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ANNUAL REPORT 2001

This year the Fachbeirat of our institute met to evaluate the state of the institute within the context of the international scientific community for the second time. Besides a high level of productivity as measured by publications and by participation in international forums, the Fachbeirat appreciated the general intellectual and multidisciplinary work atmosphere in the institute, which seemed to the committee a remarkable level of success in this fundamental aspect of the life of a scientific research establishment.

Another appreciable event was the decision of the executive committee of the Max Planck Society to enable a still closer scientific cooperation between our institute and the Max Planck Institute of Psychological Research in Munich by financing some joint PhD positions for a common research initiative on 'Action Control and Action Perception'. We easily agreed on mutually interesting projects merging the conceptual and behavioral expertise of Wolfgang Prinz group in Munich with our 'know how' in the neurosciences and in particular in the field of imaging science. First results are encouraging and projects are shaping up very well. Most importantly, the dialogue between the participating researchers is blossoming to an extent that we expect a major synergy effect by binding together the strengths of both institutes.



We should mention that David Norris, the leader of our NMR group left the house to accept a Full Professorship at the University of Nijmegen. David had helped to build up the institute and in particular our NMR system from scratch and to shape young post-docs and PhD students into a well organized group of internationally competitive physicists. We very heartily thank David for his committment and wish him all the best for his new position. Despite fluctuation in its permanent staff, the activities of the NMR group continued to comprise both imaging methodology developments and research into fundamental biophysics and physiology. In October we could welcome the new leader of the NMR group, Harald Möller, who came to us from the University of Münster.

Angela D. Friederici D. Yves von Cramon Leipzig, February 2002



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2

NEUROCOGNITION OF LANGUAGE PROCESSING 2.1

Research over the last years in the Neurocognition of Language group was guided by a neurocognitive model by Friederici published in 1995 (Brain and Language). This model has received support from some of the work conducted in the past years and, moreover, has gained considerable specification with respect to certain subprocesses (2.1.1, to appear in Trends in Cognitive Sciences, February 2002).

Sentence processing. The neural basis of the processing of syntactic violations was investigated in an fMRI experiment using those sentences which were administered in a number of previous ERP studies focusing on the different processing stages in the proposed model (2.1.2). An additional fMRI study explicitly examined the role of Broca's area during syntactic processes by manipulating syntactic complexity parametrically (2.1.3).

The issue of syntactic hierarchy and thematic hierarchy is addressed in two studies, using ERPs (2.1.4) and time sensitive behavioral measures (SAT) (2.1.5). Aspects of word order variations are treated in a number of studies: a first indicating that grammar generally overrides frequency of structure (2.1.6), a second one showing that prosodic structure plays a crucial role in processing syntactically ambiguous sentences (2.1.7), a third one demonstrating that prosodic information is used to license a particular non-canonical word order (2.1.8) and a fourth one suggesting qualitative processing differences between participants with different memory capacity (2.1.9).

Word and phrase level processing. In an fMRI study it was shown that syntactic gender information and word category information are processed by two different networks with Broca's area being the common denominator and two additional areas being activated as a function of gender and word category processing respectively (2.1.10). The processing of syntactic gender mismatch is investigated in an ERP study using words and pictures (2.1.11). The processing of abstract and concrete words reveals different fMRI patterns supporting the notion of a dual coding (word and image) for concrete words (2.1.12). This notion also explains observed differences and similarities in the ERP pattern for the processing of words and pictures (2.1.13). Interestingly, reading of words acquired early evokes an increase in the activity in areas known to be activated during auditory processing, whereas late acquired words does not (2.1.14). Two additional experiments studied the neural basis (fMRI, 2.1.15) and the time course of priming (ERP, 2.1.16) during word perception. The effect of auditory and visual prime fragments on lexical access was investigated in two further ERP studies (2.1.17, 2.1.18).

A model describing lexical access of compound words as a prosody-assisted dual-route mechanism built on findings from nine behavioral experiments is proposed (2.1.17). Two ERP studies investigate the effect of morphosyntax and semantic transparency on compound processing (2.1.19, 2.1.20). The investigation of the influence of emotional-prosodic parameters on word processing reveals that women not only use this information type earlier than men (2.1.21) but, moreover, do not ignore this information even when being task irrelevant (2.1.22).

Two studies explored the neural basis (fMRI, 2.1.23) and the time course (ERP, 2.1.24) of semantic and phonological information during production. The results from the fMRI study support the notion of a common phonological processing network for production and comprehension.

2.1.1 Towards a neural basis of auditory sentence processing

Friederici, A.D.

A neurocognitive model of sentence comprehension is proposed whose temporal parameters are based on electrophysiological data and whose neurotopographical specifications are based on brain imaging data. The temporal characteristics of the model are described as consisting of three phases. Phase 1 (100-300 ms) represents the time window in which the initial syntactic structure is built up on the basis of word category information. During Phase 2 (300-500 ms), lexical-semantic and morphosyntactic pro-



Figure 1: Neurocognitive model of auditory sentence processing. The boxes represent the functional processes, the ellipses the underlying neural correlate identified either by fMRI/PET or by ERPs. Note that the neuroanatomical specification indicated by [] is based on fMRI/PET data, but that the ERP components specified in their temporal structure at the figure's left margin are assigned to their neural correlate by means of the function rather than by the localization of their generator. This holds true for the ERP components of Phase 2 and 3 as late components are hard to localize. The different distributions of the P600 and their functional nature are discussed in Friederici et al. (J. Psycholing. Research, in press). The neural correlate of the ELAN, however, has been verified by dipole localization (Friederici et al., 2000, Hum. Brain Mapp., 11, 1-11). [BA=Brodmann's area, STG=superior temporal gyrus, MTG=middle temporal gyrus, MTL=middle temporal lobe, IFG=inferior frontal gyrus]

cesses with the goal of thematic role assignment take place. During Phase 3 (500-1000 ms) the different types of information are integrated. While syntactic phrase structure building is autonomous and precedes semantic processes in the early time windows, these processes interact in the late time window. From this perspective, we argue that both psycholinguistic views, autonomous processing and interactive processing, hold in principle, but describe different processing phases during language comprehension, i.e., early versus late. The present model is thus comparable with syntax-first models as well as with those interactive models which assume late interaction, but certainly not with those that claim immediate or even predictive interaction. The model proposed does consider the interaction of prosodic and syntactic information during auditory sentence comprehension, however, without specifying its temporal structure.

The functional neuroanatomy of auditory language comprehension is described as a bilateral temporo-frontal network with the left temporal regions supporting processes of identification of phonetic, lexical and structural elements and the left frontal cortex subserving sequencing and the build up of structural, semantic and thematic relations. The right temporal region is viewed as supporting the identification of prosodic parameters, and the right frontal cortex as being involved in the processing of sentence melody. A schematic view of this model concerning the left hemispheric processes is given in Figure 1. This figure, moreover, sketches the role of working memory for the process of language comprehension. The present model is based on empirical evidence from neurophysiological studies using event-related brain potentials (ERPs) and magnetic fields (ERFs) and from imaging studies including positron emission tomography (PET) and functional magnetic resonance imaging (fMRI).

Localization of syntactic and semantic processing areas: An event-related fMRI study

The present study was centered around earlier ERP studies, in which the processing of semantic and syntactic errors in spoken sentences was investigated. Syntactic violations brought on an early negativity at around 180 ms (ELAN) followed by a P600 effect over the posterior parietal scalp. Semantic errors induced a centro-parietal N400 effect.

Using similar experimental materials we utilized event-related fMRI to investigate the neural correlates underlying these ERP results. For syntactically violated sentences vs. correct sentences we observed increased activation in the superior temporal sulcus (STS) bilaterally. In the left hemisphere increased activation is present in the inferior frontal cortex (BA44/6) extending into the anterior insular. An additional, smaller, area showing increased activation is located in the supramarginal gyrus, in the inferior parietal cortex.

Semantically anomalous sentences brought on increased levels of activation in the STS bilaterally and the insular cortex bilaterally. The STS activation increase was more pronounced than that brought on by syntactic errors, however covers less area.

2.1.2

Rüschemeyer, S.-A., Fiebach, C.J., Hahne, A. & Friederici, A.D. Our findings suggest that syntactic processing is supported by the STS, bilaterally in conjunction with left inferior frontal and left inferior parietal cortices. This largely coincides with previous studies examining auditory syntactic processing (Caplan, 2001; Ni et al., 2000; Meyer et al., 2000; Friederici et al., 2000). One goal was to examine the neural correlates of the ELAN and P600 described by Hahne (2001). A previous attempt to localize these components using MEG concluded that the ELAN is evoked from both a frontal and a temporal generator (Friederici et al., 2000). Our data support the fact that syntactic processing in this violation condition is indeed carried out in superior temporal as well as left frontal cortices.

The processing of semantic violations, on the other hand, elicited more focused bilateral activation in the STS, as well as bilateral activation in the insular cortex. In contrast to the syntactic condition, anterior portions of the left STS were not activated. These data demonstrate that semantic and syntactic violations in sentences elicited activation increases in shared superior temporal regions, but also in distinct areas. In particular, the detection (and repair) of word category violations seems to rely on left inferior frontal and inferior parietal brain regions.



Figure 2. Activation for syntactic condition vs. correct condition (above) and semantic condition vs. correct condition (below).

2.1.3 A parametric approach to syntactic processing in the brain

Fiebach, C.J.¹, Bornkessel, I.¹, Schlesewsky, M.² & Friederici, A.D.¹ ¹ Max Planck Institute of Cognitive Neuroscience, Leipzig ² Department of Linguistics, University of Potsdam

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While clinical neurolinguistic studies have established that Broca's region is involved in syntactic processing (e.g., Swinney et al., 1996; Grodzinsky, 2000), the results of functional neuroimaging experiments manipulating syntactic complexity so far are controversial in this respect. Some researchers have, mostly based on PET studies with blocked paradigms, argued that syntactically complex sentences elicit activation increases in Broca's region (e.g., Caplan et al., 1998, 1999). Other studies, however, have been unable to replicate this finding using event-related fMRI (Caplan et al., 2001; Fiebach et al., submitted). It has been suggested that previous findings of activation in Broca's region might be due mainly to syntactic working memory costs rather than to processes of syntactic integration as such (e.g., Stowe, 2000; Fiebach, Schlesewsky & Friederici, 2001).

In the present event-related fMRI study, we manipulated syntactic complexity parametrically by including an increasing number of object arguments which are moved from their canonical positions between the subject noun phrase and the verb of the sentence to the 'Mittelfeld' of the sentences. This syntactic transformation, known as scrambling, changes the word order within the sentences but does not change their meaning essentially or render sentences ungrammatical. Previous ERP work has demonstrated that scrambled sentences are harder to process and elicit a LAN component reflecting a local syntactic mismatch (Rösler et al., 1997; Friederici, Schlesewsky & Fiebach, in press). The sentences used in the present study contained three complexity conditions (i.e., low complexity, reflecting the canonical order of verb arguments; medium complexity; high complexity):

[low, canonical]	Vielleicht hat der Vater dem Baby den Schnuller gegeben. probably has the _{NOM} father the _{DAT} baby the pacifier _{ACC} given
[medium]	Vielleicht hat dem Baby der Vater den Schnuller gegeben. probably has the _{DAT} baby the _{NOM} father the _{ACC} pacifier given
[high]	<i>Vielleicht hat dem Baby den Schnuller der Vater gegeben.</i> probably has the _{DAT} baby the _{ACC} pacifier the _{NOM} father given

[translations given are word by word]

The processing difficulty induced by the increasing number of scrambled object noun phrases was assessed in a behavioral pre-test using a speeded acceptability judgement. These ratings, which reflected the theoretically assumed syntactic complexity, were used as parameters to model hemodynamic responses in the general linear model. Figure 3 shows that neural activity in the inferior tip of the inferior frontal gyrus/pars opercularis (BA44/Broca's region) correlated with this three-staged manipulation of syntactic complexity. This region, as well as a homologous area in the right inferior frontal gyrus and the pre-SMA in the medial frontal wall, exhibited increasing hemodynamic responses when the number of scrambled object noun phrases was increased. These results demonstrate that syntactic integration processes during phrase structure building indeed rely on the classical area of Broca. However, this region is not contributing in isolation but in a network comprising also a right-hemispheric homologue and medial frontal premotor regions.



Figure 3. Left inferior frontal gyrus activation reflecting an increase in hemodynamic response with increasing syntactic complexity (A). The timecourse of the BOLD response (B) reflects the activation increase from sentences with low (blue line) or medium (green line) complexity to sentences of high syntactic complexity (red line) in the area shown in (A).

2.1.4 Interactive relational processing: The role of the thematic hierarchy

Bornkessel, I.¹, Schlesewsky, M.² & Friederici, A.D.¹ ¹ Max Planck Institute of Cognitive Neuroscience ² Department of Linguistics, University of Potsdam

How and when different information types interact during sentence comprehension constitutes a central domain of investigation in psycholinguistic research. A precise characterisation of such interaction is especially important with regard to the question of how the relations between obligatory sentential constituents that determine interpretation are established.

The present ERP study examined the interaction between two information sources which contribute to a specification of the relation between subject, object and verb, namely subject-verb agreement and the thematic hierarchy. To this end, participants read ambiguous German verb-final sentences such as (1).

(1)	Gestern wurde erzählt,	dass Maria Sängerinnen folgt/folgen.		
	yesterday was told	that $Maria_{AMB.SG}$ singers $_{AMB.PL}$ follow $_{SG}$ /follow $_{PL}$		
	'Yesterday, it was said	that Maria follows singers / singers follow Maria."		

Both arguments in (1) are case ambiguous, i.e. the word order of the embedded clause is determined via the subject-verb agreement specified by the number marking of the clause final verb. Additionally, the thematic properties of this verb were varied such that it either required a hierarchical thematic ordering of the arguments in which the subject was higher than the object (active verbs, as in (1)) or a reversal of this ordering (object-experiencer verbs, e.g. *gefallen*, 'to be appealing to').

Figures 4 and 5 show grand average ERPs for active and object-experiencer verbs, respectively. Disambiguation towards an object-initial order gave rise to an N400 com-

ponent, which was smaller in the case of object-experiencer verbs. Additionally, subject-initial sentences completed by an object-experiencer verb elicited a left-anterior negativity (LAN).

We interpret the N400 as reflecting a reanalysis of the preferred object-initial order at a processing stage when no prior association between the arguments and the verb needs to be revised. Object-experiencer verbs aid this recovery, hence the smaller N400, by immediately providing the alternative hierarchisation between the arguments. The LAN, by contrast, reflects a principled mismatch between the grammatical function hierarchy (requiring that the initial argument be the hierarchically higher subject) and the thematic hierarchy (requiring that the subject be the thematically lower ranked argument). Thus, subject-verb agreement and thematic information are processed interactively within the same time range, i.e. approximately between 300 and 500 ms post onset of a word.



Figure 4. Grand average ERPs for subject- vs. object-initial sentences with active verbs.



Figure 5. Grand average ERPs for subject- vs. object-initial sentences with object-experiencer verbs.

2.1.5 The N400 as an index of reanalysis: Evidence from processing dynamics

Bornkessel, I.¹, McElree, B.², Schlesewsky, M.³ & Friederici, A.D.¹ ¹ Max Planck Institute of Cognitive Neuroscience

² Psychology Department, New York University

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Reanalysis processes in sentence comprehension are typically associated with the P600 event-related brain potential. However, a non-preferred resolution of subject-object ambiguities in German sentences such as (1) has been shown to elicit an N400 component (Bornkessel, Schlesewsky & Friederici, 2001).

(1) Gestern wurde erzählt, dass Maria Sängerinnen folgen.
yesterday was told that Maria_{AMB.SG} singers_{AMB.PL} follow_{PL}
'Yesterday, it was said that singers follow Maria.'

The present study examined the hypothesis that the N400 observed for sentences such as (1) may indeed be interpreted as reflecting reanalysis processes by means of the multiple response speed accuracy tradeoff (SAT) method (McElree, 1993). In this paradigm, participants continually judge the acceptability of a sentence while reading (by means of a button press every 350 ms). The time-course functions thus obtained may be described by three parameters: (a) an asymptote, reflecting the level of accuracy ultimately reached, (b) an intercept, describing when performance departs from chance level, and (c) a rate of rise showing how quickly accuracy increases from chance to the asymptote. Crucially, parameter differences between a condition involving a reanalysis process and a control condition should differ from those between two conditions resulting from plausibility differences (typically thought to be reflected by the N400). A reanalysis should result in a decrease in processing speed (as reflected by an intercept or a rate difference) in comparison to a control condition, since additional time will be required to compute the non-preferred reading. However, this should not be the case for an implausibility, since for these only the probability that the sentence will be judged acceptable is lower (as reflected by an asymptotic difference).



Figure 6. Time course functions for subject- and object-initial sentences (with active and object experiencer verbs). The smooth curves indicate the best fits.

Results showed that object-initial sentences required both a lower asymptotic value and a higher (i.e. slower) intercept value than their subject-initial counterparts (cf. Figure 6). The finding of a difference in processing dynamics (i.e. the intercept difference) indicates that the processes reflected in the N400 observed for sentences such as (1) may indeed by interpreted in terms of reanalysis. We assume that this particular type of reanalysis differs from a P600-eliciting reanalysis of subject-object ambiguities in that disambiguation is effected by a semantically contentful verb rather than a clause-final auxiliary, i.e. at a stage of processing when no associations between the predicate and its arguments have as yet been made.

Grammar overrides frequency: Evidence from the processing of word order variations

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Supported by DFG

Frequency-based accounts of on-line sentence processing difficulty have become increasingly popular with the advent of probabilistic parsing models (e.g., Jurafsky, 1996; Crocker & Brants, 2000). However, we show that online processing difficulties induced by word order variations in German cannot be attributed to the relative infrequency of the constructions in question, but rather appear to reflect the application of grammatical principles during parsing.

Event-related brain potentials (ERPs) revealed that dative-marked objects in the initial position of an embedded sentence do not elicit a neurophysiologically distinct response from subjects, whereas accusative-marked objects elicit a centrally distributed negativ-



Figure 7.

2.1.6

Bornkessel, I.¹, Schlesewsky, M.² & Friederici, A.D.¹ ity between 300 and 450 ms post-onset of the noun phrase (cf. Figure 7). These differences are predictable on the basis of grammatical distinctions (i.e., underlying linguistic properties), but not on the basis of frequency information (i.e., a superficial linguistic property). We therefore conclude that the former, but not the latter, guide syntactic integration during online parsing.

2.1.7 Word order variations in German:The processing of syntactic and prosodic structure

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A series of studies have shown that silent reading is accompanied by *inner speech*, which refers to a phonological representation of words and a representation of prosodic characteristics of sentences (Van Orden et al., 1988; Slowiaczek & Clifton, 1980). We made use of this phenomenon to investigate the time course of prosodic and syntactic processes during reading using event related brain potentials (ERP). For these purposes, we presented participants sentences with word order variations.

German has a relatively free word order. For instance, the first determiner phrase (DP, determiner + noun) after the complementizer can be either the subject or the object of the complement clause as a result of case ambiguity (nominative vs. accusative). Sentences can be constructed which are ambiguous until the number information of the finite verb appears:

Subject before Object

(1a) Maria hat gesagt, daß [die Mutter die Kinder beschäftigt hat]_F

Object before Subject

(1b) Maria hat gesagt, daß die Mutter, $[die KINDER]_{F}[t_{i}]$ beschäftigt haben.

The object-first order in (1b) results not only in a more complex syntactic structure, but also in a change of prosodic structure.

Two reading experiments allowed us to differentiate between processes of syntactic reanalysis on the one hand and the revision of the prosodic structure on the other hand.

The data analysis showed two different components in Experiment 1: An early positivity (300-400 ms, FZ), which could be interpreted as reanalysis of the syntactic structure, and a right anterior negativity (400-600 ms, F8), which might be seen as the correlate of prosodic structure revision.

To further test this hypothesis, we eliminated the difference in the prosodic structure between the two sentence types by insertion of a focus particle in front of the second DP, thus preventing the parser from a prosodic structure revision. As predicted, there was no right anterior negativity in Experiment 2, whereas the early positivity (300-400 ms) was still elicited and followed by a later positive component (500-900 ms). We



Figure 8.

interpret this later component as reflecting a syntactic process. This result indicates that the late syntactic process interacts with prosodic revision processes.

All in all, our results show that prosodic and syntactic processes can be differentiated in the ERP by their time course and distribution. Furthermore, our results suggest that prosodic structure plays a crucial role in the processing of syntactically ambiguous sentences.

Prosodic licensing of gaps in sentence comprehension

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Supported by the Leibniz Prize of the DFG awarded to Angela D. Friederici

The constraints that prosody imposes on sentence structure building are subject to recent parsing research. Most studies deal with prosodic disambiguation effects on the processing of ambiguous syntactic structures. Besides, the role of prosody in predictive parsing is discussed. There is some evidence that prosody may help to identify the base position (the gap or trace) of a fronted constituent (Nagel, Shapiro & Nawy, 1994). It has been suggested that prosodic information gives rather indirect than direct hints to the location of gaps (Straub, Wilson & Badecker, 2001).

In a series of cross-modal lexical priming experiments, we explored prosodic effects on gap-filling in German verb-final sentences. Crucially, verb-specific subcategorization information that might license the gap is not available in a preverbal position. We claim that German intonation structure gives a hint to the location of a preverbal object gap. The neutral sentence accent typically falls on the constituent immediately preceding the sentence-final verb (Féry, 1993). This regularity might help to predict the sentence-final verb position. As the verb is adjacent to the direct object's base position, the parser might exploit the predictability of the verb position for the identification of the preverbal

2.1.8

Muckel, S.¹ & Pechmann, T.² gap. To test for this possibility, we presented (1) sentences with neutral accentuation (NA) and (2) sentences with contrastive accentuation of the sentence-final verb (VA).

- (1) *Der Krug(i) ist [einem jungen Richter des Berliner (c) GeRICHTS (t(i)) zerbrochen]NA.*
- (2) Der Krug(i) ist einem jungen Richter des Berliner (c) Gerichts (t(i)) [zerBROchen]VA.
 the+NOM jug is a+DAT young judge of the Berlin court broken 'The jug broke on a young judge of the Berlin court.'

In Experiment 1, (1) yielded shorter lexical decision times for identical targets in the gap position (t(i)) as compared to a control position (c). No difference was found for unrelated targets. In Experiment 2, the reactivation effect found for identical targets in (1) was replicated. By contrast, no similar effect for identical targets was found in (2). In Experiment 3, there was no decision time difference for identical or unrelated targets with respect to probe positions in (2).

We conclude that prosodic information is used to license a direct object gap in German neutrally focused verb-final sentences.

2.1.9 Individual differences in the maintenance of preferred readings: Activation vs. inhibition

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

Approaches to (possible) individual differences in sentence processing have hitherto focused mainly on quantitative distinctions between the processing abilities of different groups of participants (Just & Carpenter, 1992; MacDonald, Just & Carpenter, 1992). Thus, high span readers are typically classified as more "efficient" sentence processors than low span readers. However, research into non-linguistic processing differences between high and low span readers indicates that the distinction between the two groups may be *qualitative*, rather than quantitative, since low span readers generally show a greater susceptibility to the interference of irrelevant information (e.g., Chiappe, Hasher & Siegel, 2000).

The present ERP study examined whether the degree of interfering information also plays a role in determining (qualitative) individual processing differences in sentence comprehension. To this end, two groups of participants (high and low span readers) read ambiguous sentences such as (1), the competing readings in which should increase the degree of interference, as well as unambiguous controls.

 Klaus fragte sich, welche Sängerin am Sonntag nachmittag hinter der Kirche Klaus asked himself [which singer]_{AMB} on Sunday afternoon behind the church

den/der Richter gesehen hat. [the judge]_{ACC/NOM} seen has Whereas high span readers showed a sustained negativity with a left-anterior focus for ambiguous in comparison to unambiguous sentences throughout the ambiguous region (cf. Figure 9, right), low span readers showed a sustained posterior positivity in the same contrast (cf. Figure 9, left). Furthermore, only high span readers showed a P600 when sentences were disambiguated towards a dispreferred reading. These results are in line with a proposal advanced in Friederici et al. (Friederici, Steinhauer, Mecklinger & Meyer, 1998) that high span readers process ambiguous sentences more efficiently because they more effectively inhibit dispreferred readings. Thus, low span readers must invest more effort into the suppression of such readings (hence the sustained positivity), while the processing of high span readers is better described in terms of a continued activation of the preferred reading (cf. Fiebach, Schlesewsky & Friederici, 2001, for evidence in this regard from the processing of unambiguous sentences).



Figure 9. Grand average ERPs throughout the ambiguous region for high span (left) and for low span (right) participants.

Processing different types of syntactic information in Broca's area: An event-related fMRI study

In so-called syntax-first models of comprehension (Frazier, 1987; Friederici, 1995) it is assumed that word category information is processed during an initial phase of phrase structure building while lexically bound gender information may be processed in a second phase. It is an open issue whether these two aspects of syntactic information processing are supported by the same brain systems. In the present event-related fMRI study, subjects performed either a gender decision task (GEN) on German nouns (masculine vs. neuter) or a word category decision task (WC, nouns vs. prepositions). A decision on the spacing in non-word letter strings served as a baseline for both syntactic tasks.

Reaction times in WC were faster than in GEN. Relative to the baseline, both syntactic tasks activated the inferior tip of BA44. In addition, BA45 showed activation in GEN, whereas BA47 was activated in WC. In the conjunction analysis of both syntactic tasks, the maximum of activation was located in the inferior tip of Broca's area (cf. Figure 10A - 10C). The time course of the BOLD signal in this activation focus was also analyzed separately for WC and GEN (cf. Figure 10, lower panel). However, due to the low temporal resolution of the fMRI data, no significant difference in the time course could be demonstrated for the two syntactic tasks.

2.1.10

Heim, S., Opitz, B. & Friederici, A.D. The behavioral results suggest that, in accordance with the syntax-first models, word class information processing precedes gender information processing in language comprehension. The imaging data show that the inferior portion of BA44 supports both early and late syntactic processes. Further research is necessary to investigate if the temporal delay between WC and GEN that was observed in the reaction time data and in earlier electrophysiological studies can also be demonstrated for the time course of neural activation in the inferior tip of Broca's area.



Figure 10. Sagittal views of the foci of significant activation in the syntactic tasks relative to the physical baseline. (A) Word category decision (section at x = -50). (B) Gender decision (section at x = -47). (C) Conjunction of word class and gender decision (section at x = -50) and time course of the BOLD signal for both syntactic tasks.

2.1.11 Gender of German nouns during word and picture processing

Hofmann, J., Kotz, S.A. & Friederici, A.D. During a lexical decision task we explored the possibility that pictures and words are processed in different semantic systems. For example, multiple semantic system models propose that pictures and words are processed in separate, specialized semantic systems. Paivio (1991) postulated a "logogen" system for words and an "imagen" system for pictures, which can communicate with one another, but operate independently. Common semantic system models assume one amodal semantic store for words and pictures (e.g., Pylyshyn, 1980; Snodgrass, 1984). In the present study subjects performed a gender decision task on German nouns (Is the noun's syntactic gender feminine or not?). Two conditions (match – feminine; mismatch – masculine, neuter) were tested with both words and picture representing objects. Reaction times were faster for

words than for pictures and faster in the match condition than in the mismatch condition. Percent correct were higher for words than for pictures in general. For picture percent correct was higher in the mismatch condition than in the match condition. ERPs revealed a greater negativity for words and pictures both in the mismatch compared to the match condition. For words the maximal effect was located over centro-frontal electrode-sites, for pictures over centro-parietal electrode-sites. The distributional difference suggests the involvement of different brain systems underlying the retrieval of syntactic gender information during word and picture processing.



Figure 11. Grand average of gender-match (blue) and gender-mismatch (red) condition for (A) pictures and (B) words displayed on selected electrode-sites.

Neural correlates of abstract and concrete word processing

We contrasted the processing of abstract and concrete words in a visual lexical decision task using event-related fMRI (cf. 2.1.3). While abstract words activated a subregion of the left inferior frontal gyrus (BA45) more strongly than concrete words, concrete words caused stronger hemodynamic responses in the left basal temporal cortex (Figure 12). The data support the assumption that the representations of concrete concepts have stronger associations to visual representations in the brain, as was proposed by dual coding theory (Paivio, 1986, 1991). The comprehension of abstract words, on the other hand, relied more on brain regions associated with effortful retrieval of semantic information. This finding is compatible with the assumption of the context availability model (Bransford & Johnson, 1972; Schwanenflugel & Shoben, 1983; Schwanenflugel, 1991) that processing abstract content words involves increased effort in order to activate contextual semantic information.

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



Figure 12. Brain areas exhibiting increased activity for abstract as compared to concrete words (A) and concrete as contrasted with abstract words (B).

2.1.13 Category verification gives evidence for multiple semantic systems

Hofmann, J. & Kotz, S.A.

One immanent question in psychology is how knowledge that can be related to either a word or a picture is stored and processed. Multiple semantic system models propose that pictures and words are processed in separate, specialized semantic systems. Paivio (1991) postulated a "logogen" system for words and an "imagen" system for pictures, which can communicate with one another, but operate independently. Common semantic system models assume one amodal semantic store for words and pictures (e.g., Pylyshyn, 1980; Snodgrass, 1984). In the present study we presented words and pictures in a category verification task (Is the picture / word part of a superordinate category or not?) contrasting two conditions (category match vs. category mismatch). Overall, reaction times were faster for pictures than for words. Percent correct were higher for words than for pictures and in the mismatch condition higher for pictures than in the match condition. In the mismatch condition a greater N400 amplitude was elicited for both words and pictures than in the match condition. For words the maximal effect was located over right and left frontal electrode-sites, for pictures the effect was found across all scalp sites. In a later time window (550-800 ms) only pictures in the mismatch condition elicited a larger negative-going component at frontal electrode-sites (see Figure 13). The N400 in both modalities might reflect amodal semantic processing. However, we observed different scalp distributions and latencies for the two modalities (pictures - global, words - frontal). The frontal distribution for words and pictures might correlate with imagery. West and Holcomb (2000) found a more frontal activation in an imagery task involving words. They interpreted this as the use of mental imagery. Furthermore, there is previous evidence reporting that picture mismatches elicit a double-peaking negativity. Both Barrett and Rugg (1990) and Federmeier and Kutas (2001) argued that the first peak could be the N300. This modality specific frontal component might reflect semantic feature activation which is more predominant for pictures than for words. In sum, we can conclude that the activation at frontal electrode-sites might reflect the imagery processing of words and pictures in a category verification task. Also, the N300 and late negative-going component might indicate modality specific ways of processing in a multiple semantic system.



Figure 13. Grand average of category-match (blue) and category-mismatch (red) for (A) pictures and (B) words displayed at selected electrode-sites.

Early and late learned words are represented differently in the brain: An event-related fMRI study

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Several factors such as frequency of occurrence or concreteness influence how words are processed by the brain. In the present study, we investigated whether the age with which one learns a word (i.e., age of acquisition/AoA) modulates adults' brain responses during visual word processing. In a single trial event-related fMRI experiment (12 axial slices of 5mm acquired at 3 Tesla, TR = 1.5 sec, TE = 30 ms), 12 participants performed a lexical decision task to visually presented words and pseudowords. Words were independently rated by 29 individuals regarding subjectively estimated age of acquisition, a rating which is known to be highly correlated with objective AoA norms (Gilhooly & Gilhooly, 1980; Morrison, Chappell & Ellis, 1997). These ratings were used as a regressor variable in a random effects model to identify brain areas respond-

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Fiebach, C.J.¹, Hernandez, A.E.², Müller, K.¹, von Cramon, D.Y.¹ & Friederici, A.D.¹ ing more strongly to early versus late learned words. Word frequency of occurrence was used as a second regressor in order to dissociate brain regions sensitive to word frequency from areas modulated by AoA. The regression of word frequency on hemodynamic responses replicated previous results (Fiebach et al., 2002; Figure 14a). Early learned words elicited stronger activity than late learned words in the left temporal operculum, including the transverse temporal gyrus, and the right precuneus (cf. Figure 14b, c). Stronger hemodynamic responses to late acquired words were observed bilaterally in inferior frontal areas (BA45/47, extending into posterior/lateral orbital frontal cortex), as well as in medial frontal and subcortical structures (cf. Figure 14c, d). We conclude that in adults, processing of early acquired words activates auditory representations which were relevant during the learning of these words. These codes, in turn, might have direct access to (implicit) episodic memories which are retrieved via the precunes. In contrast, later learned words which are more difficult to process elicited specific activity in brain areas known to be involved in effortful or strategic semantic retrieval.



Figure 14. (a) Pars triangularis (BA45, red arrow) and pars opercularis (BA44/6, yellow arrow) of the left inferior frontal gyrus exhibit increased activity for low frequency words (compare to Ref. 5). (b) Activity in left transverse temporal gyrus (arrow) for early learned words superimposed on the mean anatomical image of the 12 participants. (c) In addition to the temporal operculum/transverse temporal gyrus (yellow arrow), early learned words activated the precuneus (red arrow). Later acquired words elicited increased activity in inferior frontal and insular areas (blue arrow). (d) Inferior frontal activity for later acquired words was bilateral and extended into lateral and posterior orbital frontal regions.

2.1.15 A neural dissociation of repetition priming effects for words and pseudowords

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

It is commonly known that repetition priming leads to a facilitation of stimulus processing, accompanied by a decrease of neural activity to the second stimulus presentation ('repetition suppression'). However, it has recently been demonstrated that the hemodynamic responses for familiar and unfamiliar objects and faces show a dissociation between a repetition suppression effect for repeated familiar stimuli and repetition enhancement effect (i.e., an increased activity) for repeated unfamiliar stimuli (Henson et al., 2001). This activation increase has been interpreted as reflecting the build-up of a mental representation of the unfamiliar item. We adopted this paradigm to the processing of (familiar) words and (unfamiliar) pseudowords, as we hypothesized that dissociable patterns of repetition priming for these two stimulus classes might provide new insights into the way words are represented and processed by the brain. An equal number of words and pseudowords were visually presented to 14 participants in an event-related fMRI study (3 Tesla, 14 slices of 5mm, TR = 1 sec, TE = 30 ms, mean SOA = 4 sec). Participants performed a visual lexical decision task. 58 words and 58 pseudowords were repeated after 5 to 10 items (i.e., after 20 to 40 sec; mean repetition time 30 sec). Repetition of words resulted in repetition suppression effects in a network of areas involved in word processing. Affected were the fusiform gyri bilaterally, the left middle/inferior temporal gyrus, the left anterior insula, and left inferior frontal areas (BA44/6 and BA45; cf. Figure 15). Repetition of pseudowords induced repetition suppression only in the left anterior insula and the most anterior part of the left lateral occipital sulcus. In contrast, repetition enhancement was observed in several posterior regions bilaterally, including cuneus, precuneus, the lingual gyrus (Figure 16).

The observed repetition suppression effects for words suggest that visual word form processing (subserved probably by the fusiform gyri; cf. Cohen et al., 2000) and mechanisms of lexical access (involving the left inferior frontal gyrus; Fiebach et al., 2002) are facilitated in repetition priming. The increased activity for repeated pseudowords suggests that repetition priming activates additional cognitive processes which might be involved in forming new representations for these initially unfamiliar items (as suggested by Henson et al., 2000).



Figure 15. Brain areas exhibiting repetition suppression effects for repeated words, as compared to their first presentation.



Figure 16. Blue-to-white coding indicate brain areas exhibiting repetition suppression effects for repeated pseudowords (left anterior insula and left lateral occipital sulcus, anterior portion). Red-to-yellow coding represent brain areas in which repetition enhancement was observed for repeated pseudowords. Most prominent are activation increases in cuneus and precuneus, as well as the lingual gyri bilaterally.

2.1.16 Priming of unattended words: ERP evidence

De Filippis, M., Gunter, T.C. & Kotz, S.A. Prior experiments have revealed a semantic categorization effect for spatially attended as well as unattended words (De Filippis, Kotz, & Gunter, submitted). While attended word processing results in an N400 effect, the electrophysiological correlate of unattended word processing is an enhanced anterior negativity for stimuli of a given target category (CAT-effect). In order to investigate the underlying mechanisms of the CATeffect a priming paradigm was utilized. We predicted that if the enhanced negativity reflects facilitated semantic integration during unattended word processing, a priming effect should only occur for unattended words of the target category. For unattended words of the distractor category no semantic integration, thus no priming effect was expected. The priming of attended and unattended words was realized by presenting prime-target pairs of the target ('animate') and the distractor category ('inanimate') in a semantic categorization task. Words were alternately presented on both sides of the screen while participants focused their attention on one side. Simultaneously with the presented words distractors consisting of hashed marks (# # #) were presented on the opposite screen side. Subjects decided if attended words belonged to the target or distractor category. ERPs were recorded from 32 electrode-sites. The priming effects described below for attended and unattended words are shown in Figure 17. When words were attended, distractor words elicited a larger N400 than target words. In addition, unprimed words displayed a larger N400 than primed words. For unattended words an effect of screen side was found. Unattended word presentation on the left screen side



PRIMING

Figure 17. Topographic maps of the difference waves for non-primed minus primed words of the target (left) and distractor (right) category and attended and unattended words.
elicited a CAT-effect and a reversed priming effect for the target category in the CAT time window. Unattended word presentation on the right screen side showed a small enhanced negativity for the distractor category and no priming effects. These data suggest that the CAT-effect, elicited during unattended word processing, reflects the degree of semantic integration of words. The data also imply that target words are most likely fully semantically integrated. The position of unattended words is critical for eliciting a priming effect and probably relates to hemispheric specialization of language or attentional processes.

ERP correlates of word fragment priming I: Auditory fragments

The use of initial auditory input for lexical access was investigated using a cross-modal word fragment priming study. In this paradigm a spoken word fragment is immediately followed by a visual word starting with that fragment (target word) or not (control word). Control words have been found to elicit an enhanced P350 and an enhanced N400 as compared to target words (Friedrich, Kotz, Alter & Friederici, 2001). The present experiment explored the sensitivity of both components to the length of the fragments. Short, medium and long fragments were presented (see Figure 18 for an example). For all prime conditions an enhanced P350 and an enhanced N400 for control words was observed. Only the N400 effect was sensitive to fragment length. Short primes elicited the weakest, long primes the strongest N400 (see Figure 18). The results indicate that facilitation in reaction times for longer primes must be caused by controlled processes as reflected in the N400 rather then by automatic activation of lexical entries as indexed by the P350.



Figure 18. Left: Waveforms of auditory word fragments extracted from the German word Amboss (Engl. anvil), Medium: ERPs elicited by target words (black line) and control words (blue line) for the three fragment length, Right: Scalp distribution of difference waves for target words subtracted from control words between 300 and 400 ms (left) and 400 and 600 ms (right).

2.1.17

Friedrich, C.K., Kotz, S.A., Friederici, A.D. & Gunter, T.C.

2.1.18 ERP correlates of word fragment priming II: Visual fragments

Friedrich, C.K., Kotz, S.A., Friederici, A.D. & Gunter, T.C. The present experiment explored to what extent the P350 and the N400 observed in cross-modal word fragment priming vary as a function of prime modality. The same word fragments of differing length as in the cross-modal experiment (see part 1) were now presented visually (see Figure 19 for an example). As in the previous study, these fragments were immediately followed by a visual word that started with the prime fragment (target word) or not (control word). All prime conditions elicited an enhanced P350 for control words as compared to target words, however, only the long prime fragments elicited an N400 effect (see Figure 19). This result confirms the assumption that the P350 is correlated with activation processes in a modality independent mental lexicon. Moreover, it suggests that only late controlled processes underlying the N400 differ as a function of modality, i.e., visual and auditory fragments.



Figure 19. Left: Examples of the visual word fragments extracted from the German word Amboss (Engl. anvil), Medium: ERPs elicited by target words (black line) and control words (blue line) for the three fragment length, Right: Scalp distribution of difference waves for target words subtracted from control words between 300 and 400 ms (left) and 400 and 600 ms (right).

2.1.19 Lexical access to spoken German compound words: A new attempt of modelling

Isel, F., Gunter, T.C. & Friederici, A.D. The present behavioral study addressed the question of whether German two-noun compound words are processed in a discontinuous mode that requires a preliminary activation of an access code (Taft & Forster, 1976) or whether they are processed in a continuous mode similar to monomorphemic words (Marslen-Wilson, 1987). We tested the level of activation of the left constituent of the compound words with the goal to determine whether these morphemes are the crucial segment in accessing the whole word in the mental lexicon. In order to avoid a possible confound between factors of morphology and semantics, we used four categories of compound words: (1) fully transparent T-T (i.e., the two morphemes were semantically associated with the compound word: *Weinberg*), (2) truly opaque O-O (i.e., no semantic association between the morphemes and the compound word: *Luftschloβ*), (3) partially transparent regarding the left morpheme T-O (e.g., *Geldwäsche*), and (4) partially transparent regarding the right morpheme O-T (e.g., *Flohmarkt*).

In nine cross-modal (auditory-visual) semantic experiments using a lexical decision task, we demonstrated that there is no primacy of the left morphemes. A robust priming effect of these morphemes was only found for compound words with a transparent right most constituent (T *head*), which is the *head* of compound words in Germanic languages. Moreover, we demonstrated that the cognitive processing system is able to differenciate the prosodic structure of first morpheme as part of a compound from the prosodic structure of the same morpheme uttered in isolation on the basis of suprasegmental information of duration. This information is used to *guide* access mechanisms to the lexicon.

We therefore proposed a new model, e.g., the prosody-assisted parallel dual-route model or PAP model in order to account for the lexical access to German compound words.



Figure 20. The prosody-assisted parallel dual-route model or PAP model. Note that long duration indicates monomorphemes and short duration indicates that this element is part of a compound.

This model assumes two routes, i.e. a direct and a decompositional route that work in parallel. Each route is assigned for the processing of a specific type of compound word depending on the transparency versus opacity of the head. The prosodic structure of first morphemes of compound words appears to be a determining factor for the activation of the decompositional route. With respect to the duration of the first morphemes, the processing system is "set" either in a mono-route configuration (direct access of monomorphemic words) or in a dual-route configuration (temporal overlap between a direct and a decompositional route for the processing of compound words). We assume that in addition to the strong/weak prosodic pattern usually observed for German two-noun compound words, the strong/strong⁺ prosodic contrast allowing to differenciate poly- and monomorphemic words is determinant in *guiding* the word-recognition process in German.

2.1.20 The processing of German noun compounds. Part I: Separate morphosyntactic activation of constituents and their ter, D., semantic integration

Köster, D., Wagner, S., Köhler, S. & Gunter, T.C.

In the area of compound comprehension a major question is whether compounds are accessed by means of decomposition of the acoustic stream into single lexical constituents or by a direct access route to the lexicon. This experiment was set out to explore the course of constituent activation by inducing morphosyntactic violations. Semantically transparent, low frequent compounds, i.e. novel compounds, were presented acoustically preceded by a determiner, e.g. der vs. das Ballettkurslehrer (the mase vs. the neut ballet_{neut} course_{masc} teacher_{masc}). Subjects had to decide whether there was a gender incongruity between the compound and the determiner. In addition they had to judge the semantic content in 20% of the cases. Reaction times as well as event-related potentials (ERPs) were measured. The ERPs showed a left anterior negativity (LAN) for the first (see Figure 21) and for the last constituent if they disagreed with the determiner. The detection of the gender violation of the first constituent indicates that at least on a morphosyntactical level the constituents of a compound are activated separately. This is remarkable because German is a head-final language, i.e. the gender of the compound only depends on the last constituent. Furthermore, a slow negative shift across the whole compound was observed. This negativity was sensitive to the semantic content of the compound (see Figure 22) and showed an N400-like distribution. It was enhanced for those compounds where the constituents could not be integrated into a proper meaning, e.g. Pokalgastfinale (trophy guest finale) as opposed to compounds that made sense easily (e.g. Ballettkurslehrer). The modulation due to the semantic content was largest at the centro-parietal midline electrode (CPZ). The slow shift is suggested to reflect the integration process of the constituents' meanings. This is, however, a post hoc interpretation and was tested in a follow-up experiment. In general, our data suggest that novel compounds are decomposed and the constituents' meanings are integrated actively to yield the compound's meaning.



Figure 21. ERPs for congruent (black) and incongruent (red) first constituents of the compounds at a left frontal electrode (F3).



Figure 22. The negativity across the compound was greater for those compounds that were difficult to integrate. The difference was largest at CPZ which is shown here.

The processing of German noun compounds. Part II: Differences between opaque and transparent words

Köster, D., Wagner, S. & Gunter, T.C.

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From a previous experiment (cf. Part I) the prediction followed that opaque and transparent compounds should be processed differently. Since the meaning of an opaque compound cannot be deduced from the meaning of its constituents they must have an own entry in the mental lexicon, whereas the meaning of transparent compounds can be compiled from their constituents' meanings. In this experiment transparent items had a low frequency of occurrence and were, therefore, categorised as novel compounds. (Opaque compounds had the same frequency on average.) As it was shown before, it is possible to track the processing of compounds by means of gender incongruity (cf. Part I). In the present experiment we included non-compound words, and compounds made up from two and three constituents for auditory presentation together with a determiner. We varied the factors gender congruence of the first and last constituent, and *transparency* of the compounds. Subjects had to judge either the grammaticality or the semantic content of the words presented. As a replication of the former experiment we found a left anterior negativity (LAN) for the first constituent within the two-constituent compounds, our target items in this study. No effect of transparency and no interaction of gender congruence and transparency were observed within the first constituent. That is, during the time course of the first constituent of a compound there is no difference on a morphosyntactic level between a transparent and an opaque compound. In addition, a LAN was observed for the last constituent as well as a main effect of transparency (see Figure 23) but no interaction. Opaque compounds showed an enhanced negativity about 100-200 ms after onset of the second constituent. Transparent compounds were more negative than opaque ones about 500-600 ms after onset of the second constituent. Both peaks had a similarly distributed centro-parietal maximum. Our preliminary interpretation is that a more difficult lexicon search must be performed for opaque compounds because more phonetic features must be matched as opposed to only one constituent. This increased effort results in a greater negativity. For transparent compounds an integration effort is necessary, which results in a later negativity (see Figure 23) because the two constituents have to be accessed first.



Figure 23. ERPs for transparent (black) and opaque (red) two-constituent compounds were measured from the word onset at the PZ electrode.

2.1.22 Sex differentiates the role of emotional prosody during word processing

Schirmer, A., Kotz, S.A. & Friederici, A.D. The meaning of a speech stream is communicated by more than the particular words used by a speaker. For example, speech melody, referred to as prosody, also contributes to meaning. In a cross-modal priming study we investigated the influence of emotional prosody on the processing of visually presented target words. Participants listened to sentences that were spoken in a happy or a sad voice (e.g., Yesterday she had her final *exam*). Following sentence offset, they saw a word or a pseudo-word and were asked to make a lexical decision. Words were always semantically related to the preceding sentence. Half the words had a positive meaning (e.g., *success*) and half the words had a negative meaning (e.g., failure). With a short interval between sentence and target word (i.e., 200 ms) women but not men profited from emotional-prosodic congruence. They showed faster reaction times and a smaller N400 amplitude in the ERP to words that matched the valence of the preceding prosody. In men, emotional-prosodic priming effects showed only with a longer interval between sentence and target word (i.e., 750 ms). These findings suggest sex differences in the processing of emotional speech. More specifically, women seem to use emotional prosody earlier during language comprehension.



Figure 24. Stimulus presentation. Participants listened to sentences spoken in a happy or a sad voice. After a short interval they saw an emotionally valenced word or a pseudo-word.



Figure 25. ERP results. Grand average for words that matched the valence of the preceding prosody (solid line) and for words that did not macht (dotted line).

Word-prosody-interference in emotional speech: ERPs indicate processing differences between men and women

The present study investigated the interaction of emotional prosody and word valence during speech processing in men and women. In a word-prosody Stroop task, participants listened to positive, neutral and negative words that were spoken with a happy, neutral and angry prosody. Participants were asked to judge word valence while ignoring emotional prosody and vice versa. In both tasks, female participants made faster emotional judgments than males. Additionally, the event related potentials (ERPs) revealed sex differences for the interaction of prosody and word meaning.

In women, happily and angrily spoken words elicited a smaller N400 when word valence was congruent as compared to when it was incongruent. Although significant in both tasks, this N400 effect was more salient and extended over a longer time interval during the word valence judgment. Interestingly, the N400 amplitude for emotionally incongruent words did not differ from neutrally spoken words with congruent meaning (Figure 26). This suggests that the N400 effect is due to a reduction in activity in case of congruence between emotional prosody and word meaning.

The ERPs of male participants revealed no interaction between emotional prosody and word meaning. During the word valence judgment the N400 amplitude was larger for neutral and negative words as compared to positive words. During the prosodic judgment the N400 amplitude was larger for neutrally as compared to emotionally spoken words.

The results suggest that women automatically integrate emotional prosody and word meaning, whereas men can process both stimulus dimensions independently. However, the inability of women to ignore irrelevant information was no disadvantage in terms of task performance. Moreover, the interaction between prosodic and word information in women seems to make the processing of emotions in speech more efficient than in men.



Figure 26. ERP results. Grand average for emotionally spoken words that had a congruent meaning (e.g., 'loved' spoken in a happy voice; black solid line), neutrally spoken words that had a neutral meaning (blue/green solid line) and emotionally spoken words that were incongruent in meaning (e.g., 'hated' spoken in a happy voice; black dotted line).

2.1.23

Schirmer, A. & Kotz, S.A.

2.1.24

Heim, S., Opitz, B., Müller, K. & Friederici, A.D.

Segregating different aspects of phonological processes in Broca's area:An event-related fMRI study of language production

Studies on language perception showed that different regions of the superior part of Broca's area contribute to different phonological processes: the posterior junction point (BA44/8/6) subserves monitoring tasks as well as segmentation tasks, whereas the anterior portion is only active in the latter tasks. The present event-related fMRI study investigates whether the same pattern can also be observed during language production. Subjects performed phonological decisions on the German names of pictures of real objects. In the monitoring task, they decided whether the picture name started with the target phoneme /b/ or not. In the classification task, subjects indicated whether the name started with a vowel or a consonant.

The behavioral results show that the classification task takes longer than the monitoring task (reaction times) but is equally difficult (error rates). The fMRI data show the predicted pattern: The junction point and the medial-superior portion were activated in both tasks. Anterior activation was only present in the classification task (cf. Figure 27). The results support the notion of a common phonological processing network for comprehension and production. Considering results from current verbal working memory studies, the three different activation foci observed in the present study can be interpreted as neural correlates of phonological encoding (posterior), rehearsal (middle), and binding (anterior) operations which are in particular necessary for syllabification in language production.



Figure 27.

Information flow in the mental lexicon during speech planning

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Supported by DFG

In the past years, the question of whether semantic competitors to a target word become phonologically activated during speech planning has received a lot of attention, as the answer to this question is crucial to the ongoing debate on serial-discrete versus cascaded models of lexical access. Meanwhile, it has been demonstrated that near-synonyms are phonologically activated (such as *sofa*, if *couch* is the target), but no such effect has been obtained for category associates (such as *hand*, if *foot* is the target). However, it has repeatedly been pointed out that the available chronometric techniques might not be sensitive enough to reliably detect small phonological coactivation effects that are to be expected under cascaded models also for the latter type of competitors. We performed a series of experiments using a new ERP-paradigm for the study of lexical activation processes during speech planning (see Ann. Rep. 2000). It combines a delayed picture naming task with a priming technique. While speakers prepared the naming of an object, they heard an auditory target word to which the ERP was recorded. This auditory target word was related to the prepared picture name in various ways. It was either phonologically related (sand, if hand was the target), or the name of a close category associate (*foot*), or related to the phonological form of the category associate (*put*, mediated semantic-phonological condition). These experiments consistently showed semantic and phonological priming effects, as manifested in less negative going ERP-waveforms to related words in the N400 time window. However, they also consistently demonstrated the absence of mediated semantic-phonological priming, even for the case that the category associate had been named a few trials earlier.



Figure 28.

2.1.25

Jescheniak, J.D.^{1,2}, Schriefers, H.³ & Hahne, A.¹

This newly established group focuses on aspects of first and second language learning under normal and pathological circumstances. Moreover, the group also examines the domain-specificity of the processing of structure and meaning by looking at artificial grammars.

In an fMRI study using an artificial grammar as a second language to be learnt it is shown that initial learning stages depend on the left hippocampus and that increased proficiency is correlated with a decrease of hippocampal activation and an increase in the left inferior frontal gyrus (2.2.1). The effect of proficiency on the mastery of word processing (2.2.2) and the effect of global language context (2.2.3) is investigated in an ERP experiment with late German learners of English.

As part of the longitudinal German Language Development Study financed by the German Research Foundation (DFG) and our institute two ERP studies examined the basic prerequisites of language learning during early infancy: one study tested the infants ability to distinguish different consonants (2.2.4) another study tested the infants' capability to discriminate long from short vowels (2.2.5).

The development of morphosyntactic processes during first language acquisition between the age of 6 and 12 years is shown to be correlated with a systematic change in the ERP pattern over time (2.2.6). The impact of deafness corrected by cochlear implants on language processing was demonstrated in an ERP study revealing a strong focus on semantic rather than syntactic cues in the auditory input (2.2.7).

An earlier ERP study on artificial grammar processing in proficient learners revealed that the violation of a grammatical error elicits the two ERP components known to reflect syntactic processing, namely the early anterior negativity and the P600 (PNAS, January 2002). A present ERP study found that in a learned action game proficient users display an N400 for a meaning violation. The structural violation elicited a P600 and an early negativity which, however, was distributed posteriorly. These data suggest a domain-generality for the N400 and the P600, but a domain-specificity for the early negativity (2.2.8).

2.2.1 The brain circuitry mediating language learning

Opitz, B. & Friederici, A.D. As supposed by one of the most influential views on language acquisition, the underlying learning mechanisms are of a domain-general, associative nature. However, the brain structures mediating such learning processes remain to be described. Research on retrograde amnesia has pointed to the hippocampus playing a major role in associative learning, while neuroimaging studies have highlighted the importance of neocortical areas, specifically the prefrontal cortex, in learning, memory and language processing.



Figure 1. Schematic representation of the artificial grammar of BROCANTO. Nodes in the upper panel specify word classes (nouns, verbs, etc.), while arrows denote valid transitions between nodes. A correct sentence is formed by a transition from beginning ([) to end ([). The lower panel depicts the rules according to which valid phrases are formed. Thus, a sentence (S) consists of a noun phrase (NP) and a verb phrase (VP). An NP in turn is either the sequence dN or DMN, where N is one of the possible noun choices gum and trul. Word classes: N=noun, v=verb, M=adjective, m=adverb, d, D=determiner.



Figure 2. (I) Brain regions in which a significant Condition x Time interaction was observed. Sagittal sections at x = -26mm (left panel)= and x = -40mm (right panel) exhibit brain areas with changes of activity during learning relative to the recurring control blocks. Regions demonstrating decreased activity during artificial language learning included the left posterior hippocampus (A: -26, -32, 0) and the left ventrolateral thalamus (B: -18, -16, 1). Increased activity was noted in the left inferior gyrus (C: -40, 8, 18) and the left medial occipital gyrus (D: -40, -81, 28). (II) Temporal changes of activation in the hippocampus (left panel) and inferior frontal gyrus (right panel) for learning periods relative to sensorimotor control blocks. The time course shows the response collapsed across the three consecutive learning blocks and averaged across all participants.

The present study used functional magnetic resonance imaging to examine the brain circuitry involved in the acquisition of an artificial language called BROCANTO (see Figure 1) by assessing learning-related changes in hemodynamic activity.

We found that increased proficiency in artificial language use resulted in a gradual decrease of left hippocampal activity and a gradual increase of activity in the left inferior frontal gyrus (Broca's area), a region that contributes to syntax processing in natural language.

The present results, therefore, indicate a learning-related change in brain circuitry underlying language acquisition, with a transition from general learning systems in the medial temporal lobes to a language-specific processing system in the left prefrontal cortex.

The role of proficiency on processing categorical and associative information in the L2 as revealed by reaction times and event-related brain potentials

ERP studies show that L2 learners exhibit relatively native-like processing patterns in semantics but have more difficulty with syntax (e.g., Hahne & Friederici, 2001). However, different types of semantic information, namely associative versus categorical, create sub-components of semantics that also appear to be sensitive to proficiency. Processing associative relationships such as girl - boy is generally considered a lexical-level, highly automatic process that reflects spreading activation in a lexical network (Lupker, 1984). In contrast, categorical processing of pairs such as *junior – boy* that share semantic features or properties has been argued to reflect access to semantics/conceptual information (Kroll et al., 1992; Shelton & Martin, 1992). So, in a highly speeded visual sequential lexical priming task where controlled processing is not possible, categorical pairs may be less likely to yield RT and ERP N400 priming effects than associative pairs, especially if connections between concepts and L2 words are relatively weak as they are thought to be for late learners (cf. Dufour & Kroll, 1995). Associative relations, however, still require automatic processing and a well-developed L2 lexical network, so less proficient late learners may have difficulty with these relations.

Using the associative and categorically related pairs in the speeded task performed by highly proficient and less proficient late German learners of English, we demonstrate that the highly proficient learners (determined by language exposure and self-rating) showed associative RT and N400 ERP priming effects similar to early high proficient learners and native speakers (reported in Kotz, 2001), but no categorical effects. The lower proficiency group, however, showed no RT or ERP priming effects for both categorical and associative pairs (see Figures 3 & 4). Results suggest that in a speeded lexical decision task, the lower proficiency learners lack the automaticity and richness of inter-lexical L2 connections required to perform in a native-like way for associative relations. On the other hand, while the high proficiency group mastered the associative relations, they still lack the strong L2 word-concept links required for highly automatic

2.2.2

Elston-Güttler, K.E. & Kotz, S.A.

categorical processing similar to that observed for natives and even early high proficiency learners (Kotz, 2001). Even within the domain of semantics, different information types and proficiency level determine how automatic L2 lexical processing can become.



Figure 3. Difference waves comparing the N400 priming effects observed for high and low proficiency groups for associative relationships.



Figure 4. Difference waves comparing the N400 priming effects observed for high and low proficiency groups for categorical relationships.

2.2.3 Global language context:

How (non)selective is access in the bilingual mental lexicon?

Elston-Güttler, K.E.

Certain word types across the L1 and L2 are especially problematic for L2 learners. An example in German (L1) and English (L2) is when a word in L1 such as *klatschen* is a homonym and therefore has two distinct translations in the L2, i.e., *clap* and *gossip*. Another such case includes interlingual homographs where L1 and L2 share the same form, e.g. *chef*, but the L1 meaning *boss* and the L2 meaning *cook* do not overlap. The crucial question with regard to these word types is whether L1 representations can be suppressed by sentence context in L2 processing, and if so, under which conditions. This question was explored with three visual semantic priming lexical decision experiments performed in English by 32 advanced German learners of English. Targets were preceded either by single word primes or primes at the end of semantically biasing sentence contexts (with SOAs of 250 ms), i.e.,

Experiment 1	After the performance the audience began to <i>clap</i>	GOSSIP
Experiment 2	The man liked cooking so became a <i>chef</i>	BOSS

Experiment 1 showed significant priming with pairs such as *clap-gossip* (translations of the German homograph *klatschen*) compared to unrelated pairs, both in isolation (32 ms priming) and when the prime was in a sentence context (56 ms priming). On the other hand, Experiment 2 with pairs like *chef-boss*, revealed significant priming as single words (37 ms) but no significant priming in an L2 sentence context (15 ms). Experiment 3 (24 participants) used the same biased sentences in Experiment 2 to test whether the insignificant context effect builds up over time and was therefore weak overall in Experiment 2. Indeed, there was priming (120 ms) of the inappropriate German meaning in the first half of the experiment and inhibition in the second half (-40 ms); the interaction between experimental block and priming effect was significant (see Figure 5).

Overall, the nonselectivity hypothesis holds for the translated homonyms (clap - gossip) because even biased sentences could not restrict activation of the L1 translation equivalent, which then caused activation of the other L2 word. On the other hand, it appears that for false friends (chef - boss) which share only formal information across languages, sentence context can indeed create selective access, but only if the global language context is firmly established and has time to build up.



Figure 5. Block-Priming interaction indicating the build-up of language context while processing L1-L2 interlingual homographs.

Event-related potentials and mismatch negativity in 4 weeks and 5 month old infants

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Supported by DFG

Phoneme and frequency discrimination were examined in normally developed infants in the age of 4 weeks (n=85) and 5 month (n=45) as part of the German Language

2.2.4

Nubel, K.¹, Lange, K.¹, Friederici, A.D.² & Gross, M.¹ Development Study. Event-related Potentials and Mismatch Negativity were elicited by pure tones (1000 Hz vs. 1200 Hz) and naturally spoken phonemes (/da/ vs. /ga/) in an odd-ball paradigm with 500 standards and 100 deviants (150 ms stimulus length, 750 ms interstimulus interval). Signals were recorded with 11 channels.

The grand-average of the younger infants shows a positive deflection after 200 ms of the difference wave in the frontal-central electrodes for both the phonemes but with a higher amplitude for the tones. In addition, the difference waves for the phonemes reveal a negativity of about 700 ms (Figure 6).

The grand-average of the older infants shows an early positive deflection after 200 ms, too, but with a shorter latency. Also, the negativity for the phonemes was present earlier and higher in amplitude in the 5 month old infants compared to the younger infants (Figure 7).



Figure 6: Grand-average ERPs and MMN from infants (4 weeks, n = 85) elicited by phonemes (/*da*/ - /*ga*/, 64 dB SPL).



Figure 7: Grand-average ERPs and MMN from infants (5 months, n = 45) elicited by phonemes (/*da*/ - /*ga*/, 64 dB SPL).

There seems to be a preattentive discrimination in infants for pitch and phonemes /da/vs./ga/ as easy as the age of 4 weeks. The ERP-morphology of the discriminationrelated mismatch response, however, has to undergo considerable development before an adult-like MMN is observed.

ERP correlates of the discrimination of syllable length in early infancy

Supported by DFG

The comprehension of intonational languages crucially depends on the ability to discriminate long from short syllables, as duration is one of the parameters indicating syllable stress. Using a mismatch negativity paradigm we investigated 39 infants (14 female, 25 male), at the age of 2 months recording their ERPs. Twenty-nine infants (10 female, 19 male) were asleep during ERP recording, ten (4 female, 6 male) were awake. Two stimuli were used: a short CV syllable /ba/ (202 ms) and a long CV syllable /ba:/ (341 ms). Each stimulus functioned as the standard and the deviant. The probability of standard to deviant was 5:1. The interstimulus interval was 855 ms.

Both groups showed a strong mismatch response for the long deviant condition. For awake infants we observed a frontal positivity between 400-600 ms followed by a right distributed negativity between 800-1000 ms. For infants that were asleep the earlier positivity and the later negativity were also observed, although the negativity was not present at frontal sites while the positivity was spatially and temporally much more extended in the asleep than in the awake group. In the short deviant condition the mismatch response was reduced. In infants that were asleep both positivity and negativity failed to be significant. However, the awake infants showed a negative response similar to the extent observed in the long deviant condition.



Thus, it appears that infants by the age of two months are able to discriminate long from short syllables, but that a long syllable is more easily detected in a sequence of short syllables than the other way round. The former is perceived as more salient. The data, moreover, suggest that the ERP effect observed varies as a function of vigilance.

2.2.5

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

2.2.6 Speech comprehension with cochlear implants

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Supported by DFG

Cochlear implants (CI) are currently used in the rehabilitation of profoundly deaf patients with a fair degree of success. With the use of cochlear implants it becomes possible to restore auditory sensation by inserting electrodes within the cochlea to stimulate the cochlear nerve. However, hearing with the help of a cochlear implant differs severely from normal hearing, and the processes underlying the language comprehension of patients with CI are yet to be determined. We continued our work (see Ann.Rep. 2000, p.29) using event-related brain potentials to study sentence comprehension in CI-patients. By now, we tested twelve cochlear implant users who all suffered from a postlingually acquired deafness. In a first experiment, participants listened to sentences which were either correct, semantically incorrect or syntactically incorrect (phrase structure error). They were asked to judge each sentence's acceptability. Prior to the experiment, the patients were given a written instruction which included example sentences for each condition. In a second experiment, similar sentences were presented visually to the CI-participants.



Figure 9. Grand average ERPs across 12 cochlear implant patients for auditory as well as for visual sentence presentation.

We were able to demonstrate that the CI user group deviated from a control group in auditory, but not in visual sentence processing. The auditory ERP data averaged across correctly answered trials showed an N400-like effect for the semantic as well as for the syntactic condition. However, when presented visually to the CI group, the semantic and syntactic violations elicited similar patterns to those of a control group, i.e. an N400 effect for semantic violations and a modulation of a late positivity (P600) for syntactic violations.

The current findings suggest that the degraded input of a cochlear implant results in changes in auditory language processing in CI users. These patients seem to focus on semantic aspects of words relying on compensatory semantically-based strategies. This pattern was demonstrated to be a specific feature of auditory comprehension rather than a general difference in cognitive language processing as sentence reading was shown to be normal.

How brain potentials develop: An ERP study about the processing of German noun plurals in adults and children

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Previous studies using event-related brain potentials (ERPs) on adults have led to the identification of brain potentials associated with semantic, syntactic and morphological processing (e.g., Kutas & Van Petten 1994; Friederici, 1998). However, little is known as to how these language-relevant brain potentials emerge during child language development. The present study addresses this question and examines the processing of German plural nouns in adults and children of different ages adopting the ERP violation design from Weyerts et al. (1997). We developed two conditions of nouns and the nouns were incorporated into sentences, as illustrated by the following examples.

- I. Semi-regulars: feminine nouns ending on schwa: (correct plural form: -n; incorrect plural form: -s) *Die meisten Jacken haben die praktischen Kapuzen/*Kapuzes gegen den Regen.* Most coats have handy hoods against the rain.
- II. Regulars: loan words:

(correct plural form: -s; incorrect plural form: -en) *Christine lutscht am liebsten die leckeren* **Bonbons/*Bonbonen** *aus Schokolade*. Christine likes it most to suck the delicate sweets made of chocolate.

The experimental sentences were presented to participants auditorily. We examined one group of adults (N=23) and three groups of children (N=20 each): (a) aged 6.0-7.11, (b) aged 8.0-9.11, and (c) aged 11.0-12.11. For the adults, incorrect feminine nouns elicited a LAN/P600 pattern in comparison to their correct counterparts, an ERP pattern which is often observed in correlation with syntactic violations (Friederici, 1998). The incorrect loan words additionally gave rise to an N400 component, which is generally observable during the processing of semantic problems or non words (e.g., Kutas & VanPetten, 1994).

2.2.7

Lück, M.¹, Hahne, A.¹ & Clahsen, H.² The three groups of children showed a clear development with regard to the ERP pattern observable for the feminine nouns. The results for the first condition, feminine nouns, for all age groups are shown in Figure 10. Thus, group (a) showed a broadly distributed negativity for the incorrect feminine items, while group (b) showed a frontocentrally distributed negativity as well as a positivity which was restricted to occipital sites, and group (c) showed a frontal negativity with maxima at F7 and F8 and a centroparietal positivity. By contrast, there was no clear pattern and no obvious developmental effect for the loan word condition. These results show that, despite the nearly perfect production abilities of even the youngest age group, children's comprehension of inflected words clearly differs from that of adults. Most interesting in this regard is the development of the late positive component (P600) and the focusing of a negativity, which both appear to take place up to the age of 12. More generally, these findings demonstrate that event-related brain potentials enable us to shed light on fine grained qualitative changes within the process of language development.



Figure 10. Difference maps of incorrect and correct items of condition 1, feminine nouns, of all age groups.

2.2.8 Meaning and structure in action comprehension: Electrophysiological evidence

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Interpreting the actions of others is a cognitive activity frequently encountered in everyday life. Actions can be understood by their perceivers because they consist of an orderly structure of meaningful gestures in a certain context. Structure, meaning and context are also the essentials of language comprehension. It is therefore not unplausible that language and action comprehension share underlying cognitive mechanisms. This study was set out to explore this issue.

Participants were presented with a modified version of the familiar game 'Paper, Scissors, Rock'. The gesture at the end of a sequence was either valid or represented a meaning or structure violation. Event-related potentials (ERPs) elicited by the end gesture showed an N400 component for meaning violations and an early posteriorly distributed negativity followed by a P600 component for structure violations. The N400

and P600 have traditionally been observed in language comprehension for semantic and syntactic processes.

In language processing the early negativity [(E)LAN] which typically preceeds the P600 has quite a different distribution compared to the early effects found in the action game. The language related negativity is associated either with the identification of wordcategory information (ELAN: 150-200 ms) or with the identification of morpho-syntactic information (LAN: 300-500 ms; e.g. syntactic gender, case). The *identification* of the structural violation in the present action game can be done solely on the basis of visual features and not, as is the case in language processing, on the basis of abstract syntactic features. Therefore, it does not come as a surprise that the early negativity observed for the gestures is distributed over the occipital cortex, the region where visual processing takes place.

In sum, the present data give us reason to believe that the processing of action sequences in the context of a game shares common ground with language processing. Two crucial aspects of language comprehension -namely semantic integration as reflected by the N400 and rule based integration as reflected by the P600 are present in action comprehension. The clearly differently distributed early negativity, however, suggests that the detection of a rule violation is much more domain specific.



Figure 11. Example of the presented sequence in the game. Part [1] to [5] depicts the context sequence. Part [6] depicts a correct end gesture (i.e. 'paper').



Figure 12. Examples of incorrect end gestures: (a) a structural violation (wrong orientation), (b) a meaning violation, and (c) a double violation.



Figure 13. ERPs elicited by the end gesture reflecting the correct condition (solid) and he meaning violation (dashed). The meaning violations show an N400 component.



Figure 14. ERPs elicited by the end gesture reflecting the correct condition and the structural violation. The meaning violations (dashed) show an early negativity (circles) and a P600 component.

During the last year, our Music-group had three major aims: *first*, we wanted to further investigate the early right anterior negativity (ERAN), an ERP component that reflects the processing of complex musical regularities (which may be denoted as 'musical syntax'). We found additional evidence for our claim that the ERAN is elicited by violations of regularities of major-minor tonal music, and not merely by the processing of physical irregularities (2.3.1).

Second, we began to investigate developmental aspects of music cognition using EEG (2.3.2). We therefore presented the musical stimuli that we used under several experimental conditions with adults to 5-year-old and 9-year-old children. Interestingly, we observed that 5-year-olds already show electrical reflections of a remarkably competent and sensitive music processing. The finding that children show an early effect (similar to the ERAN of adults) before they show an ELAN appears to underline that musical competence is a prerequisite for the acquisition of language, a notion that is in line with an increasing number of experimental findings reported during the last decade. An unexpected finding was that boys process the 'syntactic' aspects of music with a left-hemispheric predominance, in contrast to girls who showed a more bilateral distribution. This gender difference led to a reanalysis of numerous data-sets obtained in our previous experiments with adults (2.3.3): The pooled data from three comparable experiments indicate a gender difference also for adults, the ERAN being lateralized to the right in males, and being rather bilateral in females.

Our *third* aim was to step into the investigation of emotion using music – after thoroughly investigating the more cognitive aspects of music processing during the last years. We found first evidence for a mirror system in the auditory domain, and discovered that a part of the auditory cortex might be specifically involved in the processing of auditory information with emotional valence (2.3.4).

2.3.1 Contributions of music-syntactic processing to the ERAN

Koelsch, S.¹, Sammler, D.^{1,2}, Kenntner, R.¹ & Friederici, A.D.¹ ¹ Max Planck Institute of Cognitive Neuroscience ² University of Leipzig

In our previous experiments, harmonically inappropriate chords elicited an early right anterior negativity (ERAN), taken to reflect the processing of complex musical regularities. However, in these experiments the chords eliciting an ERAN were not only harmonically inappropriate, but they also introduced new notes into the chord-sequences: All notes of the in-key chords preceding the inappropriate chords belonged to a set of the seven in-key notes of a scale. Whereas the appropriate chords contained notes that also belonged to this set, the inappropriate chords contained two notes not belonging to this set. Thus, it remained to show that the ERAN is not only elicited by this difference between appropriate and inappropriate chords. Therefore, in the present experiment the notes of both the harmonically appropriate and inappropriate chords occurred in equal proportions in the previous chords. Sequences of five chords were presented, the first four chords building up a musical context, and the last chord being (in relation to the established context) either the harmonically correct tonic or the incorrect dominant to the dominant (see Figure 1). Note that the term "harmonically correct/incorrect" refers in the present paradigm only to the regularities of the arrangement of chord functions within harmonic sequences, i.e. with respect of the complex regularities of major-minor tonal music. These regularities have been denoted as a "musical syntax". The probability for each sequence type was 0.5, each sequence was presented in another key, the order of presentation was randomized, and one sequence directly succeeded the other (see bottom of Figure 1). All participants (n=12, with varying degree of musical expertise) were instructed to indicate whether the last chord of a sequence was harmonically (in)correct. The ERPs of the correct classified chords at the fifth position show that the music-syntactically inappropriate chords elicited an ERAN, which was maximal around 200 ms after the onset of the chord and lateralized to the right (Figure 2 and 3). Because the dominant of the dominant as presented in this study did not deviate psycho-acoustically, but only music-syntactically from the tonic, results show that the ERAN can be elicited solely by music-syntactic processing. Given the similarities between ERAN and MMN, the ERAN-effect elicited in this study might be denoted as "music-syntactic MMN".



Figure 1. Examples of the chord sequences. Top: chord sequences terminated by an expected tonic chords (left), or by a dominant to the dominant (upper right). Bottom: Directly succeeding sequences as presented in the experiment.





Figure 2. ERPs of correctly classified chords, the blue line indicates the ERPs elicited by tonic chords. Incorrect (and thus unexpected) chords elicited an ERAN (arrow).

Figure 3. Potential map of the ERAN (differencewave: tonic subtracted from dominant chords), interpolated over a time-window from 170-230 ms.

Music processing in children: An ERP-study

Our previous studies using EEG, MEG, and fMRI revealed that adults process harmonic incongruities within a major-minor tonal context surprisingly well corresponding to the theory of harmony, even when they have not received formal musical training. In these studies harmonically inappropriate (unexpected) Neapolitan sixth chords were presented infrequently in a series of chord sequences. The Neapolitan chords elicit two distinct electric brain responses in adults: an early right anterior negativity (ERAN, maximal around 200 ms after the onset of the chord) and a late bilateral negativity (denoted as N5, maximal around 550 ms). It is an open question how these neural correlates of music processing develop during childhood.

In the present study, we investigated music processing in 5-year-old (n=14) and 9-yearold (n=14) children without formal musical training. Chord-sequences consisting of five chords were presented in direct succession sounding like a musical piece. In 50 percent of the sequences, harmonically incongruous Neapolitan sixth chords were presented at either the third or the fifth position of the sequences. The Neapolitans were, in music-theoretical terms, harmonically less related to the preceding musical context than the in-key chords. Most of the chords were played with a piano sound, but in 8 percent of the chord-sequences a chord was presented with a deviant instrumental sound (for example, trumpet). The children were instructed to detect the deviant instruments.

In both age groups, Neapolitan chords at the fifth position elicited in both groups an early negativity peaking around 320 ms, which was followed by a late negativity which peaked around 660 ms (Figure 4). When Neapolitans were presented at the third position of the chord sequences no ERP-effects were elicited compared to in-key chords, neither in the 5-, nor in the 9-year-olds. The finding that Neapolitan chords at the fifth position were processed differently from tonic chords indicates that 5-year-old children already processed the chords according to the principles of the theory of harmony. The fact that the children received no special musical training may allow a broad generali-

2.3.2

Grossmann, T., Koelsch, S., Hahne, A. & Friederici, A.D. zation, namely that the acquisition and application of (implicit) knowledge about musical regularities is a general human ability. However, this generalization could only be drawn within the culture-specific context of western tonal music.

Interestingly, the observed early negativity had a left hemisphere predominance in boys, whereas it was bilaterally distributed in girls (Figure 5). This sex difference is consistent with a great body of evidence indicating a more bilateral structural and functional organization of the brain in females. Notably, the earlier negativity in adults (ERAN) is predominant over the right hemisphere. The different scalp distributions between adults and children might be attributed to developmental effects, suggesting that the generally reported preponderance of the right hemisphere for music processing is established later in life, and not 'imprinted' in the functional brain organization in early life.



Figure 4. Grand-average ERPs elicited by chords at the fifth position, separately for 5-year-olds (left) and 9-year-olds (right).



Figure 5. Potential maps of the early effect elicited by the Neapolitans (difference-ERPs, in-key sub-tracted from Neapolitan chords), separately for boys (left) and girls (right).

2.3.3 Gender differences in music-syntactic processing

Koelsch, S.

In our previous music experiments, we routinely analyzed data with respect of gender differences. Although slight differences were observable in the ERPs, these differences were statistically not significant when analyzing data of single experiments. In order to increase the signal-to-noise-ratio of the ERPs, we pooled sixty-two data sets from our previous experiments. In all of these experiments, subjects were presented with chord-sequences, each sequence consisting of five chords (see also 2.3.2). On average, 45 percent of the sequences contained a harmonically inappropriate chord at either the third or the fifth position of the sequence. These inappropriate chords had in the previous experiments been shown to elicit an early right anterior negativity (ERAN) and an

N5. The ERAN is interpreted as a sound expectancy violation, the expectancies being based on knowledge about complex musical regularities (in the experiments regularities of major-minor tonal music), that is knowledge about a 'musical syntax'. The N5 is interpreted as reflecting processes of musical integration. The pooled data reveal that the ERAN is more right lateralized in males and rather bilateral in females. An ANOVA with factors chord type (harmonically appropriate vs. inappropriate), lateralization (left vs. right), and gender, conducted for the ERAN-time-interval (130-280 ms), revealed a significant interaction between the three factors. Although the N5 seems larger in females, and probably more lateralized in males, these differences were statistically not significant. The results parallel some studies that revealed more lateralized language functions, and larger structural left-right asymmetries of auditory regions in males.



Figure 6. Potential maps of the ERAN (difference-wave: in-key subtracted from Neapolitan chords), interpolated over a time-window from 130-280 ms), separately for females (left) and males (right).

Music and emotion

Music has the capacity to induce emotions. In the present study, we used music to induce feelings of pleasantness and unpleasantness. We presented musical excerpts from joyful instrumental dance tunes from the past four centuries and contrasted them with dissonant, and thus unpleasant, versions of the original excerpts.

The results reveal that listening to the consonant (pleasant) contrasted to dissonant (unpleasant) music activates a medial part of the parietal operculum in the inferior parietal lobe of the right hemisphere (Figure 7A). Based on cytoarchitectonic investi-



Figure 7. The sagittal sections show activations (A) of the medial posterior part of the parietal operculum (roughly superior of the posterior part of Heschl's gyrus) in the right hemisphere and (B) the anterior inferior part of the pre-central gyrus in the left hemisphere, extending anteriorly into the pre-central sulcus, and posteriorly into the subcentral gyrus.

2.3.4

Koelsch, S., Fritz, T., von Cramon, D.Y. & Friederici, A.D. gations, this structure has previously been described as part of the human auditory cortex, namely as rostro-caudal parakoniocortex. The present activations correspond to this cytoarchitectonic description; the combined findings might indicate that a part of the auditory cortex located in the parietal operculum is specifically involved in the distinction and processing of pleasant and unpleasant auditory input.

Furthermore, listening to pleasant music activated vocalization-related premotor areas in the inferior pre-central gyrus of the left hemisphere (Figure 7B). This finding is reminiscent of the activation of premotor areas during the observation of grasping movements. The premotor activations observed in the present study might indicate that mirror activity is not restricted to the visual, but also observable in the auditory domain. This year the reports of the MEG group are mainly methodological. Four contributions (2.4.1, 2.4.2, 2.4.3, 2.4.4) result from work within the SimBIO project (http:// www.simbio.de). The final goal of the particular part of the project, in which the MEG-group is involved, is to establish the practical feasibility of the finite-element-method (FEM) based head-modeling for brain research and for regular medical use. There are at least two main advantages of the FEM method: The geometry of the head might be described in more detail and tissue properties, like the electrical conductivity, can be given for each voxel separately. Because this information is not available within one magnetic resonance image (MRI), it is necessary to combine differently weighted MRIs and develop adapted segmentation algorithms for them (2.4.1, 2.4.4). This work was carried out in close cooperation with the SIP-group of our institute. High resolution FEM models lead to a heavy computational load with respect to both, time/computational and also memory costs. Hence, concurrent mathematical algorithms have to be used to allow for high accuracy, fast computing and feasible memory demands (2.4.2, 2.4.3).

A simulation study focused on (2.4.5) is analyzing the resultant time resolution when using the event-related desynchronization (ERD) method with different windowing algorithms by a number of simulations.

Very exciting results were found by two studies on early auditory stimulus processing: One study describes that identical stimuli tested under two different tasks (requiring a "where?" or a "what?" answer) elicit activity in significantly different regions within the vicinity of the auditory cortex (2.4.6). Another study demonstrates interactive parallel processing of word-information and voice-information during auditory language comprehension (2.4.7). A study on visual processing shows that the often described N170 also reflects Gestalt perception in addition to attentional processes and physical stimulus properties (2.4.8). The difficulty of color processing was investigated by means of evoked gamma activity analysis (2.4.9).

Finally, the work (2.4.10) aimed the computer-aided analysis of spontaneous EEG activity in an clinical environment. The program is able the classify EEG epochs e.g. into bulb artefacts, epileptic spike activity and alpha waves.

During the last year our group was growing: Dr. Michael Schauer and Dr. Thomas R. Knösche joined the group as scientific staff members. Paivi Sivonen and Dr. Akinori Nakamura are working with us as scientific guest researcher and Jens Molski as an engineer for soft- and hardware maintenance.

2.4.1 Accuracy studies for AFCM segmentation and a comparison to the ISODATA algorithm

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Accurate tissue segmentation is an important pre-requirement for the set-up of a high resolution finite element model of the human head. Elsewhere in this report (see 2.4.4), we presented a procedure to segment the human skull, using T1- and PD-weighted MRI datasets. One important tool within this proc., the Adaptive Fuzzy C-Means (AFCM) algorithm, compensates for intensity inhomogeneities while performing a fuzzy segmentation of the MR images. Within the outer loop of the algorithm, new centroids for each class and new membership and multiplier values for each voxel are determined. For the multiplier field, a large sparse linear equation system with an assumed large condition has to be solved iteratively so that preconditioning gets an important tool. We found out in synthetic model studies, that a relative accuracy of at least 10^{-1} is needed for the solver in order to accurately extract the modeled inhomogeneities. A simple preconditioning, the Jakobi diagonal scaling, does not influence the convergence/ accuracy properties of a Successive OverRelaxation (SOR) solver, but preconditions the Conjugate Gradient (CG) method, especially since the large entries on the diagonal of the matrix are clustered with the values of the centroids, so that a parallel scaled CG solver was implemented for AFCM and tested against the SOR. As the Figure (3rd from left) shows, tested settings of the parameter w for SOR failed to yield an accuracy below 0.34 for the PD-MRI, whereas the sCG converged to any given bound (e.g., 2283 iterations for 10^{-6}). The result with 4 outer AFCM-sCG iterations and 10^{-1} solver accuracy is presented in the Figure for the PD- (2nd) and the T1 image (6th). 2 hours 18 on one proc. of an SGI Origin 2000 were needed for the latter and a linear reduction is assumed for parallel



Figure 1. (left to right). PD-MRI: ISODATA (1st), AFCM-sCG (2nd) and residual consid. (3rd). T1-MRI (4th): ISODATA (5th) and AFCM-sCG (6th).

computing. Compared to results of ISODATA unsupervised clustering (1st, 5th), AFCM-sCG yielded closed skin layers and accurate white/grey matter segmentation (about 4mm cortical thickness at the observed location in the Figure 1), while large holes in the skin layer and a cortical thickness of up to 8mm were observed in the ISODATA results.

Integration of high resolution FEM forward modeling based on parallel algebraic multigrid methods with an inverse toolbox for source localization

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Supported by the European Community

The aim of this study is the development of software for high resolution EEG/MEG source reconstruction using a realistic anisotropic finite element model (FEM) of the head. The FEM is known to be able to treat geometries of arbitrary complexity and is able to model variable material properties and anisotropy in computer simulations. Due to computational complexity it is rarely applied to inverse source reconstruction. The use of parallel algebraic multigrid methods as FEM solution system on a modern parallel computer enabled the acceleration of the field computation for a given source by a rate of 75 (see 2.4.3). This enables inverse source localization with underlying high resolution FEM forward modeling, integrating anisotropic modeling of the skull layer and the white matter fibers. Therefore, we coupled our new parallel FEM simulation software NeuroFEM with a toolbox of state of the art inverse solution methods. The toolbox is developed in collaboration with ANT Software. The FEM software allows discrete and continuous source reconstruction on high resolution meshes necessary for accurate individualized modeling of the various tissues and anisotropy. First tests of inverse source localization with dipole fit and current density reconstruction using parallel computing of the FEM forward simulation were successfully carried out. The FEM model was generated via segmentation of an MR image of the subject. Figure 2 shows the result of a current density reconstruction with an FE model. The segmented cortex was used as source space for the inverse source localization for EEG signals acquired from evoked fields.



Figure 2. Linear estimation of the source current density using a high resolution finite element model (FEM) for evoked fields.

2.4.2

Anwander, A.¹, Dümpelmann, M.³, Knösche, T.R.¹ & Wolters, C.^{1,2}

2.4.3

Wolters, C.^{1,2}, Kuhn, M.³, Anwander, A.² & Reitzinger, S.⁴

Parallel algebraic multigrid preconditioner for high resolution FE based volume conductor modeling in EEG/MEG source localization

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The inverse problem in EEG/MEG requires the repeated simulation of the field propagation for a given dipolar source in the brain using a volume-conduction model of the head. High resolution Finite Element (FE) modeling allows the inclusion of tissue inhomogeneities and anisotropies (see 2.4.4). Many studies indicate the necessity of such a complex forward model. The bottleneck for a broader application is the time for solving the large sparse linear equation system with thousands of different right hand sides arising from the FE discretization. Preconditioning techniques for the iterative solution process are not only important to yield accuracy, as shown in (2.4.1), but also to speed the computation. Even if the Algebraic MultiGrid (AMG) in comparison with Incomplete Threshold Factorization methods turned out to be the fastest tested solver for relative accuracies below 10^{-4} (see Ann.Rep.2000, 2.11.3), additional speedup is required. Very short calculation times were now achieved through the combination of AMG preconditioning techniques and a non-overlapping element-wise domain decomposition (Figure 3, left) parallelization on a distributed memory platform. The AMGpreconditioned Conjugate Gradient (AMG-CG) method was compared with a Jacobi-CG (or scaled CG), the latter being a well-known solver in FE-based source localization. If the Jacobi-CG on one processor is taken as a reference, we achieved for relative accuracies between 10^{-6} and 10^{-8} speedups of 75 for a realistically shaped high resolution



Figure 3. Non-overlapping element-wise domain decomposition of the tetrahedra head model for 12 procs (left), the speedup results (bottom left) and the solver time comparison (bottom right).





tetrahedra head model with 713733 elements and 118299 nodes, 7.5 through multilevel preconditioning and 10 through parallelization on 12 procs (Figure 3, bottom left). On 12 procs, AMG-CG took 2.6 sec for a solution with rel. accuracy of 10^{-8} , (Figure 3, bottom right), for 10^{-4} only 1.2 sec.

Segmentation accuracy studies and conductivity anisotropy determination of the 2.4.4 human skull using a dual echo MR data set

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Previously (see Ann.Rep.2000, 2.8.10), we presented a procedure to segment the human skull, using a T₁- and PD-weighted MRI data set. Segmentation errors were observed for the outer skull surface. Problems were solved with an improved initial outer skull mask, generated by means of a high elastic extended region growing approach (Wagner, 1998) of the dilated inner skull surface. The initial mask is used as starting surface for a deformable model (result in Figure 4, left). In order to construct an improved electro-magnetical forward model of the human head, a tensor for every point in the skull describing the conductivity anisotropy of the skulls 3-layers upper compact (about 1.5mS/m, see Akhtari et al., Brain Top., 13(1), 2000), spongiform (about 10mS/ m) and lower compact (about 3.5mS/m) has to be taken into account. The spongiosa space is modeled by a smoothed spongiosa surface mesh (SSSM): First, the outer skull surface is eroded and a mesh is extracted from it. Then, a deformable model approach with strongly weighted inner forces for smoothing/shrinking and moderate T1 image based outer forces for fixation at the spongiosa surface is carried out, resulting in the SSSM. For each point in the skull (e.g., a mass center point of a finite element), directions perpendicular to the SSSM are assumed to be good approximations for the radial conductivity tensor eigenvector with low corresponding eigenvalue (series connection of the 3 resistors). The vector product enables the determination of the tangential eigenvectors with much higher eigenvalue. Since it is assumed that especially the inner skull surface (ISS) is substantially improved through the exploitation of the registered PD-image, we compared it with an estimated surface (EISS), solely based on a segmented brain surface from the T, modality. The EISS, used by well-known commercially available EEG/MEG source localization tools, is obtained by smoothing (with d₁) the brain surface and then



Figure 4. T1/PD skull segm. result, SSSM and comp. of ISS and EISS (from left to right).

Wolters, C.^{1,2}, Burkhardt, S.³, Kruggel, F.² & Saupe, D.⁴ dilating it with d_2 . Larger errors will thus result in regions where the CSF layer between brain and skull is underestimated. The parameter choice $d_1=15$ and $d_2=0$ in Figure 4 (middle, right, right) shows a difference between ISS and EISS of up to 8.5 mm.

2.4.5 On the time resolution of event-related desynchronization: A simulation study

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The objective of this study was to investigate the time resolution of different methods for the computation of Event-Related Desynchronization / Synchronization (ERD/ERS), including one based on Hilbert transform. In order to better understand the time resolu-



Figure 5. ERD results for brief oscillatory bursts. The bursts contain 3, 1.5, or 0.75 periods of the oscillation and are separated by 1 or 0.5 burst length. The signals are sampled with 500, 250, 100, or 25 samples per period of the oscillation. The oscillation amplitude during the bursts is twice the amplitude between them. The blue line indicates the true envelope of the burst signal.

tion of ERD/ERS, which is a function of factors such as the exact computation method, the frequency under study, the number of trials and the sampling frequency, we simulated sudden changes in oscillation amplitude as well as very short and closely spaced events. The results showed that Hilbert based ERD yields very similar results to ERD integrated over predefined time intervals (block ERD), if the block length is half the period length of the studied frequency. ERD predicts the onset of a change in oscillation amplitude with an error margin of only 10-30 ms. On the other hand, the time the ERD response needs to climb to its full height after a sudden change in oscillation amplitude is quite long, i.e. between 200 and 500 ms. With respect to sensitivity to short oscillatory events, the ratio between sampling frequency and EEG frequency band plays a major role (Figure 5). We draw the following conclusions: (1) The optimal time interval for the computation of block ERD is half a period of the frequency under investigation. (2) Due to the slow impulse response, amplitude effects in the ERD may in reality be caused by duration differences. 3. Although ERD based on the Hilbert transform yields only minor advantages over classical ERD in time resolution, it has some important practical advantages.

,What' and ,where' processing in human auditory cortex

The human visual system is divided into two pathways specialized for the processing of either objects or spatial locations. Neuroanatomical studies in monkeys have suggested that a similar specialization also divides auditory cortex into two such pathways. We used the same stimulus material in two experimental sessions in which subjects had to either identify auditory objects or localize their source in space. MEG was recorded during the experiment and dipoles were localized in individual brain models which were reconstructed from subjects' MRI datasets. The different tasks resulted in differential activations of human auditory cortex.



2.4.6



Figure 6. M100 dipole locations for auditory object identification ('what' condition, red) and for localizing auditory objects in space ('where' condition, yellow). A: Horizontal slices of the five individual brains. Horizontal (B) and coronal (C) slice of a mean brain computed from these five subjects. In the right hemisphere a clear separation of the two functional specializations can be seen: objects are processed more medially while space is processed more laterally.

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The processing of auditory spatial information leads to more lateral activations within the temporal plane while object identification leads to more medial activations. This effect was more pronounced over the right hemisphere. These findings suggest that the human auditory system is separated into two pathways, one for processing auditory objects and one for locating sounds in space. In addition, the right-hemispheric dominance of humans as compared to monkeys seems to reflect our ability to process language in the left hemisphere.

2.4.7 Early parallel processing of auditory word and voice information

Knösche, T.R., Lattner, S., Maess, B., Schauer, M. & Friederici, A.D. This study is focused on the dichotomy of content (word information) and form (voice information) in speech perception. The objective was to establish the temporal and spatial organization of the underlying neuronal processes. For this purpose, an MEG experiment was conducted using an auditory oddball paradigm. The stimuli consisted of single spoken words, whereby the deviants manifested a change of the uttered word, of the voice, or both word and voice simultaneously (combined). First, we identified the N100m and localized its generators. Spatio-temporal dipole analysis in conjunction with the boundary element method using a scaled standard head model was employed. We analyzed N100m latency, dipole localization, and dipole strength. For the deviant stimuli, we found a more anterior localization with respect to the standard bilaterally (Figure 7). Localization differences between the deviants could not be shown and must have been smaller than 3-10 mm. Hemispherical localization differences were found (right more anterior and lateral) and are likely to be due to anatomical asymmetries reported in literature. The dipole strength was larger for all deviants compared to the standard stimulus. Again, no differences between the deviants could be established. For all conditions, the dipole strength was stronger in the left than in the right. This confirms evidence from the literature that both N100 and MMN show a left lateralization for language stimuli, but not for simple tones (e.g., Paavilainen et al., 1991; Alho et al., 1998; Szymanski et al., 1999). The analysis of the latencies of the N100m revealed a significantly shorter and less variant latency for the combined stimulus, compared to all other experimental conditions (Figure 8). This points towards a parallel processing of different dimensions of deviancy. We proposed an integrative parallel model that could quantitatively explain the observed latency effect.



Figure 7. Average dipole locations overlayed to the horizontal slice of a standard brain which intersects their center-of-mass.


Figure 8. Average latencies of the N100m with 95 % confidence intervals. The last two rows represent the prediction of the integrative parallel model for the latencies for the combined stimulus.

Gestalt perception modulates early visual processing

We examined whether early visual processing reflects perceptual properties of a stimulus in addition to physical features. We recorded event-related potentials (ERPs) of 13 subjects in a visual classification task. We used four different stimuli which were all composed of four identical elements. One of the stimuli constituted an illusory Kanizsa square, another was composed of the same number of collinear line segments but the elements did not form a Gestalt. In addition, a target and a control stimulus were used which were arranged differently. These stimuli allow differentiation between the processing of collinear line elements (stimulus features) and illusory figures (perceptual properties). The visual N170 in response to the illusory figure was significantly larger as compared to the other collinear stimulus. This is taken to indicate that the visual N170 reflects cognitive processes of Gestalt perception in addition to attentional processes and physical stimulus properties.



Figure 9. A: The four stimuli used in our paradigm: The target (a), a control (b), the collinear nonillusory figure (c) and the illusory figure (d). B: ERPs at electrodes O1 and O2 in response to the Kanizsa square (d, solid) and the collinear non-illusory figure (c, dotted) reveal a larger N170 for the illusory Kanizsa figure.

2.4.8

Herrmann, C.S. & Bosch, V.

2.4.9 Evoked gamma activity in human EEG is related to the level of difficulty in a color discrimination task

Senkowski, D., Temming, H. & Herrmann, C.S.

Recent findings support the notion that EEG gamma activity is related to attentional and binding processes. In the present study we found that evoked gamma activity and different ERP components are modulated by task difficulty in a visual discrimination task. In three blocks with identical stimuli we presented two similar green stimuli and one red stimulus. Stimuli consist of simple circles. ERPs and evoked gamma activity were measured in a passive block requiring no response, in an easy discrimination task where the red stimulus was the target, and in a difficult discrimination task where one of the two green stimuli was the target. We found a pronounced posterior amplitude increase of the ERP components N170 and P300 and an increase of early evoked gamma activity in both discrimination tasks. Compared to the easy task, N2b and posterior evoked gamma activity in a time range of about 200 msec were increased in the difficult task, indicating that N2b and evoked gamma activity are crucially involved in the processing of difficult tasks. In the easy task, higher gamma activity was found in a time range of about 100 msec, indicating a higher degree of stimulus processing in this early time range for the easy task. Our study further suggests a close relation between early evoked gamma activity and different ERP components such as N2b and P300.



Figure 10. Evoked gamma activity at occipital electrodes O1 and O2 of the non-target green stimuli in three different tasks. The easy task showed highest gamma activity in a time range of about 100 msec, whereas in a later time range of about 200 msec highest gamma activity was found in the difficult task. These differences are pronounced at posterior sides.

2.4.10 Computer-aided diagnosis of clinical EEG

Arnold, T.¹, Visbeck, A.² & Herrmann, C.S.¹ ¹ Max Planck Institute of Cognitive Neuroscience ² Department of Neurology, University of Mainz, Germany

The manual diagnosis of clinical EEG describes the dominant rhythmic activities like the background rhythm and pathologic slowings. Aside from the description in the frequency domain, it also reports the occurrence of specific patterns (graphoelements), in particular spike-wave-complexes as prominent indicators of epilepsy. An important part of the diagnostic process deals with the detection of physiological and technical artefacts like eye movements or electrode shifts. Although these artefacts are usually not part of the final report, their recognition is neccessary to avoid false classifications of rhythmic activities or epileptic graphoelements. We developed a computer-aided diagnostic system (CADS) for the mimetic analysis of the clinical EEG. The goal was the generation of an automatic diagnosis containing symbolic and numeric facts, that support the neurologist in the writing of his report.



Figure 11. Structure of the computer system for the automatic diagnosis of clinical EEG.



Figure 12. Structure of the medical expert system that inferes the automatic diagnosis.

The first stage of the system implements an interface to the digital EEG data (Figure 11). It resamples the signals if necessary and applies the appropriate high- and low-pass filters for the next level of the analysis. Here, one module extracts spectral parameters from all traces on a second-by-second basis. The parameters represent the dominant frequency components of each signal and also capture the development of sustained rhythmic activities over several seconds. The second module detects graphoelements by means of so-called Active Shape Models. The module makes use of two models that mathematically describe the mean shape and the typical deformations of spike-wave-complexes. Each EEG trace is scanned individually and the detected graphoelements are stored as output.

Based on these results and recording parameters a medical expert system infers the facts of the automatic diagnosis (Figure 12). The report is built of spatio-temporal events like artefacts, topologic information like the spreading of slow activity across the scalp and neurological facts like the existence of a normal background rhythm. The rules are separated into five modules that are processed sequentially and a sixth module for statistic analysis that is used in parallel. The first module checks the input of the expert system for logical inconsistencies. Afterwards artefacts, the background rhythm and pathologic slow activities are detected, where each module depends on the facts inferred by the previous one. Finally, the detected spike-wave-complexes are validated in their spatio-temporal context and false-positive detections are rejected. A detailed description and first results of the CADS were presented in Herrmann et. al. (2001).

In the year 2001, the major interest of the Independent Junior Research Group 'Neurocognition of Prosody' lay once more in the further exploration of auditory language processing, and especially on the examination of the segmentation processes of the incoming speech stream. We therefore focused our work on the processing of prosodic domains and prosodically highlighted information in the speech stream as realized by lexical stress (2.5.1; 2.5.2) and sentence accentuation (2.5.3). Our view that these kinds of prosodic information assists the interpretation of the perceived signal is supported by the studies we conducted.

Our main goal in the second year of our existence was threefold: First, the exploration of the prosodic domains involved in auditory speech processing, i.e., intonational phrases (2.5.4; 2.5.5), accent groups, words and syllables (2.5.6). Second, the influence of so-called 'non-linguistic' properties such as voice recognition (2.5.7) and third, the localization of processes related to pitch processing and voice recognition.

Behavioral and neurophysiological similarities for the processing of different prosodic domains and 'highlighting' during auditory processing has been proved.

First of all, we found evidence that metrical information has an impact on syllable processing and word recognition. As already known, highlighting or the encoding of linguistic prominence is related to pitch, durational and other acoustic cues. Our findings suggest that pitch parameters have the most important impact on speech processing in an intonational language such as German.

Furthermore prominence on the sentence level, induced by information structure, also enhances speech processing.

A main question still remaining here is whether the segmentation of an incoming continuous speech stream will differ between varying experimental conditions and its neuropsychological correlates.

Our presently running localization studies are concerned with the identification of a cortical network responsible for segmentation. We are therefore looking for interactions or a possible disentangling of specific functions of auditory processing in the left and right cerebral hemispheres.

Most of the studies concerning the formerly mentioned issues are still in progress and first results are being mapped onto existing theories of neuroanatomy and neuro-psy-chology.

2.5.1 Pitch and spoken word recognition I: Early extraction

Friedrich, C.K., Alter, K. & Kotz, S.A. Supported by DFG

A main focus of the neurocognition of prosody regards its function during spoken word recognition. In the present experiment we isolated the processing of a single important parameter of prosody, namely pitch, with artificially manipulated words (see Figure 1b for an example of this manipulation). We wanted to explore firstly, when pitch is extracted from the speech signal and secondly, if incorrect pitch information affects spoken word recognition. ERPs were recorded while subjects made decisions to the pitch manipulated words (e.g., whether it belonged to the category 'animate'). The ERPs revealed that pitch contours are already discriminated within the first syllable of a word as indicated by a stronger P2 for words with initially unstressed pitch contour as compared to the same words with initially stressed pitch contour (see Figure 1). This result indicates an early extraction of the pitch information from the acoustic signal by the listener. Furthermore, incorrect pitch information significantly delayed the recognition.



Figure 1. a) Waveform of the German word 'Tango' (Note, that in this example the syllable boundary is indicated by the plosive burst of /g/ following the nasal $/\eta/$), b) Pitch contours of 'Tango' for the initially stressed pitch that is incorrect for this initially unstressed German word (above) and of the same word with unstressed pitch contour as required for this word, c) ERPs for a selected electrode (P7) for words with initially stressed pitch contour (solid line) and for the same words with initially unstressed pitch contour (dashed line) time-locked to the word onset.

Pitch and spoken word recognition II: Lexical access

Supported by DFG

The present two experiments set out to clarify the role of pitch information during early processing stages of the recognition of spoken words. In Experiment 1, subjects heard spoken word initial syllables with artificially modulated pitch contours (see Figure 1a for an example) and were asked to name a word starting with that syllable. Following a syllable with stressed pitch subjects more frequently answered with an initially stressed word. However, if the same syllable carried an unstressed pitch contour, subjects more frequently responded with an initially unstressed word. In Experiment 2, we investigated the electrophysiological response to visually presented words that followed an auditory syllable with a stressed or with an unstressed pitch contour (Figure 2 a,b). An ERP component named the P350 was found to be sensitive to pitch information (Figure 1c,d). We argue that this ERP component is likely to reflect lexical access of words guided by the word initial pitch contour.



Figure 2. (a) Examples of the stressed (above) and unstressed pitch contour of the syllable 'tan' used in both Experiments, (b) Examples of the visual words that were presented immediately following the auditory syllables in Experiment 2 (Note, that stressed syllables are indicated by capital letters), (c) ERPs elicited by words that did match (solid line) or did not match (dashed line) the pitch of the prime, time locked to the word onset, (d) Difference map for the ERPs elicited by pitch matching subtracted from pitch mismatching words between 300 and 400 ms.

2.5.2

Friedrich, C.K., Kotz, S.A., Alter, K. & Friederici, A.D.

2.5.3 The influence of context in the perception of prosodic boundaries

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Supported by DFG

As previous studies have shown, processing of intonational phrase boundaries (IPh) on single sentence level elicits the Closure Positive Shift (CPS) in event-related potentials. Our present studies focus on the processing of prosodic cues in dependence on context information. In a first experiment (see Ann.Rep. 2000) we presented spoken dialogues to investigate the influence of information structure (IS) on the prosodic processing of accent positions and, furthermore, on that of IPh boundaries. Acoustic analyses of speech data showed that focused constituents carry the main pitch accent in the answer sentences and, in addition, that the syntactic variation (intransitive vs. transitive verb condition) is prosodically disambiguated in the transitive condition by an IPh boundary after the first verb.

transitive condition with narrow focus on the second verb

Question:	What does Peter promise Anna to do?
Answer:	Peter verspricht] _{IPh} Anna zu entLASten] _{IPh} und das BüRO zu putzen
	(Peter promises to support Anna and to clean the office)

Data from ERP measurements indicate clearly that the comprehension process is triggered by obtaining the new information, the CPS occurred after the constituent in focus. This seems to override syntactic analyses so that no CPS occurs at the measurable first IPh boundary after the first verb (see example above). In a present experiment the answer sentences were presented in isolation either with a narrow focus on the second verb or with the neutral default intonation of German declaratives to prove whether the



Figure 3. Same acoustic input leads to different processing depending on context information. Whereas in sentences presented in isolation a CPS occurs after the first verb, the processing of such prosodic boundaries in equal sentences presented with a preceding context question failes to elicit the CPS (solid line illustrates accentuated sentences with a preceding context question and the dotted line shows the condition presented without a preceding question).

missing CPS is caused by the influence of context information or by the prosodic character of the speech data. Behavioral data of prosodic judgment showed a surprisingly high acceptance rate of sentences in the condition of narrow focus.

The ERP-data reflect that listeners switch from processing accented information to syntactically driven processing if no context is given; the CPS due to the first measurable IPh boundary occurs again. Our results suggest that the processing of prosodic cues relies strongly on the presence of context information. Cues of prosodic boundary realization seem to be used to structure the incoming speech input if no previous information is available.

How the brain reflects prosodic chunking

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The Closure Positive Shift (CPS; Steinhauer et al., 1999) was shown to be evident at Intonational phrase boundaries (IPh; Nespor & Vogel, 1986; Selkirk, 1986) even when no isomorphy of the syntactic and prosodic constituents was given.

To further explore the nature of that CPS, two syntactically and prosodically varying structures, parentheticals vs. temporal adjuncts, were chosen to modify the former stimulus corpus. Although they both are maximal syntactic projections they differ in their location in the phrase structure tree and, prosodically, in their status as independent intonational constituents (Selkirk, 1978). Associated with these differences in intonational phrasing we expected to find varying ERP patterns, especially concerning the CPS.

1 PARENTHESIS	[Peter verspricht Anna] _{IPh} [das weiß Ingo] _{IPh} [zu arbeiten] _{IPh} und das Büro zu putzen.			
	(Peter promises Anna, to clean the office)	this Ingo knows,	to work an	ıd
2 ADJUNCT	[Peter verspricht Anna] ₁ das Büro zu putzen.	_{Ph} [am Donnerstag	zu arbeiten] _{IPh} un	d
	(Peter promises Anna to clean the office)	to work on Thurse	day an	ıd

Acoustic analyses were carried out showing an IPh boundary pattern (with boundary tone, prefinal lenghtening and pause) *before* and *after* the parenthesis of condition 1 but only *before* the adjunct of condition 2.

EEG- recordings were taken from 21 right- handed students without hearing and neurological disorders. *Statistical analyses of evoked brain potentials* reveal that there are significant differences in the latency of the CPS at the parieto-central electrode reflecting the two varying intonational boundary patterns of the stimuli (PARENTHESIS vs. ADJUNCT; Figure 4). Since the CPS has been shown to reflect boundaries of full

2.5.4

Toepel, U.^{1,2}, Saddy, D.¹ & Alter, K.² Intonational phrases, the results suggest that parenthetical constructions form full Intonational phrases while adjuncts of the type and scope in condition 2 do not.



Figure 4. Illustration of the differing CPS-patterns at the PZ-electrode.

2.5.5 The brain's coping with deviant speech

Toepel, U.^{1,2}, Saddy, D.¹ & Alter, K.² ¹ University of Potsdam, Linguistics Department, Germany ² Max Planck Institute of Cognitive Neuroscience

In former studies concerning the Closure Positive Shift (CPS; Steinhauer et al., 1999) its occurence at major intonational phrase boundaries (IPh) has become well established. But so far it is not clear whether *exclusive* prosodic processing is sufficient for eliciting this ERP-component or if segmental information (i.e., syntactic and semantic) is also needed for boundary detection in the auditory speech signal and hence for the CPS.

To evolve a stimulus condition requiring the pure processing of prosodic information a delexicalization procedure (PURR; Sonntag & Portele, 1998) was used to manipulate the acoustic stimuli described above. This was proven to preserve only the suprasegmental (prosodic) attributes of the signal; i.e. the fundamental frequency and the amplitude envelope. If the CPS is indeed only due to prosodic parameters, it should occur in the same way for the delexicalized stimuli as in their corresponding conditions (PARENTHESIS / ADJUNCT) with preserved segmental content.

EEG- recordings were taken from 21 right- handed students without hearing and neurological disorders.

Statistical analyses show that in the position of the second IPh-boundary where the CPS would have only been expected for the delexicalized PARENTHESIS-condition the difference between the waveforms did not reach significance (TW 500 ms; Figure 5). The absence of the electrophysiological potential Closure Positive Shift in purely prosodic conditions could be taken as support for the dependence of the CPS on segmental, hence syntactic, as well as prosodic information.



Figure 5. Electrophysiological responses to segmental and delexicalized conditions illustrated at the FZ-electrode

The neural processing of metrical changes in tri-syllabic consonant vowel pairs and the influence of task conditions

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The comparison of temporal aspects of naturally produced repetitive consonant vowel structures with varying metrical patterns was examined in a semi-attentive study (see Ann.Rep. 2000). An enhanced positivity was elicited by the syllable boundaries and was most eminent in the infrequent item. This could reflect the existence of a neuronal memory trace for durational changes of speech-like sounds and therefore the importance of syllable boundaries for the segmentation of the continuous speech stream. In the present study the brain response to the metrical patterns (initially stressed vs. medially and finally stressed item) and additionally the influence voiced vs. unvoiced consonants (/da/ vs. /ta/) was observed with different task conditions in a passive and an active oddball presentation. During the passive recordings subjects were instructed to ignore the stimuli and concentrate on a computer game. During the active recordings subjects were instructed to count the deviants in mind.

By changing the task condition to passive listening we observed ERPs to naturally produced changes of syllable duration in tri-syllabic consonant vowel items. We found a main effect for the comparison of initially and medially stressed items which seem to reflect the neural representation of differing sequences in early time windows of ERPs. The early negativity of phoneme change strongly reminds of a MMN-component, usually observed in sound and vowel discrimination tasks. The comparison of active and passive presentation shows a large P300 which is related to the behavioral response and occurs earlier for the phoneme change than for the metrical change.

2.5.6

Kruck, S.¹, Tervaniemi, M.² & Alter, K.¹



Figure 6.

Left side: Standard (black line) and deviant (coloured line) in the passive condition at the Fz electrode.

Right side: Comparison of deviants in the passive (coloured line) and active (black line) condition at the Pz electrode.

2.5.7 Human auditory processing of pitch altered speech

Lattner, S., Alter, K., Maess, B., Wang, Y. & Friederici, A.D. Artificial speech exhibits peculiar acoustic properties that are often interpreted as sounding like a 'computer voice'. Little is known about how the perceptual system deals with this lack of 'naturalness' in synthesised speech. Here we report a change in the early brain response as a function of naturalness of the auditory speech signal. We presented a natural male voice as a frequent standard stimulus and three types of infrequent deviants: a natural female voice, a pitch manipulated voice and synthesised speech. The event-related magnetic fields in response to the deviants were recorded by a wholehead magnetometer, and current densities were modelled. As indicated by Figure7 displaying the average current density from 100 to 300 ms post onset, and Figure 8 showing the spatial distribution of the activation at two points in this time course, we found a relatively weak brain response to the natural female voice, while the natural, but pitch altered speech signal led to a medium increase of current density. The artificial signal evoked the strongest neural response. Not only do these results demonstrate an early, preconscious neural sensitivity to voice information, but the study also provides objective neurophysiological evidence for the notion of 'naturalness' of voices.



Figure 7. Current density for each deviant - averaged across channels and subjects, from 100-300 ms after stimulus onset



Figure 8. Distribution of current density for each condition in the left and right hemisphere – averaged across subjects at two time points (175 ms and 225 ms after stimulus onset)

Clinical studies in the field of neuropsychology and neuro-imaging are currently experiencing an increasing importance. No matter how well we begin to understand basic and more complex brain functions that allow us to walk, to talk, to think or to memorize, we are challenged and fascinated by an advanced knowledge of the 'pathological state': Why are we the way we are? And how can we understand, cope with and possibly cure the many dreaded afflictions and disturbances that attack the human brain? Both questions are closely linked and require patient, careful and innovative research respecting the patient in his role as main character. The Day-Care Clinic of Cognitive Neurology at the University of Leipzig and the Max Planck Institute face this major challenge in close interaction. Most importantly, the cooperation of many patients garanties the ideal setting to address this major goal.

In 2001, the Day-Care Clinic treated 165 patients. 108 (66%) of the current patients took part in clinical research projects. Moreover, 153 former patients participated in clinical studies. Including discharged patients, our database now consists of a pool of more than 660 current and former patients with brain injuries of various etiologies. This offers researchers the opportunity to carefully select patient samples and to test specific hypotheses. The detailed characterization of individual patients in terms of medical and neuropsychological profiles and the considerable amount of patients with several cognitive deficits were the starting point of many neuropsychological projects in 2001.

The clinical research focused on several issues that belong to three categories and partly overlap: Two main topics, which have been in the center of our research for several years, are the *functional neuroanatomy of the frontal lobes* (2.6.1-2.6.3) and *language processing / language organization* (2.6.4-2.6.7). Both fields profited from the clinical orientation and could further evolve. In addition, a study of regularity learning in Parkinson's disease (2.6.8-2.6.9) and a study of the cerebral microangiopathy (2.6.10) round up the picture of long-term activation. A new topic promoted by Prof. Pollmann's group at the day clinic targeted visual attention and interhemispheric transfer (2.6.11-2.6.15).

2.6.1 Deficits in sequential processing: premotor and parietal patients

Sakreida, K., Schubotz, R.I. & von Cramon, D.Y. Previous findings in fMRI (Schubotz & von Cramon, 2001) have indicated that the entire lateral premotor cortex (PMC) is involved in the processing of sequential information. Particularly, activations suggest that temporal, object-specific and spatial patterns of sequences are represented in anatomically distinct foci of the PMC. In continuation, behavioural performance in the processing of temporal, object-specific and spatial sequences was investigated in patients with premotor (n=8) and parietal (n=7) lesions. As a further control, both patients with prefrontal (n=7) lesions as well as age-balanced healthy control subjects matching each patient group were also tested. Visually stimulus sequences where presented in a block design. Twelve pictures were successively presented within each trial, with two successive pictures repeated six times. Each screen display showed two equal geometrical forms arranged on two opposite positions on a virtual circle. Four tasks were announced by visual cues. Subjects were asked to monitor stimulus sequences for dimension-specific violations, i.e., rhythm, object, or position deviants (50% of all trials). In addition, a non-sequential baseline condition was employed in order to control for perceptual requirements and motor response.



As a result, premotor patients showed significant higher error rates in all sequence tasks, but not in the baseline task, in comparison to the healthy control group (Figure 1, top panel). In contrast, parietal patients were impaired only in the object-specific task, compared to controls (Figure 1, middle panel). Prefrontal patients exposed no specific deficits at all (Figure 1, bottom panel). The findings demonstrate that sequential processing relies on an intact premotor-parietal network. Moreover, they indicate that premotor lesions cause a broader deficit in sequential processing than parietal lesions.

Figure 1.

The imitating hand

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We take it for granted that our hands do more or less what we want them to do. However, patients with so called 'alien hand syndrome' show that this is not as self evident as we might think. The term 'alien hand syndrome' describes a neuropsychological syndrome after lesion to medial brain structures, in particular to the corpus callosum. Patients with this syndrome have problems to willingly control the actions of one hand while the other hand is completely under intentional control. Although the actions executed by the 'alien' hand are not intended they are nevertheless meaningful. Therefore the question about the origin of these actions arises. In a patient with a left sided alien hand syndrome we have tested the hypothesis that the 'alien hand' executes automatic imitative response tendencies. The patient was required to lift the index or the middle finger of the right or left hand in response to a number ('1' indicates index finger and '2' indicates middle finger) which was presented between index or middle finger of a right or left videotaped hand (left part of Figure 2). In some trials the number was presented without a finger movement of the displayed hand (baseline trials). In some trials the presentation of the number was combined with a finger movement of the congruent finger (congruent trials). Importantly, sometimes the number was presented while the incongruent finger was moving (incongruent trials). While the patient had no problems to execute all three conditions with the right hand, he had severe problems in incongruent trials when using the left hand (right part of Figure 2). Our results suggest that the 'alien hand' which is only partly under intentional control tends to imitate the observed finger movements. This finding supports the assumption of an automatic tendency to imitate.



Figure 2. Left part: Last frame of the video sequences. Right part: Errors as a function of congruency and required response hand.

2.6.2

Brass, M.¹, Förstl, S.², Schroeter, M.¹ & von Cramon, D.Y.¹

2.6.3 Interactions of focal brain lesions with error processing

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Day care clinic of cognitive fictiology, oniversity of Leip

³ Clinic for Neurology, Charité, Berlin, Germany

Electrophysiological as well as hemodynamic studies have suggested that structures in the vicinity of the anterior cingulate cortex are involved in performance monitoring, particularly in detection of errors. Bidirectional interactions between the frontomedian system involved in performance monitoring and the lateral prefrontal cortex as well as the orbitofrontal cortex have been proposed, but only few studies have directly addressed this issue.

We investigated error-related ERPs in three patient groups with different focal cortical lesions employing a speeded flankers task: patients with bifrontopolar lesions extending into the orbitofrontal cortex (n=6), with unilateral lesions of the lateral frontal cortex (n=7), and with unilateral temporal lesions (n=6), respectively. The data were compared to the results from two age-matched healthy control groups.

Whereas bilateral frontopolar lesions involving the orbitofrontal cortex as well as temporal lesions did not alter the error-related negativity (ERN/Ne), lesions of the lateral frontal cortex resulted in an abolition of the ERN and a reduction of the error positivity (Pe). This suggests that frontolateral lesions rendered the generators of the ERN unable to distinguish between correct and incorrect. It could be speculated that lesions of the lateral frontal cortex led to difficulties with task-set-related processes, which may have disturbed the establishment of a representation of the correct response. It is conceivable that on the basis of incomplete response representations errors cannot be detected properly.



Figure 3. Grand mean ERP waveforms for each group at FCz and Pz from erroneous trials (dotted lines) and correct trials (solid lines). Left panel: lateral frontal and the according older control group; right panel: bifrontopolar, temporal and the according young control group.

Text comprehension after brain injury: Auditory distractability of patients with attention deficits and non-aphasic language disorders

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Brain injured patients often complain that they cannot concentrate on a conversation, when they are distracted by surrounding noise or when several people participate. Studies investigating distractability have mostly focussed on attentional influences on phoneme and word recognition and used basic language stimuli, such as syllables or short words. However, besides an attention deficit, the problems might also be caused by a non-aphasic language deficit (NALD), following frontal lobe lesions or traumatic brain injury. The goal of this project was to develop a paradigm for assessing distractability by verbal and non-verbal background noise in the context of naturally occurring connected text. Analogous to previously used text material (Walther, 2000; Nicholas & Brookshire, 1995) we wrote nine short stories with eight associated yes/no questions each. The verbal distractor consisted of party or restaurant noise, including spoken conversations, the non-verbal distractor was traffic noise, and the control condition consisted of uniform pink noise. The three distractor types were matched with respect to loudness and frequency spectrum, and three stories were combined with each of the distractor types. In the first experiment, the stories were presented auditorily without distractor. 30 brain-injured patients - including 22 with frontal lobe lesions had a mean error rate of 15%, indicating that the difficulty level of the comprehension task was appropriate. In the second experiment, we tested younger (age 25-35) and older (age 49-62) control subjects. There were no significant differences between the distractor types, but the older group had considerably more difficulties with the pink noise condition. In the third experiment, six patients with attentional deficits (ATT) and seven patients with NALD participated. Overall, the error rates were dramatically elevated. As expected, the ATT patients were distracted by those noise conditions only in which separate acoustic objects were distinguishable. In contrast, the NALD patients did not show the expected distractor effect for the verbal condition (party noise), a result which



Figure 4. Mean error rates for the different groups of participants as a function of distractor type.

2.6.4

Ferstl, E.C.¹, Guthke, T.², Rübsamen, R.³, Lange, Y.¹ & von Cramon, D.Y.^{1,2} might be due to a floor effect, i.e., to their problems in the pink noise control condition. An important conclusion is that clinical diagnosis of text comprehension difficulties must include naturalistic conditions, including background noise, and cannot be restricted to tests conducted in laboratory settings.

2.6.5 A dissociation of the P300 and the P600 components: A lesion study

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A recent discussion in event-related brain potential (ERP) research is focussed on the question of whether the P600 and P300 component are functionally distinct or not (cf. Coulson et al., 1998; Friederici et al., 2001; Osterhout & Hagoort, 1999). While the P600 is elicited by a broad range of grammatical violations, the P300 component is elicited by an unexpected event (cf. Donchin & Coles, 1988). In order to further test a functional as well as an anatomical differentiation of the two components, we tested a group of 16 aphasic patients, half of them with both anterior and subcortical lesions involving the basal ganglia and half of them with a temporo-parietal lesion. In a first ERP experiment, the patients judged auditorily presented sentences, which were either correct or incorrect as the verb was wrongly inflected. In a second ERP experiment, patients were tested in an auditory ERP oddball paradigm. In the oddball experiment, both patient groups displayed a clear P300 effect (Figure 5). However, in the language experiment, only the group with temporo-parietal lesions showed a P600 component to verb inflection errors (Figure 6). These data indicate that there is a single neurophysiological dissociation of the P300 and P600 components. It appears that the basal ganglia in particular seem to play a crucial role in the generation of the P600, but not of the P300 component.



Figure 5. Difference waves of the P300 effect displayed at selected electrode-sites for patients including basal ganglia lesions (black line) and patients excluding basal ganglia lesions (blue line). Waveforms are plotted from 200 ms prior to target onset up to 800 ms after target onset.



Figure 6. Difference waves of the P600 effect displayed at selected electrode-sites for patients including basal ganglia lesions (black line) and patients excluding basal ganglia lesions (blue line). Waveforms are plotted from 200 ms prior to target onset up to 1200 ms after target onset.

Do arachnoid cysts change the functional organization of the brain ? An fMRI and morphometric study

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This study aimed to investigate the significance of congenital and clinically quiescent arachnoid cysts in the left temporal fossa on the functional organization of adjacent cortices. Functional MR mapping was applied in five right-handed and asymptomatic patients to determine the functional organization of language. Moreover, morphometry was performed in each individual patient to gain white and grey matter volumes in adjacent brain areas as well as the mean cortical thickness of the left opercular region. Four patients showed a clear left hemisphere language dominance regardless of the size of the cyst. In the remaining patient, a mixed laterality of language organization was assessed. An interesting dissociation of morphometric data was assessed comparing the overall neighbouring and selective language related cortices. Morphometry in



Figure 7. The individual zmaps of the five patients are overlaid onto their anatomical 3D dataset. The zmap was thresholded at z>4.

2.6.6

Hund-Georgiadis, M.¹, von Cramon, D.Y.^{1,2}, Kruggel, F.¹ & Preul, C.¹ the neighbouring brain regions of the AC showed overall reduced cortical surface areas, grey and white matter volumes as well as a decrease in cortical thickness in comparison to the homologous right side. However, the surface area of the fronto-opercular region of the left inferior frontal gyrus i.e. the pars triangularis and the pars opercularis was larger on the left as compared to the right side. Both have been identified to represent the morphometric substrate of language dominance in the left hemisphere. In sum, ACs do not disturb the obviously robust normal asymmetry of hemisphere language organization, in spite of delicate locations adjacent to the left inferior frontal gyrus. The ACs account for a physical displacement of language related activations but usually patients with congental ACs employ their original language cortex even when distorted through the cyst.

2.6.7 Crossed nonaphasia in a dextral with left-hemispheric lesions: A functional MRI-study of mirrored brain organization

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This line of research is addressing the underlying physiology of abnormal lateralization of certain brain functions. So far, it is unsettled whether atypical dominance of language is accompanied by a reversed asymmetry in other domains. The functional organization of language, attention and motor performance was investigated in a 42year-old patient with crossed non-aphasia by means of functional MR-imaging. The



Figure 8. Functional activation patterns of language, attentional and motor tasks overlaid on the patient's anatomical image in the axial plane. Functional images were created by generating statistical zmaps with z-values > 4 on a single pixel level.

strongly right-handed male developed a left middle cerebral artery infarction documented by MR imaging without exhibiting aphasia. However, the left hemispheric stroke was accompanied by visuospatial impairment, right-sided slight sensory and motor paresis and right homonymous hemianopia. No history of familial sinistrality or prior neurological illness was present. Functional MR-language mapping revealed strongly right-hemispheric activation in inferior frontal and superior temporal cortices. Finger tapping with the right hand recruited exquisitely ipsilateral premotor and motor areas as well as SMA. A Stroop task - usually strongly associated with left sided inferior frontal activation in dextrals - resulted in strongly right hemisphere frontal activation. From our data there is clear evidence that different modalities such as language perception and production, attention and motor performance are processed exclusively by one hemisphere, when atypical cerebral dominance is present.

Sequence-learning deficits in Parkinson's disease depend on stimulus presentation

Supported by BMB+F / IZKF Leipzig

In this study, we investigated implicit sequence learning in 22 patients with Parkinson's disease (PD). For this purpose, a newly developed variant of the Serial reaction time task (SRT) was employed. As previous SRT studies with PD patients have reported heterogenous results, we aimed to examine in detail the preconditions of impaired sequence-specific learning in PD.

In the first experiment, we investigated whether stimulus learning or response-stimulus learning as subprocesses of sequence learning were specifically impaired in PD. Therefore, the complexity of the stimulus sequence was varied while keeping the motor sequence constant. Our results indicated that neither stimulus learning nor response-stimulus learning was specifically affected in PD.



Figure 9. Experiment 1 - Mean reaction times as a function of sequence type, block, and group. Blocks 1, 5, 9, 13, and 17 were random. Both groups show comparable sequence-specific learning.

2.6.8

Werheid, K., Ziessler, M. & von Cramon, D.Y. In the second experiment, we investigated whether sequence learning deficits depend upon the surface characteristics of the SRT task, i.e., the stimulus presentation mode. For this purpose, a spatial variant of the SRT task employed in Experiment 1 was developed. Sequence-specific learning deficits in PD patients emerged only when the stimuli were presented spatially.

Taken together, our results suggest that there is no global sequence learning deficit in PD. Reduced learning in spatial SRT variants may be due to a deficit in linking stimulus anticipations to corresponding eye movements.



Figure 10: Experiment 2 - Mean reaction times as a function of sequence type, block, and group. Blocks 1, 5, 9, 13, and 17 were random. In this visuospatial (VR) version of the task, patients show reduced sequence-specific learning as compared to controls.

2.6.9 Regularity learning in a serial reaction time task:An fMRI study on patients with early Parkinson's disease

Supported by BMB+F / IZKF Leipzig

In the present study, we investigated regularity learning as a subprocess of sequence learning in patients with Parkinson's disease and healthy participants. Functional magnetic resonance imaging and a variant of the serial reaction time task were employed to examine regularity learning independently from visuomotor learning. Prior to scanning, the participants (seven per group) received a pretraining, during which they responded to successively appearing visual stimuli by pressing spatially corresponding keys. Unbeknownst to them, a cycling 12-item sequence was presented. During the fMRI session, they received alternating blocks of sequential and random stimuli.

Regarding the functional correlates of regularity processing (see Figure 11), our main findings were that performance of previously learned sequences as opposed to random stimuli mainly activated the frontomedian and posterior cingulate cortex and that the extent of regularity learning was in both groups related to the magnitude of activations in the posterior cingulate cortex. These results point to a fronto-parietomedian network for processing previously learned regular sequences. Viewed together with earlier research, we conclude that the posterior part of this network is responsible for memory

Werheid, K., Zysset, S. & von Cramon, D.Y. retrieval, i.e., matching the actual stimuli with the previously learned regular sequence. The anterior part is rather involved in the prediction of future stimuli and in anticipating corresponding actions.



Figure 11. Z-maps depicting the contrast between 'Sequence' and 'Random' condition for healthy controls (HC) and patients with Parkinson's disease (PD).

Patients with early Parkinson's disease showed reduced visuomotor learning during pretraining, but intact regularity learning. Imaging revealed highly similar cortical activations in patients as compared to the control group, involving the same fronto-parietomedian network. We conclude that the frontostriatal dopaminergic pathway is affected in early Parkinson's disease, but the medial pathway from the ventral tegmental area to the frontomedian cortex may still be spared.

In conclusion, the results of the present study indicate that the assumption of a procedural learning deficit has to be replaced by more specific hypotheses about the pattern of cognitive deficits in Parkinson's disease. Regarding sequence learning, we conclude that despite obvious impairments of visuomotor learning in Parkinson's disease, other subprocesses, such as the processing of regularities can be spared. Further work is needed to determine the brain systems which are necessary and sufficient for the performance of other procedural tasks.

Characterization of cerebral microangiopathy by means of 3Tesla MRI: Correlation with neurological impairment and vascular risk factors

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2.6.10

Hund-Georgiadis, M.¹, Balaschke, O.², Scheid, R.², Norris, D.G.¹ & von Cramon, D.Y.^{1,2}

This study sought to investigate whether clinical and neuropsychological impairment in cerebral small vessel disease (CSVD) can be evaluated by means of morphological magnetic resonance imaging (MRI). MR-imaging at 3 Tesla in T_2 and T_1 weighted sequences was evaluated in 44 patients with cerebral microangiopathy and 30 patients with combined cerebral micro- and macroangiopathy. The MR characteristics as visualized in Figure 12 were correlated to clinical data, attentional impairment and the patients' individual vascular risk factor profiles. 15 healthy age-matched control subjects participated in the study to assess MR signal changes in non-hypertensive elderly subjects. Patients and normal controls differed significantly in the extent of MR signal changes. A close relation between age, obesity, hypertension and MR signal abnormalities was evident in all patients. Patients with pure CSVD additionally showed an association between MR defined severity of their disease, the degree of neurological impairment and their vascular risk score. In contrast, attentional impairment did not relate to the MR defined severity of CSVD.



Figure 12. Abnormal MR signal changes on the T2-weighted -image were the basis of the performed MR staging: Periventricular caps and rims, the degree of diffuse white matter hyperintensities (A) were rated as well as the severity of basal ganglia involvement (B) and the presence of lacunar infarcts (C). The enlargement of perivascular spaces as referred to as the hyperintense vessel sign (D) was further evaluated. The hyperintense vessels are marked by white arrows.

2.6.11 Splenial lesions and dichotic listening

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Previous studies demonstrated that partial lesions of the corpus callosum may lead to left ear suppression in consonant-vowel dichotic listening tasks. Initially, lesions of the posterior part of the trunk of the corpus callosum were thought to be associated with left ear suppression. In the monkey, this area contains auditory commissures. Consequently, disruption of auditory transfer to the language-dominant hemisphere was thought to be the cause for the left ear suppression. However, a more recent study, using magnetic resonance imaging and exact measurement of callosal lesion location, found left ear suppression after lesions of the posterior 25-20% of the circumference of the corpus callosum, which consist largely of the splenium, but often includes the most posterior part of the trunk of the corpus callosum. In the present study, we found lesions in the posterior 17% of the corpus callosum to be associated with left ear suppression, con-

firming the association of left ear suppression and splenial lesion. Furthermore, left ear suppression after splenial lesions was found in a rapid presentation dichotic monitoring task and a standard dichotic listening task alike, ruling out attentional limitations in the processing of high stimulus loads as a confounding factor. Moreover, directed attention to the left ear did not improve left ear target detection in our patients, independent of callosal lesion location. Our data may indicate that auditory callosal fibers pass through the splenium, more posteriorly than previously thought. However, further studies will have to investigate whether callosal fibers between primary or secondary auditory cortices, or between higher-level multimodal cortices are vital for the detection of left ear targets in dichotic listening.



Figure 13. Individual patient performance in relation to lesion location. (A) Laterality scores in the nonforced dichotic monitoring and verbal report tasks, (B) Lesion location in percent of the curvature of the corpus callosum from the tip of the rostrum (0%) to the end of the splenium (100%), (C) Left ear detection rate in the nonforced and forced left dichotic monitoring task

2.6.12 The neural basis of the bilateral distribution advantage

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When tasks are demanding, the cerebral hemispheres may share their resources for effective processing. This has been suggested by behavioral data showing faster response times when the information to be processed is presented in both visual hemifields, compared to unilateral presentation. This bilateral distribution advantage (BDA) is typically observed in computationally complex tasks, whereas it is absent in simple tasks. Using event-related functional magnetic resonance imaging (fMRI), we confirmed the hypothesis that the BDA is due to interhemispheric resource sharing when the task becomes too complex to be easily processed within one hemisphere. In contrast to simple letter shape matches, complex letter name matches showed a contralateral stimulus load effect, indicative of resource limitation in the hemisphere of input. In name matches, where the hemispheric resource limit was reached, we observed bilateral resource sharing, i.e. bilateral visual cortex activation even for within-hemifield matches, which was not observed for the simpler shape matches. In addition, a task x visual field interaction in anterior cingulate complex and posterior cingulate / retrosplenial cortex, indicated participation of these areas in interhemispheric transfer.



Figure 14. Activation elicited in letter matching in lateral occipital cortex. In the shape matching condition, letters had to be matched by physical shape, i.e. A/A was equal, but A/a different. In the name matching condition, letter identity had to be matched, i.e. a/a was now equal. Shape matches were processed in the hemisphere of input, as shown by the statistical parametric map in the upper row (bilateral – left visual hemifield (LVF) contrast) and the BOLD-amplitudes (s: shape-, n: name matches, b: bilateral, l: LVF, r: RVF), which show equal BOLD-amplitudes for bilateral and contralateral matches and negligible activation for matches in the ipsilateral hemifield. In contrast, name matches (lower row) elicited stronger activation for contralateral matches, whereas ipsilateral matches yielded as much activation as bilateral matches.

Splenial lesions and visual spatial attention

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Evidence from lesion and imaging studies suggests the temporoparietal junction (TPJ) area to be the anatomical correlate of a subprocess of visual spatial orienting: the disengagement of the attentional focus. There is further evidence that the commissures between the TPJ-corteces cross via the anterior portion of the splenium of the corpus callosum (CC). In a study (2.6.11) using the dichotic listening paradigm we found a deficit in reporting right ear target syllables. This may potentially be due to an auditory disengagement deficit. Therefore, in the present study, we predicted that patients with splenial lesions would show difficulties in disengaging attention from the current focus, compared to those with more anterior callosal lesions or to healthy controls.

Eight former patients of the Day-Care Clinic of Cognitive Neurology with splenial (n=4) and non-splenial lesions as well as eight healthy controls were tested with the spatial cueing task They had to indicate if the target - a small white diamond on a black screen - appeared at the right or the left of fixation by pressing one of two keys. The experimental manipulation consisted of presenting a cue 300 ms before the target that either correctly indicated the target position (valid cue) or indicated the position opposite the target (invalid cue) or contained no information regarding the position of the target (neutral cue). The cue was a luminance change at the respective position(s).

All groups exhibited typical validity effects, that is valid cues led to faster responses than neutral cues which in turn lead to faster responses than invalid cues. Furthermore, patients with splenial lesions had greater costs (RT _{invalid} - RT _{neutral}) than the two other groups, supporting the assumption of a disengagement deficit. However, they also showed greater benefits (RT _{neutral} - RT _{valid}), indicating that the disengagement function is not selectively impaired. It seems as if the interhemispheric exchange of information regarding stimuli in the visual field is slowed in situations of unfocused attention after splenial lesions.



Figure 15. Mean reaction times [ms] as a function of cue validity for the three experimental groups.

2.6.13

Maertens, M.¹ & Pollmann, S.^{1,2}

2.6.14 Imaging covert reorienting and inhibition of return

Lepsien, J.¹ & ¹ Max Planck Ins Pollmann, S.^{1,2} ² Day-Care Clini

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If visual attention is directed to a location by an uninformative exogenous cue, the detection of a target at this location is facilitated within a stimulus onset asynchrony (SOA) of 250 ms. After this period, valid cueing leads to inhibition in target detection (inhibition of return, IOR). The effect of facilitation is usually interpreted as stimulus-induced allocation of attentional resources. Covert reorienting becomes necessary if the target is presented at an unattended location, and it has to counteract the still active attentional capture. In contrast, IOR is observed after the attentional capture has declined, indicating a possibly different process. According to behavioral evidence, IOR is discussed to be a compound of attentional and (oculo)motor processes. We used event-related fMRI to compare the neuronal correlates of covert reorienting and IOR by applying a modified version of the Posner cueing paradigm.

Covert reorienting revealed increased activation in left frontopolar cortex (LFPC), right anterior and left posterior middle frontal gyrus and right cerebellum (see Figure 16), areas which have previously been associated with attentional processes, specifically attentional change.

In contrast, IOR was accompanied by increased activation in brain areas involved in oculomotor programming, such as right medial frontal gyrus (supplementary eye field; SEF) and right inferior precentral sulcus (inferior frontal eye field; FEF), supporting the notion that an oculomotor bias is involved in the generation of IOR.

Joint activation for covert reorienting and IOR was found in the preSEF, preFEF, and the right supramarginal gyrus, which may link attentional and oculomotor systems.

In summary, three sets of brain areas were found, supporting the idea of different processes underlying covert reorienting and IOR. a) Covert Reorienting $2 - \frac{z - score}{3.1 - 4.7}$



Figure 16. Signal increases following (a) covert reorienting, (b) inhibition of return, and (c) joint activation of covert reorienting and inhibition of return ([1] posterior middle frontal gyrus, [2] fontopolar cortex, [3] anterior middle frontal gyrus, [4] cerebellum, [5] medial frontal gyrus (SEF), [6] inferior precentral sulcus (FEF), [7] superior frontal sulcus (preFEF), [8] medial frontal gyrus (preSEF), and [9] superior frontal gyrus).

Contrasting visual dimension changes in singleton feature- and conjunction search

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Shifting attention between visual dimensions takes time. Reaction time costs increase when visual dimension changes are induced by a singleton conjunction search task compared to a singleton feature search task. Pollmann, Weidner, Müller, and von Cramon (2000) demonstrated, that dimension changes in singleton feature search lead to activations in left lateral frontopolar cortex. In contrast, Weidner, Pollmann, Müller, and von Cramon (in press) showed that changes of a secondary target defining dimension in conjunction search leads to stronger activations in pregenual anterior cingulate (ACC). To evaluate the role of those areas we contrasted dimension changes in singleton feature search and singleton conjunction search in a single fMRI-study. Observers performed both a singleton conjunction search task, where subjects searched for a target that was defined by a unique combination of features, and a singleton feature task, where targets were defined by a simple feature contrast. An event-related analysis was carried out across the feature and conjunction search tasks. The interaction of the factors search task and target change was examined. This analysis revealed a significant interaction in pregenual ACC (Z_{max} =3.4, x=-8 y=48 z=6) and a marginally significant interaction in left lateral frontopolar cortex (Z_{max}=-2.9, x=-29 y=47 z=3). Signal changes in two regions of interest (ROIs) at these locations were analyzed for all conditions. Differential activation pattern were observed in pregenual ACC and frontopolar cortex (Figure 17). In left pregenual ACC, changes of the target defining dimension resulted



Figure 17. Percent signal change in regions of interest in left lateral frontopolar cortex and in left pregenual ACC, averaged over 8 observers. (The figure displays only the subset of locations of individual peak activation lying in the viewing plane.) Left pregenual ACC showed a clear difference between dimensional change and no-change trials in the conjunction search task, but not in the feature search task (*top / yellow*). In lateral prefrontal cortex, differences between change and no-change trials were only observed for the feature search task (*bottom /orange*).

2.6.15

Weidner, R.^{1,2}, Pollmann, S.^{2,3}, Müller, H.J.⁴ & von Cramon, D.Y.^{2,3} in a stronger signal increase compared to no-change trials only in the complex singleton conjunction search task (planned t-tests, t(7)=4.09, p<0.05), but not in the simpler singleton feature task (planned t-tests, t(7)=-0.95, n.s). Exactly the reverse pattern was manifest in left frontopolar cortex. In the conjunction search task, no significant difference in signal change was obtained for dimension change relative to no-change trials (planned t-tests, t(7)=0.82, n.s). In contrast, in the feature search task, changes in the target dimension produced a strong signal increase compared to no-change trials (planned t-tests, t(7)=3.26, p<0.05). Investigating the functional role of the frontal cortex is a bold venture. On one hand, the frontal cortex shows a complex involvement in very different cognitive tasks, on the other there is no specific cognitive function related to the frontal cortex. When viewed from a broad perspective, at least three different functional aspects might be distinguished. The 'action-related' aspect which is associated with the preparation and execution of action, but also with action-related aspects of perception. The 'executive' aspect, which is related to higher order control of cognitive processes. And finally, the 'evaluative' aspect which is related to complex judgment and contextual language processing. Our work suggests that all three aspects are loosely associated with the premotor cortex, the 'executive' aspect with the fronto-lateral cortex and the 'evaluative' aspect is related to the frontal cortex. The 'action-related' aspect is are highly interconnected, a comprehensive functional neuroanatomy of the frontal cortex has to deal with all three of them, as well as their interactions.

The research group 'Neuroanatomy of the frontal cortex' carries out studies in all three fields. Methodologically, the group combines expertise in experimental cognitive psychology with neuropsychological methods, in particular functional Magnetic Resonance Imaging (fMRI) and EEG. In order to relate our brain imaging results to cognitive deficits in neurological patients, we have carried out a number of patient-studies in collaboration with the Day-Care Clinic of Cognitive Neurology which are reported in section 2.6.

In previous studies we could show that the anticipatory perceptual analysis of dynamic target patterns draws on the lateral premotor cortex. This general finding was extended and specified in a series of experiments. In (2.7.1) it was demonstrated that increasing complexity of a target motion increases activation within the lateral premotor cortex. Whether or not the analysis of abstract target motion relies on the same premotor-parietal network as the analysis of object directed action was tested in (2.7.2). A third study (2.7.3) demonstrated that the premotor cortex reveals a somatotopically organized representation for different stimulus features in the auditory domain. Study (2.7.4) extended the investigation of the premotor cortex to observed goal-directed action and the representation of action schemata. The role of the premotor cortex in representing object-related motor programs was investigated in study (2.7.5).

The 'executive' or 'task management' aspect of the frontal cortex was investigated with various classical cognitive paradigms such as task-switching, dual-task performance and the Stroop-task. In (2.7.6) we could show the involvement of the fronto-lateral cortex in task preparation using a task-switching paradigm. This finding was further elaborated (2.7.7) by dissociating preparation-related and execution-related brain areas. Response related control processes were investigated in (2.7.8). In (2.7.9) a dual-

task paradigm was used to clarify the involvement of the lateral prefrontal cortex in task-scheduling. Retesting Stroop-performance using functional fMRI was carried out to reveal how brain activation measures and reaction time measures are related when measured repeatedly (2.7.10). In (2.7.11) an ERP-study was carried out to study the functional role of the P3 component in novelty judgements and its relationship to distractibility. Finally, we carried out a memory study of the Sternberg item recognition task investigating the relationship between the number of items in a study list and cortical activation (2.7.12).

In the beginning, neuroimaging techniques were restricted to the investigation of simple cognitive processes. However, from a clinical perspective it would be desirable to understand the cortical mechanisms underlying more complex behavior. Consequently, we have started during the last few years to investigate the cortical bases of more complex cognitive demands. In (2.7.13) it was studied which fronto-median areas are related to evaluative judgements. Study (2.7.14) investigated how the emotional and temporal aspects of the situational model in text comprehension is processed cortically. The question of whether the same fronto-median regions are related to coherence judgments and theory of mind tasks was addressed in (2.7.15).

2.7.1 A blueprint for target motion: fMRI reveals perceptual complexity to modulate the lateral premotor cortex

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

The execution of movements that are guided by an increasingly complex target motion is known to draw on premotor cortices. Functional MRI was used to investigate whether in the absence of any movement, attending to and predicting increasingly complex target motion also rely on premotor cortices. Complexity was varied as a function of number of sequential elements (Number) and amount of dynamic sequential trend (Trend) in a pulsing target motion. As a result, sequential prediction caused activations in lateral premotor and corresponding parietal cortices, particularly within the right hemisphere (Figure 1, top panel). Parametric analyses revealed that the right premotor cortex was the only area that co-varied positively with both behavioral (*Difficulty*, measured by mean error rates) as well as physical measures of sequential complexity (Number and *Trend*). Foci of maximal activation corresponding to all parametric measures of perceptual complexity are indicated in Figure 1. In addition, increasing element Number drew particularly on dorsal premotor cortex, and increasing dynamic sequential *Trend* on the motion area. The present findings demonstrate that premotor involvement directly reflects perceptual complexity in attended and predicted target motion. It is suggested that when we try to predict how a target will move, the motor system generates a 'blueprint' of the observed motion that allows potential sensorimotor integration. In the absence of any motor requirement, this blueprint appears not to be a by-product of motor planning, but rather to build the basis for target motion prediction.



Figure 1. Main activation foci indicated for predicting sequential patterns in target motion, compared to baseline (top panel), as well as for behavioral parameters of perceptual complexity (task difficulty, second panel) and for physical measures of perceptual complexity (sequential element number, third panel, and sequential trend of target motion, bottom panel).

Mapping perception onto expectation in dynamic patterns: Premotor correlates of perceived action and perceived target motion investigated with fMRI

The present study aimed at the comparison between brain correlates obtained while participants attend to movies showing manual object-directed actions (*Human Action*), and those obtained while participants attend to abstract target motion sequences (*Target Motion*) showing a regular dynamic pattern of changes. While both types of stimuli are known to activate lateral premotor cortices in two separate prior experiments, the present study was designed to allow for a direct comparison of activation foci. In order to control for perceptual and motor response effects, a simple target detection task was employed as baseline condition that presented random visual patterns similar to those



Figure 2. Activations obtained during the perceptual analysis of human actions (top) and of target motions (bottom).

2.7.2

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

used in *Target Motion*. In comparison to baseline, both the analysis of action and the analysis of target motion engaged similar cortical networks. As shown in Figure 2, most significant activation was found within the ventrolateral premotor cortex, pronounced within the right hemisphere, and within the anterior intraparietal sulcus. These areas are known to build a network that serves prehension and manual object-related action. The findings indicate that the analysis of dynamic patterns within perceptual events engages a common prehension network, no matter if those are provided by abstract target motion or by other beings' action.

2.7.3 Sensory anticipation of auditory where, when, what: Implications for a premotor homunculus replicated

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

Prior fMRI findings have indicated that the anticipation of visually presented dynamic patterns engages different lateral premotor areas, dependent on which stimulus property is attended (Schubotz & von Cramon, 2001). The present study aimed at the replication of the findings, using auditory stimuli. To this end, repetitive patterns of auditory noises of different quality were presented in different rhythms from different virtual spatial sources. Announced by a trial cue, participants were asked to attend to the task-relevant stimulus domain, i.e., the stimulus' temporal, qualitative, or spatial properties. Performance in perceptual anticipation was tested by a deviant detection task.

Direct task contrasts replicated findings in the visual paradigm, showing different premotor involvement in each of the three investigated stimulus properties. Attending to temporal patterns (Figure 3, left panel) induced highest activation in the inferior part of the ventrolateral premotor cortex, as compared to qualitative and spatial patterns. In contrast, qualitative patterns induced most significant activation within the superior part of the ventrolateral premotor cortex (middle panel), compared to temporal and spatial patterns. Finally, spatial patterns caused significantly higher activations than temporal and qualitative patterns within the dorsolateral premotor cortex (right panel). In contrast to former findings in the visual paradigm, however, all kinds of auditory



Figure 3. Direct task contrasts reveal ventral (PMv), middle (PMm) and dorsal (PMd) lateral premotor activation foci for the anticipation of temporal (left panel), qualitative (middle panel) and spatial (right panel) patterns in auditory stimulus sequences.
patterns elicited additional activations in the left inferior ventrolateral premotor cortex, relative to the baseline condition. Together, present findings were taken to reflect sensorimotor mapping processes within lateral premotor cortices, triggered by anticipatory perceptual analysis and organized in a rough parallel to the primary motor homunculus.

Action retrieval or action matching? Investigation of premotor function in action observation using fMRI

The lateral premotor cortex is known to be activated by the observation of actions, which is suggested to be due to a matching process of perceived actions onto memorized action schemas. The present study aimed at the dissociation of action memory retrieval and action matching processes. In order to manipulate action memory retrieval, pictures of object sets that corresponded to no, one, or two specific actions were presented. In order to manipulate action matching, pantomimes were presented that required no, one, or two action matching processes.

The parametric analysis with no, one, and two action schemas induced by pictures of object sets did not reveal any premotor activation to be increased with increasing number of to-be-retrieved action schemas (Figure 4, top). Foci that exposed activation to increase with increasing action retrieval effort were located within the inferior frontal sulcus, the precuneus, the fusiform gyrus, and the temporo-parietal junction area.

In contrast, the parametric manipulation of the number of to-be-matched action schemas using pantomime stimuli exposed significant activation within the left lateral premotor cortex, the inferior frontal sulcus, the pre-supplementary motor area, and the posterior temporal-parietal junction area (Figure 4, bottom). Thus, when participants had to match no, one, or two memorized action schemas with a pantomime matching one of them or not, left premotor activation increased with increasing number of matching processes. The outcome indicates that lateral premotor cortex activation during action observation reflects action matching effort rather than action retrieval effort.



Figure 4. Brain activations. Top: picture presentation, bottom: movie presentation.

2.7.4

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

2.7.5

Gruenewald, C.¹, Mecklinger, A.², Friederici, A.D.¹ & von Cramon, D.Y.¹

5 The role of visual input format and task demands on activation of motor schemas

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Our research focuses on motor schemas for object use which are associated with brain activity in the lateral premotor cortex (PMC). In prior studies we found a coactivation of the left ventral PMC and the anterior intraparietal sulcus (IPS) for memorizing linedrawings of manipulable compared to non-manipulable objects (Mecklinger et al., subm.). It was suggested that this circuitry, that mediates the transformation of sensory information into hand actions, may allow the maintaining of information about manipulable objects in working memory. However, this pattern of results could not be replicated using a similar task with real world objects. We assumed that in this latter task, the initial ventral PMC-IPS circuitry was overridden by an activation pattern evoked by spatial task characteristics (see Ann.Rep. 2000, p. 68).

To clarify this issue we conducted a further fMRI study in which simple classifications with real world objects were required. Here, we again found a left lateralized neural activation pattern, including the ventral PMC and the anterior IPS for real world manipulable objects. The combined results suggest that motor programs for objects use are not automatically activated by manipulable real world objects. Rather, their activation depends on particular task and processing demands.



Figure 5. In each line the first and the second column shows examples of manipulable and non-manipulable objects, respectively. Displayed are direct comparisons of brain activation patterns related to manipulable and non-manipulable objects revealed by different tasks and stimuli. The PMC activation in the visual classification task was slightly more lateral than in the memory task. Thus the activation focus in the IPS is not visible for this task.

The role of the fronto-lateral cortex in task preparation

The ability to prepare a task is crucial for the voluntary control of our thoughts and ac-

tions. It enables us to react rapidly and flexibly to a changing environment. In cognitive psychology, the process of task preparation was dissociated from task execution related control processes by using task cueing paradigms. In order to isolate the cortical correlate of task preparation, we have used event related fMRI and a cueing paradigm. In this paradigm subjects were required to switch between two different tasks: judging whether a digit was odd or even and judging whether it was smaller or greater than 30. In some trials, a task cue was presented 1.2 sec before the target (precue-target trials). In other trials, cue and target were presented simultaneously (no-precue-target trials). Importantly, in some trials task cues were presented without a target (precue-only trials). This last condition allows one to investigate anticipatory preparation without confounding task execution related control. The results show that a fronto-parietal network was involved in cue-related processing. The key component in this network is the lateral prefrontal cortex (Figure 6a) as was indicated by a correlational analysis between the cortical activation and the behavioral cueing effect (Figure 6b). Furthermore, our data reveal that this cortical region shows a temporal delay between trials in which subjects were able to prepare the task and trials in which they were not able to prepare (Figure 6c). These results demonstrate that the lateral prefrontal cortex plays a major role in task preparation.



Figure 6. A: Cortical activation in the fronto-lateral cortex when the precue-only condition was compared with null-events. B: Correlation of cortical activation in the precue-only condition and the behavioral cueing effect. C: Time delay between precue-target trials and no-precue-target trials.

Effects of task-rule updating and task-instantiation in task-switching: fMRI insights 2.7.7

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Our experiment aimed at revealing brain areas involved in cognitive control functions engaged in flexibly switching between alternative tasks. We introduced two spatial tasks which were presented randomly with a varying preparation interval of 100 ms or 2000 ms separating task-cue and target onsets.

2.7.6

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

Ruge, H.¹, Brass, M.¹, Koch, I.², Meiran, N.³ & von Cramon, D.Y.¹ Previous behavioural studies have shown that advance preparation results in a strong reduction of switching-costs indicating that general task-rules can be updated in anticipation without knowledge of the concrete task-instance that has to be processed. Following this line of evidence we aimed at investigating whether updating of task-rules on the one hand and processing of task-instances on the other hand are separable on a functional anatomical level.

The results show that task-switching effects were exclusively observed when no preparation was possible. Furthermore, some of the switching-related brain areas showed up to be associated with cue-locked task-rule updating while others rather seemed to be involved in target-locked task-instantiation.



Figure 7. A) Whole-brain activation map for the task-switching - task-repetition contrast at 100 ms preparation interval. B) Selected timecourses for some of these regions: no differences in onset-latencies paralleled by peak-latency differences of about 1.5 sec. indicate preparatory function. Onset differences of about 1.5 sec. paralleled by peak differences of about 2 sec. indicate target-locked function. Statistics are generated by jacknife-analysis.

These results suggest that in switching trials without the possibility to update general task-rules in anticipation (at 100 ms preparation interval) the concrete task-instance is at first encoded according to the previous relevant and currently irrelevant rules. Therefore, with establishing the currently relevant task-context, brain regions related to both task-rule updating as well as task-instantiation are highly demanded in order to overcome interference. Contrarily, given a long preparation interval task-rules can be updated in advance implicating that the current task is immediately instantiated correctly as soon as the target is presented. Thus, neither task-rule updating nor task-instantiation are subject to additional demands associated with interference control.

When the same response has different meanings: Involvement of the fronto-lateral cortex in response related task management

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One of the most fascinating properties of human intelligent behavior is the flexibility with which we can adjust our behavior to different situations and tasks. We are able to execute one task and switch to a completely different task in the next moment. This flexibility requires a set of higher order cognitive control functions related to task management. By using the so called 'task switching paradigm' in which subjects are required to switch between different tasks it was demonstrated that at least two distinct mechanisms are involved: One mechanism is related to the preparation of the forthcoming task by redirecting attention from one task to the next. The other mechanism is involved in response related control. Since we have a restricted behavioral repertoire we use similar actions in different task situations to achieve different goals. While a number of brain imaging studies have investigated preparation related processes, the aim of the present study was to investigate the cortical mechanisms underlying response related task management, namely the recoding of response meaning.

In a functional MRI study we used a task switching paradigm in which subjects were required to switch between two simple spatial tasks. In 'bivalent' condition the response sets of both tasks overlapped. Each response had two meanings, one for each task. Consequently, subjects had to recode the response meaning when switching from one task to the next. In the 'univalent' condition each task had a separate set of responses and therefore no recoding of response meaning was required. The interaction of task-switch (switch vs. repetition) and valence (bivalent vs. univalent) revealed that a region in the lateral prefrontal cortex is related to the recoding of response meaning (Figure 8A). As can be seen in the signal change analysis (Figure 8B) there is a signal change difference between switch and repetition trials in the bivalent condition but not in the univalent condition. These findings demonstrate for the first time the involvement of the lateral-prefrontal cortex in response-related task management.



Figure 8.

2.7.8

Brass, M.¹, Ruge, H.¹, Meiran, N.², Rubin, O.², Koch, I.³, Zysset, S.¹, Prinz, W.³ & von Cramon, D.Y.¹

2.7.9 The influence of task-order scheduling on dual-task related activation

Szameitat, A.¹, Schubert, T.² & von Cramon, D.Y.¹ ¹ Max Planck Institute of Cognitive Neuroscience, Leipzig ² Humboldt-University, Berlin

We investigated the neuroanatomical correlates of executive functions using the dualtask paradigm of the psychological refractory period (PRP). In a previous study we showed that dual-task performance is subserved by lateral prefrontal areas along the inferior frontal sulcus (IFS) and the middle frontal gyrus (MFG) as well as by parietal areas along the intraparietal sulcus (IPS). The present study aimed at investigating the underlying dual-task specific processes in more detail. Research with the PRP-paradigm indicated that the scheduling of the order in which the concurrent tasks are processed, i.e. task-order scheduling, is specifically important for dual-task processing. To test this hypothesis, we manipulated the demands according to an approach suggested by DeJong (1995), who has shown that in trials with a changing order, relative to the previous trial, the demands on task-order scheduling are increased, compared to trials with a repeated order.

15 participants had to perform an auditory and a visual task concurrently. The stimuli of the tasks were presented with an offset of 200 msec. The presentation order varied randomly and participants had to respond in the order of task presentation. Since the processing order had to be rearranged only in order-change trials, this condition should impose higher demands on the process of task-order scheduling. In accord with this hypothesis, order-change trials showed prolonged reaction times and increased error rates as compared to order-repetition trials. The imaging results showed that order-change trials resulted in stronger activation in cortical areas along the IFS, in the MFG and along the IPS (Figure 9). We conclude that the coordination of the appropriate processing order of the tasks is a crucial dual-task related process which is mediated by lateral prefrontal and parietal cortical areas.



Figure 9. Cortical areas associated with task-order scheduling in dual-task performance.

Extensive practice of the Color-Word Matching Stroop Task

The Stroop Color-Word interference is a well investigated and robust phenomenon in cognitive psychology. The Stroop task requires a person to respond to a specific dimension while suppressing a competing stimulus dimension. Reaction times (RT) are slowed if the competing stimulus is incongruent to the relevant stimulus compared to a congruent or neutral competing stimulus. RTs are speeded with practice, but the Stroop interference effect does not disappear, even with extensive practice.

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



Figure 10. Averaged RTs and error rates for one subjects. On the x-axis the sessions are represented, while the y-axis represents the mean RT (left) and error rate (right).



Figure 11. Individual z-maps contrasting the neutral condition against the incongruent condition for session 1 through 9. All z-maps are thresholded at z = 3.1 and mapped onto the subjects brain.

2.7.10

In this fMRI-study we investigated the hemodynamic changes in the recruited neuronal network with extensive practice. Subjects completed 9 fMRI-sessions in 9 consecutive weeks with a single-trial Stroop task. The hemodynamic signal, reaction times and error rates were recorded.

Results show that RTs are reduced over time but the interference effects remains stable (see Figure 11). The difference in the hemodynamic response between the neutral and incongruent condition disappeared with practice and no significant activations remained. It appears that a clear behavioural correlate does not have a corresponding hemodynamic change anymore.

2.7.11 Interindividual differences in working memory capacity are reflected in electrophysiological correlates of novelty detection

Ullsperger, M. & Gunter, T.C.

The novelty P3 is an ERP component which has been related to orienting to and evaluation of (usually task-irrelevant) novel events. This study addresses the question of whether the novelty P3 is a measure of distractibility (the inability to inhibit orientation to irrelevant stimuli), or a correlate of the evaluation of novel events - which is necessary to recognize the relevance of novel stimuli and to suppress the response to these stimuli. We tested 2 age-matched groups with high and low reading span, respectively, while performing two (visual and auditory) novelty oddball experiments (high span group: n=18, mean reading span=4.75; low span group: n=18, mean reading span=2.64). From several lines of evidence it is known that tests of working memory capacity do not merely measure the number of items which can be maintained over a delay period, but also test the ability to suppress interfering influences during maintenance of information. It is conceivable that working memory capacity has an influence on the processing of irrelevant novel stimuli. If the novelty P3 is a correlate of orientation reactions and distractibility, higher amplitudes should be expected in the low span group. In contrast, a larger novelty



Figure 12. Grand mean average waveforms to novel and target stimuli in the high span (red line) and low span (blue line) groups. Left panel: auditory experiment; right panel: visual experiment.

P3 should be expected, if it reflects the evaluation and categorization of the novel stimulus which is necessary for classifying novel stimuli as task-irrelevant.

In both experiments novel stimuli elicited a P3a which was more than $5 \mu V$ larger in the high span group than in the low span group at central electrodes. ERPs to standard and target stimuli did not differ significantly between groups (Figure 12). It seems that high span persons allocated more processing resources to the novel stimuli than low span participants, thus favoring the hypothesis that the novelty P3 is a correlate of the evaluation of the novel events. In a second step, it will be tested whether the allocation of resources to irrelevant novels will be influenced by a primary task differently for high and low span subjects.

Retrieval of long and short lists from long term memory: An fMRI study

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Previous studies have shown that reaction time (RT) in an item-recognition task with both short and long lists is a quadratic function of list length. This suggests that either different memory retrieval processes are implied for short and long lists or an adaptive process is involved. An event-related functional MRI study with 9 subjects and list lengths varying between 3 and 18 words was conducted to identify the underlying neuronal structures of retrieval from long and short lists.

First, a contrast between short and long lists was calculated. Further, two parametric designs, a linear increase due to increasing list length and a parametric trend extracted from the averaged RTs, were tested.

For the retrieval and processing of word-lists a single fronto-parietal network, including premotor, left prefrontal, left precuneal and left parietal regions, was activated. It appears



that all activated regions showed hemodynamic changes which are best represented by a quadratic function as seen in the RTs. With increasing list length, no additional regions became involved in retrieving information from long-term memory.

Behavioral data as well as imaging data can be interpreted in a sense that the underlying processes are best represented by a one-process model, which follows a quadratic function. At this moment it is not clear in what sense these processes change or if they are highly adaptive pb nature.

Figure 13. Brain regions showing task-related activations for the short-long contrast (top), linear (middle) and quadratic (bottom) parametric design mapped onto an individual brain. Y =-41 and Z = 41. The averaged z-maps were thresholded at z = 3.1.

2.7.12

Zysset, S.¹, Müller, K.¹, Lehmann, Chr.², Thöne-Otto, A.I.T.³ & von Cramon, D.Y. ^{1,3}

2.7.13 The anterior fronto-median cortex and evaluative judgement: An fMRI study

Zysset, S.¹, Huber, O.², Ferstl, E.C.¹ & von Cramon, D.Y.¹ ¹ Max-Planck-Institute of Cognitive Neuroscience ² Department of Psychology, University of Fribourg/Switzerland

This study investigated the neuronal basis of evaluative judgement. Judgments can be defined as the assessment of an external or internal stimulus on an internal scale and they are fundamental for decision making and other cognitive processes. Evaluative judgments (*I like George W. Bush*; *yes/no*) are a special type of judgements, where the internal scale is related to the person's value system (preferences, norms, aesthetic values, etc.). We used functional magnetic resonance imaging (fMRI) to examine brain activation during the performance of evaluative judgements as opposed to episodic and semantic memory retrieval. Evaluative judgement produced significant activation in the anterior fronto-median cortex (BA10/9), the inferior precuneus (BA23/31) and the left inferior prefrontal cortex (BA45/47). Evaluative judgement, which can be referred to as a meta-control process, appears to be implemented in the anterior fronto-median cortex. The inferior precuneus serves to update the situation model, a region which is strongly needed for episodic memory retrieval. The inferior frontal gyrus is involved in evaluative judgement for the selection of available information among competing alternatives.

The findings of our study demonstrate the functional interdependence of the anterior fronto-median and the median parietal cortex. The extent of the activation in each region appears to be dependent on the specific task set. The anterior fronto-median cortex was activated mostly by the conditions that required self-referential processing of the information in contrast with the mere retrieval of semantic information. Activation of the anterior fronto-median cortex was more pronounced in the evaluative condition compared to the episodic condition, whereas for the inferior precuneus activation the reverse was true.



Figure 14. Activation maps averaged over all subjects (z > 3.09) mapped onto the mean brain of all subjects. A) View of the medial surface (x = -7) for the contrast episodic vs semantic; B) View of the medial surface (x = -7= for the contrast evaluative vs semantic; C) Coronar (y = 16) and sagittal (x = -42) view of the activation in the inferior frontal gyrus in the evaluative vs semantic contrast. Red/yellow labels positive z-values whereas blue labels negativ z-values.

Text comprehension and the brain: The processing of emotional and temporal aspects of the narrative situation model

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An important subprocess of text comprehension is building and maintaining the socalled situation model (Kintsch, 1998) in which the text information is integrated and combined with the comprehender's prior knowledge. This representation is important because of it being retained in memory longer than the representations based on the verbatim form of the text, and it is the basis for utilizing the learned information in further tasks.

In psycholinguistics, it has been shown that the situation model of narrative texts contains several dimensions useful for encoding the standard story grammar: we need to know about the protagonists, about the place and the time of the events, about their causal structure, and so on. However, we do not know yet whether these qualitatively different aspects have dissociable realizations in the brain, i.e., whether reading or listening to a story elicits distinct subprocesses dependent on the specific information presented.

In the experiment reported here we targeted the processing of emotional and temporal information by adopting the inconsistency paradigm from the text comprehension literature (Rinck et al., 2001) for an fMRI study. Twenty participants were scanned at 3 T while listening to short stories, half of which contained inconsistencies. For instance, in one scenario of the emotion condition, Laura was dancing and laughing at her birth-day party, but later in the text the sentence "*Laura had never felt so sad*" appeared. For the temporal condition, we used similar inconsistencies, but the target information concerned a temporal aspect of the story's situation model (e.g., Tim had arrived at the train station sooner than Sarah, but later Sarah was waiting for Tim). In order to avoid the usual susceptibility artefacts that gradient-echo EPI is prone to, we used a spin-echo sequence (Norris et al., in press). Time-locked at the target information (e.g., *sad*), the BOLD contrast was analyzed in an event-related analysis. A direct comparison of the activations elicited by temporal and by emotional stories is shown in Figure 15.

Aspects of situation model processing



Figure 15. Activations during story comprehension, for the contrast comparing the temporal stories to the emotion stories. The activations are superimposed onto the average brain of the 20 participants, obtained by non-linear warping. The Z-map is thresholded at Z > 3.1, and an extent of 200 mm³. For the temporal stories there was activation in the dorsal part of the precuneus, shown in orange. For the emotional stories, there was activation in the ventro-median frontal cortex (BA11/32/25), depicted in blue.

2.7.14

Ferstl, E.C.¹, Rinck, M.², Zysset, S.¹, Norris, D.G.³ & von Cramon, D.Y.¹ The results first confirm that the spin-echo sequence is sufficiently sensitive for uncovering activation related to emotion processing in ventral prefrontal regions. Second, the results suggest that the different aspects of the narrative situation model are dissociable and, in particular, that simply listening to short stories may elicit emotion processing.

2.7.15 What does the fronto-median cortex contribute to language processing: Coherence or Theory-of-Mind?

Ferstl, E.C. & von Cramon, D.Y.

The fronto-median cortex (FMC) has been shown to be important for tasks requiring the evaluation of the plausibility or coherence of language stimuli (Ferstl & von Cramon, 2001; Zysset et al., in press). Similar brain regions have been found to be important for so-called Theory-of-Mind processes (ToM), i.e., for the ability of attributing other people's actions to their motivations, beliefs or emotions. In this study, we used eventrelated functional magnetic resonance imaging at 3.0 Tesla to disentangle the relative contributions of the FMC to Theory-of-Mind and coherence building processes, respectively. The BOLD response of nine participants was recorded while they listened to pragmatically coherent or unrelated pairs of sentences. During the first block, ToM processing was rendered unlikely. 60 sentence pairs were presented that did not contain any references to people. The instructions were to evaluate whether there was a logical connection between the sentences or not. During the second block, ToM processing was explicitly induced. All 60 sentence pairs had human protagonists, and the instructions were for the participants to evaluate whether they could understand the behavior of the people mentioned, including their motivations, goals and feelings. In three of the resulting four conditions a significant increase of the BOLD response was observed in fronto-median regions: when ToM instructions were given, both coherent and incoherent trials elicited fronto-median activation. When logic instructions were given, the coherent trials, but not the incoherent trials showed fronto-median involvement. These results clearly show that the fronto-median wall plays a role for coherence processes even in the absence of concomitant ToM processes. The findings support the view of this cortex having a domain-independent functionality related to volitional aspects of the initiation and maintenance of non-automatic cognitive processes.



Figure 16. Regions of activation in the median wall of the left hemisphere. Panel A shows the contrast of all language trials against the control condition during ToM processing (Z > 3.8). As expected, both a posterior cingulate / precuneal region, as well as a region in BA 9/10 of the FMC were activated. Panel B shows the contrast of coherent against incoherent trials in the Logic block (Z > 3.1). The strong, extended FMC activation for coherent trials confirms that coherence processes are sufficient for activating the FMC, independent of ToM processes.

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 characterise different aspects of the underlying cognitive process. Because these different methods yield complementary information about the anatomical, metabolical and neurophysiological state of the brain, integrated data evaluation is highly desirable and will lead to results not achievable with a single modality.

The Workgroup 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 2001 onto the following projects:

Segmentation of anatomical and pathological MR images

One of the long-term research goals is to obtain quantitative descriptors for brain structures and to test their use in the description of pathological processes. Sections 2.8.1-2.8.5 describe approaches for characterising brain shapes, describing changes of the brain's white matter with age, and quantifying diffuse and focal brain lesions.

Analysis of multimodal datasets

A second major research topic of the SIP group is best described as "multi-modal imaging". Here, we summarise approaches for an advanced analysis of functional images, the introduction of new imaging techniques, as well as the combination of different imaging modalities (2.8.6-2.8.8).

Set-up of bio-mechanical models of the brain as part of the SimBio project

The final three sections (2.8.9-2.8.11) performed for the SimBio project. This multinational project funded by the European Union (IST-V project 10378) aims at the implementation of a generic software environment for bio-numerical simulation. The MPI is involved in the set-up of electro-magnetical models of the brain (described elsewhere in this report) and in bio-mechanical models. More complete information about the status of this project may be obtained from the project website (*http://www.simbio.de*).

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. Further clinical collaborations were initiated with the Department of Maxillo-Facial Surgery, focusing on the description of structural changes during treatment of in-born skull deformations, and with the Department of Neurosurgery, analysing the biomechanical consequences of brain tumour resection. The fruitful scientific collaboration with the Unite 494 at CHU Salpetriere in Paris was continued by jointly publishing two papers in functional MRI analysis. Dr. Xavier Descombes (INRIA Sophia-Antipolis, France), a former member of our group, was invited for a research visit, during which a new segmentation algorithm was developed. Another 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 is planned for the next year, starting with an exchange of Ph.D. students.

2.8.1 Classifying brain shapes

Kruggel, F. & Kovalev, V.

Approaches to construct a computer-based atlas of the human brain implicitly assume that all brains stem from a structural continuum, i.e., a non-linear transformation fulfilling a diffeomorphic constraint is able to transform any instant into another one. It is questionable whether brain shapes form a set of clusters in a suitable feature space that may be related to gender, ethnic groups, or certain pathologic conditions. If such "brain shape types" exist, they may show differences in the disposition to diseases (e.g., react differently to a traumatic event). In addition, it may be necessary to revise parcellation approaches for the neocortical surface with respect to multiple shape types. We were interested whether it is possible and statistically valid to set-up classes of brain shapes in a normal population. To accomplish this, we need to extract the brain from a MRI head scan, describe the brain surface by a set of shape descriptors, and analyse the statistical properties of the brains represented as points in the high-dimensional feature space spanned by the shape descriptors. We selected the so-called modal matching which characterises a study object by the amplitude spectrum of three-dimensional vibration modes required to deform it into the reference object. 210 subjects (103 male, 107 female, age 24.8 ± 3.9 years) were selected from our brain data base. We selected 500 points to represent the brain surface, and all data sets were referenced to a single, arbitrarily chosen one. Sixty-one amplitudes corresponding to the low-frequency deformation modes were computed for each data set. Thus, each of the 210 brain shapes



Figure 1. Most typical male (top row) and female data set (below). Note the difference in the structure of the corpus callosum and the somewhat smaller and flatter appearance of the female brain.

is represented by a point in the 61-dimensional coordinate system defined by the rigidbody and mid-range deformation modes. Instead of visualising a superposition of this deformation mode spectrum, we chose to find the most typical female and male brain by selecting the data set closest to the cluster centre of female resp. male brains in the mode space (see Figure 1). A hierarchical clustering was introduced in both groups using the Ward agglomeration method. An optimal clustering was achieved with three male and three female classes.

Changes of white matter texture anisotropy with age and gender as revealed by anatomical MRI

The purpose of this work was to study the texture anisotropy of the brain's white matter (WM) based on conventional high-resolution T₁-weighted MRI datasets and its changes with age and differences with gender (see Figure 2). Quantitative anisotropy (AN) and laminarity (LM) characteristics were derived using recently suggested 3D texture analysis methods. WM anisotropy differences associated with gender were evaluated on the age-matched sample of 210 young healthy subjects (mean age 24.8, SD 3.97 years, 103 males and 107 females). Changes of WM texture anisotropy with age were studied using 112 MRI-T, datasets of healthy subjects aged 16 to 70 years (57 males and 55 females). The anisotropy analysis was performed on the whole WM compartment and WM segments in brain hemispheres. It was found (see Figure 3) that WM anisotropy in females is consistently higher i.e., more regular than in males ($p < 10^6$, z-scores from 5.2 to 9.0 depending on brain region). An age-related deterioration manifests itself in a remarkable decline of WM texture anisotropy (z-scores from -5.2 to -6.2, $p<10^6$). This effect (see Figure 4) is more evident in females (z=5.02, $p<10^6$) than in males (z=2.32, p=0.02). Anisotropy characteristics varied approximately in the same range when considering brain hemispheres. Anisotropy analysis of anatomical MRI-T, brain datasets provides quantitative information, which may help to better understand the WM alterations in normal subjects, as well as help to discriminate between normal and pathological ageing.



Figure 2. Two sample subjects with high (top panel) and low (bottom panel) white matter anisotropy. *Top panel:* axial and coronal slices of subject 1 (female, 22 years old, AN=3.85, LM=0.522) and its WM anisotropy histogram viewed from the top (left picture) and back (right picture). *Bottom panel:* axial and coronal slices of subject 2 (male, 40 years old, AN=2.37, LM=0.405) and its WM anisotropy histogram viewed from the same positions in 3D. In all the cases 2D slice images are contrasted and grey matter compartments are kept for clarity.

2.8.2

Kovalev, V.A., Kruggel, F. & von Cramon, D.Y.



Figure 3. Differences in white matter laminarity associated with gender measured on 210 MRI-T₁ datasets of young healthy controls (103 males and 107 age-matched females). Two histograms represent the distribution of male (solid line) and female (dotted line) subjects with respect to the white matter laminarity feature *LM*.

Figure 4. Variation of white matter laminarity with respect to age and gender when comparing young (16-25 years, 16 female and 17 male) and elderly (50-70 years, 11 female and 11 male) healthy subjects.

2.8.3 Detection of enlarged perivascular space

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While a trained human observer still outperforms automatic approaches for lesion detection and discrimination, estimating the lesion count and describing their position is tedious due to their multitude. Typically, lesions are evaluated visually in the acquired data sets and rated by semi-quantitative scales. One such lesion type is called "enlarged perivascular space" (EPS) and corresponds to small gaps between the white matter and its supplying deep penetrating arteries. Structure and distribution of EPS have motivated an object-oriented approach based on a geometrical model. Since EPS show some regionally higher occurrence, interactions between objects were included in the model to favour clustering of EPS while suppressing an overlap of different EPS. We implemented a marked point process defined with a Poisson density measure to model the number of objects and their localisation in the scene. This process includes interactions between points such as explicit relations or clustering properties. Shape parameters are associated with the points to define the object geometry (e.g., length and orientation of an object). A Reversible Jump Markov Chain Monte Carlo algorithm in a simulated annealing scheme is used to optimise the model. Example results are shown for a dataset with a high prevalence of EPS (see Figure 5). A set of 37 brain datasets were registered to a single brain using a non-linear procedure based on fluid dynamics. The obtained displacement fields were used to transform the detected EPS into a common space. Figure 6 shows the cumulative spatial distribution of EPS collected from all datasets, together with the reference brain. A higher prevalence of EPS is found in the area supplied by the medial and lateral striate arteries (e.g., putamen and pallidum) and in the area supplied by the long penetrating arteries, especially in the frontal white matter compartment.



Figure 5. Enlarged perivascular spaces detected in an example dataset.



Figure 6. Spatial distribution of enlarged perivascular spaces collected from a set of 37 datasets.

Population-based probability maps of diffuse white matter lesions

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Changes in the brain's white matter (WM) are often found in MRI brain datasets of elderly persons. The pathogenesis, clinical significance and morphological substrate of these changes are incompletely understood. Common types of WM lesions are diffuse white matter hypointensities (DWMH), periventricular hypointensities (PVH), and enlarged periventricular spaces (EPS) (see Figure 7). In order to deduce the clinical sig-

2.8.4

Kovalev, V.A.¹, Kruggel, F.¹, Wollny, G.¹ & Gertz, H.J.² nificance of these findings, it is necessary to provide quantitative descriptors and maps of lesion locations. Probability maps of diffuse WM lesions were created based on the sample of 105 MRI-T₁ datasets of elderly subjects including 72 patients suffering from WM encephalopathy and/or mild Alzheimer's disease (23 males and 49 females, mean age 78.6 years) and 33 healthy elderly individuals (14 males and 19 females, mean age 78.5 years). Lesion mapping was performed in two steps. First, all three kinds of lesions were segmented in each individual dataset. Second, segmented lesions were mapped into a single reference brain using a thin-plate registration method. Figure 8 shows probability maps for DWMH (green component), PVH (red), and EPS (blue), which are combined as colour channels of an RGB image and superimposed to the reference dataset. Intensity of colours represents lesion probabilities. Different combinations of basic RGB colours correspond to brain regions where lesions are overlap across the mapped population (e.g., shades of yellow correspond to regions where DWMH and PVH co-occur for different subjects).



Figure 7. Typical $MRI-T_1$ datasets of elderly subjects with diffuse white matter hypointensities (left), periventricular hypointensities (middle), and enlarged periventricular spaces (right).



Figure 8. Lesion probability maps computed over 105 elderly subjects: diffuse white matter hypointensity (green), periventricular hypointensities (red), and enlarged periventricular spaces (blue).

Descriptors for focal lesions as revealed by MR tomography

T1 imag

Focal brain lesions (e.g., due to head trauma, intracerebral hemorhages and cerebral infarcts) are usually revealed by MR tomography. Segmenting lesions is difficult because they may be heterogeneous and connected to brain compartments with similar intensities. Moreover, we are interested in distinguishing between completely and partially damaged portions of a lesion. A segmentation method was developed, which compares the local intensity statistics between a brain subregion and the corresponding contralateral subregion. A joint analysis of T_1 - and T_2 -weighted images yields a better discrimination between healthy and damaged tissues. The deviance of the signal statistics in both subregions is evaluated using a Hotelling t-square test, the test score converted to a z-score and compiled in a "lesion probability map". A probable lesion is found as a connected region of voxels with z-scores above a certain threshold. The algorithm also detects tissue loss indirectly indicated by ventricular enlargement, but



area

spares sulci and cisterns as estimated from the contralateral side. The natural asymme-

CSF

T2 image



Figure 10. Example lesion segmentation in a time-series examination. The corresponding results of an intensity- and texture-based segmentation of the lesion area are shown below. These segmentations form the basis of a "damage index", a quantitative measure for the degree of tissue damage within a lesion.

2.8.5

Chalopin, C. & Kruggel, F. try of the brain manifests itself in the lesion probability map as well. Such "pseudolesions" are often easily discriminated, because they are small. A focal lesion is generally inhomogeneous. To have an idea about the amount of damaged tissue in the lesion, we compute damage indices based on the image intensities and on texture features. Both indices were shown to be related to visually noticeable changes in time-series examinations of patients with focal brain lesions.

Spatio-temporal covariance model for medical images sequences: Application to

2.8.6

functional MRI data

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When analysing fMRI data, accurate detection of human cerebral activation raises many issues concerning the spatio-temporal properties of these regions. An adequate modelling of the correlations affecting the measured signal is mandatory and hypotheses underlying these models must accurately reflect the properties of the measured data to ensure a robust detection of the activation signal. A simultaneous analysis of spatiotemporal correlations is only possible with multivariate statistical approaches. Surprisingly, these methods often assume that the spatial and the temporal error processes are independent. We extended the commonly applied univariate linear model to cover the multivariate general linear case and introduced a new method for modelling the covariance of a stationary spatio-temporal random process. This proposed covariance model is non-separable in time and space, thus providing a better model of the intrinsic properties of the hemodynamic signal. An event-related experiment was selected to illustrate the usefulness of the proposed model. Subjects performed an item-recognition task described elsewhere (see Ann.Rep. 1999, Section 2.8.6). The experiment was analysed using the SPM99 univariate model (M1), the univariate regression model correcting for temporal correlations using a damped oscillator model (M2) and the proposed multivariate model (M3). Table 1 shows estimated covariance parameters obtained using M3. Note that the model was not separable in time and space (c > 0). Figure 11 shows sample activation maps. Comparing the activation amount, M3 ranged between M1 and M2, with much more focused activation. Note that the strip-like activation, which was presumably motion-related, was not rendered as significant by the nonseparable spatio-temporal model.

Slice	Covariance Function Parameters					
	σ^2	a	b	с	α	n ²
5	18104	0.410	1.055	0.230	0.458	0.000
6	14015	0.313	0.962	0.145	0.388	0.007
7	12462	0.329	0.935	0.172	0.474	0.000

Table 1. Covariance function parameters for slices 5 to 7.



Figure 11. For slice 6, activation maps (z-scale 4-12) obtained for the probe phase and overlaid onto T_1 -weighted anatomical scans.

Functional near-infrared spectroscopy can detect brain activity during a colourword matching Stroop task in an event-related design

Functional near-infrared spectroscopy (fNIRS) enables functional imaging of brain activity by measuring changes in the concentration of oxy- and deoxy-haemoglobin (Hb), as well as the changes in the redox state of cytochrome-c-oxidase (Cyt-Ox) by their different specific spectra in the near-infrared range between 700-1000 nm. Former cognitive fNIRS studies employed blocked designs with presentation of the stimulus for 1 to 10 min. In contrast, the event-related approach allows the analysis of events whose duration is much shorter than the latency of the vascular response. To examine the feasibility of fNIRS for the event-related approach in studies with cognitive paradigms, we measured brain activation by fNIRS during performance of a colour-word matching Stroop task in an event-related design. As illustrated in Figure 12, optodes were placed over the lateral prefrontal cortex (F7/8, F3/4, FC3/4), the intraparietal sulcus (P3/4), primary visual (O1/2) and primary motor cortices (C3/4). 14 subjects were involved. During the Stroop task, concentrations of oxy-Hb increased, whereas concentrations of deoxy-Hb decreased due to an increasing cerebral blood flow (see Figure 13). The increase of oxy-Hb and decrease of deoxy-Hb were significantly stronger during the incongruent than the neutral condition at positions F3/4, F7/8 and FC3/4 over the lateral prefrontal cortex, when differences between 'vascular response' (3-8 s after trial) and 'baseline' (2 s before trial) were compared. Thus, incongruent trials led to a stronger brain activation and, hence, vascular response compared with neutral trials due to interference reduction. These results are in accordance with a functional magnetic resonance imaging study by Zysset et al. (see Ann.Rep. 2000, Section 2.6.4).



Figure 12. Optode positions according to the international 10/20 system in relation to the corresponding cortical areas as revealed by an MR dataset of a test subject.

2.8.7

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



Figure 13. Time courses for concentrations of oxy- and deoxy-haemoglobin (Hb) during a colour-word matching Stroop task at the position F3/4. Average across 14 subjects. Beginning of the Stroop task at 0 s. Changes are given in nM. Running averages over 2 s.

2.8.8 Simultaneous measurement of brain activation with fMRI and fNIRS during visual stimulation

Schroeter, M.L., Kupka, Th., Mildner, T., Kruggel F. & von Cramon, D.Y.

While fNIRS offers a good temporal resolution, fMRI excels in spatial resolution. To evaluate the advantage of a multi-modal observation of hemodynamic responses, brain activation was measured simultaneously by fNIRS and fMRI during visual stimulation with an array of rotating red 'L'-shapes. Optodes were placed over the visual cortex on the left side (position O1 according to the international 10/20-system, overlapping the calcarine sulcus). For fMRI measurements, ten coronal slices of 5 mm thickness each separated by 7 mm were recorded with an echo planar imaging sequence. During visual stimulation, the concentration of deoxy-Hb (fNIRS) decreased, whereas the blood oxygen level dependent (BOLD) signal increased in the visual cortex (see Figure 14). The concentration change of deoxy-Hb as measured by fNIRS corresponded to the concen-



Figure 14. Time courses for deoxy-haemoglobin (Hb; green) and cerebral blood volume (red) as calculated by the Balloon model from the blood oxygen level dependent (BOLD) signal (brown). In black, concentration change of deoxy-Hb as measured by near-infrared spectroscopy. Period of visual stimulation is marked by a black rectangle.

tration change of deoxy-Hb as calculated from the BOLD signal according to the Balloon model. The changes in the concentration of deoxy-Hb (fNIRS) and the BOLDsignal (fMRI) correlated best in a depth of 7-21 mm. These data are in good agreement with a theoretical depth penetration of 2 cm, when emitter and detector are separated by 4 cm. fNIRS detected the activation in the visual cortex by the stimulus, as shown in Figure 15. In conclusion, brain activation as measured by fNIRS is in accordance with fMRI data.



Figure 15. Averaged correlation maps (6 stimulation periods; r > 0.7) in one subject. BOLD contrast. In the upper map, if a boxcar function was used as a design function (delay of 6 s). In the lower map, if the time course of deoxy-haemoglobin as measured by fNIRS was used as a design function.

Analysing time-series of medical images

Time-series of medical images are used to monitor structural changes of the brain as induced by ageing, disease progression, or surgical intervention. Studying structural changes with time may reveal empirical knowledge about such processes, and therapeutical processes may be improved. An analysis of serial medical images comprises the following steps: First, differences in patient orientation during image acquisition are corrected by rigid registration, and an intensity adjustment is applied to correct for differences in the intensity distribution due to different measurement conditions. Next, changes induced by the monitored process are detected using non-rigid registration based on a viscous-fluid model. The registration yields a 3D field of displacement vectors corresponding to the tissue shift during the acquisition interval. This vector field is usually large and therefore, hard to interpret. To get a simplified description contraction mapping is used to detect critical points, i.e., repellors (indicating local growth), and attractors (local shrinking) in these fields. Results are visualised to improve understanding of the monitored medical process. A patient was scanned 3 months and 15 months after severe head trauma, leading to a bifrontal contusion and a diffuse axonal injury. Employing the tool chain as given above a displacement field and critical points were obtained to describe the spatial pattern of brain atrophy in the chronic disease stage. It is then visualised as follows (see Figure 16): for each point on the cortex surface, the displacement vector is decomposed into its normal and tangential compo-

2.8.9

Wollny, G. & Kruggel, F. nents. Inward-pointing normals are coded in red, outward-pointing in blue; colour intensity reflects its magnitude. The scale is given in mm. The displacement vectors are shown as arrows. To represent the properties of critical points, a colour scheme is implemented, where green and red indicate repelling or attracting property, and blue a rotation component. Different types of saddle points may be distinguished by mixing the respective colours.



Figure 16. Shape difference of a patients' ventricular system between two examination time points (left) and the corresponding brain atrophy (right).

2.8.10 Detection and quantification of structural changes in time-series images – Clinical applications

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Beyond visual comparison of MR image data structural changes with time may be detected by non-linear registration of the imaged brain. The result of the registration is a vector field which maps one image onto another. This displacement field leads to quantify structural changes of the brain, as explained in more detail in the previous section. Three application areas were tested with our method: a quantification of morphological change induced by head contusion, the investigation of brain shift during tumour removal, and a validation of surgical intervention to remedy inborn deformations of the human skull. As structural changes coming along with severe head contusions is well described in medical literature, we initially validated our routines with a study of a bifrontal trauma (see previous section), which was the consequence of a car accident. The ventricles (see 2.8.9, Figure 16 left) were segmented from the brain. It is interesting to note that the ventricles are clearly enlarged, most notable in superior direction. This is a consequence of a loss of brain tissue, resulting in an increase in the CSF volume. The superior orientation of the ventricular enlargement indicate a more profound tissue damage in the supra-ventricular compartment. From the displacement field critical points were extracted (see 2.8.9, Figure 16 right). The set of critical points is dominated by a strong repellor locate in the pre-frontal CSF compartment. Since the trauma occurred on the forehead, a focus of matter loss is in the frontal lobes, leading to an increase of the CSF component

close to the frontal pole. Displacement stream lines map the "flow" of tissue along the midline structures (as a correlate of a global atrophy) and reveal a retraction of the brain in the frontal-occipital direction. The strongest deformations occur in the dorsal portions of the first and second frontal gyrus on both hemispheres.

Drastic structural changes occur during surgical intervention. In a collaborative study with *Institute of Neurosurgery*, *University Clinic of Leipzig*, we applied our routines to investigate dynamic intra-operative changes, i.e., the time dependency of brain shift, the relation between the extent of tumour removal and brain deformation, the localisation of distinct anatomical and functional brain structure. MR datasets were acquired on an 0.5 T Open MR scanner at different stages during the intervention. Non-linear registration of the first vs. subsequent time points yield displacement fields describing the brain shift (see Figure 17). Clearly, the shift follows gravity (and increase with consecutive tumour removal), with the major shift at the rim of the tumour. Midline structures such as the falx limit the extent of the displacement.

Currently, another collaborative study (with the *Department of Maxillofacial Surgery, University Clinic of Leipzig*) is underway to detect and quantify changes that occur during the sequence of interventions to remedy inborn deformations of the human face, i.e. mainly cleft lip and palate. In order to adjust deformed parts of the mid-face a metal frame is tightly fixed to the head using screws. After cutting the mid-facial bone along pre-defined lines, this device exerts forces on the bone structure to be relocated. In specific time intervals a CT scan is taken to validate the result. Here, non-linear registration of the CT datasets specifically allows for quantification by yielding displacement fields that describe the bone shift during the time interval (see Figure 18).

The advantage of conducting such biomedical analysis over simple visual comparison is obvious in all three cases: the consequences of the bifrontal head trauma are understood as a circumscribed tissue loss leading to quantifiable deformations of the brain structure; the shifting of brain structure during tumour removal can not only be quantified globally but as circumscribed shifting of regions of interest like activated fMRI cortical areas. This offers perspectives to compensate inaccuracy of surgical navigation based on functional datasets. The distraction process to remedy inborn deformation could be exactly followed and quantified.



Figure 17. Visualisation of brain shape change due to the resection of a frontal astrocytoma.



Figure 18. Bone shift due to therapy of an inborn deformation of the skull.

2.8.11 Visualisation

Svensén, M. & Kruggel, F.

The purpose of this project is to develop a software module for visualisation of the simulation results produced by other SimBio modules. It is capable of visualising data defined on voxel volumes (i.e., 3D images) as well as on geometric models (e.g., finite element meshes). Efforts are made to ensure that high quality results will be available with reasonable processing times, exploiting recent advances in the fields of graphic hardware and software. A prototype of this software module, incorporating all the essential visualisation modes, has already been produced (see Figure 19) and is now being extended to include more advanced techniques such as impostors, triangle strips and vertex arrays.



Figure 19. Example view of the SimBio Visualisation Module (VM).

Significant progress has been made in linking physiological variables to measurable MR parameters by means of a balloon model for the BOLD-weighted signal, which was adapted to reflect the situation encountered at a magnetic field strength of 3 Tesla (2.9.1). For the purpose of perfusion imaging, major developments in terms of RF coil technology were a prerequisite to permit continuous arterial spin labeling based upon the use of separate labeling and imaging coils (2.9.2). As a result, perfusion maps were obtained, which were not corrupted by magnetization transfer effects. Research related to the physiology of neuronal activation finally included ongoing attempts to utilize $H_2^{17}O$ for measuring the rate of cerebral oxygen consumption. This project, aiming at a novel modality for metabolic fMRI, is performed in close collaboration with Tel Aviv University (2.9.3). In collaboration with the Medical Center of the University of Leipzig, brain metabolism was investigated in stroke patients using *in vivo* spectroscopy (2.9.4). The relationship between brain anatomy and function was investigated by approaches from two directions. A motion-compensated diffusion tensor imaging experiment is currently being implemented to measure the white matter fiber orientation in three dimensions (2.9.5). Functional connectivity was investigated using correlations of spontaneous BOLD signal fluctuations of different brain regions in the resting state (2.9.6). Besides normal volunteers, stroke patients were included in such studies in collaboration with the Department of Neurology and the Day-Care Clinic for Cognitive Neurology at the University of Leipzig (2.9.7).

Straightforward improvements in the design of a custom-built helmet coil yielded substantial reductions of the sensitivity loss in deeper parts of the brain to permit highresolution imaging and spectroscopy of the entire head (2.9.8). Functional contrast based on T_2 changes was achieved by using a spin-echo EPI sequence with the potential advantage over conventional gradient-echo EPI of a superior intrinsic spatial resolution (2.9.9). Prominent signal changes were also obtained with spin-echo EPI in the hippocampus of subjects performing a hyperventilation task, that is, in a region where conventional strategies fail due to intrinsic magnetic field inhomogeneities (2.9.10). Through the use of 'internal' navigators, the stability of interleaved (i.e., multi-shot) EPI has been greatly improved, opening up possibilities of higher resolution for fMRI and other studies without major time penalties (2.9.11).

2.9.1 A qualitative test of the balloon model for BOLD-based MR signal changes at3 Tesla

Mildner, T., Norris, D.G., Schwarzbauer, C. & Wiggins, C.J.

After the adaptation of the balloon model to a magnetic field strength of 3 T (see Ann. Rep. 2000, Section 2.9.2), the question was examined whether the BOLD response can be fitted by the balloon model that includes both the oxygen limitation model and a very simple viscoelastic form of the outflow function. Three different types of visual stimuli were applied.

Figure 1 shows experimentally obtained BOLD responses of two subjects for a 6 s visual stimulus. In all subjects, the duration of the post-stimulus undershoot was nearly constant and the amplitude of the BOLD peak was found to be similar. The rise-time to the BOLD peak and the shape and depth of the post-stimulus undershoot varied significantly among subjects.



Figure 1. BOLD signal of the sum of all activated voxels (squares) for two subjects. The visual stimulus started at a time of 12 s and lasted 6 s. Dotted lines show the diffusion-weighted (DW) BOLD signal measured interleaved with a bipolar gradient of b = 50 s/mm⁻². The solid lines show the BOLD and DW BOLD signal as obtained by the balloon model.

Fits of the experimental BOLD responses are possible yielding parameters within a reasonable physiological range. First qualitative relations between the fitting parameters were obtained and were interpreted by the dependence of the biophysical parameters on the baseline value of the blood flow. However, to obtain quantitative information, the degrees of freedom need to be reduced, and additional information, such as perfusion data, needs to be involved.

A prediction of the balloon model is a BOLD overshoot, which is a lag between the changes of blood volume and blood flow after the onset of stimulation. Experimental evidence for a BOLD overshoot was the slow decline of individual BOLD peaks towards a steady state resulting from a train of 6 short 2-s stimuli. The period of this decline was approximately equal to the duration of the post-stimulus undershoot. The balloon model allowed a good modeling of the BOLD response with an inflow function consisting of six equal trapezoids. Results are less convincing with a single stimulus of 30 s duration, because of substantial variability of the observed BOLD responses. In the later case, modeling of the BOLD response with a single trapezoidal inflow function julied poor agreement with the experiment.

In conclusion, the balloon model represents a significant attempt to relate physiological variables with measurable MR parameters, specifically the BOLD weighted signal. The good agreement between experiment and theory obtained in this study underscores the general validity of this approach, because the conditions pertaining at 3 T differ significantly from those at 1.5 T, which is the field strength previously used for such measurements.

Perfusion imaging using continuous arterial spin labeling with separate label and image coils

Perfusion imaging using magnetically labeled water as an endogenous tracer is capable of measuring cerebral blood flow (CBF) in humans. In case of the widely used continuous arterial spin labeling (CASL) approaches, the application of long off-resonance RF pulses causes magnetization transfer (MT) effects which hinder the quantification of the perfusion. In the present work, a CASL method with separate label and imaging coils was developed. The labeling coil was placed on the neck of the subject (adjacent to one of the carotid arteries), and a helmet resonator was used for image acquisition. Thus, MT effects could be completely eliminated, and multi-slice perfusion imaging was easily implemented. A problem common to all CASL methods is the variable transit time from the labeling plane to the imaging slice, which results in a transit-time dependent sensitivity due to relaxation of the spins in the arterial blood. Therefore, the possibility of quantifying the perfusion requires verification.

Spin labeling is achieved by RF irradiation, in the presence of a magnetic field gradient oriented parallel to the carotid artery, which results in an adiabatic inversion of the flowing spins. The experimental setup was optimized experimentally by measurements with a flow phantom adjusted to velocities of 20 and 40 cm s⁻¹.



Figure 2. Perfusion map obtained by arterial spin labeling at the position of the right carotid artery. The colors correspond to perfusion values in ml/100g/min.

Figure 2 shows a multi-slice perfusion map, which was obtained by a total of 120 repetitions with and without spin labeling in an alternating fashion. The labeling coil was placed over the right carotid artery of the subject, hence, the perfusion map of the right hemisphere was obtained. The duration of the label period was 4 s and the repetition time 8 s. A long post-label delay of 2 s was used to minimize transit time effects and to suppress the intravascular signal. However, the presence of remaining intravascular signal, which could result in an overestimated blood flow, cannot be completely excluded.

The obtained CBF values are within the physiological range. Thus, multi-slice perfusion mapping by the method of separate label and imaging coils is feasible, but the variation in the CBF values, be it an effect of physiology or the method, has to be further investigated.

2.9.2

Mildner, T., Trampel, R., Schaefer, A. & Norris, D.G.

2.9.3 A double-tuned ¹⁷O-¹H helmet coil for fMRI

Driesel, W.¹, Jochimsen, T.H.¹, Norris, D.G.¹ & Navon, G.² ¹ Max Planck Institute of Cognitive Neuroscience ² School of Chemistry, Tel Aviv University, Israel

¹⁷O-decoupled proton spectroscopy uses relatively long and intense RF irradiation at the ¹⁷O frequency ($B_1 \cong 250 - 300 \,\mu\text{T}$). This makes it difficult to achieve decoupling in the human brain within FDA guidelines for power absorption. It is therefore necessary to use an optimized coil configuration for in vivo ¹⁷O-decoupled proton NMR with respect to both a highly sensitive ¹H coil and an efficient one for ¹⁷O decoupling. A prototype of an anatomically shaped quadrature transmit/receive coil for ¹⁷O -decoupled ¹H MRI was mounted on a helmet-like spherical segment (diameter of 24 cm) made from PVC. The double-tuned ¹H-¹⁷O coil is based on an assembly of two coplanar dualloop coils of the split-circle design, which are arranged in crossed fashion (see Figure 3a). To obtain a double-tuned coil, the conductor is broken along its length at the marked positions and the normal tuning capacitor used in the case of a single-tuned coil is replaced with a tuning network that consists of a capacitor in series with a parallel LC circuit (Figure 3b). The drive points and the matching unit are schematically shown in Figure 4. To drive the double-tuned coil with the ¹⁷O frequency, the voltage drop over the tuning capacitor C_{low} is used. In the case of the ¹H frequency, we used the voltage drop over the tank to drive the coil.

Due to the perfect rotation symmetry of the coil assembly, a high degree of circular RF field at both frequencies is obtained within the volume of interest (e.g., the human brain). At the proton frequency, the homogeneity and the degree of polarization were measured using a cylindrical phantom (diameter 18 cm; length 22 cm) filled with 60-mM saline solution and placed in the center of the coil. Images in axial, coronal, and sagittal directions were obtained, which are comparable with corresponding ones taken with a single-tuned helmet coil. In the *xy*-plane we obtained a comparable homogenity. Along the *z*-axis there was a moderate B_1 gradient.



Figure 3. (a) Schematic wiring of the head resonator and (b) the tuning network.



Figure 4. Drive points and matching unit.

¹H NMR spectroscopy in patients with chronic infarction

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As part of a clinical study in patients with chronic infarction, metabolic parameters accessible by ¹H NMR spectroscopy were investigated for further correlation with the clinical status, structural changes of the brain seen on anatomical MR images, and MR perfusion data. ¹H NMR spectra of the brain were acquired in four volume elements (healthy appearing brain, border of the lesion, center of the lesion, ventricles) using a PRESS sequence (echo time 20 ms). The water signal from cerebrospinal fluid in the ventricles was used as an internal reference for quantitation of absolute metabolite concentrations.

A typical spectrum obtained in healthy appearing brain is displayed in Figure 5. The displayed fit is composed of signal patterns from N-acetyl-aspartate (NAA), glutamate (GLU), creatine (CRE), choline (CHO), and myo-inositol (mINO). The histogram displayed in Figure 6 shows metabolite concentrations inside the three different regions of brain tissue. Compared to healthy brain, the detected metabolites appear with decreased concentrations in the lesion. The next step will be a correlation of quantitative spectroscopic results with perfusion data.

2.9.4

Riemer, T.¹, Scheid, R.² & Hund-Georgiadis, M.³



Figure 5. ¹H NMR spectrum from a healthy brain region (top) and fitting results (bottom).



Figure 6. Histogram of absolute metabolite concentrations in the healthy appearing brain (top), border of the lesion (middle), and center of the lesion (bottom).

2.9.5 Diffusion-tensor imaging with RARE

von Mengershausen, M., Norris, D.G. & Driesel, W.

Diffusion-tensor imaging (DTI) is a method to measure anisotropic diffusion. The diffusion tensor of brain water molecules reveals information on the orientation of white matter fiber tracts connecting cortical areas; hence, it is generally assumed that it is possible to use DTI for investigating neuronal connections. Most imaging methods being currently used for this kind of experiment suffer from image artifacts, poor spatial resolution, or low signal-to-noise ratio (SNR). Our approach to overcome such problems is to use RARE (rapid acquisition with relaxation enhancement) for image acquisition. The RARE sequence was implemented with a diffusion-weighting preparation and true online motion correction using navigator echoes. The latter is necessary because bulk subject motion causes variations in the signal phase, which lead to severe artifacts in diffusion-weighted RARE images. To avoid nonrigid body motion, such as encountered shortly after the R-wave, which is not properly corrected by the navigator technique, ECG-triggering was applied. The two pictures shown in Figure 7 provide a comparison between diffusion-weighted images acquired with UFLARE (ultra-fast lowangle rapid acquisition and relaxation enhancement) and RARE sequences in two different subjects. Although the acquisition time for a single slice is 16 times longer for RARE as compared with UFLARE, the superior image quality suggests that RARE may become the method of choice for DWI.



Figure 7. Comparison of diffusion-weighted UFLARE (left; matrix: 96×128 , FOV: 19.4 cm \times 14.4 cm, *b*-value: \sim 750 s/mm², 50 repetitions) and RARE (right; matrix: 256×256 , FOV: 25.6 cm \times 25.6 cm, *b*-value: \sim 750 s/mm², 1 repetition)

Interregional correlation of low-frequency BOLD signal fluctuations in the resting state

Functional connectivity has been defined by Friston et al. as the spatiotemporal correlation of electro/neurophysiological measurements in the resting brain. Previous research mainly focused on proving that interregional correlations of low frequency BOLD signal fluctuations at rest are an appropriate technique to probe the functional connectivity of the neuronal network. In the connectivity experiment, a time series of BOLD sensitized EPI images of the resting brain were acquired. The objective was to critically examine and to further improve the experimental protocol and the data analysis in order to investigate the functional connectivity of a more extensive neuronal network.

The EPI time courses were filtered to eliminate physiological signal fluctuations due to the cardiac cycle and respiration. The imaging sequences were analyzed regarding motional artifacts, which are caused by T_1 saturation effects and instabilities of the transverse steady-state magnetization. Statistical analysis was employed to determine significant interregional correlations. In figure 8, the *t*-statistics which were computed from the cross-correlation distributions are shown for different reference voxel positions. In the displayed example, the *t*-distributions are less distorted due to motion artifacts in the 3D-EPI than in the 2D-EPI experiment. However, the interregional correlations, which originate from motion, exhibit high spatial and intertrial variability. In order to be able to compare different connectivity maps at the same level of significance *z*-statistics were calculated from the *t*-distributions. A more systematic investigation of functional connectivity of the brain is now feasible.



Figure 8: *t*-Statistics calculated from the correlation-coefficient distribution of the time course of a reference voxel with the time courses of all other voxels within the brain. The curves represent different positions of the reference voxel within the thalami, white matter, or the ventricles. The two plots correspond to resting-state experiments using a multislice 2D-EPI and 3D-EPI sequence on the same subject in the same session.

2.9.6

Goerke, U., Schwarzbauer, C. & Norris, D.G.

2.9.7

Weih, K.¹, Goerke, U.¹, Schwarzbauer, C.¹, Berrouschot, J.², Norris, D.G.¹& von Cramon, D.Y.^{1,3}

Functional resting state experiments of patients with acute stroke in the basal ganglia

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Patients with acute stroke in the basal ganglia were investigated using a novel functional MRI method, in which interregional correlations of BOLD signal fluctuations acquired without external stimulation are investigated. Such low-frequency fluctuations (<0.1 Hz) have been proposed to probe functional connectivity between different brain regions. In the course of the project, data evaluation was substantially improved in order to achieve comparability and sufficient reliability required for patient studies. The patients were examined within the first week, after one month and three months after the stroke. The connectivity maps were correlated with the clinical status of the patients.

In figure 9, connectivity maps of a patient with a hemorrhage in the left capsula is shown. The patient was paralyzed down one side a few days after the stroke. After one month he was able to walk again with a stick. The sensormotoric functionality was almost fully recovered after three months. The patient's symptoms correlate well with the results of interregional correlations of low-frequency BOLD signal fluctuations. The connectivity between the hand primary motor cortex (marked in blue, figure 9) and other cortical and subcortical brain regions was probed. After three days, no significant correlations between the left or the right primary motor cortex and the remaining motor network were found. A month later, interregional correlations with the supplementary motor area, the contralateral hand area, and both thalami are visible upon selection of the right motor cortex. Interestingly, both hemispheres show significant correlations indicating



Figure 9. Connectivity maps of a patient obtained 3 and 30 days following stroke. Two slices of the data sets for interregional connectivities of the left and the right primary hand motor cortex (marked in blue) are shown. The red-to-yellow color scale represents *z*-values in the range from 3.1 to 5.

that the healthy side takes over the function of the impaired one. After three months, the left motor system was almost normal, while the right hand region showed normalized correlations predominantly in the ipsilateral hemisphere. It was demonstrated that functional resting-state experiments are suitable for monitoring disease, especially if the patient is unable to perform a paradigme.

Anatomically shaped flower-like helmet coil for fMRI and spectroscopy at 3 Tesla

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The previously custom-built helmet coil (see Ann.Rep. 2000, Section 2.9.4) offers an improvement in the signal-to-noise ratio (SNR) by a factor of up to 3.2 as compared to the standard birdcage head coil. This allows high-resolution imaging as well as spectroscopic investigations of the upper parts of the brain with sufficient SNR. However, lower brain regions are not accessible with the current design. The coil layout was therefore redesigned to reduce the B_1 field gradient along the *z*-axis. This optimizes the sensitivity and B_1 homogeneity in deeper regions of the brain while retaining the superior SNR in upper regions.

The geometric structure of the new helmet, which is presented in Figure 10, may be described as a flower with four leaves. It meets the constraints of a high filling factor while offering sufficient space for the nose, headphones, and glasses. The improvements achieved by using the flower-like helmet coil are illustrated in Figure 11. The left part is a sagittal image of the human head acquired with the old helmet coil. Due to a marked B_1 gradient along the *z*-axis, lower brain regions cannot be displayed. By contrast, the flower-like helmet coil permits imaging of the entire head at high SNR (right part of Figure 11) as a result of substantially reduced B_1 gradients. Coverage of the brain is now comparable to the standard birdcage head coil, however, with superior SNR (improvement by a factor of up to 3.0).



Figure 10. Photograph of the flower-like helmet coil.

2.9.8

Driesel, W.¹ & Riemer, T.²



Figure 11. Sagittal images of the human head $(256 \times 256 \text{ pixels}, \text{ field-of-view } 25.0 \text{ cm}, \text{ slice thickness } 5\text{mm})$ acquired with the old (left) and the new, flower-like helmet coil (right).

2.9.9 Spin-echo based fMRI using a Stroop colour-word matching task and EPI at 3 Tesla

Norris, D.G., Zysset, S., Mildner, T. & Wiggins, C.J.

The quality of functional contrast obtained with T_2 -weighted imaging differs from that of T_2^* -weighted images in that all contributions from static dephasing are eliminated. This considerably reduces the magnitude of the signal change that can be obtained. Hence, T_2 -weighted BOLD imaging has to date found limited use, being confined to functional studies of the primary cortices or to signal changes resulting from physiological stress. The purpose of this study was to examine whether it is possible to use T_2 -weighted BOLD imaging at the main magnetic field strength of 3 T for cognitive studies. To this end, multi-slice spin-echo EPI (SE-EPI) is used in a Stroop colour-word matching task. This Stroop experiment is known to produce robust activation in a number of brain regions.

An adapted single trial version of the colour-word interference task was used. The task was presented using a blocked design. Briefly, there are three conditions involved in the task. In each condition, the subject has to determine whether the colour of the symbols presented in the top row matches the colour-word on the bottom row (printed in black). In the neutral condition the top row just contained a row of four 'X's, in the congruent condition the top row had a colour-word printed in the corresponding colour, whereas in the incongruent condition the colour-word was printed in a non-corresponding colour. Six neutral blocks alternated with 6 congruent and 6 incongruent blocks for each run. Given a fixed interstimulus interval of 1.5 sec, subjects (n=7) completed 20 trials during each (neutral/congruent/incongruent) block, 120 trials of each type during a single run, and 360 trials of each type during the three runs. Images were acquired using a single shot, spin-echo EPI sequence (TR 2000 ms, TE 75 ms) with 16 axial slices (19.2 cm FOV, 64 by 64 matrix, 5 mm thickness, 1 mm spacing), parallel to the AC-PC plane and covering the whole brain. Three functional runs with 365 time points were performed, with each time point sampling over the 16 slices.

All regions of activation that had previously been detected using GE-EPI were present in the SE-EPI data. Additional activation was detected with SE-EPI in the ventral frontomedian cortex and in the right fronto-polar cortex (see Figure 12). The ventral frontomedian activation was stronger in the neutral than in the incongruent condition. The
level of activation in this area is known to decrease during cognitive tasks with a high attentional load, as this area is believed to be associated with a default mode of brain activity. The fronto-polar activation is related to volitional, strenuous processing and problem solving. Activation in these regions is not normally detectable on standard GE-EPI data because of the presence of strong susceptibility gradients. The z-score values were, however, reduced by a factor of about 3. The activation in the SE-EPI images appears more focused than in GE-EPI, and the variance of the z-scores is lower. In conclusion it has been shown that SE-EPI at 3 T is sufficiently sensitive to be used in a cognitive fMRI study and yielded similar results to the previously published GE-EPI study. In addition, new areas of activation were found which were previously not detectable.



Figure 12. Sagittal activation maps. The left image was obtained with GE-EPI, the right image with SE-EPI. The slice is positioned at Talairach coordinate z=-5. The ventral fronto-median activation is clearly visible in the SE-EPI image, but not in the GE-EPI image due to the strong susceptibility gradients in this region, which result in signal voids in the GE-EPI data, particularly in the most inferior slices. Activation in the pre-SMA region is visible with both imaging sequences.

Regional differences of fMR signal changes induced by hyperventilation: Comparison between SE-EPI & GE-EPI at 3 T

A purpose of this study was to evaluate whether reproducible signal change of brain tissue by hyperventilation (HV) can be seen on spin-echo (SE)-echo planar imaging (EPI) at 3T. A second goal was to examine the sensitivity of SE-EPI for measuring vascular reactivity in regions such as the hippocampus, which are difficult to visualize with more commonly used gradient-echo (GE)-EPI due to susceptibility artifacts. Six healthy human subjects performed voluntarily performed a HV task. The task design was as follows: 2 min of normal breathing (rest), was followed by 2 min of HV giving a basic block of 4 min. Three blocks were repeated yielding a total scan time of 12 min for a single run. Each subject performed two runs, one with SE-EPI and another with GE-EPI.

Statistical analysis was performed to detect the area with significant cerebrovascular reactivity (p<0.05). Both GE-EPI and SE-EPI showed a significant global signal decrease in the cerebral cortex, cf. Figure 13. A slight white matter signal increase during hyperventilation was not completely understood. A purely mechanistic explanation would be a rapid increase in the resistance to blood flow in gray matter causing a transient increase of blood flow in white matter. In GE-EPI, the frontal cortex showed a larger

2.9.10

Naganawa, S., Norris, D.G., Zysset, S. & Mildner, T. signal decrease than the other gray matter areas. In SE-EPI, the differences among gray matter regions were less significant. The hippocampal formation showed the largest signal change detectable with SE-EPI. By contrast, no significant signal change in this region was observed with GE-EPI due to the presence of susceptibility artifacts.



Figure 13. Averaged *z*-map of 6 subjects. Upper row shows *z*-maps from GE-EPI and lower row shows those from SE-EPI. Blue indicates a significant signal decrease, and red indicates a significant signal increase (p<0.05).

2.9.11 Interleaved EPI with 'internal' navigators

Wiggins, C.J. & von Mengershausen, M.

The use of 'interleaved' (i.e., multi-shot) echo-planar imaging (EPI) for fMRI studies has been limited. One reason for this relates to stability issues due to shot-to-shot phase and amplitude errors. The latter are often attributed purely to movement of the subject between the acquisitions. However, we have found significant instability effects in absence of motion, for example on a gel phantom.

Attempts to use initial navigators with a conventional encoding scheme produced instable time courses despite navigator corrections. Presumably, errors arise during the echo train and so are not corrected by the navigators. Our approach to deal with this involves the combination of inter-shot navigator correction with 'internal' reference lines. The internal reference lines are obtained by removing or modifying the phase encode blips of the EPI echo train during the zero crossing of *k*-space. As may be expected, little difference was seen in the signal stability between the data without phase correction and that with a single correction for the entire data set. However, a significant improvement arises from the inter-segment correction (Figure 14). The amplitude correction only appeared to produce significant improvement when the analysis included the initial image in each time course. In this case the correction is accounting for initial saturating effects, whereas amplitude effects during the time course seem insignificant. The use of 'internal' navigators significantly improves the stability of the time course of interleaved EPI with standard phase encoding. This should allow interleaved EPI to be used for fMRI without the time penalties that arise from centered phase-encoding.



Figure 14. Improvement due to inter-segment navigator correction on four-shot *in vivo* data. Left is the standard deviation map from the reconstruction using only a single navigator pair. Right is the same data reconstructed using inter-segment correction. The grey box in the upper left corner is set at a value of 2%. One effect that is not corrected can be seen in the large blood vessel with, presumably, phase and/or amplitude variations between the acquisitions, which the navigator corrections do not account for.

Our working group focuses on developing methods for the analysis of magnetic resonance image data of the human brain. In the year 2001 we have worked on various research projects, and at the same time have provided software support for the institute. At the heart of the methodology for the analysis of functional MRI data is our software package called "Lipsia" (Leipzig Image Analysis and Statistical Inference Algorithms). Lipsia contains numerous algorithms for the pre-processing, statistical analysis, segmentation and visualisation of fMRI data. It is now firmly established as the principal software tool for the fMRI data analysis throughout the institute. Lipsia was presented to the scientific community at the Human Brain Mapping Conference in Brighton in June 2001 where it was received with considerable interest (2.10.1).

A second area of research was focused on the development of mathematical methods for analysing functional connectivities in the human brain using fMRI data. We had previously developed a new approach for analysing fMRI data that was based on a spectral analysis of fMRI time series data. An insight that resulted from the application of this procedure to fMRI data was that phase leads can be surprisingly large and can thus pose significant problems in the interpretation of fMRI data. A research project aimed at studying this problem is under way (2.10.2). A second focus of our work in modelling functional connectivities was the development of a new mathematical method based on so-called 'replicator dynamics' (2.10.3). This method enables us to identify closely coherent networks of brain activations. Surprisingly, mathematical principles that we borrowed from theoretical biology can be applied to our quite different research domain.

Two further projects are aimed at analysing structural T_1 -weighted MR data (2.10.4, 2.10.5). In the context of a project financed by the German-Israeli Research Foundation (GIF) a useful algorithm that serves as a first step towards a fully automatic inter-individual registration of fMRI data sets was developed.

In the coming year, we plan to extend our fruitful cooperation with our Israeli project partners, as well as with external cooperation partners who are interested in our software package 'Lipsia'. The focus of our research will remain in the field of methodological developments for the analysis of MRI data.

2.10.1 The LIPSIA software package

Lohmann, G., Müller, K., Mentzel, H. & von Cramon, D.Y. The LIPSIA software package comprises all aspects of fMRI data evaluation including tools for filtering, spatial transformation, statistical evaluation as well as segmentation and visualization. Because of the rising demand on the statistical evaluation of time series, the functionality of the software was increased in 2001. The tools for statistical evaluation can now handle parametric modulation, mixed epoch-/event-related designs, variable duration of events, and smoothness estimation. The second-level analysis can also be performed in terms of the general linear model. LIPSIA follows well-established algorithms and techniques. The software was improved to handle both fMRI and NIRS (near infrared spectroscopy) time series. Furthermore, software was also developed for reviewing statistical models. The design can be visualized in form of the design and session matrix, and in form of regressors in time and spectral domain.



Figure 1. Statistical evaluation of visual fMRI data using the LIPSIA software package. The transparency mode admits the visualization of anatomical details in activated regions. Several zoom modes enable a detailed visualization of special brain regions. The statistical design can be displayed in the form of design matrices as well as in the form of regressors. At a mouse click, the shape of the basis functions, the design orthogonality, and further design parameters can be visualized.

Investigating the stimulus-dependent temporal dynamics of the BOLD signal

2.10.2

using spectral methods

Müller, K., Mildner, T., Lohmann, G. & von Cramon, D.Y.

Because the reason for the different temporal behavior of the BOLD response in different brain regions is still unknown, spectral methods were applied successfully to fMRI data obtained with varying length of visual stimulation. Diffusion weighted fMRI data obtained by the interleaved-measurement technique were evaluated separately and gave no evidence for the phase shifts to be caused by larger scale vessels.

The experiments with the short and long stimulus differ mainly in the distribution of the activated voxels in the plane of percentage signal change and phase shift. We found that the height of the signal change is not independent of the phase shift. The shorter the duration of visual stimulation, the stronger the correlation between percentage signal change and phase shift. Further work including experiments with very short visual stimuli is necessary to further elucidate this interesting effect.



Figure 2. Several axial slices of an individual subject showing the estimated phase shift (color-coded) evoked by a periodic visual hemifield stimulation with a duration of 6 seconds. The maps of the phase shift of non-diffusion (first row) and diffusion weighted fMRI time series (second row) are very similar (correlation > 0.8). The right curves show trial averages that were also computed for non-diffusion and diffusion weighted fMRI time series.



Figure 3. The correlation between percentage signal changes and phase shifts is above 0.6 for all subjects with visual hemifield stimulation of 6 seconds. Voxels showing high signal changes show also a large phase shift to other voxels. Voxels showing an early response (large negative phase shift) show only very small signal changes. This behavior appeared for both non-diffusion (blue dots) and diffusion weighted data sets (red dots).

2.10.3 Using replicator dynamics for analyzing fMRI data of the human brain

Lohmann, G.,

In this work, we have introduced a new method of modelling and detecting functionally coherent networks in the human brain using functional magnetic resonance imagery (fMRI). A standard fMRI analysis yields an activation map that shows brain regions that are significantly activated under some experimental conditions. While such maps are of large value for purposes of human brain mapping, they do not reveal interdependencies between areas of activations. Therefore, the aim of this work was to develop a new algorithm for analysing fMI data that allows us to identify such interdependencies.

The algorithm that we invented is based on a concept from theoretical biology called 'replicator dynamics'. Replicator dynamics describe the evolution of interacting species. The basic idea underlying this mathematical approach is that as time evolves, species that interact closely and profitably with many other species will eventually become dominant within their eco-system. They form a "dominant clique".

In our context, we borrow the same mathematical approach to describe interacting brain regions. Brain regions - represented by fMRI time courses - that correlate closely with many other brain regions can be considered to be dominant within the experimental task under consideration. Our algorithm is capable of detecting such "dominant cliques".



Figure 4. The replicator process applied to fMRI data (Stroop paradigm). The colored dots show maxima of the activation map, the white lines indicate the sulcal pattern viewed from the left, the top and the right. Three networks were detected: items belonging to the first (most prominent) network are shown in blue (the fronto-parietal network); the second most prominent network is shown in green (sensor-motor areas); and the remaining areas are shown in red.

2.10.4 Segmentation of neuroanatomical structures

Busch, N.H., Lohmann, G. & von Cramon, D.Y. Our aim is to describe neuroanatomical structures in MR images. This process is termed segmentation. We have developed a new segmentation algorithm called probabilistic geodesic deformable model. It is a parameter-free representation of an object's boundary evolving according to a partial differential equation (PDE) comprising data terms and regularity constraints. The steady state of the front propagation is equivalent to the minimum of an objective function. The objective function is chosen to incorporate statistical boundary and region information derived from a Markov Random Field.

Additionally, the function includes a coupling term enforcing a certain predescribed distance between boundaries, e.g. for the cortical layers, the distance is set to 3 mm. The surface evolution is solved within the level set framework, where the surface is regarded as the zero level set of a n+1 dimensional embedding function, here the signed distance function. This approach offers little dependance on the initial configuration and topological variability. We extend the framework towards a multiscale approach for better robustness, convergence rate and to overcome local minima. The result is an implicit function that can be converted to a parametric description. From either representation, morphometric quantities such as volume, area or cortical thickness can be computed.



Figure 5. Segmented left and right lateral ventricles and third ventricle from T,-weighted MR image.



Figure 6. Segmented white/gray matter boundary and gray matter/CSF boundary.

The segmentation algorithm has been applied to T_1 -weighted MR images. The validity of the results has been assessed by visual inspection of surface and slice representations of the segmented structures. In addition, computational phantoms simulating the convoluted cortical surface have been used to provide quantitative error measurements

between reconstructed and true object boundaries. The experimental results demonstrate our approach to be robust against noise and accurate, while at the same time being fully automatic.

2.10.5 Fully automatic identification of AC and PC

Temming, H. & Lohmann, G. The Talairach framework is a 3-D brain coordinate system based on two anatomical landmarks, namely, anterior commissure (AC) and posterior commissure (PC). In order to reduce operator bias and effort when identifying these landmarks by hand, we developed a fully automatic procedure. First, the interhemispheric fissure or anatomical mid sagittal plane (MSP) is estimated, as AC and PC are located here. Because the human brain/skull is nearly symmetrical, the MSP can be calculated from the orientation of the symmetry axis of both the axial and the coronal slices and their position to each other.

Since AC and PC are invariant, their position can be determined by an analysis of the correlation between the original image and two coupled 3D-templates, one for each landmark, which are rotated within the MSP (see Figure 7).



Figure 7. (a) A mid sagittal plane of a human brain automatically extracted by our procedure. (b) View of the region of interest where the center point of the coupled template is moved and the correlation coefficient of different angles is determined. Note that the single templates are not rotated and their distance varies. (c) For the positions and orientations where the correlation of the coupled template had the best value we correlate the original image with the template again, but now we rotate the single templates with respect to their positions to each other. This indicates where the position for each landmark should be and we can start a last correlation with decoupled templates within a fixed range to find the proper position.

We applied our procedure to 413 data sets. The mean distance between the results obtained manually by human experts and our procedure was 1.0 mm (std. dev.: 0.4 mm) for AC and 1.4 mm (std. dev.: 0.6 mm) for PC. This is nearly within the range of the spatial resolution of 1.0 mm.

Teaching

3.1

3

SOMMERSEMESTER 2001

Wahrnehmungspsychologie Universität Leipzig *Herrmann, C.S.*

Einführung in die Psycholinguistik

Universität Potsdam Jescheniak, J.D.

Funktionelle Magnetresonanztomographie - Grundlagen und Methoden

Universität Leipzig Pollmann, S., Norris, D.G., Lohmann, G.

Methoden der biomedizinischen Resonanzbildgebung und -spektroskopie

Universität Leipzig Norris, D.G.

Musik-Denken-Verstehen: Musik als Gegenstand der Kognitionswissenschaft

Universität Leipzig Schmidt, B.-H.

Die Entwicklung der Minimalistischen Syntaxtheorie Chomskys seit 1995 [Syntax-Phonologie-Schnittstelle]

Universität Leipzig Steube, A. (Universität Leipzig) & Alter, K.

$W \ I \ N \ T \ E \ R \ S \ E \ M \ E \ S \ T \ E \ R \quad 2 \ 0 \ 0 \ 1 \quad / \quad 2 \ 0 \ 0 \ 2$

Einführung in die Akustik Universität Leipzig Alter, K. & Lattner, S.

Ausgewählte Themen der funktionellen Neuroanatomie des menschlichen Gehirns und neurologisch-motorische Rehabilitation

Universität Leipzig

Braß, M., Cramon, D.Y. von, Ferstl, E., Lepsien, J., Schubotz, R.I., Ullsperger, M., Pollmann, S., Weidner, R., (Tagesklinik für kognitive Neurologie der Universität Leipzig), Hummelsheim, H., mit MitarbeiterInnen des Neurologischen Rehabilitationszentrums (NRZ) Bennewitz

Sprache: Entwicklung und Pathologie

Universität Leipzig Friederici, A.D., Hahne, A., Kotz, S.A.

Neuropsychologie der Handlung – Seminar

Universität des Saarlandes Gruenewald, C.

Biopsychologie I

Universität Leipzig Gunter, T.C. & Kotz, S.A.

Grundlagen der Neurowissenschaft

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

Biologische Psychologie

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

Physiologische und Biologische Psychologie

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

Verarbeitung von Volumenbilddaten

Universität Leipzig Lohmann, G.

Lokalisation kognitiver Funktionen

in **Neuropsychologische Grundlagen der Förderpädagogik** Universität Leipzig Stachowiak, F.J. (Universität Leipzig) mit Köster, D. und Mitarbeitern des Max-Planck-Institutes für neuropsychologische Forschung

Bildgebende Verfahren in der Kognitiven Psychologie

Universität Fribourg/Schweiz *Zysset, S.*

Committees and memberships

Prof. Dr. Angela D. Friederici

Deutsche Forschungsgemeinschaft (DFG) / German Research Foundation

Member of the Senate

Member of the Committee "DFG-Forschungszentren"

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 Linguistics Psychology
- *Habilitation Committee* Psychology

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

Max Planck Society

- Committee: Kunsthistorisches Institut in Florenz
- Committee: Max-Planck-Institut für Hirnforschung, Frankfurt
- 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 of the Board

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

- Member of the Editorial Board of the "Journal of Psycholinguistic Research"
- Member of the Editorial Board of "Cognitive Science Quarterly"
- Member of the Editorial Board of the "Zeitschrift für Experimentelle Psychologie"
- Member of the Editorial Board of the "Journal of Memory & Language"
- Member of the Advisory Board of "Neurolinguistik"
- Member of the Advisory Board of the "Psychonomic Bulletin & Review"
- Member of the Advisory Board of the "Emerging computational neural network architectures based on neurosciences (EmerNet)"
- Member of the Scientific Board of the Zeitschrift "Gehirn und Geist"
- Member of the Program Committee of the AMLaP Board "Conference on Architectures and Mechanisms for Language Processing (AMLaP2001)"
- Member of the Program Committee of the 23. Annual Meeting of the German Society of Linguistics (DGfS) "Sprache und Kognition"
- Member of the Program Committee of the 5. Annual Meeting of the German Cognitive Science Society (KogWis2001) "Cognitive Systems and Mechanisms"

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)
 Member of the Board
 Coordinator for the "Center of Neurosciences"
- *Center for Cognitive Sciences* Member of the Board
- *Committee of Computer Resources* Member of the Board
- Coordination Center for Clinical Research, Leipzig Member of the Board
- Nomination Committees

 General Psychology and Methodology
 Paediatrics with focus on Neuropaediatrics
 Cognitive Psychology
 Physiology
 Diagnostic Radiology
- *Doctorate Committee* Neurology, Neuropathology and Neurosciences

International Neuropsychological Symposium Member

European Neurological Society

Member of the Scientific Committee of the Section Neurorehabilitation

World Federation of Neurology

Member of the Research Group on Aphasia and Cognitive Disorders

INSERM Expert Base

Member

Deutsche Akademie der Naturforscher - LEOPOLDINA

Member

Member of the Awarding Committee

Gesundheitsforschungsrat

Member of the Scientific Committee

Forschungszentrum Jülich

Scientific Board of Biomedicine

Kompetenznetz Parkinson

Member of the External Advisory Board

Deutsche Gesellschaft für Neurologie (DGN) Chairman of the DGN-Committee 1.08 "Behavioral Neurology"

Gemeinsame Kommission Klinische Neuropsychologie (GKKN) Member

Editorial Activities

- Member of the Editorial Board of "Cortex", Action Editior
- Member of the Advisory Board of "Der Nervenarzt"
- Member of the Editorial Board of "Zeitschrift für Neuropsychologie"

3.3 Visitors

Prof. Dr. Nachshon Meiran, Ben-Gurion University of the Negev, Department of Behavioral Sciences, Beer-Sheva, Israel
29-30 January 2001
9-12 September 2001

Dr. Iring Koch, Max-Planck-Institut für psychologische Forschung, München, Germany 29-30 January 2001 10-11 September 2001

Dr. Orit Rubin, Ben-Gurion University of the Negev, Department of Behavioral Sciences, Beer-Sheva, Israel
29 January – 3 February 2001
19-22 June 2001
9-12 September 2001

Dr. Padraig Monaghan, University of Edinburgh, Center for Cognitive Science, Edinburgh, UK
30 January – 1 February 2001
25 June –13 July 2001

Dr. Michael Kuhn, Johannes Kepler Universität Linz, Numerical and Symbolic
Scientific Computing, Linz, Austria
26 February – 3 March 2001

Prof. David Swinney, Department of Psychology, University of California, La Jolla, CA, USA
27 February – 5 March 2001

Dr. Dirk Wildgruber, Neurologische Universitätsklinik, Tübingen, Germany 5 – 6 April 2001

Dr. Jochen Kaiser, Institute of Medical Psychology and Behavioral Neurobiology, University of Tübingen, Germany
22 April – 1 May 2001

Dr. Jörg Keller, Institut für Deutsche Gebärdensprache und Kommunikation Gehörloser, Hamburg, Germany 29 April – 2 May 2001

Prof. Robert Zatorre, Montreal Neurological Institute, Montreal, Canada 15 – 17 May 2001

PD Dr. Dr. Hans-Otto Karnath, Neurologische Universitätsklinik, Abteilung Kognitive Neurologie, Tübingen, Germany 5-6 June 2001

Prof. Arturo Hernandez, Department of Psychology, University of California,Santa Barbara, USA15 June – 18 July 2001

Dr. Yael Nitkin, University of Toronto, Department of Psychology, Mississauga, Ontario, Canada 21 June – 21 September 2001

Dr. Jane Neumann, University of Edinburgh, Center for Cognitive Science, Edinburgh, UK 25 June – 6 July 2001

Prof. Dr. James V. Haxby, National Institute of Mental Health (NIMH), Laboratory of Brain & Cognition, Bethesda, MD, USA25 June – 8 July 2001

Dr. Maria Ida Gobbini, National Institute of Mental Health (NIMH), Laboratory of Brain & Cognition, Bethesda, MD, USA 25 June – 8 July 2001

Dr. Elizabeth Hoffman, National Institute of Mental Health (NIMH), Laboratory of Brain & Cognition, Bethesda, MD, USA 25 June – 8 July 2001

Prof. Dr. Andrei Gorea, Laboratoire de Psychologie Expérimentale,
Boulogne-Billancourt, France
30 June – 3 July 2001

Prof. Daniela Perani, Consiglio Nazionale delle Ricerche, Instituto di Neuroscienze e Bioimmagini, Milano, Italy
30 June – 17 July 2001

Dr. Xavier Descombes, INRIA, Sophia-Antipolis, Cedex, France 3 July – 27 August 2001

Dr. Andrew Wedel, Department of Linguistics, UC Santa Cruz, Santa Cruz, CA, USA 9 July – 7 September 2001

Dr. Heike Kühn-Inacker, Cochlear Implant Centrum Süd, Würzburg, Germany 13 – 20 July 2001

Dr. Matthias Schlesewsky, Institut für Linguistik, Universität Potsdam, Potsdam, Germany

1 – 31 August 2001

Prof. Jürgen Weissenborn, Universität Potsdam, Institut für Linguistik, Potsdam, Germany

2 – 3 August 2001

Prof. Harald Clahsen, Department of Language & Linguistics, University of Essex, Colchester, UK

5 - 12 August 2001

Prof. Herbert Schriefers, Nijmegen Institute for Cognition and Information (NICI),
Nijmegen University, Nijmegen, The Netherlands
6 – 18 August 2001

Prof. Arthur Jacobs, Chair of Experimental Psychology and Methodology, Catholic University Eichstätt, Germany
13 – 18 August 2001

Heiner Drenhaus, Institut f
ür Linguistik, Allg. Sprachwissenschaft, Potsdam, Germany20 – 24 August 2001

Dr. Martin Schulz, TU München, Institut für Informatik, München, Germany 20-21 September 2001

Prof. Dr. Judith M. Ford, Stanford University School of Medicine, Department of Psychiatry and Behavioral Sciences, Stanford, CA, USA 26 November – 2 December 2001

Prof. Dr. Daniel H. Mathalon, Yale University School of Medicine, Department of Psychiatry, West Haven, CT, USA
26 November – 2 December 2001

Prof. Paavo Leppanen, Department of Psychology, University of Jyvaskyla,Jyvaskyla, Finland4 – 16 December 2001

Guest lectures

Dr. Padraig Monaghan, University of Edinburgh, Center for Cognitive Science, Edinburgh, UK Modelling hemispheric asymmetries in visuospatial neglect and neglect dyslexia 31 January 2001

PD Dr. Mike Rinck, TU Dresden, Allgemeine Psychologie, Dresden, Germany Text comprehension: Constructing and updating multidimensional situation models 7 February 2001

Dr. Ole Jensen, Helsinki University of Technology, Low Temperature Laboratory, Hut, Finland Ongoing theta activity (6-8 Hz) over the frontal midline increases with load in a short-term memory task: A parametric MEG study 1 March 2001

Dr. Jochen Kaiser, Institute of Medical Psychology and Behavioral Neurobiology, University of Tübingen, Tübingen, Germany Oscillatory MEG activity and auditory processing 25 April 2001

Prof. Dr. Gisela Szagun, Institut für Kognitionsforschung,
Carl-von-Ossietzky-Universität, Oldenburg, Oldenburg, Germany
Über Hören zur Sprache: Sprachentwicklung bei Kindern mit Cochlea
Implantat im Vergleich mit normal hörenden Kindern
9 May 2001

PD Dr. Dr. H.-O. Karnath, Neurologische Universitätsklinik Tübingen, Abteilung Kognitive Neurologie, Tübingen, Germany Wie orientieren wir uns im Raum, welche Hirnstrukturen sind beteiligt? 6 June 2001

Dr. Arturo E. Hernandez, Department of Psychology, University of California, Santa Barbara, CA, USA Bilingualism and the brain: Old questions and new directions 18 June 2001 3.4

Prof. Dr. Andrei Gorea, Laboratoire de Psychologie Expérimentale, Boulogne-Billancourt, France 'Seen' vs. 'unseen': Explorations into the psychophysics of decision 2 July 2001

Prof. Dr. James V. Haxby, National Institute of Mental Health (NIMH), Bethesda, MD, USA

The representation of faces and objects in the ventral object vision pathway 6 July 2001

Dr. Daniela Perani, Consiglio Nazionale delle Ricerche, Istituto di Neuroscienze e Bioimmagini, Milano, Italy Learning new vocabulary and new grammatical rules: Implication for language acquisition 16 July 2001

Prof. Dr. Birger Kollmeier, Medizinische Physik und Kompetenzzentrum HörTech, Universität Oldenburg, Oldenburg, Germany
Von der Neurosensorik bis zu intelligenten Hörgeräten: Psychophysik, Signalverarbeitung und Modelle des auditorischen Systems
18 July 2001

Dr. Claudia Felser, University of Essex, UK Online processing in children: A study of relative clause attachment 8 August 2001

Dr. John J. Sidtis, Department of Psychiatry, New York University, Medical School, New York, NY, USA Finding the function in functional images 22 August 2001

PD Dr. Nikolaus Troje, Fakultät für Psychologie, Ruhr-Universität-Bochum, Bochum, Germany Decomposing biological motion: Identity, gender and emotion in human gait 18 September 2001

Dr. Sophie Kerttü Scott, Institute of Cognitive Neuroscience and Department of Psychology, University College London, London, UK Streams and hierarchies in speech perception; evidence from functional imaging 14 November 2001

Prof. Judith M. Ford, Department of Psychiatry and Behavioral Sciences, Stanford University, School of Medicine, Stanford, CA, USAResponse conflict and error monitoring in schizophrenia28 November 2001

Dr. Daniel H. Mathalon, Department of Psychiatry, Yale University, School of Medicine, West Haven, CT, USA Progressive brain changes in schizophrenia 28 November 2001

Congresses, workshops and colloquia

Congresses

DGfS 2001, Twentythird Annual Meeting of the German Society of Linguistics "Sprache und Kognition" Friederici, A.D., and Dölling, J., Hall, T., Haspelmath, M., Heyer, G., Hinskens, F., Max, I., Olsen, S., Pechmann, T., Siebdrat, N., Steube, A., Umbach, C., Zybatow, G. University of Leipzig and Max Planck Institute of Cognitive Neuroscience, Leipzig, Germany, February-March 2001.

KogWis 2001, Fifths Annual Meeting of the German Cognitive Science Society "Cognitive Systems and Mechanisms"
Friederici, A.D., and
Arnold, T., Hahne, A., Herrmann, C.S., Jacobsen, T., Mecklinger, A., Pechmann, T., Schröger, E., Siebdrat, N.
Max Planck Institute of Cognitive Neuroscience and University of Leipzig, Leipzig, Germany, September 2001.

Special Session on "Brain Imaging" Kruggel, F. & Rajapakse, J. 8th International Conference on Neural Information Processing, Shanghai, China, November 2001.

Workshops and colloquia

Workshop "Prosodie zwischen Produktion und Perzeption"
Alter, K., and
Mayer, J. (University of Stuttgart), Meyer, M.
23. Jahrestagung der Deutschen Gesellschaft für Sprachwissenschaft "Sprache und Kognition", Leipzig, Germany, 28.02.-02.03. 2001.

Workshop "Zerebrale Verarbeitung von Prosodie, Propositionaler Sprache und Sprechmotorik: Getrennte oder gemeinsame Neurale Netzwerke?" Alter, K., Wildgruber, D. (University of Tuebingen) & Meyer, M. Max Planck Institute of Cognitive Neuroscience, May 2001. Workshop "Sprache, Musik und Gehirn" Münte, T. (University of Marburg) & Alter, K. (sponsered by the DfG SPP "ZIZAS") Bad Salzelmen, June 2001.

Workshop "*Prosodie*" Alter, K. KogWis 2001 - 5. Fachtagung der Gesellschaft für Kognitionswissenschaft, Leipzig, Germany, 25. - 28. September 2001.

Workshop "Textverstehen und Textproduktion bei Aphasie: Diagnostik und Therapie"Ferstl, E.C. & Engell, B.4. Würzburger Aphasie-Tage. Würzburg, March 2001.

Workshop "Einführung in die Neurolinguistik: Aphasische und nicht-aphasische Sprachstörungen" Ferstl, E.C., and Guthke, T., Kotz, S.A., Regenbrecht, F. Fortbildungsakademie der Gesellschaft für Neuropsychologie, October 2001.

Symposium at the Eighths Meeting of the Cognitive Neuroscience Society (CNS)
2001 "Brain Mechanisms of Auditory Language Processing: From Sounds to Sentences"
Friederici, A.D., and
Poeppel, D.
World Trade Center, New York, USA, March 2001.

Workshop "Neuropsychopharmakologie" Ullsperger, M. & Müller, U. Akademie der Gesellschaft für Neuropsychologie, Damp, Germany, Leipzig, September 2001.

Workshop "*Kognitive Neurowissenschaft der Aufmerksamkeit*" Pollmann, S., Lepsien, J. & Weidner, R. Akademie der Gesellschaft für Neuropsychologie, Leipzig, November 2001.

Degrees

Habilitations

Dr. Frithjof Kruggel	Habilitation in Medizin, Dr. med. habil.
	Universität Leipzig
	Verleihung der Lehrbefugnis von der Universität Leipzig

Doctoral Degrees

Anja Dove	Doktor der Naturwissenschaften, Dr. rer. nat. Universität Leipzig
Kerrie Elston-Güttler	Doctor of Philosophy, Ph.D. University of Cambridge, UK
Christian J. Fiebach	Doktor der Naturwissenschaften, Dr. rer. nat. Universität Leipzig
Axel Hutt	Doktor der Naturwissenschaften, Dr. rer. nat. Universität Stuttgart
Martin Koch	Doktor der Naturwissenschaften, Dr. rer. nat. Universität Leipzig
Doreen Nessler	Doktor der Philosophie, Dr. phil. Universität Saarbrücken
Sabine Nyström	Doktor der Medizin, Dr. med. Universität Leipzig
Markus Ullsperger	Doktor der Medizin, Dr. med. Universität Leipzig
Silke Urban	Doktor der Naturwissenschaften, Dr. rer. nat. Universität Leipzig

4.1

4

Tobias Wächter	Doktor der Medizin, Dr. med.
	Universität Leipzig
Katja Werheid	Doktor der Naturwissenschaften, Dr. rer. nat.
	Universität Leipzig

4.2 Awards

Christian J. Fiebach	Scholarship for the "European Diploma in Cognitive and Brain Sciences" at the Hanse Institute for Advanced Study, Delmenhorst, Germany, and the Universidad De La Laguna, Tenerife, Spain
Christoph S. Herrmann	Professorship in temp. position at the Otto von Guericke- University Magdeburg, Department of Biological Psychology
Axel Hutt	Schloeßmann-Stipendium of the Max Planck Society
Jörg D. Jescheniak	Heisenberg Fellowship from the German research council (DFG)
Gabriele Lohmann & D. Yves von Cramon	Best Poster Award, 17th International Conference "Information Processing in Medical Imaging" (IPMI), Davis, CA, USA, 18-22 June 2001.
Markus Ullsperger	Dr. Carl Zeise Prize of the University of Leipzig
Markus Ullsperger	Poster award of the German Cognitive Science Society

5

PUBLISHED BOOKS AND BOOKCHAPTERS 5.1

Alter, K. (in press).

Prosodie.

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

Alter, K. (in press).

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

Arnold, T. & Herrmann, C.S. (Eds.) (2001).

Cognitive Systems & Mechanisms (KogWis2001). Abstracts of the 5th Meeting of the German Cognitive Science Society.

Leipzig Series in Cognitive Sciences, Leipzig: Leipziger Universitätsverlag.

Clahsen, H. & Friederici, A.D. (2001).

Sprachverlust. Methodologie.

In G. Holtus, M. Metzeltin & C. Schmitt (Eds.), *Lexikon der Romanistischen Linguistik (LRL) (Sprache in der Gesellschaft / Sprache und Klassifikation / Datensammlung und -verarbeitung)* (pp. 63-69), Tübingen: Niemeyer.

Dove, A. (2001).

Lokalisierung an internen Kontrollprozessen beteiligter Hirngebiete mithilfe des Aufgabenwechselparadigmas und der ereigniskorrelierten funktionellen Magnetresonanz. In Max Planck Institute of Cognitive Neuroscience (Ed.), *MPI Series in Cognitive Neuroscience, vol. 17*, Leipzig.

Elston-Güttler, K. (2001) [2000].

An enquiry into cross-language differences in lexical-conceptual representations and their effect on lexical processing in the L2. [Dissertation].

Dissertations in English and Applied Linguistics Series, Cambridge, UK: University Press.

Ferstl, E.C. (2001).

Learning from text.

In N.J. Smelser & P.B. Baltes (Eds.), *International Encyclopedia of the Social and Behavioral Sciences, vol.* 13: Cognitive Psychology and Cognitive Science (Ed. W. Kintsch) (pp. 8605-8609), Oxford, UK: Elsevier.

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12th Neurobiological PhD Students' Workshop (DoWo), Universität Stuttgart-Hohenheim, Germany, September 2001.

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Effects of metrical changes in tri-syllabic consonant vowel pairs: An EEG study with different task conditions.

Helsinki Summer School in Cognitive Neuroscience (HSCN), University of Helsinki, Finland, September 2001.

Kruggel, F.

Analyzing functional MRI data.

Information Processing in Medical Imaging 2001, Davis, USA, June 2001.

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Inverse biomechanical models of the brain.

Annual Bioengineering Conference, Snowbird, USA, July 2001.

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8th International Conference on Neural Information Processing, Shanghai, China, November 2001.

Kruggel, F.

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Neuronale Korrelate zur Verarbeitung von Intonationsphrasengrenzen bei Schulkindern.

15. Tagung der Fachgruppe Entwicklungspsychologie in der Deutschen Gesellschaft für Psychologie (DGP), Potsdam, Germany, September 2001.

Lohmann, G.

Volumetrische Bildverarbeitung: Neue Methoden und Anwendungen.

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Lohmann, G.

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Zentrum für Medizinische Diagnosesysteme und Visualisierung (MeVis), Bremen, Germany, November 2001.

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Phonetics Workshop, Department of Theoretical and Applied Linguistics, University of Edinburgh, UK, November 2001.

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Themawechsel! Fokussierung und die Verfügbarkeit von Diskurselementen. 23. Jahrestagung der Deutschen Gesellschaft für Sprachwissenschaft (DGfS), Leipzig, Germany, February 2001.

Wollny, G.

Analyse von pathologischen Veränderungen in MRT-Zeitreihenaufnahmen. Bildverarbeitung für die Medizin 2001, Lübeck, Germany, March 2001.

5.6 PAPERS PRESENTED AT COLLOQUIA

Alter, K.

La réponse de l'hemisphere droite pendant le traitement de la prosodie. CNRS Marseille, France, January 2001.

Alter, K.

Fenster zum Gehirn. Urania Leipzig, Germany, February 2001.

Alter, K.

Event-related brain potentials, prosodic phrasing und information structure. Oxford University, UK, May 2001.

Alter, K.

The function of the right hemisphere during pitch processing. Oxford University, UK, May 2001. Alter, K.

Prosodieverarbeitung im EEG, MEG und fMRT.

Meeting of the SPP "Zeitgebundene Informationsverarbeitung im zentralen auditorischen System" (SPP ZIZAS), Bad Salzelmen, Germany, June 2001.

Alter, K.

Prosodische Realisierung und -verarbeitung von Kontrast und Korrektur.

Meeting der Forschergruppe "Sprachtheoretische Grundlagen der Kognitionswissenschaft", Leipzig, Germany, December 2001.

Bornkessel, I. & Schlesewsky, M.

Wem ist denn da das Schwert zerbrochen? Thematische Hierarchien und andere Abhängigkeiten. Institut für Sprachwissenschaft, Universität Salzburg, Salzburg, Austria.

Cramon, D.Y. von

Der frontomediane Cortex: Von der Intention zur Handlung. Lecture, University of Ulm, Ulm, Germany, January 2001.

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Der frontomediane Cortex: Von der Intention zur Handlung.

Celebrations tributed to Prof. Dr. D. Ploog, Max Planck Institute for Psychiatry, Munich, Germany, April 2001.

Cramon, D.Y. von

Kognitive Aspekte der Multiplen Sklerose.

Neurological Colloquium at the University of Würzburg, Würzburg, Germany, May 2001.

Cramon, D.Y. von

Der anteriore frontomediane Cortex: Ein Instrument der Handlungskontrolle.

Neurobiological Colloquium at the University of Kiel, Kiel, Germany, July 2001.

Cramon, D.Y. von

Der frontomediane Cortex und das Problem Antrieb. Liselotte Gerhard Lecture, Hattingen, Germany, September 2001.

Cramon, D.Y. von

Kognitive Aspekte der Multiplen Sklerose. Lecture, Schering Deutschland GmbH, Berlin, Germany, November 2001.

Ferstl, E.C.

Textverarbeitung nach Hirnschädigung: Ergebnisse aus klinischer und bildgebender Forschung. 4. Würzburger Aphasie-Tage, Würzburg, Germany, March 2001.

Ferstl, E.C.

Die Neuropsychologie des Textverstehens: Ergebnisse aus klinischer und bildgebender Forschung. Vortragsreihe "Sprache und Kognition" am Neurologischen Therapiezentrum Hamburg, Germany, June 2001.

Fiebach, C.J.

Syntax and working memory during sentence processing. ERP and fMRI evidence from German whquestions.

Department of Linguistics, University of Essex, Colchester, UK, March 2001.

Fiebach, C.J.

Syntax and working memory during sentence processing. ERP and fMRI evidence from German whquestions.

European Diploma in Cognitive and Brain Sciences, Universidad De La Laguna, Tenerife, Spain, October 2001.

Friederici, A.D.

Neuronale Grundlagen sprachlicher Verarbeitungsprozesse.

SFB Neurokognition, Universität Bremen, Bremen, Germany, May 2001.

Friederici, A.D.

Sprachverarbeitung.

Meeting of the SPP "Zeitgebundene Informationsverarbeitung im zentralen auditorischen System" (SPP ZIZAS), Bad Salzelmen, Germany, June 2001.

Friederici, A.D.

Neuronale Dynamik der auditorischen Sprachverarbeitung.

Zoologisches Institut der Humboldt-Universität zu Berlin, Berlin, Germany, July 2001.

Friederici, A.D.

Gehirn und Sprache.

Stifterverband der deutschen Wissenschaft, Landeskuratorium Berlin/Brandenburg, Berlin, Germany, October 2001.

Gruenewald, C.

Die Rolle des prämotorischen Cortex in nicht-motorischen Aufgaben.

Universität des Saarlandes, Saarbrücken, Germany, November 2001.

Gunter, T.C.

Interaction between semantic and syntactic information: An exploration of event related brain potentials.

Chinese University of Hong Kong, China, April 2001.

Gunter, T.C.

Working memory and the processing of language: Some ERP-studies.

Fachbereich Psychologie, Universität des Saarlandes, Saarbrücken, Germany, July 2001.

Hahne, A.

Hirnelektrische Korrelate des Sprachverstehens.

4. Treffen der Pädagogischen Leiter deutschsprachiger Cochlea-Implant-Centren, Freiburg (Breisgau), Germany, February 2001.

Heim, S.

Phonologische Prozesse bei der Sprachproduktion: Eine Serie von fMRI-Studien.

Max-Planck-Institut für Anthropologie, Leipzig, Germany, October 2001.

Heim, S.

Sprache im Gehirn.

Erziehungswissenschaftliche Fakultät, Universität Leipzig, Leipzig, Germany, November 2001.

Hein, G.

Die Lokalisation von Doppelaufgabendefiziten bei neurologischen Patienten und gesunden älteren Personen.

Lehrstuhl für Kognitive Psychologie, Humboldt-Universität zu Berlin, Berlin, Germany, February 2001.

Hein, G.

Wo sind Doppelaufgabendefizite bei neurologischen Patienten und gesunden älteren Personen lokalisiert?

Doktorandentreffen der Lehrstühle für Allgemeine Psychologie, Kognitive Psychologie und Biologische Psychologie/Psychophysiologie der Humboldt-Universität zu Berlin, Eggsdorf, Germany, September 2001.

Herrmann, C.S.

Cognitive correlates of evoked gamma activity in the human EEG.

Psychology Department, University of Liverpool, Liverpool, UK, January 2001.

Herrmann, C.S.

Age differences in 40 Hz EEG activity.

Department of Psychology, University of California, Berkeley, CA, USA, March 2001.

Herrmann, C.S.

Resonanzfrequenzen im visuellen Cortex.

Zentralinstitut für seelische Gesundheit, Mannheim, Germany, April 2001.

Herrmann, C.S.

Evoked and induced gamma activity.

Forschungszentrum Jülich, Jülich, Germany, July 2001.

Herrmann, C.S.

Kognitive Korrelate von 40 Hz Aktivität im EEG.

Institut für Psychologie, Universität Jena, Germany, July 2001.

Herrmann, C.S.

Das 'was' und 'wo' im auditorischen Cortex.

Institut für Psychologie, Otto-von-Guericke Universität Magdeburg, Magdeburg, Germany, November 2001.

Herrmann, C.S.

Measuring event-related potentials in 3T MRT.

Max-Planck-Institut für Hirnforschung, Frankfurt (Main), Germany, December 2001.

Hund-Georgiadis, M.

Wie lernt das Gehirn Sprache?

Schulvorträge der Max-Planck-Gesellschaft anlässlich der Hauptversammlung der MPG, Johann-Gottfried-Herder Oberschule, Berlin, Germany, June 2001.

Hund-Georgiadis, M.

Die fantastische Welt des Gehirns in den neuen bildgebenden Verfahren.

Urania, Senioren-Akademie, Leipzig, Germany, September 2001.

Jescheniak, J.D.

Vom Gedanken bis zum Öffnen und Schließen des Mundes: Wie Psycholinguisten das Sprechen untersuchen.

Schulvorträge der Max-Planck-Gesellschaft anlässlich der Hauptversammlung der MPG, Johann-Gottfried-Herder Oberschule, Berlin, Germany, June 2001.

Jescheniak, J.D.

Wie werden Wörter aus dem lexikalen Gedächtnis abgerufen?

Psychologisches Kolloquium, Friedrich-Wilhelms-Universität Bonn, Bonn, Germany, December 2001.

Knoesche, T.R.

Functional brain imaging based on EEG and MEG.

Brain Mapping and Neuromodulation Workshop 2001, Xian, China, April 2001.

Kotz, S.A.

Priming as a function of semantic information types: Evidence from event-related potentials and event-related functional magnetic resonance imaging.

Colloquial series at the Shriver Mental Retardation Developmental Disabilities Research Center, Waltham, MA, USA, March 2001.

Kovalev, V.

Texture analysis in 3D medical images.

Bildverarbeitungs-Kolloquium, Universitäten Heidelberg und Mannheim, Germany, October 2001.

Kruck, S.

Elektrisch korrelierte Potentiale zur auditorischen Mustererkennung von metrischen Strukturen in dreisilbigen CV-Strukturen.

German Language Aquisition Study, Klinikum Lindenhof, Berlin, Germany, June 2001.

Kruck, S.

Akustisch evozierte Potentiale: Untersuchung zeitlicher Strukturen in sprachlichen Signalen mittels EEG.

Institut für Neurobiologie, Neurotee WS01/02, Universität Leipzig, Leipzig, Germany, November 2001.

Kruck, S., Alter, K. & Tervaniemi, M.

Effects of metrical changes in tri-syllabic consonant vowel pairs: An EEG study with different task conditions.

5. Jahreskolloquium des DfG-Schwerpunktprogrammes "Zeitgebundene Verarbeitung im zentralen auditorischen System" (ZIZAS), Nimbschen, Germany, November 2001.

Kruggel, F.

Image processing in brain science: Analysing the neocortical surface.

Workshop 'Unkonventionelle bildgebende Verfahren: Von den Rohdaten zum Bild', Großbothen, Germany, January 2001.

Kruggel, F.

Recording EEG during functional MRI scanning: Experimentation, data analysis and neurobiological perspectives.

Florida Atlantic University, Boca Raton, FL, USA, June 2001.

Kruggel, F.

Independent component analysis of functional MRI data.

INSERM Summer School on Functional Data Analysis, Gif-sur-Yvette, France, July 2001.

Kruggel, F.

Bildverarbeitung in den Neurowissenschaften.

Gastvorlesung, Rhein-Ahr-Campus, Remagen, Germany, October 2001.

Kruggel, F.

Morphmetry based on magnetic resonance imaging data.

Two guest lectures, National Laboratory for Pattern Recognition, Chinese Academy of Sciences, Beijing, China, November 2001.

Lohmann, G.

Segmentierung kortikaler Regionen in Magnetresonzanzbildern des menschlichen Gehirns. Forschungszentrum Jülich, Jülich, Germany, August 2001.

Lück, M., Hahne, A. & Clahsen, H.

Bluses und Waggons oder Waggonen und Blusen - EKP Studie zur Verarbeitung von deutschen Pluralnomina bei Kindern und Erwachsenen.

Fachbereich Linguistik, Universität Potsdam, Potsdam, Germany, July 2001.

Maess, B.

Verarbeitung musik-syntaktischer Verletzungen.

Meeting of the SPP "Zeitgebundene Informationsverarbeitung im zentralen auditorischen System" (SPP ZIZAS), Bad Salzelmen, Germany, June 2001.

Maess, B.

Kortikale Verarbeitung musikalischer Reize.

Neurologisches Therapiezentrum, Heinrich-Heine-Universität Düsseldorf, Düsseldorf, Germany, October 2001.

Meyer, M.

Magnetresonanztomografische Evidenz zur Bedeutung syntaktischer und prosodischer Information beim Sprachverstehen.

Kolloquium Experimentelle Neurolinguistik, Universität Bielefeld, Bielefeld, Germany, July 2001.

Meyer, M.

The role of prosodic parameters in processing speech, vocal, and non-vocal sounds evidenced by 3T fMRI.

Graduiertenkolleg am Institut für maschinelle Sprachsynthese, Universität Stuttgart, Stuttgart, Germany, July 2001.

Meyer, M.

Brain responses to speech comprehension.

Departmental Seminar, Department of Psychology, University of Edinburgh, UK, November 2001.

Meyer, M.

Neurocognition of speech evidenced by 3T fMRI.

Public Lecture, Department of Theoretical and Applied Linguistics, University of Edinburgh, UK, November 2001.

Schubotz, R.I.

Cortical representation of predicting dynamic events (fMRI).

Forschungskolloquium Biopsychologie, Ruhr-Universität Bochum, Bochum, Germany, November 2001.

Stolterfoht, B.

Verarbeitung von Wortstellungsvariationen.

Universität Potsdam, Institut für Linguistik, Potsdam, Germany, June 2001.

Ullsperger, M.

The role of prefrontal and frontomedian cortices in planning, performing, and evaluating actions. Neurobiologisches Kolloquium, Neurologische Klinik, Universität Tübingen, Tübingen, Germany, May 2001.

Wollny, G.

Nichtlineare visko-elastische Registrierung: Methode, Implementierung und Anwendung.

Kolloquium Medizinische Bildverarbeitung, Universität Lübeck, Germany, November 2001.

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