M.[2]

[1] *Max Planck Institute for Mathematics in the Sciences, Leipzig*
[2] *Max Planck Institute of Cognitive Neuroscience*
[3] *Universitätsklinikum Hamburg-Eppendorf, Neurologische Klinik*

Supported by the European Commission

In EEG/MEG source reconstruction the human head is modeled as a volume conductor. The skull and the White Matter (WM) are known to have anisotropic conductivity with a ratio of up to 1:10. Recently, formalisms have been described for relating the effective electrical conductivity tensor of WM tissue to the effective water diffusion tensor as measured by Diffusion Tensor Magnetic Resonance Imaging (DT-MRI). This study presents methods for creating realistically shaped high resolution Finite Element (FE) models of the human head with anisotropically conducting compartments skull and WM. A prerequisite for a realistic modeling is the segmentation of head tissues with different conductivity properties. We used a bimodal T1-/PD-MRI approach, yielding in particular an improved segmentation of the inner skull surface (see Annual Report 2001, 2.4.1, 2.4.4). We generated a surface-based high resolution tetrahedral FE tessellation of the relevant 5 compartments skin, skull, CSF, brain gray and white matter. The resulting model consists of 892115 tetrahedra elements. An anisotropic conductivity tensor was assigned to each element in the skull and the WM compartment. The conductivity tensors in the skull layer were determined from the radial directions in the skull (see Annual Report 2001, 2.4.4). The anisotropic WM compartment was generated from a whole head DT-MRI registered on the T1 image. For the WM finite elements we used conductivity tensors with simulated eigenvalues longitudinal and transversal to the fiber directions. The conductivity tensor eigenvectors were taken over from the DT eigenvectors. Tensor validation and visualization was carried out with the SIMBIO visualization module.

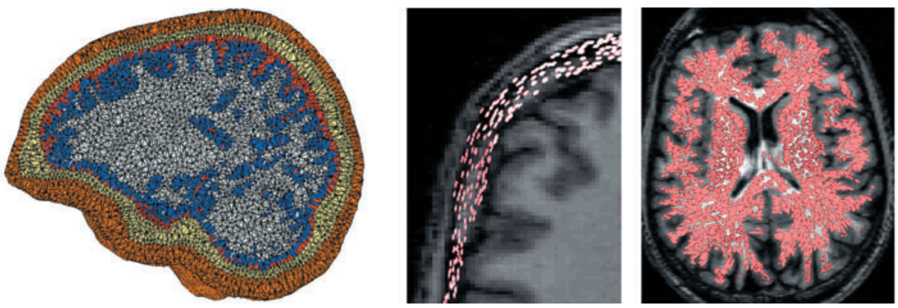

Figure 12. High resolution tetrahedral FE model (left) with conductivity tensors in the barycenters of skull elements (middle) and WM elements (right).

2.10.12 Influence of tissue anisotropy on EEG/MEG field distribution

Wolters, C.H.[1,2] *&*
Anwander, A.[2]

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[2] *Max Planck Institute of Cognitive Neuroscience*

The influence of skull and WM anisotropy in tetrahedral (see 2.10.11) and surface-smoothed hexahedral (see Annual Report 2000, 2.11.3 and 2.11.4) FE head models is studied now. Tensor eigenvalues were simulated following a volume constraint, i.e., the tensor volume was kept constant for a given anisotropy ratio. Each magnetometer flux transformer of our BTI 148 channel MEG system was modeled by means of a thin, closed conductor loop with realistic diameter, using 8 isoparametric quadratic finite row elements (see Figure 14, left). Efficient solutions for the FE linear equation systems were achieved by means of a parallel AMG-CG method (see Annual Report 2001, 2.4.3). Skull anisotropy strongly changed the head surface isopotential distribution (Figure 13, left, middle left). An increased current flow along the fibre bundles of the cortico-spinal tract can be observed in case of WM anisotropy (Figure 13, middle right, right). The MEG is only influenced by WM anisotropy (Figure 14, middle and right).

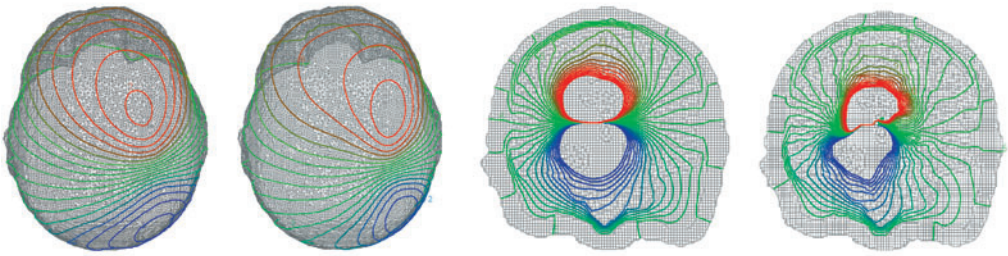

Figure 13. Isopotential distribution of a tangentially oriented somatosensory source on the head surface of the tetrahedral model for isotropic (left) and 1:10 anisotropic skull layer (middle left) and of a thalamic source on a coronal slice of the hexahedral model for isotropic (middle right) and 1:10 anisotropic WM compartment (right).

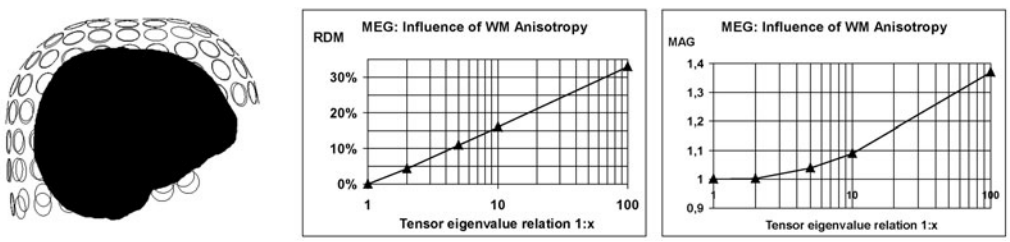

Figure 14. Modeled 148 channel BTI-MEG together with the outer surface of the head model (left) and MEG topography (RDM, middle) and magnitude error (MAG, right) due to WM anisotropy for a mainly radially oriented superficial source in the somatosensory cortex.

Sensitivity of EEG single dipole fit towards conductivity anisotropy

2.10.13

Anwander, A.[1], Wolters, C.H.[1,2], Dümpelmann, M.[3] & Knösche, T.R.[1]

[1] Max Planck Institute of Cognitive Neuroscience
[2] Max Planck Institute for Mathematics in the Sciences, Leipzig
[3] ANT Software, Enschede, The Netherlands

Supported by the European Commission

The sensitivity of the EEG continuous single dipole fit towards skull and WM anisotropy was studied for 43 mainly radially and 46 mainly tangentially oriented neocortical sources. The 71 electrode EEG forward simulation in a 1:10 anisotropic (both, WM and skull) high resolution tetrahedral FE model (see 2.10.11 and 2.10.12) was used as reference data for the inverse dipole fit procedure in the corresponding isotropic model. The reconstruction method exploited a Nelder-Mead simplex algorithm from the SimBio inverse source reconstruction toolbox. Tangential sources are localized too deeply in the temporal lobe and too superficially in particular in parietal and occipital areas. The localization error was mainly due to skull anisotropy and only to a minor degree due to WM anisotropy. A non-negligible orientation error was observed for both WM and skull anisotropy.

Anisotropic tissue	Reference source	(Abs.) Localization error (in mm)		(Abs.) Orientation error (in degrees)		(Rel.) Strength error (in percent)	
		Max	mean	Max	mean	max	mean
skull	tangential	18	8.6	55	19	201	29
	radial	8.8	4.6	35	10	154	56
white matter	tangential	5.8	2.5	26	11	43	15
	radial	6.3	2.1	25	7	63	18

Table 1. Influence of anisotropy on single dipole fit reconstruction for neocortical sources.

Figure 15 shows the EEG source localization errors due to 1:10 anisotropy of skull and WM compartment. The pole is at the position of the simulated dipole, it points to its inverse localization result. Reference sources with large radial (left) and large tangential orientation component (middle and right) are underlying the simulations. Errors are presented on (transparent) WM and inner skull surfaces.

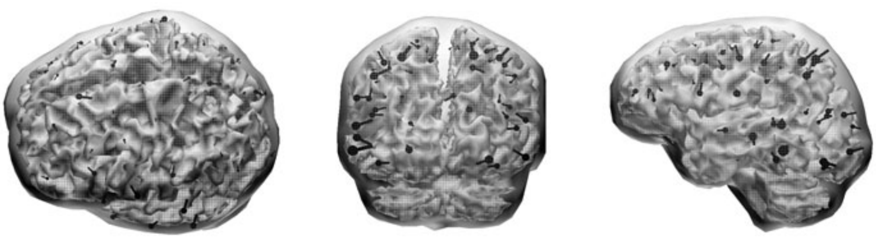

Figure 15. EEG localization errors due to 1:10 anisotropy of skull and WM compartment.

2.10.14 ELAN: Sensitivity of EEG/MEG L1 current density method towards tissue anisotropy

Wolters, C.H.[1,2], *Anwander, A.*[2], *Maess, B.*[2] & *Friederici, A.D.*[2]

[1] *Max Planck Institute for Mathematics in the Sciences, Leipzig*
[2] *Max Planck Institute of Cognitive Neuroscience*

It is currently believed that activated cortical areas in temporal as well as fronto-lateral regions of both hemispheres are responsible for evoking the Early Left Anterior Negativity (ELAN) ERP component. The supposed ELAN sources are shown in Figure 16 (left, middle left). Simulated EEG and MEG data for the 4 focal dipoles, computed either in the isotropic (corresponding reconstruction results are shown in red) or in the 1:10 anisotropic (both WM and skull) (corresponding reconstruction results are shown in blue) high resolution tetrahedral FE model (see 2.10.11 and 2.10.12), were used for the inverse current density reconstruction by means of the L1 norm method in the isotropic FE model. The L-curve method was used for the fixation of the regularization parameter. For EEG, anisotropy led to a shift of the reconstructed center of activity along the Sylvian fissure in anterior direction (Figure 16, middle right and right), whereas the MEG reconstruction result was observed to be more focused and insensitive to the modeled tissue anisotropy (Figure 17).

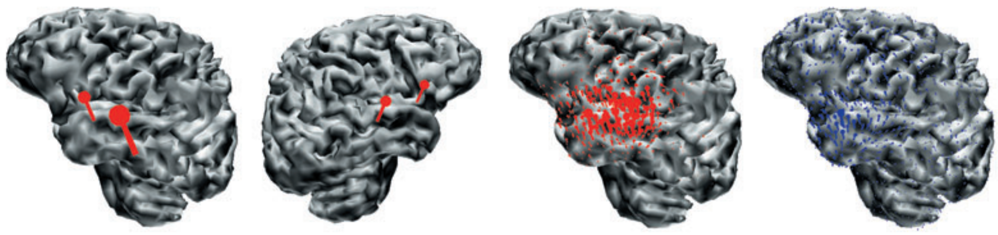

Figure 16. The 4 ELAN reference dipoles (left, middle left) and the L1 norm current density reconstruction results for 71 electrode EEG data produced in isotropic (middle right) and anisotropic model (right). The reconstruction results are only shown for the left hemisphere.

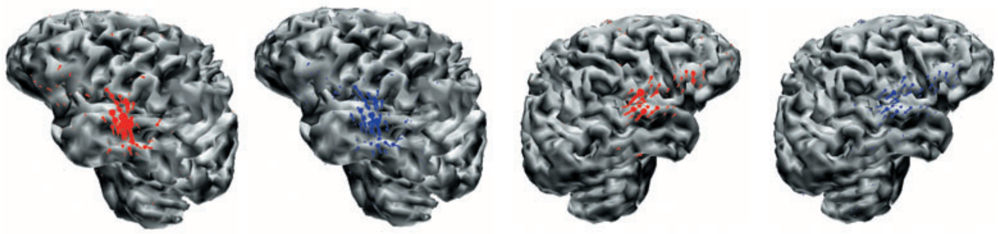

Figure 17. L1 norm current density reconstruction results for 148 channel MEG data produced in isotropic (corresponding reconstruction results are shown in red) and anisotropic model (corresponding reconstruction results are shown in blue).

An fMRI-constrained MEG source analysis with procedures for dividing and grouping activation

2.10.15

Fujimaki, N.[1], Knösche, T.R.[2], Hayakawa, T.[1], Nielsen, M.[1] & Miyauchi, S.[1]

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[2] *Max Planck Institute of Cognitive Neuroscience*

To analyze neural activity using magnetoencephalography (MEG) and functional magnetic resonance imaging (fMRI), we developed a method for fixing equivalent current dipoles of MEG in activation areas of fMRI. The method is schematically depicted in Figure 18. It includes a procedure for dividing large fMRI activation volumes into subvolumes in each of which a dipole is placed and another procedure for grouping neighboring dipoles whose temporal changes are inseparable based on MEG data. To optimize the procedures' parameters, we carried out simulations and found that any single dipole within 10 mm from a true source can explain MEG data with a correlation of 94% on average for the low signal-to-noise ratio of 3. Larger fMRI activation volumes need to be split up. This means that normally activations separated by more than 2 cm are principally distinguishable. For details, see Fujimaki et al. (2002). We applied the method to data measured in a language experiment and detected 13 significant sources. The results show that the present method is promising for detecting neural activity originating from a number of separate neural sources.

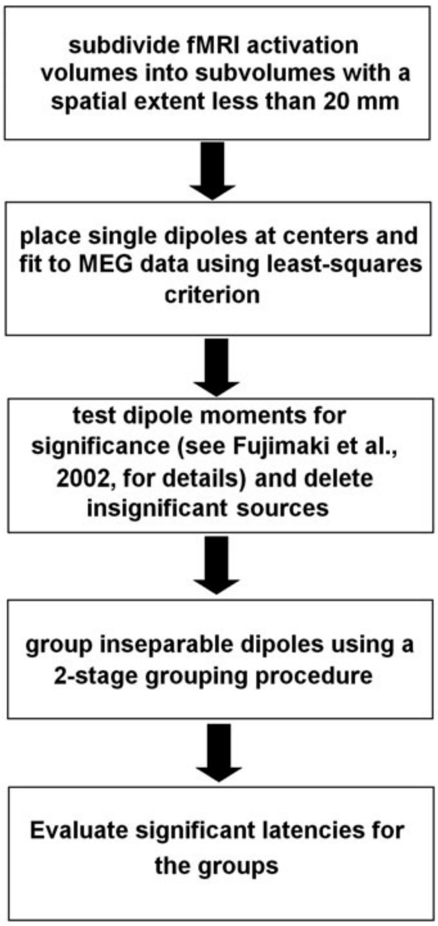

Figure 18. Schematic overview on the proposed method.

2.10.16 Multiple subjects analyses of MEG datasets

Nakamura, A., Maess, B. & Knösche, T.R.

In order to analyze multi-subjects MEG datasets more reliably, more objectively, and less time consumingly, we have developed a new procedure and its related tools. This method consists of three main parts as follows. 1) At first, we created a realistic head model using individual brain MRI, and also a brain envelope which has 1222 data points on its surface (the number of the points is changeable), for each subject. Then current density on the envelope in a realistically shaped volume conductor was calculated individually using the Minimum Norm Least Squares Technique. 2) Each individual MRI was spatially normalized onto Talairach's standard brain by linear transformation. Each brain envelope with current density data was also normalized using the same transformation parameters. Then all of the individual current density values were projected onto the standardized data points using a linear interpolation. 3) In the spatially normalized space, we could calculate averaged magnitudes of the current density (Figure 19A), condition differences of the current density (Figure 19B), statistically significant activation from the base line, and statistically significant condition differences (Figure 19C). At any region of interest on the Talairach's atlas, we could extract time courses of the brain electric activities (Nakamura et al., Annual Report 2002). Scripts for Matlab, Perl and Excel are available to automate those processes. This new analytic method provides several advantages: 1) We can extract inter-individually common activation site more easily and objectively than before. 2) We can assess the accurate functio-anatomical correlation by means of the Talairach coordinates and Broadmann's area. 3) We can easily combine/compare MEG data with other modalities, such as fMRI or PET.

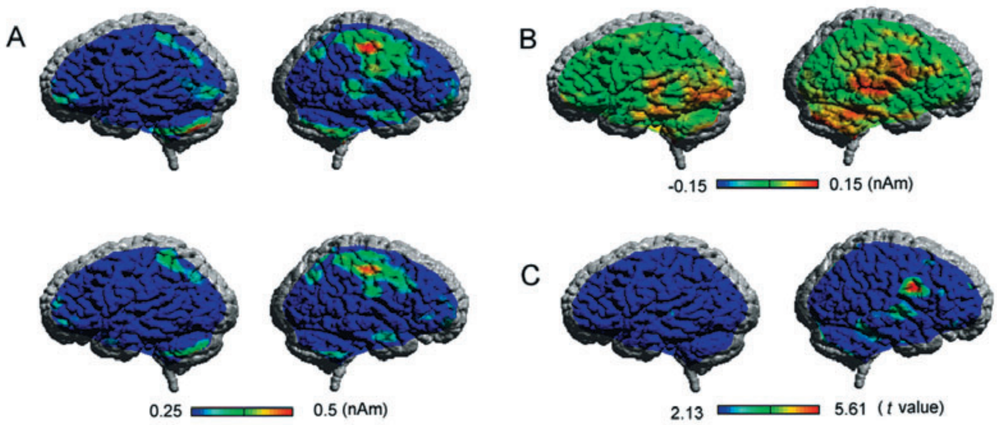

Figure 19. Representative outputs of the methods. The data sets were from the experiment for hand posture recognition (Nakamura et al., Annual Report 2002) in the time window from 360 to 380 ms after stimuli. A: averaged current density map following the meaningful hand (upper) and meaningless hand (lower) presentation. B: subtracted current density map (meaningful – meaningless). C: *t*-map of the two condition (without multiple comparison).

Teaching

3.1

SOMMERSEMESTER 2002

Methoden der kognitiven Neurowissenschaften
Katholische Universität Eichstätt
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Fiebach, C.J. & Koelsch, S.

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Otto-von-Guericke-Universität Magdeburg
Herrmann, C.S.

Grundlagen der Neurowissenschaften 1
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Herrmann, C.S.

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Schröger, E., Call, J., Gunter, T.C. & Kotz, S.A.

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Psychopharmakologie
Martin-Luther-Universität Halle-Wittenberg
Maertens, M.

Methoden der biomedizinischen Kernspinresonanzbildgebung und –spektroskopie
Universität Leipzig
Möller, H.E.

Biologische Psychologie
Universität Leipzig
Schröger, E., Gunter, T.C. & Kotz, S.A.

Committees and memberships

Prof. Dr. Angela D. Friederici

Max Planck Society

- Member of the Senate of the MPG
- Committee: Forschungsperspektiven der Biologisch-Medizinischen Sektion
- Committee: Kunsthistorisches Institut in Florenz
- Committee: Max-Planck-Institut für Hirnforschung, Frankfurt
- Committee: Max-Planck-Institut für physiologische und klinische Forschung, Bad Nauheim
- Committee: Max-Planck-Institut für Bildungsforschung, Berlin
- Committee: Nachwuchsgruppe "Neurokognition der Musik", MPI für neuropsychologische Forschung, Leipzig

University of Leipzig

- Zentrum für Kognitionswissenschaften/Center for Cognitive Science
  Director
- Member of the DFG Research Group "Arbeitsgedächtnis"/Working Memory
- Member of the DFG Graduiertenkolleg "Universalität und Diversität"/ Universality and Diversity
- Member of the DFG Schwerpunktprogramm "Zentrale auditorische Systeme"/ Central auditory systems
- Doctorate Committee
  Psychology
  Pedagogy
- Habilitation Committee
  Psychology
  Linguistics

University of Potsdam

- Member of the DFG Research Group "Konfligierende Regeln"/Conflicting Rules
- Member of the DFG Research Group "Frühkindliche Sprachentwicklung und spezifische Sprachentwicklungsstörungen"/Early Language Development and Specific Language Impairment
- Member of the Organization Committee "Leibniz Lectures"

University of Jena

- Member of the Scientific Council

Berlin Brandenburgische Akademie der Wissenschaften/BB Academy of Science

Active Member

German Academy of Natural Science (Leopoldina)
Active Member

Gesellschaft für Kognitionswissenschaft/Cognitive Science Society
Member

International Neuropsychological Symposium (INS)
Member

Cognitive Neuroscience Society
Member

International Neuropsychological Society
Member

Academy of Aphasia
Member

European Society of Cognitive Psychology
Member

European Neuroscience Association
Member

Deutsche Gesellschaft für Psychologie
Member

Deutsche Gesellschaft für Neurotraumatologie und Klinische Neuropsychologie
Member

Neurowissenschaftliche Gesellschaft
Member

Editorial Activities

- Action Editor of *"Brain and Cognition"*
- Member of the Editorial Board of the *"Cognitive Science Quarterly"*
- Member of the Scientific Board of the Journal *"Gehirn und Geist"*
- Member of the Editorial Board of the *"Journal of Memory & Language"*
- Member of the Editorial Board of the *"Journal of Psycholinguistic Research"*
- Member of the Advisory Board of the *"Neurolinguistik"*
- Member of the Advisory Board of the *"Psychonomic Bulletin & Review"*
- Member of the Editorial Board of the *"Zeitschrift für Experimentelle Psychologie"*
- Member of the Editorial Board *"Brain and Cognition"*, Action Editor

- Member of the Advisory Board of the *"Emerging computational neural network architectures based on neurosciences (EmerNet)"*
- Member of the Program Committee of the AMLaP Board *"Conference on Architectures and Mechanisms for Language Processing (AMLaP2002)"*
- Member of the National Advisory Board, *BIOMAG (13th International Conference on Biomagnetism),* Jena, August 10 – 14, 2002

Journal Referee
- Cerebral Cortex
- Cognitive Brain Research
- Journal of Cognitive Neuroscience
- Journal of Memory and Language
- Language and Cognitive Processes
- Memory and Cognition
- Nature Neuroscience
- Neuroimage
- Neuron
- PNAS (Proceedings of the National Academy of Sciences)
- Psycholinguistic Research
- Psychonomic Bulletin Review

Prof. Dr. D. Yves von Cramon

University of Leipzig
- Day-Care Clinic of Cognitive Neuroscience
  Director
- Interdisziplinäres Zentrum für Klinische Forschung
  (Interdisciplinary Center for Clinical Research)
  Coordinator for the "Neurosciences"
- Center for Cognitive Sciences
  Member of the Board
- Coordination Center for Clinical Studies
  Member of the Board
- Member of the DFG Research Group "Arbeitsgedächtnis"/Working Memory
- Member of the DFG Schwerpunktprogramm "Zentrale auditorische Systeme"/
  Central auditory systems
- Center for Magnetic Resonance Tomography
  Member of the Scientific Board
- Nomination Committees
  Psychology
  Neurophysiology
- Doctorate Committee
  Neurology, Neuropathology and Neurosciences
- Habilitation Committee
  Medicine

University of Jena

- Scientific cooperation with chairs of Neurology and Psychiatry

Deutsche Akademie der Naturforscher - LEOPOLDINA

Active Member
Member of the Scholarship Committee

Forschungszentrum Jülich

Member of the Scientific Board

BMBF Kompetenznetz Parkinson

Member of the External Advisory Board

Gesundheitsforschungsrat

Member of the Scientific Committee

World Federation of Neurology

Member of the Research Group on Aphasia and Cognitive Disorders

European Neurological Society

Member of the Scientific Committee of the Section Neurorehabilitation

International Neuropsychological Symposium

Member

Deutsche Gesellschaft für Neurologie (DGN)

Member
Chairman of the DGN-Committee "Cognitive Neurology"

Deutsche Gesellschaft für Klinische Neurophysiologie

Member

Deutsche Gesellschaft für Neurotraumatologie und Klinische Neuropsychologie

Member

Deutsche Gesellschaft für Neuroradiologie

Member

Neurowissenschaftliche Gesellschaft

Member

Referee

- Science
- The Journal of Neuroscience
- Brain

- NeuroImage
- Neuropsychologia
- Neuropsychology
- Journal of Neurology
- Neuroscience Letters
- Cerebrovascular Diseases
- Federal Ministry of Education and Research (BMBF)
- German Research Foundation (DFG)
- Netherlands Organisation for Scientific Research
- INSERM Expert Base
- Canada Research Chairs Program College of Reviewers

Visitors

3.3

Luciana Lau, Pamela Youde Child Assessment Centre, Hong Kong, China
7 January – 2 February 2002

Andrew Benjamin Wedel, Department of Linguistics, UC Santa Cruz, Santa Cruz, CA, USA
22 January – 26 February 2002
8 – 16 August 2002

Dr. Hartmut Dickhaus, Universität Heidelberg, Institut für Biometrie und Information, Abteilung Medizinische Informatik, Heidelberg, Germany
31 January – 1 February 2002

Dr. Orit Rubin, Ben-Gurion-University of the Negev, Department of Behavioral Sciences, Beer-Sheva, Israel
3 – 22 February 2002
16 – 28 June 2002

Dr. Iring Koch, Max-Planck-Institut für psychologische Forschung, Munich, Germany
5 – 8 February 2002

Prof. Dr. Nachshon Meiran, Ben-Gurion-University of the Negev, Department of Behavioral Sciences, Beer-Sheva, Israel
5 – 8 February 2002

Prof. Dr. Demetri Terzopoulos, New York University, Media Research Lab, New York, NY, USA
11 – 14 February 2002

Prof. Dr. Ulrich Hartmann, FB Mathematik und Technik, RheinAhrCampus, Remagen, Germany
17– 24 February 2002

Omer Heymann, Tel Aviv University, Department of Electrical Engineering-Systems, Tel Aviv, Israel
30 March – 6 April 2002

Prof. Dr. Kenneth Hugdahl, Biological Psychology, University of Bergen, Department of Biological and Medical Psychology, Bergen, Norway
6 – 10 May 2002
30 September – 5 October 2002
13 – 24 October 2002
18 – 24 November 2002

Beate Sabisch, Institut und Poliklinik für Kinder- und Jugendpsychiatrie, Ludwig-Maximilians-Universität, Munich, Germany
13 May – 7 June 2002

Prof. Dr. Herbert Schriefers, Nijmegen Institute for Cognition and Information (NICI), Nijmegen University, Nijmegen, The Netherlands
2 – 15 June 2002

Dr. Matthias Schlesewsky, Department of Linguistics, University of Potsdam, Potsdam, Germany
3 – 28 June 2002

Prof. Dr. Daniela Perani, Istituto di Neuroscienze e Bioimmagini, - CNR, Milano, Italy
6 – 23 July 2002

Dr. Adam Ussishkin, Department of Linguistics, University of Arizona, Tucson, AZ, USA
8 July – 16 August 2002

Dr. Sophie Scott, Departments of Psychology and Phonetics, University College London, London, UK
1 – 31 August 2002

Dr. Martin Meyer, Centre for Functional Imaging Studies, Institute for Adaptive and Neural Computation, Division of Informatics, The University of Edinburgh, UK
4 – 18 August 2002
16 – 23 November 2002

Prof. Dr. Axel Mecklinger, Experimental Neurospsychology Unit, Department of Psychology, Saarland University, Saarbrücken, Germany
5 – 16 August 2002

Dr. Jubin Abutalebi, Istituto di Neuroscienze e Bioimmagini, - CNR, Milano, Italy
3 September 2002

Dr. Matthew Davis, UK Medical Research Council, Cognition and Brain Sciences Unit, Cambridge, UK
7 – 15 October 2002

Dr. Gabriella Vigliocco, Department of Psychology, University College London, London, UK
1 – 7 December 2002

Guest lectures 3.4

Prof. Demetri Terzopoulos, New York University, Media Research Lab, New York, NY, USA
Artificial animals: From physics to intelligence
13 March 2002

Prof. Kenneth Hugdahl, Department of Biological and Medial Psychology, University of Bergen, Bergen, Norway
Auditory laterality - The forgotten dimension in brain asymmetry studies?
8 May 2002

Dr. Roman Goldenberg, Technion, Computer Science Department, Haifa, Israel
Cortex segmentation - A fast variational geometric approach
27 May 2002

Dr. Matthias Schlesewsky, Department of Linguistics, University of Potsdam, Potsdam, Germany and *Ina Bornkessel,* Max Planck Institute of Cognitive Neuroscience, Leipzig, Germany
The argument dependency model: Neurophysiological evidence and typological consequences
19 June 2002

Dr. Katrin Krumbholz, Institut für Medizin, Forschungszentrum Jülich, Jülich, Germany
Magnetoencephalographische Messungen zur Untersuchung der Darstellung von Frequenz und Tonhöhe im auditorischen Kortex
3 July 2002

Prof. Dr. Stefano Cappa, Department of Psychology, University Vita-Salute San Raffaele, Milano, Italy
Transcranial magnetic stimulation as a tool to test predictions from neuroimaging
10 July 2002

Prof. Dr. Daniela Perani, Istituto di Neuroscienze e Bioimmagini, - CNR, Milano, Italy
Language comprehension and the access to motor reprensentations
10 July 2002

Dr. Jan Modersitzki, Institute of Mathematics, University of Lübeck, Lübeck, Germany
Medical image registration
24 July 2002

Dr. Anja Ischebeck, Nijmegen Institute for Cognition and Information – NICI, University of Nijmegen, Nijmegen, The Netherlands
Reading in a regular orthography: An fMRI study investigating the role of visual familiarity
21 August 2002

Dr. Marc Pell, School of Speech and Communication Disorders, McGill University, Montreal, Canada
Emotional prosody and the brain: Insights from patients
23 September 2002

Dr. Matt Davis, MRC Cognition and Brain Science Unit, Cambridge, UK
Hierarchical processes in spoken language comprehension
8 October 2002

Dr. Antoni Rodriguez-Fornells, Departamento Psicologia Bàsica, Universitat de Barcelona, Barcelona, Spain
A neuroimage approach to word reading and language production in fluent bilinguals using ERPs and fMRI
6 November 2002

Prof. Dr. Albrecht Schneider, Musikwissenschaftliches Institut, Universität Hamburg, Hamburg, Germany
Musikwahrnehmung zwischen Psychoakustik und Kognition
27 November 2002

Congresses, workshops and colloquia

Congresses

BIOMAG 2002, 13th International Conference on Biomagnetism
Maess, B., Knösche, T.R. and
Anwander, A., Friederici, A.D., Nakamura, A., Schauer, M., Sivonen, P.H. & Wolters, C.H.
Jena, Germany, August 2002.

Conference on *"Semantic Role Universals"*
Bornkessel, I., Friederici, A.D., and
Comrie, B. (Max Planck Institute for Evolutionary Anthropology, Leipzig, Germany)
Schlesewsky, M. (Philipps University Marburg, Germany)
MPI of Cognitive Neuroscience and MPI for Evolutionary Anthropology, Leipzig, Germany
Leipzig, Germany, December 2002.

Workshops and colloquia

Symposion "Language as a Dynamical System"
Bornkessel, I., and
Schlesewsky, M. (Philipps University Marburg, Germany)
44. Tagung experimentell arbeitender Psychologen (TeaP 2002), Chemnitz, Germany, March 2002.

Workshop "Textverstehen und Textproduktion bei Aphasie: Diagnostik und Therapie"
Ferstl, E.C. and
Engell, B. (Universitätsklinikum RWTH Aachen, Germany)
5. Würzburger Aphasie-Tage, Würzburg, Germany, February 2002.

Workshop "Einführung in die Neurolinguistik: Aphasische und nicht-aphasische Sprachstörungen"
Ferstl, E.C., Kotz, S.A.,
Guthke, T. & Regenbrecht, F. (Day-Care Clinic of Cognitive Neurology, University of Leipzig, Leipzig, Germany)
Fortbildungsakademie der Gesellschaft für Neuropsychologie, Leipzig, Germany, November 2002.

Workshop "Diagnostik und Therapie nicht-aphasischer Sprachstörungen"
Ferstl, E.C.
Fortbildungsreihe zur Sprachtherapie, Brandenburgklinik Wandlitz, Bernau, Germany, September 2002.

Sprache und Gehirn: Einblicke in die aktuelle neurokognitive Forschung zur Sprachverarbeitung (Arbeitsgruppe)
Hahne, A. & Fiebach, C.J.
43. Kongress der Deutschen Gesellschaft für Psychologie (DGP), Berlin, Germany, September, 2002.

Bewusstseins-Workshop *"Forschungsansätze im interdisziplinären Dialog"*
Herrmann, C.S., Pauen, M., Rieger, J. & Schicktanz, S.
Otto-von-Guericke-Universität, Magdeburg, Germany, September 2002.

Minisymposium zur 'zerebralen Mikroangiopathie'
Hund-Georgiadis, M., Preul, C., Schroeter, M. & von Cramon, D.Y.
75. Kongress Deutsche Gesellschaft für Neurologie (DGN) mit Fortbildungsakademie, Mannheim, Germany, September 2002.

Workshop *"Forward and Inverse Modeling"*
Knösche, T.R. & Maess, B.
13th International Conference on Biomagnetism (BIOMAG), Jena, Germany, August 2002.

"Session Modeling: Forward Problem" and *"Session Modeling: Inverse Problem"*
Knösche, T.R. & Maess, B.
13th International Conference on Biomagnetism (BIOMAG), Jena, Germany, August 2002.

Tutoriumsvorlesung "Methoden der Analyse von fMRI Daten"
Lohmann, G.
Bildverarbeitung in der Medizin (BVM), Leipzig, Germany, March 2002.

Educational Program: "Bayesian Methods in fMRI"
Lohmann, G.
8th International Conference on Functional Mapping of the Human Brain (HBM), Sendai, Japan, June 2002.

Satellite Symposium "MEG – A Tool for Research on Language and Music Perception"
Maess, B., Knösche, T.R. and
Anwander, A., Friederici, A.D., Nakamura, A., Schauer, M., Sivonen, P.H. & Wolters, C.H.
13th International Conference on Biomagnetism (BIOMAG), Max Planck Institute of Cognitive Neuroscience, Leipzig, Germany, August 2002.

International Workshop "From Senses to Language: Perceptual, Cognitive, and Neuropsychological Perspectives on Normal and Impaired Language Development"
Weissenborn, J. (Universität Potsdam, Institut für Linguistik, Potsdam, Germany) and
Hahne, A. & Friederici, A.D.
organized by Max Planck Institute of Cognitive Neuroscience, Leipzig and
Research Group "Early Language Development and Specific Developmental Language Disorders", Berlin (financed by the German National Science Foundation [DFG])
Harnack-Haus, Berlin, Germany, June 2002.

Degrees 4.1

Habilitations / Venia legendi

Dr. Kai Alter	Habilitation in 'Allgemeine Sprachwissenschaften', Dr. phil. habil. Venia legendi for 'Allgemeine Sprachwissenschaften' Universität Leipzig
Dr. Christoph S. Herrmann	Habilitation in 'Psychologie', Dr.-Ing. habil. Venia legendi for 'Psychologie' Universität Leipzig Appointment to Professor of Biological Psychology (C3), Otto-von-Guericke-Universität Magdeburg
PD Dr. Harald E. Möller	Venia legendi for 'Biophysikalische Chemie', Dr. rer. nat. habil. Universität Leipzig
Dr. Ulrich Müller	Habilitation in 'Psychiatrie', Dr. med. habil. Venia legendi for 'Psychiatrie' Universität Leipzig

Doctoral Degrees

Ina Bornkessel	Doktor der Philosophie, Dr. phil. Universität Potsdam
Peggy Bungert	Doktor der Naturwissenschaften, Dr. rer. nat. Universität Leipzig
Mónica de Fillipis	Doktor der Naturwissenschaften, Dr. rer. nat. Universität Leipzig
Christin Grünewald	Doktor der Philosophie, Dr. phil. Universität Saarbrücken

Grit Hein	Doktor der Naturwissenschaften, Dr. rer. nat. Humboldt-Universität Berlin
Sonja Lattner	Doktor der Philosophie, Dr. phil. Universität Potsdam
Sandra Muckl	Doktor der Philosophie, Dr. phil. Universität Leipzig
Annett Schirmer	Doktor der Naturwissenschaften, Dr. rer. nat. Universität Leipzig
André Szameitat	Doktor der Naturwissenschaften, Dr. rer. nat. Universität Leipzig
Kristina Uhl	Doktor der Naturwissenschaften, Dr. rer. nat. Universität Leipzig
Susanne Wagner	Doktor der Philosophie, Dr. phil. Universität Potsdam
Ralph Weidner	Doktor der Naturwissenschaften, Dr. rer. nat. Universität Leipzig

4.2 Awards

Alfred Anwander, Carsten H. Wolters, Matthias Dümpelmann & Thomas R. Knösche	Young Investigators Award for Poster Presentation 13th International Conference on Biomagnetism (BIOMAG), Jena, August 2002
Marianne Maertens	PhD Fellowship of the Gertrud Reemtsma Foundation
Kirsten Volz	Jane Beattie Memorial Scholarship 2002

PUBLISHED BOOKS AND BOOKCHAPTERS 5.1

Alter, K. (2002).
Suprasegmentale Merkmale und Prosodie in der Sprachproduktion.
In H.M. Müller (Ed.), *Arbeitsbuch Linguistik* (pp. 148-169), Paderborn: UTB-Ferdinand Schöningh.

Alter, K. (2002) [2001].
Prosodie: Sprachproduktion und -perzeption.
Habilitation, University of Leipzig.

Alter, K. (in press).
Prosodie.
In G. Rickheit, T. Herrmann & W. Deutsch (Eds.), *Psycholinguistics - An International Handbook,* Berlin: Walter de Gruyter.

Bornkessel, I. (2002).
The Argument Dependency Model: A neurocognitive approach to incremental interpretation.
In Max Planck Institute of Cognitive Neuroscience (Ed.), *MPI Series in Cognitive Neuroscience*, *vol. 28,* Leipzig.

de Filippis, M. (2002).
Die visuelle Verarbeitung unbeachteter Wörter: Ein elektrophysiologischer Ansatz.
In Max Planck Institute of Cognitive Neuroscience (Ed.), *MPI Series in Cognitive Neuroscience*, *vol. 25,* Leipzig.

Fiebach, C.J. (2002).
Working memory and syntax during sentence processing. A neurocognitive investigation with event-related potentials and functional magnetic resonance imaging.
In Max Planck Institute of Cognitive Neuroscience (Ed.), *MPI Series in Cognitive Neuroscience*, *vol. 23,* Leipzig.

Friederici, A.D. (2002).
Neurobiologische Grundlagen der Sprache.
In H.O. Karnath & P. Thier (Eds.), *Neuropsychologie* (pp. 367-377), Berlin/Heidelberg/New York: Springer.

Friederici, A.D. (2002).
Sprache.
In H. Kettenmann & M. Gibson (Eds.), *Kosmos Gehirn,* 2. Aufl. (pp. 62-63), Bernau: Druckerei Blankenburg.

Friederici, A.D. (2002).
Sprache und Gehirn – Zur Neurobiologie der Sprachverarbeitung.
In Universität Kaiserslautern (Ed.), *Visionen* (pp. 63-75), Universität Kaiserlautern: Foto-Repro-Druck.

Friederici, A.D. & Lachmann, T. (2002).
From language to reading and reading disability.
In E. Witruk, A.D. Friederici & T. Lachmann (Eds.), *Basic functions of language, reading and reading disability* (pp. 9-22), Dordrecht: Kluwer.

Friederici, A.D., Schlesewsky, M. & Fiebach, C. J. (in press).
Wh-movement vs. scrambling: The brain makes a difference.
In S. Karimi & T. Langendoen (Eds.), *Word Order and Scrambling,* Boston: Blackwell.

Gruber, O. (2002).
The co-evolution of language and working memory capacity in the human brain.
In M. Stamenov & V. Gallese (Eds.), *Mirror Neurons and the Evolution of Brain and Language. Advances in Consciousness Research, 42 (Series B)* (pp. 77-86), Amsterdam/Philadelphia: John Benjamins.

Gruber, O., Arendt, T. & von Cramon, D.Y. (2002).
Neurobiologische Grundlagen der Stirnhirnfunktionen.
In H. Förstl (Ed.), *Frontalhirn. Funktionen und Erkrankungen* (pp. 21-47), Heidelberg: Springer.

Hein, G. (2002).
Lokalisation von Doppelaufgabendefiziten bei gesunden älteren Personen und neurologischen Patienten.
In Max Planck Institute of Cognitive Neuroscience (Ed.), *MPI Series in Cognitive Neuroscience*, *vol. 24,* Leipzig.

Herrmann, C.S. (2002).
Bedeutung von 40-Hz-Oszillationen für kognitive Prozesse.
In Max Planck Institute of Cognitive Neuroscience (Ed.), *MPI Series in Cognitive Neuroscience*, *vol. 22,* Leipzig.

Herrmann, C.S. (in press).
Neurowissenschaftliche Beiträge zur Bewusstseinsforschung.
In J.C. Schmidt, L. Schuster & H.J. Fischbeck (Eds.), *Der entthronte Mensch,* Paderborn: Mentis.

Jescheniak, J.D. (2002).
Sprachproduktion. Der Zugriff auf das lexikale Gedächtnis beim Sprechen.
Lehr- und Forschungstexte Psychologie. Neue Folge 12, Göttingen: Hogrefe.

Kotz, S.A. & Frisch, S. (in press).
Neurobiologie der Semantik in Wort und Satz: Elektrophysiologische Evidenz und Läsionsstudien.
In T. Goschke & M. Eimer, *Enzyklopädie der Psychologie*, Göttingen: Hogrefe.

Kruggel, F. & Herrmann, C.S. (2002).
Recording of evoked potentials during functional MRI.
In F.T. Sommer & A. Wichert (Eds.), *Exploratory Analysis and Data Modeling in Functional Neuroscience* (pp. 209-227), Boston, MA: MIT Press.

Lattner, S. (2002).
Neurophysiologische Untersuchungen zur auditorischen Verarbeitung von Sprecherinformation.
In Max Planck Institute of Cognitive Neuroscience (Ed.), *MPI Series in Cognitive Neuroscience*, *vol. 29,* Leipzig.

Laux, G., Becker, T. & Müller, U. (2002).
Monoamin-Oxidase-Hemmer, Klinik, Indikationen.
In P. Riederer, G. Laux & W. Pöldinger (Eds.), *Neuro-Psychopharmaka, Ein Therapie-Handbuch. Band 3. Antidepressiva, Phasenprophylaktika und Stimmungsstabilisierer, vol. 2* (pp. 489-507), Wien: Springer.

Meyer, M. (in press).
Bildgebende Verfahren (Functional neuroimaging).
In G. Rickheit, T. Herrmann & W. Deutsch (Eds.), *Psycholinguistics - An International Handbook,* Berlin: Walter de Gruyter.

Möller, H.E. (2002).
Grundlagen der MRT.
In E. Rummeny, P. Reimer & W. Heindel (Eds.), Ganzkörper-MR-Tomographie (pp. 1-26), Stuttgart: Thieme.

Müller, U., Becker, T. & Laux, G. (2002).
Monoamin-Oxidase-Hemmer, Klinik, Dosierung.
In P. Riederer, G. Laux & W. Pöldinger (Eds.), *Neuro-Psychopharmaka, Ein Therapie-Handbuch. Band 3. Antidepressiva, Phasenprophylaktika und Stimmungsstabilisierer, vol. 2* (pp. 507-509), Wien: Springer.

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Current issues in neuropsychological assessments in Japan.
In F.R. Ferraro (Ed.), *Minority and Cross-Cultural Aspects of Neuropsychological Assessment* (pp. 99-127), Frankfurt: Swets & Zeitlinger.

Opitz, B. (in press).
ERP and fMRI correlates of target and novelty processing.
In J. Polich (Ed.), *Detection of change: Event-related potential and fMRI findings,* Dordrecht: Kluwer.

Penner, Z., Weissenborn, J. & Friederici, A.D. (2002).
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In H.O. Karnath & P. Thier (Eds.), *Neuropsychologie* (pp. 677-684), Berlin/Heidelberg/New York: Springer.

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Spezialisierung zur Generalisierung: Anmerkungen zur funktionellen Neuroanatomie des ventralen frontolateralen Cortex.
In W. Hacke, M. Hennerici, H.C. Diener, K. Felgenhauer, C.W. Wallesch & E. Busch (Eds.), *Aktuelle Neurologie. Sonderband. Deutsche Gesellschaft für Neurologie. Neurologie 2002. Fortbildungsakademie der 75. Jahrestagung der Deutschen Gesellschaft für Neurologie* (pp. 357-360), Stuttgart: Thieme.

Schlesewsky, M. & Friederici, A.D. (in press).
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Schriefers, H., Jescheniak, J.D. & Meyer, A.S. (in press).
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In C. Habel & T. Pechmann (Eds.), *Sprachproduktion. Informationsvermittlung durch natürliche Sprache,* Wiesbaden: Deutscher Universitätsverlag.

Schröger, E., Kaernbach, C. & Schönwiesner, M. (2002).
Auditive Wahrnehmung und multisensorische Verarbeitung.
In J. Müsseler & W. Prinz (Eds.), *Allgemeine Psychologie* (pp. 66-117), Heidelberg: Spektrum Akademischer Verlag.

Schubotz, R.I. & von Cramon, D.Y. (in press).
Funktionelle Neuroanatomie und Pathologie der Exekutivfunktionen.
In M. Eimer & T. Goschke (Eds.), *Enzyklopädie der Psychologie, Kognitive Neurowissenschaft,* Göttingen: Hogrefe.

Tittgemeyer, M., Ryberg, T., Wenzel, F. & Fuchs, K. (2002).
Heterogeneities of the Earth' uppermost mantle inferred from controlled source seismology.
In J.A. Goff & K. Holliger (Eds.), *Heterogeneity in the Crust and Upper Mantle: Nature, Scaling, and Seismic Properties* (pp. 281-297), New York, NY: Kluwer.

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Witruk, E., Friederici, A.D. & Lachmann, T. (Eds.) (2002).
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Dordrecht: Kluwer.

Wolters, C.H., Anwander, A., Koch, M., Reitzinger, S., Kuhn, M. & Svensén, M. (in press).
Influence of head tissue conductivity anisotropy on human EEG and MEG using fast high resolution finite element modeling, based on a parallel algebraic multigrid solver.
In V. Macho & T. Plesser (Eds.), *"Forschung und wissenschaftliches Rechnen". Contributions to the Heinz-Billing Award, Gesellschaft für wissenschaftliche Datenverarbeitung mbH Göttingen, vol. 58,* http://www.mpg.de/billing/.

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5.5 PAPERS PRESENTED AT CONFERENCES

Alter, K.
Sequenzierung von Sprache.
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Alter, K.
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Information structure licenses syntax: An ERP correlate of focus processing.
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28. Arbeitstagung "Psychophysiologische Methodik", Tübingen, Germany, May/June 2002.

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75. Kongress Deutsche Gesellschaft für Neurologie, Mannheim, Germany, September 2002.

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28. Arbeitstagung "Psychophysiologische Methodik", Tübingen, Germany, May/June 2002.

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Gamma-band activity and event-related potentials reflect top-down and bottom-up processes of attention in an auditory novelty oddball paradigm.
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Elston-Güttler, K., Hahne, A. & Friederici, A.D.
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12th Conference of the European Second Language Association, Basel, Switzerland, September 2002.

Ferstl, E.C., Rinck, M., Guthke, T. & von Cramon, D.Y.
Wie aus Wörtern eine Geschichte wird: Untersuchungen zur Situationsmodellbildung beim Textverstehen.
2. Jahrestagung der Gesellschaft für Aphasieforschung und -behandlung, Oberhausen, Germany, November 2002.

Fiebach, C.J. & Friederici, A.D.
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Fiebach, C.J., Hernandez, A.E. & Friederici, A.D.
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8th Annual Conference on Architectures and Mechanisms for Language Processing, Tenerife, Spain, September 2002.

Fiehler, K. & Ullsperger, M.
Neural mechanisms of error detection and remedial actions: Electrophysiological evidence.
Conference on Assessing the Dynamics of Human Brain Functions, Marburg, Germany, August 2002.

Friederici, A.D.
Neural basis of syntactic and prosodic processes.
Annual Meeting of the American Association for the Advancement of Science (AAAS), Boston, USA, February 2002.

Friederici, A.D.
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10-jähriges Bestehen des Sozialpädiatrischen Zentrums an der Klinik für Kinder- und Jugendmedizin Lindenhof, Berlin, Germany, February 2002.

Friederici, A.D.
Neurotopologische und zeitliche Aspekte der Sprachverarbeitung.
6. Leibniz-Kolleg Potsdam "Die Natur der Sprache", Universität Potsdam, Potsdam, Germany, May 2002.

Friederici, A.D.
Wie wir Sprache verstehen: Neuronale Präzision in Raum und Zeit.
Jährliche MPG-Hauptversammlung, Universität Halle, Halle, Germany, June 2002.

Friederici, A.D.
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Friederici, A.D.
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International Society for the Study of Behavioural Development (ISSBD), Château Laurier, Ottawa, Canada, August 2002.

Friederici, A.D.

Language, Prosody, and Music.

13th International Conference on Biomagnetism (BIOMAG 2002), Friedrich-Schiller-Universität, Jena, Germany, August 2002.

Friederici, A.D.

Early MEG effects in processing language and music structure.

BIOMAG 2002 Satellite Symposium, Leipzig, Germany, August 2002.

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Neural basis of syntactic and prosodic processes.

International Symposium "Assessing the dynamics of human brain function", Session "Language and Memory", Marburg, Germany, August 2002.

Friederici, A.D.

The brain basis of syntactic and prosodic processes.

Workshop on "Language and motor integration: Neuroimaging and computational modelling" Institute for Adaptive and Neural Computation, University of Edinburgh, Scotland, September 2002.

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Opening Workshop: SLI, Genes, Developmental and Cognitive Neuroscience, Centre for Developmental Language Disorders & Cognitive Neuroscience, London, UK, October 2002.

Friederici, A.D.

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Conference "Logic and Creativity – Integrating Categorial Rules and Experience", Universität Osnabrück, Osnabrück, Germany, November 2002.

Friederici, A.D. & Kölsch, S.

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Conference "The Neuroscience and Music, Mutual interactions and implications on developmental functions", Venice, Italy, October 2002.

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9th Meeting of the Cognitive Neuroscience Society, San Francisco, USA, April 2002.

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11\. Multidisziplinäres Kolloquium der GEERS-Stiftung zur Förderung wissenschaftlicher Vorhaben zum Wohle der Hörbehinderten zum Thema "Hören lernen", Wissenschaftszentrum des Stifterverbandes für die Deutsche Wissenschaft, Bonn – Bad Godesberg, Germany, February 2002.

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The role of Broca's area in processing syntactic information: An fMRI study.

9th Meeting of the Cognitive Neuroscience Society, San Francisco, USA, April 2002.

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The neural correlates of syntactic processing during language comprehension: Evidence from fMRI.

1st Leipzig Research Festival, Leipzig, Germany, October 2002.

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9th Meeting of the Cognitive Neuroscience Society, San Francisco, USA, April 2002.

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28. Arbeitstagung "Psychophysiologische Methodik", Tübingen, Germany, May/June 2002.

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Neurologie-Fortbildung, Universitätsspital Zürich, Zürich, Switzerland, April 2002.

Hund-Georgiadis, M.
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1. Jahrestagung der Deutschen Gesellschaft für Computer- und Roboterassistierte Chirurgie e.V. (CURAC 2002), Leipzig, Germany, October 2002.

Jochimsen, T.H., Driesel, W., Norris, D.G. & Navon, G.
Feasibility of ^{17}O-based imaging methods for functional human brain studies.
German-Israeli Project Cooperation (DIP) on Magnetic Resonance Imaging Advanced Technologies in Medical and Material Sciences, Aachen, Germany, March 2002.

Knösche, T.R., Neuhaus, C., Haueisen, J., Maess, B., Alter, K., Friederici, A.D. & Witte, O.W.
An electrophysiological marker for phrasing in music, neurosciences and music.
The Neurosciences and Music, Venice, Italy, October 2002.

Köster, D.
Arbeiten am Max-Planck-Institut für neuropsychologische Forschung.
8. Psychologiestudierenden-Kongress des Bundesverbandes der Psychologie-Studierenden im BDP, Leipzig, Germany, December 2002.

Kotz, S.A.
A psychophysiological investigation of syntactic processes in patients.
Societa Italiana di Psicofisiologia, IX Congresso Nationale, Milano, Italy, January 2002.

Kotz, S.A.
Elektrophysiologische Untersuchungen syntaktischer Prozesse bei Sprachpatienten.
Bundesverband Klinischer Linguisten, Workshop Klinische Linguistik XV, Leipzig, Germany, April 2002.

Kotz, S.A., Frisch, S. & Friederici, A.D.
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9th Meeting of the Cognitive Neuroscience Society, San Francisco, USA, April 2002.

Kotz, S.A.
An electrophysiological investigation of syntactic language processes in aphasic and non-aphasic patients.
28. Arbeitstagung "Psychophysiologische Methodik", Tübingen, Germany, May/June 2002.

Kotz, S.A.
The processing and lateralization of emotional prosody: ERP and fMRI evidence.
8th International Conference on Cognitive Neuroscience, Porquerolles, France, September 2002.

Kotz, S.A.
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European Science Foundation – EMRC Exploratory Workshop, Cambridge, UK, September 2002.

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Untersuchung zur Dynamik der interoperativen Brainshift und deren Abhängigkeit vom zeitlichen Verlauf und dem Ausmaß der Tumorsektion.
2. Jahrestagung der Sektion Neuroendoskopie, Neuronavigation und intraoperative Bildgebung der DGNC, Leipzig, Germany, October 2002.

Maertens, M., Pollmann, S., von Cramon, D.Y., Lepsien, J. & Hugdahl, K.
Visuelle und auditorische Aufmerksamkeitsdefizite nach Läsion des Spleniums.
43. Kongress der Deutschen Gesellschaft für Psychologie (DGP), Berlin, Germany, September 2002.

Mengershausen, M. von, Norris, D.G. & Driesel, W.
High resolution diffusion tensor imaging with RARE at 3 Tesla.
Symposium 2002 des Sonderforschungsbereichs 294 "Moleküle in Wechselwirkung mit Grenzflächen", Leipzig, Germany, October 2002.

Möller, H.E.
NMR techniques for functional investigations of biological tissues.
Symposium "New Developments in High-Field NMR", Leipzig, Germany, April 2002.

Möller, H.E., Mildner, T. & Trampel, R.
Brain perfusion imaging based on arterial spin labeling.
German-Czech Neuroscience Meeting, Berlin, Germany, May/June 2002.

Möller, H.E.
The importance of brain phenylalanine levels: Indications from NMR spectroscopy.
Elsinore Meeting II "Phenylketonuria – Present Knowledge and Future Challenges", Elsinore, Denmark, June 2002.

Möller, H.E.
Funktionelle Charakterisierung biologischer Gewebe.
9. MDR-Treffen (Mittel-Deutsche Resonanz), Leipzig, Germany, July 2002.

Möller, H.E.
Investigation of energy metabolism in skeletal muscle using dynamic ^{31}P NMR spectroscopy.
1st International Conference on Biomedical Spectroscopy: From Molecules to Men, Cardiff, UK, July 2002.

Möller, H.E.
Strategies for functional imaging in living systems.
35th Polish Seminar on Nuclear Magnetic Resonance and its Applications, Kraków, Poland, December 2002.

Müller, J., Hahne, A. & Clahsen, H.
Storage and decomposition of morphologically complex words: How second language learners process German participles and plurals.
24. Jahrestagung der Deutschen Gesellschaft für Sprachwissenschaft (DGfS), Mannheim, Germany, February 2002.

Opitz, B. & Friederici, A.D.
Artificial language acquisition: Changes in brain activity during the course of learning.
9th Meeting of the Cognitive Neuroscience Society, San Francisco, USA, April 2002.

Schirmer, A. & Kotz, S.A.
What women can't ignore: ERPs indicate sex differences in a prosody-word-interference task.
8th International Conference on Cognitive Neuroscience, Porquerolles, France, September 2002.

Schlesewsky, M. & Bornkessel, I.
On incremental interpretation: Degrees of meaning accessed during sentence comprehension.
Conference on Variation in Form versus Variation in Meaning, Nijmegen, The Netherlands, July 2002.

Schroeter, M.L., Abdul-Khaliq, H., Diefenbacher, A. & Blasig, I.E.
Serum S100B as a marker for astrocytes and the function of the blood-brain barrier in psychiatric disorders.
5th Symposium on Signal Transduction in the Blood-Brain Barrier, Potsdam, Germany, September 2002.

Schroeter, M.L., Abdul-Khaliq, H., Diefenbacher, A. & Blasig, I.E. (2002).
Serum S100B is related to early treatment with typical antipsychotics, deficit syndrome and thought disturbance in schizophrenia.
32th Annual Meeting of the Society for Neuroscience, Orlando, FL, USA, November 2002.

Schroeter, M.L.
Imaging the empty brain. Towards a negative phrenology?
Conference "Körper aus Zahlen. Digitale Bildgebung in der Medizin und ihre Implikationen", Helmholtz-Zentrum für Kulturtechnik, Berlin, Germany, November 2002.

Senkowski, D., Herrmann, C.S., Busch, N.A., Hanisch, M. & Galliant, J.
Reduced evoked gamma activity and P300 amplitude in medication-free patients with schizophrenia indicates impaired network processing.
28. Arbeitstagung "Psychophysiologische Methodik", Tübingen, Germany, May/June 2002.

Stolterfoht, B., Hahne, A., Friederici, A.D. & Bader, M.
Word order variations – Syntactic, focus structural and prosodic revision processes.
15th Annual CUNY Conference on Human Sentence Processing, New York, NY, USA, March 2002.

Strüber, D., Herrmann, C.S., Basar-Eroglu, C. & Stadler, M.
The functional significance of alpha and gamma oscillations in EEG/MEG during the perception of multistable patterns.
28. Arbeitstagung "Psychophysiologische Methodik", Tübingen, Germany, May/June 2002.

Tittgemeyer, M., Wollny, G. & Kruggel, F.
Inverse bio-mechanical models of the human brain – Clinical applications.
Workshop on Visual Analysis, Imaged Based Computing and Applications, Warsaw, Poland, June 2002.

Trantakis, C. & Tittgemeyer, M.
Investigation of time-dependency of intercranial brain shift and it's relation to the extent of tumor removal using intraoperative MRI.
Computer Assisted Radiology and Surgery (CARS), Paris, France, July 2002.

Ullsperger, M. & von Cramon, D.Y.
Performance monitoring, error processing, and subjective error relevance.
8th International Conference on Cognitive Neuroscience, Porquerolles, France, September 2002.

Volz, K.G., Schubotz, R.I. & von Cramon, D.Y.
Brain correlates of uncertain predictions: Degrees and types of uncertainty investigated by functional Magnetic Resonance Imaging (fMRI).
Arbeitstreffen des Schwerpunktprogramms "Exekutive Funktionen" der Deutschen Forschungsgemeinschaft (DFG), Herrsching, Germany, April 2002.

Volz, K.G., Schubotz, R.I. & von Cramon, D.Y.
Brain correlates of uncertain predictions: Degrees and types of uncertainty investigated by functional Magnetic Resonance Imaging (fMRI).
2002 Annual Meeting of the Society for Judgment and Decision Making, Kansas City, MO, USA, November 2002.

Weber, C., Friedrich, M. & Friederici, A.D.
Diskrimination von Vokallänge bei Säuglingen.
2. Interdisziplinäre Tagung über Sprachentwicklungsstörungen, ISES[2], Universität Potsdam, Institut für Linguistik/Allgemeine Sprachwissenschaft, Potsdam, Germany, April 2002.

Weber, C., Lange, K., Nubel, K., Friedrich, M., Gross, M. & Friederici, A.D.
Event related potentials to speech stimuli in infants.
Joint Conference of the 9th International Congress for the Study of Child Language and Symposium on Research in Child Language Disorders, Madison, WI, USA, July 2002.

Wedel, A. & Hahne, A.
L1 influence on L2 gender processing: An ERP study comparing English and Russian native speakers' response to gender violations in German.
24. Jahrestagung der Deutschen Gesellschaft für Sprachwissenschaft: *Mehrsprachigkeit heute,* Universität Mannheim, Mannheim, Germany, March 2002.

Wolf, A., Hahne, A., Kiefer, J. & Müller, J.
Kognitive Prozesse des Sprachverstehens bei Erwachsenen und Kindern mit Cochlear-Implant.
5. Jahrestagung der Deutschen Gesellschaft für Audiologie (DGA), Zürich, Switzerland, February/March 2002.

Wollny, G., Hierl, T., Kruggel, F. & Klöppel, R.
Die Analyse von Zeitreihenaufnahmen am Beispiel einer suturalen Mittelgesichtsdistraktion.
Bildverarbeitung für die Medizin, Leipzig, Germany, March 2002.

Wollny, G., Hierl, T. & Kruggel, F.
Die Analyse von Zeitreihenaufnahmen am Beispiel einer suturalen Mittelgesichtsdistraktion.
52. Kongress der Deutschen Gesellschaft für Mund-, Kiefer- und Gesichtschirurgie, Leipzig, Germany, July 2002.

Wollny, G., Hierl, T., Kruggel, F. & Klöppel, R.
Die Analyse suturaler Mittelgesichtsdistraktion.
1. Jahrestagung der Deutschen Gesellschaft für Computer- und Roboterassistierte Chirurgie e.V. (CURAC 2002), Leipzig, Germany, October 2002.

Wolters, C.H.
Influence of tissue conductivity inhomogeneity and anisotropy to EEG/MEG source localization in the human brain.
SFB-Conference on "Computational Methods for Inverse Problems", Strobl, Austria, August 2002.

Wolters, C.H.
Fast anisotropic high resolution finite element head modeling in EEG/MEG-source localization.
13th International Conference on Biomagnetism (BIOMAG 2002), Jena, Germany, August 2002.

5.6 PAPERS PRESENTED AT COLLOQUIA

Alter, K.
Kontrastfokus in Sprachproduktion und –perzeption.
University of Leipzig, Leipzig, Germany, January 2002.

Alter, K.
Processing of laughter.
University of Saarbrücken, Saarbrücken, Germany, January 2002.

Alter, K.
Speech segmentation: The influence of informational structure.
University of Saarbrücken, Saarbrücken, Germany, January 2002.

Alter, K. & Jacobsen, T.
Articulation and acoustics: Formant structures in German vowels.
University of Leipzig, Department of Psychology, Leipzig, Germany, February 2002.

Alter, K.
Pitch processing in the right hemisphere?
University of Tübingen, Tübingen, Germany, February 2002.

Alter, K.
Processing of intonational phrases: An ERP investigation.
University of Stuttgart, Stuttgart, Germany, February 2002.

Alter, K. & Jacobsen, T.
Synthesizing German vowels.
University of Leipzig, Department of Psychology, Leipzig, Germany, May 2002.

Alter, K.
Speech segmentation in the brain.
Workshop on 'Neurobiological basis of communication', Brain Research Unit, Cambridge, UK, September 2002.

Alter, K. & Toepel, U.
Neural responses on the processing of contrastive accents.
Symposium on 'Information Structure', Lund, Sweden, December 2002.

Alter, K.
Sentence segmentation: On the influence of prosodic boundaries and accents on speech perception.
University of Lund, Lund, Sweden, December 2002.

Brass, M. & von Cramon, D.Y.
Kortikale Korrelate kognitiver Kontrolle.
Max-Planck-Institut für psychologische Forschung, München, Germany, July 2002.

Cramon, D.Y. von
Der anteriore frontomediane Cortex und "die menschliche Subjektivität"
University of Bonn, Clinic for Epileptology, Bonn, Germany, March 2002.

Cramon, D.Y. von
Der anteriore frontomediane Cortex: Theory-of-Mind oder mehr?
University of Oldenburg, Zentralkrankenhaus Bremen-Ost, Oldenburg, Germany, May, 2002.

Cramon, D.Y. von
Einblicke in die funktionelle Architektur des Frontalhirns.
Philipps-University of Marburg, Institute of Philosophy, Studium Generale "Geist und Gehirn", Marburg, Germany, June 2002.

Cramon, D.Y. von
Einblicke in die funktionelle Architektur des Stirnhirns.
Lecture, University of Ulm, Studium Generale, Ulm, Germany, October 2002.

Cramon, D.Y. von
Vorhersagen unter Unsicherheit: Eine Funktion des frontomedianen Cortex.
Scientific Colloquium at the "Freie Universität Berlin", Berlin, Germany, October 2002.

Cramon, D.Y. von
Einblicke in die funktionelle Architektur des Stirnhirns.
University of Leipzig, Studium Universale, Leipzig, Germany, November 2002.

Cramon, D.Y. von
Funktionelle Anatomie exekutiver Funktionen.
Otto-von-Guericke-University of Magdeburg, Magdeburg, Germany, December 2002.

Elston-Güttler, K., Carroll, S., Mueller, N. & Isel, F.
The (neuro)cognition of bilingualism/second language processing.
23. Jahrestagung der Deutschen Gesellschaft für Sprachwissenschaft, Mannheim, Germany, March 2002.

Ferstl, E.C.
Textverarbeitung nach Hirnschädigung: Ergebnisse aus klinischer und bildgebender Forschung.
Universitätsklinikum Aachen, Aachen, Germany, January 2002.

Ferstl, E.C.
Neuropsychologische Untersuchungen zur Sprachverarbeitung im Kontext.
Technische Universität Dresden, Dresden, Germany, January 2002.

Fiebach, C.J. & Friederici, A.D.
Syntax und die Funktion der Broca-Region: fMRT-Studien zur Verarbeitung syntaktisch komplexer Sätze.
Graduiertenkolleg Universalität und Diversität, Universität Leipzig, Leipzig, Germany, March 2002.

Friederici, A.D.
Gehirn und Sprache.
Max-Planck-Institut für Verhaltensbiologie Seewiesen, Starnberg, Germany, January 2002.

Friederici, A.D.
Processing a second language: Evidence form ERPs
The City University of New York, The Graduate Center, New York, USA, May 2002.

Friederici, A.D.
Neurokognition der Sprachverarbeitung.
Universität Potsdam, Potsdam, Germany, July 2002.

Friederici, A.D.
The interplay of syntactic, semantic and prosodic processes during comprehension: Temporal and neurotopographic constraints.
Max-Planck-Institut für Psycholinguistik, Nijmegen, The Netherlands, October 2002.

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A

Alter, K. 18, 23, 50, 56-59, 62, 163
Anwander, A. 145-148, 161, 162, 164
Arendt, T. 108, 110
Arnold, T. 128

B

Bach, P. 34-36
Becker, R. 119
Berti, S. 59
Besson, M. 61
Bornkessel, I. 19, 20, 21, 161, 163
Brass, M. 72, 84, 86, 94
Brückner, M.K. 108
Bungert, P. 163
Busch, N.A. 140, 143

C

Call, J. 151
Chalopin, C. 104, 111
Chen, H.C. 30
Comrie, B. 161
Cramon, D.Y. von 24, 33, 38, 56, 64-67, 69-74, 82-95, 97, 99, 102, 129-131, 152, 155, 162

D

de Fillipis, M. 163
Derrfuss, J. 94
Dietrich, J. 70
Driesel, W. 116, 117, 120, 122, 123
Dümpelmann, M. 147, 164

E

Elston-Güttler, K. 44, 45
Engbert, R. 151
Engell, B. 161

F

Ferstl, E.C. 95, 96, 161
Fiebach, C.J. 24, 28, 37, 43, 62, 151, 162
Fiehler, K. 31, 90
Fingberg, J. 112
Föhlisch, F. 108
Forstmann, B. 84
Friederici, A.D. 18, 20, 21, 23-25, 28, 29, 34, 36, 37, 42, 43, 44, 46, 47, 50, 56, 58, 60, 61, 69, 70, 134, 135, 148, 153, 161, 162
Friedrich, C.K. 30
Friedrich, M. 46
Fujimaki, N. 149

G

Gallinat, J. 136, 143
Georgiadis, D. 67
Gertz, H.J. 110
Görke, U. 119, 120, 124
Goschke, T. 85
Grigutsch, M. 136
Grimm, S. 139
Grube, M. 73
Gruber, O. 85, 87
Grünewald, C. 163
Gunter, T.C. 30, 32, 34, 35, 51, 52, 151, 152
Guthke, T. 161

H

Hahne, A. 43, 44, 47, 53, 162
Hanisch, M. 136
Haueisen, J. 50
Hayakawa, T. 149
Hein, G. 164
Heim, S. 25, 29
Heinke, W. 52, 62
Hensel, A. 110
Herrmann, C.S. 136, 137, 139, 140, 143, 151, 152, 162, 163
Hierl, T. 112
Hies, T. 59
Hofmann, J. 27, 69, 71
Hruska, C. 56
Huber, O. 96
Hübsch, T. 102
Hummelsheim, H. 142, 152
Hund-Georgiadis, M. 64, 66, 67, 131, 162

I

Isel, F. 58

J

Jänicke, H. 105
Jescheniak, J.D. 151, 152
Jochimsen, T.H. 117, 118, 125

K

Karch, S. 85
Keller, J. 33
Kenntner, R. 52
Khoromskaia, V. 105
Kittel, S. 87
Knoblich, G. 34
Knösche, T.R. 36, 50, 142, 146, 149, 150, 161, 162, 164
Koch, I. 72, 84
Koch, M. 145
Koelsch, S. 52, 53, 151
Körber, M. 125
Köster, D. 32
Kotz, S.A. 27, 31, 45, 51, 56, 61, 69, 70, 151, 152, 161
Kovalev, V.A. 106
Kruck, S. 59
Kruggel, F. 65, 82, 83, 103-106, 108, 110, 111, 112

L

Lattner, S. 60, 164
Lepsien, J. 75, 76
Lindner, D. 113
Lohmann, G. 64, 128, 129, 130, 131, 151, 152, 162
Lorenz, D. 106

M

Maertens, M. 74, 78, 152, 164
Maess, B. 36, 50, 134, 135, 148, 150, 161, 162
Marschhauser, A. 70
Mengershausen, M. von 118, 123
Merkle, H. 116
Meyer, M. 33, 61, 62
Mildner, T. 67, 120
Miyauchi, S. 149
Möller, H.E. 119, 121, 124, 151, 152, 163
Morrillo, M. 77
Muckl, S. 164
Müller, K. 119, 128, 129
Müller, U. 163

N

Naganawa, S. 66
Nakamura, A. 35, 36, 150, 161, 162
Navon, G. 117
Neuhaus, C. 50
Neumann, J. 130
Nielsen, M. 148
Norris, D.G. 66, 117, 119, 120-123

O

Oberauer, K. 151
Olthoff, D. 52, 62
Opitz, B. 25, 28, 29, 42

P

Pauen, M. 162
Penney, T.B. 30
Pilz, K. 134
Pollmann, S. 74-78, 151
Preul, C. 64, 113, 131, 162
Prinz, W. 34

R

Regenbrecht, F. 161
Reichert, K. 72
Riedel-Heller, S.G. 110
Rieger, J. 162
Riemer, T. 116, 125
Rinck, M. 94
Röttger, S. 139
Rübsamen, R. 38, 73
Rüschemeyer, S.A. 43

S

Sammler, D. 52
Samson, A. 97
Schauer, M. 135, 141, 161, 162
Schicktanz, S. 162
Schirmer, A. 30, 164
Schlesewsky, M. 19, 20, 21, 161
Schmidt, B.H. 51
Schönwiesner, M. 38
Schroeter, M. 162
Schroeter, M.L. 65, 82, 83
Schröger, E. 151, 152
Schubotz, R.I. 92-93

Schwarzbauer, C. 62, 119
Senkowski, D. 136, 137, 139, 140, 143
Siebörger, F. 96
Sivonen, P.H. 134, 161, 162
Smith, E.E. 37
Stolterfoht, B. 23
Strüber, D. 139
Svensén, M. 145
Swinney, D.A. 37
Szameitat, A. 164
Szymanowski, F. 98

T

Talsma, D. 137
Tittgemeyer, M. 102, 105, 108, 111, 113
Toepel, U. 33, 57
Trampel, R. 120
Trantakis, C. 113

U

Uhl, K. 164
Ullsperger, M. 88-90, 98

V

Volz, K.G. 91, 92, 164

W

Wagner, S. 32, 164
Waldmann, G. 141, 142
Weber, C. 46
Weidner, R. 164
Weih, K. 67, 122
Wendling, K. 99
Werheid, K. 72
Wetzel, T. 125
Wiggins, C.J. 121
Winterer, G. 143
Witte, O.W. 50
Wittfoth, M. 53
Woldag, H. 141, 142
Woldorff, M.G. 137
Wolf, A. 53
Wolf, H. 110
Wollny, G. 111, 112
Wolters, C.H. 145-148, 161, 162, 164

Y

Yang, F. 103

Z

Zysset, S. 66, 82, 83, 93, 97, 98, 129, 130