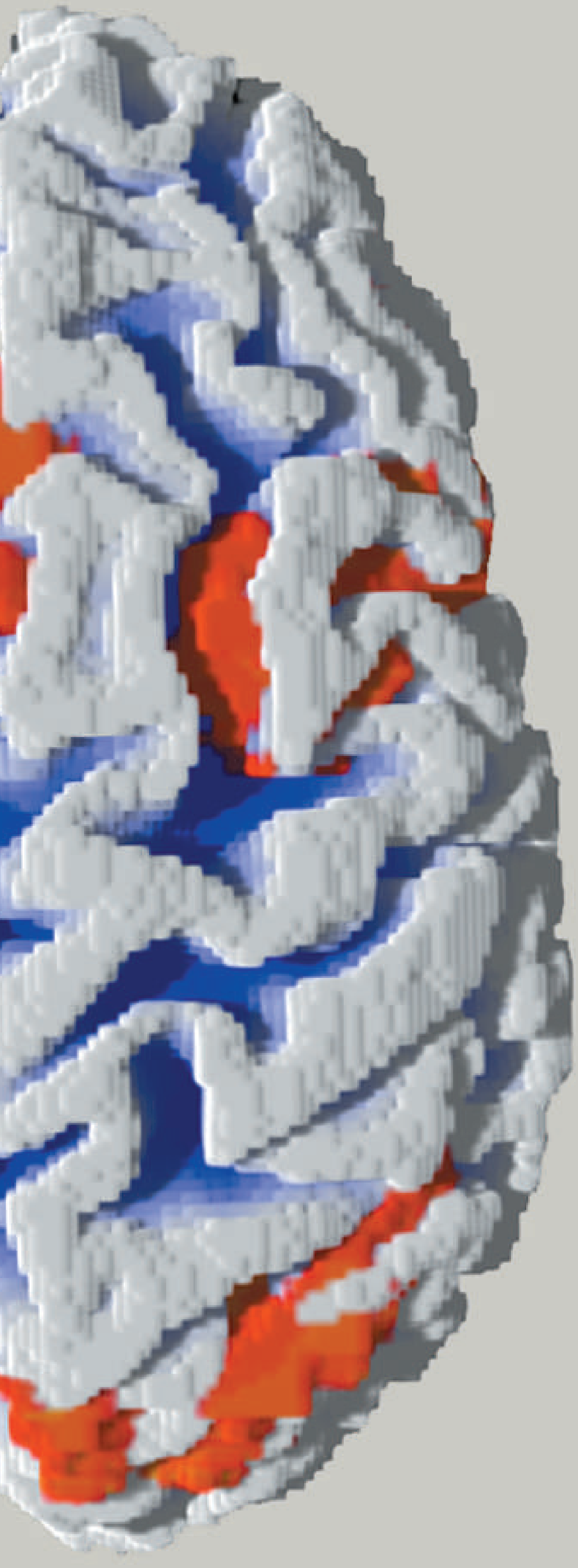

Annual Report 2000

Max Planck Institute of Cognitive Neuroscience Leipzig

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Annual Report 2000

Photo: Stefan Müller-Naumann, München

The year 2000, five years after the official opening, was characterized by major changes in the institute's personnel. The first 'generation' of scientists left the institute. Quite a number went as post-docs either to the United States, Canada, United Kingdom, or to Universities in Germany. Trevor Penney accepted an Assistant Professorship for Psychology at the Chinese University of Hongkong, Axel Mecklinger accepted a C3 Professorship for Psychology at the University of Saarbrücken, and Stefan Pollmann a C3 Professorship for Cognitive Neurology at the University of Leipzig.

The cooperation with the University of Leipzig was strengthened through the renewal of a number of research initiatives such as a joint research group on *Working Memory* (Forschergruppe), a focused research program on *Central Auditory Systems* (Schwerpunktprogramm) and a joint graduate program in *Linguistics* (Graduiertenkolleg) supported by the German Research Foundation (Deutsche Forschungsgemeinschaft).

The Interdisciplinary Center for Clinical Research (IZKF) at the University of Leipzig had its site visit in October. It found broad recognition by its external advisory board for the substantial program made in extending and improving its scientific and clinical infrastructure.

Under the handling of Prof. Michel (Department of Physics and Geology) and actively supported by our institutes, facilities and expertise of six faculties of the University of Leipzig in Magnetic Resonance Physics were amalgamated in a Center for Magnetic Resonance.

Together with the University of Potsdam, the Free University of Berlin and the Humboldt University of Berlin, a major project on *Language Development and Specific Language Impairment* was launched. This project, which is supported by the German Research Foundation, will investigate 250 children, 100 of whom come from families at-risk for language impairment, longitudinally from birth to the age of 6 years with respect to audition, language behavior, non-language cognitive behavior, social interaction as well as the neural correlates of auditory perception and language processing. The project was installed at the Children's Hospital Lindenhof in Berlin in November.

With these cooperations and initiatives we hope to contribute to the necessary strengthening of the scientific landscape in the East of Germany.

Angela D. Friederici
D. Yves von Cramon

Leipzig, February 2001

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(n) University of Rome, Italy
(o) Max-Planck-Institut für Mathematik in den Naturwissenschaften
(*) left the institute during 2000

NEUROCOGNITION OF LANGUAGE 2.1

This year's research focused on three topics: first, on *syntactic processes during comprehension*, and their neurophysiological substrate; second, on *lexical-semantic processes* and their neuronal underpinning at the word and sentence comprehension level; and third, on aspects of *language production*.

Syntactic processes have been reported to be reflected in distinct ERP components: the early left anterior negativity (ELAN) appears to be correlated with initial phrase structure building processes, whereas the late centro-parietal positivity (P600) is correlated with difficulties of syntactic integration. A first study (2.1.1) demonstrated that the P600 differs in its topography as a function of the type of integration difficulty: the processing of syntactically incorrect sentences elicits a centro-parietal positivity, whereas complex sentences lead to a more frontally P600, thus suggesting the involvement of different underlying brain systems. A second study (2.1.2) indicated that the P600 even reflects the cost of predicting a syntactic structure e.g., the prediction of a determiner phrase at the determiner. A third study (2.1.3) demonstrated a similar P600 at the verb which varies as a function of the projected complexity of the verb's argument structure. Two further studies focused on the processing of the relation of the verb's argument. One study conducted showed that a hierarchical relation between arguments can be built up on the basis of morphological information (case) even in the absence of verbal information (2.1.4). In another study, patients with anterior and with temporo-parietal lesions were tested to differentiate semantic from syntactic aspects when processing verbs with respect to their number of arguments (see section 2.5).

Three studies focused on the early left anterior negativity (ELAN) as a marker of initial syntactic processes: one study showed that this effect is still present in patients with Parkinson's disease (see section 2.5), supporting the view that the generation is not based in the basal ganglia. A second study showed that this ELAN effect can be segregated from physical deviances (MMN) (2.1.5). A third study demonstrated that the laterality of this effect changes as a function of prosodic information (2.1.6). Different types of morphosyntactic violations were investigated using ERP (2.1.7, 2.1.8). Different aspects of syntactic information, such as word category and syntactic gender, were examined in an fMRI study (2.1.9).

Syntactic and lexical semantic processes during auditory language comprehension were investigated in subjects who learned German as a second language after puberty (2.1.10, 2.1.11) and in subjects with cochlear implants (2.1.12). These studies indicate that early syntactic processes, as reflected by the ELAN, are more vulnerable under these processing conditions than late syntactic processes, as reflected by the P600; and lexical semantic processes, as reflected by the N400.

Lexical semantic processes were investigated at the word and the sentence level. An fMRI study identified the neural correlates of lexicality and frequency (2.1.13). Two studies examined the influence of attentional process on word perception (2.1.14, 2.1.15), one study the influence of task demands (2.1.16). This influence of emotional prosody on word recognition was the focus of an additional series of experiments (2.1.17). The semantic representation and processing of compounds as well as the influence of working memory was investigated in a series of experiments (2.1.18, 2.1.19, 2.1.20, 2.1.21, 2.1.22). The latter four used the N400 as an indicator for activation (or inhibition) of the dominant or subdominant reading during the processing of ambiguous lexical elements. The neural generators of the N400 at the sentence level were identified in an MEG study (2.1.23).

Production models assume that phonological (word form) information is represented and processed separately from syntactic and meaning information (lemma). In an ERP study (2.1.24), we explored the time course of activation of phonological and semantic activation. In an MEG study (2.1.25), we were able to spatially locate the processes of lexical selection in the left temporal cortex.

2.1.1 Syntactic complexity and syntactic repair elicit differently distributed P600 responses

Friederici, A.D.[1], *Hahne, A.*[1] & *Saddy, D.*[2]

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[2] *Department of Linguistics, University of Potsdam*

Aspects of syntactic complexity and syntactic repair were investigated by comparing the event-related brain potentials (ERPs) for sentences of different syntactic complexity to those containing a syntactic violation. Previous research had shown that both aspects of syntactic processing are reflected in a late positivity (P600).

A direct comparison between syntactic violation and syntactic complexity was possible using the following German constructions (1) - (3).

(1) correct, minor complexity:
Dem Vater trug er den Mantel.
The $_{\text{DAT}}$ father carried $_{\text{PAST TENSE, SINGULAR}}$ he $_{\text{singular}}$ the coat.
(He carried $_{\text{SINGULAR}}$ the coat for the father.)

(2) correct, major complexity:
Dem Vater getragen hat er den Mantel.
The $_{\text{DAT}}$ father carried $_{\text{PARTICIPLE}}$ has he the coat.
(He has carried the coat for the father.)

(3) incorrect:

(a) minor complexity:

* *Dem Vater trugen er den Mantel.*

The $_{\text{DAT}}$ father carried $_{\text{PAST TENSE, PLURAL}}$ he $_{\text{singular}}$ the coat.

(He carried $_{\text{PLURAL}}$ the coat for the father.)

(b) major complexity:

* *Dem Vater getragen er den Mantel.*

The $_{\text{DAT}}$ father carried $_{\text{PARTICIPLE}}$ he the coat.

(He carried $_{\text{PARTICIPLE}}$ the coat for the father.)

Twenty-four right handed subjects (13 female) read 360 sentences; 120 sentences of type (1), 120 sentences of type (2) and 120 sentences of type (3) [60 sentences of type (3a) and 60 sentences of type (3b)].

ERP results from a reading experiment using these sentence types demonstrate that although both processing aspects, i.e., complexity and violation, elicit a late positivity, they differ in distribution (see Fig. 1 and 2). The repair-related positivity (following a negativity) elicited by syntactic violation a centro-parietal distribution, whereas the complexity-related positivity showed a fronto-central distribution. These data indicate that the P600 is not a unitary phenomenon. Moreover, the distributional differences strongly suggest that different neural structures underlie the two aspects of processing, namely syntactic repair and syntactic integration difficulties.

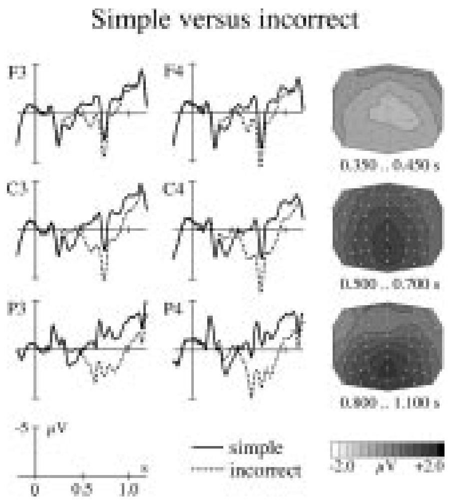

Figure 1. Left: Grand average ERP waveforms for 6 selected electrode positions for the simple and the incorrect conditions (3a and 3b were collapsed as not significant differences were found for the two incorrect sentence types). Right: Topographic maps of the differences between the ERP response to the incorrect and the simple condition for two time windows. Dark areas indicate positive differences between conditions and bright areas indicate negative differences. Electrode positions are marked by small circles.

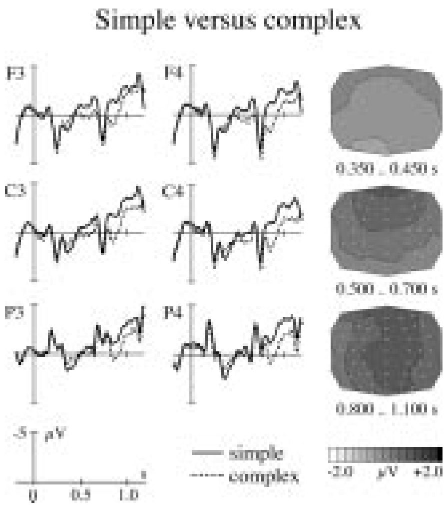

Figure 2. Left: Grand average ERP waveforms for 6 selected electrode positions for the simple and the complex condition. Right: Topographic maps of the differences between the ERP response to the complex and the simple condition for two time windows.

2.1.2 Syntactic mismatch and the cost of prediction: Event-related potentials elicited by word order variations

Schlesewsky, M.[1], *Friederici, A.D.*[2] & *Frisch, S.*[1]

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[2] *Max Planck Institute of Cognitive Neuroscience*

Following a study by Rösler and co-workers (1998), we used event-related brain potential (ERPs) in order to trace effects of word order variation. In addition to Rösler et al., the type of argument in non-canonical position was varied between full NP and pronoun in our experiment. Sentences were presented in a word-by-word manner and were followed by a question controlling thematic role assignment.

ERPs revealed several interesting observations:

(1) in sentences with nonpronominal arguments:
Dann hat dem Jäger der Lehrer den Roman gegeben.
Then has the$_{DAT}$ hunter the$_{NOM}$ teacher the$_{ACC}$ novel given.
(Then the teacher gave the novel to the hunter.)

the determiner of a non-canonical noun phrase elicited a broadly distributed negativity (see Fig. 3);

(2) in sentences with pronominal arguments:
Dann hat ihm der Lehrer den Roman gegeben.
Then has him$_{DAT}$ the$_{NOM}$ teacher the$_{ACC}$ novel given.
(Then the teacher gave him the novel.)

no differences were observed for non-canonical word order (see Fig. 4);

(3) independent of word order and structural position, a determiner elicited a late positivity compared to a pronoun or noun.

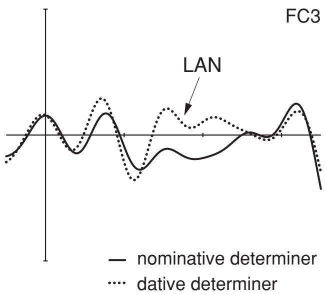

Figure 3.

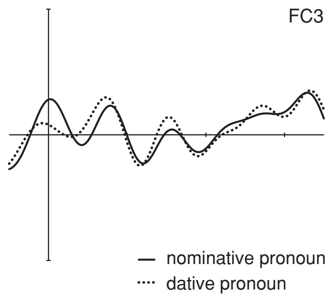

Figure 4.

By showing that the ERP-pattern induced by scrambled constituents depends on the type of the scrambled NP, we were able to demonstrate that the negativity induced by scrambled nonpronominal NPs is a reflection of a local syntactic violation and not of preparatory storage mechanisms (as suggested by Rösler et al., 1998). Furthermore, it is evident from our data that the parser's prediction of an element is costly. This is reflected in what we have termed a 'predictive P600' component. From the perspective of psycholinguistic theory-building, these results make two substantial contributions to our understanding of processes during online sentence comprehension: firstly, it is now clear that the parser is sensitive to fine-grained categorical information and its interaction with grammatical requirements, and secondly, the finding of a predictive P600 provides a further piece of strong evidence for the fact that language processing proceeds according to criteria of simplicity.

Processing of syntactically complex sentences: Evidence from two ERP studies

2.1.3

Lück, M.[1], *Hahne, A.*[1], *Clahsen, H.*[2] & *Friederici, A.D.*[1]

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The aim of our studies was to explore whether differences in syntactic complexity as proposed by linguistic theory are reflected in sentence processing. The complexity of sentences is higher, if the argument structure of the embedded verbs requires an empty category (= category with no phonological representation). Examples for these verb classes are raising verbs or subject control verbs. In our studies event-related potentials were recorded while participants heard or read sentences with different syntactic structures. With reference to Featherston et al. (2000), we generated 144 German basic sentences. These were presented in three different conditions. The first condition contained a transitive verb in the matrix sentence, in the second condition we used a subject control verb, and in a third condition a raising verb was embedded.

(1) *Der Friseur* ***entfernte*** *allerdings den Bart des Kunden ganz zum Schluss.*
The barber cut indeed the beard of the client at the end.

(2) *Der Friseur$_i$* ***hoffte*** *allerdings $_{PRO(i)}$ den Bart des Kunden rasieren zu können.*
The barber hoped indeed to cut the beard of the client at the end.

(3) *Der Friseur$_i$* ***schien*** *allerdings $_{trace(i)}$ den Bart des Kunden rasieren zu können.*
The barber seemed indeed to cut the beard of the client at the end.

The three conditions differ in their proclaimed syntactic structures: condition (1) has only a direct object and no need for an empty category before the object position, whereas conditions (2) and (3) contain an infinitival complement of the matrix verb and have an understood covert subject (PRO$_i$, trace$_i$). The difference between condition (2) and (3) lies in the nature of the dependency on the unexpressed subject. The raising construction (3) produces a movement chain between the subject position of the matrix verb and the embedded verb. In contrast, the two subject positions in the subject-control condition (2) build a referential dependency and no movement chain.
The results of both experiments showed a central positivity on the verb for condition (3) in comparison with the other two conditions. Although the P600 has generally been observed in correlation with differences in structural complexity (Kaan et al., 2000; Friederici et al., in press), the sentences do not differ with regard to their phrase structural complexity on the verb. Rather, the observed effect can best be interpreted as reflection of a prediction of higher sentence complexity (see also 2.1.2).

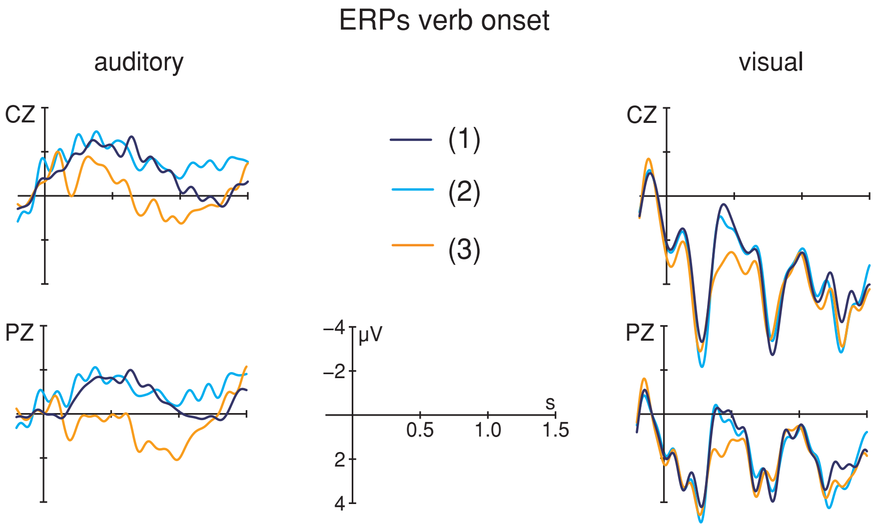

Figure 5.

2.1.4 Establishing thematic relations in the absence of verbal information: The influence of case and word order

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

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The question of how arguments are associated with their respective predicates is central to any understanding of the mechanisms involved in language comprehension. It becomes especially interesting to ask this question, namely how the human language processing system determines "who is doing what to whom", with respect to languages displaying a relatively free word order, where structural and non-structural factors might interact. In this paper, we will present an ERP study examining verb-final clauses in German, the aim of which was to dissociate between case, thematic roles and word order as possible factors that are utilized during predicate argument association.

To this purpose, we varied the word order (SO vs. OS) in sentences with unambiguously case marked arguments. Additionally, the verb in final position either subcategorized for dative or for accusative case and either required the subject to be higher on the thematic hierarchy than the object (subject-experiencer verbs) or vice versa (object-experiencer verbs). The dative-accusative manipulation served to examine the widely acknowledged assumption that only dative object-experiencer verbs in German truly require the assignment of the higher thematic role to the object argument, while accusative object-experiencer verbs also allow a causative reading in which the subject is thematically higher than the object. The resulting experimental conditions are illustrated in (1) for accusative verbs.

(1) *Daniel glaubt, …*
Daniel believes …

a. SO-Order / Subj-Exp. Verb
... dass der Senator den Bischof fürchtet und ...
… that the$_{NOM}$ senator the$_{ACC}$ bishop fears and …

b. SO-Order / Obj-Exp. Verb
... dass der Senator den Bischof ängstigt und ...
… that the$_{NOM}$ senator the$_{ACC}$ bishop frightens and …

c. OS-Order / Subj-Exp. Verb
... dass den Senator der Bischof fürchtet und ...
… that the$_{ACC}$ senator the$_{NOM}$ bishop fears and …

d. OS-Order / Obj-Exp. Verb
... dass den Senator der Bischof ängstigt und ...
… that the$_{ACC}$ senator the$_{NOM}$ bishop frightens and …

In accordance with previous results (Roesler et al., 1998; Schlesewsky et al., 2000), scrambled object NPs [*den Senator*, in (1b) and (1c)] elicited a centrally-distributed negativity in the ERP. Additionally, dative object-experiencer verbs elicited a P345 in comparison to dative subject-experiencer verbs (see Fig. 6), while accusative object-experiencer verbs elicited an N400 in comparison to their subject-experiencer counterparts.

These results strongly indicate that, in German, the language processing system builds up a hierarchical relation between the arguments on the basis of their morphological case, even in the absence of verbal information. When the verb is reached, this hierarchy is either confirmed (by a subject-experiencer verb) or must be revised (by a dative object-experiencer verb). This revision, which consists of a reordering of the thematic hierarchy that has been established, is reflected in the P345. By contrast, when the thematic ordering between arguments may be kept the same, but expectations with regard to the conceptual structure must be revised (causativization for accusative object experiencers), an N400 result.

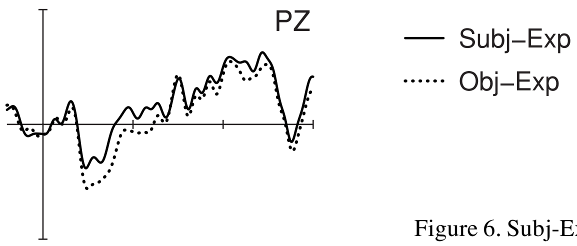

Figure 6. Subj-Exp vs. Obj-Exp Dative Verbs.

2.1.5 Types of verb form violation: An ERP study

Urban, S. &
Gunter, Th.C.

In this study, we investigated the comprehension of German verbs by violating their form differently. A German complex verb like *anrufen* ('to call in') must be separated into its stem and its particle when occurring in the second position of a sentence.

The following example will illustrate this:

(1) *Er ruft den Mann an und ...*
He called the man in and ...

We hypothesized that the violation of this requirement, compare example (2), would involve the consultation of the lexicon in order to verify that *anrufen* ('to call in') is an existing complex verb in the language (Schreuder, 1990). It was therefore assumed that this violation would be recognized by the comprehension system as a lexico-morphological inappropriate verb form.

(2) **Er anruft den Mann und...*
*He incalls the man and...

This violation type was contrasted with another kind of inappropriate verb form, namely a subject-verb agreement violation being morpho-syntactic in nature.

(3) **Er rufen den Mann an und ...*
*He call the man in and ...

Our proposed classification - both violations being of different linguistic nature - was tested by using the method of event-related brain potentials (ERP). The set of stimuli used in the experiment contained an equal number of correct and incorrect verb forms. Thirty-two students of the University of Leipzig were presented with 36 experimental sentences per condition. Sentences were presented in a RSVP-format.

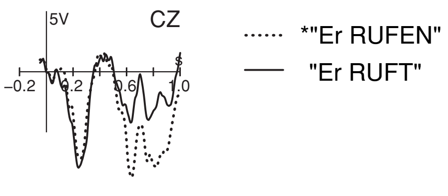

Figure 7. Grand average for CZ contrasting correct verbform with agreement violation.

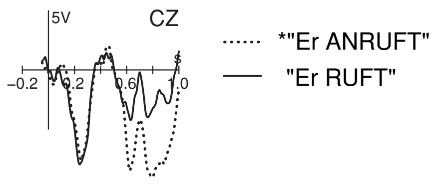

Figure 8. Grand average for CZ contrasting correct verbform with continuous violation.

Surprisingly, the result of our study is that both types of violation elicited a positive parietal component around 600 milliseconds after the verb onset. The fact that there are no different brain responses for both types of verb violation as reflected by ERP measurement indicates that the P600 seems to represent a general process reflecting the attempt of the comprehension system to find a grammatical interpretation for different types of inappropriate linguistic input. This is in accordance with Kaan et al. (2000), who suggested that the P600 reflects the difficulty in syntactic integration.

Two mechanisms to inflect a noun: An auditory ERP study of German plural formation

2.1.6

Lück, M.[1], *Hahne, A.*[1] & *Clahsen, H.*[2]

[1] *Max Planck Institute of Cognitive Neuroscience,*
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There is some evidence that two qualitatively different mechanisms of inflection can be distinguished: whereas irregulars seem to have separate lexical entries stored in the mental lexicon, regulars are processed via a set of affixation rules (Pinker & Prince, 1991; Marcus et al., 1995). Weyerts et al. (1997) examined this model for German plural formation in the visual modality. They found different ERP patterns for the processing of regularly pluralized nouns and irregular ones. The aim of the present study was whether we can replicate their results with similar materials presented in the auditory modality.
Following Weyerts and co-workers we created four conditions: two containing irregular inflected nouns, the other two regular inflected nouns. While recording event-related potentials each subject heard each noun four times in different sentence contexts, twice with the correct and twice with an incorrect plural form. For the incorrect items the irregulars were regularized and the regulars were irregularized.

(1) Irregulars:
Löwen beobachten an Wasserstellen die ruhenden ***Leoparden/*Leopards*** *im Gras.*
On ponds lions are watching the sleeping leopards in the grass.

(2) Irregulars:
Die meisten Jacken haben die praktischen ***Kapuzen/*Kapuzes*** *gegen den Regen.*
Most coats have handy hoods against the rain.

(3) Regulars:
Der Hund beschützt die ängstlichen ***Lehnerts/*Lehnerten*** *vor dem Dieb.*
The dog is protecting the fearful Lehnerts from the thief.

(4) Regulars:
Christine lutscht am liebsten die leckeren ***Bonbons/*Bonbonen*** *aus Schokolade.*
Christine likes it most to suck the tasty sweets made of chocolate.

Using the ERP violation paradigm, we compared incorrect vs. correct nouns in each condition. The incorrect irregulars (1, 2) produced a biphasic ERP-pattern, similar to a LAN/P600 pattern (also been observed in processing of syntactic violations). In the regular condition (3) we observed a broadly distributed negativity, resembling a N400, for the incorrect nouns compared to the correct ones (also seen for processing of pronounceable nonwords). The results of the fourth condition showed a broadly distributed negativity as well as a later centro-parietal positivity. Thus we can partially confirm the results of Weyerts and co-workers. The differences between the results of the two studies may be due to the specifics of auditory word processing (e.g., incremental left-to-right processing; change or no-change in syllable structure of the inflected words). Nevertheless, these ERP findings support the theoretical assumption, that the processing routes correspond to the morphological structure of the inflected word.

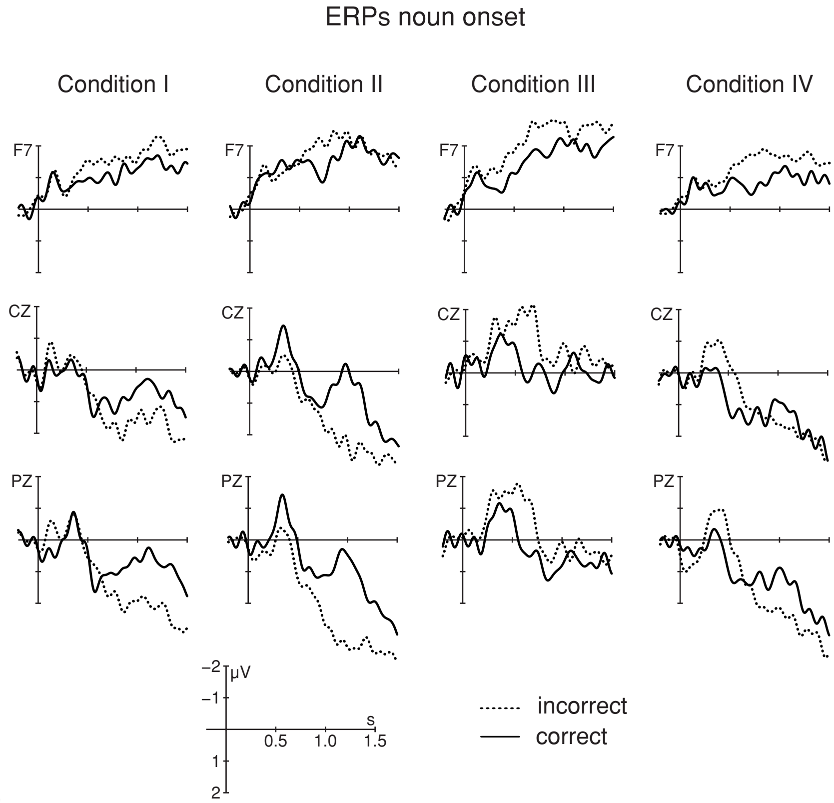

Figure 9.

2.1.7 Separating two types of syntactic information: Word category versus gender

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

This work was supported by the Leibniz-Prize of the German Research Foundation (DFG) awarded to Angela D. Friederici.

We conducted a series of fMRI experiments involving the processing of syntactic aspects at the lexical level. In a first experiment, subjects were required to either perform a syntactic task, i.e. word class judgment or a semantic task, i.e. concreteness judgment after perceiving a word (see Ann.Rep. 99, p. 24/25). The syntactic task selectively activated the inferior tip of the left fronto-opercular cortex (BA44) in addition to the junction of inferior frontal and inferior precentral sulcus (BA44/6). The semantic task selectively activated the inferior frontal gyrus (BA45) and the middle temporal gyrus (BA21/37). In a second experiment investigating production processes, subjects were presented with pictures and required to indicate whether the syntactic gender of the picture's name is feminine or masculine (syntactic gender task). In this task, a selective activation was found in the inferior frontal gyrus/sulcus (BA45/46/47) and in the middle temporal gyrus. Thus, during production the retrieval of syntactic gender information activates a neural network known to support semantic processes. The differential activation for the gender judgment tasks (in production) and the word class judgment task (in comprehension) raises the issue of whether these two aspects of syntactic information processing are supported by partly non-overlapping brain systems. Thus, in the present experiment we investigated the neuronal network underlying the processing of word class and syntactic gender during comprehension by means of fMRI. The task design was similar to the syntactic/semantic comprehension study (see Ann.Rep. 99, p. 24/25). In replication of previous results, the word class judgment activated the inferior tip of the left fronto-opercular cortex (BA44 - Fig. 10A) and the junction of inferior frontal and inferior precentral sulcus (BA44/6 - Fig. 10B). The gender judgment task activated the inferior frontal gyrus slightly anterior to the activation found during the word class judgment (cf. Fig. 10C). No temporal activation was observed. This might suggest that a temporo-frontal network is differentially activated depending on the type of syntactic information (word class or gender) and processes involved (comprehension or production). However, the precise nature of the underlying processes remains to be elucidated in further experiments contrasting comprehension and production processes directly.

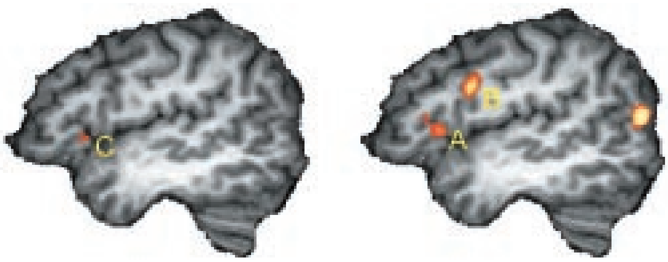

Figure 10. Sagittal section through the left hemisphere. Activation during the gender judgment task is displayed in the left panel and during the wordclass judgment in the right panel. (A) inferior tip of the left fronto-opercular cortex, (B) junction of inferior frontal and inferior precentral sulcus, (C) inferior frontal gyrus.

Segregating early detection systems for physical and syntactic deviances

2.1.8

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Hahne, A.[1], Schröger, E.[2] & Friederici, A.D.[1]

We examined whether the detection systems for physical and syntactic deviances in auditory language processing can be segregated using event-related brain potentials (ERPs). Sentences were presented auditorily as connected speech. In the physical manipulation condition, the terminal word of the sentence was presented either from the same or from a different location than the preceding sentence fragment. In the syntactic manipulation condition, the terminal word was either a syntactically correct continuation of the preceding sentence fragment or violated the syntactic constraints. These two factors were completely crossed. Physical deviances elicited the mismatch negativity (MMN) and syntactic deviances elicited the early syntax-related negativity (ELAN), both deviance-related components of the ERP. Sentences which violated physical as well as syntactic constraints elicited a negativity which was larger than that elicited by only a physical or only a syntactic deviance. This finding suggests that the physical and the syntactic deviance-detection systems act - to a high degree - in parallel and independently from each other.

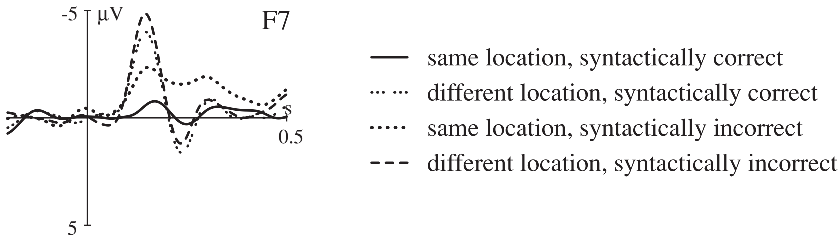

Figure 11. Grand average ERPs across 24 participants for a left anterior electrode position. Compared to correct sentences which did not switch their location, syntactically incorrect sentences without location switch elicited an early negativity. Correct sentences which switched their location showed a mismatch negativity. Syntactically incorrect sentences which additionally switched their location elicited a negativity which was larger than the location switch of a syntactically correct sentence.

2.1.9 Pitch flattening of spoken language changes laterality of syntax-related brain response

Herrmann, C.S., Friederici, A.D., Oertel, U., Hahne, A. & Alter, K.

The brain processes underlying spoken language comprehension comprise auditory encoding, syntactic parsing and semantic integration. While auditory encoding of stimuli is a process which activates both brain hemispheres, later stages which are specific for language comprehension usually activate the left hemisphere stronger than the right. Syntactic parsing, especially the detection of a syntactic violation, often leads to left-lateralized brain responses. Some studies have reported a more bilateral brain response for syntactic violations in auditorily presented sentences. Here the hypothesis is tested to what extent prosodic information might influence the lateralization of the brain response correlated with syntactic parsing. We used stimulus material from a previous MEG experiment in which syntactic violations lead to a bi-lateral brain response for syntax violations. In contrast to the previous experiment, the pitch of the sentences was flattened to diminish prosodic cues. This resulted in a dominance of the right hemisphere for the brain's syntax response. The statistical analysis revealed by a significant interaction of hemisphere x condition in an ANOVA. Post-hoc comparisons showed that the factor condition (correct vs. syntactically incorrect) yielded significant differences only in the right hemisphere ($F(1,10) = 13.73$, $p < 0.005$). Such a lateralization was not found in the previous experiment with unflattened pitch. Thus, the data show that prosodic cues such as pitch variations affect the lateralization of syntax-related brain responses. They suggest that the relative contribution of the right hemisphere depends on the interaction of prosodic and syntactic information.

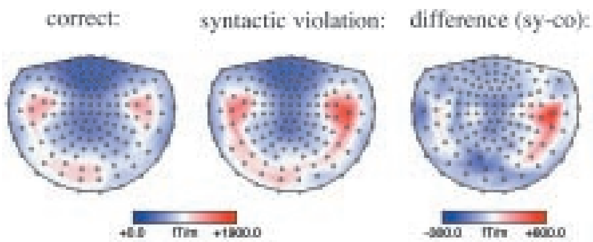

Figure 12. MEG responses (120..200 ms) to correct (left) and syntactically incorrect (middle) sentences, as well as the difference (right). Event-related fields are lateralized to the right hemisphere for the syntactic condition when the pitch of sentences has been flattened.

Processing a second language: Comprehension mechanisms of auditory German sentence processing in Japanese participants

2.1.10

Hahne, A. & Friederici, A.D.

Learning a second language and using it efficiently becomes more difficult with increasing age. Up to now, the particular brain mechanisms underlying language comprehension in less proficient language learners who appear to have incomplete syntactic knowledge but comprehend most utterances during normal conversation remain to be uncovered. The present study used ERP measures to investigate the processing mechanisms underlying late L2-learners' comprehension of auditorily presented sentences. Native Japanese speakers who had learned German as a second language after puberty listened to German sentences which were either correct, semantically incorrect, syntactically incorrect or both semantically and syntactically incorrect. Brain responses were registered while participants listened to these sentences. Grammaticality judgments required after each sentence revealed that their overall performance was not perfect but clearly above the level of chance. When comparing the L2-learners' brain responses to those of native listeners, a variety of differences were observed. Whereas semantically incorrect sentences showed an ERP pattern similar to that of native listeners (a centro-parietal N400-effect), correct sentences elicited a greater positivity in L2-learners than in native listeners, possibly in reflection of greater difficulties in syntactic integration. For sentences containing a phrase structure violation, L2-learners did not show significant modulations of the syntax-related ERP components usually seen in native listeners (i.e., the early anterior negativity and the P600). Furthermore, sentences containing a pure semantic or a combined syntactic and semantic violation elicited a late right anterior-central negativity, an effect which has not been observed for native language processing. The topography of the effect may suggest that these additional processes are based on conceptual-semantic rather than on lexical-semantic aspects.

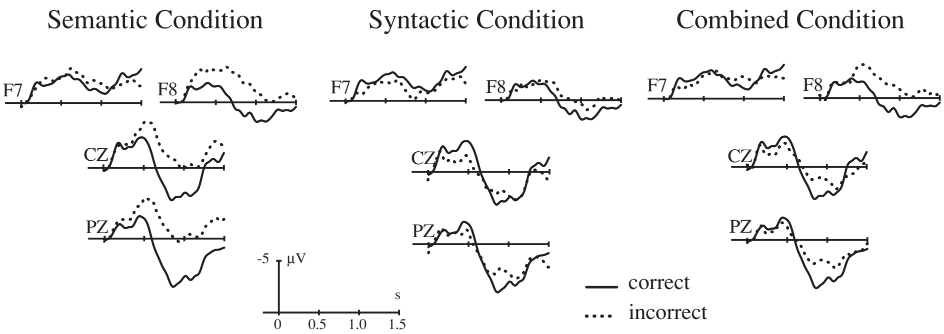

Figure 13. ERPs for semantic, syntactic and combined semantic and syntactic violations in native Japanese participants listening to their second language, German. Whereas the semantic effect resembled that of native German listeners, there were no significant effects in the syntactic as compared to the correct condition.

2.1.11 What is different in second language processing? Evidence from Russian and German native listeners

Hahne, A.

German sentences which were either correct, contained a selectional restriction violation or a word category violation were presented auditorily to 16 native speakers of German (L1-group) and to 16 native speakers of Russian who had learned German after the age of 10 (L2-group). Semantic violations elicited an N400-effect for both groups but with a reduced amplitude and a longer peak latency in the L2-group. Compared to correct sentences, sentences with a phrase structure violation elicited an early anterior negativity followed by a broad centro-parietal positivity in native speakers. By contrast, there was no differential modulation of the early anterior negativity in the L2-group. A late positivity was also elicited in the second language learners but it was slightly delayed compared to that shown by native speakers. Most interestingly, in two studies on bilingual sentence processing using similar materials, we did not observe a modulation of the P600 in participants whose native language was either Japanese (see 2.1.10) or French (see 2.1.18). However, in both experiments we observed an N400 effect for semantic violations. When comparing the behavioral data across these three bilingual groups, it becomes obvious that the performance of the Japanese and the French participants was roughly comparable but much lower (about 20% errors) than the present group of Russian native listeners (about 8% errors). This suggests that the ERP responses in the syntactic condition vary systematically with the proficiency level in L2. During second language acquisition, semantic integration processes seem to be the first to achieve a status similar to that in native listeners. The difference between the Japanese and French participants on the one hand and the Russian participants on the other hand suggests that with increasing proficiency late syntactic processes reflected in the P600 seem to come into play.

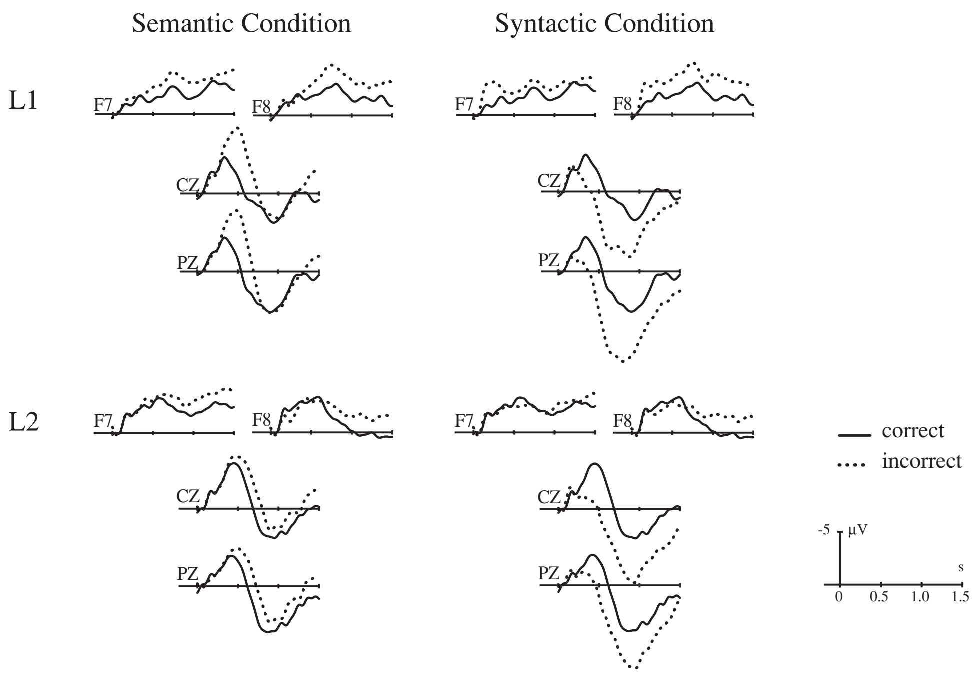

Figure 14. ERPs for native listeners and second language learners for semantic and syntactic violations. Second language learners display an N400 and a P600 similar to native listeners but no modulation of the early anterior negativity.

Language comprehension with cochlear implants

2.1.12

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[2] *University of Frankfurt,*
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Hahne, A.[1], *Wolf, A.*[1], *Kiefer, J.*[2] & *Müller, J.*[3]

supported by DFG

Cochlear implants (CI) are able to restore hearing abilities in postlingually deaf adults. However, the perceived auditory input deviates substantially from normal hearing and the language comprehension mechanisms in these patients are unclear. ERPs may be a useful method in examining language comprehension in cochlear implant users. In 1999, we reported first data on sentence comprehension mechanisms in two patients (see Ann.Rep. 99, pp.18-20). Up to now, we have tested eleven cochlear implant users who all suffered from a postlingually acquired deafness. 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.

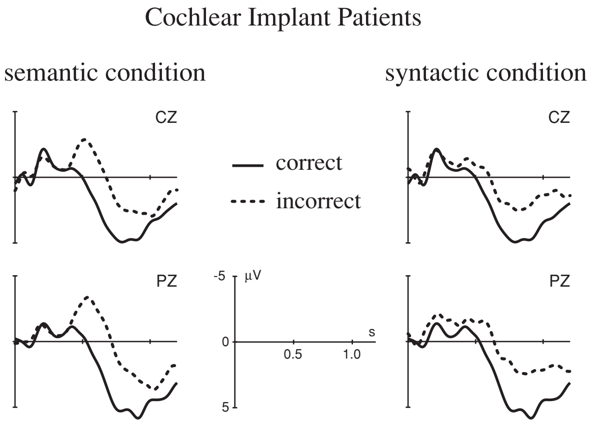

Figure 15. Grand average ERPs across 11 cochlear implant patients. Semantic violations elicited an N400 component comparable to unimpaired listeners. Syntactic violations which showed a late positivity in unimpaired listeners also elicited an N400-like negativity in hearing impaired patients.

The data confirmed our preliminary results. Although the performance data showed a large variability, the ERP data averaged across correctly answered trials were remarkably similar across participants. Semantic as well as syntactic violations elicited an N400-like negativity relative to the correct condition. This is in clear contrast to unimpaired participants who show clearly distinct ERP patterns for the two conditions, namely an N400 component for semantic violations and an early negativity followed by a late positivity for phrase structure violations. The N400-like effect for both violations conditions in cochlear implant users suggests that these participants focus on semantic rather than on syntactic information in auditory sentence comprehension. Cochlear implant users seem to rely on compensatory semantic comprehension strategies as a consequence of the impoverished auditory input.

2.1.13 Neural correlates of lexicality and word frequency in a lexical decision task

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

Event-related fMRI was used to investigate the neural correlates of lexicality and word frequency effects in the lexical decision task. Stimulus material were pseudo-randomized lists of words and phonologically legal pseudo-words. The word stimuli were further subdivided into words of low and high frequency of occurrence. Bilateral inferior occipito-temporal brain areas and portions of the posterior left middle temporal gyrus were more strongly activated when legal words were processed as compared to the processing of pseudo-words (cf. Figure 16A). Within the word stimuli, low frequency words elicited greater activations then high frequency words in the pars opercularis (BA44) and the pars triangularis (BA45) of the left inferior frontal gyrus (cf. Figure 16B). The results strongly support dual-route models of visual word processing. Inferior occipital and temporal brain regions are involved in the mapping of orthographic percepts onto word form representations stored in the orthographic input lexicon. These areas are thought to constitute the direct route to the mental lexicon. Neural activity in the superior left pars opercularis is likely to reflect activation of phonological information during lexical access, thus suggesting an involvement in grapheme-to-phoneme conversion. Left inferior frontal regions, thus, are involved in the indirect or 'assembled' route to the mental lexicon.

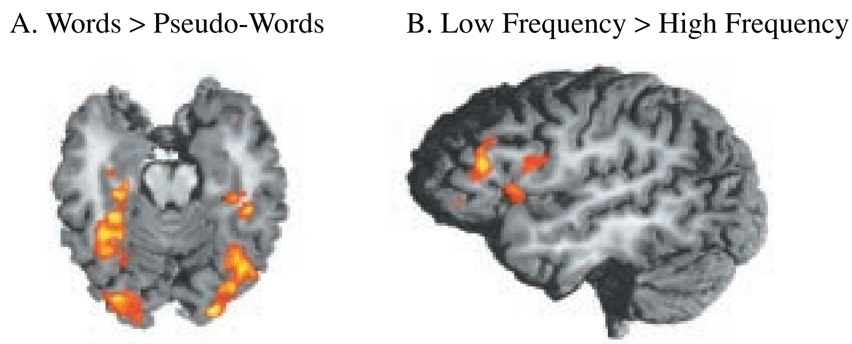

Figure 16.

2.1.14 The semantic processing of parafoveal words: Part I

De Filippis, M., Kotz, S.A. & Gunter, Th.C.

A previous study (Kotz & De Filippis, 1998) showed that a shift of spatial attention after stimulus onset can facilitate semantic processes for 'not to be attended' stimuli which is visible in an enhancement of the N400. This enhancement occured independently of a modulation of early spatial attentional processes as reflected in the P1-N1 complex (McCarthy & Nobre, 1993).

The aim of the present event-related potential (ERP) study was to investigate whether semantic word processing can happen without attention and with parafoveal word presentation. Words were presented alternately on both sides of the screen while participants were instructed to focus their attention on one side only. To prevent attentional shifts a distractor consisting of hashmarks (#) was presented simultaneously with every word on the opposite side. Eye movements towards the attended side were induced to control spatial attention during the whole stimulus presentation time of 300 ms (Shepherd et al., 1986). ERPs of 36 subjects were recorded from 32 electrodes while either a categorization task or a combined categorization/letter detection task had to be performed.

An enhancement of the P100 at contra-lateral as compared to ipsi-lateral electrodes was found in both tasks, indicating the successful direction of spatial attention towards the attended side (Luck et al., 1990). An effect of semantic categorization for words on the unattended side was only found for the simple categorization task. It was reflected in an enhanced frontally distributed N400 for stimuli of the target category (see Fig. 17).

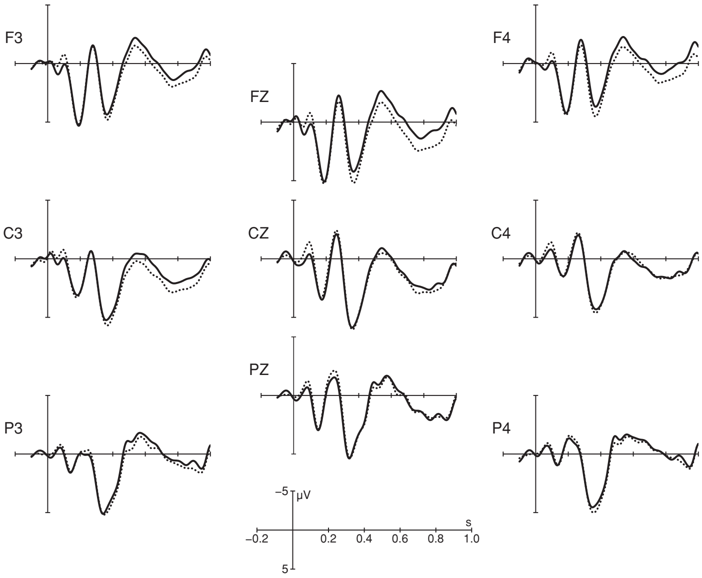

Figure 17. ERPs for unattended words of the target (solid) and nontarget (dotted) categories for word presentation on the unattended side (simple categorization task).

Therefore, we could not confirm the engagement of spatial attention at prelexical stages (Broadbent & Gathercole, 1990). However, the influence of task demands on 'unattended' word processing speaks against simple automatic semantic processing of parafoveal and unattended words (Fuentes et al., 1994), but rather for the engagement of attention in a selection process occurring after spatial selection.

2.1.15 The semantic processing of parafoveal words: Part II

De Filippis, M., Kotz, S.A. & Gunter, Th.C.

Prior experiments showed an N400 effect of semantic categorization for unattended and parafoveally presented stimuli. This effect was found to be dependent on task demands. This finding questions the automatic processing of unattended and parafoveally presented words and asks for attentional selection mechanisms other than the controlled ones: spatial attention and the attentional focus.

To confirm this hypothesis and to identify the corresponding event-related potentials (ERPs) a former experiment (De Filippis et al., 2000) was replicated changing the distractor material. Words were alternately presented on both sides of the screen while participants focused their attention on one side. Simultaneously with the presented words distractors were presented on the opposite side. The distractors used in the former experiment consisted of hashmarks (#) and were exchanged for randomly mixed letters (X, Y, V, W and Z), because it is assumed that letters are processed at a higher level than hashmarks. If the processing of parafoveal words is dependent on processing words in the center of the attentional focus, this change in distractor material should influence the semantic categorization as well as the assumed attentional selection process.

ERPs of 24 subjects were recorded from 32 electrode-sites while a categorization task was performed. An enhancement of the P100 for contra-lateral as compared to ipsi-lateral electrodes was found, indicating the successful direction of spatial attention towards the attended side (Luck et al., 1990). No effect of semantic categorization for words on the unattended side was found. Therefore, no autonomous automatic semantic categorization of words (Fuentes et al., 1994) but a dependency on processes occurring simultaneously in the focus of attention was shown.
Additionally, a previously observed negativity peaking at about 290 ms disappeared. Initially, this negativity was discussed in connection with a following positivity peaking around 390 ms as an attempt to process the simultaneously presented distractor in the focus of attention. The current results speak against this conclusion. The negativity could reflect a selection process similar to the N2b (Smid et al., 1999) that engages selection between and not within dimensions and shares resources with the processing of foveal and attended stimuli.

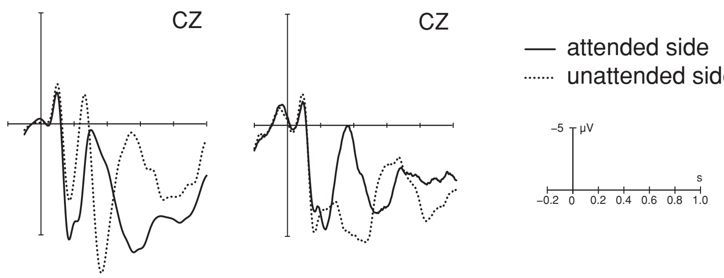

Figure 18. ERPs for one selected electrode (CZ) for stimuli on the attended (solid) and unattended (dashed) side of the screen using hashmark (left) and letter distractors (right).

2.1.16 Task demands influence the activation pattern of the inferior frontal cortex

Kotz, S.A.[1], *Friederici, A.D.*[1], *Cappa, S.F.*[2] & *von Cramon, D.Y.*[1]

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[2] *Facolta' di Psicologia, Universita' Vita Salute San Raffaele, Milan, Italy*

It has been a matter of debate whether activation of the left inferior frontal cortex correlates with task demands rather than semantic processing per se. While Thompson-Schill et al. (1995) have reported left inferior frontal activation with selectional demands or the choice among multiple alternatives in semantic tasks, Demb et al. (1995) have shown that this activation, associated with semantic encoding, is not related to task difficulty.

We recently reported single trial fMRI data (Kotz et al., 1999) exploring auditory priming via means of a lexical decision task (LDT). While lexical decision resulted in increased bilateral activation of the primary and secondary auditory cortices, semantic priming was restricted to bilateral activation of the superior temporal region. Furthermore, the hemodynamic response was modulated as a function of semantic information type in the right posterior temporal region. However, we did not find activation in the left inferior frontal cortex. We hypothesized that, if the activation in the left inferior frontal cortex varies as a function of task demand, the use of an explicit semantic task such as semantic categorization as compared to an implicit task such as the LDT should result in the activation of the left inferior frontal cortex.

The present data provide evidence that the activation of the left inferior frontal cortex varies as a function of task demand rather than as a function of semantic information since the activation occurred in the semantic categorization task but not the lexical decision task (see Fig. 19; Kotz et al., 2000).

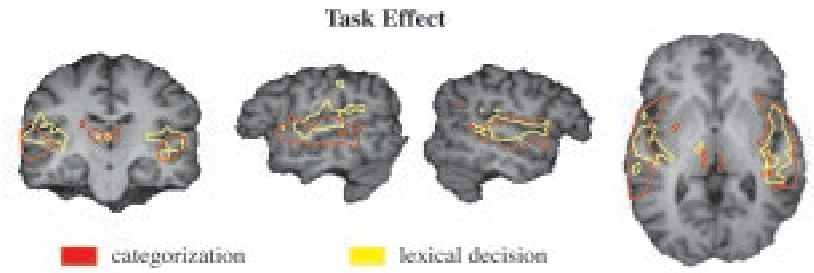

Figure 19. The presentation shows the extension of the activated areas during the semantic categorization task (red) and the lexical decision task (yellow) superimposed upon each other in a coronal, left and right sagittal and an axial view.

2.1.17 The influence of emotional prosody on word recognition: A behavioral and ERP-study

Schirmer, A. , Kotz, S.A. & Friederici, A.D.

The influence of semantic context on the processing of semantically related and unrelated words is known to be reflected in the N400 component. The present study examined the effect of prosodic context on word recognition. In a cross-modal priming paradigm, semantically neutral sentences with either a happy or a sad intonation were presented as auditory primes (e.g., *Yesterday she had her final exam.*). Each sentence was followed by a visually presented word or a non-word. Words were always semantically related to the sentence but only prosodically related half the time (e.g., *success/failure*). The subjects had to perform a lexical decision task on the target by pressing one of two buttons. Response latencies and ERPs (64 electrodes) were recorded.

Subjects responded faster to positive words as compared to negative words. Furthermore, positive words were responded to faster when the preceding prime also had a positive intonation. There was no such effect for negative words. ERPs showed a stronger negativity between 280 and 380 ms for the emotional-prosodic match condition, which became significant only for the negative target. Following this negativity there was a large positivity. In the time range between 500 and 800 ms, both mismatch conditions as well as the match condition for the negative target were more positive than the match condition for the positive target. However, between 800 and 1000 ms this positivity was smaller for both match conditions as compared to their equivalent mismatches.

The present results clearly demonstrate an effect of emotional-prosodic information on word processing. Dependent on the preceding prosodic context, a negative target ERP effect was found around 280 ms. Effects of prosodic context on the positive target appeared around 500 ms. In sum, ERPs and reaction time data suggest specific mechanisms for the processing of negative and positive information. The stronger positivity for the two mismatch conditions as opposed to the two match conditions in the time range between 800 and 1000 ms might reflect the reinterpretation of the preceding context which becomes necessary after the target word is lexically accessed.

2.1.18 Semantic representation and processing of German compounds: An RT study

Isel, F., Gunter, Th.C. & Friederici, A.D.

We addressed the question of whether the first constituents of German compounds (e.g., *Wein*/wine in *Weinberg*/wineyard) is the determinant segment for the access to the representation of compounds (Taft & Forster, 1976) or not (Marslen-Wilson, 1987). Four cross-modal (auditory-visual) priming experiments were run in order to test the activation level of left constituents. To avoid the confound between morphology and semantics, four categories of compound words were used: (1) fully transparent (the two constituents were semantically related with the compound: *Weinberg*), (2) fully opaque (no semantic relation between the morphemes and the compound: *Luftschloss*), (3) partially transparent regarding the left constituent (only the left constituent was semantically related to the compound: *Geldwaesche*), and (4) partially transparent regarding the right constituent (only the right constituent was semantically related to the compound: *Flohmarkt*). Experiment (1) with visual targets presented at the acoustic offset of the compounds provided evidence in favor of an access via the left constituent but only when the right constituent, the *head* of the compound, was transparent. When visual targets were presented at the acoustic offset of the left constituent [with coarticulation between the two constituents: Experiment (2); without coarticulation between the two constituents: Experiment (3)], no activation of these constituents was found. This finding indicates that the semantic representations of the left constituents

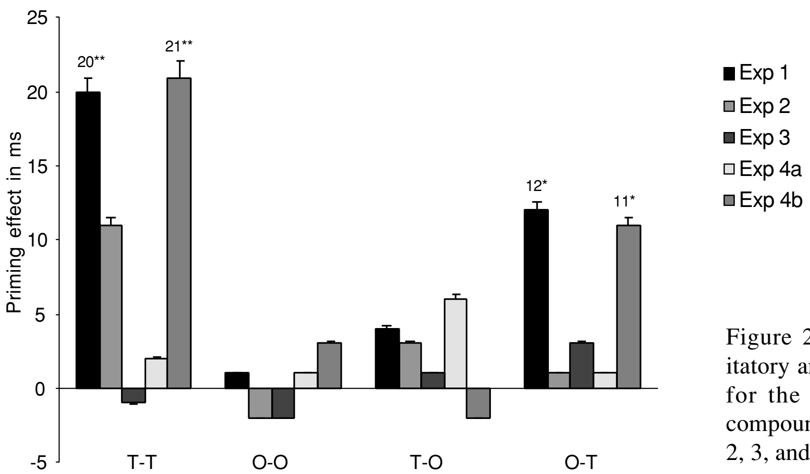

Figure 20. Amount of facilitatory and inhibitory priming for the left constituents of compounds in Experiments 1, 2, 3, and 4 (in msec).

are not activated during an early stage of processing. In Experiment (4a), where the right constituents were replaced by white noise, no activation of the left constituents was found at the acoustic offset of the truncated compounds, but, for the processing of the compounds [Experiment (4b)], results of Experiment (1) were replicated.

To account for the present findings we propose a model in which lexical access to compounds in German does not proceed from left-to-right but in a hierarchical fashion, with the transparency of the head being the crucial factor to determine the mode of lexical access.

2.1.19 Processing of ambiguous words in German compounds. Part I: Working memory constraints

Wagner, S. & Gunter, Th.C.

supported by DFG

For sentence processing, working memory capacity was found to influence the meaning selection of ambiguous words (cf. 2.1.21). In this series of four experiments, it was studied how the relevant meaning of an ambiguous word was selected within compound words and how this is related to working memory capacity. In a cross-modal priming paradigm, 60 two-part compounds were presented auditorily. Visual targets were either related to the dominant meaning of the ambiguous part of the compound (*Spiel*/game), unrelated (*Tisch*/table) or nonwords (*Malg*/malg). They were presented at four different positions within the speech signal of the compound: around the recognition point of the ambiguous first part of the compound in Experiment 1, at the immediate end of the ambiguous component in Experiment 2, at the end and 400 ms after the end of the compound in Experiment 3 and 4. A trial scheme using an example set of words is drafted in Figure 21.

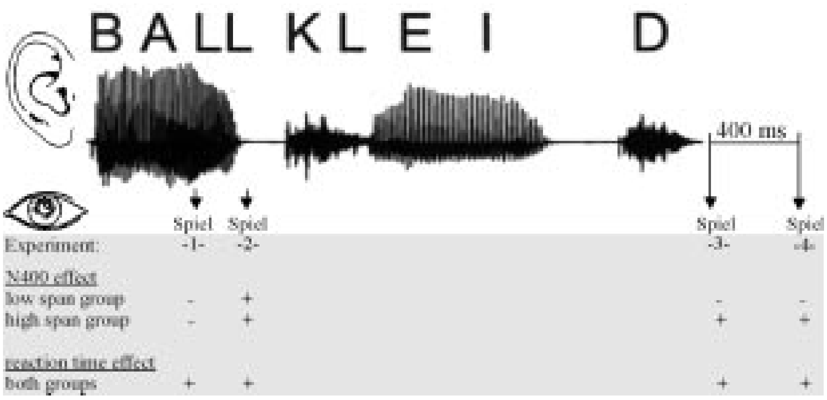

Figure 21.

Results for both high (4.5-6.0) and low (2.0-3.5) working memory groups were as listed in the lower part of Figure 21.
The differing findings for the behavioral and ERP level indicate that these measurements do not reflect identical processes. In Experiment 1, the dominant meaning of the ambiguous word was active in the semantic network but elicited no N400 effect. This

supports the assumption of Chwilla et al. (2000) that behavioral priming reflects spreading activation, whereas the N400 component is rather a marker of semantic integration processes. Moreover, our data indicate that spreading activation produces reactions faster than the processes the N400 component is based on.

As we define the resource which semantic integration relies on to be the verbal working memory, we used the N400 component as a tool to study the activation of a specific meaning in the working memory. Thus, for high span subjects, the N400 effects in Experiments 2-4 indicate that they had the dominant meaning of the ambiguous first constituent of the compound active in their working memory at all times. The results of the low span subjects show that the disambiguating second constituent had an influence on the meaning selection of the ambiguous first constituent before the end of the compound but it is not clear whether this influence was a simple decay, inhibitory in nature or a result of the interfering activation of the subordinate meaning (cf. 2.1.20).

2.1.20 Processing of ambiguous words in German compounds. Part II: The subordinate meaning becomes relevant

Wagner, S. & Gunter, Th.C.

supported by DFG

In an earlier Annual Report (Ann.Rep. 98), we reported that the dominant meaning of an ambiguous word which was the first part of a compound (e.g., *Ball* in *Ballkleid*/ball dress) was already active in working memory at the end of the ambiguous word. We found that a visually presented target which was related to the dominant meaning of the ambiguous word elicited a smaller N400 component compared to an unrelated target - when it was shown at the end of the ambiguous part of the auditorily presented compound. At the end of the compound, the activation of the dominant meaning was less strong. We report this effect of working memory constraints in 2.1.19.

In a second series of experiments, we used the same cross-modal priming paradigm with the same 60 German two-part compounds. As in the first series, visual targets were presented which were either related to one meaning of the ambiguous first part of the compound (*Tanz*/dance), unrelated (*Tisch*/table) or nonwords (*Malg*/malg). In contrast to the first series, where targets were always related to the dominant meaning of the ambiguous word, exclusively subordinately related targets were used in the present one.

Preliminary data analyses show no N400 effect when targets were presented at the immediate end of the first constituent. Thus, at the end of the ambiguous part, the subordinate meaning was not yet active in working memory. At the end of the compound, however, the subordinately related targets did elicit a smaller N400 component compared to unrelated ones.

The findings indicate that the activation of the two different meanings of an ambiguous word follow a different time course. Whereas the dominant meaning was already active in working memory at the end of the ambiguous word (cf. 2.1.19, N400 effect in Experiment 2), the subordinate meaning was activated later (no N400 effect in Experiment 1 but in Experiment 2, actual series).

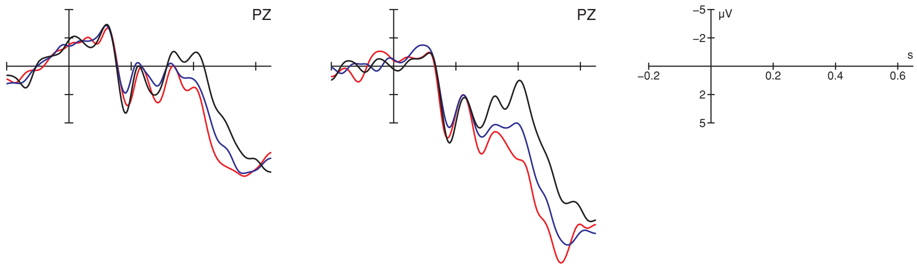

Figure 22. No significant N400-effect in the middle (a), but at the end (b) of the compound for subordinated targets (red line) compared to unrealated ones (blue). Nonwords in black.

Working memory and processing of semantically ambiguous words: Inhibition or activation? Part II: Relieving and loading WM

2.1.21

Gunter, Th.C., Wagner, S. & Friederici, A.D.

supported by DFG

In a previous study (see Ann.Rep. 98), which set out to explore the underlying mechanisms of WM, it was found that inhibitory processes play a very important role. High and low span subjects had to read German sentences containing an ambiguous word on the second position, followed by a nominal predisambiguation-cue at 5th and final disambiguation per verb at 6th position. The data at the cueing position showed that the subordinate meaning was inhibited to a larger extent for the high span subjects, whereas low span subjects had both meanings of the homograph in their WM. If there was a switch from the subordinate to the dominant meaning between 5th and 6th position in the sentence it was found that subjects with high WM-capacity suppressed the irrelevant meaning very quickly, whereas subjects with a smaller WM-capacity had difficulties inhibiting the dominant meaning. Thus, low-span subjects clearly showed problems with inhibiting irrelevant memory items (i.e., irrelevant meaning of a homonym). The question remained, however, as to whether the observed effects were due to an inefficiency in mastering inhibition and activation successfully or whether they were due to the timing of inhibition and activation. If it is due to timing, low span readers should do as well as high span readers if they are given more time to inhibit the irrelevant meaning.

In this follow-up experiment, we investigated if the inhibition difficulty of the low span readers can be diminished when they get more time between the cueing and the final disambiguation. We therefore included a proper name between the disambiguation-cue and the final disambiguation, thereby adding an extra 500 ms of processing time. (Example: *Der Ton wurde vom Sänger* ***Harry*** *gesungen, als ...* ; *The tone was by the singer Harry sung, when ...*; see also 2.1.22). The ERPs of 32 subjects were measured.

As in the earlier experiment, high span readers showed a bigger N400-component for the cue related to the subordinated meaning than low span readers who had a similar N400 for the cue related to the subordinate and dominant meaning. If there was a switch from the subordinate to the dominant meaning between 5th and 7th position (i.e., at the verb position) it was found that subjects with high WM-capacity suppressed the irrelevant meaning. In contrast to the original experiment where low span subjects had problems suppressing the dominant meaning, in the present experiment they were able to suppress the dominant meaning. Thus, the data support the hypothesis that, if low span subjects get more time, they can suppress the dominant meaning as do high span subjects under less time.

We return now to consider the finding that at the point of cueing the low span subjects appear to have both meanings present in their working memory. Would it be possible for low span subjects to continue using this memory demanding strategy (keep both meanings active) if the load on memory was increased by inserting an additional subclause between the ambiguous word and the disambiguation-cue? (Example: *Der Ball wurde, **als die Sonne schien, vom Spieler eröffnet**; The ball was, when the sun shined, by the player opened*). In this experiment too, 32 subjects were measured.

The data showed that indeed the low span participants were still holding both meanings, whereas the high spans only had the dominant meaning present as in the previous less memory demanding experiments. In addition, high span participants showed, in comparison to the other 2 experiments, a relatively large N400 effect, indicating that they were highly focused on the dominant meaning.

The situation involved in processing of homonyms is as follows: High span subjects read a homonym and activate (probably) both meanings. By the time they arrive at the disambiguation-cue they have inhibited the subordinate meaning. The longer the unbiased passage, the stronger the inhibition. If the disambiguation-cue indicates that a subordinate meaning is probably correct, they shift meanings very swiftly to the

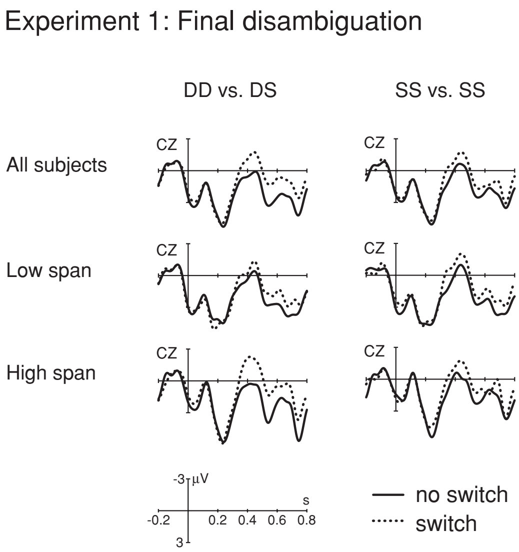

Figure 23. ERPs for the verb position of Experiment 1, where the final disambiguation was given. In the left panel, cueing was dominant, the final disambiguation was either dominant (DD, solid line) or subordinate (DS, dashed line). In the right panel, cueing was subordinate, the final disambiguation was either subordinate (SS; solid line) or dominant (SD, dashed line).

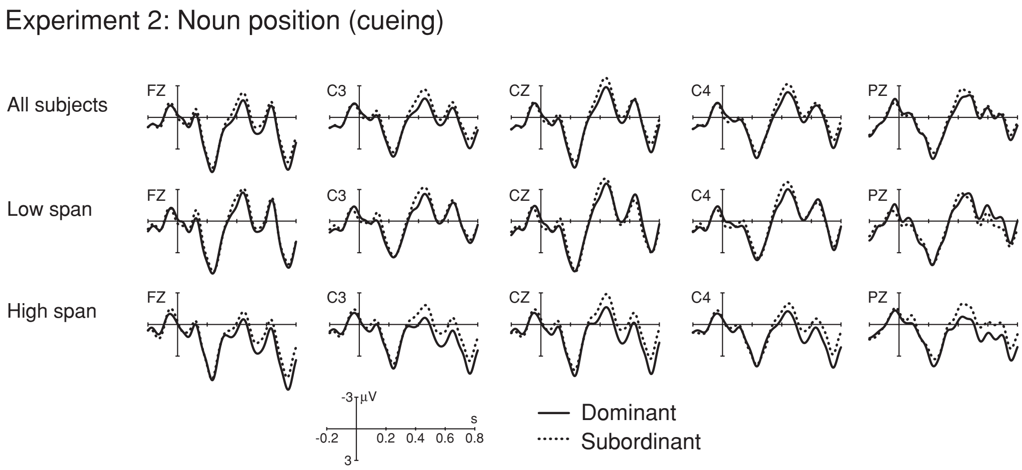

Figure 24. ERPs for the noun position of Experiment 2 where the disambiguation-cue was given. The solid line shows the ERPs elicited by the dominant disambiguation-cue whereas the dashed line shows the subordinate disambiguation-cue. The upper panel presents the data across all participants, the middle panel of the 12 low span participants, and the lower panel of the 12 high span participants.

subordinate meaning, but only for a short duration. If the sentence continues and does not give any additional confirmation that their switch towards the subordinate meaning was correct, they switch back to the dominant meaning and run then into trouble when the sentence turns out to require a subordinate meaning. Low span subjects read the homonym and activate both meanings. When they arrive at the disambiguation-cue they have both meanings present in WM. This is even the case when WM is loaded by an extension to the neutral part of the sentence. If the disambiguation-cue indicates that they probably have to switch meanings, they can do so when sufficient time is given; however, if a fast response is needed they have problems inhibiting the dominant meaning.

2.1.22 Working memory and processing of semantically ambiguous words: Inhibition or activation? Part III: Aging

Gunter, Th.C., Kotz, S.A., Wagner, S. & Friederici, A.D.

In our earlier experiments (see part II), it was shown that WM and inhibitory processes are closely related. In order to establish this relationship more solidly an aging study was carried out, because numerous studies indicate that loss of inhibitory control is a hallmark of aging, and that WM-capacity has been shown to decline gradually through adulthood (for a recent study on aging, WM, inhibition and reading skills see Chiappe et al., 2000).

Thirty elderly subjects (mean age: 56.8 years; range: 41-69) were presented with the original materials of the experiment discussed already in 1998 (see Ann.Rep. 98).
ambiguous word: ***Ton*** (either *tone* or *clay*)

(1) *Der Ton wurde vom Sänger gesungen, als ...*
(The tone was by the singer sung, when ..)
Dominant disambiguation-cue, **D**ominant disambiguation (**DD**)

B *Der Ton wurde vom Töpfer gebrannt, weil ...*
(The clay was by the potter baked, because...)
Subordinate disambiguation-cue, **S**ubordinate disambiguation (**SS**)

C *Der Ton wurde vom Sänger gebrannt, obwohl ...*
(The clay was by the singer baked, although ...)
Dominant disambiguation-cue, **S**ubordinate disambiguation (**DS**)

D *Der Ton wurde vom Töpfer gesungen, während ...*
(The tone was by the potter sung, while ...)
Subordinate disambiguation-cue, **D**ominant disambiguation (**SD**)

At the noun position, no differences were found for the cue related to the dominant and the subordinate meaning. This pattern of results looks like that of low span subjects in the original experiment. At the verb position where in half of the cases a meaning switch had to be performed, it was found that DD vs. DS showed a large N400 effect, whereas in SS vs. SD a minor difference was present. This result can be interpreted that the older subjects had problems inhibiting the dominant meaning of the homonym. Thus, both the cue and the verb position show results indicating that older subjects react like low span subjects. Since aging has been associated with loss of inhibitory control, these data strengthen the hypothesis of inhibitory processes as an important underlying mechanism for the processing of semantically ambiguous words in WM.

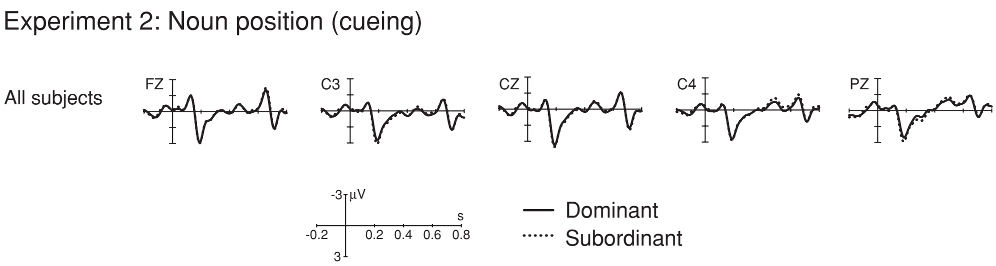

Figure 25. ERPs for the noun position where the disambiguation-cue was given. The solid line shows the ERPs elicited by the dominant disambiguation-cue, whereas the dashed line shows the subordinate disambiguation-cue.

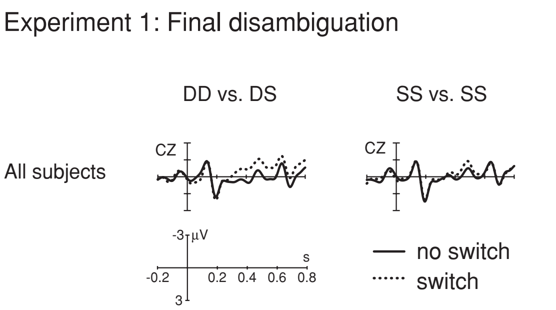

Figure 26. ERPs for the verb position where the final disambiguation was given. In the left panel, cueing was dominant, the final disambiguation was either dominant (DD, solid line) or subordinate (DS, dashed line). In the right panel, cueing was subordinate, the final disambiguation was either subordinate (SS, solid line) or dominant (SD, dashed line).

Unraveling the N400: The hemispheric interplay during semantic processing

2.1.23

Friederici, A.D., Wang, Y. & Maess, B.

The aim of this study was to investigate the temporal structure of the N400 and its underlying sources. The N400 effect is usually present between 350-500 ms and has a centro-parietal distribution slightly lateralized to the right. In the present experiment sentences which were either correct or semantically incorrect due to selectional restriction violations were presented auditorily to six subjects (3 female). Subjects were required to judge whether the sentence heard was a plausible German sentence. Event-related magnetic fields were registered by 148 channels. A new source localization procedure which averaged the individual trials in the source space prior to the grand average (see section 2.11) was applied.

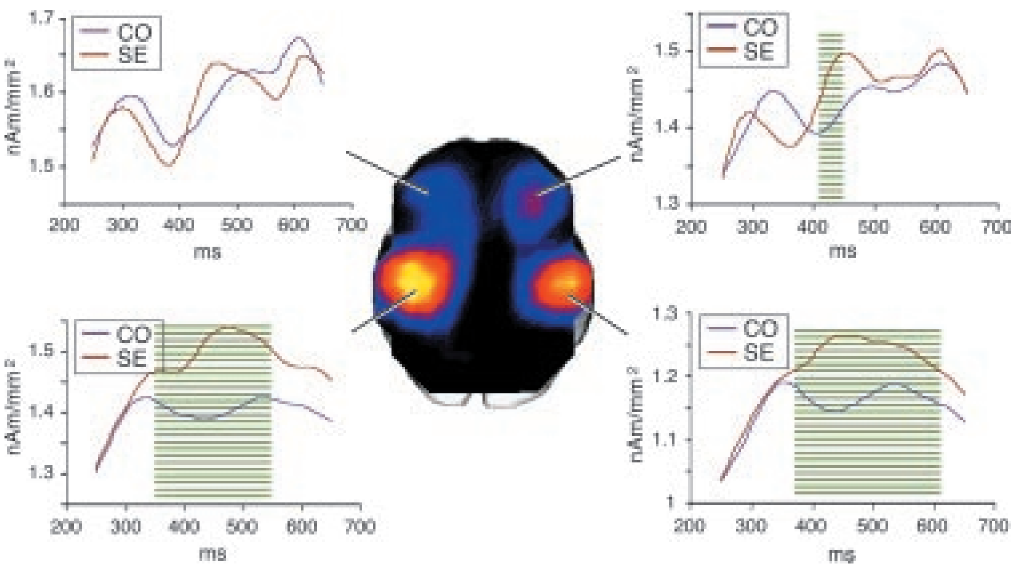

Figure 27. The marked time window are when the difference is significant.

Localization of the N100m was based on the sentence onset. The grand average demonstrates a N100m peaking at 113 ms which was of the same amplitude in the left and the right hemisphere. As expected, N100m activation was located in the temporal lobe bilaterally. The activation structure underlying the N400m clearly involved temporal and frontal foci (see Fig. 27). Interestingly, the time course of the N400m effect (difference between critical word in correct and semantically incorrect sentences) differed in the left and the right hemisphere. Analysis for significant difference between the correct and the incorrect condition (shaded green in Fig. 27) computed in 20 ms steps revealed a significant difference in the temporal region between 350-550 ms in the left hemisphere, and between 370-610 ms in the right hemisphere. Thus, the N400m effect is present earlier in the left than in the right hemisphere and it has a shorter duration in the left than in the right hemisphere. This might suggest that lexical aspects of processing located in the left hemisphere (i.e., in the medial temporal gyrus as shown by a number of fMRI studies) precede aspects of semantic association, possibly activating the association cortices bilaterally. In addition to these temporal activations, a significant difference between correct and semantically incorrect sentences was present in the right frontal cortex between 410-450 ms. This activation can be related to aspects of episodic memory demonstrated to involve this area in recent fMRI studies. Whether this frontal activity is due to the task demands or implicit to semantic processing as such can not be decided on the data from the present experiment.

We concluded that the scalp recorded N400 component with its centro-parietal right lateralized distribution appears to be based on bilateral temporal and possibly frontal sources. The right lateralization, for which a number of different explanations are proposed in the literature, can be explained by the present data as being due to a stronger involvement of the right (than left) frontal cortex.

2.1.24 Exploring the activation of semantic and phonological codes during speech production with event-related brain potentials

Jescheniak, J.D.[1,2], Schriefers, H.[3], Garrett, M.F.[4] & Friederici, A.D.[1]

[1] Max Planck Institute of Cognitive Neuroscience,
[2] Center of Cognitive Science, University of Leipzig,
[3] Nijmegen Institute of Cognition and Information, Nijmegen University, The Netherlands,
[4] University of Arizona, Tucson, USA

supported by DFG

We developed a new ERP-technique for studying the activation of semantic and phonological codes in speech production. It combines a delayed picture naming task with a priming procedure. While participants prepared the production of a depicted object's name, they heard an auditory target word. If the prepared picture name and the target word were semantically related (same semantic category) or phonologically related (shared initial consonant-vowel sequence), the ERP waveform to the target word had a less negative tendency when compared to an unrelated control (selected electrode sites are depicted in Fig. 28, left). Both effects were widely distributed. The semantic effect started about 400 ms after target onset, while the phonological effect was observed as

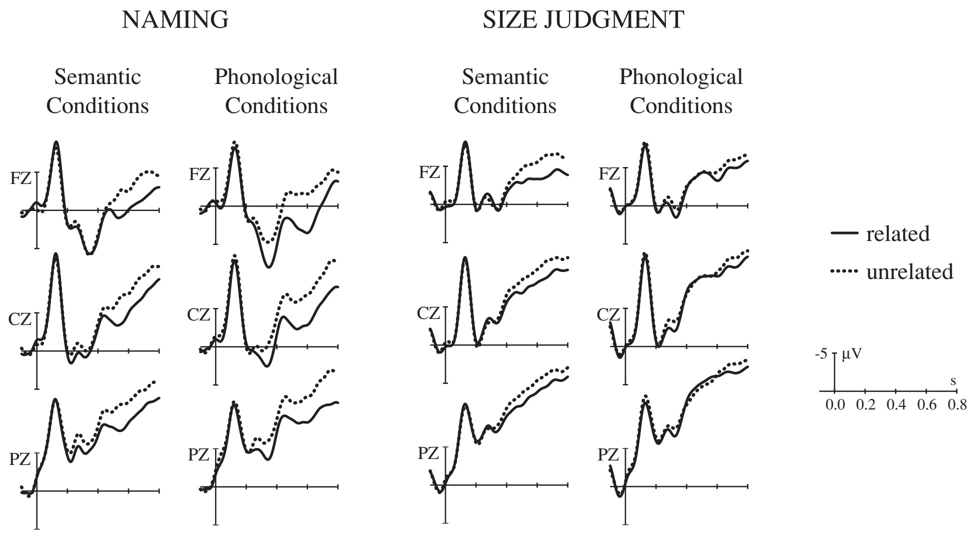

Figure 28.

early as 250 ms after target onset. By contrast, if participants performed a non-linguistic task on the depicted object (natural-size judgment), the semantic effect was still obtained while the phonological effect disappeared completely (Fig. 28, right). This suggests that the former effect indexes semantic activation involved in object processing while the latter effect indexes word-form activation specific to lexical processing. Hence, the paradigm provides a novel tool for exploring details of the lexicalization procedure during speech production which are not easily addressed with existing neurophysiological paradigms.

Semantic category interference in overt picture naming

2.1.25

Maess, B.[1], Friederici, A.D.[1], Damian, M.[2], Meyer, A.S.[3] & Levelt, W.J.M.[3]

[1] Max Planck Institute of Cognitive Neuroscience,
[2] University of Bristol, UK,
[3] Max Planck Institute for Psycholinguistics, Nijmegen, The Netherlands

The study investigated the neuronal basis of the retrieval of word forms from the mental lexicon. The semantic category interference effect was used to locate lexical retrieval processes in time and space. This effect reflects the finding that for overt naming volunteers are slower when naming pictures out of a sequence of items from the same semantic category than from different categories. Participants named pictures blockwise, either in the context of same- or mixed-category items while the brain response was registered using magnetoencephalography (MEG). Fifteen out of twenty participants showed longer response latencies in the same-category compared to the mixed-category condition. Event-related MEG signals for the participants demonstrating the interference effect were submitted to a current density (CD) analysis. A principle component analysis (PCA) was applied to decompose the grand average CD distribution into 9 spatial subcomponents (factors). The spatial Factor 6 (displayed in Fig. 29) indicating left temporal activity revealed significantly different activation for the same-category compared to the mixed-category condition in the time window between 150 and 225 ms post picture onset. These findings indicate a major involvement of the left temporal cortex in the semantic interference effect. As this effect has been shown to take place at the level of lexical selection, the data suggest that the left temporal cortex supports processes of lexical retrieval during production.

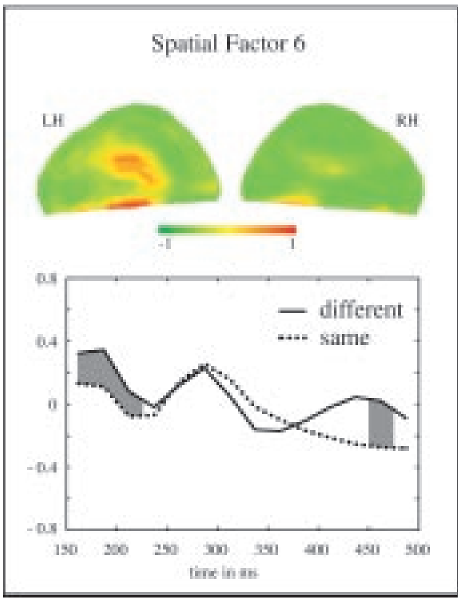

Figure 29. Spatial distribution and time course of factor 6 as revealed by spatial PCA performed for all subjects showing a significant behavioral effect.

The initial work of our neurocognition of music-group (see Ann.Rep. 98, 99) was more intensified during the last year. Music has turned out to be a useful tool to study both auditory and visual information processing in the brain. Within the auditory domain, music can be employed to study sensory memory processes using rather simple tones or tone-patterns (2.2.1), as well as the perception of complex major-minor tonal music (2.2.1, 2.2.5). This approach allows us to differentiate systematically different stages of auditory information processing. Within the visual domain, score-reading, i.e. reading musical notes, can serve the investigation of associative visual information processing (2.2.6, 2.2.7). The results of our investigations in both the auditory and the visual domain prepare us for the investigation of visuo-acoustic interfaces in the brain, a new future research topic.

In the last year, we succeeded in conducting an fMRI-study with musical stimuli (2.2.2). The results revealed that music is processed by a cortical network known to support language processing. This provides evidence for our hypotheses (based on previous EEG- and MEG-studies) about the relationship of music and language processing. Continuing this research will provide more information about how syntactic, semantic, and prosodic information is linked in the brain for the purpose of understanding language.

Another research focus of our group is the description of music, i.e. the investigation of models of music theory by means of cognitive neuroscience. Besides the investigation of "musical syntax" (2.2.1, 2.2.2, 2.2.5, see also previous Annual Reports), we intensified our research on musical meaning (2.2.3, 2.2.4). Interestingly, the latter two studies support the notion that meaning in music is, like the processing of semantics in language, reflected in N400-like ERP-components that are maximal around 400-550 ms at fronto-central leads. Moreover, study (2.2.3) provides contributions to theories of phrasing, whereas study (2.2.4) contributes to the theory of harmony.

2.2.1 Differences between ERAN and MMN: An EEG-study

Koelsch, S. & Gunter, Th.C.

Previous experiments (e.g., Koelsch et al., 2000) revealed both similarities and differences between the early right anterior negativity (ERAN) and the mismatch negativity (MMN). The present experiment is aimed at investigating the two ERP-components under comparable experimental conditions.

Three blocks were performed. Stimulation of the second block was similar to the previous experiments (cf. Ann.Rep. 99, p. 36/37), i.e. chord-sequences consisting of five chords each were presented to the subjects. One sequence directly succeeded the other, infrequently containing a Neapolitan Sixth chord at the third (p=0.2) or fifth (p=0.2) position of the sequence. Neapolitan chords were expected to elicit an ERAN. In the first block, tone-pairs raising in pitch were presented as standard stimuli with the same time-course as in the second block (for a similar paradigm, see Paavilainen et al., 1998). Tone-pairs with descending pitch were employed as deviant stimuli. Deviants occurred, as the Neapolitans in the second block, only at the third and fifth position (also with a probability of 0.2 each). The number of possible tone-pairs was matched with the number of chords that occurred at each position in the second block. The deviant pairs were expected to elicit an abstract-feature-MMN. In the third block, only one frequency was employed for a single standard-tone (presented with the same time-course as stimuli of blocks 1 and 2). The deviant stimulus was a frequency-deviant (10% difference), occurring, as in the previous blocks, at the third and fifth position (each with p=0.2). The deviants were expected to elicit a frequency-MMN. In all three blocks, participants (all "non-musicians") were instructed to ignore the stimuli and play a Video-Game.

Whereas the ERAN was distinctly larger in amplitude when elicited at the fifth position (reflecting that the processing of chords depended on the degree of musical context build-up), both abstract-feature-MMN and frequency-MMN did not differ in amplitude between third and fifth position (Fig. 1). Moreover, the latencies of the MMNs were clearly shorter compared to the latency of the ERAN, though the amplitude of the ERAN was larger than both MMNs. Finally, the ERAN, but not the abstract-feature-MMN, showed a clear polarity inversal at mastoidal sites when referenced to the nose-tip.

Results demonstrate that the ERAN differs with respect to scalp-distribution, time-amplitude relation, and functional significance from both the abstract-feature- and frequency-MMN.

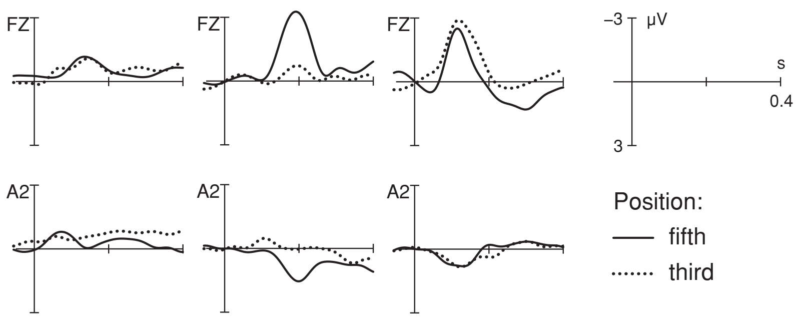

Figure 1. Grand-average ERPs (difference-waves: standards subtracted from deviants, from a frontal [Fz] electrode and at right mastoid [A2]). Effects were elicited by deviant tone-pairs (left), Neapolitan chords (middle), and deviant tones (right). Solid line indicates effects elicited at the fifth position of the sequences (dotted line: third position).

Bach speaks: An fMRI-study

2.2.2

Koelsch, S.,
Gunter, Th.C.,
von Cramon, D.Y.,
Zysset, S.,
Lohmann, G. &
Friederici, A.D.

Hemodynamic responses were measured while participants (all "non-musicians") listened to chord-sequences (chord-sequences were similar to the sequences employed in Koelsch et al., 2000). Infrequently, chord-sequences contained unexpected musical events, namely (a) a dissonant tone-cluster, (b) chords played on deviant instruments instead of on a piano, or (c) chords modulating to a different tonal key.
The processing of unexpected musical events activated a cortical network comprising the area of both Broca and Wernicke, the superior temporal sulcus, Heschl's gyrus, both planum polare and planum temporale, as well as the anterior superior insular cortices (Fig. 2). All these brain structures are known to perform important functions for the understanding of language. Up to now, the neuronal network comprising these structures has been thought to be domain-specific for auditory language processing. To what extent this network might also be activated by the processing of non-linguistic information has remained unknown.
The present fMRI-data reveal that the human brain employs this neuronal network also for the processing of musical information (though with a right-hemispheric predominance) indicating that the cortical network known to support auditory language processing is less domain-specific than previously believed.

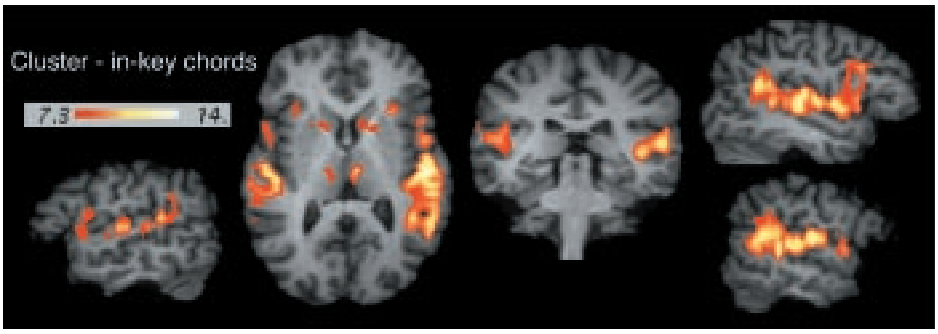

Figure 2. Statistical z-maps of clusters-sequences contrasted to sequences consisting of in-key chords only and mapped onto an individual brain. The panel shows views from left sagittal (left, Talairach coordinate x=-52), axial (middle-left, Talairach coordinate z=18), coronal (middle-right, Talairach coordinate y=-30), right medio-sagittal (top right, Talairach coordinate x=43), and right latero-sagittal (bottom right, Talairach coordinate x=51).

Music - structure and meaning and their ERP correlates

2.2.3

Schmidt, B.-H. &
Kotz, S.A.

When familiar melodies are structurally violated with an incongruous singletone, a late positive ERP component is elicited in comparison to a congruous singletone (Besson, 1978, 1995). An open question that remains is whether this type of violation can induce an ERP component in response to violations at the meaning level in music perception. Hence, we compared 80 familiar melodies from the classical instrumental repertoire with 80 familiar melodies that were cross-spliced with the first 80 familiar sequences and with 80 unfamiliar sequences by composing the counterpoints to the cross-spliced 80 familiar violations. The best twenty-five items in each condition were analyzed separately because they included no breach of rhythm, measure or harmonies. Two points were investigated. First, we looked at the first wrong tone in the initial familiar melody by comparing congruous and incongruous singletons. Secondly, if one assumes that a phrase is a meaningful unit in music (Bierwisch, 1979), it is expected that an integration problem could occur for the first phrase of the two cross-spliced violation conditions. Thus, we expected a different ERP response than the late positivity.

Figure 3. To exemplify the violation: (a) Grieg, Edward, Morning from *Peer Gynt* - normal condition; (b) Morning from *Peer Gynt* plus Bach, Joh. Seb., Brandenburg Concerto No. 1, Third Movement Theme - familiar violation; (c) Morning from *Peer Gynt* plus the counterpoint of Brandenburg Concerto No. 1, Third Movement Theme - unfamiliar violation.

For the first comparison we got a significant late positive ERP component. This positivity confirms a structural violation to the singletone in comparison to the forth-going familiar melody, because the incongruous singletone cannot be integrated in the developing hierarchical musical structure (see Besson, 1995; Verleger, 1990).
The analysis of the second position based on the twenty-five best created items showed a pronounced negativity for the familiar vs. unfamiliar violation at frontal electrode-sites with a latency of 376 to 500 ms.
We propose that at the end of the first phrase, familiarity of a musical phrase is verified. Therefore, the cross-spliced familiar sequence is not compatible with the context built by the initial familiar melody. For the unfamiliar violation condition the integration process is ongoing. Thus, the elicited negativity for this condition is smaller. Hence, we see an example of integration problem on the meaning level reflected by the negative ERP component for familiar sequences.

2.2.4 Processing of chord-inversions: An ERP-study

Koelsch, S.[1] & Overath, T.[2]

[1] Max Planck Institute of Cognitive Neuroscience,
[2] Humboldt University of Berlin

The aim of the present study was to investigate the processing of chord-inversions, i.e. of chords with the root-tone ("root position"), the third ("sixth chord"), or the fifth ("six-four chord") as base-note. Chord-sequences were presented, each sequence consisting of five in-key chords. With equal probability, chords at the third position were chords in root position, sixth-chords and six-four chords. All chords at other positions within the sequences were presented in root position. Two blocks were employed, in the first block chord-inversions were task-irrelevant, in the second block, participants (all "non-musicians") were asked to discriminate the different chord-inversions.

Behaviorally, participants could not differentiate between the inversions. At centro-parietal electrode-sites, sixth- and six-four-chords elicited a negativity which was maximal around 270 ms (N270, Fig. 4). Moreover, these chords elicited an N400 which was centrally maximal.

Due to the different interval-structure of inverted chords, the N270 might reflect a structural mismatch; taking the musical interval as analogous to the linguistic phoneme, this mismatch is reminiscent of the Phonological Mismatch Negativity. The N400 might reflect processes of integration, since the extraction of the function of inverted chords was more difficult compared to chords presented in root position. Since inverted chords elicited characteristic ERP-effects, results also indicate a surprising sensitivity of "non-musicians" to musical information.

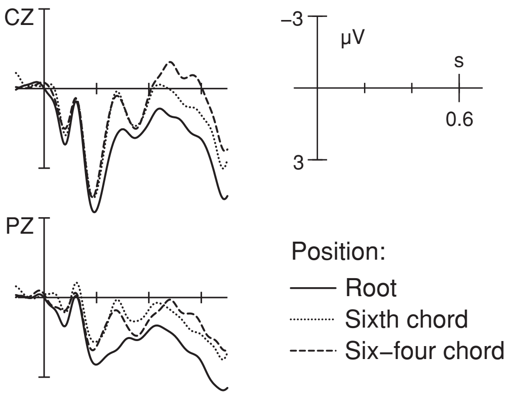

Figure 4. Grand average ERPs elicited by chords at the third position of the sequences (from a central (Cz) and parietal (Pz) electrode). Solid line indicates effects elicited by chords in root position, dotted line: Sixth chords, dashed line: Six-four chords.

2.2.5 Beethoven electrifies: An ERP-study

Koelsch, S.[1], Mulder, J.[2] & Gunter, Th.C.[1]

[1] Max Planck Institute of Cognitive Neuroscience,
[2] University of Groningen, The Netherlands

ERP-studies reported in the literature concerned with the investigation of multi-part music-processing employed rather unnatural, or uncommon musical stimuli. Stimuli were, e.g. played by a computer with all notes having the same loudness, the same attack and decay, and rhythmically quantilized notes, i.e., stimuli had no agogics and dynamics. In the study from Koelsch et al. (2000), each sequence always consisted of five chords; in the study from Patel et al. (1998), unusual part-writing was employed. The aim of the present study was to investigate whether LPC, ERAN, RATN, and N5 are elicited even while listening to "real", expressive music.
Therefore, excerpts (commercial CD-recordings) from piano-sonatas of Mozart, Haydn, Beethoven, and Schubert were employed as experimental stimuli. Brain responses of expected (in-key) chords were compared to chords that were harmonically less related to the preceding musical context (and therefore perceived as less expected than the in-key chords).
Different chord-types elicited ERAN, RATN, LPC and N5, indicating that prior experiments reporting these components actually investigate music-perception.

Moreover, results provide an additional difference between ERAN and MMN: in the present experiment, an ERAN was elicited even though unexpected chords were not preceded by repeating "standard stimuli" (which are necessary to elicit the MMN).

2.2.6 Lets face the music: Reading the score elicits different ERPs as hearing the music

Gunter, Th.C. & Schmidt, B.-H.

In language processing it is found that ERP-components like the N400, (E)LAN and P600 can be elicited in visually and in auditory presented materials. The main question of this experiment was whether or not reading diatonic violations in musical score elicits similar ERP-components (i.e., a P600-like ERP wave, cf Besson & Faita, 1995) as hearing such violations in an auditory played piece of music. We used the same musical pieces as Besson & Faita (1995), but presented the violations at a different position.

In the behavioral version of the experiment 8 musicians were presented with 120 scores of familiar musical pieces, in which, in half of them, a diatonic violation was incorporated somewhere in the middle of the piece, but in the beginning of the measure. The score was presented in a selfpaced manner in such a way that every time a button was pressed a new measure was presented in the middle of the screen. After the whole score was presented, the participants had to indicate whether or not there was a violation in the score and if they knew the musical piece the score was coming from. The RT-data for the correctly rated scores revealed that at the measure where the violation was presented the processing of that measure (as reflected in selfpaced reading time) was significantly delayed with approximately 500 ms. No other significant differences in reading times were found. It therefore seems that reading a diatonic violation costs additional effort.

In the ERP-version of the experiment the same musical phrases were presented to 20 musicians in a 'RSVP' like manner (3000 ms per measure, 200 ms 'blank' screen). We expected, on the basis of the Besson & Faita 1995 study, that the diatonic violation would elicit a late positive component in our musicians. The preliminary analysis of the ERP-data was carried out on 11 participants whose performance on the post score task was above 60% correct (mean 74%). The ERP-data of the measure where a violation was presented showed not a positivity but a negativity instead. The negativity started around 600 ms and was present during the whole trial (up to 3000 ms). In the next trial the negativity disappeared. These data indicate that the processing of auditorily and visually presented music differs more from each other than is the case in the linguistic domain.

2.2.7 Do musicians hear what they read?

Gunter, Th.C. & Koelsch, S.

In this experiment we tried to explore the plausibility of the commonly shared experience of musicians that they hear the music when they read the score. The idea was to use the mismatch negativity as marker for auditory processing. If musicians have an internal auditory 'perception' of visually presented notes, they should elicit a MMN-like ERP-wave when confronted with a deviant stimulus. Musicians were presented with three different visually presented notes. The standard note was a G, the frequency deviant note was an H and the visually deviant note was a G.

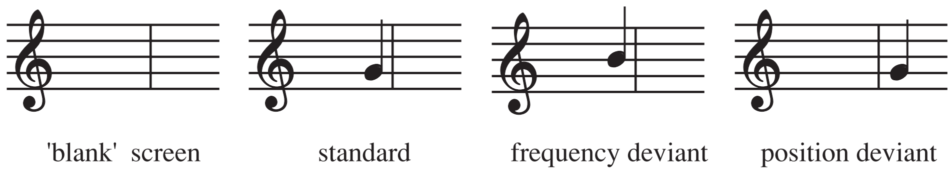

Figure 5.

The presentation was such that, embedded in standard stimuli, every third note was spatially deviant and every sixth note was frequency deviant. The three blocks, containing 324 stimuli each, were presented to 20 musicians. In the first block, the participants were instructed to look at the screen and listen to a piece of piano music (nocturnes from Chopin played by Rubinstein). In the next block the notes were presented simultaneously with the auditory version of the notes. In the last block, the presentation of the first few dummy-trials was, as in the second block, a combination of visual and auditory information. After approximately 10 trials the auditive signal had been faded away. The next stimuli were visually presented notes and subjects were asked to 'hear'/ 'imagine' the associated tones.

The preliminary analysis of the ERPs shows that, as expected, the frequency deviation in the second block elicited a large MMN component which must be due to the auditive part of the stimulation. The frequency deviation in the third block, where participants were asked to imagine the tones, did not reveal any MMN-like components. This findings suggest that even if musicians have the experience of hearing the notes, they do this in an abstract way and the auditory cortex is probably not involved in this process. If one compares the difference between standard and frequency deviant in block 1 and in block 3, the onset of this difference is later in block 1 than in block 3. The spatial deviant did not show such an effect. Thus, if the participants could not imagine the notes because of the interference by the played piano piece in block 1, the frequency related difference was delayed in time. In this respect it is interesting to note that the frequency related difference had a right occipito-parietal distribution which is in accordance with the fMRI-study of Nakada et al. (1998), where the right transverse occipital sulcus was shown to be involved in music reading.

In the year 2000, the Independent Research Group on 'Neurocognition of Prosody' became active in several areas on prosodic processing using various methods and approaches. Our research focused on different prosodic domains such as {sub-} syllabic elements, words, phrases and contextually embedded utterances. We also established tools for acoustic data analysis and speech signal manipulations, such as filters and speech resynthesis techniques.

Behavioral as well as electroencephalographic data (EEG) were assessed to explore the processing of these aspects of prosodic information. We investigated the influence of context, i.e. of information structure on the prosodic processing of accent position (2.3.1), and furthermore on that of intonational phrase boundaries (2.3.3). Moreover, we analyzed prosodic realizations of several speakers in order to identify intraindividual differences in speech production (2.3.4).

To investigate the processing of purely prosodic information, syntactic and semantic cues have been removed from the speech signal. For this purpose, a special filtering procedure, i.e. delexicalization was evaluated in a behavioral study (2.3.5). We furthermore investigated the role of the pitch parameter being crucial in German by means of pitch flattening adaptation in the speech signals (2.3.2).

In accordance to the examination of intonation contours in German sentences and nouns, we examine the microstructure of stress parameters in polysyllabic speech-like items with EEG measurements. The analysis of the acoustic parameters and the electrophysiological correlates of metrical patterns allow explicit acoustic manipulations and, hence, the investigation of speech relevant factors at lower levels of prosodic domains such as at the syllabic (2.3.6) and word (2.3.7) level.

Recently voice selective areas in the human brain were localized using fMRI and PET, i.e. methods of a high spatial but coarse temporal resolution (Belin et al., 2000; Scott et al., 2000). In behavioral and neurophysiological experiments using magnetoencephalography (MEG), we investigated how the perceptual system reacts to natural and manipulated voices. Particularly the time course and the interaction of this extralinguistic information and the lexico-semantic content were of interest (2.3.8, 2.3.9).
Besides the temporal characteristics of prosodic processing the research also focused on the identification of brain regions subserving in prosodic aspects of speech comprehension by means of functional magnetic resonance imaging (fMRI). In particular, the fMRI data at hand indicate that different cortical areas are involved in

the processing of unique prosodic parameters (accentuation, phrasing; c.f. 2.3.10). In a further study, we demonstrated that linguistic and affective aspects of prosody generally share the same cortical regions but specifically with some remarkable differences to be mentioned (2.3.11, 2.3.12).

2.3.1 ERP effects of sentence accents and violation of information structure

Hruska, C., Steinhauer, K., Friederici, A.D. & Alter, K.

supported by DFG

This auditory study aims at identifying ERP correlates both for the processing of sentence accents as such and their compatibility relative to a context question (information structure). The spoken German sentence material is based on that introduced by Steinhauer and co-workers (1999) but varies the positions of accents. All sentences were preceded by context questions establishing a narrow focus on one sentence constituent in such a manner that only the corresponding accentuation pattern provided an appropriate answer. Two types of context questions were presented, one with focus on the second noun and one focusing on the second verb phrase in the answer sentences. In spoken language new information is triggered by prosodic parameters. Acoustic analyses of the 48 speech signals in each of the four conditions confirms that the respective prosodic patterns are reflections of the information structure. Note that incompatible answers violate the required information structure in two ways: (1) they do not provide the required accent on the element in focus and (2) they contain an inappropriate accent. Twenty-one subjects participated in this experiment and judged the prosodic compatibility of questions and answers.

ERP data suggest that the same auditory input is processed differently depending on the dialogue context. Frontal negativities in the ERP at corresponding focus positions might reflect expectancies concerning the accent, possibly along with a subvocal activation of the prosodic pattern. If the answer carries the wrong accentuation pattern, missing accents at the element in focus rather than superfluous accents on other elements seem to trigger mismatch detection (see Fig. 1). The system appears to wait for an appropriately accentuated element as long as possible during the utterance but stops waiting once the mismatch is obvious.

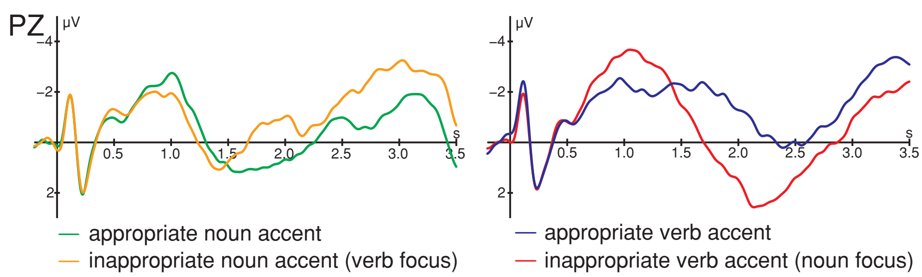

Figure 1. Same acoustic input (left panel shows noun accentuated sentences and right panel verb accentuated sentences) leads to different processing depending on question focus.

ERP effects due to violated information structure and the role of fundamental frequency

2.3.2

Hruska, C., Steinhauer, K., Friederici, A.D. & Alter, K.

supported by DFG

The present study employed ERPs to investigate how the brain identifies accent positions in information structure. Here we focused on the processing of wrong accent patterns. German being an intonational language, we expected that the F0- contour (fundamental frequency; speech melody as perceptual parameter of sentence prosody) is the most important parameter to identify the sentence accent position. We propose that the participants rely more on the speech melody than on any other parameter of prosody such as duration, pauses or intensity.
We designed auditory experiments based on the previous experimental material (see Ann.Rep. 99) to investigate the processing of prosodic information in dialogues. Again, Wh-questions requiring narrowly focused constituents in the answers were presented in each experiment. Answers were given in four conditions: correct or incorrect prosodic patterns either with normal pitch information or a flattened pitch contour. Acoustic analyses of the normal conditions confirm that prosodic patterns reflect the information structure. No more pitch variation was shown in the flattened condition while other prosodic parameters remained unchanged.
The participants had to judge whether the answer had the appropriate intonation according to the question or not. Behavioral data suggest that the participants switched their strategy for identifying wrong prosodic information from the most important prosodic parameter (F0) to durational parameters resulting in a less successful performance. The ERP data show an increased frontal negativity for the pitch-flattened sentences in contrast to normal sentences (see Fig. 2). We presume this increased negativity correlates with a reinforced effort for identifying accent positions.

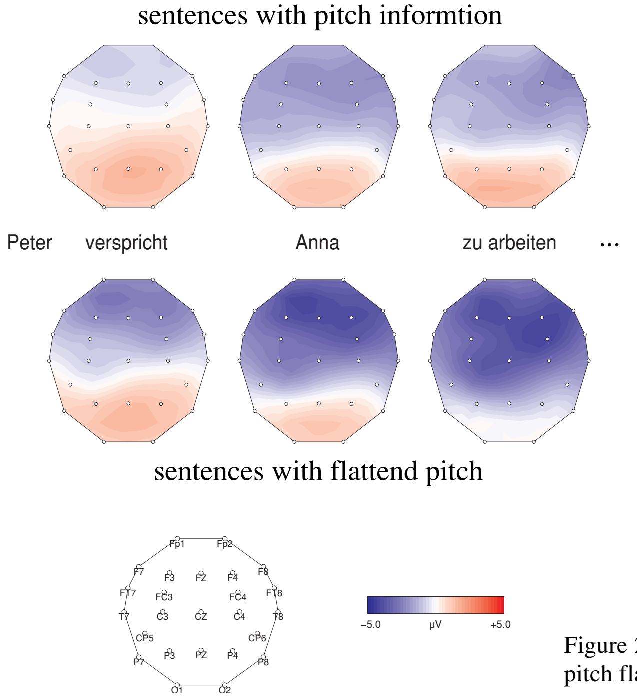

Figure 2. Increased frontal negativity for pitch flattened sentences.

2.3.3 Missing CPS due to intonational phrase boundaries in dialogues

Hruska, C., Steinhauer, K., Friederici, A.D. & Alter, K.

supported by DFG

Former studies examined the processing of sentences presented in isolation with prosodic default patterns. In this study we were interested in the influence of context on the processing of prosodic cues for different syntactic structures. Thereby, questions establishing a narrow focus on one sentence constituent preceded all sentences such that only the corresponding accentuation pattern provided an appropriate answer. Acoustic analyses of speech data confirm that prosodic patterns reflect the information structure established by context questions. The prosodic realization of different syntactic structures (see Steinhauer et al., 1999) thereby depends on the content of information given by the questions. So the questions establishing focus on NP2 provided more information than VP2-questions resulting in an unclearly marked IPh boundary after VP1 (in the transitive condition).

ERP data suggest, in accordance with the speech data, that the former syntax-driven CPS patterns were overridden as phrasing was now determined by the requirements of the information structure; no CPS occurs in the transitive sentences. Additional accent positions led to completely different ERPs in the two conditions. If the VP2 was focused, then the CPS was shifted towards the offset of this verb ('*arbeiten*') and if NP2 was focused, the CPS elicited after the focused position.

Processing of focused constituents was followed by a large positivity which resembles the CPS (see Fig. 3). The same pattern was observed for sentence type A (intransitive) and B (transitive) and for different focus conditions. Speech signals and ERPs both demonstrate that syntactically driven prosodic patterns can be completely overridden by the requirements of information structure (focus domains) in dialogues. In the listener's ERP, Closure Positive Shifts following focused constituents suggest that focused elements are critical for phonological phrasing (Alter & Hruska, 2000).

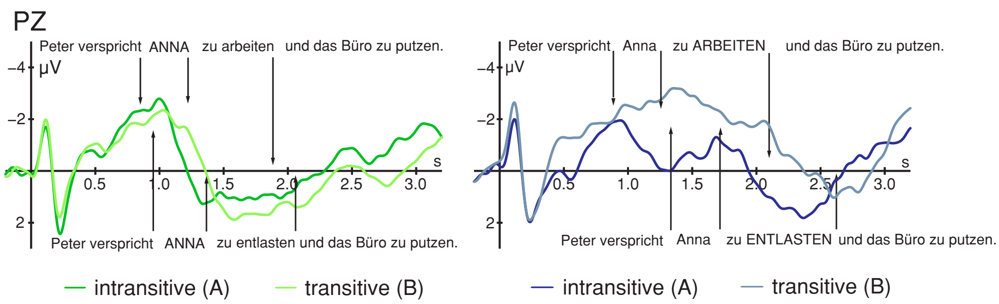

Figure 3. Missing CPS for transitive verb conditions after '*verspricht*'.

Speaker differences in information structure: Production and perception

2.3.4

supported by DFG

Hruska, C., Steinhauer, K. & Alter, K.

We investigated the production of sentences from eight speakers and asked how the differences in their use of prosodic cues is being processed by listeners. Acoustic analyses of production data indicate that answers to Wh-questions inducing narrow focus were variably realized by different speakers. Furthermore, cluster building due to values of fundamental frequency seems to be the best way of classifying different speaker's realization.

In a perception experiment, the produced sentences were then presented with preceding questions to explore how precisely the answers were produced by each speaker. Rating values of 15 participants show that answers from speakers with a prominent focus accentuation were preferred.

In a second experiment, we created prosodically appropriate as well as inappropriate dialogues that were presented auditorily. Listeners had to judge whether the answer was appropriate or not. Behavioral data (percent correct) suggest that judgment of appropriateness was easier for speakers producing a distinct pitch contour.

The results from the acoustic analyses and the two perception studies show that fundamental frequency seems to be the dominant prosodic parameter in distinguishing focused and background information.

The influence of the sentence melody on grammatical judgments

2.3.5

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[2] Department of Psychology, University of Leipzig

Toepel, U.[1], Meyer, M.[1], Blauert, C.[2] & Alter, K.[1]

To investigate the unique influence of prosodic information during auditory sentence perception, one has to remove syntactic and lexical cues from the speech signal. The PURR filtering procedure (Prosody Unveiling through Restricted Representation) realizes such a manipulation by removing all acoustic information above the 3rd harmonic as well as aperiodic portions comprised in the speech signal.

To confirm the success of intonational manipulations with the PURR- procedure, two behavioral experiments (preceding a follow- up fMRI- study) were performed in a perception paradigm, to test whether the manipulated (delexicalized) stimuli were recognizable.

The material consisted of (a) sentences with a sentential intonation, (b) sentences with an enumerating intonation, (c) word lists with a sentential intonation and (d) word lists with an enumerating intonation. Furthermore, these four conditions were filtered with the PURR- method to remove all segmental content (syntactic, semantic and phonemic information) only leaving suprasegmental parameters.

In the first experiment, subjects were required to perform a prosodic judgment task (*sentential or enumerating intonation?*), whereas in the second experiment participants were asked to do a grammatical judgment (*active or passive mode?*). For the second experiment, word list conditions were excluded from the study .

According to the data from the first experiment it can be concluded that sentential or enumerating intonation contour can be classified reliably, irrespective of the absence/ presence of syntactic information in speech utterances.

In the second experiment, the subjects' performance on segmental and suprasegmental utterances clearly demonstrated that delexicalized speech does indeed not comprise lexical and syntactic information. When subjects were required to rely on syntactic cues they responded at chance rate in the case of the filtered stimuli, whereas correctness of answers was above 80% for intelligible utterances.

2.3.6 Electrophysiological correlates due to metrical parameters: Syllable duration

Kruck, S.[1], Opitz, B.[1], Tervaniemi, M.[2] & Alter, K.[1]

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Intonation in words and sentences alters the acoustic parameters: frequency, duration and intensity. These and other acoustic parameters, like pitch, seem to be context-sensitive. A central question of prosodic processing concerns the relative contribution of each parameter. The present preliminary study aimed to investigate neurocognitive processes triggered by temporal aspects of syllable duration in a word-like pattern with preserved acoustic parameters of natural speech. To reveal the relative importance of metrical structures, we examined different intonation contours of tri-syllabic consonant vowel (CVCVCV) structures, recording ERPs during the perception. The vowel quality was always /a/ with either a voiced /d/ or an unvoiced /t/ consonant to vary the segmental structure of syllable onset. The stimuli were naturally produced by a German female speaker with either an initial or medial stress. Acoustic analyses showed that increased duration was the main correlate of syllable stress in both conditions. The four items were presented in a mismatch negativity design with a distractor task. Preliminary ERP data suggest that the stimulus onset of the initial syllable was always reflected by an early negativity, most distinct for the deviant conditions. The comparison of the ERP response to initial versus medial stressed items seems to reflect the syllable boundaries by enhanced positivity most eminent in the infrequent item, reflecting the existence of neuronal memory trace for durational changes of speech sounds.

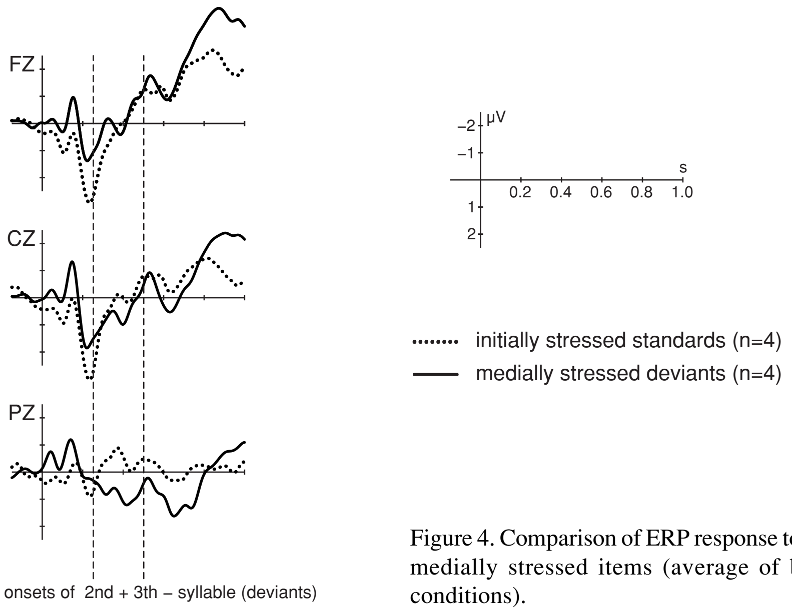

Figure 4. Comparison of ERP response to initially versus medially stressed items (average of both consonant conditions).

2.3.7 The use of suprasegmental information during word recognition as indicated by ERPs

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

Suprasegmental information on the word level is established by several acoustic parameters that distinguish the single syllables of a word. Such parameters include the pattern of fundamental frequency, duration, amplitude and spectral tilt. Our aim was to focus on two research questions: first, is there an ERP component that differentiates suprasegmental information? Second, is an ERP component that reflects processes of word recognition, namely the N400, influenced by incorrect suprasegmental information?

To explore the first question we examined the processing of bisyllabic words beginning with either a strong syllable (e.g., *Fóto*) or a weak syllable (e.g., *Fasán*). The influence of stress on word recognition was explored by presenting each word twice. One version received correct suprasegmental information, the other version received incorrect suprasegmental information, i.e., a stress shift (e.g., *Fotó*, *Fásan*). All stimuli were spoken by a female native speaker. Twenty-four subjects listened to these words and decided in two separate tasks if a word was correctly stressed (stress task) or if the word was animated or not (semantic task). Another group of 24 subjects listened to the words and pseudowords. They had to decide if the presented stimulus was a word (lexical task) or if the word or pseudoword was stressed on the first syllable (prosodic task). ERPs were recorded from 64 scalp-sites referenced to the nose.

No differences for strong versus weak-initial stressed words were found. The failure to replicate a 'stress sensitive' component as presented by Böcker et al. (1999) may result from the use of full vowels in all syllables of the words that were presented. In contrast, all initial syllables of weak-initial words in the Dutch study had reduced vowels.
The stress shift decreased the number of correct responses in the lexical task and in the stress task. For the stress task an enlarged N400 for incorrectly stressed strong-initial

words as compared to correctly stressed strong-initial words but not for correctly vs. incorrectly stressed weak-initial words occurred. In the lexical task, incorrectly stressed strong-initial words but not incorrectly stressed weak-initial words elicited an enhanced late positivity. Thus, the effects of the stress shift differed for strong- and weak-initial words. The question remains if this differentiation results from the speakers tendency to establish the stress shift via different acoustic parameters for both groups of words.

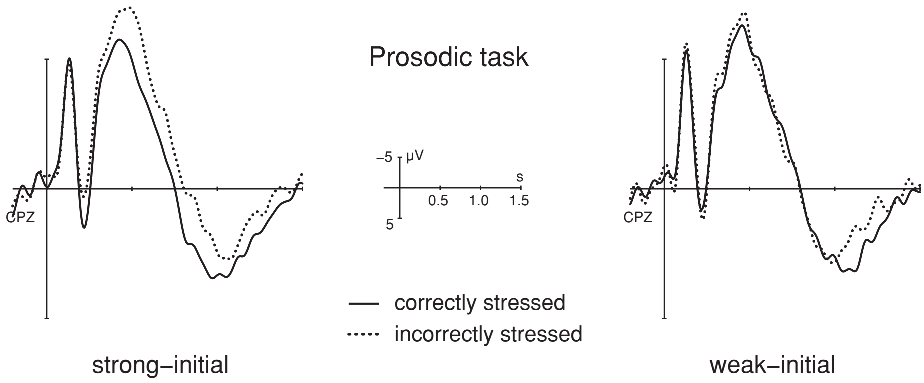

Figure 5.

2.3.8 Early auditory processing of linguistic and extralinguistic information as reflected by Magnetic Mismatch Fields

Lattner, S.[1], Alter, K.[1], Ziegler, W.[2], Friederici, A.D.[1], Maess, B.[1] & Wang, Y.[1]

[1] Max Planck Institute of Cognitive Neuropsychology,
[2] Clinical Neuropsychology Research Group, City Hospital Munich / Bogenhausen

The acoustic speech signal does not only transmit the linguistic message but also information about the speakers sex, age, health etc. The aim of the present study was to explore whether speakerspecific features and linguistic cues in the acoustic speech signal are dealt with differently with by the auditory system. Magnetic Mismatch Fields (MMFs; commonly interpreted as a correlate of the brain response to a deviating stimulus in a series of standard stimuli) were collected with a 148 channel whole-head MEG. Based on the fact that the MMFs vary according to the dimension of deviancy, we investigated the following types of deviants (a German single word uttered by a male speaker was employed as standard stimulus): (a) deviating word (b) deviating (female) speaker (c) both (i.e., another word uttered by a female speaker). Brain responses were collected from 6 female and 3 male subjects. Event-related brain surface current densities (BSCD) were calculated. All stimuli showed a mismatch response peaking around 130 - 220 ms post onset. As shown in Figure 6, the BSCD maps of the brain response to the deviating word showed a lateralization to the left hemisphere in the time range of 150 - 200 ms post onset. In contrast, the speaker deviancy led to a significantly higher current density in the right hemisphere. Stimuli deviating in both dimensions elicited a generally stronger response and a tendency of being lateralized to the left hemisphere, suggesting that the perceptual system might be tuned to phonetic deviancy rather than voice information, even in early stages of auditory processing. This assumption is also supported by behavioral results.

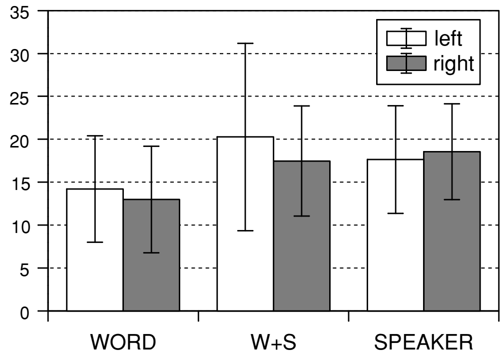

Figure 6. Mismatch-related Current Densities [mAm/m^2] of left and right hemisphere in the time window of 150-200 ms.

Words and voices: A behavioral study of linguistic and nonlinguistic discrimination

2.3.9

Lattner, S., Alter, K. & Friederici, A.D.

The speech material consisted of two words (monosyllabic, concrete German nouns) uttered by 4 male and 3 natural female speakers as well as one female voice whose fundamental frequency was lowered to about 80 Hz. The stimuli were presented in pairs to 30 subjects. Fifteen participants had to detect whether the word was uttered by the same speaker (speaker task), while the others had to indicate whether they had heard the same word or not (word task). Reaction times were measured. Considering the unmanipulated sounds only, there were significantly longer RTs for the speaker task than for the word discrimination (Fig. 7 vs. Fig. 8), suggesting that the processing of speaker information is a fast and highly unconscious process. Furthermore, there was a

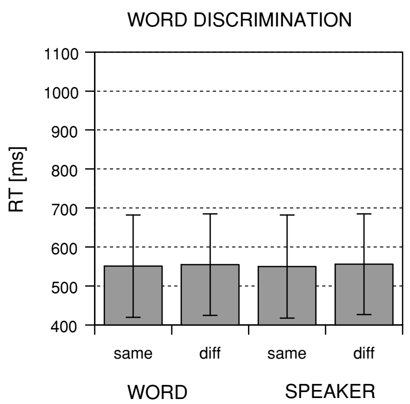

Figure 7. Reaction times to identical vs. different words uttered by the same or another speaker (word discrimination task).

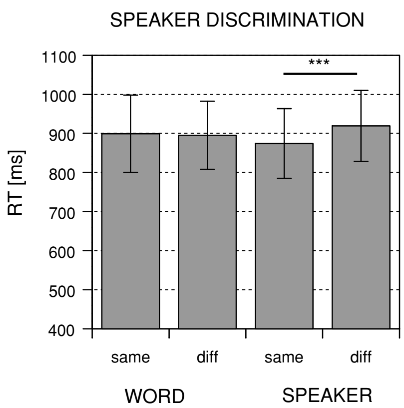

Figure 8. Reaction times to identical vs. different words uttered by the same or another speaker (speaker discrimination task).

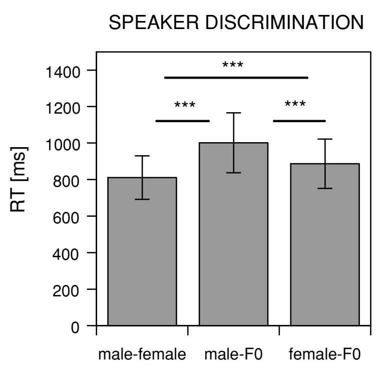

Figure 9. Reaction times to identical and different words (a) uttered by a male and a female voice, (b) coming from a male voice and the F0-manipulated signal, and (c) from a female voice and the F0-manipulated signal (speaker discrimination task).

significant main effect of speaker change in the speaker task. In particular, the discrimination between speakers of the same sex appeared to be difficult in the given setting. As shown in Figure 9, the pitch adapted voice finally appeared to be peculiar: it led to significantly longer reaction times when presented in combination with a female as well as (and in particular) in combination with male voice. This result might indicate that the role of pitch, often underestimated because of its inter- and intraindividual variability, is of a major importance in the processing of speaker-related information.

2.3.10 Event-related fMRI reveals the role of pitch modulation during the comprehension of spoken utterances

Meyer, M., Alter, K., Steinhauer, K., Friederici, A.D. & von Cramon, D.Y.

In intonational languages like German, linguistic prosody is realized particularly by pitch information. Modulations in pitch contour help speakers (and listeners) to mark (and recognize) differences at the sentence-level, e.g. distinguishing questions from statements. Empirical evidence provided by previous neuroimaging studies points to an involvement of human right inferior and dorsolateral frontal cortex in pitch processing while subjects listened to sentence melody (Meyer et al., 2000), musical melody (Zatorre et al., 1994), and syllables (Zatorre et al., 1992). This is in agreement with several lesion studies also proposing a right hemisphere contribution to pitch processing in spoken language (f.e., Schirmer et al., 2000). The present study employed behavioral and fMRI measures to investigate systematically, how selective pitch manipulations in natural, re-synthesized, and low-pass filtered sentences affect the hemodynamic responses in cerebral regions subserving comprehension of fluent speech, particularly in the right hemisphere. Four experimental conditions were created: (1) sentences with wide focus and normal intonation, (2) sentences with flattened pitch contour, (3) pure pitch contour [i.e., sentence melody exclusively], and (4) sentences with narrow focus. Fourteen neurologically healthy participants performed a prosodic rehearsal task while listening to a pseudo-randomized order of experimental (German) sentences. Gradient-echo EPI T_2* images were collected from eight axial slices parallel to the AC-PC plane using a Bruker 3T scanner. Data analyses suggest that functional brain activation clearly varies as a function of specific pitch manipulation applied to the sentences. Intonational marking of sentence focus corresponded to weak activation in the left anterior superior temporal region (STR) [(1) vs.(4)]. Increased activation in several right inferior frontal and posterior temporal areas was observed when subjects listened to flat-pitch sentences [(1)+(4) vs. (2)]. Processing sentence melody corresponded to reduced activation in the anterior and mid STR bilaterally, but to bilateral signal increase in the posterior STR (planum temporale/planum parietale), in the anterior insula, and in subcortical regions, particularly in the right hemisphere [(1)+(4) vs. (3)]. Emphasizing syntactic and lexical information led to stronger activation in the left inferior frontal gyrus (pars triangularis) and in the STR bilaterally, whereas focusing on prosodic processing involved the fronto-opercular cortex with a right hemisphere preponderance [(2) vs. (3)]. As a function of task rehearsal of pitch contour activated left inferior frontal cortices for all conditions except for pitch-flattened sentences. These findings emphasize the essential role of pitch modulation in the comprehension of spoken utterances and unveil the underlying neural substrates.

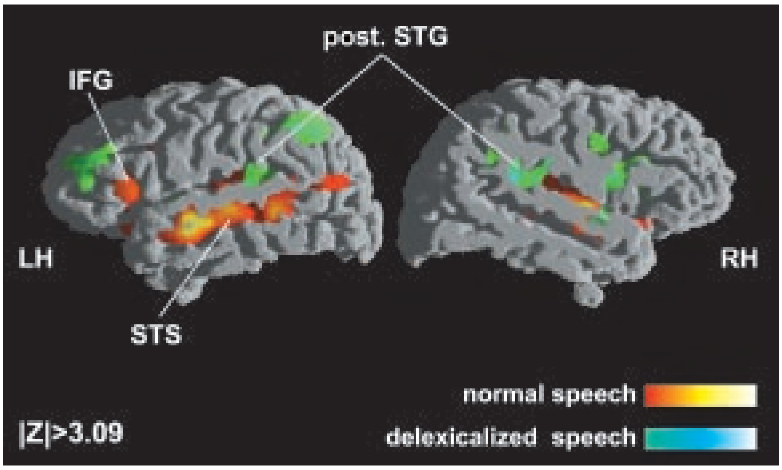

Figure 10.

Accentuation and emotions - Two different systems?

2.3.11

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Current investigations point to a relationship between syntax and prosody. However, prosody can also be linked to emotional markers of an utterance. In the present study, the relation between accent placement and different acoustic parameters of emotional speech was analyzed using the online response method of event-related brain potentials (ERPs).
The sentence material varied in emotional state (happy, neutral, angry) and accent position (last NP of the sentence or sentence final verb).
In addition to ERP- measures, the material was further analyzed using (a) an estimation of the harmonics-to-noise ratio (HNR), (b) a measure for spectral flatness and (c) the maximum prediction gain for a speech production model computed by the mutual information (MI) function. For that, the vowels of the NP and of the sentence final verb (accented and unaccented) were used.
The results suggest that accentuation and emotional state seem to be two different systems indeed. Firstly, a correlation between the maximum prediction gain and the differentiation of ERP- traces with different emotional states was found. Utterances comprising neutral emotional state are characterized by a higher maximum prediction gain and a more negative ERP- trace than utterances with positive and negative emotional states. Thus, the maximum prediction gain can be used as an indicator of arousal, i.e. positive or negative emotional state of the speaker in comparison with the neutral state.

Since sentence accent is not a necessary target point for the encoding of emotions, the ERP traces with its millisecond time resolution provide a more detailed picture of emotional state differentiation than an averaged measurement, such as the maximum prediction gain.
The HNR estimation, on the other hand, was found to correlate with accentuation of the sentence final verb vs. default accentuation on the NP.

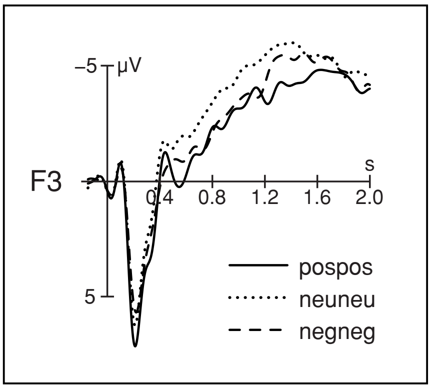

Figure 11. The differenciation in the ERP between neutral (dotted line) and happiness/cold anger (straight/dashed line). Waveforms illustrate the averages for all three conditions from 150 ms prior to sentence onset to 2000 ms at a selected frontal electrode site.

2.3.12 Differentiation of affective prosody: An fMRI investigation

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Only a few RT and ERP experiments have investigated the effect of prosodic cues on linguistic processes such as syntax (e.g., Cutler et al., 1997; Steinhauer et al., 1999; Warren et al., 1996). The effect of prosodic cues on non-linguistic processes, such as affect, has mainly been explored in patient populations and a few brain potential studies (Pihan et al., 1997; Kotz et al., 2000). Controversy exists, as to how affective prosody is lateralized in the brain (e.g., Blonder et al., 1991; Kotz et al., 2000; Pihan et al., 1997, 2000; Starkstein et al., 1994) and whether the lateraliztion varies as function and of linguistic prosodic parameters such as fundamental frequency, intensity and duration (e.g., van Lancker & Sidtis, 1992).

Therefore, we set out to explore whether types of affective prosody can be differentiated by means of fMRI by contrasting lexicalized and de-lexicalized (low-pass filtered) affective prosody. Twelve subjects judged the prosodic contour of a sentence on a five-point scale during the fMRI scan. *Condition effects*: While bilateral (left accentuated) activation was found in the temporal and subcortical regions in the lexicalized condition, there was bilateral inferior frontal and prefrontal activation in the de-lexicalized condition (Fig. 12). *Prosody effects*: In the lexicalized condition the contrast between neutral and negative prosody showed activation of the middle insula, while the contrast between neutral and positive prosody resulted in bilateral activity of BA44, BA45 and the right posterior STS. In the de-lexicalized condition the contrast between neutral and negative prosody resulted in bilateral activation of BA46, BA44/45 (right) and the left planum polare, while the contrast between neutral and positive prosody showed enhanced activation in BA44, BA45 (left) and the supratemporal plane. Thus, lateralized brain activation related to affective prosody varies as a function of condition (lexicalized vs. de-lexicalized) and affect (negative vs. positive).

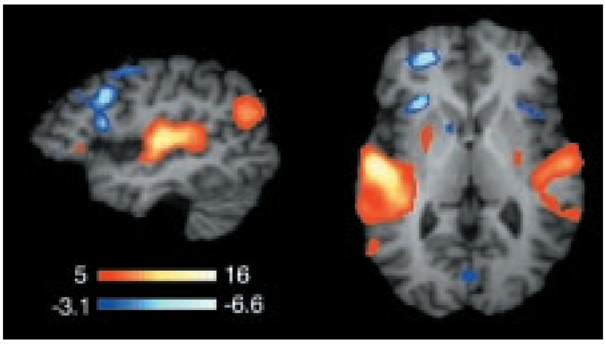

Figure 12. The presentation shows the activation across all prosodic conditions in the lexicalized (red) and de-lexicalized (blue) version in a sagittal and an axial view.

This research program examines memory systems and processes and their functional representation in the brain. In accordance with recent developments in memory research, memory is regarded as process specific, that is memory performance is examined in terms of specified processes such as encoding, storage and retrieval. Second, memory is considered to be comprised of multiple systems, such as working memory, semantic and episodic memory.
The two main research topics are working memory and memory retrieval. Behavioral measures, electrophysiological measures (ERPs and EEG spectral analysis), measures of hemodynamic brain activation (fMRI) and ERP recordings from depth electrodes in the human medial-basal temporal lobes are used to examine memory-related brain activation patterns.

One focus of this research program is on working memory, a brain system that enables temporary storage and manipulation of information necessary for the guidance of goal-directed behavior. Working memory can be separated into executive control functions that allow the coordination of lower level cognitive functions and information specific maintenance functions that enable storage of information. One fMRI project (2.4.1) focused on the role of prefrontal and premotor brain regions when information is retained in working memory, whereas in a second project we examined brain activation patterns associated with executive functions, i.e. the inhibitory control of irrelevant information (2.4.2). Another project (cf. section 2.11) used EEG spectral analysis to examine the functional role of gamma band oscillations during working memory operations.

The second research focus is on memory retrieval. Here we focus on the subprocesses contributing to memory retrieval such as familiarity assessment, recollection and post-retrieval processing (cf. Mecklinger, 2000) using ERP and fMRI measures. Project (2.4.3) examined the relevance of familiarity assessments for illusory memory judgments. The role of frontal cortices in retrieval and monitoring processes during item specific recognition was investigated in patients suffering from frontal lobe lesions (2.4.4). In project (2.4.5) we examined the functional significance of two ERP effects evoked by task-relevant and irrelevant stimulus repetitions: the fronto-medial old/new effect and the (inverse polarity) parietal old/new effect. Project (2.4.6) evaluates differences and similarities between familiarity and facilitation in direct and indirect tests of memory. The combined analysis of ERP and fMRI measures was used in project (2.4.7) to disentangle the temporal and spatial characteristics of auditory episodic memory and project (2.4.8) examines object-based and spatially-based memory processes in the hippocampus proper.

Two additional projects (2.4.9, 2.4.10) were concerned with the attentional modulation of auditory sensory memory traces using ERP and fMRI recordings.

2.4.1 Codes in visual working memory: Motor codes and processing strategies in working memory tasks

Gruenewald, C., Mecklinger, A. & Friederici, A.D.

supported by DFG

We continued our work on identifying which codes are used to maintain visual information in an active state in working memory. In previous studies we identified motor schemas (i.e., ensembles of neurons related to a given action) as important representation formats in working memory (see Ann.Rep. 99, p. 42-43). In particular, we found that manipulable (graspable) objects activated the left lateral premotor cortex and the ascending branch of the intraparietal sulcus (Fig. 1), two regions which have been associated with the representation of motor schemas in animal studies.
Important questions for further investigation concern (a) the precise functional characteristics and neuronal realization of these motor schemas and (b) the influence of task variables. As our previous results were based on schematic line drawings of manipulable and non-manipulable objects, in a first step we generated and evaluated a set of realistic real world stimuli (i.e., indoor and outdoor photographs of objects and animals). From this pool 200 objects were selected and entered in a rating study, in which 32 subjects rated each object's name typicality, associated action typicality, familiarity and manipulability (i.e., the existence of typical actions associated with the object). On the basis of this evaluation we generated pools of objects with variable action valences.
In a second step, we examined the brain activation patterns evoked by these real world stimuli in a working memory task. Rather than using a task that entails a mental rotation component as in the aforementioned study (i.e., requiring subjects to judge whether a test stimulus is identical or a mirror image of the one held in working memory or not), in the current study, we used a task that focused on the processing of object features (i.e., subjects had to indicate whether a black shape matches the outline of the object presented previously or not). In contrast to the above mentioned study, manipulable and non-manipulable objects lead to highly similar premotor cortex activation and to bilateral activation in the frontal eye fields (FEF), the pre-SMA, along the intraparietal sulcus and in non-primary visual areas (BA19 and MT), a neuronal network presumably engaged by an internal shape scanning strategy. Consistent with the aforementioned study, manipulable objects relative to non-manipulable objects activated the ascending branch of the intraparietal sulcus. This pattern of results suggests that motor schemas are not automatically activated and held in an activated state in working memory tasks. In particular, the premotor component seems to be modulatable by task demands.

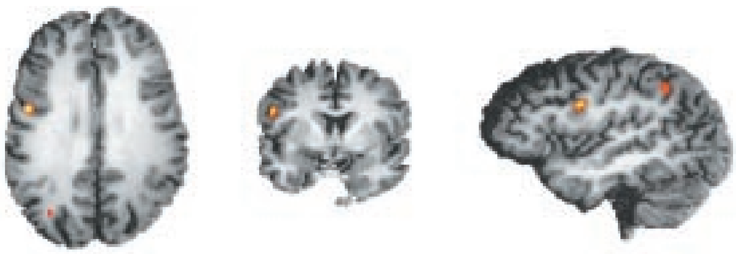

Figure 1. Brain regions showing enhanced BOLD responses for manipulable relative to non-manipulable objects in a delayed response interval. Activations were found in the left lateral premotor cortex (-47, 3, 27) and in the ascending branch of the left intraparietal sulcus (-44,-46,47).

Differential proactive interference effects in item recognition tasks for subjects with high and low working memory (WM)-capacity: Behavioral and fMRI evidence

2.4.2

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Two behavioral and an event-related fMRI study were performed to investigate inhibitory control processes in working memory. We used an item-recognition task with abstract visual objects to investigate sequential interference effects, which were assumed to reflect inhibitory control mechanisms employed to minimize the distracting influence of no longer relevant information from the preceding task trial on the current task trial. Furthermore, the task was designed to differentiate between inhibition of a mere stimulus representation in the Low Interference (LI) condition and inhibition of a stimulus-response-set as the unit of inhibition in the High Interference (HI) condition. We predicted higher interference costs in the latter case. We found higher costs in the interference conditions compared with a control condition, but no significant differences between HI and LI.
Since WM capacity seems to be correlated with the ability to suppress irrelevant information, individual differences in WM-capacity may have contributed to the absence of differential interference costs in the HI and the LI condition. In a second experiment, we contrasted subjects with high (HS) and low (LS) working memory spans. Taking into account individual differences in the capacity for controlled attention and active inhibition, it was possible to separate interference caused by an activated stimulus representation and interference caused by an activated representation of a stimulus-response-set.
Experiments 1 and 2 were aimed to do a precise analysis of the unit of inhibition in an item recognition task. Neuroimaging findings on prefrontal cortex indicate that this region supports executive control processes such as inhibitory processing of task-irrelevant information. An event-related fMRI study was performed to investigate neuroanatomical correlates of inhibitory control mechanisms for familiar (letters) and unfamiliar stimuli (unknown objects) in HS and LS subjects. We examined whether proactive interference effects in item recognition are content specific (i.e., activate different brain regions for familiar and unfamiliar stimuli) or reflect the operation of a general control process. Participants performed a letter and an object recognition task. On interference trials, the probe did not match a current target, but it was target-set-member and probe on the previous trial (consistent with the HI condition of Experiment 1 and 2). In the letter task, interference trials activated a bilateral network along the upper banks of the inferior frontal sulcus and along the banks of inferior precentral sulcus. This activation pattern was more pronounced for low span than for high span subjects. In the object task, interference trials led to enhanced activation in the right posterior parietal cortex along the banks of the intraparietal sulcus, with this pattern being more pronounced for high span subjects. These results suggest that HS subjects may be more efficient in generating episodic memory traces, especially for unfamiliar objects, and by this need to engage more attentional control mechanisms to inhibit these stimuli. Conversely, the LS subjects seem to be more susceptible to interference from familiar

and highly over learned stimuli. This pattern of results is consistent with the view of content specific inhibitory control mechanisms and, moreover, suggests that the brain regions mediating these inhibitory mechanisms are differentially recruited by high span and low span subjects.

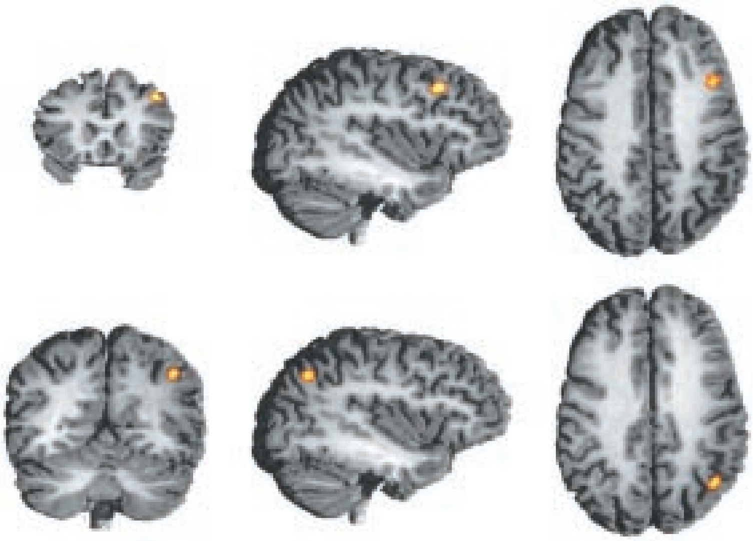

Figure 2. Averaged z-maps of the contrast interference vs. control across all subjects. The upper row shows coronar, lateral (right) and axial views of the activated areas in the letter task. The corresponding views in the lower row show the brain activation in the object task. In this figure, the threshold was set to z=3.1 for the letter task and to z=2.6 for the object task.

2.4.3 Is false recognition always based on illusory familiarity?

Nessler, D. & Mecklinger, A.

Prior ERP experiments revealed that the rate of false recognition as well as strategic processes during encoding are important factors in determining electrophysiological differences between true recognition of previously studied words (OLD) and false recognition of non-studied, but semantically related words (LURE) (see Ann.Rep. 99, pp. 46-47). Most models of false recognition assume that such erroneous responses arise from an illusory feeling of familiarity. However, in our prior studies we did not consistently find an early frontal old/new ERP effect for false recognition, an effect that is seen as a correlate of familiarity assessment. Consequently, in this experiment we examine directly the relationship between familiarity and false recognition rate. For this purpose event-related potentials (ERPs) elicited by true and false recognition were investigated after short (40 s) and long retention delays (80 s). Prior studies showed that recognition memory performance as well as familiarity decrease with longer delays. With regards to these results, we expected an increase in the rates of false recognition, i.e., a decrease in performance as well as a decrease in familiarity, as revealed by a smaller early frontal old/new ERP effect for the long delay. If, however, this increase in false recognition is accompanied by enhanced illusory familiarity, there should be larger frontal old/new effects in the long delay.
Results revealed decreased performance in the long delay, that was most pronounced for the rates of false recognition. Further, ERPs to true recognition were more positive than ERPs to new responses to NEW words in an early time window (300-600 ms) at

frontal locations, indistinguishable for both delay condition. However, an early frontal old/new effect for false recognition, seen as a correlate of familiarity assessment, was only found for the short delay (cf., Fig. 3). In showing that the performance decrement is not always accompanied by enhanced illusory familiarity, the findings indicate that there is no strong relationship between familiarity and false recognition. They rather suggest that false recognition of semantically related words in the long delay condition arose from less readily accessible memory traces.

As an additional result, response-related averages showed an error-related negativity (ERN) for false and true recognition. The presence of an ERN to true recognition indicates that this effect is not related to error trials per se, but rather may reflect a misrepresentation of the correct response. Larger and slightly topographically different ERNs for false recognition suggest an additional contribution of high task demands under conditions of response uncertainty to this effect.

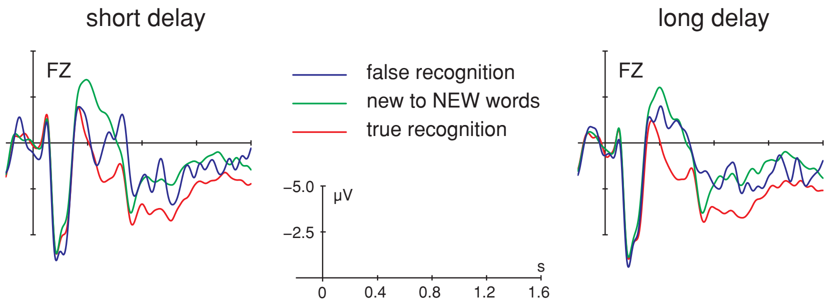

Figure 3. ERPs elicited by true recognition, false recognition and new responses to NEW words at middle frontal electrode site (Fz) for the short retention delay (left) and the long retention delay (right).

2.4.4 Modulating the ERP repetition effect by manipulating stimulus characteristics

Wiegand, W., Penney, T.B. & Mecklinger, A.

Previously, we reported that responses to immediately repeated non-target stimuli elicited less negative ERP waveforms at frontal sites (250–500 ms) and less positive ERP waveforms at parieto-occipital sites (after 400 ms) as compared to first presentations (see Ann.Rep. 99, p. 48). Furthermore, immediate stimulus repetitions in an intentional memory retrieval task elicited a similar frontal ERP effect, but more positive ERP waveforms to repeated as compared to first presentations over parietal sites. We proposed that the frontal effect reflected stimulus familiarity in both tasks and depended, in part, on semantic information, whereas the parietal effect in the target detection task reflected access to a short-term memory representation, i.e. a token, and was distinct from the representations accessed by intentional retrieval. To determine whether physical and semantic properties of repeated stimuli differentially modulate the frontal and parietal ERP effects observed in the target detection task, we used a stimulus stream in which the repeated stimuli were either physically identical or were physically different but represented the same object. For example, in the former case the same line drawing of a hammer would be presented twice, whereas in the latter case two different hammer line drawings would be presented. We hypothesized that if the frontal effect was driven by semantic information, then the form of stimulus repetition would fail to have an influence and the two repetition conditions would yield equivalent effects. In contrast, if the parietal effect reflected access to a token representation, then physically identical, but not semantically identical, stimuli would elicit an effect. The results supported both hypotheses. First, physically identical and semantically identical stimulus repetitions elicited equivalent frontal effects that were similar to those described above. Second, only physically identical stimulus repetitions elicited less positive ERP waveforms at parieto-occipital sites as compared to first presentations. Taken together, the results provide further support for the claim that the frontal effect reflects stimulus familiarity that depends on conceptual-semantic information, whereas the parietal effect is due to the availability of a short-term memory representation that precludes the generation of a new token.

2.4.5 Familiarity is more than facilitation: Differential ERP components evoked by familiarity assessment and item repetition

Mecklinger, A., Nessler, D., Dupke, C. & Penney, T.B.

In previous studies, we found a medial-frontal ERP old/new effect between 300 and 500 ms during recognition memory judgments. We interpreted this effect as reflecting the assessment of links in long-term memory that do not necessarily form the large representational units that allow conscious recollection to occur (Mecklinger, 2000). Although these results suggest that familiarity assessments can be dissociated from the processes leading to recollection experience, the precise functional characteristics of familiarity assessment, i.e. the processes that lead to the experience "that a particular event reminds one of something", are still a matter of debate.

Here, we examined whether the ERP old/new effects elicited by familiarity assessment and by item repetition differed in their temporal and/or topographic characteristics. In Experiment 1, participants were presented with famous and non-famous faces (repeated with a lag of 6 to 12 items) and were required to indicate whether the face was famous. Familiarity assessment was assumed to be reflected in the ERP difference between first presentations of famous and non-famous faces. Notably, given that the task required explicit fame judgments active recollection may also have contributed to this contrast. Repetition effects were defined as the difference between first and second presentations of non-famous faces. Second presentations of famous and non-famous faces were classified faster than first presentations. Familiarity assessment elicited an early (200 to 250 ms) centro-parietally focused old/new ERP effect; a result that has not been, to our knowledge, reported previously. Furthermore, consistent with prior studies we obtained a pronounced fronto-medial old/new effect between 300 and 500 ms. In contrast, repetition elicited an old/new effect between 350 and 500 ms that was right-lateralized and had a centro-parietal focus.

In Experiment 2, we examined whether the differential ERP effects were due to the task requirement of fame judgment by requiring participants to monitor the same stimulus sequence as used in Experiment 1 for the occurrence of rare target events. Obtaining the same ERP effects for the famous vs non-famous first presentation as in Experiment 1 would indicate that these effects indeed reflect familiarity assessment rather than a combination of familiarity assessment and active recollection. First presentations of famous faces relative to first presentations of non-famous faces as in Experiment 1 elicited an early (centro-parietal) and a later (medial-frontal) old/new effect, whereas repetition elicited a right lateralized centro-parietal effect. The results suggest that familiarity assessment, i.e. the processes by which a particular event reminds one of something, can clearly be dissociated from the facilitated processing that occurs when items are repeated.

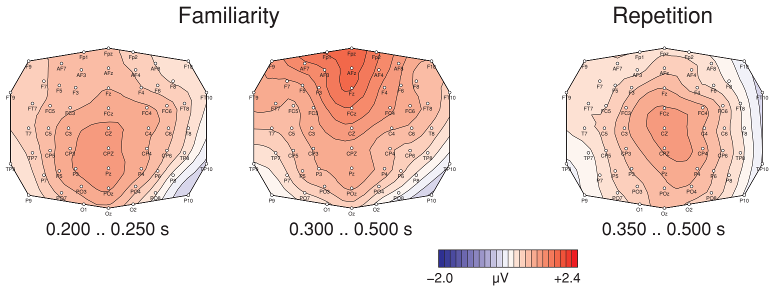

Figure 4. Topographic distributions of the difference waves for ERPs elicited by the first presentation of famous and non-famous faces between 200 and 250 ms and between 300 and 500 ms in Experiment 1 as reflection of familiarity assessment are shown on the left. The effect of repetition is displayed on the right by the topographic distributions of the difference waves for ERPs elicited by the second and first presentation of non-famous faces between 350 and 500 ms in Experiment 1.

2.4.6 Content-specific lateralization of human prefrontal cortex in episodic memory: Combined ERP and fMRI evidence

Opitz, B., Mecklinger, A. & Friederici, A.D.

This work was supported by the Leibniz-Prize of the German Research Foundation (DFG) awarded to Angela D. Friederici.

Last year (see Ann.Rep. 99, pp. 51-52), we reported results of an episodic memory task in which subjects were required to remember identifiable or nonidentifiable environmental sounds under different task instructions. Using fMRI, we observed an increased activity in a distributed neuronal network, including bilateral superior temporal, gyrus, anterior insula and dorsolateral prefrontal cortex (PFC). However, given the poor temporal resolution of the fMRI technique, the temporal relationship of these brain activations had to be analyzed in a more detailed manner using event-related potentials (ERPs). Therefore, a combined analysis of ERP and fMRI was carried out in 18 subjects. In the study phase of the memory task, subjects were required either to judge the sound's loudness (nonverbal task) or to decide whether or not a sound could be verbally described (e.g., ringing bell - verbal task). In the following test phase, subjects performed a recognition test. ERPs (1500 ms duration) were computed separately for recognized as well as not recognized novels in both. The ERP results during encoding showed a frontally distributed novel P3 followed by a slow potential starting around 800 ms that was more positive going for subsequently recognized than for non-recognized novels. In agreement with the fMRI findings, this subsequent memory effect (SME) was present at right frontal electrode sites irrespective of task and at left frontal sites only in the verbal task. As indicated by the earlier onset of the SME for identifiable novels (cf. Fig. 5), the access to verbal codes of nonverbal material during encoding is faster than the access to nonverbal codes. The present results suggested a content-specific rather than process-specific lateralization of activity in the dorsolateral PFC. Other brain regions, such as the superior temporal cortex, had been found to be only active in the encoding task. Furthermore, the novel P3 of the ERP behaves very similarly, showing a substantial reduction from encoding to recognition, suggesting an involvement of the STG in novelty processing. This view is consistent with recent findings demonstrating bilateral activation of the superior temporal gyrus in a novelty detection task. In contrast, the differential reduction of the novel P3 for identifiable and nonidentifiable novels with stimulus repetition points to additional processes, such as attentional modulation and/or categorization of novel stimuli, reflected in the novel P3.

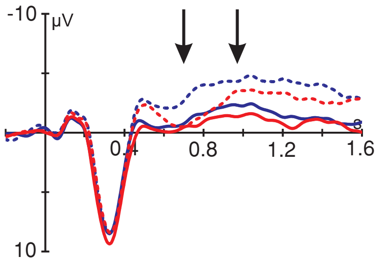

Figure 5. Time course of the subsequent memory effect of the ERP for identifiable (blue trace) and nonidentifiable (red trace) novel sounds at a representative, left frontal electrode. Note, the earlier onset of the SME for identifiable novels as indicated by the arrows. Solid lines – recognized sounds, dotted lines – not recognized sounds.

2.4.7 Object and location processing in the human hippocampus

Penney, T.B.[1], Grunwald, T.[2], Mecklinger, A.[1], Pezer, N.[2], Lehnertz, K.[2], Helmstaedter, C.[2] & Elger, C.E.[2]

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The placement of bilateral depth electrodes in the medial temporal lobes (MTL) of patients undergoing presurgical evaluation for resective surgery provides a unique opportunity to examine processing within distinct neuroanatomical structures of the medial temporal lobe on a millisecond time scale. To examine the functional response of the hippocampus proper during object and spatial information processing, we recorded from intracranial depth electrodes in patients with epilepsy as they performed object and location target detection tasks.

A number of authors have suggested that the left MTL is specialized for object processing, whereas the right MTL is specialized for location processing. More recent proposals, however, suggest that the distinction between left and right MTL function reflects whether or not information can be semantically encoded. The main empirical finding of the present study was that object targets elicited a larger MTL-P300 than location targets in the right hippocampus, whereas in the left hippocampus the two target types elicited equivalent amplitude MTL-P300's. We propose that the MTL-P300, in both hemispheres, is elicited by stimuli that are verbalizable and can be conceptually recoded. Targets in the object-task could be conceptualized easily, resulting in a robust MTL-P300 in both hippocampi. In contrast, conceptualization difficulty for targets in the location-task resulted in a much weaker right hippocampus MTL-P300 whereas the robust MTL-P300 elicited in the left hippocampus may have been because the left hippocampus can, when necessary, serve a compensatory function and conceptually recode spatial information.

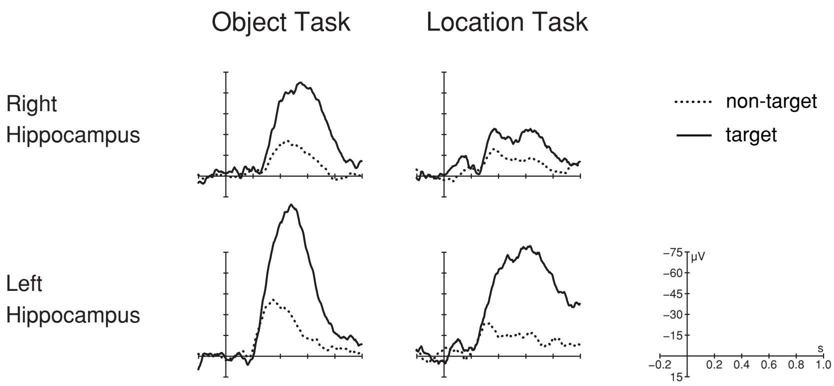

Figure 6.

On the functional significance of the frontal MMN generator

2.4.8

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Opitz, B.[1], Rinne, T.[2], Mecklinger, A.[1], Schröger, E.[3] & von Cramon, D.Y.[1]

This work was supported by the Leibniz-Prize of the German Research Foundation (DFG) awarded to Angela D. Friederici.

Psychophysiological research suggested that the mismatch negativity (MMN) is generated by a temporofrontal network subserving change detection processes and an attention switch towards environmental changes. There is an ongoing debate about the functional role of the frontal lobes in deviancy processing due to heterogeneous reports regarding the conditions under which frontal brain activity has been observed. The present study addresses this issue by systematically varying the degree of pitch deviancy. Three different deviant types, small, medium and large deviants (10%, 50% and 100% deviation, respectively) were randomly presented among standard tones of 500 Hz. ERPs were continuously recorded from 64 electrodes in 13 subjects. In a second session with the same subjects fMRI, measures were obtained at 3T from eight axial slices. When tested under MR background noise conditions large and medium but not small deviants elicited a robust MMN, indicating that the latter could not be detected under MR recording conditions (cf. Fig. 7). Consistent with this finding, significant activations in the superior temporal gyri (STG) bilaterally and the right frontoopercular cortex were found for large and medium deviants. In temporal regions, the signal change was larger for large compared to medium deviants, suggesting that change detection processes are subserved by the STG. For the right frontoopercular cortex the opposite pattern was observed, medium deviants generated a larger signal change than large deviants. This finding does not support the view of an attentional switch mechanism reflected in the frontal MMN generator but rather points to other mechanisms modulating change detection, such as amplification/contrast enhancement of the deviance detection system or sequencing the stream of the incoming sounds.

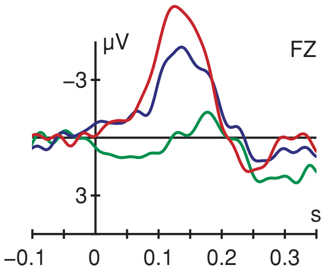

Figure 7. Deviant minus standard difference waveforms for large (red), medium (blue) and small (green) deviants. Note, that no statistically significant MMN was elicited by small deviants.

2.4.9 Refractoriness or memory trace? Neural structures underlying MMN

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This work was supported by the Leibniz-Prize of the German Research Foundation (DFG) awarded to Angela D. Friederici.

The occurrence of a physically deviant sound in a repetitive auditory environment elicits a distinctive negative component in the event-related potential (ERP), the so-called mismatch negativity (MMN). The MMN is assumed to be associated with automatic, preattentive change detection processes. Two possible mechanisms are currently discussed. The first view holds, that the MMN could be the result of a differential state of refractoriness between neural populations being sensitive to the features of the repetitive environment and those being sensitive to the features of the deviating sound. In an alternative view, the MMN may be regarded as the outcome of a memory comparison process. The aim of the present study was to disentangle the neuronal basis of the different contributions (differential refractoriness and memory comparison) to the scalp recorded MMN component. Using event-related fMRI, we recorded the BOLD response while subjects listened to tone trains either consisting of 9 standard tone and one deviating tone (traditional MMN condition) or ten different tones including the standard and the deviant tone (control MMN condition). When comparing the BOLD response in the traditional MMN condition with the control MMN condition, both

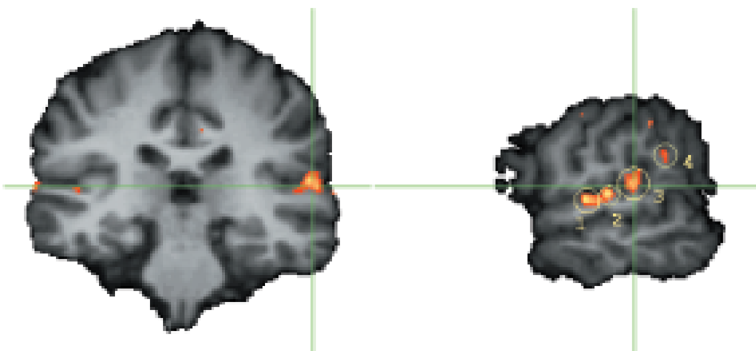

Figure 8.

standard and deviant tones elicited a similar activation pattern, including the planum polare (1), the anterior and posterior banks of the transverse temporal gyrus (2, 3 respectively) and the supramarginal gyrus (4).

Whereas the activation in the anterior and posterior banks of the transverse temporal gyrus reflect refractoriness effects, the activation in the planum polare might be associated with tonal context integration. It is conceivable that a tone can be easier integrated (and therefore leads to less activity) in a repetitive sequence as compared to a sequence of different tones. However, the precise nature underlying such tonal context integration remains to be elucidated.

The Day Clinic of Cognitive Neurology at the University of Leipzig and the Max Planck Institute have had close ties since the clinic was founded in February 1996. The ultimate goal of this interaction is to improve both the diagnosis and the rehabilitation of cognitive deficits after brain injury. To reach this goal, results from patient studies must complement those from neuroimaging. Thus, the therapists' and, most importantly, the patients' cooperation is an invaluable prerequesite for neuropsychological research.

In 2000, 164 patients received treatment at the Day Clinic, and 78% of them gave their informed consent to participate in clinical research projects. Including discharged patients, our database now consists of a pool of more than 500 current and former patients with brain injuries of various etiologies. Based on detailed information concerning neuropsychological and medical profiles, researchers have the opportunity to carefully select patient samples for testing specific hypotheses on brain-behavior relationships. During the last year, 136 brain-injured individuals volunteered to take part in neuropsychological experiments.

The clinical studies targeted a wide variety of issues, which can be loosely grouped into four, partly overlapping categories. Two main topics, the *functional neuroanatomy of the frontal lobes* (cf. section 2.6), and *language processing* (cf. section 2.1), both of which have been in the center of attention for many years, were further elaborated. Several studies concerned the neuropsychology of specific clinical populations, in particular *Parkinson* patients, and finally, a number of studies investigated the applicability of *recent MRI technology* to clinical issues.

The *functional neuroanatomy of the frontal lobes* was studied using paradigms classically associated with so-called executive functions, such as working memory, monitoring and inhibition. Gruber studied two patients to test his hypothesis on different maintenance mechanisms in phonological working memory (2.5.1), and Mecklinger et al. (2.5.2) investigated right fronto-lateral contributions to item-specific recognition memory. Ullsperger et al. (2.5.3) were interested in impairments of error detection and performance monitoring processes. Derrfuss et al. (2.5.4) used a finger tapping paradigm and showed that frontal lobe patients had difficulties inhibiting imitative movements. Hein et al. (2.5.15) compared inhibitory mechanisms in the context of a multi-tasking paradigm for healthy elderly participants, frontal lobe patients, and Parkinsons's patients.

Different aspects of *language processing* were studied as well. Extending their research program on non-aphasic language disorders, Ferstl and Guthke and their colleagues conducted several studies on text comprehension processes after frontal lobe lesions (2.5.5 - 2.5.7). In particular, they compared specific discourse production deficits with associated comprehension problems, studied the effects of encoding perspectives on narrative comprehension, and showed that lesion location in part predicts difficulties with inference processes. Schirmer et al. (2.5.9) examined the lateralization of prosody in the brain and found differential sensitivity of the two hemispheres to distinct prosodic parameters. How lateralization of language processing is influenced by task design, performance level and stimulus modality was studied by Hund-Georgiadis and Cramon (2.5.11). Kotz and co-workers found evidence for differential processing of semantic and syntactic aspects of verb-argument structure in aphasic patients (2.5.10).

Syntactic processing was the topic of a study on patients suffering from Parkinson's disease. Friederici et al. (2.5.12) argue that these patients have problems mainly with late processes, such as repair and integration. Werheid et al.'s (2.5.13) results on procedural learning support the view that motor learning rather than sequence-specific learning is impaired in PD patients, and an additional fMRI study (2.5.14) indicates that PD patients activate fronto-median regions during the processing of structured sequences. Interhemispheric transfer for a patient group with callosal lesions was studied by Pollman et al. (2.5.16) using a dichotic listening paradigm. Müller et al. (2.5.17) found evidence for pathological crying being associated with a low level of brainstem serotonin transporter expression.

Recent developments of MRI technology were applied to clinical issues. Wiggins et al. (2.5.19), used T_2* weighted MR images for making visible indicators of diffuse axonal injury in patients, whose standard MRI scans did not show any lesions. Hund-Georgiadis et al. (2.5.20) combined preoperative fMRI, neuronavigation and intraoperative electrophysiological localization of the motor cortex in patients with brian tumors. Finally, in a pharmacological study, fMRI methodology was successfully applied for examining the effect of subanesthetic isoflurance (2.5.18).

A patient study on the functional relevance of the anterior prefrontal cortex for phonological working memory

2.5.1

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

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Previous fMRI studies in our institute have consistently revealed anterior prefrontal activations during the performance of verbal item-recognition tasks under articulatory suppression. Based on our findings of these studies, an evolutionary-based model of human working memory has been proposed that distinguishes two different phonological short-term memory systems, i.e. an explicit verbal rehearsal mechanism, and a presumed second, phylogenetically older mechanism which is supported both by the supramarginal gyrus and the prefrontal cortex along the anterior intermediate frontal sulcus (2.6.9, Fig. 8). According to this model, verbal short-term memory performance of patients with lesions affecting the cortex along the anterior intermediate frontal sulcus should be normal under non-interfering conditions, but extremely reduced during articulatory suppression. Completing the double dissociation of the two proposed systems, patients with lesions in brain areas subserving verbal rehearsal should show reduced performance under non-interfering conditions and diminished effects of articulatory suppression. Using the same paradigm as in the fMRI study described in the previous section, these predictions were confirmed in two patients with circumscribed brain lesions in the anterior prefrontal cortex (P300) and in Broca's area (P403), respectively (Fig. 1). Moreover, the effects in the former case were shown to be specific to the verbal domain, i.e., they were not attributable to central executive deficits which should also become apparent during interference in visuospatial working memory. Thus, the present lesion study provides convergent evidence for a critical role of the anterior prefrontal cortex in non-articulatory maintenance of phonological information.

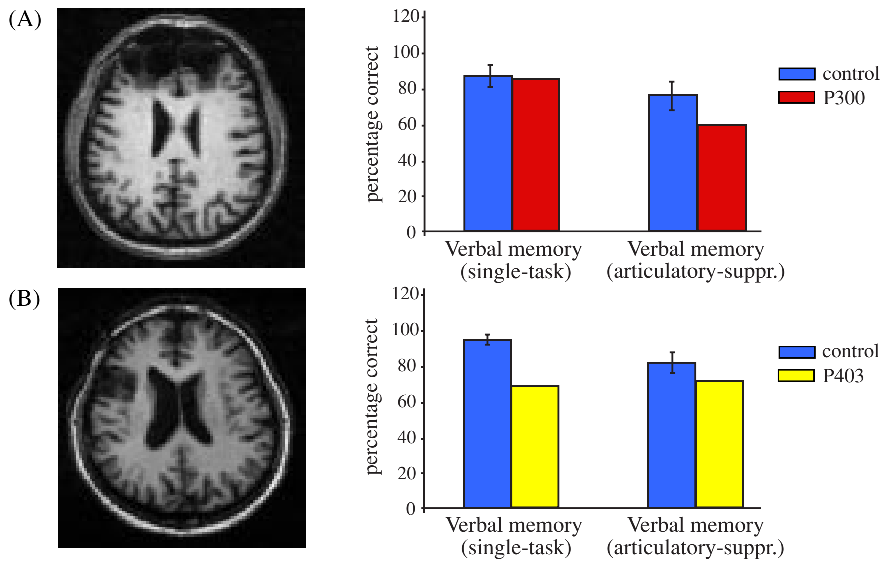

Figure 1. (A) Selective impairment of phonological storage due to bilateral lesion of the anterior prefrontal cortex. (B) Selective impairment of rehearsal due to lesion of Broca's area.

2.5.2 The role of the right frontal lobes in recognition memory: Evidence from frontal lobe lesions

Mecklinger, A.[1], *Nessler, D.*[1], *Schüller, A.*[1], *Matthes-von Cramon, G.*[2] & *von Cramon, D.Y.*[1,2]

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The frontal cortices are important for retrieval and monitoring processes required for item specific recognition. Neuropsychological evidence for this view was provided by a patient (BG) suffering from a right fronto-lateral brain lesion in front of the precentral gyrus, who exhibited large false alarm rates for items that were conceptually similar with previously studied items. Here we examined whether this selective deficit in item specific recognition memory is a general characteristic of frontal lobe pathology.

Six frontal lobe patients and 12 controls performed a recognition memory task. The test words included studied words (OLD), new words (NEW) and new words which were semantically related to studied words (LURE). As expected, patients and controls showed higher rates of old responses to LURE words (false recognition) than to NEW words and performance in both groups decreased from a short (40 s) to a long (80 s) retention delay. Patients with bilateral and left lateral fronto-polar lesions showed poorer recognition memory performance (i.e., lower hit rates and longer reaction times) than controls. However, for these patients there was no selective enhancement of false alarm rates to LURE words. This latter effect was obtained only in one patient with an extended right-hemispheric lesion including the posterior division of the middle and inferior frontal gyri. This lesion area is comparable to the lesion of patient BG. Extending the findings on patient BG, these results suggest that the right posterior fronto-lateral cortex is more relevant for item specific recognition memory than other right frontal regions. Currently, the latter view is investigated in more detail by an examination of item-specific recognition memory in patients with focused lesions to the posterior part of the right frontal cortex.

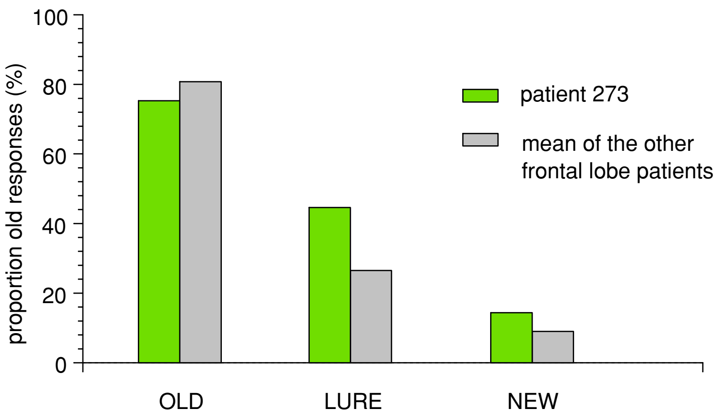

Figure 2. Percent old responses for the different item types (OLD, LURE, NEW words) for patient 273 compared to the mean of the other frontal lobe patients. Patient 273 made fewer true old responses to OLD words and more false old reponses to NEW words. However, especially noticeable is his enhancement in false old responses to LURE words.

The influence of different brain lesions on error processing

2.5.3

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Ullsperger, M.[1]*,*
Müller, N.G.[3] *&*
von Cramon, D.Y.[1,3]

The error-related negativity (ERN), a negative deflection with frontomedian scalp distribution which is elicited about 80 ms after an error has been committed, has been interpreted as a correlate of error detection. An ERN is evoked when the comparison of the representations of the correct (intended) response and the actual response yields a mismatch. In this ERP study employing a speeded flankers task, error processing was investigated in three patient groups with different focal brain lesions [lateral frontal lobe lesions (n = 9), bifrontopolar lesions extending into orbitofrontal cortex (n = 6), frontal lobe and additional basal ganglia lesions (n = 6)] and a matched control group. In all groups but the patients with additional basal ganglia lesions an ERN was elicited by errors (see Fig. 3). In addition, an ERN-like deflection was also found on correct trials. Compared to controls, patients with lateral frontal lobe lesions had a larger ERN on correct responses, indicating that the lateral frontal cortex plays an important role in error detection. It was suggested that the lateral prefrontal cortex is involved in maintenance of the task demands which is necessary for a representation of the correct response. Uncertainty about the correct response as a result of frontal lobe lesions could lead to problems in the error detection process which are reflected by the ERN on correct responses. In contrast, patients with frontopolar and orbitofrontal lesions showed a larger ERN on errors. This finding might result from disinhibition and supports the notion that the ERN has an affective-motivational dimension. Patients who suffered from lesions of the basal ganglia in addition to frontal lobe damage did not have any ERN, neither on erroneous nor on correct trials. This finding indicates that the basal ganglia could be involved in the comparison of the response representations.

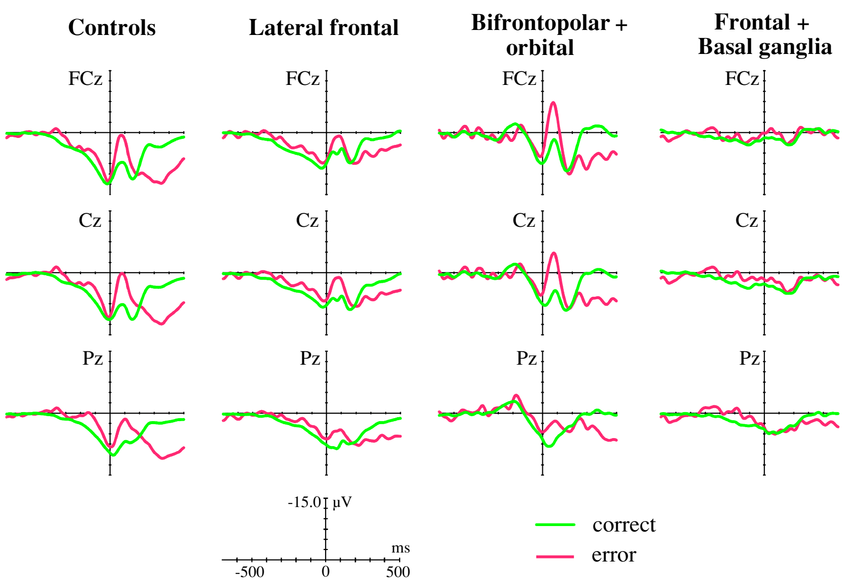

Figure 3. Response-locked ERPs on correct and erroneous trials in the three patient groups and healthy controls.

In sum, it can be concluded that not only the anterior cingulate cortex (ACC) and the pre-SMA are involved in error processing. A larger network including lateral prefrontal cortex, orbitofrontal cortex, and subcortical structures, such as the basal ganglia, seems to be responsible for online performance monitoring. Further electrophysiological, hemodynamic and lesion studies will be conducted to reveal the specific roles of these structures in response representation, error detection, and remedial actions.

2.5.4 Inhibition task performance and frontal lobe lesions

Derrfuss, J.[1], *Brass, M.*[1], *Matthes-von Cramon, G.*[2] & *von Cramon, D.Y.*[1,2]

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[2] *Day Clinic of Cognitive Neurology, University of Leipzig*

Inhibition of prepotent responses has often been reported to pose major problems on patients with frontal lobe lesions. Frontal lobe patients were reported to have difficulties in the inhibition of overlearned responses (Perret, 1974; Vendrell et al., 1995) as well as in the inhibition of imitative actions (Luria, 1966; Lhermitte et al., 1986).
We applied a new paradigm, the finger-lifting interference (Flint) task (Brass et al., 2000), to further investigate the role of the frontal lobes in the inhibition of imitative actions. In the Flint task (see Fig. 4), subjects have to respond with an index or a middle finger movement to a number presented between the fingers of a video-taped hand while the hand on the screen carries out the same (congruent condition), a different (incongruent condition) or no finger movement (baseline condition).
We studied 26 patients (16 with frontal, 10 with posterior lesions) and 16 healthy controls with the Flint task and other tests reported to be sensitive to lesions of the frontal lobes. The Flint task was the only task that revealed significant differences between the frontal and the posterior group (see Fig. 5). The Stroop task, the Modified Card Sorting Test and a verbal fluency measure did not reliably discriminate between the frontal and the posterior group.
Our results provide evidence that there is a deficit in the inhibition of imitative responses in frontal lobe patients. Since the Flint task was capable of revealing significant differences between frontal and posterior patients, it might prove a useful tool for neuropsychological diagnosis.

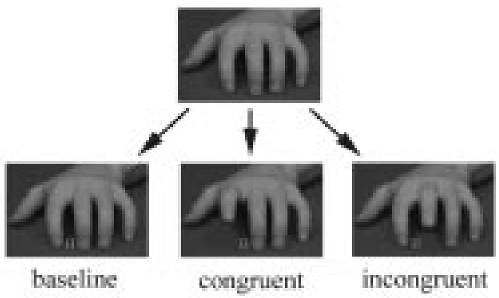

Figure 4. The Flint task.

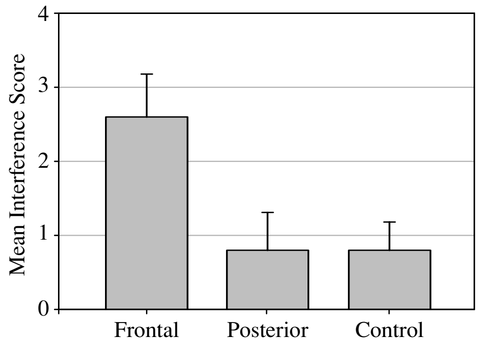

Figure 5. Group means and standard errors of Flint task interference score.

Text comprehension after brain injury: Effects of an encoding perspective on the recognition of story contents

2.5.5

Ferstl, E.C.[1],
Wilke, M.[2],
Guthke, T.[3] &
von Cramon, D.Y.[1,3]

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Non-aphasic language disorders are deficits of communicative language use in the absence of aphasic symptoms on the word and sentence level. Some of these deficits are probably related to frontal brain injury, and thus are likely to co-occur with executive dysfunction. In a previous study (Ferstl et al., 1999), we showed that patients with left-frontal lesions were less likely than brain injured patients without such lesions to make goal-oriented use of one of two alternative perspective cues in recall (cf. Anderson & Pichert, 1978). The question of whether this failure to utilize the cue was due to insufficient encoding of story information or to inadequate use of a revised retrieval strategy could not be answered. The present study attempted to further delineate the processing differences by using a recognition task instead of free recall. By this task manipulation, it was expected that encoding differences would be reflected in different patterns of recognition performance, while retrieval strategies would not play a role. The same story was used as in the original experiment, and 96 words were selected for recognition. Half of the words were mentioned in the text, and half were new. The items in each of the categories further differed with respect to their perspective relevance (encoding perspective, alternative perspective, neutral). After receiving a perspective cue ("Imagine you are a burglar overhearing this story"), the participants read the story, and then performed the recognition task presented by the computer. In the first experiment, 60 healthy control participants of different age groups were tested. The results showed clear age effects: While the hit rates were comparably high for all ages, the older participants (40-70 years) had elevated false alarm rates. This effect was most apparent for those items relevant to one of the two perspectives, rather than for the neutral items. In the second study, 33 patients with brain injuries were tested. Of particular interest were those patients with lesions involving the left prefrontal cortex. Overall, the patients' performance level was lower. Most importantly, however, there were group differences depending on lesion location: only patients with left-frontal lesions had fewer false alarms for the items relevant to the encoding perspective compared to the items relevant for the alternative perspective. This result suggests that the perspective instructions did have an impact on the encoding of the story, but that the missing perspective switch effect in the recall experiment was due to problems with utilizing appropriate retrieval strategies.

2.5.6 Text comprehension after brain injury: The effect of explicitness and salience on question answering performance

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Non-aphasic language disorders have been mostly described as deficits of pragmatic communication and discourse production. Patients affected by this type of language deficit include closed-head injury patients and frontal lobe patients. The present study focused on text comprehension processes of these patient groups. Using the approach of Nicholas and Brookshire (1995), we used a yes/no-question format to evaluate how story comprehension is influenced by the salience and explicitness of narrative information. Sixteen questions to each of two stories were written, with four questions in each of the four cells of the Salience (main idea vs. detail) x Explicitness (explicit vs. implicit) design. The number of required yes-responses was counterbalanced across conditions. In a first experiment, we tested 50 healthy control participants, ranging in age from 20 to 69 years. While Salience greatly influenced response accuracy, neither Explicitness nor age had a significant impact. In the second experiment 55 brain injured patients of various etiologies were tested. As expected, the overall performance level was lower (19% errors) than for the control group (14%). In addition to the significant main effect of Salience, the patient group also exhibited the expected effect of Explicitness (15% error rate for explicit information, compared to 19% for implicit information). In addition, this effect was modulated by etiology and lesion location. The performance on questions requiring inferences (implicit information) was significantly impaired for patients with diffuse brain injuries, such as diffuse axonal injury or small vessel disease, as compared to patients with focal cortical lesions (see Fig. 6). When further subdividing the focal lesion group, it can be seen that particularly those patients with right-sided fronto-temporal lesions had difficulties with implicit information (see Fig. 7). These results confirm that with the appropriate text comprehension test, qualitative differences between patient groups become visible.

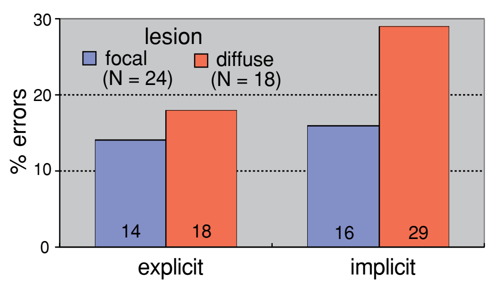

Figure 6. Percent errors as a function of explicitness and brain lesion.

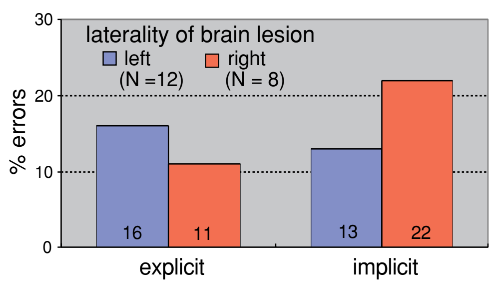

Figure 7. Percent errors as a function of explicitness and laterality of focal brain lesion.

A comparison of text comprehension and discourse production profiles in patients with non-aphasic language disorders

2.5.7

Siebörger, F.[1], Ferstl, E.C.[2], Guthke, T.[3] & von Cramon, D.Y.[2,3]

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[3] *Day Clinic of Cognitive Neurology, University of Leipzig*

Patients with non-aphasic language disorders exhibit several distinct discourse production profiles (e.g., Hartley & Jensen, 1992). For this extended case study, we selected two profiles, characterized by the amount of language output produced. In hypophasia, language production is reduced overall, and spontaneous speech lacks detail and content. In hyperphasia, the output is greatly enhanced, with a tendency for redundancy and tangentiality, as well as frequent deviations from the general theme of the conversation. The question of interest was whether we could identify corresponding text comprehension profiles, i.e., whether patients' discourse behavior would be reflected in predictable comprehension deficits. To this end, we selected four brain injured patients, two of each discourse profile, and administered a battery of production and comprehension tasks. The production tasks differed with respect to their structural complexity, and included spontaneous speech ("Tell me about your weekend."), cartoon story description, and the production of a procedural text. The comprehension tasks included a homonym priming task, a word recognition task testing the levels of text representation (cf. Guthke, 1991), an inferencing task (Ferstl & von Cramon, 2000), story comprehension (2.5.6) and story recall (cf. Ferstl, Guthke & von Cramon, 1999). These tasks were selected for the evaluation of different subprocesses of language comprehension. The results of the production tasks confirmed that the discourse production profiles differed not only with respect to quantitative measures, but also with respect to content and task demands. The hyperphasic behavior (T.R. & B.R.) was apparent mostly during the loosely structured spontaneous speech task, but less so during the production of procedural texts (cf. Fig. 8). The sparsity of information in the hypophasics' discourses (K.O. & D.O.) concerned less important information, while main ideas were mentioned (see Fig. 9). For the comprehension tasks, the picture was not as clear-cut. The two word level tasks did not yield interpretable

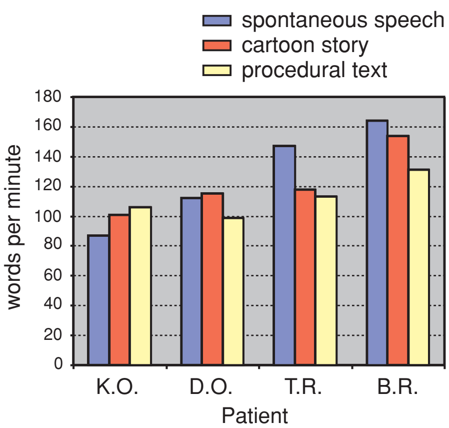

Figure 8. Rate of speech during the three discourse production tasks.

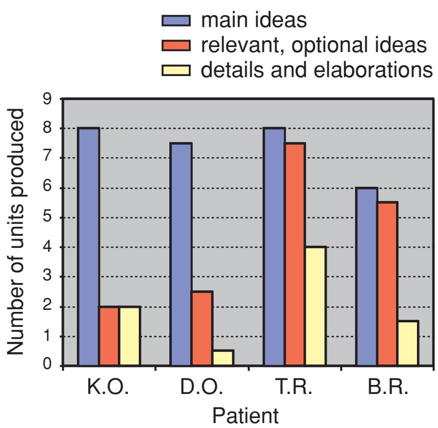

Figure 9. The average number of content units as a function of their rated importance (averaged across procedural and cartoon tasks).

results on a single case basis. In contrast, there was evidence for both hypophasic patients being impaired in the story comprehension task, but lesion location better predicted the patterns of the story recall and inferencing task. Taken together, these results did not provide evidence for text comprehension profiles that directly map onto the identified discourse production profiles. Nevertheless, the study confirms the necessity for a clinical diagnosis of text comprehension skills in non-aphasic patients.

2.5.8 Orbito-frontal cortex regulates cortical synchronicity

Herrmann, C.S.[1], *Hartikainen, K.M.*[2], *Soltani, M.*[2], *Ogawa, K.H.*[3] & *Knight, R.T.*[2]

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[2] *Department of Psychology, University of California, Berkeley, USA,*
[3] *Saint Mary's Hospital, Department of Psychology, Moraga, USA*

Investigating patients with orbito-frontal brain lesions and age-matched control subjects, we were able to demonstrate that orbito-frontal cortex differentially affects the synchronicity of alpha activity in response to visual stimuli. EEG was recorded from 5 patients with orbito-frontal lesions and 10 age-matched controls, who were presented visual stimuli and had to classify them as targets or standards.

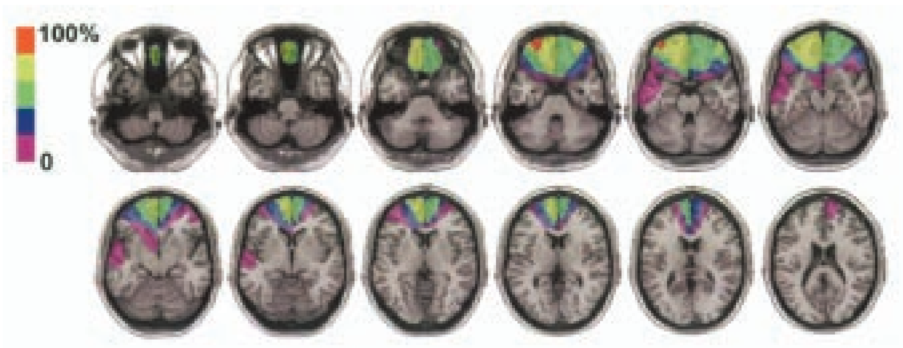

Figure 10. Degree of overlap of the orbito-frontal lesions in the 5 investigated patients.

A wavelet analysis was applied to the EEG data to extract the alpha activity. While induced alpha activity (alpha power) decreased after stimulation, evoked alpha (phase-locked activity) increased. This is due to a phase resetting of the alpha rhythm after stimulus onset. The increase of evoked alpha activity was significantly stronger for orbito-frontal patients than control subjects.

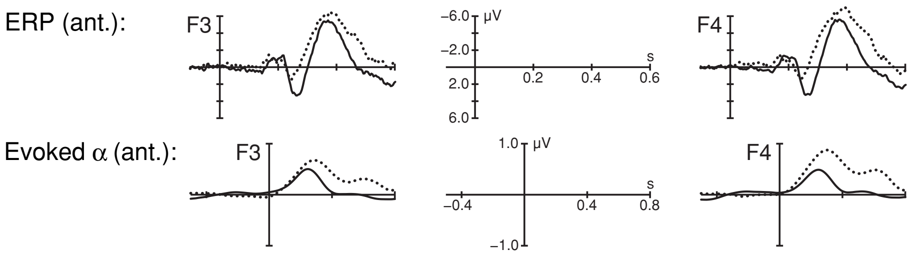

Figure 11. ERPs (top) and evoked alpha activity (bottom) of orbito-frontal patients (dotted) and control subjects (solid). ERPs show a suppression of early components, while evoked alpha shows an increase due to excessive synchronization.

Previous findings have reported larger evoked alpha responses after stimulation for elderly than for young subjects. It has been speculated that frontal cortex is responsible for this increase of evoked alpha activity. Our findings support the previously formulated hypothesis that frontal cortex regulates cortical alpha activity in the human EEG.

Lateralization of prosody during language production: A lesion study

2.5.9

Schirmer, A., Alter, K., Kotz, S.A. & Friederici, A.D.

The present study is aimed at specifying the lateralization of prosody in the brain. Therefore, the speech production of six right hemisphere lesion patients and five left hemisphere lesion patients was compared to that of seven normal controls using a question-answer-paradigm.
In the experimental session, subjects were asked to read a sentence aloud (e.g., *Peter promised to support Anna and to clean the office*.). Then the examiner asked a question concerning a sentence constituent (e.g., *Who promised to support Anna?*). In order to answer this question, subjects had to repeat the sentence with the correct intonation, i.e. focusing on the questioned constituent. Using this procedure we induced two focus conditions. 'Wide focus', i.e. non-restricted focus, was realized when subjects read a sentence the first time. When reading the sentence a second time subjects had to realize 'narrow focus' while stressing the questioned constituent. Subjects' speech production was recorded and later analyzed for fundamental frequency and time structure.
Acoustic analyses indicated a preserved ability in patients to differentiate between the experimental conditions via prosody. Nevertheless, there were some deficits. Under wide focus, left hemisphere patients showed time structure deficits as they made long pauses, exhibited a short word duration and failed to realize prefinal lengthening. When realizing narrow focus, both patient groups had difficulties with fundamental frequency, as they some times failed to show the typical pattern for the focused constituent found in normals. Stronger prosodic deficits in left hemisphere patients, as compared to right hemisphere patients, suggest a left hemisphere superiority when processing linguistic prosodic information. However, the fact that right hemisphere patients mainly exhibited difficulties in fundamental frequency whereas left hemisphere patients showed stronger difficulties when expressing time structure information suggests a specialization of the two hemispheres in handling the different prosodic parameters. The present results, therefore, support functional as well as parameter dependent hypotheses of the lateralization of prosodic processing in the brain.

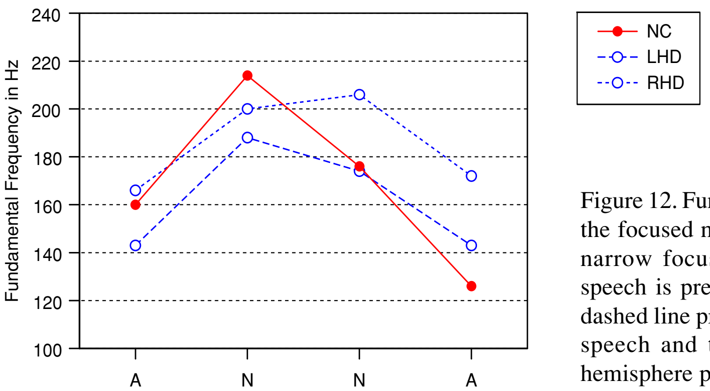

Figure 12. Fundamental frequency contour for the focused noun phrase (e.g., 'Anna') in the narrow focus condition. Normal control's speech is presented with the solid line. The dashed line presents left hemisphere patient's speech and the dotted line presents right hemisphere patient's speech.

2.5.10 Processing of verb-argument structure and subcategorization information in brain-damaged patients: Event-related potential evidence

Kotz, S.A.[1], Frisch, S.[2] & Friederici, A.D.[1]

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The processing of verbs is characterized by the fact that verbs can (or must) take complements. These complements are semantically as well as syntactically specified in the lexical entry of each verb. Semantically speaking, a verb such as '*besuchen*' (to visit) expresses an event which has two participants, one doing the visiting (agent) and one who is visited (patient). Syntactically speaking, the verb '*besuchen*' needs two expressions as complements in order to form a grammatical sentence, namely two noun phrases (e.g., *Der Junge besucht den Mann* / The boy visits the man). ERP recordings of verb argument violations (e.g., *Der Junge grinst den Mann* / The boy grins the man) elicit a biphasic ERP pattern, namely a negativity (resembling an N400 component) and a positivity (P600) (e.g., Frisch, 2000). This pattern suggests that violations of this type involve semantic as well as syntactic processing.

Processing of verb complements also play a central as well as a controversial role in the discussion of agrammatism (e.g., Grodzinsky, 2000; Friederici & Gorrell 1998; Frisch et al., 2000). It is assumed that Broca's aphasics detect argument structure violations (e.g., complements), but their detection may rely on semantic aspects inherent to an argument structure violation. On the other hand, Wernicke's aphasics seem not to be able to detect an argument structure violation, possibly due to missing the semantic aspect of the verb argument structure. We therefore set out to test verb argument violations in patients with anterior (including Broca's area) and temporo-parietal lesions measuring the ERP.

Preliminary results indicate that the biphasic pattern of a negativity followed by a positivity in the ERP is modulated as a function of lesion site. While patients with anterior lesions display a negativity, but no positivity, patients with temporo-parietal lesions show the reversed picture. Functionally speaking, this indicates differential sensitivities towards the semantic and syntactic aspects of verb-argument structure processing in the two groups of aphasic patients as reflected in the ERP.

2.5.11 Functional MRI language lateralization: Contributions from task design, performance and stimulus modality

Hund-Georgiadis, M.[1] & von Cramon, D.Y.[1,2]

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The influence of different task demands, task designs and presentation modalities on the functional MRI activation patterns during a language lateralization task was investigated in a group of 14 right-handed control subjects. A word classification task was presented as an appropriate target task to evoke language-related activation in the inferior frontal gyrus (IFG). The choice of the contrasting baseline task was demonstrated to have a major impact on the functional outcome: while a fixation baseline elicited activations in the inferior frontal gyrus of both hemispheres, a non-semantic perceptual control task helped to isolate the relevant target task of word classification. The modality of stimulus presentation did not influence the functional data: auditory and visual presentation modes broadly evoked activations in similar brain regions during word classification. Moreover, minor differences in task performance and the side of the responding hand did not interfere with the functional activation patterns of the target task. Our study clearly shows that the choice of an appropriate baseline task in a blocked design is essential to obtain reliable functional maps of the target task of lexico-semantic processing. In particular, our data suggest that a pure resting condition is not an appropriate baseline because it evokes activations in other cognitive networks that may interfere with the relevant activation and result in flooding of the functional data. Whenever functional MR data analysis is performed based on contrasting or subtracting target task and control condition, knowledge thereof is important for the understanding of the data.

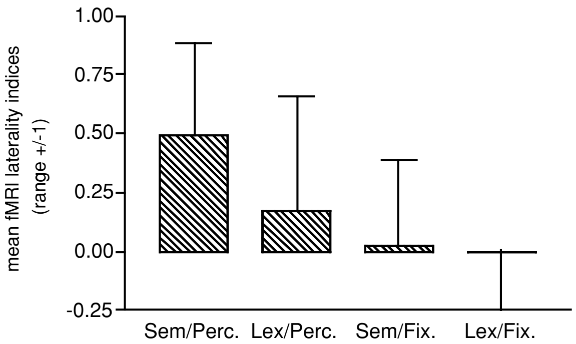

Figure 13. Influence of the applied baseline task on the overall laterality index in different word classification tasks, contrasted with a fixation baseline and a non semantic structural classification task.

On-line syntactic procedures in Parkinson patients: Evidence from ERPs

2.5.12

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Friederici, A.D.[1], Kotz, S.A.[1], Werheid, K.[1], Heim, S.[1] & von Cramon, D.Y.[1,2]

This project investigated lexical and syntactic aspects of language processing in patients with Parkinson's disease. We used ERPs as an indicator of processing syntactically or semantically incorrect and correct sentences presented auditorily. Previous studies in healthy subjects in the auditory domain have shown that syntactic phrase structure violations correlate with an ELAN component followed by a P600, whereas semantic violations correlate with an N400 component. Studies in patients with circumscribed lesions demonstrate that the ELAN is selectively absent in patients with left anterior cortical lesions, whereas the ELAN is present in patients with subcortical left anterior (basal ganglia) lesions. From these data we concluded that cortical rather than subcortical brain regions in the left hemisphere support early automatic syntactic processes.

Recently Ullman et al. (1998) argued that syntactic procedural knowledge is supported by the frontal/basal ganglia circuit. Our data with the basal ganglia patients, however, appear to be evidence against this view. However, Ullman (CUNY, 2000) reasoned that the conflicting results could be explained in the following way: impaired output from the basal ganglia (as in Parkinson patients) may hamper syntactic processes more than no output from the basal ganglia (as in basal ganglia lesioned patients).

This hypothesis was tested in a study investigating Parkinson patients with the same paradigm previously used with lesion patients.

A total of 8 Parkinson patients were submitted to an auditory sentence processing ERP study including correct, syntactically incorrect and semantically incorrect sentences. We used ten age matched participants as controls. As expected, control subjects displayed an N400 component for the semantically incorrect sentences and an ELAN followed by a P600 for the syntactically incorrect sentences. Parkinson patients also displayed an N400 component for semantically incorrect sentences. Most interestingly, these patients showed a clear ELAN component reflecting early syntactic processes, whereas no clear P600 could be observed (see Fig. 14). These data suggest that early automatic parsing procedures are intact in these patients. It is rather the late syntactic processes, such as syntactic repair and syntactic integration, which are affected by Parkinson's disease.

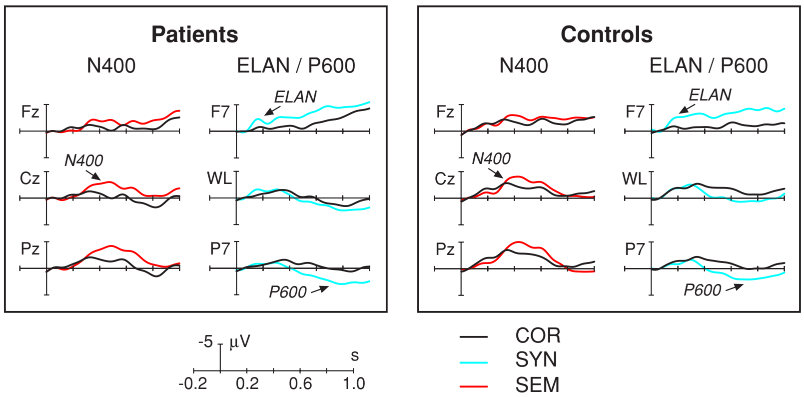

Figure 14. ERPs elicited by correct (black),semantically incorrect (red;) and syn-tactically incorrect (blue) sentences. The comparison of correct and incorrect sentence types is shown at selected electrode-sites for the patients (left side) and the controls (right side).

2.5.13 Intact implicit sequence-specific learning in advanced Parkinson's disease

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supported by BMB+F / IZKF Leipzig

In the face of a growing body of neuropsychological research on the cognitive alterations in Parkinson's disease (PD), deficits in motor-based procedural learning are still controversial. One of the standard paradigms for implicit procedural learning is the serial reaction time task, in which visual stimuli successively appear at different locations and participants respond by pressing corresponding keys. During training of a regular sequence, reaction times decrease due to general training effects. When switching to a random sequence thereafter, reaction time increments indicate sequence-specific learning, even if explicit knowledge about the sequence remains fragmentary. In this study, we used a patient version of a serial reaction time task devised by Ziessler and Nattkemper (in press). In this task, the complexity of interstimulus (S-S) and response-stimulus (R-S) transitions can be varied while the response sequence remains constant.

We examined 18 patients with PD and 18 age-matched controls. As previous research indicates that deficits in procedural learning tasks may be dependent on disease severity, only patients with advanced PD (Hoehn & Yahr, 1967, stage ≥ 2) were included in the sample. Participants were assigned to condition S1 (low S-S/R-S complexity) or S4 (high S-S/R-S complexity). Comparison of patients and controls revealed a reduced reaction time decrement throughout the task, but equal reaction time increments when switching to the random blocks (see Fig. 15). Our findings support the view that motor learning in general, but not sequence-specific learning is impaired in Parkinson's disease.

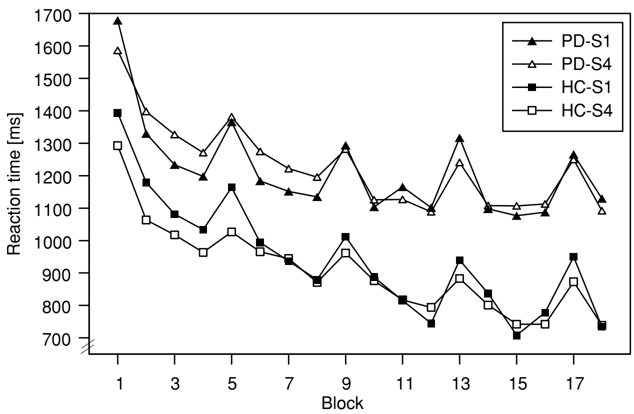

Figure 15. Mean reaction times per block and condition in patients with Parkinson's disease (PD) and healthy controls (HC). Random sequences were administered in Blocks 5, 9, 13, and 17.

2.5.14 Performance of implicitly learned sequences in early Parkinson's disease: An fMRI study

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supported by BMB+F / IZKF Leipzig

In this study, the effects of implicit procedural learning were investigated by an fMRI-adapted variant of the Serial Reaction Time task. In this task, participants respond to series of visual stimuli appearing at different locations by pressing corresponding keys. Unbeknown to the subjects, regularly cycling sequences are administered during a training phase. Usually, reaction times decrease during the training phase (general training effects) and increase again after switching to a random sequence (sequence-specific learning). Previous imaging studies have found a large variety of cortical and striatal regions activated during regular versus random sequence conditions. While the striatum is assumed to be involved in sequence learning, there are no imaging studies on patients with striatal dysfunction so far.

Our fMRI study was aimed at investigating brain activation in seven patients with early Parkinson's disease (Hoehn & Yahr, 1967, stage ≤ 2) and age-matched controls during performance of regular versus random sequences. To focus on the effect of previous sequence learning, subjects were pretrained before scanning. Patients showed reduced general training effects during pretraining, but similar sequence-specific learning during the fMRI session. Imaging revealed highly similar brain activations of the two groups, involving frontomedian, anterior cingulate, and precuneate/retrosplenial areas (s. Fig. 16A). Activation of the right putamen was found in controls, but not in patients (s. Fig. 16B). A second level analysis revealed that the magnitude of individual learning effects was significantly correlated with mean z-values of left medial prefrontal activation. Thus, after the initial training phase, frontomedian rather than striatal activations are decisive for performance of structured sequences.

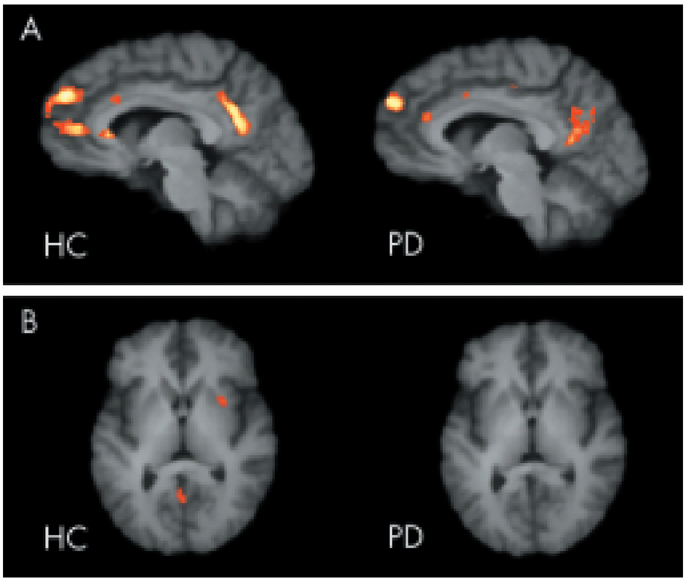

Figure 16. Comparison of sequence and random blocks for patients with Parkinson's disease (PD, z value > 4.0) and healthy controls (HC, z-value > 4.5). (A): Activations in the medial plane (x = 8). (B): Activation of the right putamen in controls (z = 0).

Localization of multitasking deficits in neurological patients and older subjects

2.5.15

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supported by BMB+F / IZKF Leipzig

The issue of this study was to localize multitasking deficits in healthy older subjects and two groups of neurological patients. Based on the dual-task paradigm we asked whether multitasking deficits are caused by interference between the perception processing stages of the different stimuli. Older subjects (M= 57 years), patients with Parkinson's disease (PD) and patients with frontal lobe damage following closed head injury (CHI) were presented with an auditory and a visual choice reaction task, separated by varying SOAs. The perceptual difficulty of the visual stimulus was manipulated by presenting high intensity visual stimuli (easy Task 2 condition) and low intensity visual stimuli (hard Task 2 condition). If the perception stages of both task do not interfere, the locus-of-slack logic (Schweickert, 1983) predicts an underadditive interaction between SOA and perceptual difficulty on visual Task 2 reaction time. Older subjects, PD patients and CHI patients failed to show this underadditive interaction. Surprisingly a decline of performance for older adults, patients with PD and CHI patients was observed under condition of high intensity (easy Task 2 condition) and short SOA (Fig. 17, upper and lower panel/ left). In a second experiment we could prove that older adults and PD patients are capable to process the auditory and the visual perception stages without interference if the high intensity of the easy Task 2 stimuli was diminished (Fig. 17, upper panel/ right). On the contrary, it was not possible to optimize perception processing for CHI patients with frontal lobe damage (Fig. 17, lower panel/ right).
These results indicate increased input interference following frontal lobe damage. Probably, this increased input interference is caused by a generalized inhibitory deficit, resulting in decreased ability to coordinate different input channels in dual-task situations. The conclusion is drawn, that increased vulnerability for input interference should contribute to multitasking deficits in older subjects, PD patients and CHI patients.

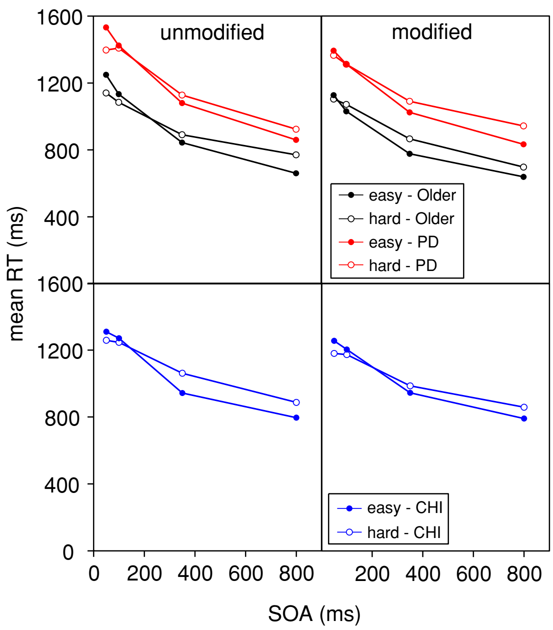

Figure 17. Mean Task 2 reaction time as a function of SOA and perceptual difficulty (easy = high intensity visual stimuli; hard =low intensity visual stimuli) for older subject, PD patients (upper panel) and CHI patients (lower panel) under unmodified (left) and modified (right) stimulus conditions.

2.5.16 Dichotic listening in patients with splenial and nonsplenial callosal lesions

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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 include 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, confirming 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

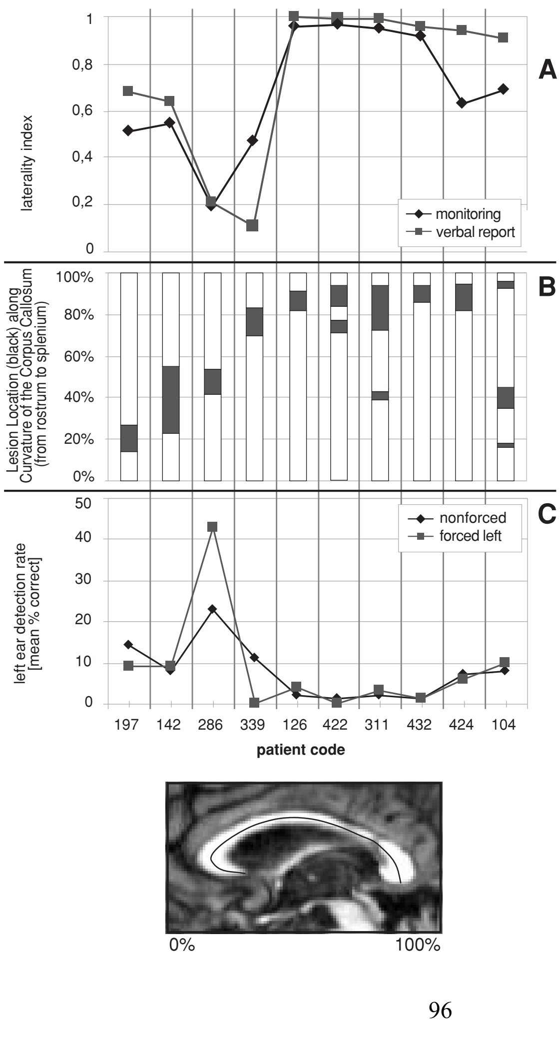

Figure 18. Individual patient performance in relation to lesion location. (A) Laterality scores in the nonforced dichotic monitoring and verbal report tasks, (B) Lesion location in percent of the curvature of the corpus callosum from the tip of the rostrum (0%) to the end of the splenium (100%), (C) Left ear detection rate in the nonforced and forced left dichotic monitoring tasks.

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, an alternative explanation may be that left ear suppression is not caused by disruption of auditory callosal transfer, but by disruption of interhemispheric transfer of attentional target detection signals originating in the temporo-parietal junction area.

Reduced serotonin transporter density in post-stroke pathological crying: A [123I]β-CIT SPECT study

2.5.17

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[4] *Cognitive Neurology, and*
[5] *Psychiatry, University of Leipzig*

Background: Pathological crying (PC) is a neuropsychiatric disorder characterized by an excessive tendency towards crying after brain damage. Selective serotonin reuptake inhibitors are very effective in treating this condition (Müller et al., 1999). To elucidate the role of serotonin (5-HT) neurotransmission for PC the central 5-HT transporter density was investigated with [123I]β-CIT SPECT (Murai et al., in press).
Method: Six patients with PC and nine patients without PC after unilateral cerebral infarction were investigated. The specific to non-specific binding ratios were calculated for midbrain/pons and thalamus/hypothalamus.
Results: In the PC group, the midbrain/pons binding ratios were significantly lower than those of the non-PC group (1.26 ± 0.51 vs. 1.93 ± 0.59, respectively; $p = 0.025$). There was no significant difference in the thalamus/hypothalamus binding ratios between these two groups (Fig. 19).
Conclusions: These preliminary findings suggest that a low level of brainstem 5-HT transporter expression is associated with PC after stroke.

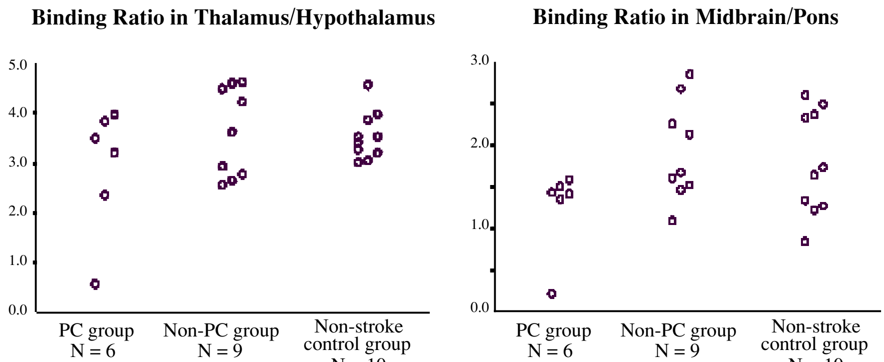

Figure 19. [123I]β-CIT binding ratios in stroke patients with pathological crying (PC), stroke patients without PC, and non-stroke control subjects.

2.5.18 Subanesthetic isoflurane affects task-induced brain activation in a highly specific manner: An fMRI study

Schwarzbauer, C. & Heinke, W.

Investigation of sedative effects produced by anesthetics in conscious volunteers offers the possibility to study the interaction of these drugs with cognitive processes. It should therefore provide further evidence for a better understanding of the general mechanism of anesthetic action. In the present study, we investigated the effect of subanesthetic isoflurane on functional brain activation induced by a visual search task.

In order to separate isoflurane-related effects from carry over effects (e.g., habituation, fatigue, learning) we performed a statistical comparison between an isoflurane group and an independent control group; each group consisted of 10 healthy male volunteers. The resulting interaction map is depicted in Figure 20. The red-to-yellow color scale displays the level of significance. The threshold was set to z = 3.1. Significant decrease in task-induced activation is visible in three distinct cortical regions: the right anterio-superior insula, the left intraparietal sulcus (ascending / horizontal branch), and the right intraparietal sulcus (horizontal branch). Voxels with a significant increase in task-induced activation were not found at this level of significance. Regions of significant task-induced activation, which were not affected by isoflurane, are shown in uniform blue. These regions include the lateral geniculate nucleus, the striate and extrastriate visual cortex, the motor cortex, the supplementary motor area, and the left putamen as well as large parts of the anterior insula, and the banks of the intraparietal sulcus.

In conclusion, our findings indicate that subanesthetic isoflurane affected task-induced activation in specific neural networks rather than causing a global decrease in functional activation.

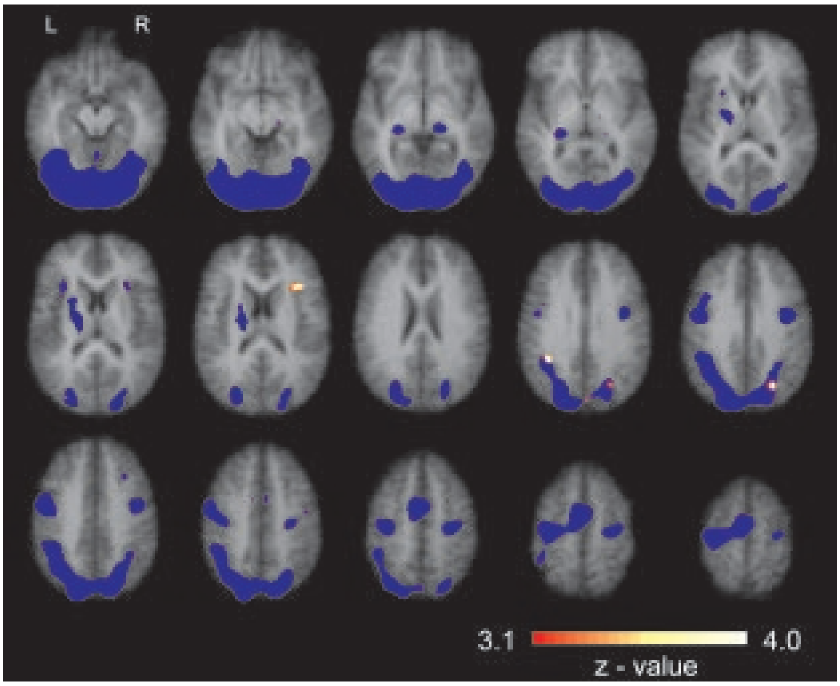

Figure 20. Functional interaction map showing isoflurane-related changes in functional brain activation induced by a visual search task. L = left; R = right.

T_2*-weighted MR imaging as a tool to examine diffuse axonal injury

2.5.19

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Wiggins, C.J.[1], *Gruber, O.*[1], *Scheid, R.*[2] & *von Cramon, D.Y.*[1,2]

The appearance of focal signal losses in T_2*-weighted MR images has been attributed to remaining iron-containing deposits resulting from cerebral microbleeds (Atlas, 1998). This interpretation has been recently confirmed with histopathological methods (Roob, 1999; Fazekas 1999). On this basis, we have added a T_2*-weighted protocol to the set of standard measurements we perform at 3T on patients.

A section of this patient population has shown neurological deficits that were attributed to traumatic brain injury. Prior to the addition of the T_2*-weighted protocol, many of the T_1- and T_2-weighted scans of these subjects showed no evidence of lesions.

The factors that induce diffuse axonal injury, with shearing of the nerve fibers, can also lead to the rupturing of small, adjacent blood vessels. The resultant iron deposits are then clearly detectable on a T_2*-weighted image. The images below show the same area using a T_2 and a T_2*-weighted sequence. While an area of hypointensity is seen on the T_2-weighted image (2.6.8, Fig. 7), several further lesions are observed on the T_2* image (2.6.9, Fig. 8).

In addition to providing evidence of diffuse axonal injury, in cases where no evidence is found on T_1- and T_2-weighted images, the T_2*-weighted protocol has also helped in classification of small hypointensities seen on T_1-weighted images, where no corresponding signal changes could be seen on the T_2-weighted scans.

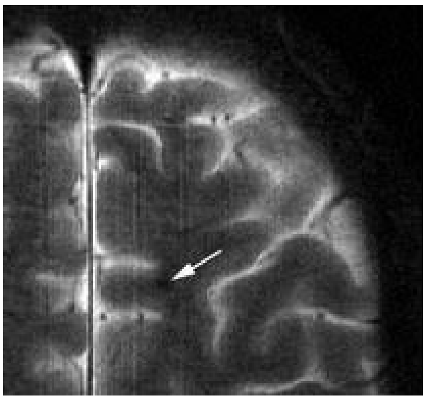

Figure 21. T_2-weighted image. A single lesion is detectable. Sequence details: RARE, FOV=25cm, TE=21.7ms, TR=8500ms, RARE factor=16, Matrix=512x512, FOV=25x25cm, Slice thickness=5mm.

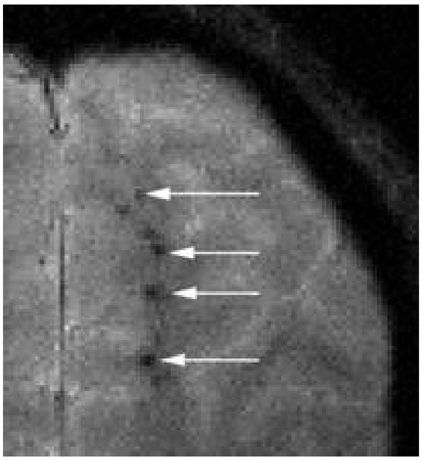

Figure 22. T_2^*-weighted image. Note the lesions that were not apparent on the T_2 image. Sequence details: Gradient echo, TE=15ms, TR=700ms, Flip angle=25, Matrix=256x256, FOV=19.2x19.2, Slice thickness=5mm.

2.5.20 Integration of functional MR and neuronavigation in patients with brain tumors adjacent to primary motor cortices

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Combination of preoperative fMRI, neuronavigation and intraoperative SSEP reversal was used to define eloquent cortical areas pre- and intraoperatively in patients with brain tumors. The aims of this cooperative study were to improve pre-operative neurosurgical planning, to evaluate the reliability of acquired functional data and to control the patient's outcome after surgery. Neuronavigation has become an important tool for presurgical planning and intraoperative guidance. Online fusion of functional and structural information may be essential to reduce the risk of surgical complications. Thirteen patients with tumors adjacent to the primary motor cortex were examined. FMRI based motor mapping and a neuronavigational planning procedure including image fusion of functional data were performed preoperatively. After intraoperative definition of the central sulcus by SSEP phase reversal and localization of the premotor cortex by direct cortical stimulation, patients underwent a tumor resection or biopsy.

In all patients, the central sulcus and the motor cortex were successfully located with the help of SSEP phase reversal and direct electrical stimulation and were correlated with the fMRI data. Neurological control could verify a good postoperative outcome. Two patients had progredient paresis after surgery, which remitted within a month completely, the others were discharged from hospital without further complications and neurological deficits.

Preoperative fMRI, neuronavigation and intraoperative electrophysiological localization of the motor cortex are reliable methods to improve neurological outcome. Our results justify the additional expense for preparing and realizing surgery in favor of a better benefit risk ratio.

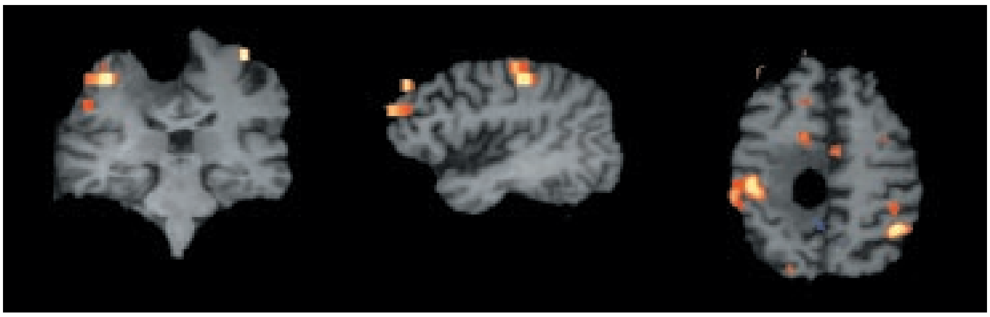

Figure 23. Integration of anatomical data and functional MR motor mapping results prior to neurosurgical management in a patient with a precentral and paramedian brain tumor.

Thirty years ago, Nauta (1971) noted that *"The frontal lobe, despite decades of intensive research by physiologists, anatomists, and clinicians, has remained the most mystifying of the major subdivisions of the cerebral cortex."* With the development of modern neuroimaging techniques and more sophisticated cognitive theories we are now in a position to attempt a further delineation of the functional neuroanatomy of the frontal lobe in humans.

While the traditional approach to frontal lobe functions focuses on the study of executive functions, i.e., those cognitive processes required for the planning, organization and conduction of complex behaviors, we take a more comprehensive approach and include, besides studies on prefrontal brain regions, research projects concerned with precentral and premotor cortices. In addition, in comparing and contrasting the results from various imaging studies from our laboratory, it has become increasingly clear that the functions of fronto-median structures, - including the anterior cingulate cortex (ACC), the supplementary motor cortex (SMA) and the pre-SMA - , must be included in a description of the frontal lobes.

After having established activation in the premotor cortex during sequencing tasks, a series of experiments were conducted to further describe the factors influencing this activation. (2.6.1, 2.6.2, 2.6.3). Issues investigated were the information type (object-specific, spatial, or temporal properties of serial events), perceptual influences on ventrolateral premotor hand field activation (graspability of objects), and effects of predictability and periodicity in serial processing.

Working memory processes, in particular those related to the maintenance and manipulation of working memory contents, have also been ascribed to the frontal lobe. Using suppression and dual task designs, (2.6.8, 2.6.9, 2.6.10) tested a model postulating different maintenance mechanisms in working memory. Furthermore, a neuro-pharmacological study investigated the effects of noradrenergic modulation on manipulation aspects of working memory (2.6.11).

A series of experiments built on previous work on tasks targeting the use of executive functions, such as inhibition, task set management, and response scheduling. Using a Stroop paradigm (2.6.4) showed that while stimulus interference tended to activate lateral regions, response conflict involved the pre-SMA more. (2.6.7) studied the costs of executive processes during dual-task performance. When two tasks were to be carried out concurrently, their coordination led to activation in lateral prefrontal cortex. The interference between an effector-related imitation tendency and a task-induced response requirement was the topic of (2.6.6). Once more, lateral activation was observed when an inhibition of imitative response tendencies was required.

Combining ERPs and fMRI for studying error detection and response competition, (2.6.5) could dissociate functions of the pre-SMA from those of the ACC. Error detection in the context of complex everyday actions was studied in (2.6.13). The perception of action slips led to activation both in premotor cortex and the ACC.

Finally, we extended our work on higher level cognitive processes. We continued the project on coherence building during language comprehension. A study using auditory presentation confirmed that fronto-median activation for coherent sentence pairs is modality-independent (2.6.12). Second, an experiment on judgment processes showed that evaluative or uncertain decisions also activate fronto-median regions (2.6.14).

Although the main focus of our research was on functional brain imaging, we also conducted a fNIRS study (see 2.8.7) using the Stroop paradigma and an extensive number of patient studies. By describing the functional deficits of patients with frontal lobe lesions, we attempt to collect converging evidence for the interpretations of our imaging data. When possible, we use the same methodology for both patient and imaging experiments. A more detailed description of some of these studies is given in section (2.5).

2.6.1 Functional organization of the lateral premotor cortex: FMRI reveals different regions activated by anticipation of object properties, location and speed

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

Previous studies have provided evidence that the lateral Premotor Cortex (PMC) is involved in representations triggered by attended sensory events. However, little is known about functional specialization within human lateral premotor areas. In the present study, fMRI was used to investigate if attending to object-specific (O), spatial (S), or temporal (T) properties of the same sensory event, i.e., moving objects, involves different premotor areas. Twelve students (4 male, mean age: 23.6) participated in the study. Tasks were presented in a random trial design and announced by visual cues. A baseline condition (B) controlled for perceptual and motor effects. We found a frontoparietal 'prehension network' comprising the Pre-Supplementary Motor Area, the ventral PMC, and the left anterior Intraparietal Sulcus to be activated independently of the attended stimulus property, but most intensively during object-related attention. Moreover, several areas were exclusively activated according to the attended stimulus property, as shown in Figure 1. Particularly, different PMC regions responded to the Object (O) task [left superior ventrolateral PMC], the Spatial (S) task [dorsolateral PMC], and the Timing (T) task [vPMC/BA44]. These results indicate that the representation of different stimulus dimensions engage distinct premotor areas and, therefore, that there is a functional specificity of lateral premotor subregions.

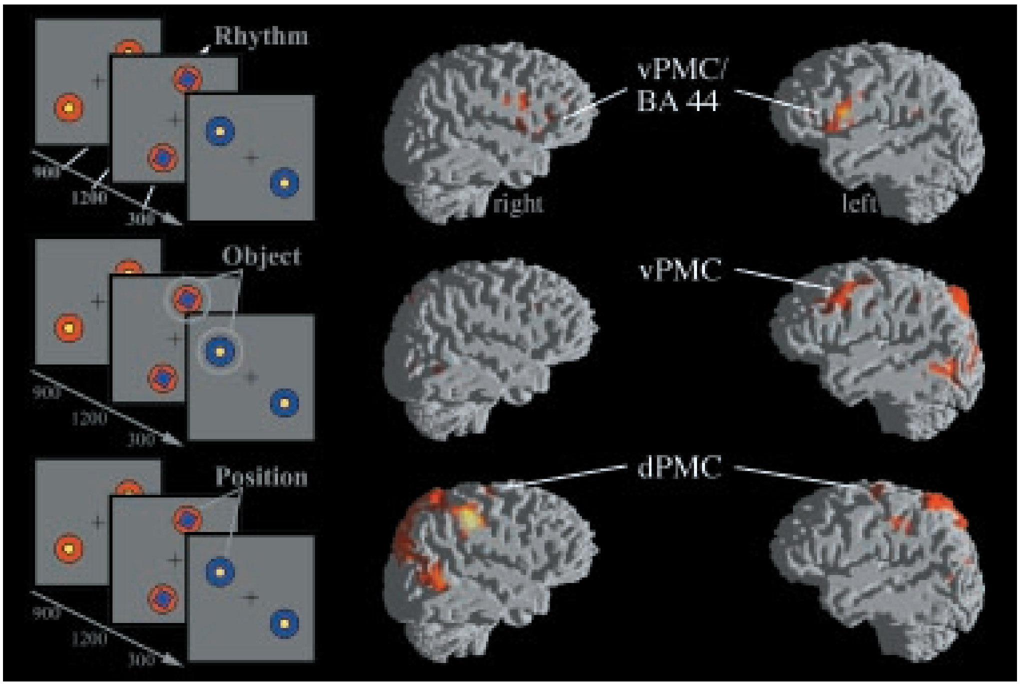

Figure 1. Attending to different properties of sequential events (direct task contrasts). An example for trial stimulation is given at the left. According to the attended property, different premotor areas responded preferentially to movement rhythm (most inferior ventrolateral, extending into BA44), object features (ventrolateral), and spatial positions (dorsolateral).

2.6.2 Influence of expectation and repetitive structure in sequence processing on premotor activation in fMRI

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

Previous fMRI studies have shown that the lateral Premotor Cortex (PMC) is highly responsive to repetitive events, which are characterized by both repetitive and expectable structures. The present study investigated if only one of these two factors is exclusively effective on lateral premotor activation. Four conditions were presented in a random trial design. In each trial, 12 pictures of circles with different diameters were presented subsequently for 500 ms. Subjects had to decide at the end of the trial if one of the last three pictures was somehow irregular, i.e., a color deviant (Random Series, RA) or a diameter deviant (Order Series). In the RA condition, diameters of circles changed randomly (not repetitive, not expectable). In three Order Series conditions were presented, where diameters of circles changed orderly: monotone series (MO) (not repetitive, but expectable), repetitive series (RE) (both item repetitive and expectable) and alternating series (AL) (formally repetitive and expectable). Effects of expectancy were tested by contrasting monotone with random series. Effects of repetitivity were tested by contrasting repetitive with monotone series.

As shown in Figure 2, both expectancy and repetitivity elicited lateral PMC activation, with Z-scores and extension slightly pronounced by repetitivity (middle panel). Moreover, formally repetitive series elicited even additional activation within the same area relative to item repetitivity (right panel). These findings indicate that the lateral PMC is sensitive to both expected and repetitive events, with a dominance of repetitive structures.

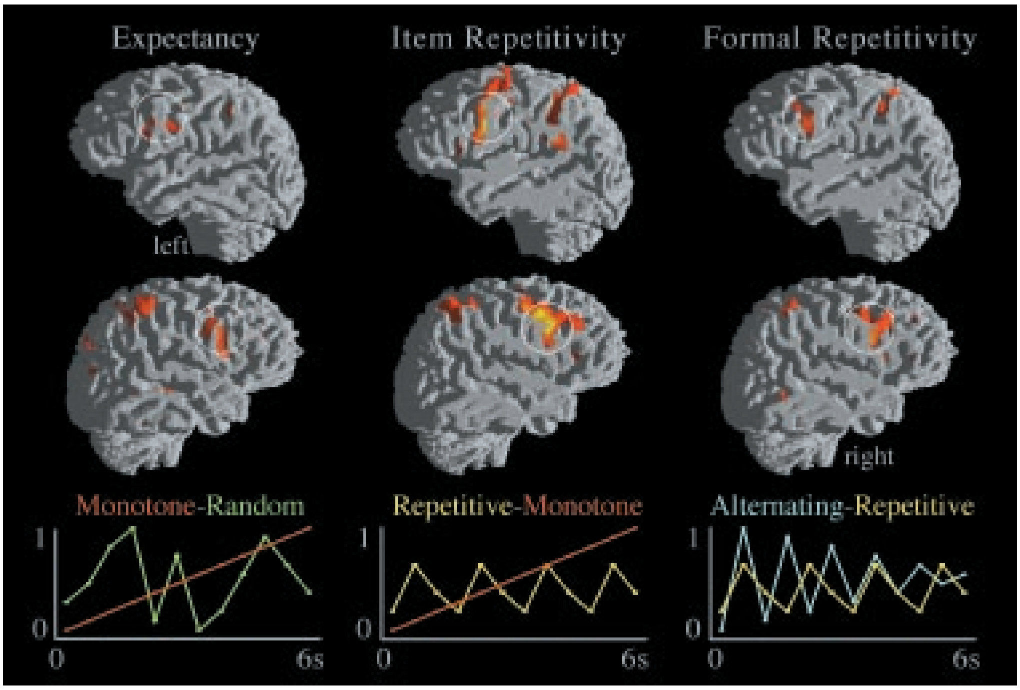

Figure 2. Effects of expectancy and repetitivity in serial processing. The lower panel shows the contrasted series in a time by difference diagram. The x-axis displays the time course of the stimulus presentation within one trial, with one stimulus each 500 ms. The y-axis displays the diameter differences between the presented circles from minimal (0) to maximal (1).

2.6.3 Perceptual responses in the ventrolateral premotor 'handfield': Effects of object graspability

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

Proceeding on the monkey model of ventral Premotor Cortex (vPMC, 'hand field') function in transforming object perception into manual action, two fMRI studies investigated if vPMC activation depends on the graspability of objects. Twelve healthy right-handed students participated in both experiments. In Experiment 1, abstract objects were presented in graspable (Item, *I*) and in non-graspable size (Pattern, *P*). In Experiment 2, abstract objects with (Contour, *C*) and without distinct contours (Non-contour Pattern, *N*) were presented. Except for the object presentation mode, tasks were identical in both studies. Subjects were asked to monitor a repetitive sequential stimulation for missing objects and indicate these order violations immediately. Baseline conditions not related to object processing controlled for visual perception and the go-nogo response mode. As shown in Figure 3, results were consistent in both experiments. Premotor handfield activation was found *both* during graspable and non-graspable object stimulation, relative to baseline, as long as distinct contours were presented (conditions *I, P,* and *C*). In contrast, no premotor hand field activation was found during the Non-contour Pattern condition (*N* condition). The findings suggest that the monkey model of object-action transformation within the vPMC apply also to the human brain. Particularly, distinct object contours appear to be an essential prerequisite for activating the premotor hand field.

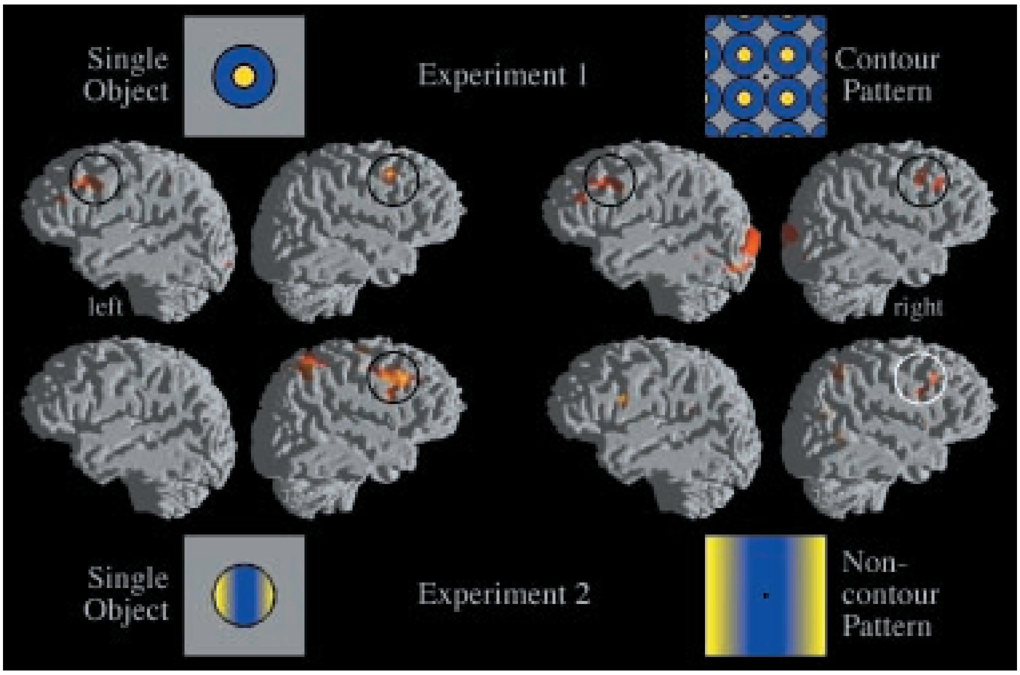

Figure 3. Attending to 'graspable' objects and to 'non-graspable' objects in Exp. 1 (upper panel) and Exp. 2 (lower panel), relative to baseline condition. The object tasks elicit activations within the vPMC hand field only if distinct object contours are presented.

2.6.4 Color-Word Matching Stroop task: Separating interference and response conflict

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

Cognitive interference occurs when the processing of a specific stimulus feature impedes the simultaneous processing of a second stimulus attribute. The Stroop task (Stroop, 1935) has become a prototypical interference task. It requires a person to respond to a specific dimension of a stimulus while suppressing a competing stimulus. Previous PET and fMRI studies argued that interference is reduced within the 'cognitive division' of the cingulate cortex (Bush et al., 1998; Pardo et al., 1990; Carter et al., 1995) . An alternative view put forward in recent articles is that the anterior cingulate cortex (ACC) is primarily involved in functions contributing to the process of selecting, preparing and executing motor responses determined by decision-making processes mediated by lateral prefrontal cortex (Paus et al., 1995, 1998).

In our study, we used a variation of the Stroop task, which is based on a version from Treisman & Fearnley (1969). In this Color-Word Matching Stroop version, interference takes place at a conceptual level and is separated from the response preparation. Subjects were presented two words (e.g., GREEN written in blue ink; BLUE written in black ink), and they had to match the color of the first word with the meaning of the second word (e.g., 'Does the color of the first word correspond with the meaning of the second word?'). Varying the dimension of the first word (neutral, congruent or incongruent words to the presented color) allows for the investigation of interference effects. The conceptual interference between the two dimensions of a stimulus within a matching process was separated from the response preparation and execution process. The main difference between the two tasks is that subjects in the Matching Stroop task compare two attributes of a stimuli while in the traditional Stroop task they generate a response to match one attribute of a stimulus.

There were three main findings: (1) The Color-Word Matching Stroop task produced reliable and pronounced interference effects. This version allows the investigation of facilitation effects in a event-related design, an advantage which is not available with other versions of the Stroop task suitable for fMRI. (2) No significant ACC activation could be found, indicating that the ACC is not involved in interference per se, but in response conflict (see Fig. 4). It is argued that the ACC is involved in response selection, a process which was held low in the presently used version of the Stroop task. (3) Regions along the IFS appear to be involved in solving interference and task management (see Fig. 4).

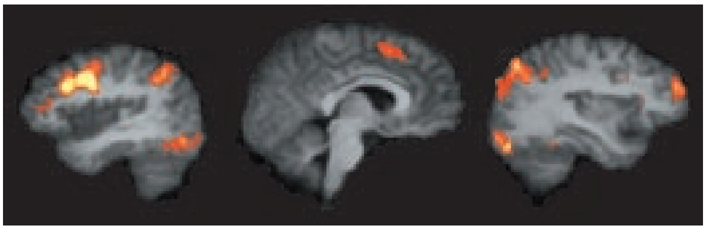

Figure 4. Averaged z-maps of the contrast comparing the interference vs the neutral condition mapped on a mean brain of 9 subjects. Left column: left lateral cortex (x = -40); middle panel: the left medial surface (x = 3); right panel: right lateral cortex (x = 29).

2.6.5 Error detection or response competition: A combined event-related fMRI and ERP study

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

Performance monitoring can be implemented by two possible systems, one that specifically detects and registers errors or one that is more generally sensitive to response competition, which is often associated with the commission of errors. In order to disentangle the neural substrates of response competition and error processing fMRI and ERP data were collected in two separate sessions from 12 young healthy subjects, who performed a speeded modified flankers task yielding a sufficient number of errors. In the fMRI experiment, similar networks were activated by response competition and error processing with several important subregional and extent differences (see Fig. 5, left). These differences were particularly obvious at the frontomedian wall: The pre-SMA (BA6 and BA8) was activated by response competition to a much higher extent than during errors. Especially BA8 responded selectively to response competition. In contrast, the cortex along the anterior cingulate sulcus (ACC, BA32/24c') was significantly more activated by error processing. In the response competition contrast, additional activations were found in the lateral premotor cortex (BA6) and even in the left sensorimotor cortex (left hand field; Note: subjects responded with the right hand). It seems plausible to interpret the motor cortex activation in the response competition contrast as a measure of response competition. Interestingly, no residual motor cortex activation was found in the error contrast, suggesting that response competition was not higher in erroneous than in correct incompatible trials, which is inconsistent with the response competition model.

Figure 5 (right) displays the response-locked ERP waveforms for compatible correct, incompatible correct, and incompatible erroneous trials. A clear error-related negativity

(ERN) was identified on erroneous incompatible trials peaking about 80 ms after the response. Interestingly, no negative deflection of similar properties is present in the response-locked averages of the correct trials as would be expected by the response competition model.

In sum, the data show a dissociation between the neural activities elicited by response competition and error processing. Therefore, they favor a dual-process model of performance monitoring based on two systems specialized on (1) error detection and (2) detection of response competition.

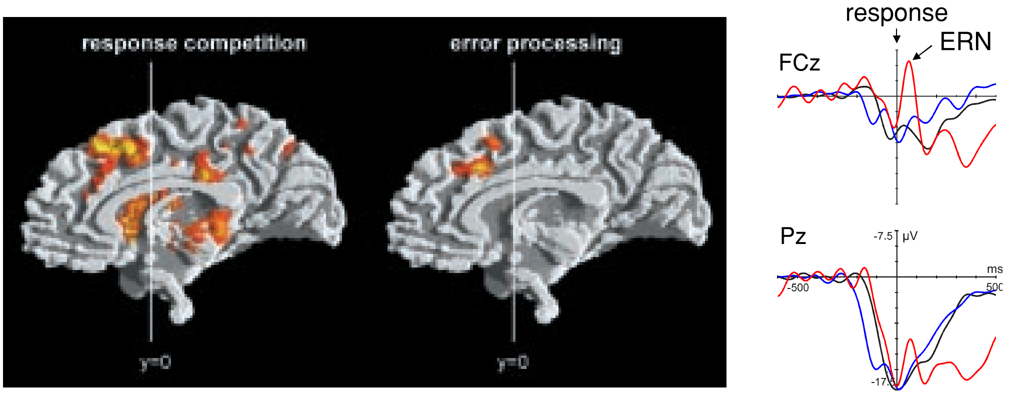

Figure 5. FMRI activations within 7 mm depth in the two contrasts of interest projected on the median wall of a white matter segment, z > 3.09 (left side); response-locked ERPs in the same subjects during the same task (right side).

2.6.6 The inhibition of imitative response tendencies

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

Recent neurocognitve findings show that perception and execution of actions are intimately linked. The mere observation of an action seems to evoke a tendency to execute that action (Brass et al., 2000). Since imitation is not sensible in many everyday situations, imitative response tendencies usually have to be inhibited. From neuropsychological research it is known that patients with frontal lesions sometimes have problems inhibiting imitative response tendencies (Lhermitte et al., 1986; Luria, 1980). Nevertheless, the inhibition of imitative response tendencies has never been investigated using brain imaging techniques. Former work on response inhibition and interference control has focused on tasks like the stroop-task or the go/no-go task.

We have carried out an event-related functional magnetic-resonance imaging study (efMRI) in order to investigate the cortical mechanisms underlying the inhibition of imitative response tendencies. The experiment utilizes a simple response task, in which subjects were instructed to execute predefined finger movements (tapping or lifting of the index finger) in response to an observed congruent or incongruent finger movement (tapping or lifting). The comparison of brain activation in incongruent and congruent trials revealed strong activation in the right dorsolateral prefrontal cortex (middle frontal gyrus), the right frontopolar cortex as well as the precuneus (see Fig. 6).

In sum, the results demonstrate that the inhibition of imitative response tendencies is achieved by a network of prefrontal and parietal brain regions. The key component of this network is the right dorsolateral prefrontal cortex, which might be responsible for updating the instructed action goal when a conflicting action goal is induced by the observed incongruent finger movement.

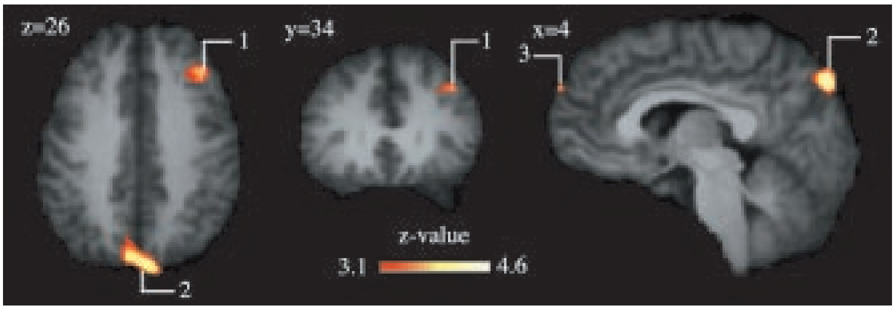

Figure 6. BOLD-response increase related to incongruent trials versus congruent trials in the middle frontal gyrus (1), the precuneus (2) and the frontopolar cortex (3).

2.6.7 The influence of temporal task overlap on executive control in dual-task performance

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The aim of our studies is to investigate the detailed characteristics of prefrontal cortex activity caused by executive control processes in dual-task performance. For this, a thorough theory about the underlying processes is necessary. To account for this, we used the paradigm of the psychological refractory period (PRP). In this paradigm, two stimuli are presented in rapid succession, separated by a variable amount of time (the stimulus-onset-asynchrony, SOA), with each stimulus requiring a response. Behavioral results typically show slowing of the second response with decreasing SOA. This is taken as evidence that the processing streams of the two tasks interfere with each other and that the amount of interference depends on the SOA. Based on Meyer and Kieras (1997) and DeJong (1995), we assume that executive processes are needed for resolving this interference. In a previous study incorporating the PRP-paradigm, we localized these executive functions with fMRI in the dorsolateral prefrontal cortex (inferior frontal sulcus, IFS and middle frontal gyrus, MFG).

As mentioned above, the amount of interference depends on the SOA, and executive control is needed for resolving this interference. Consequently, also the demands on executive control should depend on the SOA. Further on, if prefrontal activity represents this executive control, as indicated by our first study, the degree of activation should covary with the SOA. We tested this assumption by using three conditions incorporating large (100 ms SOA), moderate (300 ms SOA) and small or no (800 ms SOA) temporal overlap. As in our first study, subjects had to perform an auditory and a visual 3-choice-reaction task either concurrently (dual task) or separately (single tasks) during fMRI measurement. Dual task related activation was preliminary (7 subjects), assessed by an interaction contrast, which tests for activation which cannot be explained by the combined effects of the single tasks. First, we replicated the findings of our previous study: dual-task related activation was located along the IFS/MFG. Second, we were able to show, that these areas were less but still significantly activated with moderate overlap compared to large overlap. However, with small overlap, only an area located along the anterior IFS, was less activated in comparison to a large overlap, while there was no difference in posterior areas along the IFS/MFG previously also defined as dual-task related. So we carefully conclude, that activation along the IFS/MFG increases with decreasing SOA. With regard to the above mentioned theory, that the degree of executive control depends on the temporal overlap of the tasks, this would imply that prefrontal cortex is implementing this control in dual-task performance.

2.6.8 Domain-specific distribution of working memory processes along human prefrontal and parietal cortices

Gruber, O. & von Cramon, D.Y.

In a previous study, silent articulatory suppression was shown (1) to eliminate memory-related activity in classical verbal working memory areas and (2) to lead to the occurrence of other memory-related activations in prefrontal and parietal cortices. The present fMRI study was set in to investigate whether these brain regions activated by phonological working memory under articulatory suppression could be anatomically differentiated from prefrontal and parietal areas that are known to underlie visual working memory processes. Subjects performed different phonological and visual item-recognition tasks, during which colored letters in different fonts were presented and either the letters themselves or their colors or specific forms were to be remembered. Under conditions of articulatory suppression, both phonological and visual working memory processes activated similar prefronto-parietal networks but were found to be differentially distributed along several identical anatomical structures. In particular, while the phonological task variant yielded strong activations along the anterior intermediate frontal sulcus and the inferior parietal lobule, working memory for visual letter forms or colors preferentially activated more posterior prefrontal regions along the intermediate and superior frontal sulci as well as the superior parietal lobule (Fig. 7). In close analogy to the well-established functional neuroanatomy of working memory in non-human primates, we assume that these brain structures represent a multimodal working memory system whose subdivisions deal with different informational domains (see Fig. 7). Thus, the present study may provide new, convergent evidence for a functional homology between the intermediate frontal sulcus in humans and the principal sulcus in monkeys. Overall, the results suggest that a domain-specific topographical organization of neural working memory mechanisms in the primate brain is conserved in evolution. However, the findings also underline the critical dynamic influence that the additional availability of language may have on working memory processes and their functional implementation in the human brain.

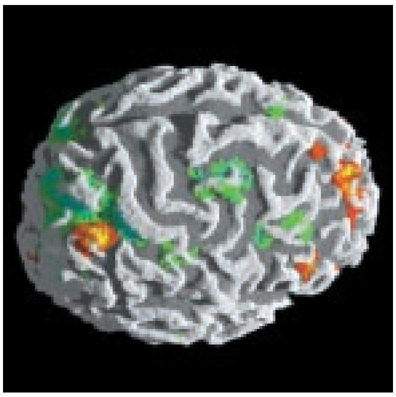

Figure 7. Brain regions predominantly activated by phonological (yellow/red) and visual (blue/green) working memory task performance under articulatory suppression.

2.6.9 An fMRI study of domain-specific interference in verbal and visuospatial working memory: Further support for the evolutionary-based model of human working memory

Gruber, O. & von Cramon, D.Y.

In the present event-related fMRI study we explored the neural implementation of verbal and visuospatial working memory both during non-interfering and interfering conditions due to articulatory and visuospatial suppression. A factorial design was used with two different memory tasks (verbal and visuospatial item-recognition) and a motor-perceptual control task, as well as with two different concurrent dual-task components (counting and tracking). For verbal memory during single-task and non-interfering dual-task conditions we replicated the findings of left-sided activations in premotor cortices including Broca's area, along the left intraparietal sulcus and in the right cerebellum. Correspondingly, we found activations related to visuospatial memory bilaterally along the posterior superior frontal and intraparietal sulci, in the superior parietal lobule and precuneus, and along the precentral and lateral occipitotemporal sulci. Candidate regions for domain-specific interference effects were determined by searching for common activations evoked by the respective primary and secondary tasks, e.g. verbal rehearsal and counting. They included the left precentral gyrus for articulatory suppression and almost the complete network subserving visuospatial memory (as described above) for visuospatial suppression. Memory-related activity in these regions was significantly reduced during suppression. Conversely, additional memory-task related activations during interference in verbal working memory occurred in a bilateral network comprising the regions along the anterior intermediate and inferior frontal sulci and the supramarginal gyrus. Since these activations were specific to the verbal domain, the present results indicate that not only the supramarginal gyrus, but also anterior prefrontal regions along the intermediate and inferior frontal sulci participate in phonological storage. Together, these findings corroborate the evolutionary-based model of human working memory that distinguishes an explicit verbal rehearsal mechanism from a phylogenetically older mechanism which is also able to maintain phonologically coded information (Gruber, 2000; see Fig. 8).

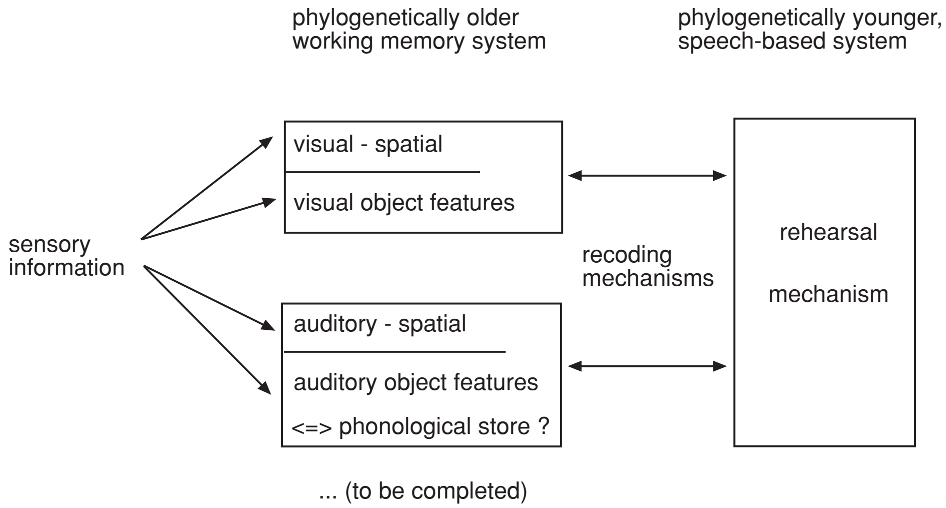

Figure 8. An evolutionary-based model of human working memory.

The role of the anterior prefrontal cortex in verbal working memory: An fMRI study on its sensitivity to domain-specific interference and memory load variations

2.6.10

Gruber, O., Kittel, S. & von Cramon, D.Y.

Anterior prefrontal activations during verbal working memory performance have not only been observed under articulatory suppression but also in high memory demand conditions (e.g., Rypma et al., 1998). In the present study, we attempted to further specify the functional contribution of anterior prefrontal cortices to phonological short-term memory by parametric variations of these two factors (memory load and articulatory suppression rate). Fifteen healthy right-handed volunteers underwent functional magnetic resonance imaging (fMRI) at 3 Tesla (Bruker Medspec 30/100). Gradient echo-planar image series (TR = 1.5 s, TE = 4 ms, FA = 90°, voxel size =3x3x5 mm^3) were obtained in 18 slices covering the entire brain. Subjects performed a Sternberg task requiring phonological maintenance of verbal items. Different memory load and articulatory suppression conditions were arranged in a bifactorial manner. Verbal rehearsal elicited activations in left premotor cortices including Broca's area, along the left intraparietal sulcus and in the right cerebellum. Additionally, bilateral activation along the anterior intermediate frontal sulcus was found both in the highest memory load condition without suppression and (to a comparable extent and at nearly identical location) in lower memory load conditions under articulatory suppression. While this pattern of occurrence cannot be fully explained by the actual memory demands, the results suggest that the cortex lining the anterior intermediate frontal sulcus participates in phonological storage whenever the capacity of mechanisms that commonly underlie articulations and rehearsal is exceeded. These findings are consistent with the recently proposed evolutionary-based model of human working memory (Gruber, 2000; 2.6.9, Fig. 8).

Noradrenergic modulation of manipulation processes in working memory

2.6.11

Müller, U.[1,2], Mottweiler, E.[1], Steffenhagen, N.[1], Regenthal, R.[3] & Bublak, P.[1,4]

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[4] Institute of Psychology, LMU Munich

Background: Working memory processes are mediated by the prefrontal cortex (D'Esposito et al., 2000) and modulated by monoamine neurotransmitters (Arnsten, 1999). To further investigate the effects of noradrenergic stimulation and blockade two pharmacological studies were performed.

Methods: A total of 40 healthy students were investigated. The first study compared two beta-blockers with different liposolubility (50 mg of atenolol vs. 25 mg of propranolol) and placebo. In the second study a noradrenergic psychostimulant drug (200 mg of modafinil) was administered, again in a balanced double-blind placebo-controlled design. Drug effects were further controlled by cardiocirculatory monitoring or plasma concentrations. Manipulation processes were investigated with a verbal working memory paradigm that requires short-term storage and cued manipulations of four-digit-sequences (Bublak et al., 2000).

Results: There were higher ($p < 0.05$) manipulation costs after propranolol as compared to atenolol or placebo. The effect was only observed in low anxiety subjects. In study two there was a reduction of errors in the manipulation conditions but not in the no-manipulation condition after modafinil ($p < 0.01$). Attentional control tasks (letter cancellation, trail-making) were not affected by any of the drugs.
Conclusions: Noradrenergic blockade and stimulation affect manipulation processes in working memory bidirectionally. Our data indicate central effects that depend on endogenous activity of the noradrenergic system as well as complex interactions between arousal and working memory processes.

2.6.12 Inference processes during text comprehension: Do they depend on stimulus modality?

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

Text comprehension requires inference processes for bridging gaps between successive sentences. In neuropsychological studies and brain imaging studies, these coherence building processes have been ascribed to the right hemisphere. Previously, we presented data from an event-related, whole-head fMRI study that did not support this proposal (Ferstl & von Cramon, 2000). When the coherence of visually presented sentence pairs was to be judged, we found regions in the left fronto-median wall and in the left retrosplenial / precuneal cortex to be activated more strongly for coherent than for incoherent sentence pairs.
To further support these results, we tested collected data in an auditory version of the experiment. The questions of interest were whether the previously reported fMRI results were modality specific. The same design and the same materials were used: 30 sentence pairs occurred in each of four conditions resulting from crossing the factors Coherence (yes vs. no), and Cohesion (the presence or absence of lexical connectives, such as pronouns or conjunctions). Furthermore, we used 30 pseudo-sentence pairs for a baseline task to control for perceptual processing. The 150 sentence pairs were tape recorded, combined in a pseudo-random order, and presented auditorily to 12 participants. When the fMRI results of the two experiments were analyzed together, we found expected modality differences for the comparison of stimulation vs. rest. In contrast, the coherence effect was comparable across experiments. Independent of modality, reliable activations were found in the fronto-median cortex and in the retrosplenial / precuneal region (Fig. 9). The results of this experiment further confirm the role of the fronto-median wall for the initiation of non-automatic inference processes.

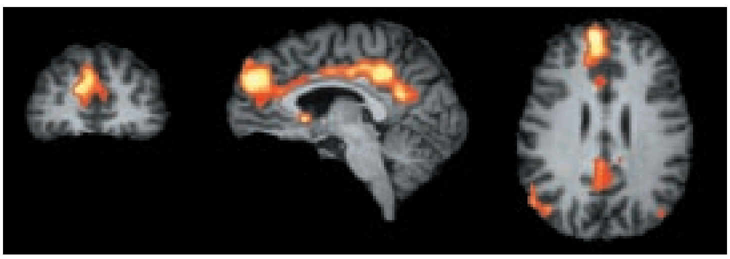


Figure 9. Activations evoked by the coherent sentence pairs as compared to the incoherent sentence pairs. Shown are the group data across 24 participants, projected onto an individual brain. The views are centered in the fronto-median area (Talairach-coordinates x=-5, y=46, z=13).

What are action slips doing to the brain? An fMRI-study

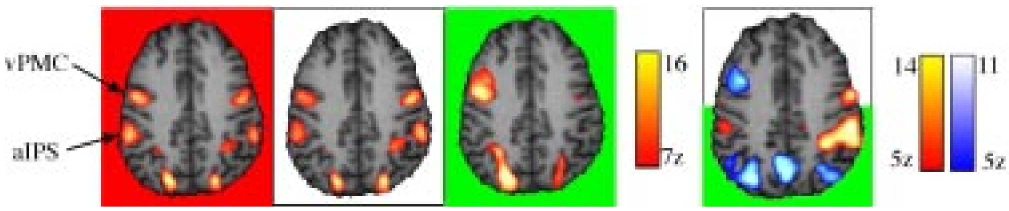
2.6.13

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

The cerebral correlates of observed action slips presented by movies were investigated using whole-brain fMRI. Recently, imaging studies with healthy participants focussed their attention on biological motion and action, but not on action slips. Therefore, the present study set out to investigate (1) which cortical areas in the frontal lobes are activated by observing action slips versus correct actions, and (2) whether activations differ according to different types of action slips. Our interest focussed on the neural circuit of the vPMC and aIPS, which is involved in visuomotor transformations in manual action (*grasping circuit*, Rizzolatti et al., 2000).

Twelfe participants were scanned while performing a classification of different conditions presented in randomized order. In the correct action condition (CA), participants observed hands successfully completing an action. In the qualitative action slip condition (QAS), observed hands made insufficient movements. In the substitutional action slip condition (SAS), observed hands selected the incorrect object. In the object manipulation baseline (BA), observed hands took one object and "thoughtlessly" moved it. The participants classified the moves pressing one of three optional buttons (*correct action*, *action slip*, *movement*). Pure motor and perceptual effects were subtracted out by BA.

Relative to the baseline, all conditions showed bilateral activations within the ventrolateral Premotor Cortex (vPMC) and the caudal cingulate zone (CCZ). The anterior Intraparietal Sulcus (aIPS) was only activated by CA and QAS. However, activations were modulated significantly by the different conditions (Fig. 10). With regard to the *grasping circuit*, the SAS condition showed the highest activation of all conditions in the left vPMC, but the lowest activation in the right vPMC. Activations of the aIPS were not significant for the SAS condition. In contrast, the activations in the QAS condition did not differ significantly from the activations in the CA condition. In summary, the CCZ, an area proposed to be involved in error detection, was activated in all conditions. Moreover, brain activations in the *grasping circuit* differed significantly both between observing correct and incorrect actions versus meaningless movements, as well as between different types of action slips.



qualitative action slips minus movement

correct actions minus movement

substitutional action slips minus movement

correct actions minus substitutional action slips

Red: correct actions,
Blue: subst. action slips

Figure 10.

2.6.14 Evaluative judgment and judgment under uncertainty

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In this study, we investigate the neuronal basis of personal judgments. We compared evaluative judgments and judgments under uncertainty to memory retrieval. We consider a judgment to be the assessment of a stimulus (e.g., object, person), an act/event or a cognitive element (e.g., religious content, art work) on an internal scale. Judgments differ from memory retrieval tasks in that there is often no objectively correct answer. We contrasted three types of tasks: (1) memory retrieval, (2) evaluative judgments, and (3) judgments of uncertainty.

A memory retrieval task (*Leipzig is the capital of Germany; yes/no*) needs to activate the knowledge base of the person. There exists an objective truth. This condition was split into a semantic condition and an episodic condition.

An evaluative judgment (*I like Leipzig; yes/no*) needs the knowledge base, because the person has to identify the elements, but also emotional/motivational components need to be activated. No absolute true or false exists.

A judgment of uncertainty (*I will live in Leipzig for the rest of my life; yes/no*) needs the knowledge base, but also components involved in planning, construction of events or chains of events. Furthermore, it is often assumed that uncertainty is in most cases experienced as unpleasant.

In this investigation, we are interested in the question, whether these three types of tasks (memory retrieval, evaluative judgments, judgments of uncertainty) involve the same brain areas, or whether additional regions become involved when aspects of evaluation and uncertainty are introduced.

Evaluative judgment produced significant activations in the medial part of the frontopolar cortex and precuneus (see Fig. 11), regions known to be involved in personal and social decision making. Judgment under uncertainty produced less pronounced activations in the frontopolar cortex and precuneus, but additional activation were found in the cuneus and the right dorsolateral prefrontal cortex (see Fig. 12).

Figure 11. Activations evoked by the evaluative judgment compared to the semantic memory retrieval condition.

Figure 12. Focus of activation in frontomedian wall (left) and the right prefrontal cortex (middle and right) evoked by the judgment under uncertainty condition in contrast to the semantic memory retrieval condition.

Over the last year, we have carried out a number of experiments to investigate the functional neuroanatomy of attention changes. In a spatial attention experiment, we investigated which areas would be involved when subjects were cued to expect a target at one location, but the target would appear at an uncued location. In this situation, a prominent activation was found in left lateral frontopolar cortex (2.7.1). In a previous experiment (Pollmann et al., *J. Cognit. Neurosci.*), virtually the same activation was observed when subjects would attend to a given visual dimension, such as motion or color, and would then be forced to switch attention to a new dimension. Frontopolar cortex thus seems to be involved in the allocation of attention to previously unattended aspects of our environment. Furthermore, this reallocation seems to be more rather exogenously than endogenously driven, since the pattern of activation shifts from lateral frontopolar cortex to the anterior frontomedian wall, when changes between visual dimensions are carried out under top-down control (2.7.2).

In a further experiment, we investigated the functional neuroanatomy of visual marking (2.7.3). It turned out that temporal shifts of the BOLD-response between experimental conditions indicated a specific role of the right superior parietal lobule in the suppression of irrelevant distractors, whereas parts of the inferior parietal lobule seemed to be involved in target detection and response preparation.

In addition to these studies of visual attention, we started to investigate the functional neuroanatomy of auditory attention processes. Using the dichotic listening paradigm, we found that partial lesions of the corpus callosum led to left ear suppression for CV-syllables when the callosal lesions affected the splenium, but not for more anterior callosal lesions (2.5.16). We are currently following up this result to investigate whether splenial lesions lead to a specific deficit of interhemispheric auditory transfer or rather a supramodal deficit of interhemispheric transfer.

2.7.1 Different mechanisms in redirecting visual spatial attention

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If visual attention is directed to a location by an exogenous cue, the detection of a target at this location is facilitated, even if the cue is uninformative (giving a valid prediction only in 50% of all cases). This holds, if the target appears 200 ms after cue onset. After this period, valid cues lead to inhibition in target detection (inhibition of return, IOR) (Posner & Cohen, 1984). The most common explanation of this effect is that after the non-appearance of the target, attention is shifted away from the cued position. The return to this location is inhibited and novel positions are favored (Taylor & Klein, 1998; Klein, 2000). Whereas facilitation at short SOA is considered to be a purely attentional phenomenon, IOR is argued to be a compound of at least partly independent attentional and occulomotor processes.

We used event-related fMRI to investigate the functional neuroanatomy of these different processes in directing visual spatial attention.

Analysis of functional data revealed a significant interaction of cue validity (valid, invalid) x SOA (100 ms, 500 ms) in left frontopolar cortex (FPC, BA10), right anterior middle frontal gyrus (MFG, BA10), left posterior MFG (BA9), right angular gyrus (AG, BA19), right anterior superior temporal sulcus (STS, BA 21), and left middle insula (BA13) (see Fig. 1).

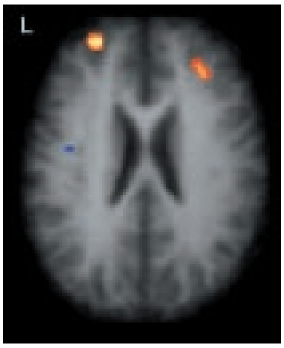

Figure 1. Activations in left frontopolar cortex, left insula and right anterior middle frontal gyrus, revealed by the interaction contrast.

Anterior MFG and STS showed signal increases with IOR, whereas decreases were found in the insular. Activity in FPC, posterior MFG and AG increased with invalid cues at SOA = 100 ms.

We conclude that the redirection of attention to invalidly cued targets and the process related to IOR are supported by different neural systems. However, there was a tendency for increased activation with initial inhibition (invalid cues, SOA 100 ms), as well as inhibition of return in the left FPC and the right anterior MFG, indicating a possible overlap of both networks.

Left FPC was also activated following changes of visual dimension (color and motion) in a previous study. This structure may be involved in the stimulus-induced reallocation of attentional resources.

Imaging visual dimension changes in a conjunction search task

2.7.2

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Detection reaction times in pop-out-out search tasks are faster when targets on consecutive trials are defined within the same rather than a changed visual dimension (Found & Müller, 1996). We demonstrated similar dimension-specific intertrial effects in conjunction search. Subjects saw a display of colored squares (red, blue or green) of two different sizes, each of which moved in one of three possible directions (horizontal, 45° or 125° from horizontal axis). Subjects had to indicate the presence or absence of a target defined by unique combination of size and a second dimension, either motion direction or color. In two within-dimension conditions, the target was consistently defined within the same visual dimension but with varying feature values. In a cross-dimensional condition, the second of the target-defining dimensions varied randomly across trials. Changes of the second dimension across trials, but not changes of the target feature within the second dimension, increased the time required to detect the target.

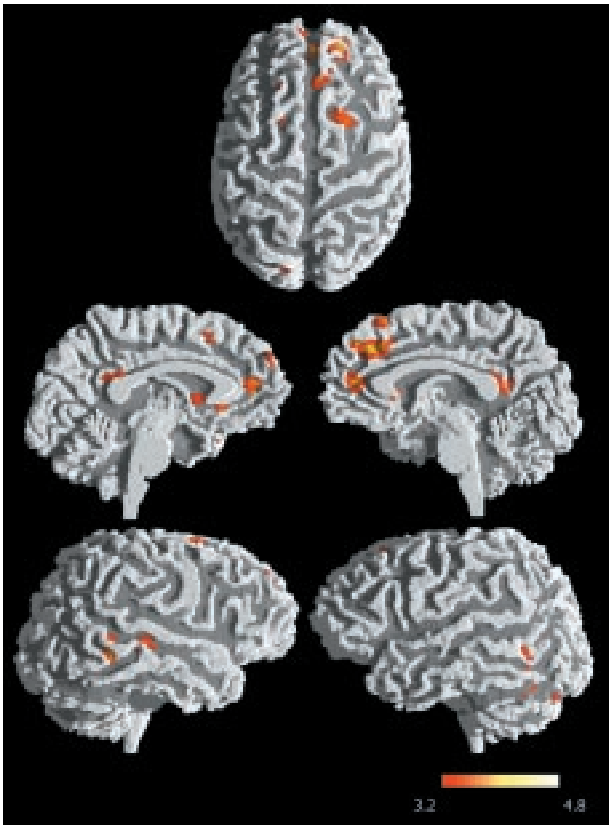

Figure 2. Brain areas with significant interaction of search (within-, cross-dimension) x change condition (change, no change) projected onto a surface rendering of an individual brain.

The physiological correlate of this effect was investigated with event-related fMRI. Data were collected at 3T using a gradient recalled EPI sequence (TR = 2000 ms, TE = 40 ms, flip angle = 40°). Conjunction search (versus a fixation baseline) led to pronounced activations in a network subserving visuospatial attention, consisting mainly of the frontal eye fields, lateral premotor cortex and ascending and descending portions of the intraparietal sulcus.

To identify areas specifically activated during dimension changes, we carried out an ANOVA with the factors condition and change. This analysis revealed a significant interaction, indicating stronger activation in change trials vs. no-change trials specific for cross-dimensional search along the dorsal and medial surface of right superior frontal gyrus, the pregenual division of both anterior cingulate gyri as well as both posterior cingulate gyri (Fig. 2). Further dimensional change-related activation was found in the posterior divisions of the right superior and middle temporal gyri and subcortical areas. Changes to color (resp. motion) led to increased activation in V4 (resp. V5). Thus, top-down controlled dimensional change led to frontal activation mainly in medial anterior prefrontal cortex, whereas stimulus-driven dimensional change in pop-out search led to lateral frontopolar activation in a previous study.

2.7.3 Visual marking processes analyzed with event-related fMRI

Pollmann, S.[1,2], Weidner, R.[3], Humphreys, G.W.[4], Müller, K.[1], Lohmann, G.[1], Wiggins, C.J.[1], Olivers, C.[4] & Watson, D.[5]

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Successful survival in a competitive world requires the employment of efficient procedures for selecting new in preference to old information. Recent behavioral studies have shown that efficient selection is dependent not only on properties of new stimuli, but also on an intentional bias that we can introduce against old stimuli, a process termed 'visual marking'.

In the present study we use event-related fMRI procedures to investigate the neural mechanisms of visual marking. Subjects had to search for a pretermined target stimulus. The target was presented along with distractor stimuli which rendered the search more or less efficient. The critical manipulation was the presence or absence of advance information on one set of distractors. Throughout the experiment, all trials contained two successive displays of 2 s duration each. Subjects had to detect target presence in the second display. The target, present in 50% of the displays, was always a blue 'H'. In one condition, the blue H was presented along with blue As distractor items. Here the target differed by a single feature (form) from the distractors. In a more difficult, serial search condition, the blue H was presented along with green H and blue A distractors.

In a third, preview condition, the second display was identical to the conjunction search condition. However, one set of distractors (the green H's) was presented in advance in the first display. To control for effects of physical stimulus presentation, the search display in the single feature and conjunction search conditions were preceded by a set of red Os, which occupied the same locations as the green H distractors in the preview condition but which differed in color and shape from the stimuli in the actual search display.

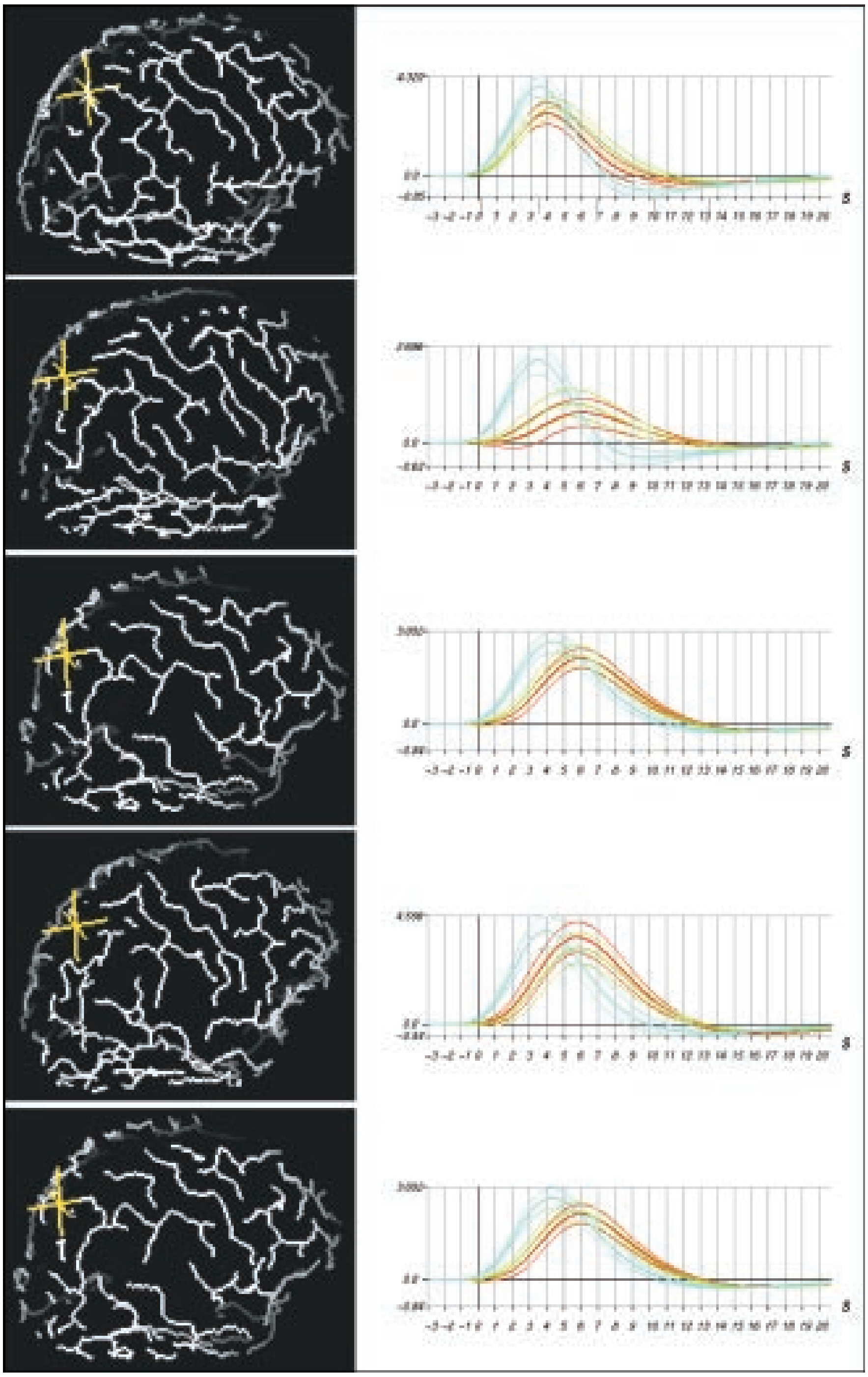

Figure 3. Early onset of the evoked response in right superior parietal lobule in the preview condition (blue), compared to single feature (red) and conjunction search (green). Thin lines represent standard errors.

Event-related analysis of functional magnetic resonance imaging data indicates that the right superior parietal lobule is specifically involved in the inhibition of old items, whereas the temporoparietal junction area and the horizontal limb of the right intraparietal sulcus are involved in the detection of new items and in response preparation. The study provides evidence for the functional segregation of brain regions within the posterior parietal lobe.

Cognitive processes in humans are usually studied by stimulation experiments. Responses are recorded by methods, such as functional MRI, EEG, MEG, SPECT and PET, which characterize different aspects of the underlying cognitive process. Because these different methods yield complementary information about the anatomical, metabolical and 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 2000 onto the following projects:

- the segmentation of pathological MR images (5 sections),
- the analysis of multimodal datasets (4 sections),
- the setting-up of bio-mechanical models of the brain as part of the SimBio project (3 sections).

As announced in the previous Annual Report, the SIP group takes part in the SimBio project (IST-V project 10378, funded by the European Community), which focuses on bio-mechanical simulations of the human head using Finite Element Models. 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. The software partnership with the Neuroimaging Group at the Forschungszentrum Jülich yielded a mutual exchange of additions to our BRIAN software package. The fruitful scientific collaboration with the Unite 494 at CHU Salpetriere in Paris was continued in the form of a research visit of Dr. H. Benali to our lab, which resulted in common projects in functional MRI analysis.

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. The following 5 sections describe approaches for characterizing changes due to diffuse and focal brain diseases, volumetric measurements of brain compartments in healthy subjects and patients with diffuse brain diseases, regional measurements of the cortical thickness, and an initial attempt to classify the neocortical fine-structure.

2.8.1 3D texture analysis of MR brain datasets

Kovalev, V.A.[1], Kruggel, F.[1], Gertz H.-J.[2] & von Cramon, D.Y.[1]

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It has long been recognized that textural features play an important role in a wide variety of image analysis problems. While 2D texture analysis has been extensively studied, there has been very little work done in the area of characterization and analysis of 3D (volumetric) textures. Continuous increase of spatial resolution of neuroimaging techniques and strong practical needs challenge for new, natively 3D texture analysis methods.

We have suggested a new method for 3D texture analysis of MR brain datasets. The method is based on extended, multi-sort co-occurrence matrices that combine intensity, gradient and anisotropy image features in a systematic and consistent way. Proposed co-occurrence descriptors are reflection and translation invariant and, to some extent, rotation-insensitive. Normalization of co-occurrence descriptors provides a basis for inter-subject analysis and comparisons of brain regions with different size. A comparative study revealed that general 6D matrices are the most sensitive texture descriptors. Traditional integral texture features appear too robust for analyzing faint, not well-defined brain textural changes. Another important issue is the dependency of textural properties with spatial image scaling, which renders this operation as unacceptable in neurological research involving texture measurements.

The ability of suggested 3D texture descriptors is demonstrated on two non-trivial tasks for pathologic findings in brain datasets. The first one is related to the characterization and clustering of patients with mild cognitive disturbances and normal, healthy elderly subjects (see Fig. 1). A clear separation of 28 patients and 15 controls is achieved, which manifests also certain inter-hemispheric differences of the severity of pathological changes. In Figure 2, we have demonstrated the use of the method for an automatic segmentation and quantitative evaluation of diffuse white matter hypo-intensities as a common type of WM lesion. These measures may then be compared with clinical features such as cognitive abilities measured on performance scales and help to understand various diffuse pathologic processes in the brain.

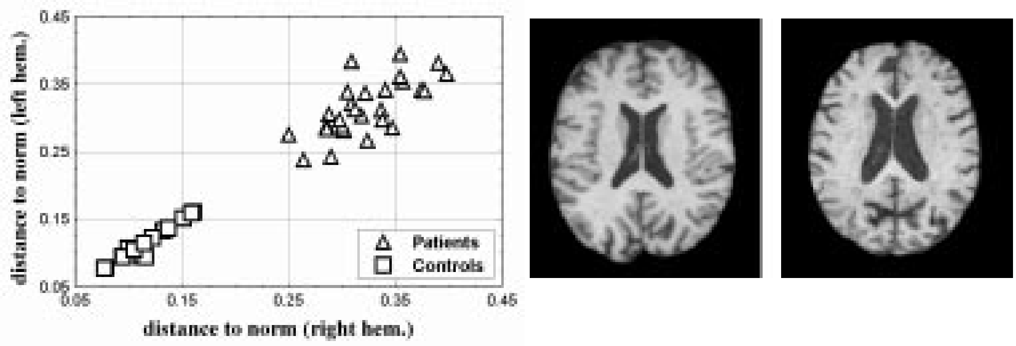

Figure 1. Clustering of healthy elderly subjects (see example top right) and patients with mild cognitive disturbances (example bottom right) based on texture properties as revealed by MRI.

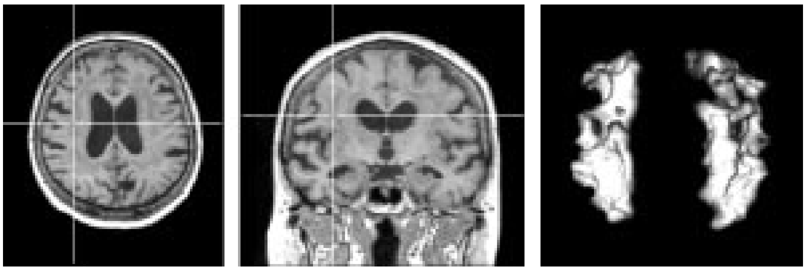

Figure 2. Automatic segmentation and estimation of diffuse white matter hypointensity.

Descriptors for focal lesions as revealed by MR tomography

2.8.2

Chalopin, C. & Kruggel, F.

The study of subjects with acquired brain damage is highly interesting to better understand human brain functions. Focal lesions (such as consequences of head trauma, intra-cerebral hemorrhages or cerebral infarcts) are revealed in clinical practice using high resolution T_1-weighted MR images. In order to relate lesion properties with the cognitive abilities of a patient, a precise segmentation and classification of a lesion is necessary. We developed automatic methods providing descriptors of the lesions from MR images.

An initial segmentation step, which extracts the lesion from the brain, is necessary. The task is complex, because the lesions are inhomogeneous and may include completely and partially damaged areas. Moreover, lesions resulting from focal brain damage are characterized by low intensities on T_1-weighted images, and are hard to distinguish from other brain compartments, such as the external or internal CSF. A segmentation method was developed, which compares the intensities of two symmetrical brain voxels relatively to the middle-plane separating the two hemispheres. Since the symmetrical area of a lesion is generally healthy, the algorithm detects automatically damaged voxels, but also artefacts due to the natural asymmetry of the brain or indirectly caused by lesions such as ventricle enlargement. In order to remove these artefacts and also to automatically locate the lesion, the algorithm extracts asymmetrical voxels in both T_1- and T_2-weighted images. An intersection of the selected areas provides then the lesion.

Then, geometrical descriptors, such as lesion size and compactness, are computed. To characterize tissue properties within the damaged areas, voxels were clustered by using image intensities and Haralick's texture parameters. A damage index of the lesion is calculated from both cluster analyses. Now, we plan to study the performance of this algorithm in a larger group of patients, in order to achieve a better understanding of the characteristics of such lesions and their evolution with time.

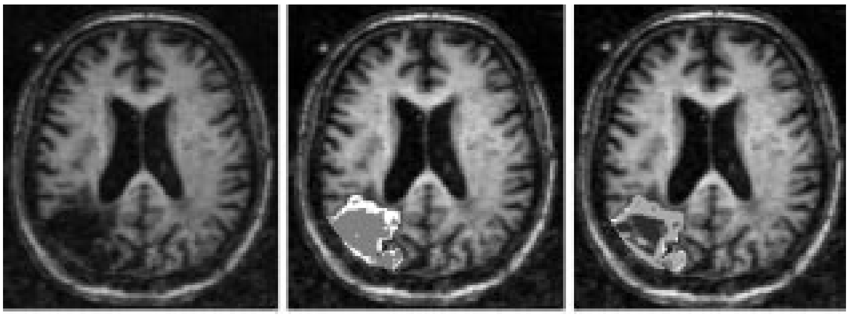

Figure 3. Automatic segmentation and clustering of a focal brain lesion.

2.8.3 Measuring volumes of brain compartments in normal subjects and patients with diffuse brain diseases

Hensel, O., Kruggel, F. & von Cramon, D.Y.

The goal of this project is to obtain volumetric measures of the major brain compartments (i.e., frontal, parietal, temporal, occipital lobe, brain stem, basal ganglia, cerebellum, intern/extern cerebral fluid and the insula). A brain subdivision scheme was defined based on anatomical landmarks which are visually detectable 3-D MR Images. At this time, manual delineation of compartment boundaries is the "gold standard". We analyzed the volumes of lobes in 30 young, healthy brains. At a later stage, manual segmentations will serve as expert knowledge for devising an automatic segmentation scheme for morphometry of brain compartments.

Compartment	Male (in ml, n = 15, age = 26.5 years)		Female (in ml, n = 15, age = 25.4 years)	
	left	right	left	right
brain	1405		1313	
frontal lobe	203	208	186	193
parietal lobe	120	113	111	106
temporal lobe	125	124	117	112
occipital lobe	70	75	66	68
insula	14	13	12	11

Measuring the cortical thickness

2.8.4

Kruggel, F. &
von Cramon, D.Y.

Besides normal aging, a number of brain diseases are known to reduce the amount of gray matter in the brain. To better understand the nature and progression of these disease processes, quantitative measurements of relevant brain structures, such as the regional cortical thickness, are highly desirable. Starting from high resolution volumetric MR images of the human head, a reliable segmentation procedure for the gray matter compartment was designed which allows thickness measurements at sub-voxel resolution.

A fuzzy c-means classification algorithm is used to determine per-voxel class probabilities while correcting for the inhomogeneity of the B_1 field of the MR scanner. Both brain hemispheres were extracted from the class containing mostly white matter (WM) voxels. A surface of this WM segmentation was obtained by the marching tetrahedra algorithm and optimally adapted to the gray-white matter boundary by treating the initial surface as a deformable model. Adjusting parameters of this model, a second surface representing the gray matter (GM)-CSF boundary was obtained. The cortical thickness is finally computed as the local minimal distance between both surfaces.

Regional values for the cortical thickness may be obtained by parcellation of the surface into patches, using the previously developed notation of "sulcal basins". Gyral crowns and fundi, which exhibit significant differences in their cortical thickness, are discriminated by their depth (as measured from the convex hull of the brain) and the sign of the local curvature.

Two M.D. theses were started (by S. Morgenstern and C. Nikolaus) to derive quantitative thickness measurements for healthy young and elderly subjects, and patients with diffuse brain diseases (M. Alzheimer, cerebral hypoxia and diffuse axonal injury).

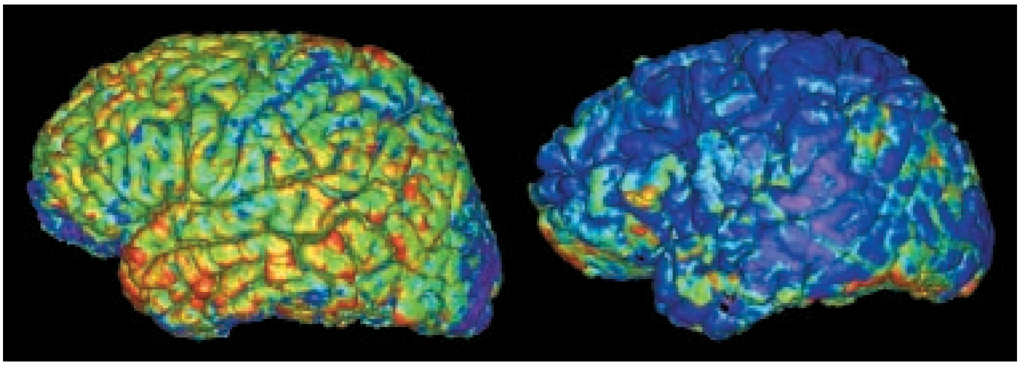

Figure 4. Cortical thickness determined in a healthy subject (left) and an elderly patient suffering from M. Alzheimer (right).

2.8.5 Analysing the neocortical fine-structure

Kruggel, F.[1], Brückner, M.K.[2], Arendt, Th.[2], Wiggins, C.J.[1] & von Cramon, D.Y.[1]

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[2] Paul Flechsig Institute for Brain Research, Leipzig

Cytoarchitectonic fields of the human neocortex are defined by characteristic variations in the composition of a general six-layer structure. It is commonly accepted that these fields correspond to functionally homogeneous entities. Diligent techniques were developed to characterize cytoarchitectonic fields by staining sections of post-mortem brains and subsequent statistical evaluation. Fields were found to show a considerable inter-individual variability in extent and relation to macroscopic anatomical landmarks. With upcoming new high-resolution magnetic resonance (MR) scanning protocols, it appears worthwhile to examine the feasibility of characterising the neocortical fine-structure from anatomical MR scans, thus, defining cytoarchitectonic fields by in-vivo techniques.

An isolated left brain hemisphere (fixed in formalin and embedded in agar gel) was scanned using a high resolution T_1-weighted 3D MDEFT protocol (matrix 256x512x512, voxel size 0.375x0.375x0.25 mm, scanning time 12 h). The GM and WM surface were computed by a similar procedure as described above, and intensity profiles were determined across the cortex. Exact and consistent positions of the GM-WM boundary and the GM-background (BG) boundary were computed from these profiles. Between these points, a normalised profile of equidistant data points was interpolated. Intensity profiles were characterized by a set of measures within a local surface patch and classified statistically.

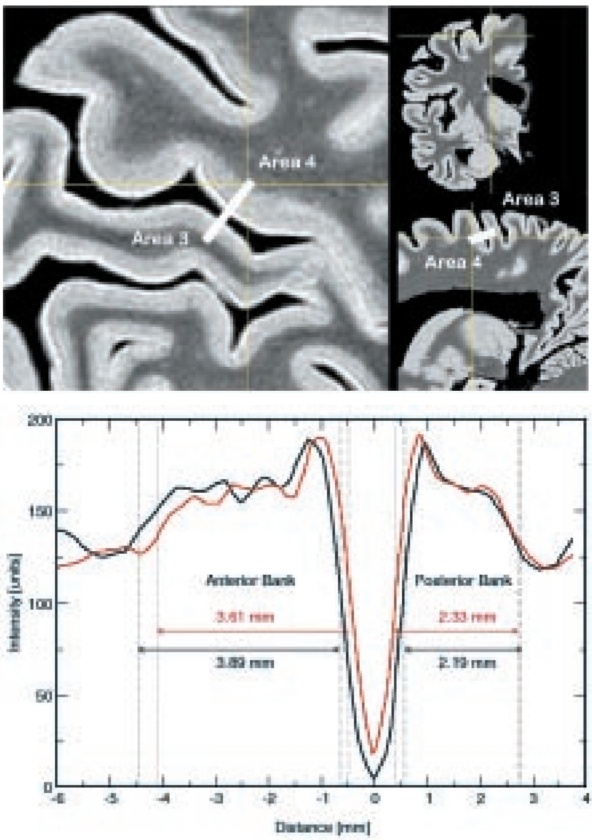

Figure 5. Top: Sagittal, coronal and axial slice (enlarged) through the anterior (Area 4, motor cortex) and posterior (Area 3, sensory cortex) bank of the central sulcus. The position of the intensity profiles through Areas 4 and 3 is marked by a white bar. Below: two intensity profiles through Area 4+3. The motor cortex is thicker than the sensory cortex and shows more substructure.

As an example, we tried to differentiate the primary motor cortex (Area 4) on the anterior bank of the central sulcus from the somato-sensory cortex (Area 3) on its posterior bank. The most distinctive feature here is the cortical thickness: on the anterior bank, the motor cortex reaches values up to 3.8 mm, while the sensory cortex is less than 2.2 mm thick. Intensity profiles in Area 4 mostly showed three maxima (see Fig. 5), which roughly correspond to the transition between layer II/III, layer III/V and layer V/VI as described by Amunts et al. (1995). The somato-sensory cortex on the posterior bank exhibited much less substructure.

A statistical classification was initialised by a manually specified region close to the hand field and yielded the full extent of the motor cortex well in agreement with previously published histological classifications. The border between the anterior and the posterior bank is sharp, although some small spots, especially at crowns of other gyri, respond to this classificator as well.

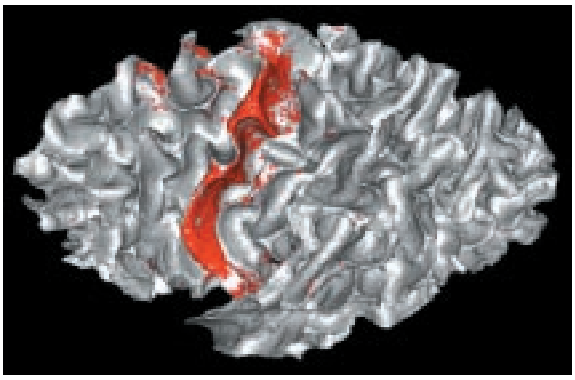

Figure 6. Top lateral view of the white matter surface. Area 4 is colour-coded as detected using a model region on the anterior bank of the central sulcus.

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 Independent component analysis of fMRI group study data

Svensén, M.[1], Kruggel, F.[1] & Benali, H.[2]

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Building on work from the previous year (see Ann.Rep. 99, 2.8.4–5), we have developed an approach for applying independent component analysis (ICA) to functional magnetic resonance imaging (fMRI) data from group studies. This yields a set of time courses common to the whole group and a set of independent images with corresponding spatial response patterns given individually for each subject in the group. The underlying idea is that, since the same stimulation is administered to all the subjects in the group, their temporal responses should exhibit a common behavior.
This approach has been shown to be capable of separating out not only components which show a direct correlation with the stimulus, but also other components which

have a more complex coupling to the given stimuli. Examples of both kinds of components are shown in Figure 7, which shows results from an fMRI experiment with a block trial design and visual stimulation. The experiment was carried out with a group of 5 subjects, but for reasons of space economy, the spatial response patterns are shown for a single subject only; the corresponding patterns found in the other subjects were very similar.

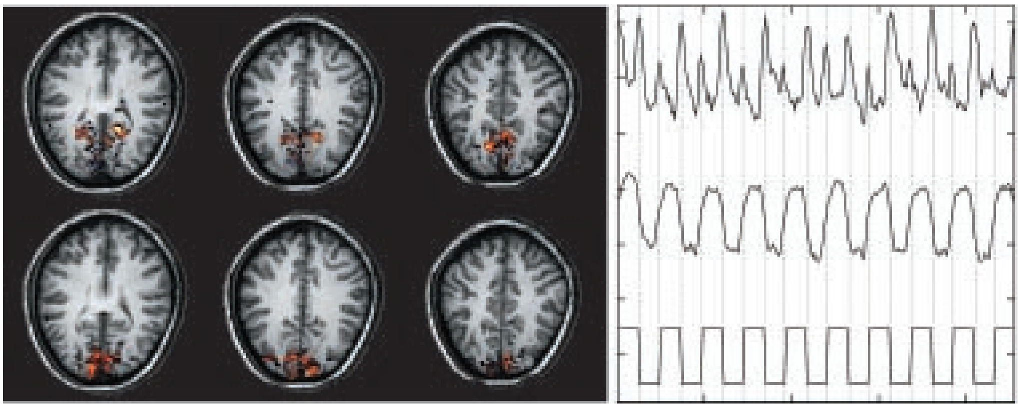

Figure 7. The right plot shows a boxcar function representing the stimulus (bottom), the time course corresponding to the spatial response pattern shown in the image bottom left (middle) and the corresponding time course for the top left image (top).

2.8.7 Brain activity as examined by functional near-infrared spectroscopy during a Color-Word Matching Stroop task in an event-related design

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

Brain activity may be detected by near-infrared spectroscopy (NIRS), which measures concentration changes of oxy- and deoxy-haemoglobin by their different spectra. Recent NIRS studies have mostly employed block designs for the cognitive task with stimulus durations of 18 s to 10 min. In order to investigate the potential of NIRS to detect brain activation in an event-related design, we selected a Color-Word Matching Stroop task (see Ann.Rep. 99, 2.6.1). Eleven healthy subjects were examined at optode positions F7/8, F3/4, C3/4, C3a/4a (in the middle of C3/4 and F3/4), P3/4 and O1 according to the international 10/20 system. Activations for the incongruent (mismatch between a

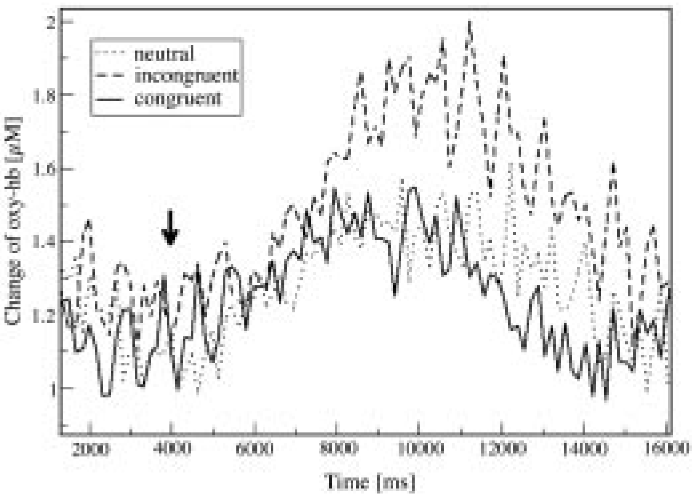

Figure 8. Change in concentration of oxy-haemoglobin (oxy-hb) in position F3 during Stroop task performance (one subject; each curve resulted from averaging over 10 trials). Time of onset of the cognitive task is marked by an arrow. The incongruent condition leads to higher increases of oxy-haemoglobin than the congruent and neutral conditions, corresponding to higher brain activation due to interference in the lateral prefrontal cortex.

color word and its color producing interference), congruent (match between a color word and its color) and neutral conditions (color only) were compared in a temporal window of 3–8 s after stimulation onset and baseline (2 s before stimulation onset). At positions F3/4, F7/8 and C3a/C4a, significantly higher concentration changes were observed for oxy- and total haemoglobin in the incongruent vs. neutral condition (Fig. 8). At F3/4, this difference was found as significant for deoxy-haemoglobin as well. Significance values were higher on the left side in comparison to the right side. Thus, brain activation is higher in the incongruent compared to the neutral condition of the Stroop task in the lateral prefrontal cortex, which is in accordance with previous results from functional MRI. Thus, it is feasible to detect brain activation using NIRS and event-related designs.

Fixed point clustering and its application to visual event-related potentials

2.8.8

Hutt, A.[1], Kruggel, F.[1], Herrmann, C.S.[1] & Friedrich, R.[2]

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[2] *Institute of Theoretical Physics, University of Stuttgart*

Spatio-temporal analysis methods based on dynamical systems theory have been applied to EEG/MEG-signals in several works. The basic idea considers a high-dimensional signal as a temporal sequence of data points in a high-dimensional space, where each point corresponds to a spatial intensity distribution at one time point. This sequence of points in data space represent a trajectory. We assume that the trajectory passes several fixed points, which show attractive and repelling properties. Thereby, the signal slows down when approaching a fixed point and accelerates when moving away from a fixed point, attracted by the next fixed point. Thus, spatio-temporal models for the whole signal are replaced by a sequence of models, where each model describes the behavior near a fixed point. We apply a clustering method (see Ann.Rep. 99, 2.8.9) for detecting these regions near fixed points. Applications on visual event-related potential (ERP)-data (see Ann.Rep. 99, 2.11.9) illustrate features of the proposed approach.

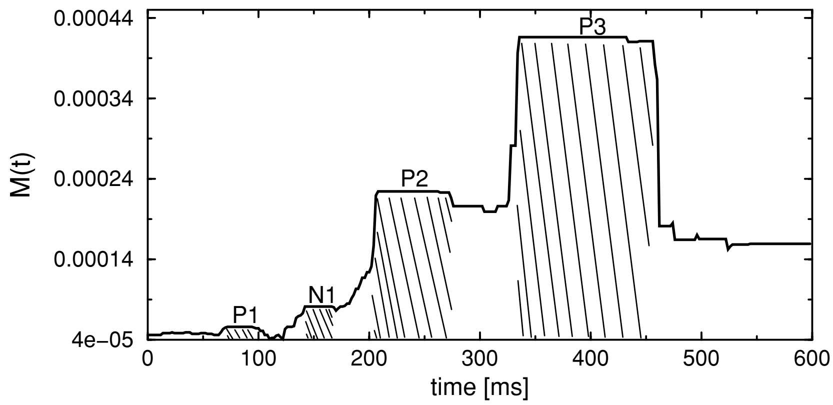


Figure 9. As a result of the clustering algorithm, we obtain a probability M(t) for each time point, that the data point belongs to a region near a fixed point. In Figure 1, increases of M(t) can be recognized in time windows, where ERP-components P100 (60 ms - 110 ms), N170 (130 ms - 170 ms), P200 (190 ms - 270 ms) and P300 (330 ms - 450 ms) occur. This correspondence indicates a relationship between underlying fixed points and functional ERP-components.

2.8.9 Recording of event-related potentials while functional MRI scanning

Kruggel, F., Herrmann, C.S. & von Cramon, D.Y.

As described previously (see Ann.Rep. 99, 2.8.8) we were able to reliably record a visually evoked potential (VEP) during functional MRI scanning. The obvious next step was to record an event-related potential (ERP) related to a cognitive task.

We selected a well-studied visual oddball paradigm (see Ann.Rep. 99, 2.11.9, 2.11.10). We used Kanizsa figures and non-Kanizsa figures as stimulus material: figures consisted of either three or four inducer disks, which we will consider the shape feature, and either constituted an illusory figure or not. Stimuli were presented for 1000 ms, followed by randomized inter-stimulus-intervals (ISI) of 1000 to 2500 ms. The ISI duration followed an exponential distribution. A total of 900 trials were presented in three runs within 45 min. EEG was recorded using 18 electrode in a standard 10/20 set-up while functional MR scanning using an EPI protocol (5 axial slices oriented parallel to AC-PC, TR 1500 ms). The time period during which the images were acquired was 270 ms, leaving a period between 1730 and 3230 ms for MR relaxation and EEG acquisition.

Functional MRI data were analyzed using conventional regression statistics and by an adaptation of a non-linear model to the hemodynamic response in the time-series (see Ann.Rep. 99, 2.8.6). The same ordering of the amplitude vs. experimental conditions was found for the visual N170 potential and the hemodynamic response of secondary visual cortices. Experimental experience and collected results demonstrate the feasibility of conducting combined EEG-fMRI studies using cognitive tasks.

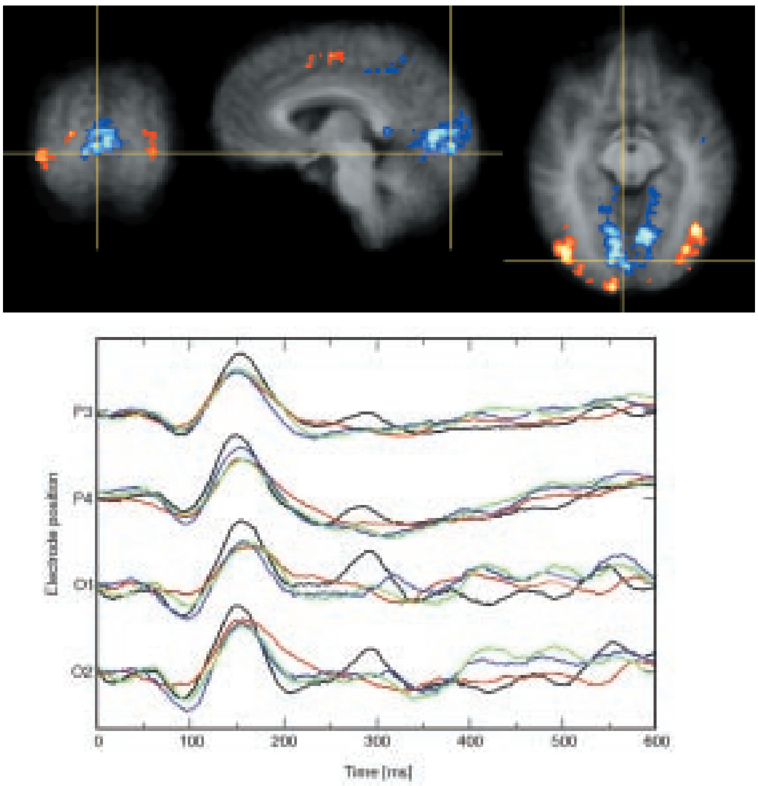


Figure 10. Regions activated by the visual stimulus as detected by functional MRI (top) and ERPs recorded at selected electrode positions (below: black: Kanizsa square, red: Kanizsa triangle, blue: non- Kanizsa square, green: non-Kanizsa triangle).

The final three sections summarize work performed for the SimBio project. This multinational project funded by the European Union aims at the implementation of a generic software environment for bio-numerical simulation. The MPI is involved in the setting-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.

Segmentation of the skull from dual-echo MR data sets

2.8.10

Burkhardt, S.[1,2,3], Kruggel, F.[1] Saupe, D.[3] & Wolters, C.H.[1,2]

[1] *Max Planck Institute of Cognitive Neuroscience,*
[2] *Max Planck Institute for Mathematics in the Sciences,*
[3] *Department of Computer Science, University of Leipzig*

A correct model of the skull is important for many applications. The identification of the CSF-boundary solely based on T_1-MRI is only approximated by smoothing and dilating the segmented brain surface. Proton-Density-Weighting (PD) MRI, leading to a large gray value difference between the CSF and the skull, is suitable for this problem. Therefore, multi-MR-imaging protocol acquisition, registration and segmentation leads to an improved skull modeling. The T_1-weighted MR image was acquired using a MDEFT sequence, the PD-weighted image by a FLASH protocol, both with a resolution of 1x1x1.5 mm.

First, the PD-weighted image was registered onto the T_1-weighted data set by an affine transformation. Optimal parameters were determined using a Downhill-Simplex algorithm in a multi-resolution approach by a cost function based on mutual information. Then, segmentation was carried out while correcting for intensity inhomogenities by means of an adaptive fuzzy-C-means algorithm. The results are an intensity corrected image and a classification of the voxels, from which an initial skull mask was computed. The inner and outer surfaces of the skull were obtained as triangle meshes by the "marching tetrahedra" algorithm, simplified and adapted to sub-voxel precision by treating the mesh as a deformable model. The resulting meshes were converted to voxel space and the space between them was filled to yield a final skull mask.

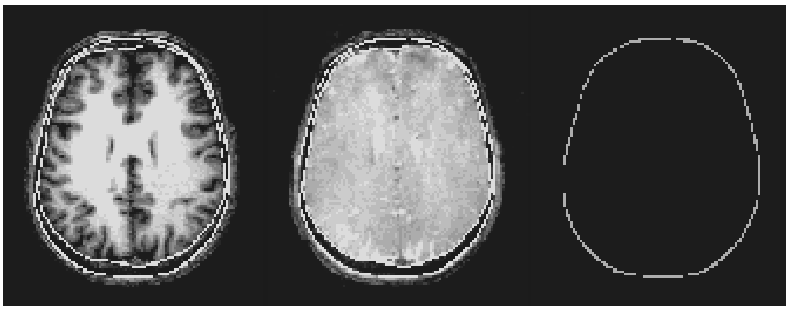


Figure 11. Inner and outer skull surface in a T_1-weighted MR image (left), a PD-weighted MR image (middle) and the corresponding skull mask (right).

2.8.11 Deformations induced by disease processes in the brain

Wollny, G., Tittgemeyer, M., Kruggel, F. & von Cramon, D.Y.

As there is no prior information on underlying forces of pathological processes in the brain available, MRI time series examinations are employed and analyzed for (non-linear) vector field transformations. Deformation fields are used to derive a force field, based on incorporated realistic material parameters. Such analyses may yield empirical knowledge about the pathological process and help to predict the disease progress.

The problem of deducing forces leading to tissue deformations from time-series examinations is equivalent to performing a (non-linear) registration between the time-series examinations. Thus, in a first approach, mathematical techniques may be applied for registering anatomical modalities via vector field transformations, which map template images to a respective target. The resulting deformation field corresponds to the forces induced by the disease process.

In a first approach, we model the brain as a viscous-fluid material here, which can be described by the equations of viscous-fluid mechanics. The study image is registered to the reference by minimizing the mean square of the intensity difference. To reduce the computation time various approaches for solving the underlying linear partial differential equation system, such as the use of scale-space convolution, conjugated gradients and successive (over-) relaxation were studied. Finally, relaxation, enhanced with an adaptive update scheme and combined with a multi-grid approach, proved to be the best solution.

Transformations have to be constrained, however, to be consistent with the physical properties of deformable elastic solids. Unfortunately, a fundamental problem with a large class of image registration techniques is that those techniques are inconsistent [a transformation from one image to another (forward registration) does not necessarily equal the transformation of the inverse registration]. In a second approach, we attempt to overcome this limitation by means of a consistent approach to elastic registration, which essentially relies on a joint inversion of both the forward and its inverse transform, and on the mapping being topologically invariant. By addressing the topological issues involved with volume transformations, we put explicit constraints on the bio-mechanical plausibility of such vector field transformations, i.e., we guarantee that connected sub-regions of an image remain connected, neighborhood relationships between structures are preserved, and surfaces are mapped to surfaces.

Instead of pixel based approaches we prefer to base the analysis on the Euclidean space, in which brain structures actually reside. Maps are used to analytically compute classical formulas from differential geometry on transformations on tangent spaces in the brain. Herefore, transformations must be established on a continuum. A great advantage of the method is that it can handle segmented images - and is thus applicable to FE meshes directly - which allows us to achieve a better performance (less nodes than image pixels) and to gain vantage from robust knowledge of tissue elasticity.

Based on the consistent registration, we extract displacement fields and detect force fields. These data are analyzed for normal biological variability as well as for pathological processes. In doing so, the respective vector fields might be simplified by finding critical points like attractors, repellors and saddle points, which are immanent to the field. These points are of special interest: a growth center is indicated by a repellor, while a center of loss of brain matter corresponds to an attractor. Anatomical landmarks may serve as a co-ordinate system basis to describe the position of these critical points. The resulting map of internal forces can be passed to a finite element (FE) program for forward simulation on the initial MR data. Visualization of the MR image data together with the deformation (see Fig. 12) reveals a deeper insight into the physics of the disease process.

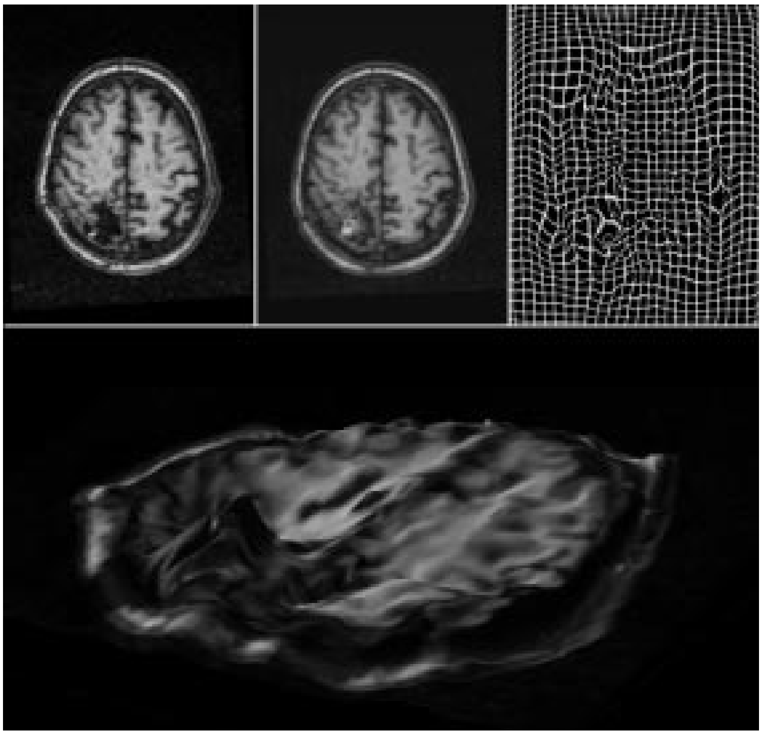


Figure 12. Top row: reference, study, visualization of deformation as a mesh. Below: 3D view of the deformed study slice.

Visualization

2.8.12

Svensén, M. & Kruggel, F.

The purpose of this project is to develop a software module for visualization of the simulation results produced by other SimBio modules. It will be capable of visualizing voxel volumes (i.e., 3D images) as well as geometric models. Efforts will be 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.

In its first phase, we pursue a standard model for software development, with requirements specification, technical design, implementation and testing. The goal of this first phase is a working software module with all the necessary basic functionality.

In the second phase, commencing upon completion of the first phase, this basic software will be extended to incorporate more advanced visualization techniques. At the time of writing, this work package is in the first phase, with the requirements specification completed and the technical design being in progress.

The new millennium has seen the NMR group concentrate its activities in three core areas:

- The relationship between anatomy and function
- The relationship between functional signal changes and physiology
- Methodological support and development.

Most activities within the group can now be assigned to one of these aims. The relationship between anatomy and function is currently being investigated by combining diffusion tensor imaging and spontaneous fluctuations in the BOLD signal (2.9.1). Significant progress has also been made in understanding how physiological changes affect the BOLD signal by means of an extended balloon model (2.9.2). It is now intended to support this endeavor by developing arterial spin labeling as a means of measuring perfusion, and to examine the possible use of ^{17}O imaging as a means of determining the rate of metabolic oxygen consumption. The latter project is part of an international collaboration, with the main partner being the University of Tel Aviv (Gil Navon). In terms of methodological developments, one of the more imaginative projects was that of imaging on curved planes (2.9.3). There have also been valuable developments in terms of RF coil technology (2.9.4) and in understanding the motion sensitivity of the diffusion weighted imaging experiment (2.9.5). One of the easiest methodological developments was that of T_2^*- weighted imaging, which has, however, proven extremely useful for clinical studies (2.5.19). One project that has yielded interesting results is the result of a collaboration with the Department of Anesthesiology at the University of Leipzig. In this, volunteers were investigated under varying degrees of anesthesia while performing a cognitive task (2.5.18).

2.9.1 An investigation of functional and anatomical connectivity using diffusion tensor imaging

Koch, M., Norris, D.G. & Hund-Georgiadis, M.

It has been observed that in a time series of T_2^* weighted images the signal fluctuations of right and left human primary motor cortex without stimulation are correlated. The phenomenon is known as functional connectivity and has also been observed in primary visual cortex and in the amygdalae. It has been discussed that the fluctuations are caused by spontaneous bursts of electrical activity that occur irrespective of whether a task is performed or not. The correlation is a manifestation of an increased conditional probability that a neuron in region 'A' fires provided that a neuron in 'B' has fired immediately before. This coincidence can be due to a direct influence mediated by an anatomical link between the regions. Diffusion tensor imaging reveals information on fibre tracts that connect cortical areas. It has been postulated that it is possible to use DTI as a tool to investigate functional connectivity. If the correlations are a result of a strong neuronal connection, then two regions that in DTI fibre maps appear to be strongly connected in an anatomical sense should also exhibit a high correlation of signal fluctuations. In order to investigate whether this is the case, we measured the anatomical and functional connectivity of areas on adjacent cortical gyri.

For fluctuation imaging, 1024 gradient-recalled blipped EPI images were acquired for a single 5-mm axial slice. The signal time courses of all image pixels above a noise threshold were low-pass (<0.08 Hz) frequency filtered to remove signal fluctuations due to the respiratory and cardiac cycle. Correlation coefficients between time courses were calculated for all possible pairs of pixels. Subsequent to the EPI scans, diffusion tensor imaging was performed for the same slice. The tensor eigenvector corresponding to the largest eigenvalue represents the estimated fibre direction. In order to find a numerical measure of anatomical connectivity, a Monte-Carlo type algorithm was implemented. The path of a virtual particle performing a random walk in the plane of image pixels can be confined preferentially to the white matter fibres if the probabilities for the jump directions are made dependent on the diffusion tensors. By counting how often a particle starting in a region 'A' reached region 'B', we obtained a (relative) measure of the anatomical connectivity between regions 'A' and 'B'.

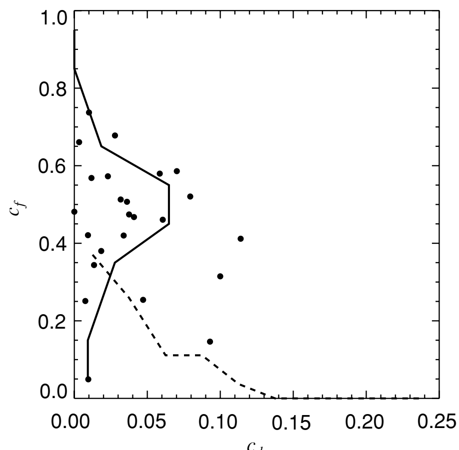


Figure 1.

As expected, for many cortical regions the correlation maps showed a high correlation with the homologous contralateral area. To assess how strongly gyral crowns were interconnected we selected gyri on the convex surface of the brain and defined manually regions of interest on the crowns which were defined as the cortical regions at the origin of a fibre tract. Figure 1 shows a plot of correlation coefficients c_f between regions on adjacent gyri (max. over region) versus the corresponding anatomical connectivity measure c_d for the 4 subjects. The situation with large c_d and small c_f rarely occurs. This may suggest that a strong anatomical connection implies a high functional correlation.

The balloon model for BOLD-based MR signal changes applied to a magnetic field strength of 3 Tesla

2.9.2

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

The most prominent approach developed to date for modelling the blood oxygenation level dependent (BOLD) signal is given by Buxton's balloon model, which was initially derived for a magnetic field strength of 1.5 Tesla. The aim of this work was to adapt the balloon model to the magnetic field strength of 3 Tesla and to validate the underlying biophysical assumptions. The main difficulty for a quantitative test of the balloon model is the lack of knowledge about the exact time courses of the changes of the blood flow (CBF) and the oxygen consumption ($CMRO_2$). The balloon model uses the oxygen limitation model for the coupling between CBF and $CMRO_2$, which has not yet been validated experimentally. In addition, it could be shown that physiological parameters such as the mean transit time τ_0 or the parameter τ_v, which describes the resistance of the vasculature against fast volume changes, strongly influence the shape of the BOLD response, although neither of these parameters changes its steady state. Experimental BOLD responses of the primary visual cortex were obtained for 8 subjects by use of a short and strong visual stimulation. Satisfactory stability of the BOLD response for the same subject within the same experimental session was found, whereas considerable variability among subjects was observed. The maximum peak of the BOLD response within the 8 subjects varied between 2.5 % and 4.5 %. The measurement of the diffusion-weighted BOLD response by use of a bipolar gradient with $b = 50$ smm^{-2} gives a further tool for the comparison of the balloon model with the experiment, because this experiment can be modelled independently. The attenuation of the maximum BOLD signal by the diffusion gradients was between 20 % and 40 %.

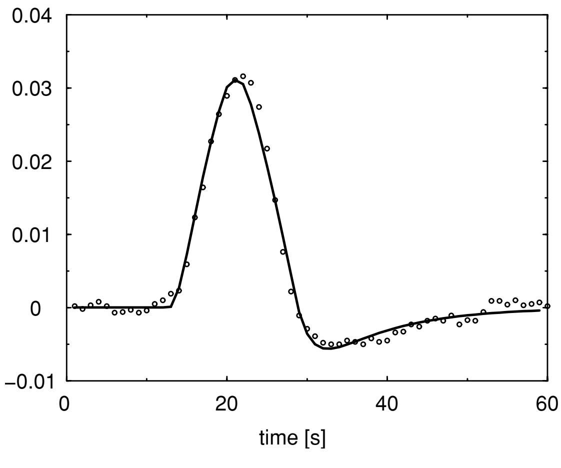


Figure 2. Percentage change of the BOLD signal (circles) for all activated voxels due to a visual stimulation of a subject. The stimulation lasted 6 s and started 12 s after the start of the cycle. The solid line corresponds to the fit by use of the balloon model at 3 Tesla. A CBF change of 50% with ramp times of 7 s, a mean transit time of 1.8 s and a parameter τ_v of 25 s were used for the fit.

Taking the sum of the time courses of all activated voxels as the experimental BOLD response, the use of reasonable values for the CBF change between 40 % and 80%, a blood volume fraction of 2 %, a mean transit time of about 2 s and a parameter τ_v of about 25 s yielded good agreement between experiment and theory, cf. Figure 2. However, the "standard" balloon model is not able to explain the very intense post-stimulus undershoots in a few experiments. The reason for this has to be further investigated.

2.9.3 Single-shot imaging on curved slices

Jochimsen, T.H. & Norris, D.G.

The examination of extended anatomical structures generally requires the acquisition of 3D or multi-slice 2D data sets. Particularly in the case of objects that resemble a folded or distorted slice it may be advantageous to shape the excitation profile so that it is matched to the object. Such a scheme may well be less time-consuming than a multi-slice experiment but requires a considerable overhead to obtain the information needed to generate the necessary 2D image. This may, however, be justified when imaging the cortex of the brain. The previous publication to this theme excited a curved slice which was then imaged in projection on a flat 2D plane. Although the imaging experiment required to achieve this is then standard, there may be difficulties caused by the effective spatial resolution varying within the slice. In this abstract, the possibility of imaging on a coordinate system in the slice-plane is examined. The resulting image then has uniform resolution and represents an un-warping of the curved excitation slice onto a 2D plane.

Excitation was performed using a standard 2D RF pulse. This permitted a 2D curved excitation with the third dimension unrestricted. This third dimension was oriented parallel to the read gradient in a GRASE imaging experiment using non slice-selective refocusing pulses. The problem then simplifies to finding a *k*-space trajectory in the other two dimensions that captures the in-plane information. The most practical method found to date approximates the curved slice with a polygon. Each segment of the polygon in image-space requires a radial *k*-space trajectory, which is parallel to it. The *k*-space information regarding the slice profile is perpendicular to this. Provided that the slice profile information does not interfere with the in-plane information from another polygon-segment, it is possible to uniquely reconstruct an image. Experiments were performed on a Bruker 3 T/100 Medspec system equipped with 45 mT/m, 300 µs gradients. Images were obtained from healthy volunteers who had previously given

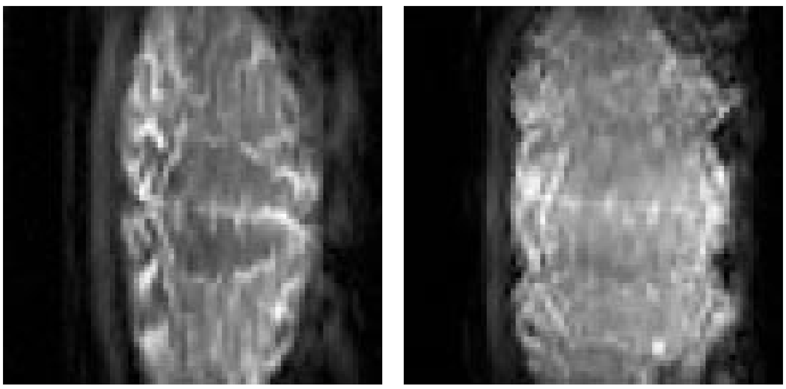


Figure 3. An approach to obtaining images from non-flat planes has been successfully demonstrated. With further development it should find useful application in fMR.

informed consent. In the GRASE sequence 3 gradient echoes per spin echo were acquired at a *TE* of 11 ms. A three segment polygon was acquired with 198 phase-encoding steps. The TIPE phase-encoding scheme was used and the data multiplied by a resolution-enhancing filter to ameliorate the effects of signal decay during the acquisition period. Resulting images are shown in Figure 3.

2.9.4 Transmit / receive Helmet Coil for imaging and spectroscopy applications at 3 Tesla

Driesel, W. & Norris, D.G.

The application of surface coils in MR imaging and spectroscopy offers the possibility to detect the signal from specific regions of interest, and gives an improvement in the signal to noise ratio (SNR). This is important for spectroscopic applications as well as high resolution or functional imaging. Generally, the effective imaging depth of a surface coil is proportional to the coil size. For that reason, the helmet coil described by Merkle et al. (Proc. ISMRM 2000, p.565) is limited to the upper part of the brain. Our goal was now to develop a circular polarised transmit / receive helmet coil for *in-vivo* imaging and spectroscopic studies of the whole brain. In order to maximise the sensitivity as well as the homogeneity of the B_1 field in special regions of the brain we built a swivelling helmet coil which enables the helmet to be rotated about the *x*-axis.

Figure 4. Photograph of the swivelling helmet coil.

The B_1 field distribution for the coil was mapped by using a standard multislice spin echo imaging (SE) sequence implemented on the Bruker 3T/100 MEDSPEC system. A spherical phantom (diameter 16.5 cm; filled with gel) was placed in the centre of the coil. For SE imaging sequences using an excitation pulse with a flip angle of ϕ and a 180° refocusing pulse, the signal intensity (SI) is related to ϕ by $SI \propto \sin\phi$. If two SE images are acquired with identical scan parameters ($TR > 5T_1$), but with different flip angles ($\phi_2 = 2*\phi_1$), the intensity ratio of the two images has the relationship $SI_1 / SI_2 = \sin\phi_1 / \sin\phi_2$. According to this relationship the B_1 field can be calculated with $B_1 = \phi_1 / \gamma\tau$ where γ is the gyromagnetic ratio and τ the duration of the excitation pulse. In our experiment, two sets of axial images where acquired using a multislice SE sequence (8 slices, distance 10 mm, thickness 7 mm, TE = 13 ms, TR = 10000 ms, FOV = 20 cm, τ = 3.2ms) with different flip angles (ϕ_1 = 45° and ϕ_2 = 90°). The homogeneity obtained in the x-y-plane is better than 15 %. Along the z-axis there is a moderate B_1 gradient. As an example a high-resolution image is shown in Figure 5.

Figure 5. High resolution IR image of the human brain (512×512 pixels, in-plane resolution 0.375 mms, slice thickness 1.5mm, inversion time 922 ms, repetition time 2.8 s).

2.9.5 Characterization of motor sensitivity depending on diffusion weighting time

von Mengershausen, M., Weih, K. & Norris, D.G.

Diffusion weighting preparation experiments are sensitive to spin motion due to bulk or physiological motion (e.g., blood flow) of the subject resulting in phase errors. Hence, combining diffusion weighted preparation with the segmented imaging techniques needed for higher spatial resolution is only possible with correction methods like navigator echoes (keeping the phase information of each segment of an image) to correct bulk motion. To overcome the effect of physiological motion, like the pulsatile motion of the brain, ECG-triggering has been proposed. Another possibility is to use moment nulled gradient schemes for diffusion weighting, thus avoiding the requirement for navigator echos. These schemes are insensitive to constant spin velocity. As it is necessary for the diffusion weighting to take a certain time to produce a detectable contrast in diffusion, this leads to the question as to what is the limit of the assumption of constant spin velocity during the diffusion weighting period.

In this work a method was developed to measure the additional phase errors due to bulk motion and their effect on segmented diffusion weighted EPI, depending on the duration of the diffusion weighting. Two diffusion weighting gradient schemes (no-m1 and no-m1-m2), both insensitive to spin motion with constant velocity, and no-m1-m2 with negligible sensitivity to spin motion with constant acceleration, were compared. The aim was to look for differences between these schemes because this is a measure for accelerated spin motion, at least for shorter diffusion times.

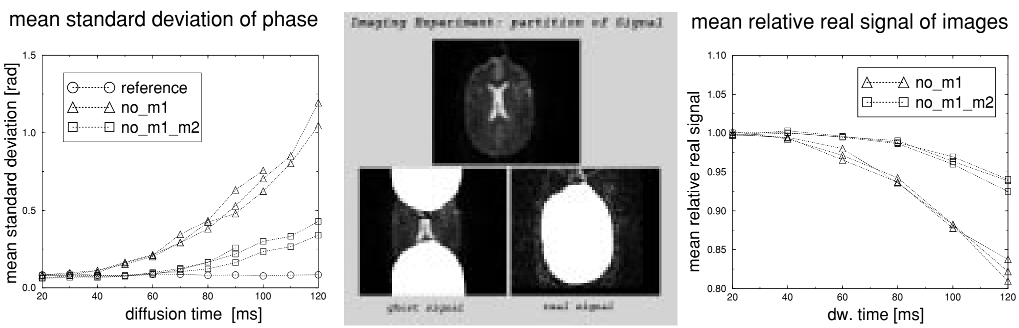


Figure 6. Left side: Result of phase experiment ; middle: illustration of signal distribution for the imaging experiment (the slice shown here is not the slice used in the experiments); Right side: result of imaging experiment.

Measurements of signal phase following the diffusion-weighting period and imaging were performed on six healthy subjects. For each subject 500 repetitions for the phase measurement and 100 for the imaging experiments were obtained. For both experiments the slice from which data was obtained was positioned in an area of the brain weakly influenced by pulsatile motion.
As a measure of phase errors first the standard deviation of each repetition and then the mean of the 500 repetitions was calculated. This value is called the mean standard deviation of phase (see Fig. 6, left side).
The effect of phase errors on the DWEPI imaging sequence was determined by the fraction of the signal appearing in the place where 100% of the signal would be in case of no phase errors. The mean of this value was calculated and is called the mean relative real signal (see Fig. 6, right side). If this value is 1, the image data is undisturbed. In Figure 6, in the middle, the signal distribution of disturbed image data (ghost signal) and artefact free image data (real signal) can be seen.

The graphs in Figure 6 show that the effect of accelerated spin motion increases with diffusion weighting time. This result indicates that the assumption of constant spin velocity for diffusion weighting times greater than times about 30 ms is not valid. Therefore, it cannot be expected that gradient moment nulled schemes sufficiently compensate phase errors due to spin motion for diffusion weighting times longer than 30 ms.

The main focus of our workgroup is to develop methods for the analysis of magnetic resonance image data of the human brain. Automatic image analysis as well as statistical methods play a fundamental role in this context. In the year 2000 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 visualization of fMRI data. It has by now become the principal software tool for fMRI analysis throughout the institute (2.10.1). Software development and user support have taken up much of our time, but we think that the success has justified the time and effort spent. This year, we have begun to distribute the Lipsia-package (non-commercially) to a few external co-operation partners. We hope that through external co-operations and comments from other people we will gain new insights and get some new ideas for improving Lipsia.

A second area of our research was focused on the development of mathematical methods for analyzing functional connectivities in the human brain using fMRI data. We developed a new approach that is based on a spectral analysis of fMRI time series data. Under the assumption of weak stationarity, coherence measures between any two voxels are used to detect functionally coherent clusters in the brain. Since these measures are defined in the frequency domain, we obtain additional temporal information about the phase lead of one voxel against another. Thus, we can analyze the BOLD signal as it propagates from one brain area to the next (2.10.2).

In another research project, we investigated factors that determine the process of gyrification. Together with a doctoral student in medicine, we examined MR images of 195 subjects using new image analysis algorithms and structural equation modeling. The analysis revealed that a purely mechanical model of the cortical folding is not consistent with the covariance structure found in our data (2.10.3).

Another doctoral thesis project was started that aims at providing a highly accurate segmentation of the human cortex using a level set approach. As a first step, an interactive visualization tool called LIMA (Lipsia Image Manipulation and Analysis Package) was developed that will help us to visualize segmentation results as well as other data types (2.10.4). In the context of this work, we had a very fruitful co-operation with the Max Planck Institute of Mathematics in the Sciences in Leipzig, for which we are very grateful.

In the coming year, we will continue our various research projects. A special emphasis will again be placed on techniques for detecting and modeling functional connectivities in the brain using fMRI data. We will expand our collaboration with partners in Israel. We are grateful that we have received a grant from the German-Israeli Research Foundation, that will allow us to begin a new project with a focus on surface flattening and inter-individual registration methods.

2.10.1 LIPSIA - Leipzig Image Processing and statistical inference algorithms

Lohmann, G., Müller, K., Bosch, V., Mentzel, H., Heßler, S. & von Cramon, D.Y.

LIPSIA (Leipzig Image Processing and Statistical Inference Algorithms) is the in-house software-system for the data processing and evaluation of functional magnetic resonance images. It was used throughout the institute for virtually all fMRI experiments conducted in the past year.

The analysis of fMRI data comprises various aspects including filtering, spatial transformation, statistical evaluation as well as segmentation and visualization. A number of well established and peer-reviewed algorithms were implemented in Lipsia that allow an efficient and user-friendly processing of fMRI data sets. The statistical evaluation in LIPSIA is based on the general linear model. Various hemodynamic modeling functions are supported. In its statistical methodology, LIPSIA closely follows well-established techniques. Other parts of the software such as registration, segmentation and visualization are algorithmically novel.

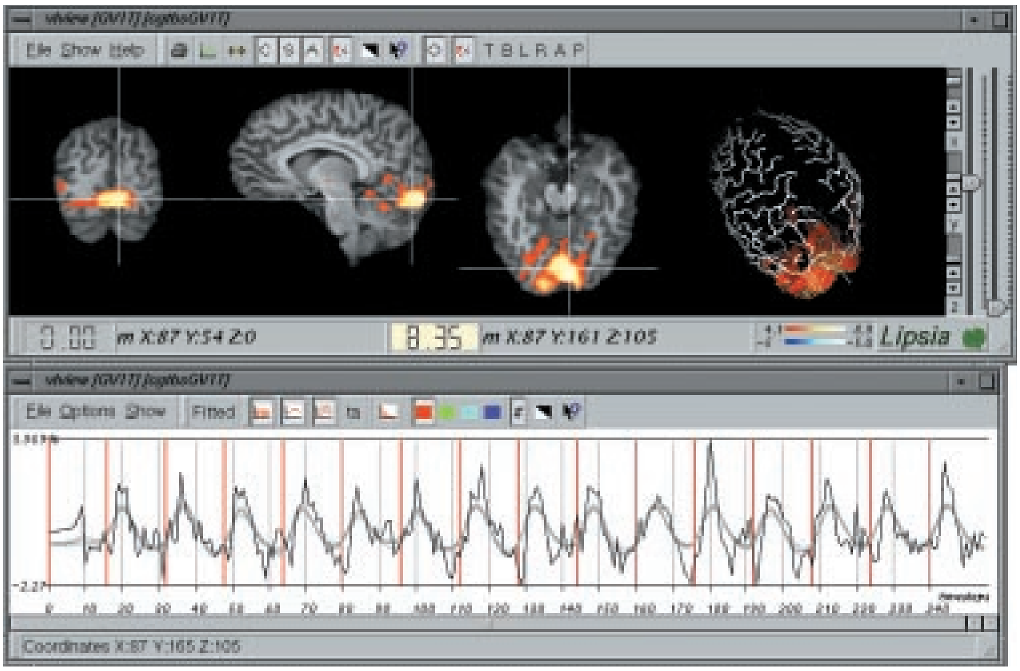


Figure 1. Visualizing activation areas in fMRI experiments. Time courses, design information as well as many other types of information such as the power spectrum, trial averages, evoked response are shown at a mouse click. The cortical folding patterns of individual subjects can be displayed and geometrically linked to the raster data so that a mouse click highlights corresponding locations in both display windows.

Particular emphasis was placed on the development of new visualization and segmentation techniques that support visualizations of individual brain anatomy. Figure 1 gives an example: sulci are represented as three-dimensional polygonal lines that can be rotated in real time and geometrically linked to the anatomical raster data so that the anatomical locations of activation areas can be easily assessed.

As the amount of data that must be handled is enormous, an important aspect in the development of LIPSIA was the efficiency of the software implementation. It currently functions in an environment in which fMRI experiments are conducted for about 10 h/day, generating about 2 GByte of data every day.

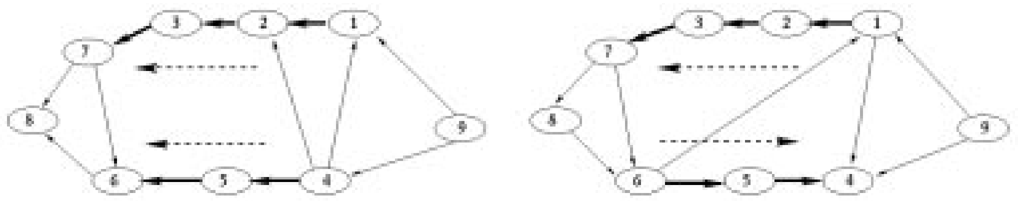
The LIPSIA software is implemented in C and C++ and runs within the Unix operating system. Most programs additionally run in a parallelized version implemented on a 16-processor parallel computer (SGI origin 2000). FMRI time series are stored in a user-friendly 4D format requiring only one data file per subject.

2.10.2 Investigating the formation of the human frontal cortex using structural equation modeling

Lohmann, G., von Cramon, D.Y., Huttner, H. & Bosch, V.

There is an ongoing debate about the factors that determine the cortical folding. In general, one can distinguish between two opposing views in this debate (Welker, 1990; Armstrong et al., 1995). One view assumes a 'proximal cause that is mechanical in nature' as the predominant factor that determines the development of cortical convolutions. This view has sometimes been termed the 'mechanical hypothesis' (Richman, 1975; Armstrong et al., 1995). The opposing view assumes a summation of many factors that are related to active instrinsic processes (e.g., Rakic et al., 1985; Welker, 1990; Smart et al., 1986). According to this view, the sulcal fundi are anchored to the lissencephalic brain while other growth processes move the gyral crowns outward. Movements of sulcal fundi should then primarily occur as a consequence of global deformations of the lissencephalon. We addressed this issue using structural equation modeling (SEM) techniques applied to 195 high-resolution T_1-weighted MRI data sets acquired from 96 female and 99 male subjects. Structural equation modeling was used to fit causal models that describe spatial interactions between sulcal fundi of the left frontal cortex.

We investigated two alternative SEM models. Local mechanical forces as hypothesized by the 'mechanical view' should manifest themselves as local influences between adjacent sulcal fundi. Therefore, our first model was designed to express these influences (see Fig. 2a). At the same time it is consistent with current knowledge about the temporal process of gyrification. The second model expresses global deformations such as scaling and shearing (Fig. 2b). Both models agree well with the observed covariances in our data.



(a) (b)

Figure 2. Structural equation models that express spatial influences between sulcal fundi. Model I is consistent with the temporal process of gyrification, whereas model II is not.

However, the first model breaks down in the presence of a global scaling transformation applied to our input data. In other words, the reason why it initially fitted the data was simply that it expressed a global linear deformation. Therefore, we conclude that the major factors that determine the positioning of sulcal fundi — in so far as they are visible at the macroscopic level — are global in nature. This finding agrees well with the hypothesis that sulcal fundi are anchored to the lissencephalon so that movements of sulcal fundi can be interpreted as consequences of global deformations of the lissencephalic brain rather than as local mechanical influences.

2.10.3 On multivariate spectral analysis of fMRI time series

Müller, K., Lohmann, G., Bosch, V. & von Cramon, D.Y.

Functional connectivities in human brain can be described using the correlation structure of fMRI time series in the time or spectral domain. Our new approach is based on the spectral theory for multivariate time series that goes back to the findings of Wiener and Kolmogorov on prediction theory for weakly stationary stochastic processes.

We assume weak stationarity, and therefore our approach is suitable for analyzing experiments with periodic stimuli. The experimental paradigm is characterized by the fundamental frequency. The core of the method is the estimation of the cross-covariance function and the spectral density matrix. This matrix contains bivariate spectral measures for all combinations of two voxels of the whole brain. The entries of that matrix can be used for computing estimations of *coherence* and *phase lead* that is a central issue in our approach.

Coherence of time series was also introduced by Wiener, and it is a measure of the degree of linear association between time series. Roughly speaking, we may refer to the coherence as a correlation coefficient in the frequency domain. The squared coefficient of coherence can be interpreted as the proportion of the power in one of the two time series that can be explained by its linear regression to the other time course. Brain regions with a high coherence value are considered as areas that belong to the same network structure. Maps of coherence can be generated for any interesting frequency. The nature of periodic designs ensures that the components of the spectral measures attributable to the response to the stimulus will occur at a few discrete frequencies in the spectral domain.

For clusters of voxels with a high sample coherence, the pairwise average phase lead can be computed at frequencies suggested by the experimental task. Dividing the phase lead by the frequency, the parameter of *time lead* of the harmonic of the selected time series can be obtained. Because this is exactly the time lead of the measured signal at two selected voxels, this parameter can be considered as the temporal displacement of the BOLD response in a brain region with respect to another region. For our interpretation, we pay attention to confidence intervals to evaluate the quality of the estimation. By calculating the time lead for all voxels of cluster of high coherence, we are able to investigate the temporal dynamics of functional connectivities. Brain regions with an early maximum of the response can be separated from those areas with a late BOLD response.

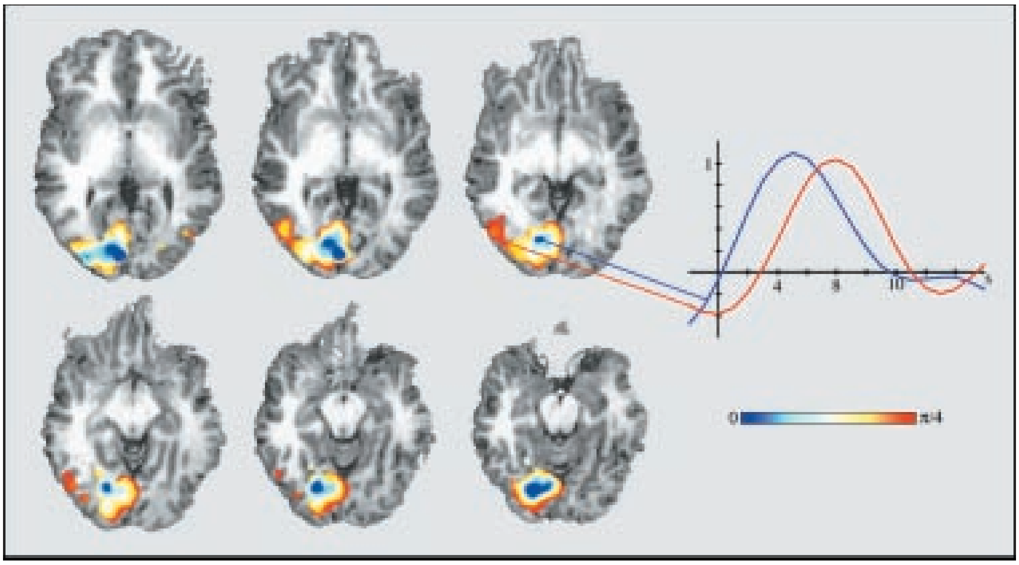


Figure 3. Several axial slices of an individual subject showing the estimated phase lead evoked by a periodic right visual hemifield stimulation with a cycle of 30 seconds. The phase is computed for brain regions that show at least a sample coherence of 0.75 (visual cortical areas V1/V2 and a region in the vicinity of the lateral occipital sulcus covering O2). The curves show trial averages of the data in two brain regions with an early and a late response.

2.10.4 LIMA: An object-oriented visualization and analysis framework for large volumetric datasets

Busch, N.H. & Lohmann, G.

The ability to interactively process, visualize and explore large volumetric datasets (LVD) is crucial for the understanding of data common in neuroscience, e.g. anatomical and functional MRI datasets. Furthermore, the validation of algorithms acting upon the data by visual and quantitative inspection is of great importance. However, the form of data and its most suitable visual representation varies greatly from one context to another. Therefore, a versatile and modular visualization and analysis framework has been developed to meet these requirements.

LIMA (Lipsia Image Manipulation and Analysis package) is based upon an object-oriented framework, offering a modular concept for representing three different entities occurring in visualization and analysis tasks. The framework distinguishes between data modules, representation or scene modules and compute modules. They form the base of a class hierarchy, from which specialized modules can be derived. Data modules encompass n-dimensional volumetric datasets (scalar, vector, tensor) or polygonal meshes. To each data module, a certain set of visualization components can be attached by the scientist through an intuitive graphical user interface. Among possible representation modes for volumetric datasets are, for instance orthogonal and oblique cutting planes, isosurfaces with geometrical simplification and smoothing operations or arrow plots. Data modules can also be further processed through different compute modules, forming new data modules as output of the processing chain. An interactive segmentation module is an example of this. When the need arises, the framework can easily be extended by new modules, e.g. a new visualization method for tensor data. The exchange of data to and from LIMA is possible through the Vista file format and VRML (Virtual Reality Markup Language), a standardized file format for 3D data and scene descriptions, thereby allowing a wide distribution of data produced by LIMA.

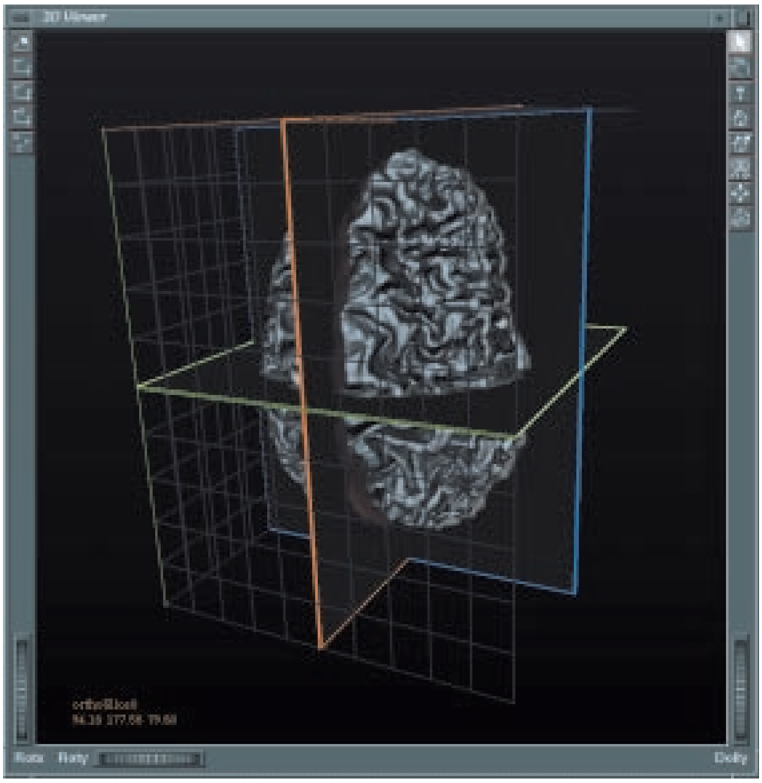


Figure 4. A typical session for visualizing data with LIMA. Axial, saggital and coronal cutting planes through an MRI volume are displayed together with an isosurface.

The MEG group continued their applied research on analysis of MEG and EEG data. One contribution (2.11.1) deals with the heart artifacts, which have to be removed from the data because one cannot reject contaminated epochs. The suggested method could also be used more generally, e.g. for the reduction of eye artifacts. Another method (2.11.2) allows for calculation of a cortical magnetic field distribution, which is due to the much smaller distance between sources and the virtual sensors less distributed than the measured magnetic field distribution. This opens an alternative way to derive the appropriate source model directly from the experimental data, at least if the cortical sources are dominant.

Two contributions (2.11.3, 2.11.4) result from work within the SimBIO framework (http://www.simbio.de). This project is very demanding in respect to the necessary couplings of different experimental, mathematical, numerical and computational methods. The two subsections describe important partial problems, which have to be solved before the finite element method may be introduced to routine applications of very fine meshes (in the order of 1 mm to localize brain activity from MEG/EEG data).

Another important field in our research is the analysis of oscillations observed in EEG or MEG channels. Based on EEG data, (2.11.5) presents an interesting observation of clear resonance phenomena within the human brain during periodic visual stimulation. This offers a nice explanation why the human brain prefers frequency bands like alpha and gamma. A visual search paradigm (2.11.6) demonstrates that illusory figures (Kanizsa) can be processed pre-attentively by an analysis of reaction time differences. A comparison of two EEG studies using Kanizsa and non-Kanizsa type stimuli but different targets reveals that the early Gamma response is strongest to the target stimulus (2.11.7). That shows that the intensity within the gamma band is also influenced by higher cognitive processes like attention.

The analysis of the dynamic properties of ERP data opens an alternative view, which even allows for single subject data analysis when comparing effects different in latency, distribution and amplitude (2.11.8).

Further projects are presented in other chapters of this Annual Report: namely, an MEG study on how the laterality of previously studied language syntactic violations depends on prosodic features like the pitch (2.1.9), a language production study, which was able to identify the left temporal cortex being significantly different activated when producing words of the same semantic category in comparison of words of different categories

(2.1.21), and a study investigating unattended deviancy detection on a word and a voice level (2.3.9).

Parts of our work are directly related to clinical applications. One paper (2.11.9) deals with automatic spike classification in ongoing EEG data. This work is funded by the BMB+F and is continuation of a project described earlier (see Ann.Rep. 98; section 3.7.9; Ann.Rep. 99, section 2.11.11). Within our cooperation project with the Neurological Rehabilitation Clinic, Machern, we could demonstrate the feasibility of MEG measurements for monitoring motor rehabilitation processes of brain injured patients (2.11.10). A further clinical study revealed that orbito-frontal brain lesions result in enhanced evoked alpha oscillations after visual stimulation (2.5.8).

The last year was also marked by severe alterations in the MEG group: Dr. Yunhua Wang left our group to continue his career at the McGill-University, Montreal, Canada, because the Canadian government had offered him permanent residency. Dr. Ian Walker finished his stay as a visiting research fellow and is now at the University of Bath, UK. Ulrich Oertel is now working on micro-sensors for a commercial company. Alfred Anwander has joined our group as a new member and co-worker of Carsten Wolters within the SimBIO project.

2.11.1 Reduction of cardiac artifacts in magnetoencephalogram

Wang, Y.

Technological developments in recent years have made it possible to simultaneously record multi-channel MEG signals with whole-head magnetometers, and the relevant research is providing more and more impressive results which are enriching our understanding of the functions and pathologies of the human brain. One problem in MEG signal analysis is that the magnetoencephalographic signal is often contaminated by cardiac artifacts which can be several times stronger in magnitude than spontaneous brain activities. Although coherent averaging can reduce the effect of cardiac artifacts on event-related fields (ERFs), the potential effect of such strong artifacts is still a concern of many studies based on MEG, particularly when studying spontaneous brain activities. In the present study, we address this problem by applying the common spatial subspace decomposition (CSSD) algorithm. This method is based on the dissociation of topographical subspaces common and specific to the MEG measurement matrix and the pure artifact matrix. The artifact signal was obtained by averaging MEG measurement time-locked to the R wave of the cardiac activity. Applying CSSD to these two signal matrices can decompose the original MEG measurement into two parts: one part with the same spatial subspace as that of heart beat artifacts, the other part relating to brain activities. The artifact can then be removed as the common components.
Simulations were curried out by mixing artifact free MEG measurements and pure artifacts (averaged) from different subjects. When artifact amplitude is 3000 fT, the correlation coefficient between artifact free MEG and artifact contaminated MEG is about 0.75. After CSSD, this value was improved to 0.97, demonstrating that the artifact cab be effectively removed by the present algorithm. Among 6 subjects with strong

heart beat artifacts (1500 ft ~ 3000 fT), using CSSD can reduce the amplitude of the artifacts by a factor of 50 on average. To test the effects of the current algorithm on source localization, a phantom experiment with planted artificial dipole sources was conducted. Results show that the localization accuracy can be improved by 3-4 mm for superficial dipoles, 5-6 mm for sources at moderate depths, 6-9 mm for the deep source.

Estimating scalp MEG from whole-head MEG measurements 2.11.2

Wang, Y. & Oertel, U.

Studies based on whole-head MEG recordings are providing more and more impressive results. In such recordings, the MEG sensors are several centimeters away from the scalp and the positions of the MEG sensors with respect to the head differ from subject to subject, and from session to session for the same subject. To overcome these difficulties, we proposed a method to estimate the scalp MEG distributions from whole-head MEG measurements. The goal is to remove the discrepancy of MEG measurements caused by the various sensor positions with respect to the head, as well as to reduce the smearing effect caused by the distance of the MEG sensors from the scalp. The method was based on an indirect projection of MEG measurements to the scalp surface. The measurement was first projected to a hypothetical dipole layer within the head volume conductor model using the inverse solution. The scalp MEG estimation was then obtained from the resultant dipole layer by the forward solution. To test the method, first, simulations were carried out using a spherical head model and 148-channel MEG sensors (Bti) with different simulated dipole source configurations and noise levels. Results demonstrate that, with a reasonable signal to noise ratio (>6), scalp MEG can reveal more detailed spatial information about the underlying brain source than the original measurements. Second, the method was applied to a phantom experiment where two measurements were carried with the same planted dipole sources but different dewar positions. The results show that the discrepancy between the MEG measurements, caused by different dewar positions, was removed efficiently by estimating the scalp MEG distributions. Third, auditory evoked magnetic field (AEF) using pure tone stimulus was analyzed with the present method. The estimated scalp MEG has more localized distributions over both left and right temporal regions. This is consistent with our knowledge about the neural generators of N100 activity, demonstrating that the present method is applicable to experimental MEG data.

2.11.3 Improved tissue modeling and fast solver methods for high resolution finite element modeling in EEG/MEG source localization

Wolters, C.H.[1,2], Reitzinger, S.[3], Basermann, A.[4], Burkhardt, S.[1,2], Hartmann, U.[4], Kruggel, F.[2] & Anwander, A.[2]

[1] Max Planck Institute for Mathematics in the Sciences,
[2] Max Planck Institute of Cognitive Neuroscience,
[3] SFB F013, Johannes Kepler University, Linz, Austria,
[4] NEC Europe C&C Research Laboratories, St.Augustin

The inverse problem in EEG and MEG amounts to finding a realistic source distribution in the human brain for a given set of field observations on the surface of the head. This requires the repeated simulation of the field propagation for a given dipolar source in the brain using a volume-conduction model of the head. For most realistic modeling, the different tissues have to be segmented and assigned individual conductivity tensor material parameters. Layers like the skull or fibrous tissues like brain white matter are known to be anisotropic up to a ratio of 1:10. The radial and tangential direction of the conductivity tensor in the skull are computed through improved skull segmentation from registered T_1- and PD-MR images (2.8.10). The structural information about the white matter fiber directions are acquired in an MR-diffusion tensor imaging protocol (Wolters et al., 1999). A realistic high resolution anisotropic 3D FE model of the head requires fast numerical solver techniques to compute the electric field. Figure 1 shows isopotential lines on a coronal layer of an FE mesh with smoothed (node-shift) surfaces (left) and the solver comparison for the solution of one forward calculation on a realistic head model (right). The algebraic multigrid-preconditioned conjugate gradient method (AMG-CG) is a factor 2 to 3 times faster than the best-tuned incomplete threshold factorization (ILDLT) preconditioned Krylov method (Wolters et al., 2000). Future examinations will include skull anisotropy and white-matter tensor measurements. With regard to the inverse problem, acceptable calculation times are reached by the parallelized versions of the presented solvers. An efficient concept based on a non-overlapping element-wise domain decomposition can be especially designed for the AMG-CG (see Haase et al., 2000).

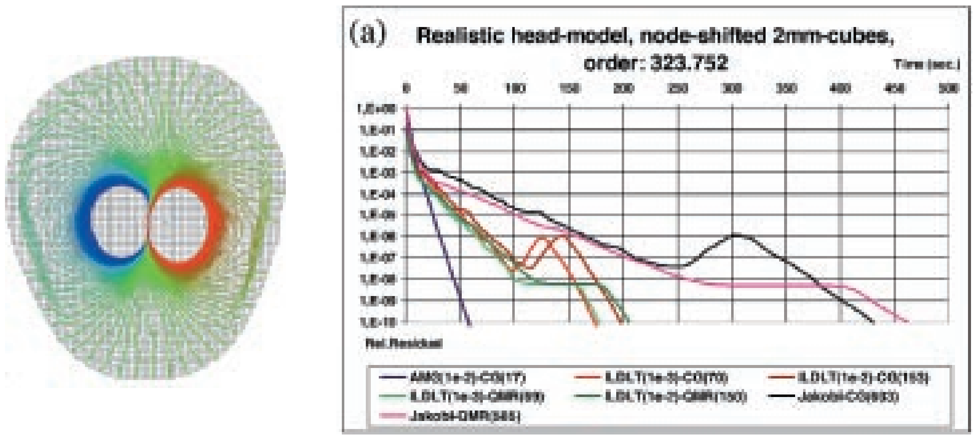


Figure 1. Isopotential lines (left), solver comparison (right).

Validation of subtraction method and FE mesh generation in multi-layer sphere model

2.11.4

Wolters, C.H.[1,2], Anwander, A.[2], Hartmann, U.[3] & Kruggel, F.[2]

[1] Max Planck Institute for Mathematics in the Sciences,
[2] Max Planck Institute of Cognitive Neuroscience,
[3] NEC Europe C&C Research Laboratories, St.Augustin

For the forward problem in EEG/MEG-source reconstruction, the potential distribution in the human head for a given dipolar source in the brain is simulated using models for the source and the head volume-conductor. The source is usually modeled as a mathematical equivalent current dipole, i.e. a current source and a sink, which are infinitively close together in the human cortical layer. This point-like equivalent current dipole has been shown to be an adequate model for the synchronous polarization of a cortical surface of about 30 mm^2. The point-like source leads directly to a singularity in the related potential which has to be treated numerically. One possibility is the "blurred dipole", where current monopoles are placed at neighboring FE-mesh nodes around the dipole location, such that the resultant moment matches that of the mathematical dipole (Buchner et al., 1997). Another possibility is the subtraction method where the "singularity-potential" for a mathematical dipole in an unbounded homogeneous conductor is calculated analytically and the correction is carried out numerically on the realistic geometry (von Rango et al., 1996; Pohlmeier, 1996). The correction is calculated with the FE method so that the sum of "singularity-" and "correction", the "total-potential", obeys the charge continuity law within the head and the Neumann boundary conditions at the surface. The subtraction method and the node-shift (ns) mesh generation approach (2.11.3) have been validated in a 4-layer sphere model where a spherical harmonics series expansion of the dipole potential can be derived for anisotropically conducting layers (de Munck, 1988, 1993). To validate the ns, we assumed the following isotropic conductivities in the 4 layer model: 0.33, 0.0049, 1.0 and 0.34 S/m. Node-shift improved the magnification error (optimum 1) from 1.115 (model without ns) to 1.053 and the relative difference measure (optimum 0) from 0.027 to 0.023 for 6 electrodes at all extreme sphere surface positions.

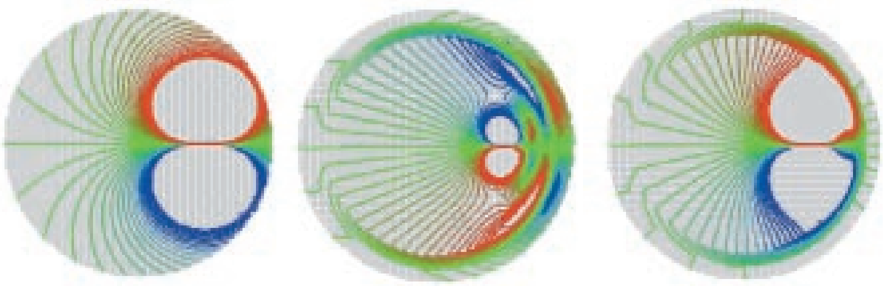


Figure 2. Isopotential lines in ns-models: singularity-potential (left) and FE-correction potential (middle) from –0.5 to 0.5 µV, total-potential from –1 to 1 µV (right).

2.11.5 Resonance frequency in human visual cortex and its putative role for cognitive phenomena

Herrmann, C.S.

The individual properties of visual objects, like form or color, are represented in different areas in our visual cortex. In order to perceive one coherent object which is composed of distributedly represented features, they have to be bound together. This was found to be achieved in cat and monkey brains by temporal correlation of the firing rates of neurons which code the same object. This firing rate is predominantly observed in the gamma frequency range (approx. 30-80 Hz, mainly around 40 Hz). In addition, it has been shown in humans that stimuli which flicker at gamma frequencies are processed faster by our brains than when they flicker at different frequencies. These effects could be due to neural oscillators which preferably oscillate at certain frequencies - so-called resonance frequencies. It is also known that neurons in visual cortex respond to flickering stimuli at the frequency of the flickering light. If there exist neural oscillators with resonance frequencies they should respond more strongly to stimulation with their resonance frequency. We performed an experiment, where 10 human subjects were presented flickering light at frequencies from 1 to 100 Hz in 1 Hz steps. The event-related potentials exhibited steady-state oscillations at all frequencies up to at least 90 Hz.

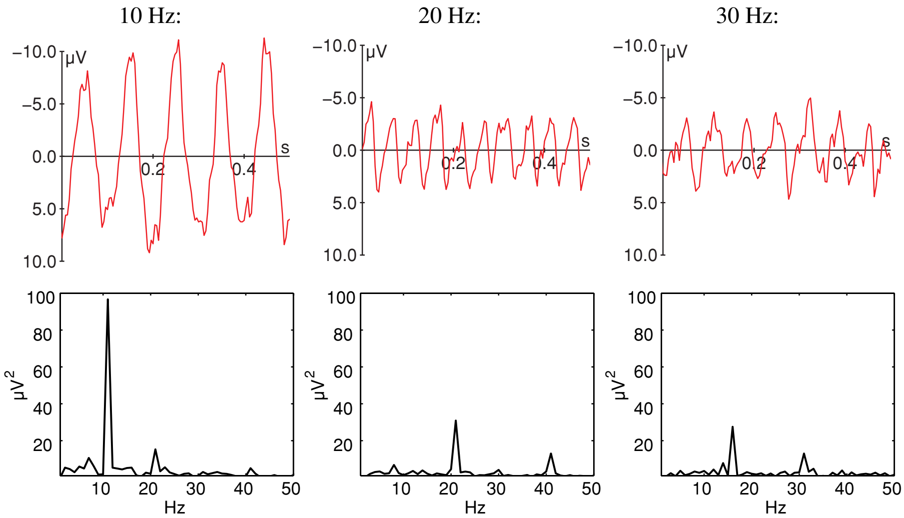


Figure 3. Steady-state event-related visual responses (SSVEPs) of a single subject in response to 10, 20 and 30 Hz stimulation. All three frequencies lead to SSVEPs of different amplitude.

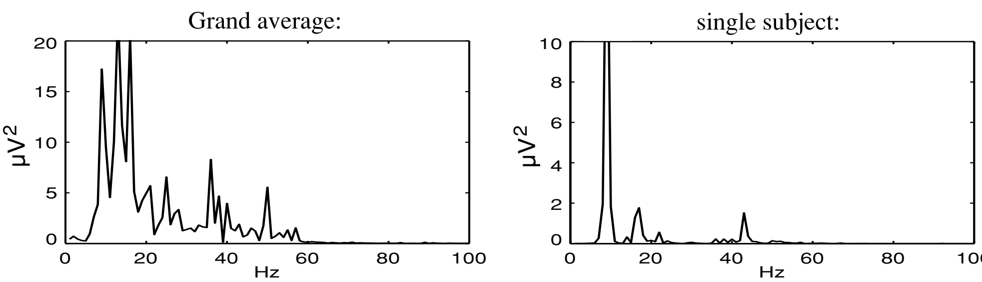


Figure 4. When the amplitudes of the SSVEPs of all frequencies are mapped into one diagram, so-called resonance frequencies become visible, which reveal at which frequencies the cortex responds most strongly to visual input.

Interestingly, the steady-state potentials exhibited clear resonance phenomena around 10, 20 and 40 Hz. This could be a potential neural basis for gamma oscillations in binding experiments. The pattern of results resembles that of multi-unit activity and local field potentials in cat visual cortex.

Kanizsa figures pop out of visual search displays

2.11.6

Herrmann, C.S.

It is a matter of debate whether or not illusory contours are processed pre-attentively and can lead to subsequent shifts of spatial attention. Previous studies have demonstrated the pre-attentive processing of Kanizsa squares but failed to demonstrate the same effect for Kanizsa triangles. We performed two visual search experiments, in which illusory Kanizsa squares and triangles had to be detected among distractors. Ten right-handed students participated in this study. All subjects were investigated in each experiment. RTs were recorded while subjects had to indicate whether or not a Kanizsa figure was present in a visual search display. Target present trials were significantly faster than target absent trials. RT slopes were around 2-3 ms/item, indicating parallel visual search.

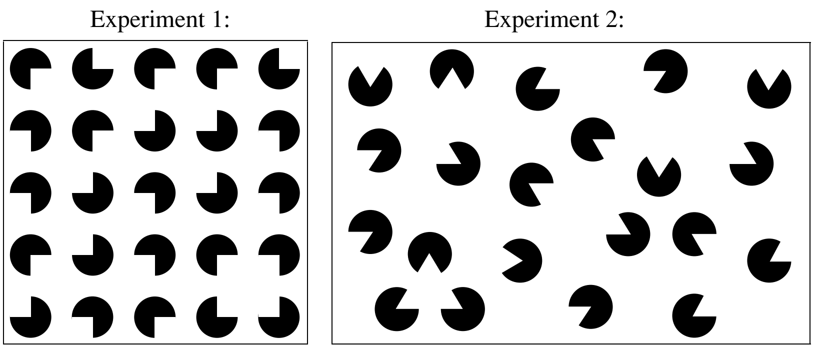


Figure 5. Regular (left) and irregular (right) arrangement of inducer disks showing a Kanizsa square and triangle which serve as targets.

Flat slopes of reaction time per item suggest pre-attentive binding mechanisms. While local stimulus properties (collinear lines / non-collinear lines) were constant across experiments, differences between the two experiments were related to global (ordered/ unordered) stimulus properties. Together with previous findings, these data seem to suggest that the pop-out effect of local stimulus features is affected by global stimulus characteristics, such as regularity in the display structure.

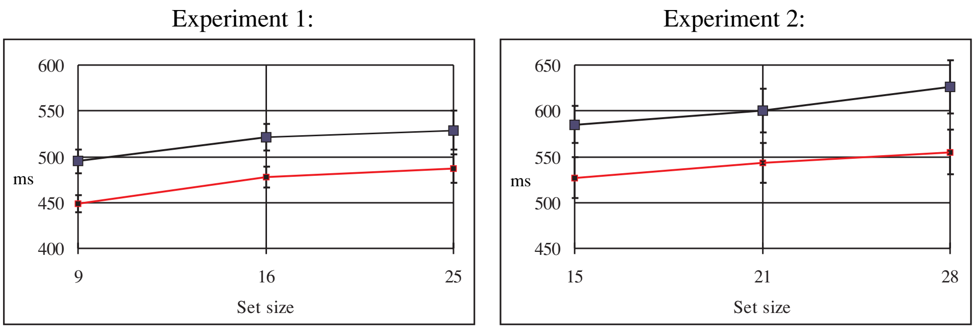


Figure 6. RT slopes to the two experiment suggest parallel pop-out search for illusory figures.

2.11.7 Gamma activity in human EEG is related to attention, memory and motor response

Herrmann, C.S. & Mecklinger, A.

Among the most important processes of the brain in order to correctly perceive the outside world and act within it are binding, attention and memory. All three functional mechanisms have been associated with brain activity in the gamma frequency range. It needs to be clarified, however, which subprocesses within the gamma frequency range relate to which perceptual or cognitive functions. In a visual discrimination task, we used Kanizsa figures, whose constituent inducer disks need to be bound together to perceive the illusory contours. By a variation of the task requirements, we manipulated the allocation of object selective attention as compared to a previous study. One out of four objects had to be detected. This detection process requires the comparison of two object dimensions (form and collinearity) with a working memory template. In order to get behavioral and electrophysiological measures, EEG and reaction-times were recorded from 16 and 10 subjects, respectively. Gamma activity was evaluated via a wavelet analysis.

In a previous detection task, in which the Kanizsa square was the target, it evoked the most gamma activity in a time interval from 50..150 ms. In the present experiment, the non-Kanizsa square was the target and again evoked the most gamma activity in this time interval. This demonstrates that the early evoked gamma activity reflects the process of allocating attention to a selected object as early as 50—150 ms after stimulus onset. We propose that the underlying mechanism is a high-speed memory comparison.

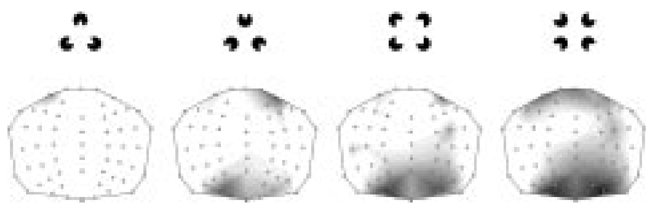


Figure 7. The four stimuli used and the topographical distribution of early evoked gamma activity (50..150 ms) in response to these stimuli. From left to right: Kanizsa triangle, non-Kanizsa triangle, Kanizsa square, and non-Kanizsa square (target). The target evokes the most gamma activity, while stimuli which are similar in one dimension evoke some and stimuli which are dissimilar in both dimensions evoke almost none. Gray-scale is form 0 (white) to 0.5 (black) µV.

In addition, we were able to show that this early gamma activity also determines the reaction times needed to respond to the different stimuli. We correlated the average of early evoked gamma activity in all electrodes with the reaction times and found a significant correlation of 0.97.

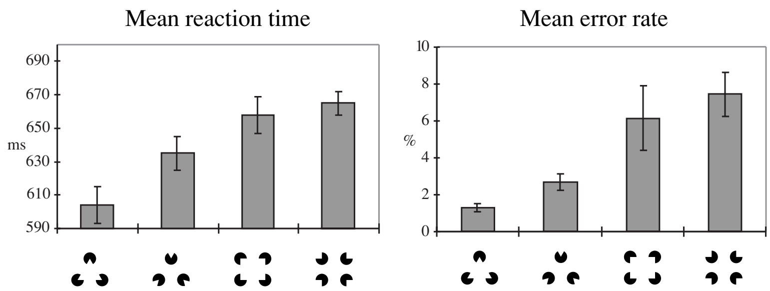


Figure 8. The reaction time and error rate in response to the four stimuli: The pattern closely resembles that of early evoked gamma activity.

New ways to analyze ERP data by methods of dynamical systems theory

2.11.8

Kotz, S.A. &
Hutt, A.

In an acoustic word list priming experiment, we examined whether the N400 priming effect in the ERP varies as a function of semantic relation (associative vs. categorical). Thirty-two subjects listened to associatively and categorically related primes and targets (CAT-DOG vs. LOCK-CHAIN), unrelated primes and targets, and pseudowords and were asked to make a lexical decision to each word.

Results show that both associative and categorical relations elicit an N400 component. However, the strength, the latency and the distribution of the ERP priming effects differ. In order to separate these subtle differences in the ERP pattern of the two conditions we applied a dynamical systems analysis.

The probability function M(t) (see Ann.Rep. 99, 2.8.9) indicates which data points belong to an ERP component: low values represent transition parts, while high values of M(t) define time windows of ERP-components. Figure 1 presents results from single-subject data for associatively (ar) and categorically related(cr) targets. Both conditions show an ERP component at [180 ms; 280 ms], while following ERP-components of condition ar appear time shifted by 50 ms as compared to condition cr.

This new method to detect dynamical states in the ERP allows a more fine-grained analysis of subtle ERP differences not only in group data, but also single subject data.

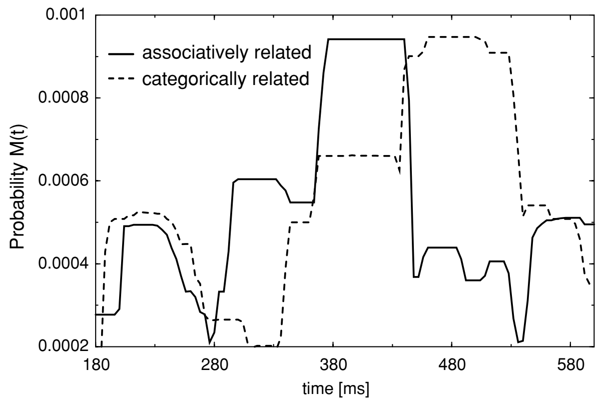


Figure 9. The probability M(t) being member of an ERP-component, plotted for all points and one subject.

Pattern recognition in clinical EEG using 'Active Shape Models'

2.11.9

Arnold, T.[1]*,*
Visbeck, A.[2] *&*
Herrmann, C.S.[1]

[1] *Max Planck Institute of Cognitive Neuroscience,*
[2] *Department of Neurology, University of Mainz*

Aside from the description in the frequency domain, the detection of characteristic graphoelements (specific patterns in the EEG trace) is an important part of clinical EEG analysis. We developed a new method of pattern recognition in ongoing EEG that can be easily adapted to a wide range of graphoelements. The effectiveness of this approach could be demonstrated in an application to spike wave detection, a crucial task in the diagnosis and treatment of epilepsy.

The method is based on an algorithm for pattern recognition known as 'Active Shape Models'. The general idea is to use a set of representative examples of the pattern (training set) and extract their average shape and typical deformations with a principal component analysis (PCA).

At first, the training patterns have to be marked in the EEG by a neurologist. These EEG sections are extracted from the signal, and are afterwards normalized and aligned to each other. Figure 10a shows our results of this procedure for the spike-wave model. In the second step, the average shape and the typical deformations are extracted from the aligned patterns. The deformations are obtained as eigenvectors of the PCA with the corresponding eigenvalues describing their standard deviation. An example of deformation of the spike-wave model can be seen in Figure 10b.

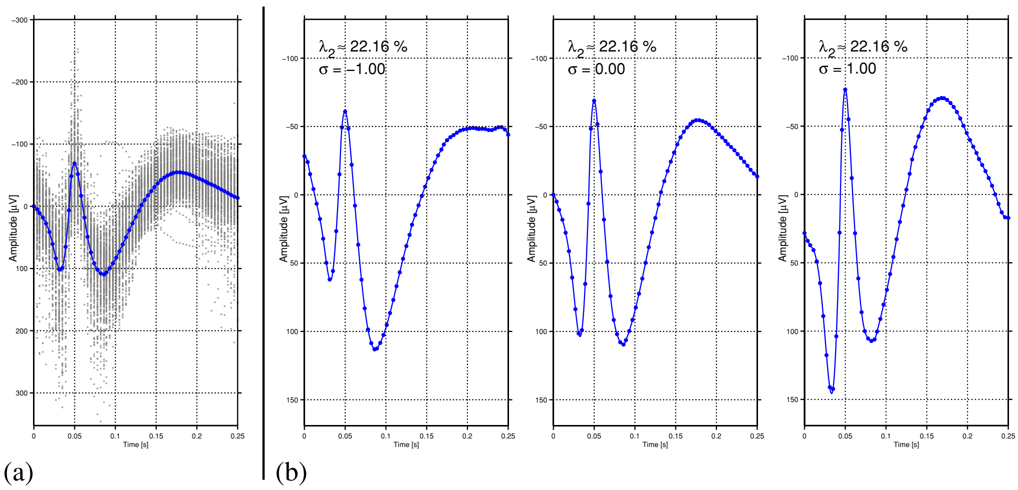


Figure 10a. Cloud of 251 aligned training patterns (gray) with overlaid average shape (blue).
Figure 10b. Extracted deformation varying by plus / minus one standard deviation from the average shape.

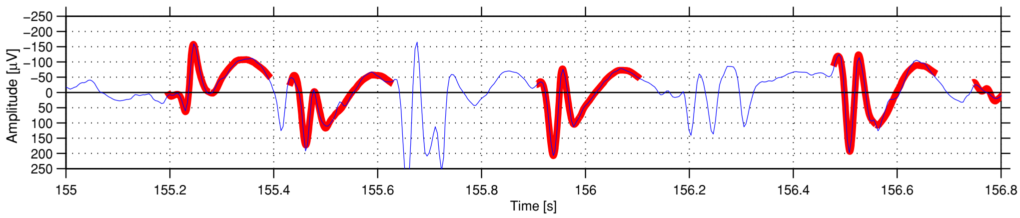


Figure 11. Automatically detected spike-wave complexes (red) in ongoing EEG (blue).

In order to apply the extracted model, the EEG trace is scanned with a sliding window for sections that are similar to the average shape. Every possible match is extracted from the signal, normalized and then aligned to the average shape. Finally, the Mahalanobis distance of the resulting shape to the average shape is computed using the eigenvalues and eigenvectors belonging to the model. If this distance is smaller than a suitable value (typically two standard deviations) the EEG section in question is accepted as being similar enough to the patterns of the training set. Figure 11 shows examples of automatically detected spike-wave complexes in an EEG trace.

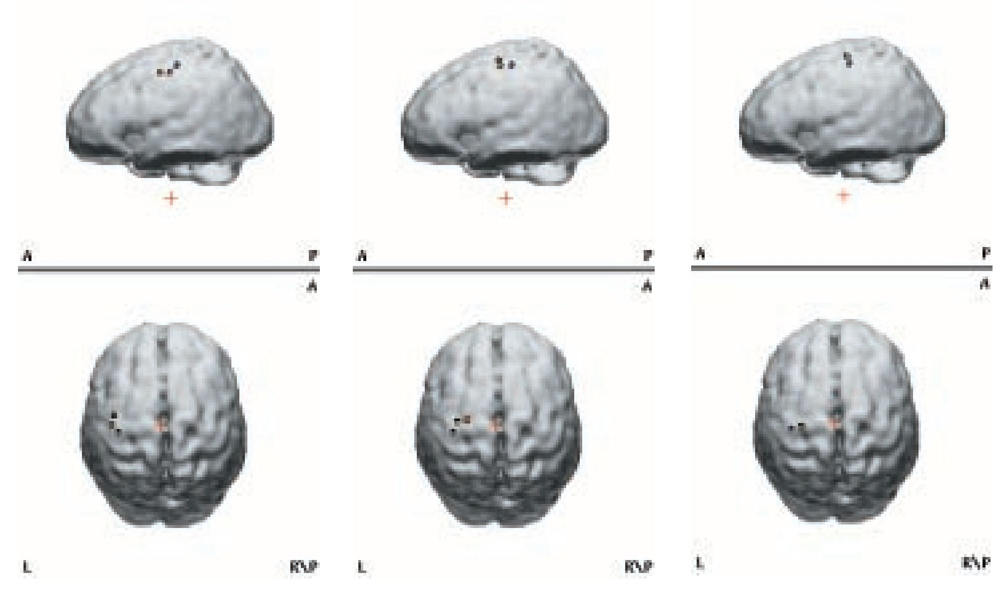
Current density analysis of movement-related cortical magnetic fields

2.11.10

Oertel, U.[1], Waldmann, G.[2], Maess, B.[1], Schubert, M.[2], Woldag, H.[2], Hummelsheim, H.[2] & Friederici, A.D.[1]

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

The aim of this study is the development of a standard MEG measurement protocol to monitor progress of clinical motor rehabilitation applied to brain injured patients. This study compares the evoked fields and localization results based on whole head MEG data measured during three different types of a horizontal right hand movement in three subjects: (a) triggered movement: volunteers were asked to move their hand towards the direction of an arrow presented on a screen; (b) voluntary movement: volunteers were asked to move their hand in a self paced rhythm; (c) passive movement: The hand of the volunteer was moved by a second person. In all cases the interval between movements was about 3 seconds. Data from triggered and voluntary movements were analyzed with Current-Density (CD) reconstruction of the first peak in the signal at about movement onset, the Motor Evoked Field I (MEF I). The CD calculations on passive movement data were conducted at the first peak, the passive field (PF), occurring about 50 to 80 ms after movement onset. The localization results yield a contralateral activation close to the sulcus centralis for all three types of movement (Fig. 12) in accordance with other studies (Lange et al., 1999). Passive movements show a slightly more posterior activation at the identical position for all subjects. The locations of the activity during the triggered and voluntary movement show small variations. This is probably caused by a superposition of the activation in area 4 and 3 (Weiller et al., 1996). Active and passive movements seem to be both feasable for evaluation of motor rehabilitation programs.



#1 #2 #3

Figure 12. Locations of the CD maxima for three volunteers in the contralateral sensorimotor area: triggered movements (MEF I) –red ; voluntary movements (MEF I) – yellow; passive movements (PF) – blue).

Library Report

3.1

Lewin, G.

The development of the Internet and the WWW has seriously changed the practice of publication, sale and use of scientific information. New forms for publication of scientific results, new forms for retrieval of these publications and the necessary effective retrieval-elements are all newly required. In 1995, the Dublin Core Metadata Initiative began to elaborate metadata standards to achieve an international agreement about the use of a defined set of metadata, which describes digital and conventional resources of information.

The mission of the Dublin Core Metadata Initiative is to make it easier to use the Internet through the following activities:
- Developing metadata standards for resource discovery across domains
- Defining frameworks for interoperation of metadata sets
- Facilitating the development of community-or domain-specific metadata sets that work within these frameworks.

Despite the Dublin Core Initiative there are series of other projects which try to use the multimedia potential for modern information management.

In an enormous undertaking, the librarians of the different MPIs started to change the existing practice of the MPG and set up a new concept. This integrated approach involves establishment of uniformity comprises uniformity in the presentation of the data, as well as the development and the investment of service and tools which are geared to the own needs (i.e., linking the resources, Data Mining Tools, investigation of data for a better control of the resources). The first step will be the preparation of an inventory of the entire stock of current literature in the MPG as Web-OPAC. This way an observable improvement of the service of the librarians will be available to the scientists. In the autumn of this year all criteria of the institutes in general which will be necessary to achieve this intention were collected. A prerequisite for all libraries which will participate in the Web-OPAC will be that they have library software at their disposal which allows the import and export of data. To carry out the data exchange at our institute, the library software "Biblio Light", which we use in our house, will be further developed.

Since 1995, the budget of the library has been fixed at a constant amount. The rising prices of the publishing houses for journal titles, an increasing production of literature, the increased demand for journal titles and a temporarily unusual high dollar rate have put the library in a very critical budget position, which has been absorbed through the institute. Therefore, as of yet there have not been reductions in the purchase of foreign monographs and the procuring of older years of journals.

The work of the library committee was concentrated on counteracting the exploding rise in prices, by:

- permanent evaluation of the current journal titles and cancellation of infrequent titles.
- all new purchases were strictly made on the main foci of research.
- an inventory/ audit was carried out to minimize the rate of loss of literature.

Unfortunately, there have been increases in the prices of the document delivery service "Subito" since 1st September 2000. This is caused by a copyright tax which must be paid to the utilization company "Word" for the direct dispatch of copies.

At present, the "printmodel" is still the main one for production and dispatch of journals. In addition to the printversion, scientists can have access to the electronic version in the electronic journal library of our institute. This includes:

- E-journals licensed throughout the MPG
- free E-journals of the subscribed journals in printed version
- parallel versions of the subscribed journals in printed version

Meanwhile, the electronic journal library contains over 1450 specialist journals.

Work with the very different license and acquisition conditions of the suppliers of electronic journals (which change over relatively short intervals) requires a lot of time and energy on the part of the librarians. In addition, there still exists the need to optimize the management of electronic journals (archivation, online access, downloading).

In this year, the entire stock of the library has grown to over 8700 media units.

4100	monographs
185	current journal titles
4450	bound volumes of journals
1	CD-ROM Data base
10	data bases with access via Internet

SOMMERSEMESTER 2000

Zu ausgewählten Themen der funktionellen Neuroanatomie des menschlichen Gehirns
Universität Leipzig
Cramon, D.Y. von, mit MitarbeiterInnen der Medizinischen Fakultät der Universität Leipzig und des Max-Planck-Instituts für neuropsychologische Forschung

Verarbeitung von Bilddaten in der Hirnforschung
Universität Leipzig
Lohmann, G.

Methoden der biomedizinischen Resonanzbildgebung und -spektroskopie
Universität Leipzig
Norris, D.G.

Lexikale Verarbeitung
Humboldt-Universität zu Berlin, Institut für deutsche Sprache und Linguistik
Jescheniak J.D.

Einführung in die Psycholinguistik
Humboldt-Universität zu Berlin, Institut für deutsche Sprache und Linguistik
Jescheniak J.D.

Psycholinguistisches Experimentalpraktikum
Humboldt-Universität zu Berlin, Institut für deutsche Sprache und Linguistik
Jescheniak J.D.
Cholin, J. (Institut für deutsche Sprache und Linguistik, Humboldt-Universität zu Berlin)

Analyse von neurophysiologischen Daten aus kognitionspsychologischen Experimenten
Universität Leipzig
Herrmann, C.S. & Maess, B.

WINTERSEMESTER 2000 / 2001

Neuropsychologie von Sprache und Musik
Universität Leipzig
Friederici, A.D., Hahne, A. & Koelsch, S.

Forschungsorientierte Vertiefungsrichtung "Kognition" im Hauptstudium Psychologie
Universität Leipzig
Friederici, A.D. & Gunter, T.
Schröger, E. mit MitarbeiterInnen des Institutes für Allgemeine & Biopsychologie

Zur funktionellen Neuroanatomie und neurologischen Rehabilitation - ausgewählte Themen
Universität Leipzig
Cramon, D.Y. von, mit MitarbeiterInnen der Tagesklinik für kognitive Neurologie
Hummelsheim, H., mit MitarbeiterInnen des Neurologischen Rehabilitationszentrums (NRZ) Bennewitz

Verarbeitung medizinischer Volumenbilddaten
Universität Leipzig
Lohmann, G.

Methoden der biomedizinischen Kernresonanzbildgebung und -spektroskopie
Universität Leipzig
Norris, D.G. & Schwarzbauer, C.

Besprechung aktueller Forschungsvorhaben - Seminar
Universität Leipzig
Pollmann, S.

Neuropsychologie
Universität Leipzig
Pollmann, S.

3.3 Committees and memberships

Prof. Dr. Angela D. Friederici

Deutsche Forschungsgemeinschaft (DFG) / German Research Foundation
Member of the Senate

State of Brandenburg
Member of the Landeshochschulrat / Scientific Council of the State Universities

University of Leipzig
- *Zentrum für Kognitionswissenschaften / Center for Cognitive Science*
  Director
- Member of the DFG Research Group "Arbeitsgedächtnis" / Working Memory
- Member of the DFG Graduiertenkolleg "Universalität und Diversität" / Universality and Diversity

- Member of the DFG Schwerpunktprogramm "Zentrale auditorische Systeme" / Central auditory systems
- *Doctorate Committee*
  Psychology

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"
- *Doctorate Committee*
  Psychology
  Linguistics
- *Habilitation Committee*
  Psychology

University of Jena

Member of the Scientific Council

Berlin Brandenburgische Akademie der Wissenschaften / BB Academy of Science

Active Member

Gesellschaft für Kognitionswissenschaft / Cognitive Science Society

Member of the Board

Editorial Activities

- Member of the Editorial Board of the *"Journal of Psycholinguistic Research"*
- Member of the Editorial Board of the *"Cognitive Science Quarterly"*
- Member of the Editorial Board of the *"Zeitschrift für Experimentelle Psychologie"*
- Member of the Advisory Board of the *"Neurolinguistik"*
- Member of the Advisory Board of the *"Psychonomic Bulletin & Review"*

HBM 2000, Sixth Annual Meeting of the Human Brain Mapping

Member of the Scientific Advisory Board

42. Kongress der Deutschen Gesellschaft für Psychologie / 42. Congress of the German Society of Psychology

Member of the Program Committee

Conference on Architectures and Mechanisms for Language Processing (AMLaP2000)

Reviewer and Member of the AMLaP Board

University of Leipzig

- *Day-Care Clinic of Cognitive Neuroscience*
  Director
- *Interdisziplinäres Zentrum für Klinische Forschung / Interdisciplinary Center for Clinical Research*
  Coordinator for the "Neurosciences"
- *Center for Cognitive Sciences*
  Member of the Board
- *Committee of Computer Resources*
  Member of the Board
- C*oordination Center for Clinical Research, Leipzig*
  Member of the Board
- *Nomination Committees*
  Neurology, Psychiatry, Psychology
  Cognitive Psychology
  Experimental Physics
  Neurology
  Membrane and Cellbiophysics
  Physiology
  Diagnostic Radiology
  Nuclear Medicine
- *Doctorate Committee*
  Neurology, Neuropathology and Neurosciences
- Member of the DFG Research Group "Arbeitsgedächtnis"/ Working Memory
- Member of the DFG Schwerpunktprogramm "Zentrale Auditorische Systeme"/Central auditory systems
- Member of the Reha-Forschungsverbund Berlin-Brandenburg-Sachsen (BBS)

International Neuropsychological Symposium
Member

European Neurological Society
Member of the Scientific Committee of the Section Neurorehabilitation

Deutsche Akademie der Naturforscher - LEOPOLDINA
Member

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

Neurowissenschaftliche Gesellschaft / Neuroscience Society
Member

Roman, Marga and Mareille Sobek Award
Member of the Scientific Committee

Forschungszentrum Jülich
Scientific Board of Biomedicine

Member of the *"Gemeinsame Kommission Klinische Neuropsychologie" (GKKN)*

Gesundheitsforschungsrat
Member of the Scientific Committee

Kompetenznetz Parkinson
Member of the External Advisory Board

Kuratorium ZNS
Member of the Scientific Board

Editorial Activities

- Member of the Editorial Board of *"Cortex"*
- Member of the Advisory Board of *"Der Nervenarzt"*
- Member of the Editorial Board of *"Zeitschrift für Neuropsychologie"*

Visitors 3.4

Dr. Mari Tervaniemi, Cognitive Brain Research Unit, Department of Psychology, University of Helsinki, Helsinki, Finland
2 Feb. - 30 April 2000
14 - 18 May 2000

Prof. Herbert Schriefers, Nijmegen Institute for Cognition and Information (NICI), Nijmegen University, Nijmegen, The Netherlands
13 - 19 Feb. 2000

Dr. Mireille Besson, Center for Research in Cognitive Neuroscience, CNRS - CRNC, Marseille, France
23 - 31 March 2000

Prof. Harald Clahsen, Department of Language & Linguistics, University of Essex, Colchester, UK
8 - 19 May 2000

Angela Scardina, Psychology Department, Fairfield University, Fairfield, CT, USA
12 June - 23 July 2000

Prof. Gabor Szekely, ETH Zürich, Institut für Kommunikationstechnik, Zürich, Switzerland
26 June 2000

Prof. Stefano F. Cappa, Department of Psychology, Vita Salute San Raffaele, S. Raffaele University, Milano, Italy
4 - 9 July 2000

Dr. Randall Engle, Georgia Institute of Technology, Atlanta, GA, USA
15 July - 15 Aug. 2000

Dr. Habib Benali, INSERM, Paris, France
17 - 29 July 2000

Dr. Monica Fabiani, Department of Psychology, University of Missouri, Columbia, MO, USA
20 July - 5 Aug. 2000

Dr. Gabriele Gratton, Department of Psychology, University of Missouri, Columbia, MO, USA
20 July - 5 Aug. 2000

Prof. David Swinney, Department of Psychology, University of California, La Jolla, CA, USA
27 July - 7 Aug. 2000
27 Sept. - 30 Nov. 2000

Dr. Matthias Schlesewsky, Institut für Linguistik, Universität Potsdam, Potsdam, Germany
7 Aug. - 7 Sept. 2000

Prof. David Barber, Medical Physics & Clinical Engineering, University of Sheffield, Sheffield, UK
4 - 5 Sept. 2000

Prof. Anne Cutler, Max Planck Institute for Psycholinguistics, Njmegen, The Netherlands
1 - 6 Oct. 2000

Dr. Jens Haueisen, Klinik für Neurologie, Biomagnetisches Zentrum, Friedrich-Schiller-Universität Jena, Jena, Germany
4 - 12 Nov. 2000

Dr. Lawrence L. Latour, Applied Science, IGC-Medical Advaces, Inc., Milwaukee, WI, USA
4 - 12 Nov. 2000

Dr. David S. Tuch, MGH-NMR Center, Charlestown, MA, USA
4 - 12 Nov. 2000

Dr. Peter Jezzard, FMRIB Centre, John Radcliffe Hospital, Headington, Oxford, UK
12 - 14 Dec. 2000

Guest lectures 3.5

Dr. Randall W. Engle, Georgia Institute of Technology, Atlanta, GA, USA
What is working memory capacity?
18 January 2000

Dr. Jörg Keller, Institut für Deutsche Gebärdensprache und Kommunikation Gehörloser, Universität Hamburg, Hamburg, Germany
Raumsyntax in der Deutschen Gebärdensprache
20 January 2000

Dr. Julio Cesar Martinez Trujillo, Neurologische Universitätsklinik, Tübingen, Germany
Effects of attention on single cell responses in MT/MST areas of the macaque monkey
26 January 2000

Dr. Thomas Grunwald, Klinik für Epileptologie, Bonn, Germany
Neue Untersuchungen zur Funktion des menschlichen Hippokampus mit Hilfe limbischer ereignis-korrelierter Potentiale
2 February 2000

Prof. Denis Le Bihan, Service Hospitalier Frédéric Joliot, Commissariat a l'énergie atomique, Orsay, France
FMRI at 3 T: The Orsay Group Experience
23 February 2000

Dr. Armin Heinecke, Institut für Psychologie, Abteilung für Allgemeine Psycholgie, TU Braunschweig, Braunschweig, Germany
Unbewusste Wahrnehmung - Die Einflüsse selektiver visueller Aufmerksamkeit auf die Verarbeitung maskierter primes
6 March 2000

Dr. Hartmut Leuthold, Institut für Psychologie, Humboldt-Universität zu Berlin, Berlin, Germany
Kopplung von sensorischen und motorischen Prozessen: Elektrophysiologische Analysen zur sensumotorischen Integration
8 March 2000

Dr. Jörg Mayer, Institut für Maschinelle Sprachverarbeitung, Stuttgart, Germany
FMRI-Studien zur Sprachproduktion: Artikulation, Prosodie, Syntax
22 March 2000

Dr. Joachim Groß, Institut für Neurologie/MEG, Universität Düsseldorf, Düsseldorf, Germany
Die Analyse kortiko-kortikaler und kortiko-muskulärer Interaktionen mit MEG und EEG
19 April 2000

Dipl.-Phys. Stefan Bleeck, TU Darmstadt, Darmstadt, Germany
Die erstaunliche Fähigkeit von Absoluthörern, komplexe Signale zu diskriminieren
6 June 2000

Dr. Jens Haueisen, Biomagnetisches Zentrum, Friedrich-Schiller-Universität, Jena, Germany
The role of tissue anisotropy in bioelectromagnetism
28 June 2000

Dr. Amy Schafer, Department of Linguistics, University of California, Los Angeles, CA, USA
Effects of intonational phrasing on the integration of preceding linguistic context
12 July 2000

Dr. Jean-Baptiste Poline, Service Hospitalier Frederic Joliot, Orsay, France
FMRI signal detection on the cortical surface
18 July 2000

Dr. Elyse Sussman, Department of Otolaryngology, Albert Einstein College of Medicine, Bronx, NY, USA
Mismatch negativity and sensory memory
19 July 2000

Dr. Heather K. J. van der Lely, Department of Psychology, Birkbeck College, University of London, London, UK
SLI children, subgroups and grammar-specific deficits: Theoretical implications for the development of cognitive systems
26 July 2000

Dr. Nicolas Francisco Lori, Neuroimaging Laboratory, Washington University, School of Medicine, St. Louis, MO, USA
Diffusion tensor tracking of neuronal fiber pathways in the living human brain
2 August 2000

Dr. Markus Bader, Institut für germanistische Linguistik, Friedrich-Schiller-Universität Jena, Jena, Germany
Subjekt-Objekt-Ambiguitäten im Kontext
16 August 2000

PD Dr. Dr. Horst Mueller, Institut für Linguistik und Literaturwissenschaften, Universität Bielefeld, Bielefeld, Germany
Repräsentation lexikalischer Kategorien: Neurolinguistische Ergebnisse
13 September 2000

Dr. N. Jon Shah, Institut für Medizin, NMR, Forschungszentrum Jülich, Jülich, Germany
Methodological development of keyhole imaging, T_1 and T_2* mapping for fMRI
18 October 2000

Dr. Nikolai A. Bondarenko, Institute of Radio-Engineering and Electronics, Russian Academy of Sciences, Moscow, Russia
The study of human primary visual cortex using MEG
1 November 2000

Dr. Judith Streb, Institut für Psychologie, Philipps-Universität Marburg, Marburg, Germany
Brain potentials during processing of anaphoric forms
8 November 2000

Dr. Jens-Max Hopf, Klinik für Neurologie, Otto-von Guericke-Universität Magdeburg, Magdeburg, Germany
Neural mechanisms of visual search
15 November 2000

Prof. Dr. David Swinney, Department of Psychology, University of California, La Jolla, CA, USA
Lexical properties and processes in service of combinatorial (language) processing
4 December 2000

Dr. Peter Jezzard, FMRIB Centre, John Radcliffe Hospital, Headington, Oxford, UK
High field human MRI: Successes, potentials and pitfalls
13 December 2000

Dr. André Brechmann, Leibniz-Institut für Neurobiologie, Magdeburg, Germany
FMRI-Studien zur Repräsentation frequenzmodulierter Töne im Auditorischen Cortex
20 December 2000

Internal / Informal Talks

Mitglieder der Projektgruppe 'RT-Linux', Fachhochschule Fulda, Fulda, Germany
Linux - mehr als eine Alternative für 'Echtzeit'-Arbeitsplätze
26 May 2000

Dr. Christian Uhl, Philips Research Laboratories, Man Machine Interfaces (MI), Aachen, Germany
Subspace methods for signal enhancement
24 October 2000

Wilhelm-Wundt-Lecture

Prof. Dr. Robert Desimone, Scientific Director, Division of Intramural Research Programs, NIMH NIH, Bethesda, MD, USA
Cortical mechanisms for visual selective attention
15 March 2000

3.6 Congresses, workshops and colloquia

Congresses

CUNY 2000 'Thirteenth Annual Conference on Human Sentence Processing'
Friederici, A.D., and
Bouck, V., Hickok, G., Love, T., Nicol, J., Shapiro, L., Swinney, D. & Zeidell, A.
University of California, La Jolla, California, USA, March-April 2000.

Workshops and colloquia

Workshop *'Development and Interaction of Linguistic and Non-Linguistic Cognition in Infants'*
Friederici, A.D., and
Weissenborn, J.
unterstützt durch die Otto und Martha Fischbeck-Stiftung am Wissenschaftskolleg zu Berlin, MPI Leipzig & das durch die DFG geförderte Innovationskolleg "Formale Modelle Kognitiver Komplexität" an der Universität Potsdam, Berlin, Germany, February 2000.

Workshop *'Textverstehen und Textproduktion bei Aphasie: Diagnostik und Therapie'*
Ferstl, E.C., and
Engell, B.
3. Würzburger Aphasie-Tage, Würzburg, Germany, February 2000.

Symposium *'Neural binding of space and time: Spatial and temporal mechanisms of feature-object binding'*
Herrmann, C.S., Mecklinger, A., and
Humphreys, G.W. (University of Birmingham, United Kingdom)
Elliot, M.A., Müller, H.J. (University of Leipzig)
MPI, Leipzig, Germany, March 2000.

Workshop *'Textverstehen und Textproduktion nach Hirnschädigung: Diagnostik und Therapie'*
Ferstl, E.C., and
Engell, B.
Deutscher Berufsverband für Logopädie, Naumburg, Germany, March 2000.

Special Session I at the CUNY 2000 *'The structure of language comprehension as revealed by electrophysiology'*
Friederici, A.D.
University of California, La Jolla, California, USA, March-April 2000.

Workshop *'Foundations of Language'*
Jackendoff, R., and
Friederici, A.D. & Urban, S.
MPI & University of Leipzig, Leipzig, Germany, May 2000.

Workshop *'Störungen der Kommunkationsfähigkeit bei Frontalhirnläsionen ohne aphasische Sprachstörungen'*
Ferstl, E.C.
Neurologische Klinik der Universität Zürich, Switzerland, July 2000.

Workshop *'Neuropsychopharmakologie - Teil 1 + 2'*
Müller, U. & Ullsperger, M.
Akademie der Gesellschaft für Neuropsychologie (GNP), Würzburg, Germany, July 2000.

Workshop *'SimBio Project Meeting'*
Kruggel, F.
MPI, Leipzig, Germany, July 2000.

Workshop *'Cognition and Action'*
Prinz, W., and
Friederici, A.D. & von Cramon, D.Y.
MPI Leipzig, Leipzig, Germany, July 2000.

SummerSchool TuBBS 2000 - Tutorials in Behavioural and Brain Sciences :
'Cognitive Processing and its Representation in the Brain'
Fiebach, C.J. & Weber, K.
Wörlitz, Germany, July/August 2000.

Workshop *'Neuropsychopharmakologie - Teil 1'*
Müller, U.
Akademie der Gesellschaft für Neuropsychologie (GNP), Leipzig, Germany, October 2000.

Workshop *'Special session on prosodic modeling and transcription'*
Mixdorff, H.J., and
Grabe, E. & Alter, K.
PROSODY 2000: Speech Recognition and Synthesis, Krakow, Poland, October 2000.

Workshop *'Arbeiten mit Texten in der Sprachtherapie: Die Analyse von Makrostrukturen'*
Ferstl, E.C.
27. Jahrestagung der Arbeitsgemeinschaft für Aphasieforschung und -behandlung, Munich, Germany, November 2000.

Workshop *'Einführung in die Neurolinguistik: Aphasische und nichtaphasische Sprachstörungen'*
Guthke, T., and
Ferstl, E.C., Kotz, S.A. & Regenbrecht, F.
Akademie der Gesellschaft für Neuropsychologie (GNP), Leipzig, Germany, November 2000.

Workshop *'Models to generate individual anisotropic conductivity maps of head tissues from multimodal-MR and influence on EEG/ MEG-source localization'*
Wolters, C.H. & Anwander A.
MPI, Leipzig, Germany, November 2000.

Workshop *'On the nature of case'*
Bornkessel, I.
University of Potsdam & MPI Leipzig, Potsdam, Germany, December 2000.

Degrees 4.1

Habilitations

Dr. Jörg D. Jescheniak	Habilitation im Lehrgebiet Psychologie, PD Dr. phil. habil. Universität Potsdam

Doctoral Degrees

Stefan Frisch	Doktor der Philosophie, Dr. phil. Universität Potsdam
Martin Meyer	Doktor der Naturwissenschaften, Dr. rer. nat. Universität Leipzig
Karsten Steinhauer	Doktor der Naturwissenschaften, Dr. rer. nat. Universität Berlin
Stefan Koelsch	Doktor der Naturwissenschaften, Dr. rer. nat. Universität Leipzig
Thomas Jacobsen	Doktor der Naturwissenschaften, Dr. rer. nat. Universität Leipzig

Awards 4.2

D. Yves von Cramon	Member of the Scientific Board of the Gesundheits-forschungsrat
Angela D. Friederici	Member Elect of the Deutsche Akademie der Naturforscher / German Academy of Natural Sciences LEOPOLDINA Member Elect of the International Neuropsychological Symposium

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
Andreas Hauptmann*	Nachwuchsförderpreis der GNP

* (University of Leipzig, Dissertation advised at the Max Planck Institut, by E. Ferstl, Ph.D.)

PUBLISHED BOOKS AND BOOKCHAPTERS 5.1

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

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

Clahsen, H. & Friederici, A.D. (in press).
Sprachverlust.
In G. Holthaus & M. Metzeltin (Eds.), *Lexikon der Romanistischen Linguistik,* Tübingen: Niemeyer.

Cramon, D.Y. von & Markowitsch, H.J. (2000).
Human memory dysfunctions due to septal lesions.
In R. Numan (Ed.), *The Behavioral Neuroscience of the Septal Region* (pp. 380-413), New York, NY: Springer.

Elliott, M.A., Müller, H.J. & Mecklinger, A. (2000).
Oscillatory characteristics of visual persistence.
In E. Schröger, A. Mecklinger & A.D. Friederici (Eds.), *Working on Working Memory* (pp. 27-42), Leipzig: Leipziger Universitätsverlag.

Ferstl, E.C. (in press).
Learning from text.
In N.J. Smelser & P.B. Baltes (Eds.), *International Encyclopedia of the Social & Behavioral Sciences,* vol. III/13: Cognitive Psychology and Cognitive Science (Ed. W. Kintsch), Amsterdam: Elsevier.

Friederici, A.D. (2000).
Sprache und Gehirn: Zur Neurobiologie der Sprachverarbeitung.
In N. Elsner & G. Lüer (Eds.), *Das Gehirn und sein Geist* (pp. 71-85), Göttingen: Wallstein.

Friederici, A.D. & Hahne, A. (in press).
Developmental patterns of brain activity for semantic and syntactic processes.
In B. Höhle & J. Weissenborn (Eds.), *Approaches to Bootstrapping in Early Language Development,* Amsterdam-Philadelphia: John Benjamins.

Friederici, A.D. & Hahne, A. (2000).
Neurokognitive Aspekte der Sprachentwicklung.
In H. Grimm (Ed.), *Enzyklopädie der Psychologie: Sprache,* vol. 3: Sprachentwicklung (pp. 273-310), Göttingen: Hogrefe.

Friederici, A.D. (in press).
Event-related brain potentials and aphasia.
In R.S. Berndt (Ed.), *Language and Aphasia. Handbook of Neuropsychology,* vol. 3, Amsterdam: Elsevier.

Friederici, A.D. (in press).
Neural basis of syntax.
In J.L. McClelland (Section-Editor), *International Encyclopedia of the Social and Behavioral Sciences,* Oxford: Elsevier.

Friederici, A.D. (2000).
The neuronal dynamics of language comprehension.
In Y. Miyashita, A.P. Marantz & W. O'Neil (Eds.), *Image, Language, Brain,* (pp. 127-148) Cambridge, MA: MIT Press.

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

Frisch, S. (2000).
Verb-Argument-Struktur, Kasus und thematische Interpretation beim Sprachverstehen.
In Max Planck Institute of Cognitive Neuroscience (Ed.), *MPI Series in Cognitive Neuroscience,* vol. 12, Leipzig.

Gruber, O., Arendt, T. & von Cramon, D.Y. (in press).
Neurobiologische Grundlagen der Stirnhirnfunktionen.
In H. Förstl et al. (Eds.), *Der Frontallappen: Funktionen und Erkrankungen*, Heidelberg: Springer.

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

Gruenewald, C., Mecklinger, A. & Friederici, A.D. (2000).
Segregating semantic from phonological codes in working memory: A dual task interference approach.
In E. Schröger, A. Mecklinger & A.D. Friederici (Eds.), *Working on Working Memory* (pp. 61-78), Leipzig: Leipziger Universitätsverlag.

Herrmann, C.S. (2000).
AI and cognitive science: Feedback leads to a new neural concept.
In S. Hölldobler (Ed.), *Intellectics and Computational Logic: Papers in Honor of Wolfgang Bibel* (pp. 175-188), Dordrecht: Kluwer.

Herrmann, C.S. (2000).
Erforschung von Wahrnehmungs- und Denkprozessen.
In C. Kirk (Ed.), *Wirtschaftsstandort Leipzig* (pp. 78-79), Darmstadt: Europäischer Wirtschaftsverlag.

Herrmann, C.S. (in press).
Gamma activity in the human EEG.
In J. Polich (Ed.), *Detection of Change: Event-Related Potential and fMRI Findings,* Dordrecht: Kluwer.

Jacobsen, T. (2000).
Characteristics of processing morphological structural and inherent case in language comprehension.
In Max Planck Institute of Cognitive Neuroscience (Ed.), *MPI Series in Cognitive Neuroscience,* vol. 10, Leipzig.

Koch, M. (2000).
Measurement of the self-diffusion tensor of water in the human brain.
In Max Planck Institute of Cognitive Neuroscience (Ed.), *MPI Series in Cognitive Neuroscience,* vol. 14, Leipzig.

Koelsch, S. (2000).
A contribution to the investigation of central auditory processing with a new electrophysiological approach.
In Max Planck Institute of Cognitive Neuroscience (Ed.), *MPI Series in Cognitive Neuroscience,* vol. 11, Leipzig.

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

Laux, G., Becker, T. & Müller, U. (in press).
MAO-Hemmer. Indikationen.
In P. Riederer, G. Laux & W. Pöldinger (Eds.), *Neuro-Psychopharmaka,* vol. 4: Antidepressiva und Phasenprophylaktika, Wien: Springer.

Matthes-von Cramon, G. & von Cramon, D.Y. (2000).
Störungen exekutiver Funktionen.
In W. Sturm, M. Herrmann & C.W. Wallesch (Eds.), *Lehrbuch Klinische Neuropsychologie* (pp. 392-410), Frankfurt: Swets & Zeitlinger.

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

Müller, H.J., Elliott, M.A., Herrmann, C.S. & Mecklinger, A. (Eds.) (in press).
Neural binding of space and time.
Visual Cognition (Special Issue).

Müller, U., Becker, T. & Laux, G. (in press).
MAO-Hemmer. Dosierung.
In P. Riederer, G. Laux & W. Pöldinger (Eds.), *Neuro-Psychopharmaka,* vol. 4: Antidepressiva und Phasenprophylaktika, Wien: Springer.

Müller, U., Ullsperger, M. & von Cramon, D.Y. (2000).
Pharmakologische Interventionen in der neuropsychologischen Rehabilitation.
In W. Sturm, M. Herrmann & C.W. Wallesch (Eds.), *Lehrbuch Klinische Neuropsychologie* (pp. 697-709), Frankfurt: Swets & Zeitlinger.

Müller-Plath, G. (2000).
Formale Modellierung visueller Suchstrategien mit Anwendungen bei der Lokalisation von Hirnfunktionen und in der Diagnostik von Aufmerksamkeitsstörungen.
In Max Planck Institute of Cognitive Neuroscience (Ed.), *MPI Series in Cognitive Neuroscience,* vol. 9, Leipzig.

Murai, T., Hadano, K. & Hamanaka, T. (in press).
Current issues in neuropsychological assessments in Japan.
In F.R. Ferraro (Ed.), *Minority and Cross-Cultural Aspects of Neuropsychological Assessment,* Frankfurt: Swets & Zeitlinger.

Murai, T. & Hamanaka, T. (2000) [1999].
Memory and its assessment: Semantic memory [Japanese].
In M. Asai & H. Kashima (Eds.), *Clinical Aspects of Memory (Enzyclopedia of Clinical Psychiatry),* Special Issue 2 (pp. 101-112), Tokyo: Nakayama Pub.

Norris, D.G. (in press).
Safety considerations in static magnetic fields and pulsed magnetic field gradients.
In Institute of Physics and Engineering in Medicine (Ed.), *Report,* York, UK.

Opitz, B. (in press).
ERP and fMRI correlates of target and novelty processing.
In J. Polich (Ed.), *Detection of Change: Event-Related Potential and fMRI Findings,* Dordrecht: Kluwer.

Schriefers, H. & Jescheniak, J.D. (in press).
Lexikalischer Zugriff und grammatische Kodierung.
In G. Rickheit, T. Herrmann & W. Deutsch (Eds.), *Psycholinguistics - An International Handbook,* Berlin: Walter de Gruyter.

Schriefers, H., Jescheniak, J.D. & Meyer, A.S. (in press).
Grammatisches Genus in der Sprachproduktion.
In Ch. Habel & Th. Pechmann (Eds.), *Sprachproduktion. Informationsvermittlung durch natürliche Sprache,* Wiesbaden: Deutscher Universitätsverlag.

Schröger, E., Mecklinger, A. & Friederici, A.D. (Eds.) (2000).
Working on Working Memory.
Leipzig Series in Cognitive Sciences 1, Leipzig: Leipziger Universitätsverlag.

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

Schwarzbauer, C. (2000).
NMR-Forschung in Leipzig mit langer Tradition und guten Zukunftsaussichten.
In C. Kirk (Ed.), *Wirtschaftsstandort Leipzig* (pp. 76-77), Darmstadt: Europäischer Wirtschaftsverlag.

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