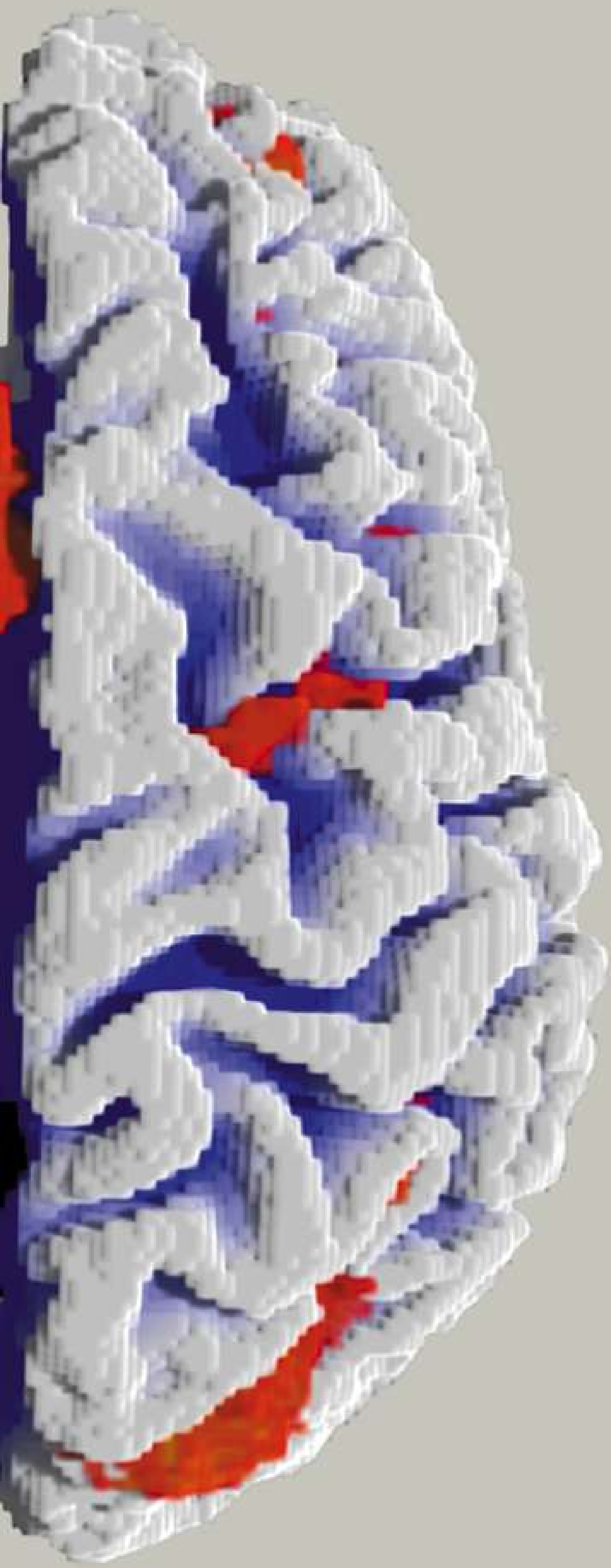

Annual Report 1999

Max Planck Institute of Cognitive Neuroscience Leipzig

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Annual Report 1999

Except for a costly burst in a water pipe in the basement of our new building in the Stephanstrasse, some minor problems with the dewer of the MEG system, and the much longed for installation of a new gradient tube in our NMR system, the year 1999 was a year of steady progress in many ways.

First of all, we are happy to announce a new junior research group under the guidance of Dr. Kai Alter, who has taken up its work on the "Neurocognition of Prosody" in November. Together with our intensified efforts in investigating both central auditory processes (in cooperation with our Day-Care Clinic at the University of Leipzig) and music processing, we were able to complete a chain of projects covering aspects from the pre- and non-verbal level of auditory processing to the level of language comprehension.

This year, tremendous progress has been made in applying the MEG system to research questions concerning the temporal and neurotopological aspects of language and music processing showing that the MEG system plays a major role in clarifying some of these questions. A cooperation of the MEG group with our external Scientific Member, Prof. James Haxby, is under way.

In contrast to last year's Annual Report, we gave up the section "Psychological Methods in Neuroimaging" and focused this group's activities on two topics closely related to functional neuroanatomy. The results of this work are presented in chapter 2.6 under the rubric "Functional Specialization of the Frontal Lobe" and "Functional Specialization of the Parietal Lobe". Due to the natural change in the staff personnel, major parts of this group had to be replaced in the second half of the year.

We should still mention that the institute has successfully engaged in acquiring grant money from several national and international grant givers; among them the "Deutsche Forschungsgemeinschaft" (Schwerpunktprogramm: Zeitgebundene Informationsverarbeitung im zentralen auditorischen System), the European Union (5^{th} European Research Framework Programme) and the German Israeli Foundation for Scientific Research and Development.

Angela D. Friederici
D. Yves von Cramon

Leipzig, February 2000

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NEUROCOGNITION OF LANGUAGE 2.1

Language processing and its functional representation on the brain are major research areas in our institute. Psycholinguistic theorizing as well as neuropsychological and neurophysiological modeling, together with empirical data from both normals and from patients with circumscribed brain lesions, are considered in building a picture of the language-brain relationship. Measurements of language-related brain activity with high temporal resolution (EEG, MEG) and high spatial resolution (fMRI) are used to specify the processes and systems underlying language comprehension.

This year's research was characterized by three main topics: first, *syntactic processes* and their underlying neuronal substrate were investigated at the sentence level as well as at the word level; second, a number of studies focused on the *influence of working memory* on processes of language comprehension; and third, we further investigated the *impact of prosodic information* on language comprehension.

Syntactic processes of local phrase structure building which are correlated with an early left anterior negativity in the ERP already have been characterized with respect to a number of important parameters (see previous Annual Reports). In 1999, we were able to complete an MEG study localizing the early syntactic processes in frontal and temporal cortical areas (2.1.1). The involvement of subcortical structures during syntactic processes was investigated in a fMRI study (2.1.2). The interesting question, "to what extent does background noise (as, for example produced by the MRI scanner) affect early syntactic processes" was evaluated in a MEG study. This study showed that early auditory processes, but not early syntactic processes, are influenced by noise in the normal hearing subject (2.11.5). Patients with cochlea implants suffering from a post-lingual acquired deafness, in contrast to normal hearing subjects, do not show an early anterior negativity in response to local phrase structure violations, but they rather appear to rely on compensatory semantic comprehension processes reflected by the N400 (2.1.3). The way early syntactic processes and semantic processes are realized in a Romanic language was evaluated using French as a testing ground (2.1.4). In an earlier experiment we had shown that a local phrase structure violation can block the integration of a content word indicating the primacy of phrase structure building processes. One additional study systematically varying word order and plausibility, presented here, supports the view that semantic integration is primarily driven by the on-line analysis of syntactic relations (2.1.5). The primacy of syntactic phrase structure building processes over verb argument structure assignments was demonstrated in a further ERP study (2.1.6). The impact of case information for the assignment of the verb's argument was investigated in an ERP experiment in which subject and object NP were marked incorrectly by the same case (2.1.7). The on-line use of case information during verb argument assignment was further evaluated in an ERP experiment using split particles which in German appears in sentence final position. The data from this study suggest that the parser exhaustively accesses all possible argument structures when encountering the verb (i.e., the structure of the no-particle verb as well as the structure of the particle verb) and assigns the ultimate structure when encountering the sentence final particle (2.1.8). The on-line characteristics of the use of case information for the resolution of syntactic ambiguity was investigated using behavioral and ERP measures (2.1.9).

Syntactic, semantic and morphological aspects of processing at the word level were examined in four studies. In a first study using fMRI, participants were presented with content words and function which were either concrete or abstract. Different activation patterns were observed as a function of task (syntactic task versus semantic task), rather than as a function of class membership or concreteness (2.1.10). A second fMRI study focused on the semantic relations between content words, i.e. nouns and their possible neuronal substrate (2.1.11). Differences in processing nouns and verbs were found in an MEG study. These differences were maximal over the right hemisphere when words were presented in isolation and over the left hemisphere when presented in minimal syntactic context (2.1.12). A third study focused on the processing and possible representation of compound words in German. Data from this reaction time study indicate that German compounds are not accessed from left-to-right with a primacy of the left constituent of the compound, but that they are rather accessed via the head of the compound (the right constituent) which carries information about the compound's word class and in case of nouns also information about the compound's syntactic gender (2.1.13).

The *influence of working memory* on sentence comprehension is still in the center of psycholinguistic discussions. Two studies focused on the interaction of working memory and syntactic aspects of processing, one of them on its interaction with lexical-semantic aspects. In an ERP study varying the distance between the interrogative pronoun moved to the sentence-initial position and its original position in the sentence a sustained left anterior negativity was observed as a function of the distance manipulation. This suggests that the pronominal element is held active in working memory until it can be linked to its original position (2.1.14). In order to disentangle brain areas that might subserve working memory and those supporting syntactic processes, an fMRI experiment was conducted using the same sentence material. Differential brain areas were activated as a function of syntactic complexity and of working memory requirements (2.1.15).

The *impact of prosodic information* on sentence processing was examined in three studies, two of them focusing on syntactic aspects and one focusing on semantic aspects. Following up earlier ERP work on the processing of prosodic boundaries, two ERP studies were conducted to demonstrate the universal nature of the particular ERP component found in correlation with the processing of prosodic boundaries, namely the so-called CPS, the Closure Positive Shift (2.1.16, 2.1.17). The interaction between prosody and semantics was evaluated in an ERP study systematically crossing sentence content and emotional tone coded in the sentence's intonation. Differential ERP patterns for prosodic judgments and for semantic judgments suggest distinct neural substrates for these two aspects of processing (2.1.18).

2.1.1 Localization of early syntactic processes in frontal and temporal cortical areas: A magnetoencephalographic study

Friederici, A.D., Wang, Y., Herrmann, C.S., Maess, B. & Oertel, U.

Earlier electrophysiological studies had found an early anterior negativity often with the lateralization to the left hemisphere (ELAN) to correlate with the early detection of an error in the syntactic structure of a sentence (see Ann. Rep. 1995/1996). The aim of the present study was to localize the cortical areas involved in the processes reflected in ELAN.

Six healthy, right handed German native speakers volunteered as participants in this study (three of them males, age 18-29 years, mean age of about 23 years). Data from one of them were disregarded from further analysis because of the low signal to noise ratio (SNR). The sentences were presented as connected speech, including 50% correct, 25% syntactically incorrect, and 25% semantically incorrect. The syntactic incorrectness was realized as word category error. The MEG was recorded with a 148-channel whole-head magnetometer (MAGNES WHS 2500, BTi). To improve the SNR, for each subject 6 experimental blocks were recorded. The signal was band-pass filtered (2-10 Hz) off-line to further improve the SNR and remove the baseline offset. The averaged responses (locked to the onset of the critical word) for syntactic incorrect condition were subject to further analysis of source localization.

For the source analysis, the realistically shaped one-compartment boundary element model for the interior of the skull from the standard Warp model in CURRY was adopted as the volume conductor. From results of an fMRI study, two locations for each brain hemisphere were selected as the seed points for the constrained dipole fitting. To account for the variation of the individual head volume conductors and the difference between fMRI and MEG, the dipoles were fitted within a sphere region centered at the respective seed points with a radius of about 10 mm. The dipole fitting was carried out for a 20 ms time interval around the ELAN peak.

The results demonstrate that syntactic processes reflected by ELAN are supported by tissue at or in the vicinity of the planum polare as well as brain tissue in the fronto-lateral cortex bilaterally. A clear left hemisphere dominance was obtained for all the three male subjects and one female subject, whereas another female subject displayed a right lateralization. As indicated by the dipole strength, the contribution of the left temporal region to the ELAN appears to be larger than the contribution of the left fronto-lateral regions.

2.1.2 The role of subcortical structures in syntactic processing

Opitz, B., Friederici, A.D. & von Cramon, D.Y.

Neuropsychological research and brain imaging studies indicate that the processing of syntactic information relies on left frontal brain structures described as Broca's area. More recent neuroimaging studies (cf. Ann. Rep. 98, pp. 6-17) and findings from intracranial recordings (cf. Ann. Rep. 98, pp. 20-21) emphasize the contribution of thalamic structures or the hippocampal formation to syntax mechanisms. The present study specifies subcortical contributions to syntactic processing during speech comprehension by using fMRI.

Twelve volunteers were randomly presented with two types of auditory sentences extracted from a larger set of stimuli (cf. Ann. Rep. 98, pp. 16-17). These sentences were normal prose sentences and syntactic prose sentences, i.e. a syntactically correct structure in which content words were replaced by phonologically legal pseudowords. To disentangle thalamic and hippocampal contributions to brain activity, 16 BOLD volumes from 8 slices (thickness = 3 mm, gap = 1 mm) parallel to the longitudinal axis of the hippocampus were acquired at a rate of 1 per sec during comprehension of a single sentence.

In the present study, we were able to replicate findings described by us last year (see Ann. Rep. 98, pp. 16-17). Thus, both types of sentences elicited a bilateral hemodynamic response in the posterior part of the superior temporal gyrus and the thalamus. The left frontal opercular cortex, previously reported to be activated during syntactic processing, was not covered by the slice arrangement, which was optimized for hippocampal assessment. Despite this, a hippocampal BOLD response related to the processing of syntactic structures was not found. There are at least two possible explanations: one concerning the stimulus material and one a methodological issue. In contrast to Mecklinger et al. (cf. Ann. Rep. 98, pp. 20-21) who found electrophysiological responses within the hippocampus while investigating syntactic violations, the present study only used syntactically correct structures. On a methodological point of view one could argue that the low neural density of the hippocampus caused a low signal-to-noise-ratio of the BOLD signal, and therefore the hemodynamic response of hippocampal system evoked by syntactic processing not be sufficient to be extracted from hemodynamic changes elicited by more general processing aspects.

2.1.3 Auditory sentence comprehension in patients with a cochlea implant: ERP evidence for semantic comprehension strategies

Hahne, A.[1] & Kiefer, J.[2]

[1]Max Planck Institute of Cognitive Neuroscience, [2]Medical Center of the Johann Wolfgang Goethe-University, Frankfurt

Cochlear implants (CI) have become a successful method for restoring hearing in deaf patients. However, the perceived auditory input deviates substantially from normal hearing and the language processing mechanisms in these patients are largely unclear.

The present study was an attempt to study auditory sentence comprehension processes in two CI patients using event-related brain potentials.

The two patients both suffered from a post-lingually acquired deafness. We tested them 8/16 months after implantation. Their performance could be classified as very good with 75 or 85% correct monosyllabic word understanding. Three types of sentences were presented auditorily. The sentences ended with a target word that was either correct, semantically incorrect, i.e., violating the selectional restriction of the verb, or syntactically incorrect, i.e., violating the phrase structure. The participants were asked to judge the correctness of each sentence. ERP averages were computed for 11 artefact-free electrodes 1500 ms after the onset of the critical participle.

The patients' performance was very high. While participants with normal hearing showed clearly distinct response patterns for syntactic as opposed to semantic violations in our previous studies, the ERP responses of the CI-patients did not differ for the two violation types. Both incorrect sentence types elicited a similar N400-like negativity relative to the correct condition. The syntactic conditions did neither elicit an early anterior negativity (assumed to reflect rather automatic first-pass parsing processes) nor a P600 (assumed to reflect processes of structural repair). The data suggest that the CI-patients were unable to perform first-pass parsing processes which guarantee the early detection of the syntactic word category in unimpaired listeners. Rather, the patients appear to rely on compensatory semantic comprehension strategies possibly as a result of the omnipresent experience of impoverished auditory input. The paradigm applied in this study seems to be a suitable extension of the evaluation of language comprehension processes in cochlear implant patients.

2.1.4 Syntactic and semantic processes in French spoken sentences: ERP evidence

Isel, F.,
Hahne, A. &
Friederici, A.D.

In our project, which aims to study the syntactic and the semantic processes by French late bilinguals (French/German) during the auditory processing of German sentences, we first conducted a pilot experiment to investigate the temporal and the spatial characteristics of these processes in French. We registrated event-related brain potentials (ERP) when French listeners were processing syntactically or semantically correct or incorrect short French sentences which were comparable to German sentences used in prior studies. The critical item was the last word of the sentence, which was either syntactically or semantically congruent or incongruent with the preceding context.

Conditions	Linguistic materials
correct	*L'enfant qui est dans la maison dort* [The child, who is in the house, is sleeping]
semantically incorrect	*Le caillou qui est dans la piscine dort* [The stone, which is in the swimmingpool, is sleeping]
syntactically incorrect	*L'enfant qui est dans la dort* [The child, who is in the is sleeping]

Semantically incorrect sentences elicited an N400 component present between 300 and 600 ms after the onset of the critical item. It was distributed over centro-parietal sites but was also pronounced over frontal areas. This frontal distribution has previously been observed with auditory presentation of semantic incongruity. Syntactically incorrect sentences elicited a negativity mostly distributed over frontal areas of both hemispheres starting around 200 ms and a late positivity (P600) pronounced over parietal sites. The onset of the negativity was earlier than the N400 component observed in the semantic condition but later than the early left anterior negativity (ELAN) found in similar German sentences by Hahne and Friederici (1999) for word category violations. However, when using German words for which the category uniqueness point was only available in the suffix, Friederici et al. (1996) observed a left anterior negativity starting 370 ms after word onset, i.e. 50 ms after the mean word category uniqueness point. Therefore, the present data support the notion that the onset of the early anterior negativity is temporally closely linked to a word's category uniqueness point. Furthermore, these findings give us a solid reference to determine the temporal and the spatial specificities of syntactic and semantic processes implied in French native speakers when processing their native language, i.e. French, versus a foreign language, i.e. German.

2.1.5 When syntax guides semantics: Evidence from event-related potentials

Steinhauer, K. & Frisch, S.

In a recent study using event-related brain potentials (ERPs), we showed that semantic integration of a content word is blocked if this word violates the local phrase structure (PS) of the sentence (Friederici, Steinhauer & Frisch, 1999). Words carrying both a semantic and a PS violation did not elicit increased N400s in the ERP. The amplitude of a word's N400 component can therefore be small for two very different reasons: either because the word was semantically primed, or because the process of semantic integration does not take place at all. In the latter case, even implausible content words do not elicit a large N400.

Our claim is that lexical integration in sentences generally depends on legal phrase structural relations and thus differs from the less specific semantic processing observed for word lists or 'scrambled sentences' (e.g., Van Petten & Kutas, 1991). According to this view, even in legal and unambiguous sentences the same sequence of content words should elicit different N400 amplitudes if the underlying PS and the associated theta role assignments change.

Previous ERP findings that seem to support this notion could not provide final answers as they can alternatively be explained by lexical differences across conditions (Garnsey et al., 1989; Mecklinger et al., 1995). Here, we use plausible and implausible German subject and object relative clauses (SR, OR) in which subject NP (agent) and object NP (patient) swap positions. The plausibility does not depend on the NP order or the clause type per se, but rather on a combination of both.

SRplaus ... *der Lehrer, der* (Nom) *den* (Acc) *Schueler geprueft hat.*
ORimpl ... *der Lehrer, den* (Acc) *der* (Nom) *Schueler geprueft hat.*
(the teacher that (Nom/Acc) the (Acc/Nom) pupil examined has)

SRimpl ... *der Schueler, der* (Nom) *den* (Acc) *Lehrer geprueft hat.*
ORplaus ... *der Schueler, den* (Acc) *der* (Nom) *Lehrer geprueft hat.*
(the pupil that (Nom/Acc) the (Acc/Nom) teacher examined has)

The ERP reading experiment was conducted with 24 right-handed German native speakers. As predicted, the N400 elicited by the past participle (*geprueft* / examined) did not depend on the noun order but on the plausibility of the sentence given the theta role assignments associated with the phrase structure. Thus, the plausible sentences SRplaus and ORplaus elicited smaller N400s as compared to the implausible sentences SRimpl and ORimpl, respectively. The data suggest that semantic integration during sentence reading is primarily driven by the on-line analysis of syntactic relations rather than by unspecific associations between words.

2.1.6 Argument structure information defeated: ERP evidence for the autonomy of phrase structure processing in sentence comprehension

Frisch, S., Hahne, A. & Friederici, A.D.

One of the core issues in psycholinguistic research is the question whether argument structure (e.g., transitivity) information of verbs is used in the same initial phase of parsing in which word category information is supposed to play its role in phrase structure build-up. Although quite early influences of verb information on syntactic ambiguities have been demonstrated in numerous studies, it was disputed that such results necessarily implied the use of argument structure information within the same time range as phrase structure information. It was argued that these early influences might be understood as post-initial filtering effects (cf. Frazier, 1987; Mitchell, 1994). The whole discussion has led to some skepticism regarding the methods used so far (cf. Mitchell, 1994).

We addressed this question by presenting sentences with combined violations, that is, with violations of two types of information being realized on the identical item (cf. Friederici, Steinhauer & Frisch, 1999). In two ERP experiments (visual vs. auditory presentation), we presented German sentences with either (a) no violation at all, (b) a phrase structure violation, (c) an argument structure violation or (d) both a phrase structure and an argument structure violation.

All violations were realized on the critical item in the sentence, namely a past participle. Phrase structure violations were realized by a preposition followed by the past participle (instead of a noun), whereas in sentences with argument structure violations, the past participle was derived from an intransitive verb but embedded in a passive construction with a subject NP. Several filler conditions were used in order to avoid predictability.

Under the assumption that phrase structure information is processed autonomously (as, for example, Frazier (1987) and Mitchell (1987) propose), we would expect nonadditivity of the two information types and thus identical patterns in conditions (b) and (d). Argument structure violations should exhibit a biphasic N400-P600 pattern only in the case that the phrase structure of the sentence is correct, but not if there is an additional phrase structure violation. This is exactly what the ERPs showed in both the visual and the auditory modality.

Results support phrase structure driven models of parsing according to which word category information is processed with priority over verb transitivity information.

2.1.7 The specificity of diagnosis of case ungrammaticalities: ERP evidence from argument doubling in German

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

[1] Max Planck Institute of Cognitive Neuroscience, [2] Institute of Linguistics, University of Potsdam

A recent ERP study by Coulson, King and Kutas (1998) on the processing of double nominative ungrammaticalities in English showed that sentences such as (1) elicit a biphasic LAN-P600 pattern on the mismatching second pronominal NP in comparison to correct sentences.

(1) The plane (Nom) took *<u>we</u> (Nom) / <u>us</u> (Acc) to paradise.

In an ERP experiment, we examined the ERP pattern for double nominative as well as double accusative ungrammaticalities in German. The language-specific differences between English and German led us to predict a pattern for German that differs from the one found by Coulson et al. (1998). English has a rigid word order in which linear positions determine the grammatical function of the NP arguments, thus making interpretation possible despite incorrect case marking on the NPs. By contrast, in a language with free word order such as German, grammatical functions are determined by overt case marking on the NPs rather than by their linear positions. In German sentences with two nominative NPs, e.g. (2) below, assignment of grammatical functions and therefore thematic interpretation is impossible.

(2) *Welcher Botschafter* (Nom) *beobachtete* *der Richter* (Nom)?
Which ambassador (Nom) observed the judge (Nom)?

Given that the N400 is a marker of uninterpretability, while the LAN is not, we expected an *N400*-P600 pattern for German sentences such as (2). In an ERP experiment using such NP-V-NP structures, we found the expected N400-P600 pattern for both double case conditions as opposed to the correct ones. In the double nominative condition, however, the N400 was delayed and shorter in duration compared to the double accusative N400. This may be due to the fact that double nominatives are initially easier to interpret (cf. Schlesewsky, Fanselow & Frisch, submitted).

The fact that the N400 effects differed between the two incorrect conditions suggests that the verb confirms the subject interpretation of an initial nominative (but not of an initial accusative) NP and therefore enhances the parser's expectation that an object NP will follow. Contrary to input-driven models of reanalysis (cf. Fodor & Inoue, 1999), we assume that it is the second NP that is overlooked because the parser is driven by expectations built up on the basis of prior information.

Verb information in sentence comprehension processes

2.1.8

Urban, S. &
Friederici, A.D.

We performed several EEG experiments with two different groups of verbs manipulating the syntactic and semantic environment in which these verbs can or cannot occur. Lexically constraint based approaches have claimed that verbs restrict their sentential context because they immediately activate information whose arguments allow a particular verb (Boland, Tanenhaus & Garnsey, 1990). Others propose that every input following the verb is attached in the same way (cf. Frazier, 1987). That means at a first stage the processor uses a generalized rule and does not rely on specific verbal information. We used an on-line measurement (EEG) in order to disentangle first-pass parse and reanalysis processes.

Our experiments support the thesis that the verb feeds in information related to the number of its arguments. That is, at 550 ms after the onset of a verb transitive and particle verbs show a more negative wave compared to intransitives. (Note that in German the particle follows the object NP.) This negativity points towards an increased memory load as the storage of information in memory has been reported to be reflected in frontal negativities. In our experimental material the difference in memory load is probably caused by the activation of the possible argument slots a verb can take and the fact that the number of arguments is larger in the case of transitive compared to intransitive verbs.

Additionally, our interpretation of this difference at the verb position receives support from an additional ERP effect observed at the position of the particle. Here, a P300 effect for the correct particle was found in the grammaticality judgment task. Given the finding that particle verbs behave like transitive verbs at the verb position (suggesting that the processor keeps open the option for an object) forces the interpretation that the ERP effect at the particle position does not reflect processes of reanalysis but rather processes of uncertain resolution. It is at this point that the uncertainty about the correctness of the structure initially built is resolved.

Finally, the failure to record predicted differences at the position of NPs following the two verb groups (intransitive and transitive) can be explained when considering data from a related experiment. Conducting an experiment with argument and adjunct NPs, we found that the attachment of both the NPs is carried out equally regardless of preceding verb group information. Consequently, the processing of a given verb and its connection with its sentential partners is neither purely syntactically driven nor lexically driven. Substantially different ERP effects, i.e. the local effect at the verb position and the global effect at the sentential level, suggest on the one hand that lexical access of verbs is exhaustive concerning the activation of all possible argument structures, and on the other hand that phrasal attachments are governed by a general rule independent of the preceding verb.

2.1.9 ERPs elicited during NP/S ambiguity resolution

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

Behavioral studies investigating NP/S attachment ambiguities indicate that there is an NP preference. The experiment explored this ambiguity in German, a language in which case marking can disambiguate very efficiently. ERPs were measured in sentences which either contained an unambiguous case marked NP (a/c) or had an ambiguous case marking (b/d).

Der Dirigent besucht den Apotheker,
The conductor visits the pharmacist,

(a)	***der***	*Trainer*	*besucht den Bruder, und ...*
	$\text{the}_{\text{masc, nom}}$	$\text{trainer}_{\text{masc}}$	visits the brother, and ...
(b)	***die***	*Trainer**in***	*besucht den Bruder, und ...*
	$\text{the}_{\text{fem, nom/acc}}$	$\text{trainer}_{\text{fem}}$	visits the brother, and ....
(c)	***den***	*Trainer*	*und den Bruder auch gerne ...*
	$\text{the}_{\text{masc, acc}}$	$\text{trainer}_{\text{masc}}$	and the brother especially ...
(d)	***die***	*Trainer**in***	*und den Bruder auch gerne ...*
	$\text{the}_{\text{fem, nom/acc}}$	$\text{trainer}_{\text{fem}}$	and the brother especially ...

The nominative NP *der Trainer* indicates an S conjunction, whereas the accusative NP *den Trainer* signals another NP to come. In the case-ambiguous NP, *die Trainerin,* there is no disambiguation until the verb (b) or the conjunction (d).

At the conjunction, (d) compared to (c) elicited a large P600. At the verb, (b) compared to (a) elicited a larger N400. Thus, even though behavioral measures demonstrate an NP-preference, ERPs indicate that developing this preference is not without mental effort. Furthermore, the data suggest that the way in which syntactic disambiguation is achieved depends on the structure of the target sentence.

2.1.10 Dissociation of semantic and syntactic processes in the human brain: Functional MRI investigations of word comprehension

Opitz, B., Friederici, A.D. & von Cramon, D.Y.

Psycholinguistic models assume that lexical-semantic and syntactic processes are distinct. This separation has often been exemplified in the distinction between two word classes (open class - semantic processes and closed class - syntactic processes). It was shown, however, that words of a particular class are processed differently as a function of the amount of semantic information a particular element carries. The present study, in contrast to previous research (see Ann. Rep. 98, pp. 19-20), used event-related fMRI to disentangle the effect of class membership, concreteness and task on the word processing in a systematic way.

Twelve subjects were required to judge whether a visually presented word was a noun or a function word (syntactic task) or whether it was a concrete or an abstract word (semantic task). In an additional physical task subjects were asked to indicate whether or not a consonant letter string was written in a normal spacing or with enlarged spacing between each letter. Gradient EPI images (matrix = 64x64, TE = 40 ms) were acquired from 10 axial slices.

We found a major difference in the activation as a function of task. While both semantic and syntactic tasks (compared to the physical baseline task) evoked activation in the left pars opercularis and in both thalami, clear differences between the semantic and syntactic task were found in other regions. For the *semantic task* we observed a selective additional activation of the left BA45 and the posterior part of the middle temporal gyrus (MTG) exceeding the superior temporal sulcus, whereas the *syntactic task* selectively evoked the inferior part of BA44 and of cortex lining the inferior precentral sulcus. Moreover, for these latter areas a word class by concreteness interaction was observed when a *syntactic judgment* was required. This interaction can be interpreted as a prototypicality effect: non-prototypical members of a word class showed larger activation than prototypical members.

From the present data we conclude that neither syntactic class membership nor semantic concreteness per se predicts the processes underlying word perception. Rather, it appears that the activation differences of the neuronal network supporting word processing are largely determined by task requirements focusing either on semantic or syntactic aspects.

Functional MRI evidence for priming of semantic word types

2.1.11

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

Recent evidence from event-related-brain potential (ERP), research reaction time (RT) studies and lesion studies report that priming effects vary as a function of type of semantic information. In particular, activation related to associative priming (*dog-cat* or *mouse-cheese*) seems to be more left lateralized, while categorical priming (*chicken-cat*) appears to be more right lateralized. To our knowledge there is very little PET or fMRI evidence of semantic priming probably given the temporal window of these imaging techniques. However, the application of the single trial technique in fMRI now allows one to better specify the neuroanatomical correlates of semantic information processing via means of an auditory lexical decision task (LDT) correlated with priming. The goal of the study was to identify the activation in the left and right hemisphere correlated with semantic information types as well as with priming.

A pseudo-randomized list of 320 word and pseudo-word pairs (prime and target) were presented auditorily via head phones in a single-trial paradigm. Thirteen subjects (seven of them female) were asked to decided whether a target word was a word of the German language or not. Each auditory stimulus was presented for its duration. The ISI between prime and target items was 100 ms, the ITI 6.8 s. Four echo planar images (TE = 40 ms, TR = 2 s) per trial were acquired in eight axial slices (thickness = 4 mm, interslice distance = 2 mm) using a Bruker 3T/100 scanner. The calculation of activation maps for each subject utilized voxelwise Pearson correlation coefficients. After normalizing images to Talairach space, group averages were calculated. Activation correlated with each critical condition was evaluated by means of z-score ($p < .05$, $z >= 2$).

Associative condition: bilateral activation was found in Heschl's Gyrus as well as a left lateralized activation of the planum temporale and the posterior insula. *Categorical condition*: comparable activation was found for the categorical targets. However, the activation was more enhanced in Heschl's Gyrus and the left planum temporale. While there was no activation in the left posterior insula, there was additional activation in the right anterior temporal operculum. *Related condition*: there was increased bilateral activation in the Heschl's gyri, the planum temporale and theanterior temporal operculum (planum polare) across semantic information types. *Unrelated condition*: in comparison to the related condition, there was additional left lateralized activation of the posterior insula, the temporal opercular cortex and the thalamus. Furthermore, there was enhanced right hemisphere activation of the temporal operculum and along the superior temporal sulcus and along the transverse sulcus.

The differential activation patterns of related versus unrelated target items indicate that computational resources in the right hemisphere increase as a function of the degree of semantic relatedness. Furthermore, it appears that both the role of the inferior frontal cortex related to semantic network activation as well as the lateralization of semantic information types need to be reconsidered under different task demands.

2.1.12 Differences of processing of nouns and verbs in the human brain: Neuromagnetic evidence

Fiebach, C.J., Maess, B., Walker, I. & Friederici, A.D.

The present study was intended to identify brain regions differentially activated by verbs and nouns during a syntactic task. Magnetic fields were measured with a 148 channel whole-head MEG while participants listened to nouns (e.g., *Draht*, *Nasen*) and verbs (e.g., *geht*, *lachen*). Subjects were required to make word category classification judgments. The stimulus words were either presented in isolation or with a preceding minimal syntactic disambiguating context. In these conditions, nouns were presented together with an article (*der*, *die*, or *das*) and verbs were preceded by a pronoun (*er* or *sie*). Stimulus words were controlled for frequency of occurrence and length. Eight participants listened to blocks of verbs and nouns without context first, while another eight listened to the blocks of items with context first.

Statistical analyses in the time window of 400 to 600 ms (i.e., the time range known to show the N400 component) were performed on root mean square values which were aggregated for channels of the four quadrants left-anterior, left-posterior, right-anterior, and right-posterior. The results show (i) that words presented in isolation produce stronger signals than words presented with context (significant main effect of context $p < .005$), and (ii) a significant interaction of context with quadrant and condition ($p < .01$). This interaction is due (a) to increased signal strength in the left posterior quadrant for nouns as compared to verbs when a disambiguating context is present ($p < .05$) and (b) to an increased signal strength context over the right hemisphere for verbs as opposed to nouns when context is absent ($p < .1$).

These results are supported by brain surface current density maps (BSCD) that were calculated using the CURRY software package. In order to identify the anatomical regions responsible for the observed activations, BSCD maps were overlaid with the cortex segmentations of the individual participants. Figure 1 shows BSCD maps of nouns and verbs presented without context for both hemispheres for one representative subject at 600 ms. Strongest activation is visible in the right inferior frontal gyrus for the verbs. This is in correspondence with the statistical analyses of root mean squares reported above (see ii, b).

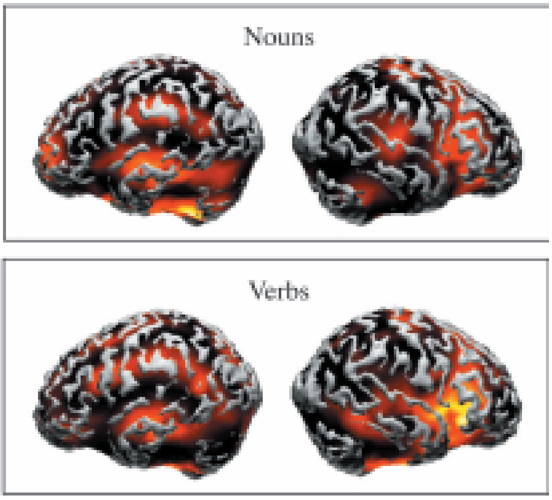

Figure 1. BSCD maps of nouns and verbs without context for one single participant.

It appears that the left hemisphere reflects differences between nouns and verbs when these are presented in a syntactic context, and that the right hemisphere rather demonstrates differences between nouns and verbs when these are presented in isolation.

Semantic representation and processing of German compounds: A RT study

2.1.13

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

The research we reported here was concerned with the nature of the mental representation of German compounds (e.g., *Weinberg*). Three cross-modal (auditory-visual) priming experiments were run in order to test the activation level of left constituents (*Wein* in *Weinberg*). To avoid a possible confound between morphology and semantics, four categories of compounds were used: (1) fully transparent (the two constituents were semantically related with the compound: *Weinberg*), (2) fully opaque (no semantic relation between the constituents 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 compounds in German, was transparent. When visual targets were presented at the acoustic offset of the left constituents (with coarticulation cues between the two constituents: Experiment 2; without coarticulation cues between the two constituents: Experiment 3), no activation of these constituents was found. This finding indicates that the semantic representations of the left constituents are not activated during an early stage of processing.

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.

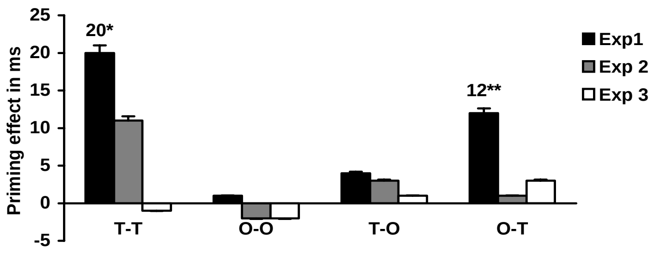

Figure 2. Amount of facilitatory and inhibitory priming for the left constituents of compounds in Experiments 1, 2, and 3 (in ms).

2.1.14 Multiword ERPs reflect syntactic working memory during the processing of embedded WH-questions in German

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Many psycholinguistic models of language processing postulate influences of working memory (WM) capacity on syntactic processing (e.g., Just & Carpenter, 1992; Caplan & Waters, 1999). However, little empirical evidence from on-line measurements is available to specify the nature of WM processes evoked during parsing. In the present study, multi-word event-related potentials (ERPs) were used to identify syntactic WM processes during parsing.

ERPs were recorded while 21 participants read indirect German WH-questions of the following type:

(SUBJECT) *Karl fragt sich, wer* (NOM) ___ *am Dienstag den Doktor verständigt hat.*
(OBJECT) *Karl fragt sich, wen* (ACC) *am Dienstag der Doktor* ___ *verständigt hat.*

Although no ambiguity resolution strategies are required for parsing questions involving the German masculine interrogative pronoun (*wer*/*wen*), reading time studies (Schlesewsky et al., submitted) suggest that object WH-questions are more difficult to process because the interrogative pronoun has to be maintained active in WM until it can be linked to its gap (indicated by ___ in the examples).

To manipulate WM demand, we introduced a length manipulation with four prepositional phrases (PPs) in long, and only one PP in short sentences. By this, the distance between the WH-filler and its gap in the object condition was increased and the filler had to be maintained active for a longer time.

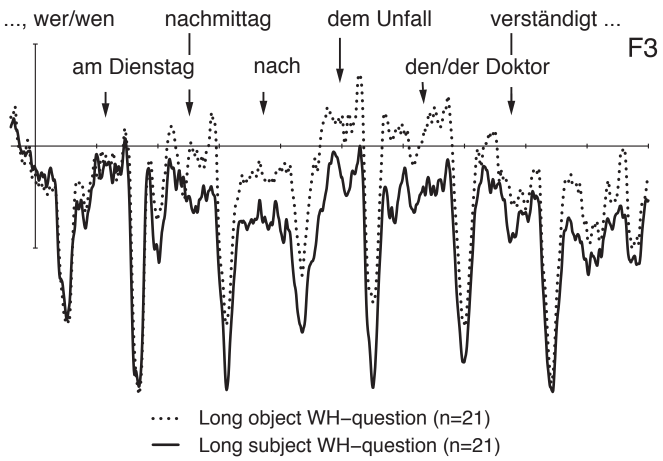

Figure 3.

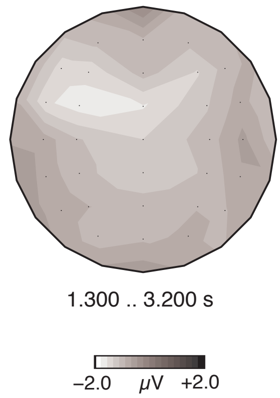

Figure 4.

ERPs averaged from the beginning until the end of the embedded question reveal a sustained frontal negativity for the long object relative to the long subject questions (see, for example, electrode F3 in Figure 3). This negativity starts with the first PP and becomes very pronounced during the additional PPs in the long object condition. As Figure 4 shows, it has its maximum over left-anterior electrode sites. No comparable effect was found in the short WH-questions. This sustained negativity is taken to be correlated with the use of WM resources for maintaining the object WH-filler active in working memory until it can be linked to its gap.

Broca's area and syntactic working memory: Functional MRI reveals distinct brain regions for syntactic complexity and syntactic working memory

2.1.15

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

Recent neuroimaging studies comparing processing of relative clause sentences of varying complexity suggest that left pars opercularis and pars triangularis activations correlate with increased syntactic complexity (Stromswold et al., 1996; Just et al., 1996; Caplan et al., 1999). The exact nature of the processes subserved by these brain areas, however, could not be specified so far. It has been argued that increased processing difficulty in syntactically more complex relative clause sentences is not only caused by more difficult processes of syntactic or semantic integration, but is also partly due to working memory processes such as maintaining unintegrated linguistic constituents active in working memory (Gibson, 1998).

We dissociated these two aspects of sentence processing using indirect German WH-questions. In a related ERP study (see 2.1.14) it was shown that during processing of object WH-questions, the interrogative pronoun has to be kept active in working memory until it can be linked to the canonical object position. In an event-related fMRI study (3 Tesla, EPI, axial slices, TR=1 s, TE=30 ms) participants read WH-questions adapted from the ERP study. The questions varied on the factors (1) syntactic complexity (i.e., subject vs. object questions), and (2) syntactic working memory costs (i.e., short vs. long movement of the question word in the object question).

Preliminary data from five participants suggest that syntactic memory costs were correlated with significant activations in a network comprising deep left inferior fronto-opercular cortex (BA44; see Figure 5) and its left superior portion, as well as four foci along the left middle temporal gyrus. In the syntactic complexity contrast significant activation foci were found in the parietal operculum bilaterally and in the left middle and right anterior insular cortex.

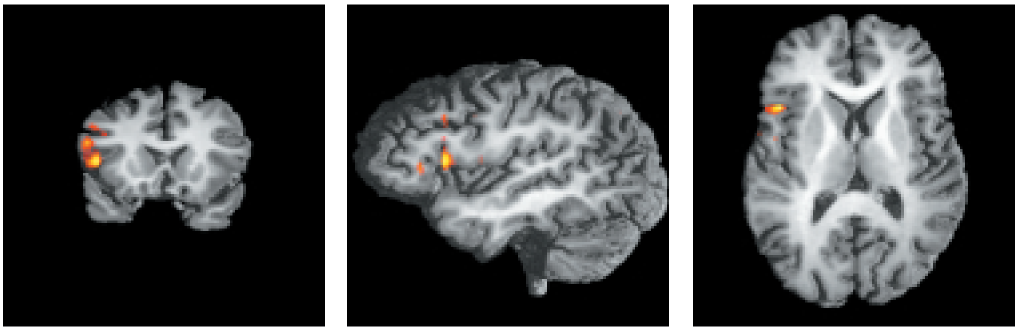

Figure 5.

Our data suggest that Broca's area plays a role in syntactic working memory during sentence processing. Moreover, they demonstrate that activations observed in Broca's area cannot be attributed to syntactic complexity as such but must be dissociated from syntactic working memory processes.

2.1.16 Prosodic boundaries, comma rules, and brain potentials

Steinhauer, K. supported by the DFG

In a recent study, we demonstrated that the processing of prosodic boundaries in natural speech was reflected in a large positive going ERP component, the Closure Positive Shift (CPS) (Steinhauer, Alter & Friederici, 1999). A pilot study with written sentences revealed that commas mimicking the prosodic boundary elicited a large negative slow wave instead which was preceded by a small CPS-like positivity in some subjects only. These data suggested significant differences in the mechanisms underlying the processing of speech boundaries and commas. In the meantime, additional subjects entered the reading study. Subjects were grouped according to their punctuation habits as assessed by a completion test. Separate analyses for each group show that amplitudes of both ERP components are much larger for subjects accustomed to strict insertion of disambiguating commas at potential boundary positions (Figure 6). Both easy-to-read judgments and ERP data suggest that participants with deviant punctuation rules were also less susceptible to commas during reading.

A second reading experiment examined whether the negative slow wave was either a reflection of the comma processing proper or rather a so-called contingent negative variation (CNV) triggered by the need to prepare for a severe garden-path. Thus, all garden-path sentences were excluded from the materials of this study. As hypothesized, commas elicited only the CPS-like positivity and no negative slow wave (Figure 7).

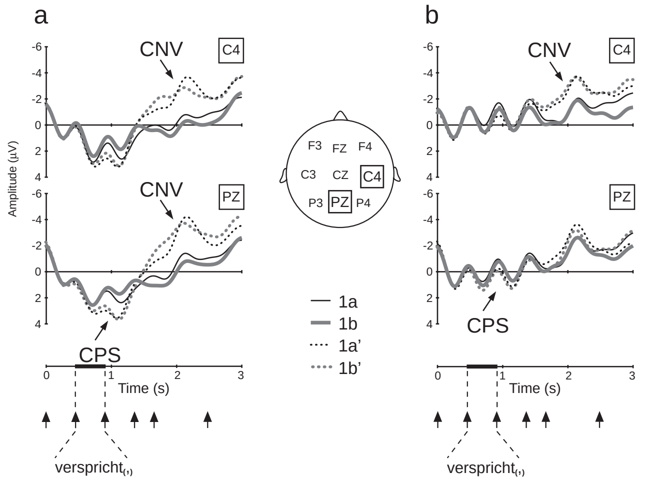

Figure 6. ERPs in the first reading experiment. Commas elicit a positivity followed by a negative slow wave, both being larger for subjects with strict punctuation habits (a) than for those with deviant habits (b).

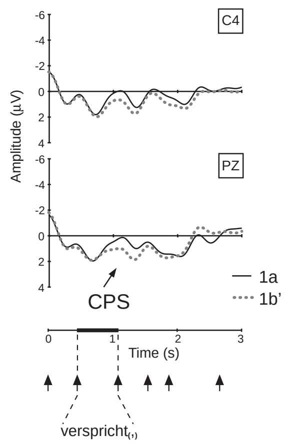

Figure 7. ERPs in the second reading experiment. As commas did not indicate a potential garden-path sentence no CNV followed the CPS-like positivity.

Is the Closure Positive Shift a universal marker for prosodic phrasing?

2.1.17

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

supported by the DFG

The finding that both the processing of prosodic boundaries in speech and that commas in written language were reflected in the Closure Positive Shift (CPS) seems to suggest that commas trigger similar prosodic processing subvocally (see 2.1.16).

The present ERP study both confirms and extends this notion. Here, subjects first listened to a pure 'sentence melody' that was stripped of any lexical information with a special filtering procedure (PURR). Half of these prosodic patterns contained an additional prosodic boundary. After a short pause interval, subjects were instructed to replicate the previously heard melody during the silent reading of a visually presented (word-by-word) sentence. Although the written word sequence always allowed this sentence melody mapping, the syntactic structure of the sentence was either compatible or incompatible with the number of prosodic boundaries.

Both the prosodic boundaries in the pure melody and the boundaries replicated during reading elicited CPS-like positive ERP components, which resembled those found for comma perception. Thus, the CPS appears to be a universal on-line reflection of both overt and covert phonological sentence phrasing independent of the input modality.

2.1.18 ERP evidence for the interface of prosodic and semantic processes

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Current behavioral investigations point to a relationship between syntactic and prosodic processes during sentence processing (i.e., Cutler et al., 1997; Warren, 1996). However, prosody can also be linked to semantic content and affective markers of an utterance. In particular, there is ample evidence from patient studies indicating that affective prosodic parameters (i.e., Blonder et al., 1991; Starkstein et al., 1994) are processed in the right hemisphere while linguistic prosodic parameters are processed in the left hemisphere (i.e., Emorey, 1987). However, the evidence for the later parameter is more controversial in terms of its lateralization (i.e., Ross et al., 1997).

We set out to test the possible interface between semantic content and affective prosodic markers in an event-related brain potential (ERPs) study. Our primary goal was to explore to what extent prosody can be processed independent of the comprehension of meaning. Forty subjects listened to a set of sentences in which semantic content (positive, neutral, negative) was fully crossed with affective prosodic information (happy, neutral, angry). This resulted in nine match and mismatch conditions. Half of the subjects judged the semantic content whereas the other half judged the prosodic contour of the sentences on a five point scale.

Behavioral results indicate that subjects were able to judge semantic content or prosodic contour above 95%, respectively. This means that they were able to solely focus on the information that they were asked to evaluate irrespective of the other sentence information. ERP evidence from the match conditions show that processing of negative as compared to neutral and positive sentence content and prosody elicits a larger negativity in both the prosodic and semantic judgment tasks. The prosodic judgment task data from the mismatch conditions (i.e., positive content with angry prosody) display a combination of two negativities, one around 200 ms and one at 500 ms post-stimulus onset at fronto-temporal right hemisphere electrode sites. In the semantic judgment task only the later negativity is predominant at centro-parietal electrode sites. The preliminary data indicate that affective prosodic information is processed earlier during sentence processing as a function of task instruction. Semantic information on the other hand is processed at a later point in time. Further work is under way to extend the data.

This year, we intensified our investigation of music processing. Besides being motivated by a general interest in music processing as such, investigating this issue with the present studies particularly aimed at exploring differences and similarities between the neural processing of music and language. Means of investigation were EEG and MEG. Up to now, electrophysiological reflections of language perception have been extensively examined. In contrast, only little is known about the neural correlates of music perception. Thus, for the most part it is still unknown which cognitive processes and brain regions are activated by the processing of both music and language (and which specifically by either of them).

It may be speculated that at least some cognitive processes, or brain structures, might be employed for the processing of both language and music, since both have many features in common. Undoubtedly, both music and language are means of communication. Both language and music are 'sign-systems' which allow the generation of messages. Like language, music also has a semantic dimension that refers to the meaning of signs. In both language and music, the meaning of a sign has to be 'extracted' by an active process of interpretation, whereby the meaning of signs has to be seen as lying in their systematic relation to each other. Further, the sign-systems refer to rules, or a 'syntax', according to which (acoustic) information can be interpreted. That is, in both language and music, rules serve the attribution of meaning to information.

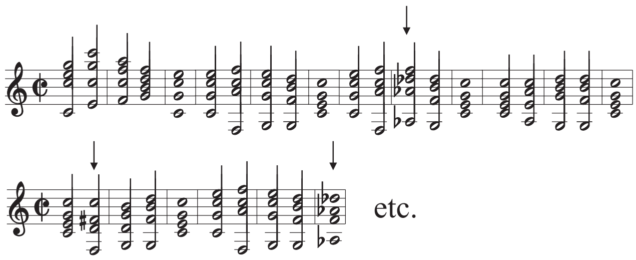

Figure 1.

In order to investigate the processing of syntactic and semantic aspects of music, we use chord-sequences (each consisting of five chords), composed in a way that each sequence builds up a musical context towards the fifth chord (and can thus be imagined as the musical equivalent to a spoken sentence in language). During an experiment, the sequences are presented one directly succeeding the other, sounding like a musical piece. Infrequently, a chord of a chord-sequence contains e.g. unexpected 'out-of-key' notes (see Figure 1, chords with out-of-key notes are indicated by the arrows). It was found that unexpected chords elicit an early right anterior negativity (as a working term labeled 'ERAN') and a late frontal negativity (labeled 'N5'). The ERAN is taken to reflect music-syntactic processing, and the N5 to reflect a processing of semantic aspects of music. Interestingly, the ERAN resembles (though with right-hemispheric scalp distribution), the early *left* anterior negativity (ELAN). The N5 reminds to the N400 elicited by semantically incongruous words in a sentence (see Ann. Rep. 1998).

This year's research focus was to examine influences of the degree of musical sound-expectancy violation (2.2.1), task-relevancy (2.2.2), probability (2.2.3), and attention (2.2.4) on the processing of music as reflected in both ERAN and N5. Additionally, we investigated the processing of changes in a tonal key (2.2.5), and attempted to localize the neural generators of the ERAN (2.2.6).

2.2.1 Sensitivity of ERAN and N5 to the degree of sound expectancy violation

Koelsch, S.[1], Gunter, Th.C.[1], Friederici, A.D.[1] & Schröger, E.[2]

[1]*Max Planck Institute of Cognitive Neuroscience*, [2]*Department of General Psychology, University of Leipzig*

In a previous EEG experiment, unexpected Neapolitan chords infrequently presented at either the third or the fifth position within the chord-sequences elicited an ERAN and an N5. In the present experiment, Neapolitan chords (which are harmonic triads and consonant) were replaced by clusters (which are not triads and may thus be referred to as 'non-harmonic'). Clusters contained the same amount of out-of-key notes as Neapolitan chords. The sound expectancy of listeners was thus violated not only with respect to the occurrence of unexpected notes, but additionally with respect to harmony. Stimuli were presented under the instruction to ignore the harmonies. Participants were 18 'non-musicians'.

Clusters at both the third and the fifth position of the chord-sequences elicited compared to in-key chords an ERAN and an N5 (see Figure 2). Both components were larger at the fifth compared to the third position, and both components were larger when elicited by clusters compared to Neapolitans.

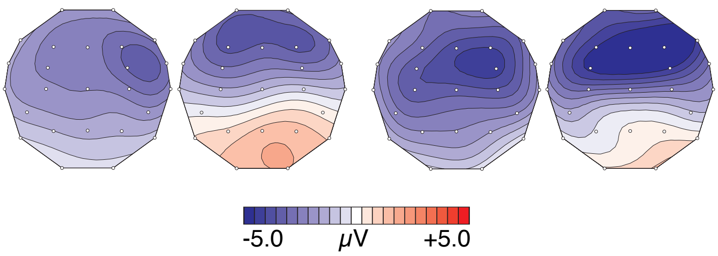

Figure 2. ERAN (190-250 ms) and N5 (550-610 ms) elicited at the third (left) and fifth (right) position.

Results strengthen the hypothesis that the ERAN reflects a violation of musical sound expectancy and the N5 processes of musical integration. Results of the present experiment also indicate that the amplitude of the ERAN (and, consequently, of the N5) is a function of the degree of expectancy induced by a preceding musical context. Scalp-distribution of both ERAN and N5 virtually did not differ when elicited by Neapolitans compared to clusters, thus the present data do not yield that the neural processes elicited by a dissonant sound differ essentially from effects elicited by harmonically unrelated consonant sounds.

Effects of task-relevancy on music processing

2.2.2

Koelsch, S.[1], Gunter, Th.C.[1], Friederici, A.D.[1] & Schröger, E.[2]

[1]*Max Planck Institute of Cognitive Neuroscience,* [2]*Department of General Psychology, University of Leipzig*

In all our previous ERP studies, ERAN and N5 were elicited under the instruction to ignore the harmonic context and to detect deviant instrumental sounds. This suggests that both ERAN and N5 are elicited even when unexpected musical events are not task-relevant. In order to determine a possible influence of the task-relevancy of unexpected chords on ERAN and N5, chord-sequences were presented under the condition of focusing the participants' attention onto unexpected Neapolitan chords, which infrequently occurred at either the third or the fifth position of the chord-sequences ($p=0.25$). Participants were informed about the presence of Neapolitan chords and their nature, and instructed to detect the Neapolitan chords.

Participants detected more Neapolitan chords at the fifth position compared to when presented at the third position. Correspondingly, the ERAN was (just as in previous experiments) larger in amplitude at the fifth compared to the third position. Compared to a previous experiment in which the Neapolitan chords were task-irrelevant, the ERAN did not differ between both experiments, suggesting that the early processing of music is rather insensitive to influences of task-relevancy.

The N5 elicited by detected Neapolitans was almost compensated by the potentials of the P3. Interestingly, *undetected* Neapolitans at the third position did not elicit an ERAN, but a distinct N5. This finding suggests (1) that both ERAN and N5 seem to reflect processes which are independent from each other, and (2) that harmonically unrelated chords were processed differently compared to in-key chords, even when subjects were not able to detect these chords consciously.

Effects of probability on music perception

2.2.3

Koelsch, S.[1], Gunter, Th.C.[1], Friederici, A.D.[1] & Schröger, E.[2]

[1]*Max Planck Institute of Cognitive Neuroscience,* [2]*Department of General Psychology, University of Leipzig*

The present study was designed to investigate an influence of probability on ERAN and N5. The experimental design was the same as in a previous experiment (see 2.2.2), except that Neapolitan chords occurred with a probability of 0.5 at the fifth position only (in the previous study, the same amount of Neapolitan chords was distributed equally over the third and the fifth position, resulting in a probability of 0.25 for each position).

Neapolitan chords elicited a small ERAN and virtually no N5, that is both components were distinctly smaller in amplitude compared to the previous experiment. (Though the over-all probability for Neapolitan chords was identical for the two experiments!) The amplitude-reduction of the ERAN is taken to indicate that subjects got familiar with the Neapolitan chords and therefore became able to anticipate them (at least to a certain extent), which made the sound of the Neapolitans less unexpected. The reduction of the N5 is suggested to reflect that after a few trials, when the notes of a Neapolitan are (at least by some subjects) recognized as leading downwards to the tonic, the integration of Neapolitan chords becomes easier or even unnecessary. Results are suggested to indicate that musical experience can very quickly alter the perception of music with respect to musical expectancies and the integration of musical events.

2.2.4 Pre-attentive musicality of the human brain

Koelsch, S.[1], Schröger, E.[2], Gunter, Th.C.[1] & Friederici, A.D.[1]

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The present experiment was conducted to investigate whether ERAN and N5 can be evoked pre-attentively, i.e. even when a musical stimulation is ignored. Therefore, chord-sequences were presented to the participants (all 'non-musicians') under the instruction to read a self-selected book. Chord-sequences consisted of five chords each. Infrequently (p=0.2), a chord at the third or at the fifth position was a Neapolitan sixth chord (which was harmonically only distantly related to the preceding in-key chords).
Progressing in-key chords elicited a bilateral N5 which was larger in amplitude when elicited at the beginning compared to the end of a cadence (see Figure 3), reflecting, surprisingly, the build-up of musical context even in the absence of attention. ERPs of Neapolitan chords opposed to expected in-key chords revealed both ERAN and N5. Findings are taken to indicate that the sound-expectancy of listeners was violated by the Neapolitans, and that participants integrated the Neapolitan chords into the musical context. That is, participants distinguished musically between in-key and out-of-key chords, even under "ignore" conditions. Due to the build-up of harmonic context, both components were larger at the fifth compared to the third position, according to the principles of music-theory. The brain responses of participants thus indicate a pre-attentive musicality of the human brain.

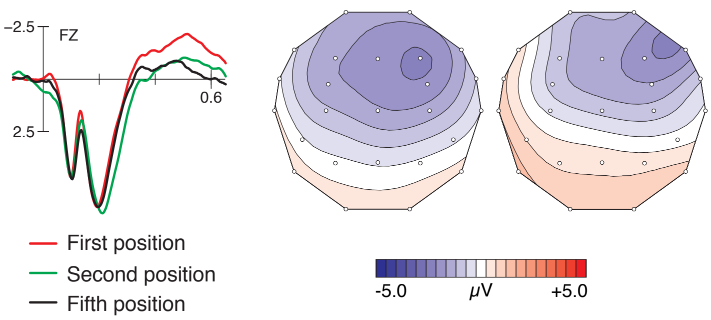

Figure 3. ERPs of in-key chords (left); and effects of Neapolitans at the fifth position (left: ERAN, right: N5).

In a control block, participants were asked to detect the Neapolitans. The ERAN slightly increased in amplitude, indicating that the processes underlying the generation of the ERAN are (only) marginally influenced by attention.

Processing of changes in tonal key

2.2.5

Koelsch, S.[1], Gunter, Th.C.[1], Friederici, A.D.[1] & Schröger, E.[2]

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A common stylistic mean in western tonal music is the change of key within a musical sequence (in musical terms modulation). The aim of the present study was to investigate the cognitive processing of modulations. Participants (all 'non-musicians') listened to sequences of chords which were infrequently modulating. Participants were instructed to detect infrequently occurring deviant instrumental sounds (subjects were not informed about the presence of modulations or their nature).

ERPs of in-key chords revealed a CNV-like sustained and increasing negativity, taken to reflect the increasing specificity of musical expectancy (i.e., anticipation) for tonally related chords to follow. Modulating chords elicited distinct effects in the ERPs: an ERAN and an N5. The ERAN is thought to be elicited by a violation of sound expectancy, since modulations introduced out-of-key notes whose sound is perceived as unexpected with respect to the precedingly established tonal context. The abstract distinction of 'in-key' and 'out-of-key' must refer to a processing of harmonic relations. Harmonic relations (to be understood literally in the sense of harmonic relatedness) are described by music theory and reflected psychologically in terms of the degree of musical expectancy. Results are taken to support the hypothesis that the principles of harmonic relatedness constitute (at least a considerable part of) a musical syntax.

The N5 is taken to reflect processes of harmonic integration. Modulating chords contained out-of-key notes (with respect to the old key), which could hardly be integrated into the old, but more successfully into the new key. Modulating chords thus needed more musical integration than in-key chords.

Additionally, modulations elicited a tonic negative potential (maximal around 500-1500 ms), suggested to reflect the restructuring of the hierarchy of harmonic stability entailing working memory operations. Interestingly, the final dimension of such a restructuring correlates with the term 'strong dynamic aspect of modulations in time' by C. Krumhansl, that is modulations induce a strong expectation for the completion of the modulation.

2.2.6 Localizing neural correlates of music perception as reflected in the ERAN with MEG

Maess, B., Koelsch, S., Gunter, Th.C. & Friederici, A.D.

It is commonly agreed that music has 'some kind of' syntax. However, which aspects of music may be described as 'syntactic' has remained matter of debate. In order to investigate the processing of a musical 'syntax', previous ERP studies performed by the authors simply took advantage of the psychological reality of musical syntax as demonstrated by the brain's ability to expect musical events to a higher or lower degree. A violation of musical syntax has been found by the authors to be reflected electrically as the ERAN which was elicited when a harmonically unexpected chord occurred within a sequence of in-key chords.

Using the same experimental paradigm as in a previous EEG experiment, unexpected ('Neapolitan') chords opposed to in-key chords elicited a particular early magnetic field which was largest around 200 ms and taken as magnetic counterpart of the ERAN (ERANm). The dipole solution for the ERANm (calculated as grand-average of Talairach-transformed individual dipole solutions, which had an explained normalized variance of above 95%) revealed in each hemisphere one dipole located within the lower part of the pars opercularis (i.e., in the lower part of BA44, see Figure 4). In the left hemisphere, this area is classically called Broca's area.
During language perception, Broca's area is thought to be responsible for the processing of syntactic elements and syntactic sequences, involved in the syntactic analysis of incoming language input (in the sense of determining grammatical relations in a sentence), and specialized for fast and automatic access to syntactic information. Analogously, Broca's area may also be involved in determining harmonic relations within a musical phrase. It is suggested that the determination of harmonic relation is a 'syntactic' analysis of incoming musical input.

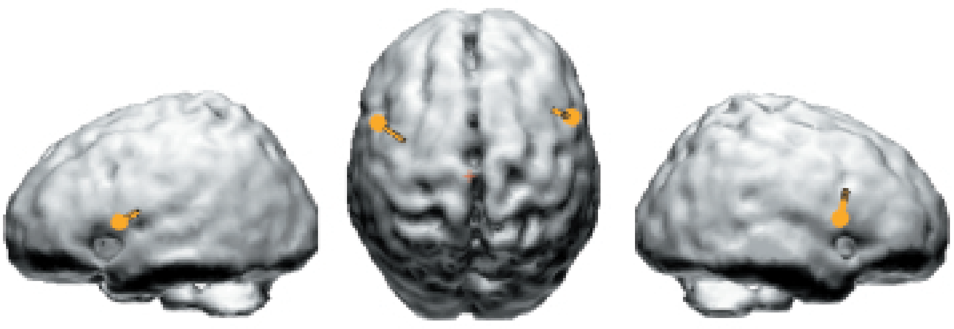

Figure 4. Positions of dipolar activity based on the difference fields between Neapolitan and in-key chords around 200 ms.

During the last few years, neuroscientific research on language processing has been mostly related to lexical access and to syntactic and semantic processing.
The Independent Research Group on 'Neurocognition of Prosody', working since November 1st 1999, will focus on the processing of prosody and its interfaces to syntax, semantics and pragmatics.
We are using the term 'prosody' in a broad sense including abstract phonological properties and their concrete acoustic realization.

Prosody has various functions in language processing: spoken language provides prosodic cues in order to express both linguistic (e.g., syntactic and semantic) and non-linguistic (e.g., affective) information. However, in order to realize a certain prosodic effect (e.g., accentuation, prosodic phrasing, etc.) speakers can use a variety of prosodic parameters such as pause insertion, constituent lengthening, and pitch or loudness variations (Cutler, Dahan & Donselaar, 1997). The listener, on the other hand, has to decode and to integrate these different parameters. Thus a central question of prosodic processing concerns the relative contribution of each single parameter. A crucial prerequisite for addressing this question empirically is the separation and systematic variation of single parameters. This is a non-trivial enterprise as the different parameters are usually not completely independent of each other. For this purpose, we will use speech synthesis and resynthesis techniques.

Traditional neuropsychological observations associated right hemisphere brain damage with disturbances of patients' capability to deal with prosodic information. Since these results are mostly based on single-case studies and fail to identify precisely the location of the lesion, little is known about the cortical representation of prosody. To date there is a widely held belief that language is represented predominantly in the peri-sylvian cortex (e.g., Broca's and Wernicke's areas) of the left hemisphere, whereas emotional and affective prosody appear to involve particularly right hemispheric areas (cf. Baum & Pell, 1998).
This raises the question as to where in the brain the different aspects of linguistic prosody, such as intonation, accentuation and prosodic phrasing are processed.

Recent fMRI-studies provide evidence that peri-sylvian areas in the right hemisphere play a decisive role in processing prosodic information, e.g. non affective intonation comprised in connected speech. This holds, in particular for the deep frontal operculum, that is directly adjacent to an area in the right inferior frontal cortex better known as the Broca's homologue. This finding is in concordance with neuropsychological observations as well as a dichotic listening study which also emphasize the right hemisphere with respect to sentence intonation. Currently, a fMRI-study with healthy subjects and brain damaged patients is in preparation which aims at dissociating and localizing specific aspects of prosodic processing during auditory language comprehension. Moreover, it is intended to investigate whether the same brain areas subserving prosodic information in healthy subjects are involved when non hearing subjects comprehend language utterances.

Presently, we are planning several investigations of prosodic parameters or closely related aspects of speech using magnetoencephalography (MEG). By means of this technique, we hope to localize characteristic MMNm (magnetic mismatch negativity) components for the various acoustic features comprised in natural or manipulated speech signals. We will also investigate the relevance of prosodic parameters indicating properties of information structure. We do acoustic analyses of speech signals and compare behavioral data, such as reaction time, with EEG-measurements, in order to investigate the cognitive processing of prosodic features, in particular their role in comprehending information structure.

From cooperation with various in-house groups we hope to get synergetic effects on the following research areas:

- the processing of information structure (Karsten Steinhauer, Angela D. Friederici),
- the processing of emotions (Sonja A. Kotz, Angela D. Friederici, Mireille Besson),
- concepts of the processing of melodic structures in speech (Th.C. Gunter),
- studies with brain damaged patients (Day-Care Clinic, D. Yves von Cramon, Sonja A. Kotz),
- fMRI studies (D. Yves von Cramon),
- MEG studies (Angela D. Friederici, MEG group).

Two grants from the German Research Foundation (DFG) allow us to carry on with research cooperation with the University of Leipzig (Department of Linguistics) concerning the influence of word stress on lexical access (Angela D. Friederici, Anita Steube, Sonja A. Kotz) and the relation between semantics and prosody (Anita Steube).

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 at first, 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 (EEG and MEG) and measure of hemodynamic brain activation are used to examine memory-related brain activation patterns.

A major 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 in information specific maintenance functions that enable storage of information. In extension of two prior fMRI studies (see Ann. Rep. 98, 3.2.1) two projects focused on the functional role of premotor (2.4.1) and prefrontal cortical areas (2.4.2) when information is maintained in working memory. Project (2.4.3) used spectral EEG parameters to examine maintenance process in a delayed matching-to sample task. Two other projects were concerned with control functions of working memory and focused on inhibitory mechanisms (2.4.4) as well as motivational aspects during working memory performance (2.4.5).

The second research focus is on memory retrieval. Most of our projects are concerned with the subprocesses contributing to intentional retrieval. Based on dual process models that assume that recognition memory comprises two processes; familiarity and recollection, we investigated the temporal aspects and neuronal realization of these two aspects. Projects (2.4.6) and (2.4.7) examined the subprocesses underlying illusory memories for semantic and episodic information using ERPs and behavioral measures. The spatio-temporal ERP patterns underlying familiarity and recollection were examined in more detail in (2.4.8) using the source memory technique. Projects (2.4.9) and (2.4.10) combined ERP and MEG recordings to investigate the time course and neuronal sources of incidental retrieval mechanisms in a repetition paradigm. Three fMRI projects (2.4.11-2.4.13) focused on the interplay of the mesial temporal lobes and the frontal lobes during recollection and encoding using words (2.4.11, 2.4.12) and sound patterns (2.4.13) as stimulus materials. Using depth electrode recordings in epileptic patients in an additional project we, tried to specify the contribution of the mesial temporal lobes to memory updating processes (2.4.14), and a final project examined the neuronal realization of implicit memory processes for natural and schematic faces and objects (2.4.15).

2.4.1 Holding in mind: Motor representation and their role in visual working memory

Gruenewald, C.[1], Mecklinger, A.[1], Besson, M.[2] & von Cramon, D.Y.[1]

[1]Max Planck Institute of Cognitive Neuroscience, [2]CNRS, Centre de Recherche en Neurosciences Cognitives, Marseille, France

Retention processes in visual working memory are realized by a neuronal network including prefrontal, parietal and premotor areas. We used fMRI to specify the functional role of the lateral premotor cortex in this network. Previous studies suggest that the lateral premotor cortex is activated by viewing of graspable objects in the absence of any overt motor demands. In the present study we examined whether the lateral premotor cortex is more strongly activated with graspable objects as compared to non-manipulable objects which have to be maintained in working memory for several seconds. To examine this, two classes of stimuli were used, that according to a pre-experimental rating were either manipulable or non-manipulable. To ensure that any manipulability specific activations were not confounded with encoding and/or decision processes, event-related brain activation was measured in a modified delayed matching paradigm.

A direct comparison of manipulable and non-manipulable objects in the retention interval revealed significant activation (manipulable > non-manipulable) in the ventral premotor cortex (Figure 1). This area was previously found to be activated by imaging grasping movements and by object use naming. In addition, for manipulable objects relative to the baseline task significant activation was found in the same ventrolateral premotor cortex region. This suggests that motor schemata for object use are activated when graspable objects are maintained in working memory. Retention of non-manipulable objects relative to the baseline recruited the left fronto-opercular cortex (Broca's area), suggesting that phonological recoding and rehearsal takes place for the latter objects. The results indicate a differential involvement of hand motor and verbal motor representation in working memory depending on the motor valence of the objects to be memorized. We assume that the premotor cortex reflects the activation of general motor schemata for object use, which provide a mnemonic reference structure in working memory tasks.

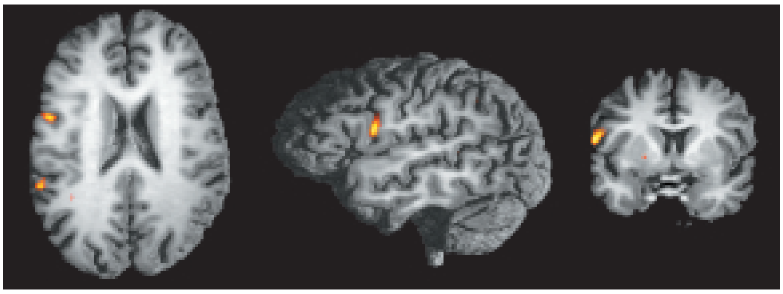

Figure 1. Across subject activation pattern for manipulable relative to non-manipulable objects ($z=2.6$, $p<.005$).

On the relationship between working memory and semantic retrieval

2.4.2

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

In 1998, two fMRI experiments were performed to examine the domain specificity of visual working memory systems (see Ann. Rep. 98, pp. 40-41). These experiments revealed a pronounced domain specific lateralization pattern within the banks of the inferior frontal sulcus (IFS). That is, retention of unfamiliar faces recruited the left IFS to a larger extent than retention of abstract biological objects (butterflies). One inter-pretation for this frontal lateralization pattern could be that verbal labels for faces or face parts were more easily retrievable than for abstract biological objects and that this is associated with enhanced left IFS activation. To test this hypothesis we performed two dual task reaction time experiments. The primary tasks were identical to those used in the fMRI experiment and required subjects to maintain either unfamiliar faces or butterflies in working memory. In the dual task conditions subjects made semantic judgments (Experiment 1) or phonological judgments (Experiment 2) upon a word presented in the retention interval. Experiment 1 shows that maintaining faces in working memory interferes with semantic classification to a larger extent than maintaining butterflies in working memory. This result is consistent with the view that verbal labels for faces and face parts were more easily retrievable from semantic memory. Preliminary analyses of Experiment 2 suggest a differential pattern for the phonological classification task. The observation that semantic but not pho-nological classifications interfere to a larger extent with the maintenance of faces than butterflies suggests that semantic retrieval processes are important though often neglected aspects of working memory.

Induced but not evoked alpha activity reflects short-term memory in a delayed-matching-to-sample task

2.4.2

Herrmann, C.S. & Mecklinger, A.

We conducted a delayed matching to sample experiment with 15 subjects. Stimuli were pac-men arranged to either constitute a Kanizsa square or not. All stimuli were presented at three different rotation angles. In a memory task, subjects had to compare the rotation angle of the first (S1) and second (S2) presentation. A random dot pattern was presented in the variable delay between S1 and S2. In a perceptual control task, subjects only had to tell whether the rotation was maximal for S2. EEG was recorded from the 19 electrodes of the 10-20 system at 500 Hz. Individual frequency bands were analyzed via a time-frequency method using a wavelet approach. Alpha, beta and gamma bands were investigated. We found increased evoked gamma activity for the illusory figures as compared to non-illusory figures. In addition, we found increased induced alpha activity in the delay for the memory as compared to the control task. No differences were found for evoked alpha. Consistent with previous findings reporting event-related desyn-chronization in correlation with memory processes (Klimesch, 1999), the results suggest that the alpha generators might be continuously active but vary in synchrony.

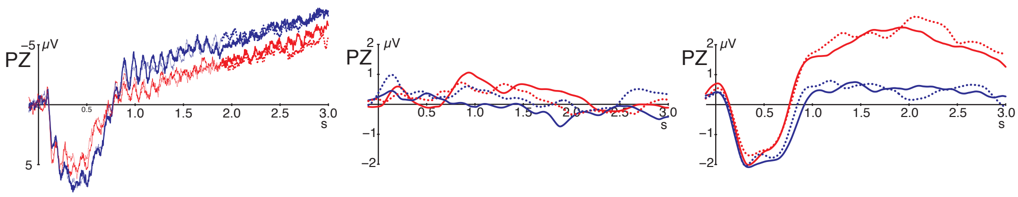

Figure 2. Left: Event-related potential in response to first presentation (0-400 ms) of a stimulus showing oscillatory activity during the delay (400-3000 ms). Middle: Evoked alpha activity doesn't show a differentiation between the memory task (blue) and the perceptual control task (red). Right: Induced activity clearly dissociates memory and perception processes.

2.4.4 Proactive interference and inhibition in working memory

Weber, K., Mecklinger, A. & Gunter, Th.C.

In working memory information is maintained in an active state for a short period of time and depending on task requirements modulated by executive control processes. An example for such control processes is inhibition of irrelevant information.

In two behavioral studies we investigated inhibitory control processes using a S1-S2-paradigm. Subjects performed item-recognition-tasks in which they had to decide whether a probe stimulus (S2) matched a target stimulus (S1) or not. The target set (S1) consisted of two abstract figures followed, after a brief interval, by a single probe figure (S2). In critical trials the probe did not match the target figure and therefore required a no-response. There were three conditions: in the High Interference (HI) condition the probe that had to be rejected in the current trial had been a member of the target set (S1) and probe (S2) in the previous trial. In the Low Interference (LI) condition the critical probe had only been member of the target set (S1). In the control condition the probe had not been presented in the previous five trials.

We hypothesized that in the LI condition a memory trace of the critical S1 from the previous trial would interfere with the comparison of the probe to the S1 in the current trial resulting in longer latencies and higher error rates. Further, we expected even longer latencies and higher reaction times in the HI condition, in which an activated representation of the whole stimulus-response-set from the previous trial is assumed to interfere with the actual probe comparison.

We found higher reaction times and error rates in the interference conditions compared with the control condition. It may reflect processing costs to reject unwanted response tendencies associated with probes presented in the previous trials (see also Jonides et al., 1998). No significant differences between the two interference conditions were obtained, although the pattern of results was in line with our hypotheses (larger costs in the HI than in the LI condition).

Since working memory capacity according to Rosen and Engle (1997) is correlated with the ability to suppress irrelevant information, in a second experiment we contrasted high span (HS) readers (rs S 4.0) and low span (LS) readers (rs R 2.5).

For the error rates the following pattern was obtained (Figure 3): LS readers made most errors in the HI condition and fewer errors in the LI condition. HS readers showed the opposite pattern.

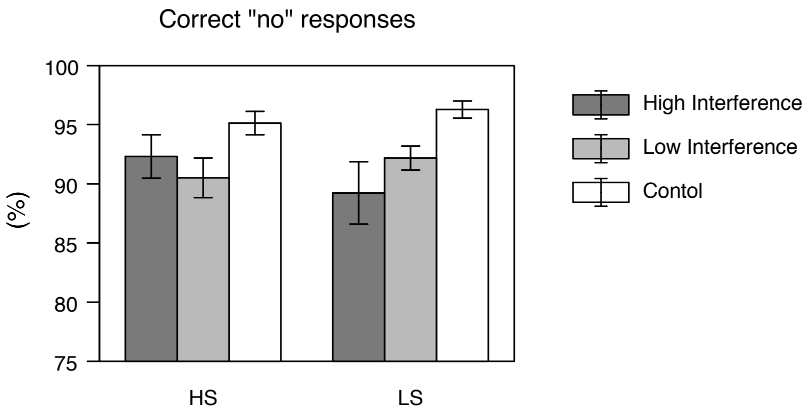

Figure 3. Error rates for high span compared to low span subjects.

An additional analysis that took into account the duration of the preceding response showed that the performance pattern of HS readers (more errors in the LI than in the HI condition) is most pronounced when the preceding response is fast. This differential cost pattern for HS and LS readers can be interpreted as follows: LS readers are less efficient in inhibiting irrelevant information and by this show higher cost in the HI as compared to the LI condition. The error pattern of the HS readers suggests that they might actively inhibit the S2 stimulus of the preceding trial. This results in lower error rates in the HI condition in which the S2 from the previous trial has to be rejected in the actual trial as compared to the LI condition in which no relationship between the S2 in the preceding trial and the S2 in the actual trial exists.

2.4.5 Effects of monetary reward and differential feedback on performance in a visuo-spatial delayed-matching paradigm

Müller, U. & Brattge, S.

Monetary reward and feedback can be used to modify the motivation of human volunteers participating in cognitive experiments. Monetary reward has been shown to improve performance and to influence several physiological parameters like heart rate, blood pressure, P300, rCBF in the dorsolateral prefrontal cortex, and striatal dopamine release. The effects of different kinds of feedback on performance in cognitive tasks are more complex and have so far not been investigated in psychophysiological studies. The aim of this working memory study is to investigate which kind of motivational enhancement is most effective and reliable.

We used a visuospatial delayed-matching paradigm (1, 4 and 8 s delays) similar to a previous one that has been shown to be sensible to dopaminergic treatment (Müller et al., 1998). In the monetary reward experiment, 12 students were investigated twice using a balanced design and error dependent financial compensation. The second experiment was between subjects' (n = 18) comparison of trialwise and blockwise feedback.

Delay-dependent error and RT increases were observed in both experiments. Monetary reward as compared to no reward did not influence error rates, however, it resulted in faster RTs in the longer delays (significant delay x reward interaction). Blockwise feedback did not significantly influence RTs, however, it reduced the overall error rate.

Working memory performance in a relatively boring, long-lasting (30-40 min.), and difficult (20-40% errors) visuospatial working memory paradigm can be influenced by manipulations of motivation and consecutive effort. High financial incentives may result in over-motivation and performance decreases as observed in single subjects. Both feedback and monetary reward manipulation will be used in further pharmacological and neuroimaging studies to investigate the dopaminergic link of motivation and working memory performance.

2.4.6 ERPs and illusory memories: The effects of recognition performance and encoding

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

We conducted two ERP studies to examine ERP correlates of true and illusory memories. Recent studies on false memory suggest processing differences between true recognition of previously studied words (OLD) and false recognition of non-studied, but semantically related words (LURE). However, to date no ERP or fMRI study using randomized test presentation has shown a plausible neuronal correlate of this difference. It is conceivable that this has to do with the fact that in most studies the degree of semantic association between LURE and OLD words is higher than between the subsets of OLD words. Therefore, we examined whether dissociable ERPs occur when OLD and LURE words have the same degree of within category semantic association. In Experiment 1, correctly recognized OLD words showed more positive ERPs than correctly rejected NEW words in an early time window at frontal and parietal sites and also in a late time window with a maximum at right frontal locations. Similar old/new ERP effects were elicited by incorrectly recognized LURE words for poor performers only. This performance related effect may depend on the use of different retrieval strategies that are determined by the memory representation of the studied words. Participants that encoded and searched for word specific information would be less susceptible to LURE words than participants that encoded and searched for more general category information. To test this assumption, in Experiment 2 one group of participants focused on item specific information during study (Item Group) while the other group focused on category specific information (Category Group). Both groups made equivalent rates of true recognition and false alarm to LURE words, even though the Category Group made fewer false alarms to NEW words. Old/new ERP effects for OLD words were similar to both groups, but only the Category Group showed an early frontal old/new effect for LURE words, possible due to the higher familiarity of the LURE words after categorical encoding. This frontal effect was absent for the Item Group, that also showed a reduced parietal old/new effect to LURE relative to OLD words. The proposed relation of the parietal effect to successful recollection suggests a smaller amount of conscious recollection of LURE words through associative mechanisms during study for the Item Group.

In summary, the results show that differences in brain activity elicited by true and false recognition are also evident using randomized test presentation and that encoding processes is an important factor in determining such neuronal differences.

2.4.7 False memory for everyday and novel visual stimuli

Penney, T.B., Wiegand, K., Pataki, K., Pelz, D. & Gehrhardt, J.

In an effort to examine the influence of item specific and general information (i.e., the influence of visuo-spatial representations, category or schema information) on false memory we developed two false memory paradigms using visual stimuli.

In the Everyday Scene paradigm, cartoon drawings of everyday scenes (e.g., a beach scene) or written descriptions of those scenes were presented during study, and probe items, either drawings of objects or their verbal labels, were presented in a subsequent recognition memory test. There were three types of probe item: presented scene appropriate stimuli (OLD; e.g., shell), unpresented scene appropriate stimuli (LURE; e.g., beachball) and unpresented scene inappropriate stimuli (NEW; e.g., snowman). Study of both visual scenes and verbal descriptions of scenes elicited strong false memory effects, as indicated by a significantly higher false alarm rate to LUREs than to NEW stimuli. The size of the false memory effect was uninfluenced by the probe used at test (word or picture) but was influenced by the study format. The false memory effect was much larger following study of verbal descriptions than following study of pictures. Studying pictures may elicit a smaller false memory effect because subjects have visuo-spatial (i.e., item specific) representations of studied stimuli available in memory as well as verbal labels and a general scene schema. Verbal description of scenes may encourage gist or schema related strategies (i.e., categorical) to a greater extent, such that a schema appropriate item, i.e. LURE, is more likely to be classified as old.

In our second paradigm, the Novel Insect paradigm, we used stimuli that did not have a pre-existing representation in memory, thereby placing the use of category or item specific information under greater experimental control. Here, we presented cartoon line drawings of fantasy insects during study. In test, studied insects (OLD), unstudied insects from the same category as studied insects (LURE), and unstudied insects from unstudied categories (NEW) were presented. During study stimuli were presented in random order or blocked by category. In both conditions there were highly robust false memory effects for LURE items but the false memory effect was larger following random study order than blocked study order. It is possible that blocked study order encourages subjects to focus on stimulus differences whereas random order encourages subjects to focus on stimulus similarities. Consequently, blocked order may lead to stronger item specific representations and a reduced susceptibility to false memories. We are currently pursuing this possibility with encoding instruction manipulations.

2.4.8 ERP correlates of familiarity and episodic memory for visual stimuli

Penney, T.B.[1], Mecklinger, A.[1], Hilton, H.J.[2] & Cooper, L.A.[2]

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Old items evoke more positive ERP waveforms than new items in explicit recognition tasks. The recognition related positivity, however, consists of both a brief early frontal effect and a slightly later, longer lasting, more widespread effect that is frequently focused over left-parietal cortex. These two effects have been interpreted within the framework of dual process theories of recognition, which claim that distinct familiarity and active recollection processes underlie recognition performance. One approach for ensuring active recollection in a recognition task is to require subjects to make a source judgment in addition to the old-new recognition judgment.

We recorded ERP responses to studied and non-studied line drawings following intentional encoding in a recognition memory paradigm that also required retrieval of the screen location of studied stimuli (source memory). Beginning at about 300 ms and localized to frontal electrode sites, waveforms to studied objects were more positive than the waveforms to non-studied objects, an effect that may reflect stimulus familiarity. In a time range from 500 to 900 ms correct source judgments were more positive than incorrect source judgments across a broad temporo-parietal region of scalp, reflecting successful retrieval of episodic (source) information.
In the same time window, at right frontal electrode sites the ERP waveforms to correct and incorrect source judgments were more positive than those to new items, but did not differ from each other. This source-accuracy independent difference between old and new items may reflect a strategically controlled evaluation of episodic memory contents.

2.4.9 The three R's of memory: Repetition, recognition and representation

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

Repetition of a stimulus elicits a neural response that is different from that elicited by the initial presentation, undoubtedly reflecting the influence of some form of memory. The quantitative and qualitative features of this difference depend, at least in part, on the processing the stimulus requires, i.e. whether memory access is incidental or intentional.

We recorded behavioral and event-related potential (ERP) responses to initial and repeated presentations of line drawings of everyday (possible) objects and combinations of parts of everyday (impossible) objects in a simple target detection task (Experiments 1 & 2) and in an explicit recognition memory task (Experiment 3). In Experiments 1 and 3, stimulus repetitions were immediate whereas in Experiment 2 there were between three and five intervening items.

In Experiment 1, responses to repeated items were significantly faster (40 ms) for both object types. Second presentations of non-target stimuli elicited less negative ERP waveforms than first presentations in an early time window (250-500 ms) at frontal sites. At parieto-occipital sites, beginning at about 400 ms, the repeated stimuli elicited less positive ERP waveforms than did first presentations. In Experiment 2, responses to repeated stimuli were significantly faster (10 ms) for possible objects only. Second presentations of non-target stimuli elicited less negative ERP waveforms than first presentations in an early time window (250-500 ms) at frontal sites but there was no parieto-occipital ERP difference. In Experiment 3, the same stimulus stream was used as in Experiment 1, but subjects indicated if an item was presented for the first time or was repeated. Here, repeated stimuli of both types elicited more positive ERP waveforms than first presentations at both frontal and parietal sites.

The early frontal ERP effect observed in both Experiments 1 and 2 is most consistent with stimulus familiarity, mediated by increased processing fluency during stimulus categorization. The effect was present when behavioral responding was facilitated (Experiment 1, possible and impossible; Experiment 2, possible) and absent otherwise (Experiment 2, impossible). The parietal reduction in positivity to repeated stimuli (Experiment 1; see also Ann. Rep. 98, p. 47) may reflect availability of a short term memory representation, i.e. a token, that facilitates repeated processing but either quickly decays or is written over by intervening stimuli. Hence, the absence of this effect in Experiment 2 because of the longer delay and intervening stimuli between repetitions. The token appears to be a distinct form of representation from that accessed by intentional retrieval, as repeated stimuli elicited more positive parietal ERP waveforms under conditions of intentional retrieval (Experiment 3).

2.4.10 Parietal and temporal cortex activity is reduced with stimulus repetition: An MEG analysis

Penney, T.B., Maess, B., Busch, N., Derfuss, J. & Mecklinger, A.

Last year (see Ann. Rep. 98, p. 47), we reported results from a target detection task in which a proportion of the non-target stimuli, line drawings of structurally possible and impossible geometric figures, were immediately repeated. Relative to initial presentations, repeated presentations elicited a less negative ERP waveform at frontal electrode sites between 250-350 ms and a less positive ERP waveform at parietal sites between 300-600 ms. Determining the neural tissue responsible for these effects, however, is not a trivial matter. One option is to attempt dipole source modeling, however, this approach is most effective when there are strong a priori constraints on the initial dipole locations (e.g., hemodynamic activation patterns obtained in a parallel fMRI experiment). An alternative method is to take advantage of the spatial and temporal sensitivity of magnetoencephalography (MEG) to localize neural sources. Therefore, we conducted the same target detection task while recording whole head MEG from 148 channels.

Using brain surface current density mapping we found that repeated non-target stimuli elicited less brain activity relative to first presentations at recording sites over the anterior temporal and parietal cortex. This suggests that the frontal effect in the ERP study was a consequence of reduced neural activity in the temporal lobe whereas the parietal ERP effect was due to a widespread reduction of parietal cortex activity.

The spatial and temporal distribution of the temporal lobe activity reduction resembles results from single unit recordings in macaques showing infer temporal lobe (IT) neurons that suppress their firing rate when non-task relevant stimulus repetitions occur. This suppression mechanism could be the basis for the familiarity component of recognition. The parietal cortex reduction is suggestive of reductions in posterior cortical activity obtained in neuroimaging studies of implicit memory. The time course of the ERP and MEG effects, however, does not necessarily suggest a facilitation of perceptual processing. Instead, it may be related to an alternate form of short term memory representation.

2.4.11 Event-related fMRI dissociates recollection-based and illusory recognition memory

Mecklinger, A., von Zerssen, C., Opitz, B. & von Cramon, D.Y.

Several studies revealed remarkably high levels of illusory recognition of items that are semantically related to studied items. Under some circumstances they are equivalent to the level of true recognition. However, the issues of what brain mechanisms are recruited by both forms of recognition and whether recollection and familiarity contribute similarly to both forms is not yet resolved. In a project last year (see Ann. Rep. 98, p. 51), a first event-related fMRI study was conducted to study the brain mechanisms recruited by both types of recognition. A direct comparison of different test stimuli revealed differential brain activation for correct and illusory recognition judgments in the basal forebrain and the medial frontal cortex. In the same year, an additional event-related fMRI study was conducted in which baseline trials that were matched for stimulus and response characteristics and did not require any retrieval operations were incorporated in the test phase. Using event-related fMRI we recorded the BOLD response (TR. 2.25 s; TE: 40 ms) while 12 subjects made recognition judgments to old words, new words and words that were categorically similar to old words (lures). The stimulus materials comprised a total of 300 concrete nouns (30 semantic categories à 10 exemplars) and were identical to those used in two related ERP studies (see 2.4.6). Relative to baseline trials all recognition judgments recruited cortex lining the left inferior frontal sulcus and the anterior insula, presumably reflecting general task-coordination processes. Correct old responses and correct rejections of lures but not false alarms to lures led to strong activation in the retrosplenial cortex (BA29/30), posterior cingulate (BA23) and precuneus. Given that recollection contributes not only to the recognition of old words but also to the rejection of similar words, this result suggests that these regions are recruited by the recollection of episodic information. Notably, basal forebrain structures (nucleus accumbens) and fronto-median cortex (BA9/10) were more strongly activated for correct old responses than for other judgments, suggesting that either an internal reward or an expectancy confirmation mechanism accompanied correct old judgments. The results show that a network including the hippocampal-anterior thalamus axis is involved in recollection of episodic information and dissociates recollection-based from illusory recognition.

The effect of slice orientation and number of stimuli on fMRI activation of the human hippocampus

2.4.12

Opitz, B., Mecklinger, A. & von Cramon, D.Y.

Neuropsychological data from amnestic patients as well as some neuroimaging studies with normal subjects provide evidence that the hippocampal formation is involved in episodic encoding and retrieval tasks. However, several neuroimaging studies of encoding or retrieval failed to provide such evidence. These negative findings have led to various explanations for the unexpected absence of hippocampal activity. It has been suggested that the hippocampal formation may not show sufficiently robust hemodynamic changes across conditions to be detected by fMRI. For fMRI studies, multi-slice EPI is a commonly used technique. Brain images acquired using EPI are sensitive to T_2^* changes, reflecting the level of blood oxygenation (BOLD contrast). This contrast relies upon the neuron density and the vascularization of a certain brain region. The small neuron density in the hippocampal formation might be one of the reasons for diminutive hemodynamic changes. The present study set out to disentangle the effects of slice orientation and the number of stimuli used on fMRI activation of the human hippocampus. Therefore, we investigated the hemodynamic response in the test phase of a visual word recognition task. Prior to scanning, the subject heard a total of 150 words at a rate of 1 every 2 s and performed an animacy judgment. During recognition the hemodynamic response of the hippocampal formation was recorded using EPI (TR = 1 s, TE = 40 ms) from 8 slices oriented either parallel (3x3x3 mm spatial resolution) or orthogonal (3x3x5 mm spatial resolution) to the longitudinal axis of the hippocampus.

In single subject analyses, correctly recognized words elicited a weak activation in the left hippocampal formation in only six out of 11 subjects. This could be attributed to the high noise level in the present data. Despite this, in the group analysis an activation focus in the left hippocampal formation was obtained with orthogonal but not with parallel slice orientation. This could be due to the larger voxel volume and the resulting higher signal intensity. Regarding the influence of stimulus number on the BOLD-response we found that only reducing the number of stimuli to a quarter of the initial number led to a substantial reduction in signal intensity. The results suggest that at a high number of stimuli the BOLD response is less sensitive to changes in the number of stimuli.

A more fine grained analysis will be performed to evaluate possible implications for studies investigating the role of the hippocampal formation in memory processes.

Content-specific lateralization of human prefrontal cortex in episodic memory

2.4.13

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

Recent memory research focuses on encoding and retrieval related brain activity. There are several views about the organization of memory functions in the human prefrontal cortex. One view assumes a process specific brain lateralization according to different memory subprocesses. An alternative view emphasizes content-specific lateralization of brain systems involved in memory processes. The present study addresses this apparent inconsistency between process- and content-specific lateralization of brain activity by investigating the effects of verbal and nonverbal encoding on prefrontal activation during encoding and retrieval of environmental novel sounds using event-related fMRI.

15 subjects were presented with novel sounds embedded in a tone-sequence. In the study phase of an intentional memory task, subjects were required either to judge the sounds' loudness (non-verbal encoding task) or to decide whether or not a sound could be verbally described (e.g., ringing bell - verbal encoding task). Retrieval processes were examined in a subsequent 'yes/no' recognition test. During the entire experiment, echo planar images (TE = 40 ms, TR = 1 s) of eight axial slices were acquired.

In the study phase, the right posterior dorsolateral prefrontal cortex (PFC) was activated in both tasks. During verbal encoding, additional activation of the left dorsolateral PFC was obtained. Retrieval related fMRI activity varied as a function of the encoding task: for the non-verbal task we detected an activation focus in the right posterior dorsolateral PFC while for the verbal task an activation in the left dorsolateral PFC was observed. Moreover, the encoding related activation of the left dorsolateral PFC in the verbal task was positively correlated with subsequent memory performance. In contrast, in the non-verbal task the activity of the right PFC was correlated with memory performance. These findings indicate that the right dorsolateral PFC is engaged in encoding of auditory information irrespective of encoding task. Furthermore, the lateralization of PFC activity during retrieval depends on the availability of verbal codes, with left hemispheric involvement for verbally and right hemispheric activation for nonverbally coded information.

An ERP study is currently being conducted that will allow a more detailed analysis of the time course of the effects under investigation.

2.4.14 Lateralization of the AMTL P300 to object and spatial targets

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Encoding, maintenance, and retrieval of information about the relationships between objects and their positions in space is one postulated role of the hippocampus. In an ongoing collaboration with the Department of Epileptology at the University of Bonn, we recorded intracranial event-related potentials (ERPs) in the hippocampi of patients with temporal lobe epilepsy while they performed visual target detection tasks. We were specifically interested in whether targets defined by object and spatial features elicit equivalent electrophysiological responses in the physiologically normal hippocampus. Last year, we reported (see Ann. Rep. 98, pp. 54-55) that targets defined by object features, but not targets defined by spatial location, elicited a MTL-P300, a hippocampal analog of the scalp recorded P300 component. The results were interpreted as suggesting that the MTL P300 reflects memory updating and is only elicited in situations in which unique object features can be bound with spatial information.

Continued data collection has brought an additional pattern to light. The failure to show a MTL P300 in the spatial task is restricted to left temporal lobe epileptics, right temporal epileptics show a robust MTL P300 in the spatial task. A possible explanation is that the left hemisphere is not specialized for spatial processing and is inefficient in representing and maintaining spatial information. Consequently, memory updating occurs in the left hippocampus whenever an object appears in a target location because the representation of the target position had deteriorated since the last target presentation. The representation in the right hemisphere is maintained across the experiment without deterioration, so memory updating does not occur in that hemisphere and the MTL P300 is not elicited.

Differential brain activation pattern to schematic and natural faces

2.4.15

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A variety of neuropsychological, neuroimaging and electrophysiological studies suggest that faces are processed by specifically tuned neuronal systems. To further probe the functional and neuroanatomical characteristics of these face processing systems we conducted an fMRI study in which we examined whether or not face processing modules can be activated by impoverished visual input. FMRI was recorded in five blocks. In the first block, subjects saw pairs of X's separated horizontally by 10 cm. In the second block the X's were encircled by an ellipse and a nose and a mouth were added to form a schematic face. Block 3 was identical with block 1 and block 4 and 5 included natural eyes and faces. All 5 blocks elicited pronounced bilateral activation in the face area (middle fusiform gyrus), with this activation only differing in degree rather than in kind across the five blocks (see Ann. Rep. 98, p. 55). Staying with the initial logic of the design in this year an additional fMRI study was conducted using stimulus materials that enhanced differential processing across blocks. In blocks 1 and 3, different pairs of stimuli presented at variable locations were used, non biological objects were added to blocks 2 and 4 and all five blocks included baseline trials matched for luminance with the experimental stimuli. Within block comparisons, enhanced activation in the right middle fusiform gyrus was revealed when schematic faces and natural faces were contrasted with schematic and real word objects, respectively. Areas that were more strongly activated for schematic and real world objects include bilateral areas medial to the fusiform gyrus (in the lingual gyrus and extending to the collateral sulcus). Notably, schematic faces but not natural faces activated the posterior portion of the inferior temporal sulcus bilaterally. A direct comparison of the identical blocks 1 and 3 revealed bilateral activation in the fusiform gyrus, though partially overlapping the fusiform gyrus activity of blocks 2 and 4 was distributed more posteriorly. The data suggest a clear dissociation in the processing of biological and non-biological objects with the ventral processing stream regardless of their visual impoverishment.

In the last year, 163 neurological patients took part in the assessment or therapy program of the Day-Care Clinic of Cognitive Neurology at the University of Leipzig. Again, a majority of them (80% compared to 87% in 1998) gave us their informed consent to participate in one or several clinical projects. More than the half of those patients who were not involved in any study in 1999 had been treated in the clinic before and took part in studies during their former stay. 51% of the patients were tested in studies other than the anatomical MR-scanning. 126 patients (compared to 75 in 1998) participated in studies after having been discharged from the Day-Care Clinic, 79 of whom were discharged before January 1999. Meanwhile, there is a pool of patients who cooperate with the Max Planck Institute on a regular basis, 20 of whom were examined in 10 or more experiments.

In continuation of our previous studies, clinical projects in 1999 focused on

- investigation of cognitive functions in patients with circumscribed lesion, with particular emphasis on:
  a) language processing
  b) memory
  c) executive functions

- understanding of cognitive deficits in defined patient groups, especially patients with
  a) Parkinson's disease
  b) transient global ischemia

- MRI investigation of neurological patients

For the examination of *executive functions*, one of our main topics, a separate group was founded in 1999 (Functional neuroanatomy of the frontal lobe). Therefore, patient studies on executive functions or frontal lobe lesions will be presented there (2.6.5, 2.6.6, 2.6.7, 2.6.11).

In the field of *language processing* we made progress in the development of psycho-acoustic test tools, which on the basis of dichotic stimulus presentation enabled us to evaluate hemispheric-specific auditory processing (2.5.1). Several ERP studies were conducted with aphasic patients for a better understanding of phonological (2.5.2) and semantic processes (2.5.3, 2.5.4, 2.5.5).

With the help of fMRI-technique we developed a paradigm on the basis of which lateralization of language functions may be predicted, in order to replace the invasive WADA-test used in presurgical assessment (2.5.6). Several experiments tried to further understand text processing in brain injured patients (2.5.7). The results could be confirmed in an fMRI experiment with healthy control subjects (2.6.8). In another study (2.5.8), we analyzed the effect of context and categorizability on verbal learning in young and old healthy subjects, as well as in patient groups.

For the examination of cognitive deficits in patients with *Parkinson's disease* (PD), we used ß-CIT SPECT and three-dimensional MRI to show that degeneration of nigrostriatal dopamine neurons and a dysfunctional serotonergic raphé system contribute differentially to motor deficits and neuropsychiatric symptoms (2.5.9) and further examined subprocesses of implicit sequence learning (2.5.10).

In the field of *memory processes*, an ERP experiment examined age effects on spatial memory (2.5.11). In continuation of previous studies, visual P300 scalp distribution was examined in *transient global ischemia* in order to improve measurement of anoxic-ischemic encephalopathy (2.5.12). In a project concerning the use of telemedicine in clinical neuropsychology, we made progress in the development of hard- and software of an electronic memory device especially adapted to the needs of brain injured patients (2.5.13).

We used new *MRI techniques* in order to examine the development of vasogenic edema in acute stroke patients (2.5.14) and segmentation of white matter lesions from volumetric MR images in a group of clinically diagnosed Alzheimer's disease and patients with diffuse white matter lesion (2.5.15).

2.5.1 Psychoacoustic test tools for evaluation of hemispheric-specific auditory processing

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The knowledge of the specificity of cortical auditory signal processing is a necessary condition for the establishment of hypotheses regarding the processing of spoken language. We also need to know the functional differentiation of primary auditory cortex areas and of the neighboring auditory association cortices. The development of test tools, which aim at such a differentiation (as a whole constituting a central psycho-acoustics) is challenging, since these tests should not only be applicable in normal hearing subjects, but also in neurological patients who suffer from lesions in alleged auditory cortical areas. Moreover, such tests must selectively enable the evaluation of auditory processing in either of the two forebrain hemispheres, and should allow the allocation of specific deficits in auditory processing to the position and the size of brain lesions. What complicates the design of such tests is the fact that the auditory cortex of each side receives input from both ears, i.e. a lesion in one cortical hemisphere cannot be directly recognized by contralateral perceptual deficits. Therefore, such tests cannot be based on monaural acoustic stimulation. Instead, we have applied the dichotic stimulus paradigm to non-speech acoustic signals in order to selectively route test stimuli from one ear to the contralateral cortical hemisphere and 'mask' the weaker ipsilateral input. The tests aim at the evaluation of threshold values for frequency- and sound pressure level differentiation and at thresholds for temporal discrimination. In all tests which are based on the three-interval forced-choice procedure, the test signals are presented through earphones to one ear, while the contralateral ear is simultaneously stimulated with bandpass noise. These tests were successfully applied in neurological patients which suffer from various temporal lesions including the temporal operculum and Heschl's gyrus of either the left or the right cortical hemisphere or from unilateral disruption of the medial geniculate body or the acoustic radiation. While monaural-successive stimulus presentations to either ear did not disclose any impairment in auditory processing, the dichotic stimulation identified the reduction in the discrimination of frequency-, intensity- and temporal cues.

2.5.2 Phonological discrimination in aphasia: Perception and short-term memory

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

The current reaction-time experiment aimed to study auditory language perception and short-term memory in aphasic patients using a same-different decision paradigm to test a possible correlation between verbal short-term memory and phonological discrimination deficits. Vallar et al. (1992) showed that aphasic patients can suffer from an auditory memory span impairment in an immediate recall condition and might also display subtle phonological processing deficits. However, Blumstein (1995) claims that nearly all aphasic patients have problems in discriminating phonological contrasts independent of short-term memory deficits.

One possible confounding aspect in previous studies might have been that similar synthetic syllables were used without really testing phonological discrimination. Therefore, we used real words with one or two syllables and minimal phonological contrasts (similar vs. identical) to test phonological discrimination. Furthermore, phonological discrimination was tested in two short-term memory conditions (memory set 1 vs. set 2) with an ISI of 2 s. We predicted that aphasic patients with discrimination deficits and/or short-term memory deficits would often chose the "identical" target when they hear phonological similar words and that phonological discrimination of similar items should be more difficult with the increase of the memory set size. In addition, an increased interstimulus interval (ISI) between items could either lead to an increased miss or false rate during phonological discrimination or could improve the hit rate since the increase could allow subjects to develop strategies to better discriminate items.

The patient group selected for the study had minimal or no deficit in short-term memory, phonological processing or both, according to their cerebral lesions (temporo-parietal). Age and gender-matched controls for all patients were also tested. Patients and controls did a training of 12 trials per memory condition before the experimental conditions. The two experimental conditions (memory set 1 and 2) were presented in a randomized fashion, whereby a question mark on the screen indicated whether two or three words had to be discriminated.

Overall, controls responded faster and more accurately to both identical and similar phonological targets than patients across memory set size. Controls showed the expected effect responding slower to phonologically similar targets than identical targets in both memory sets. However, error rates for similar targets were only significantly lower in memory set size 1, but not 2. The patient data displayed comparable results related to the RTs of the controls. In comparison, the error rates showed the right tendency with patients making more errors judging similar targets than identical targets in both memory sets.

In summary, the current data confirm that patients with temporo-parietal lesions display phonological discrimination deficits that are not necessarily correlated with short-term memory deficits.

2.5.3 Auditory word list priming in left and right temporal lobe lesion patients

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

A well-known and replicated behavioral and electrophysiological finding is that the processing of a word is facilitated when it is preceded by a semantically related word. This priming effect is reflected in shorter reaction times and less errors to related words than unrelated words in lexical decision tasks (e.g., Neely, 1991) and in the N400 component in electrophysiological studies (e.g., Anderson & Holcomb, 1995). In addition, some research has focused on whether semantic information type (*associative* vs. *non-associative*) and presentation type (*word pair* or *word list*) can influence priming effects. Kotz (1998) reported auditory and visual word list priming effects for associative relations in reaction time measures (RTs) and an event-related potential (ERP) priming effect for associative *(cat-dog*) and non-associative *(horse-dog*) relations.

Priming studies in aphasic patient populations have shown controversial results. However, most research indicates that the lexical-semantic deficit in aphasics is the result of modified processing operations (controlled or automatic) rather than a loss of knowledge representation (Milberg et al., 1987).

The current experiment followed up on a previous ERP priming experiment with language patients (Hagoort et al., 1996). We further explored priming by manipulating semantic information type (associative functional, associative categorical, and semantic categorical) and word list presentation as a function of lesion sites. Eight patients with left hemisphere temporal lesions and seven patients with right hemisphere temporal lesions as well as normal controls participated in the experiment. Words were presented auditorily in a word list (SOA 1025 ms) and subjects were required to press a button when they heard a verb or an adjective (10%). ERPs were recorded from 32 electrodes.

Normal controls made fewer errors detecting targets in the word list. They showed the expected associative (functional/categorical) and semantic (categorical) N400 priming effects. Overall, the error rate between left and right hemisphere temporal lesioned patients was comparable. Patients with left hemisphere temporal lesions displayed no associative functional priming effect, an associative categorical priming effect (extended latency) and a delayed semantic categorical priming effect. Patients with right hemisphere temporal lobe lesions, in contrast, showed an associative functional priming effect as well as an associative categorical priming effect. They also displayed a small semantic categorical effect, which was modified by a positivity around 200 ms at left hemisphere electrode sites.

In conclusion, these data indicate that word list priming in language impaired patients is differentially modulated by semantic information type and word list presentation depending on lesion site. The different ERP patterns for the two patient groups suggest that the left temporal lobe might monitor functional associative priming whereas the right temporal lobe might be involved in aspects of semantic categorical priming.

2.5.4 Semantic sentence processing in patients with anterior temporal lobe lesions

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

The current study attempted to further specify the neuronal sources that partake in the generation of the N400 component which is thought to reflect semantic integration processes (Kutas & Hillyard, 1980). There is some evidence from intracranial recordings (i.e., McCarthy et al., 1995; Nobre et al., 1994) that point to the anterior medial temporal lobe (AMTL) as the source of the N400. However, the topography at the scalp surface of the N400 varies as a function of modality, task and degree of context (word vs. sentence). Thus, it appears unlikely that the AMTL is the only source of the N400. In addition, ERP surface recordings from other patient studies indicate that a specific type of semantic information (categorical) is absent in right hemisphere lesion patients (Hagoort et al., 1996) or reduced in right anterior temporal lobe lesion patients (Kotz et al., 1999). Therefore, the main goal of the study was to find out whether there is a lesion-specific failure or modulation of the electro-physiological activation of the N400 component in specific lesion patients. This would allow us to identify brain structures which might be engaged in the generation of the N400 component.

We tested a group of patients with left hemisphere temporal lobe lesions (n=8) in comparison to a group of patients with right hemisphere temporal lobe lesions (n=7) in a delayed auditory sentence judgment paradigm. Data from a patient with bilateral temporal lobe lesions were also collected. Standard clinical classification defined all patients as non-aphasic. However, in controlled linguistic tests most of the left anterior temporal lobe patients have a subtle semantic differentiation problem, while patients with right anterior temporal lobe lesions sometimes show difficulties integrating or rearranging content into a sentence. All patients were at the chronic stage at the time of ERP measurement. In addition, age- and gender matched controls were tested.

Results show that both patient groups, the single patient and the controls are comparable in their judgment of the sentences (above 95%). ERPs of the left anterior temporal lobe group display a delayed N400 component with a reduced amplitude relative to the right anterior temporal lobe group and the normal controls. In comparison, the data from the bilateral anterior temporal lobe lesion patient show no N400 effect.

In conclusion, it appears that in patients with non-aphasic language deficits the modulation of the N400 as reflected by the delayed latency indicates a stronger impact of the left anterior temporal lobe in the generation of the N400 than the right anterior temporal lobe. It also becomes apparent that neither a selective left anterior temporal lesion nor a right anterior temporal lobe lesion suffices to eliminate the N400 component. However, the example of a bilateral temporal lesion allows the tentative conclusion that the right anterior temporal also plays a role in the generation of the N400 that might be dependent on the activation pattern in the left anterior temporal lobe. The implications of these modulations of the N400 might be a different timing/integration pattern of semantic information in the left vs. right hemisphere for semantic information.

2.5.5 Semantic differentiation in patients with head trauma: Behavioral evidence

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

One behavioral finding is that patients with frontal lobe lesions have difficulty recognizing the focus of a theme and/or selecting correct items from a set of stimuli. Also, they often give vague definitions about familiarity topics (Yasuda, Watanabe & Ono, 1997). Several patients show category specific impairments such as disturbance for living (biological) things (De Renzi & Lucchelli, 1994). Given this evidence it can be assumed that patients with frontal lobe lesions might have category specific impairments.

In contrast, it is well-known that patients with language impairments show more difficulty processing verbs than nouns (Kohn et al., 1989; Zingeser & Berndt, 1990). For example, there is an effect of verb transitivity. Intransitive verbs are more independent from a syntactic frame and proclaim meaning in itself. They often refer to states (e.g., sleep; swing → concrete verbs; fail → abstract verb). However, verbs also give information about argument structure and transitivity. For example, transitive verbs contain more information (syntactic and semantic complexity) than intransitive verbs. Jonkers and Bastiaanse (1997) presented one patient who retrieved intransitive verbs significantly better than transitive verbs. Therefore, verb representations contain not only syntactic information, but also meaning and phonological form.

Given previous evidence, we assume that patients with head trauma would have problems with transitive verbs due to their semantic complexity as well as problems with category specific noun information.

The current study utilized both nouns and verbs at the single word, dual word and sentence level in the visual modality. Each level was presented in a close and distant distractor version. The task required patients to select the correct noun or verb in either version. The test material contained controlled dichotomies across the two test versions: high frequency vs. low frequency, concrete vs. abstract, biological vs. man-made for nouns. Verbs were controlled for frequency, degree of concreteness and transitivity. These dichotomies allow to control targets for semantic and lexical criteria to insure a conclusive result with respect to the nature of a semantic deficit in language impairment in patients with head trauma. In this study, 23 patients were grouped to participate at either the single word, dual word or sentence level responding to both the noun and the verb version at the respective test level.

Patients at all three test levels chose more close distractors at a faster rate than distant distractors across all tested dichotomies in the noun version. The same was true for transitive verbs. It appears that patients with head trauma suffer from a semantic differentiation deficit when having to select target nouns or verbs according to semantic information. However, the effect is qualified by a speed-accuracy trade off, meaning that whenever patients chose a close distractor speed and error rate go hand in hand. This could be indicative of a modified inhibition process during target selection in head trauma patients.

Interhemispheric distribution of language lateralization

2.5.6

Hund-Georgiadis, M. & von Cramon, D.Y.

Lateralization of language functions plays an important role in the benefit-risk evaluation of presurgical decision making in patients with tumors and epileptic foci in the vicinity of eloquent cortices. Presently, the invasive WADA-test (WT) is the Gold Standard of language lateralization. The latter includes - given the brief examination time available - testing of certain language modalities such as spontaneous speech, semantic encoding, syntactic encoding and sometimes verbal memory. In any case, language lateralization is best understood as a continuous variable rather than a discrete category, such as 'left', 'right' or 'mixed'. A yet open question is, why the different components of the language network show inhomogeneous lateralization effects and even more important, what are the clinical implications. Furthermore, no comprehensive functional mapping study about lateralization effects of verbal memory is available. The current functional MR language lateralization research in our institute aims to replace the WT. A set of paradigms is established that show activation in different subcomponents of the language network. This includes the inferior frontal, the medial and superior temporal gyrus. Furthermore, the activation patterns of other non-eloquent cortices and the assumed subdominant hemisphere are comprehensively examined in terms of functional lateralization. Figure 1 shows fMR group data of 14 right-handed subjects in a word classification task. During lexical encoding of nouns and verbs activation was assessed in the left inferior frontal gyrus, the putamen and the lateral premotor cortex as well as in the right insular cortex. There is evidence that even the subdominant right hemisphere contributes to word processing to some degree.

Before applying the lateralization protocol in patients, cohorts of normal controls are being examined. In particular, the question of language dominance in the inhomogeneous group of left-handed subjects is presently addressed, taking into account various characteristics such as age, sex, familiarity and writing hand.

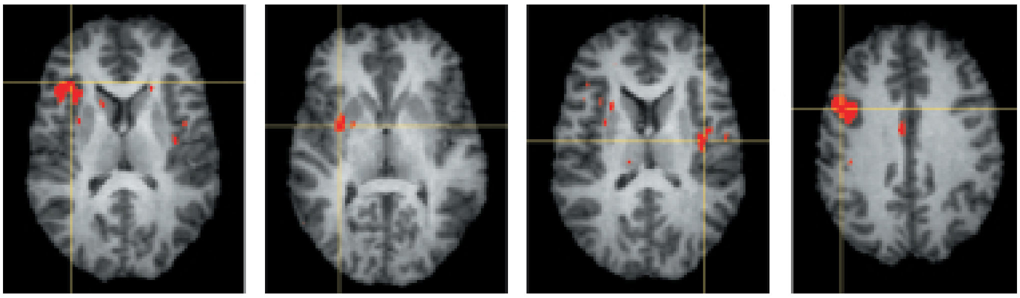

Figure 1. Functional activation patterns of a word classification task in a group of 14 right-handed subjects.

2.5.7 Text comprehension after brain injury: The role of Cohesion and Coherence

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Some brain-injured patients show deficits of higher level language processing without the presence of aphasic symptoms on the word- and sentence level. For example, patients with frontal lobe injuries sometimes fail to organize their discourse in a coherent manner, so that it becomes difficult for the listener to derive the gist of the utterances. Similarly, it has been suggested that patients after right-hemisphere lesions have difficulties with inferences required to establish a coherent representation of text (e.g., Brownell et al., 1986).

There are several explanations for possible inference deficits. One hypothesis is that patients do not notice coherence gaps, and thus, that they do not initiate necessary strategic inference processes. An alternative explanation is that the general world knowledge needed is not available, or that it is not successfully integrated with the current language input.

The goal of this study was to develop a paradigm for dissociating these two hypotheses. We created 160 context-target pairs that were pragmatically coherent, but required a non-automatic inference. Example sentences are

(1) Mary took the train to work. The newspaper was interesting.
(2) Robert was in a car accident. *His* insurance went up.

An incoherent condition was created by switching the context sentences, so that no pragmatic relationship could be detected. Crossed with *Coherence* there was a second factor: *Cohesion*. Each target sentence occurred in one version with a cohesive tie (2), i.e., a lexical item specifying the type of relationship (such as pronouns or conjunctions), and in a second version without (1).

In the first experiment, the sentences were presented to 24 students in a self-paced reading paradigm. Error rates for the coherence judgments were less than 10% in all conditions.

The results for the reading times of the target sentences, corrected for sentence length, are shown in Figure 2. As expected, there was an interaction between Cohesion and Coherence. When the sentence pair was coherent, the cohesive ties facilitated the inference. When the pair was incoherent, longer reading times indicated that the misleading cohesive marker rendered detection of a coherence gap more difficult.

In the second experiment, 14 brain-injured patients at the Day-Care Clinic were tested using a subset of 80 sentence pairs. The patients were grouped according to their lesions: 6 patients had no frontal lesion, 4 patients a uni-lateral right-frontal lesion, and 4 patients a left-frontal or bifrontal lesion. Only the latter patients made errors in the coherent condition, indicating that left-frontal lesions lead to an inference deficit (see Figure 3). These results are consistent with an fMRI study with similar materials (see 2.6.8), showing predominantly left lateralized prefrontal activation.

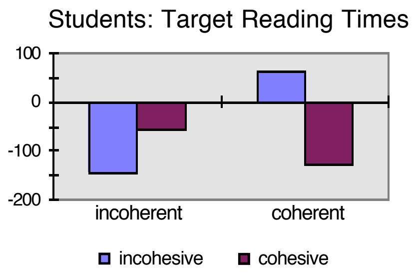

Figure 2.

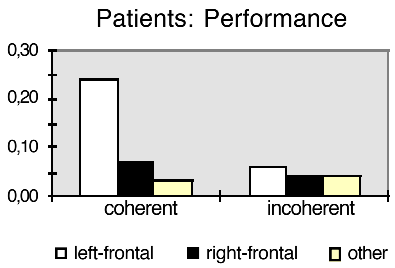

Figure 3.

The effect of context and categorizability on verbal learning

2.5.8

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Guthke, T.[1]*,*
Ferstl, E.C.[1,2] *&*
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For therapy of verbal learning deficits, it is necessary to evaluate whether memorizability of verbal information can be enhanced by providing additional context, or whether a reduction of information to the essential content is more beneficial. The aim of this project was to compare the effects of semantic categorizability (a reductive strategy) and of a story context (an elaborative strategy) on verbal learning. Two German verbal learning tests, only one of which contains categorizable words, were used. The same words were embedded then in short stories. The first question of interest was whether the story context would aid verbal learning even if it was not self-generated but experimenter-provided. Second, we wanted to know whether an eventual difference between the story and the list versions depends on the categorizability of the words.

In the first experiment, 24 healthy participants of two different age groups were tested to explore whether the two strategies are facilitative and, if so, whether there are age differences in the application of learning strategies. As can be seen in Figure 4, there was an advantage of text for both age groups, but only older people benefited from the categorizabality.

In the second experiment, a group of ten well-selected brain-injured patients was tested. As expected, their learning performance was lower, but as a group, the patients showed a qualitatively similar pattern as the control participants. However, in evaluating the results of individual patients we found the expected differences. For example, we compared the results of two patients with two different types of non-aphasic communication disorder after frontal lobe injury. The patient with hypophasia (reduced language output) benefited from the additional context in the story condition. In contrast, the patient with hyperphasia (increased language output) benefited from the categorizability only, while showing a very low performance level in the text condition (without categorizability). One possible interpretation is that reduced speech output might reflect a failure to activate relevant information. Therefore, providing additional, external information during encoding is facilitative. In contrast, enhanced speech output might reflect the failure to inhibit irrelevant information or to select context appropriate content, so that the additional story context interferes with the successful encoding of the relevant words.

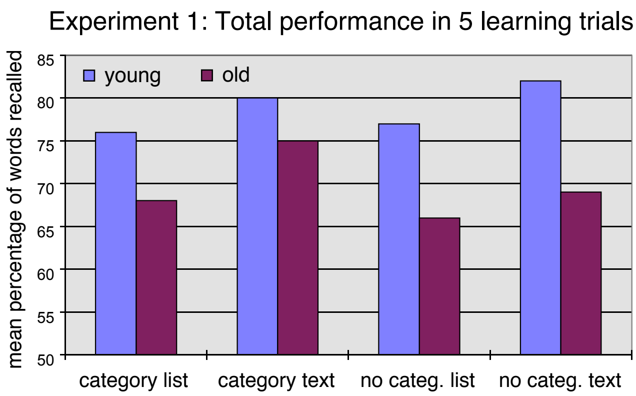

Figure 4.

2.5.9 In vivo evidence for differential association of striatal dopamine and midbrain serotonin systems to neuropsychiatric symptoms in Parkinson's disease

Murai, T.[1], Barthel, H.[2], Werheid, K.[1,3], Reuter, M.[4], von Cramon, D.Y.[1,3] & Müller, U.[5]

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Neuropathological findings indicate that Parkinson's disease (PD) involves various neurotransmitter systems, namely dopamine (DA) and serotonin (5-HT) systems. β-CIT SPECT allows to estimate regional DA and 5-HT transporter densities in vivo. Sixteen patients with PD underwent [^{123}I]β-CIT SPECT and a three-dimensional MRI. ROIs were determined on individual MRI and transferred to manually co-registered SPECT images. β-CIT binding ratios of the early images (2 hours after injection) were calculated for the caudate (head), putamen, thalamus, and dorsal midbrain over cerebellum and correlated with clinical ratings of the motor and cognitive/psychiatric subscales of the UPDRS. β-CIT binding ratios of striatum, which reflect mainly regional

DA transporter densities, were correlated with the UPDRS3, UPDRS-total, HY stage and the duration of the disease. On the other hand, binding ratios of the dorsal midbrain, which reflect mainly regional 5-HT transporter densities, were correlated only with UPDRS1 ($r = -0.66$, $p < 0.01$) but not with the motor ratings. The findings of this pilot study indicate that degeneration of the nigrostriatal DA neurons and a dysfunctional serotonergic raphé system as evaluated with β-CIT SPECT contribute differentially to motor deficits and neuropsychiatric symptoms in PD.

	UPDRS1 mentation, behavior, and mood	UPDRS2 ADL	UPDRS3 motor	UPDRS-total	HY stage	duration
head of caudate	-0,19	-0,48	-0,55*	-0,58*	-0,53*	-0,56*
putamen	-0,21	-0,38	-0,56*	-0,57*	-0,62*	-0,55*
medial thalamus	-0,36	-0,17	-0,57*	-0,51	-0,61*	-0,27
dorsal midbrain	-0,66**	-0,19	-0,38	-0,38	-0,22	-0,01

* $p < 0.05$; ** $p < 0.01$ (2-tailed significance); [a] Partial correlations with the effects of age removed.

Table 1. Correlations[a] between [^{123}I]β-CIT binding ratios and behavioral scales.

Implicit sequence learning: Differentiation between learning subprocesses

2.5.10

Werheid, K.[1,2], Ziessler, M.[3] & von Cramon, D.Y.[1,2]

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supported by BMBF / IZKF Leipzig

Research on implicit learning has shown that sequences of stimuli and sequences of movements can be learned in the absence of explicit knowledge about the underlying regularities. Sequence learning experiments typically consist of several consecutive learning blocks intersected by blocks of stimuli in random order. The amount of learning is shown by a reaction time (RT) increment in the random blocks compared to regular sequence blocks.
Whereas sequence learning is usually assumed to rely on relations between subsequent stimuli (S-S) or subsequent responses (R-R), Ziessler and Nattkemper (Ziessler, 1989; Ziessler & Nattkemper, 1999, submitted) could demonstrate that learning of relations between a performed reaction and a subsequent stimulus (R-S) represents an important, dissociable subprocess in sequence learning. The present study is part of a series of studies investigating sequence learning in Parkinson's disease. The aim was to replicate

the findings of Ziessler with student volunteers performing a task version adapted for future use in a patient study.

The task consists of three conditions (RS1, RS2, RS4) with 13 learning blocks and 5 random blocks (blocks 1, 5, 9, 13, 17). While the three conditions do not differ with respect to R-R relations, sequences are constructed in such a way that S-S relations get increasingly complex from RS1 to RS4. R-S relations are equally complex in RS2 and RS4 and simpler in RS1.

Figure 5 presents the reaction times per block by a total of 34 subjects investigated so far.

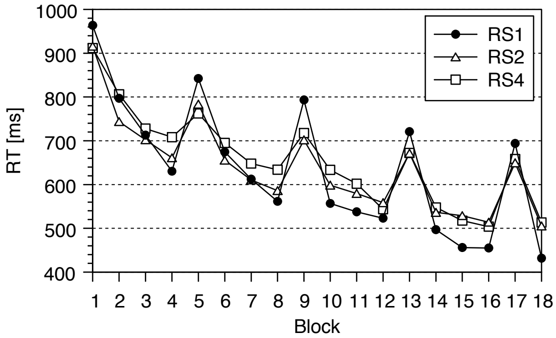

Figure 5. Mean reaction times per block for each condition (Random blocks: 1, 5, 9, 13, 17).

Obviously, RTs in condition RS1 differ from both RS2 and RS4 with respect to RT increments in random blocks and gradual RT decrements in sequence blocks. Furthermore, a trial-based evaluation revealed that R-S relations in random blocks corresponding to those in regular sequence blocks facilitate RTs to the next stimulus.

Our results confirm the findings of Ziessler and Nattkemper. The amount of sequence learning corresponds to the complexity of the R-S relations, but not of S-S or R-R relations. It can be concluded that the association of responses and subsequent stimuli (R-S learning) represents an important subprocess in implicit sequence learning. The paradigm will be used in a patient study on sequence learning in Parkinson's disease to investigate if deficits in sequence learning are connected with a specific learning subprocess.

2.5.11 Age effects on spatial memory

Müller, N.G.[1] & Knight, R.T.[2]

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Normal aging is known to affect prefrontal function preferentially. Thus, by comparing healthy old to young subjects, inferences about prefrontal contribution to different cognitive processes, e.g. spatial memory, can be made.

We tested young and old subjects in non-delayed and delayed-matching-to-sample tests for spatial locations (3 s and 6 s delays) while event-related potentials (ERPs) were recorded.

So far, old subjects performed as accurately as young subjects in the non-delay task but their reaction times were slower. Accuracy for old subjects was impaired in the 3 s delay condition. Young subjects elicited a posterior scalp P3b in all tasks with the largest amplitude observed in non-delay trials. The younger subjects' P3b was larger than older subjects' for all stimuli. The enhanced amplitude P3b indicates that young subjects may allocate more processing resources for stimulus evaluation. An earlier latency frontally distributed P3a was observed in young subjects during the non-delay task which may reflect a novelty reaction to stimulus rarity. Irrespective of task, old subjects elicited an equipotentially distributed P3 with prolonged activity observed over frontal electrodes. The age-related frontal ERP enhancement may reflect additional frontal activation in an attempt to compensate for processing deficits in other brain regions.

Taken together, the results provide evidence of age-related deficits in discrimination, encoding and retrieval of spatial information. More subjects will be tested to confirm these assumptions.

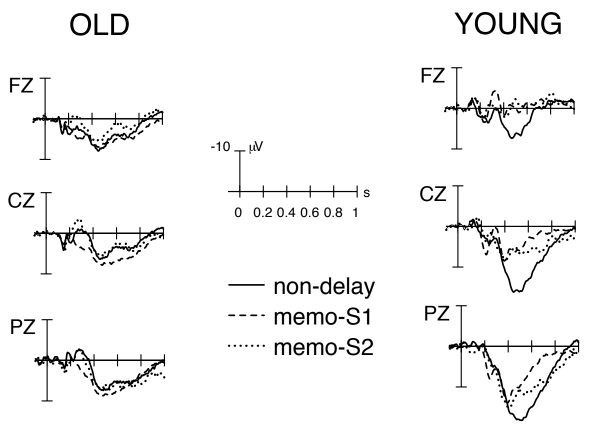

Figure 6.

Transient global ischemia specifically modulates visual P300 scalp distribution

2.5.12

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Ullsperger, M.[1], Mecklinger, A.[1], von Cramon, D.Y.[1,2] & Matthes-von Cramon, G.[2]

In continuation of our previous studies (see Ann. Rep. 1997, p. 72; Ann. Rep. 1998, p. 74) of neuropsychological deficits and psychophysiological markers of transient global ischemia (TGI), we examined latency, amplitude, and scalp topography of the P300 component elicited in a visual oddball task in a group of 11 patients, all of whom had suffered a period of TGI due to cardiac arrest (TGI group), 8 neurological patients with brain lesions not resulting from TGI (clinical control group), and 9 healthy controls. The three groups were matched for age, socioeconomic status, and intelligence scores. Based on neuropathological post mortem findings indicating that the triple watershed zone, a region located in the posterior parietal cortex and the transitional parieto-occipital area supplied by the most distal branches of the cerebral arteries, is vulnerable to TGI, we hypothesized that P300 activity in TGI patients could be selectively modulated at posterior recording sites.

Compared to healthy controls, mean latency of the P300 component was prolonged in both patient groups. Changes in scalp distribution, however, appear to be specific to anoxic-ischemic encephalopathy. The topographical change in TGI patients was due to a selective amplitude reduction at posterior recording sites. In nine out of eleven TGI patients the amplitude of the P300 was larger at frontal and central electrodes compared to parieto-occipital recording sites, whereas only in two out of nine healthy control subjects a similar topographical pattern was found. The results suggest that the selective amplitude reduction might reflect a damage of the most vulnerable parts of the cerebral cortex, i.e. the triple boundary zone. It is important to note that neuroimaging studies did not reveal macroscopically visible structural brain damage in any of the TGI patients under investigation. Taking into account that the diagnostic value of structural brain imaging in TGI is limited, ERPs, particularly recording of the visual P300 component, seem to be an easily performed, inexpensive, and sensitive measure for anoxic-ischemic encephalopathy. Currently, we are examining the extent to which posterior P300 amplitude reduction is correlated with visuo-spatial processing deficits.

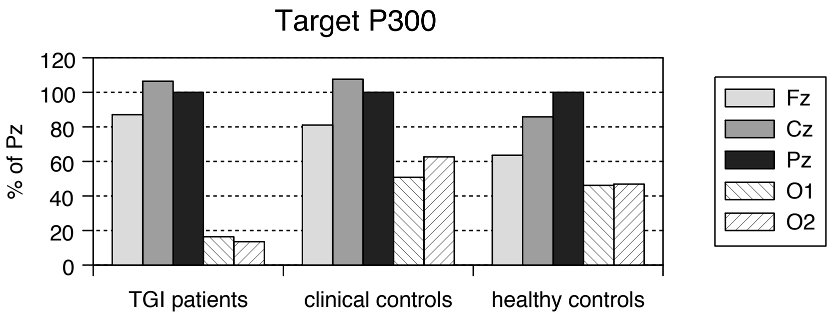

Figure 7. Mean amplitudes for target P300 at Fz, Cz, Pz, O1, and O2 electrodes recorded in the three groups. The amplitudes were normalized by converting them to the percentage of the P300 amplitude at Pz to allow a better evaluation of topographical differences.

2.5.13 Use of telemedicine in clinical neuropsychology

Kopp, U.A.[1], Thöne, A.I.T.[1], von Cramon, D.Y.[1,2], Rüdiger, G.[2], Irmscher, K.[3], Schulze, H.[3], Voinikonis, A.[3], Richter, J.[4] & Romanowski, T.[4]

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supported by SMWK

Deficits in prospective memory performance are of high relevance for patients' everyday life functioning. They are based on memory deficits for future intentions, but may as well be due to a lack in self-initiated retrieval processes, i.e. a lack of executive functioning. The use of external aids has often failed due to several difficulties inherent in the patients' functional deficits, e.g., patients forget to write down appointments, they do not remember to look into their diaries at the right time etc. Modern electronic timers or organizers on the other hand, often are too complicated to deal with and thus patients are not able to learn their use.

Thus, the aim of the project is the construction and evaluation of an external aid which clearly improves the patient's life-quality by providing active support in situations where normal function is impaired by disturbances of memory or executive functions.
In the beginning of 1999, we decided to use the processor "Strong Arm SA 1100" (Intel) and the operating system Windows CE as a platform for the development of our software. The implementation of Windows CE on the handheld device by an authorized Microsoft developer still is in progress. Meanwhile, a complex exemplary task was worked out by the Day-Care Clinic, thereby taking into account findings from engineering psychology and neuropsychological requirements. Furthermore, the task specified rules for the management of adverse events, like the subject not answering an alarm. This exemplary task was the starting point for the development of our own syntax (Mobtel Markup Language) that will be used to guide processes in both the handheld device and the server.

One part of the project concentrated on selection and evaluation of GSM-modules providing the communicational base between server and handheld device. For this module a stable and reliable data transfer mode was developed. As for the hardware, we now have a CPU with storage interface and power management features. An LCD display with touch screen capabilities and a power supply for bias- and backlight was integrated in the prototype. A codec-interface with digital speech recording capabilities was also implemented.

In parallel to the hard- and software development, the Day-Care Clinic evaluated the relationship between neuropsychological functioning, memory aids used in everyday life and the degree of autonomy in a group of 26 former patients. We found strong evidence that the degree of autonomy a patient may reach is related to intact executive functions as assessed via neuropsychological expert rating and the Behavioral Assessment of the Dysexecutive Syndrome (Wilson et al., 1996).

Furthermore, the Day-Care Clinic started to evaluate a commercially available paging system in order to gain experience with reminding strategies and the patients' compliance. We will prepare the clinical evaluation of the prototype (starting in June 2000) by identifying suitable patients and collecting baseline data of behaviors being triggered by the external aid.

2.5.14 MR investigation of acute stroke

Weih, K. & Norris, D.G.

Stroke is characteristically abrupt in onset being caused by a vascular insult, an arterial stenosis or an occlusion. The relatively new MRI techniques of diffusion-weighted imaging (DWI), perfusion-weighted imaging (PWI), and magnetic resonance angiography (MRA) can rapidly visualize and quantify the changes associated with acute stroke. During the first hours after stroke onset, the PWI lesion is typically larger then the DWI lesions. The observed PWI/DWI mismatch is assumed to reflect the ischemic penumbra, "tissue at risk" that is potentially salvageable. Combined DWI, PWI, and MRA studies may be an important diagnostic tool for the application and development of new acute stroke therapies.

In cooperation with the stroke unit of the Leipzig university hospital, MRI examinations of acute stroke patients are being performed. The standard stroke protocol includes T_2-weighted imaging (T_2WI), EPI-based DWI and PWI, and MRA. T_2WI is capable of depicting the vasogenic edema within 12 h after onset of ischemia, and can also identify intracerebral hemorrhages. Two DWI experiments using different diffusion encoding schemes are performed: the first, to localize the infarct; and the second with diffusion encoding in different directions, to average out anisotropy effects in white matter. PWI is performed using dynamic first-pass bolus tracking of the paramagnetic contrast agent Magnevist® using an EPI gradient-echo sequence. The dynamic perfusion series are processed computing relative perfusion maps of summary parameters, maximum peak (MP), time-to-peak (TTP), and peak area. MRA of the Circle of Willis is performed using 3D time-of-flight (TOF) measurement. Figure 8 shows an example of an infarct measurement The lesion is depicted as hyperintense in T_2WI and DWI, a haematoma is depicted as an area of signal loss.

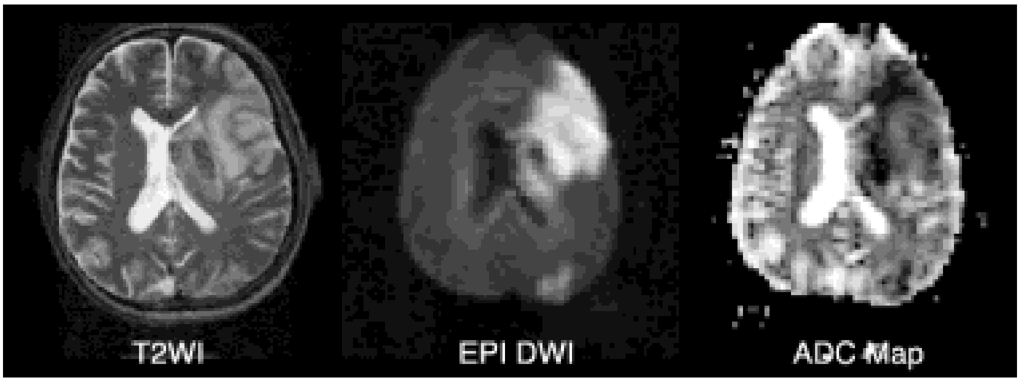

Figure 8.

The research plan aims to correlate acute stroke MRI data with functional deficits in the chronic state, and to compare PWI and SPECT data in acute stroke.

2.5.15 Segmentation of white matter lesions from volumetric MR images

Hojjatoleslami, S.A.[1], Kruggel, F.[2], Gertz, H.J.[3] & von Cramon, D.Y.[2]

[1]School of Computer Science, University of Birmingham, UK, [2]Max Planck Institute of Cognitive Neuroscience, [3]Department of Psychiatry, University Clinic Leipzig

Quantitative analysis of the changes to the brain's tissues is an important objective for a better understanding of pathological changes in various forms of degenerative brain diseases. The extraction of such quantitative measures is concerned with computing a number of descriptors representing the properties of anatomical structures in the brain. White matter (WM) lesions are one of the main signs of various forms of degenerative brain diseases. In T_1-weighted MR images, they appear as faint, dark, arbitrarily shaped blobs, which range from a few millimeters to several centimeters in size. Reliable detection of these lesions is difficult: fuzzy lesion boundaries, noise and non-uniformity in MR images produce a severe lack of definition of WM lesions. They may also lead to a reduction of the WM volume, which is also detected indirectly as an increase of the cerebrospinal fluid (CSF) compartment.

First, main tissue compartments (WM, GM and CSF) were segmented from T_1-weighted MR data using a region growing method. The CSF compartment is splitt into internal and external cisterns using cutting planes relative to the position of the anterior and posterior commissure. Finally, a region growing method is applied to detect lesions inside the white matter. Since lesions may be adjacent to the gray matter, we use the external cisterns as a clue to prevent the algorithm from absorbing low gray level points in the gray matter.

The method was fully applied to detect the WM lesions and relevant structures from a set of 41 MR images of normal subjects, patients suffering from clinically diagnosed Alzheimer's disease and patients with diffuse WM lesions. Subjective assessment of the results demonstrates a high performance and reliability of this method.

In 1999, we established a research group especially dedicated to the functional neuroanatomy of the frontal lobes. The cognitive functions ascribed to frontal brain structures have been termed "executive functions". Although it seems to be clear that all organization and planning of behavior in time depends on executive functions, a precise definition or classification of subprocesses is still lacking.

One of the goals of this group is to further specify these concepts. We want to take advantage of the interdisciplinary make-up of the group, so that a thorough description of the frontal regions involved in higher level cognition becomes possible. In particular, we attempt to combine expertise on anatomical constraints with a task analysis based on cognitive psychology.

The most prevalent method is functional Magnetic Resonance Imaging (fMRI), but we also use ERPs and behavioral studies with non-standard populations for converging evidence on frontal lobe functions. We follow two parallel approaches. First, we extend and replicate results for tasks shown to be sensitive to frontal lobe functions, such as the dual-task, switch or Stroop paradigm. Second, we venture into areas that have been studied less thoroughly, such as processing of sequential information and text level language processes.

Whether the preparatory set for a possible task switch and its subsequent performance could be dissociated in fMRI was investigated in (2.6.10). Although the switch costs declined with longer preparation periods, the activation patterns during preparation and execution were remarkably similar.

Two studies were concerned with dual-task processes. In (2.6.9) we attempted to identify brain regions activated by additional task management requirements. In (2.6.7) we used a similar paradigm for showing that dual-task performance in older adults can be disrupted by interference from an especially salient stimulus.

Interference was the topic of the project (2.6.1). In this study, two Stroop-Tasks were employed for testing the hypothesis of the anterior cingulate cortex being relevant for suppressing competing responses.

For a test of executive functions of working memory, we compared an elaborate digit reordering task to an easier task without demands on the manipulation of information in working memory (2.6.4).

An important prerequisite for the successful organization of behavior is error detection. The error related negativity, an ERP-component elicited in erroneous trials, was used in (2.6.5) to test the error detection ability of patients with frontal lobe lesions.

Using ERP methodology as well, we investigated the false memory effect in recognition memory (2.6.6). The susceptibility to distraction by categorically related lures was compared for a group of healthy control participants and a group of frontal lobe patients.

Another aspect of memory, prospective memory, was studied in (2.6.11). In this project we targeted the question of whether a deficit in this area is caused either by forgetting the intentions, or by the lack of their self-initiated and goal-oriented retrieval.

Planning and monitoring involve the processing of sequential information. Two fMRI studies (2.6.2, 2.6.3) employed modified serial learning paradigms to test the hypothesis that sequencing functions are particularly based on premotor areas.

Finally, there was an initial fMRI study on higher level language (2.6.8). We mapped the brain regions involved in strategic inferences needed for integrating successive sentences into a coherent whole (see also 2.5.6).

2.6.1 Color-Word Stroop-Task and the anterior cingulate cortex

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

Cognitive interference occurs when the processing of stimulus features impedes the simultaneous processing of a second stimulus attribute. The Stroop-Task has become a prototypical interference task. A color word, such as GREEN appears in an ink color such as red. By naming the word and ignoring the color, there is no evidence of difficulty relative to reading the word in black ink. However, if the subject's task is to name the ink color and ignore the word, there is considerable difficulty relative to naming a color patch. This is the phenomena of *Stroop interference*. Numerous previous PET and fMRI studies using the Stroop paradigm have shown increased activity in the cognitive division of the anterior cingulate cortex. The main purpose of this study was to validate the involvement of the anterior cingulate cortex in the Stroop-Task with fMRI. The second purpose was to evaluate two different versions of the Stroop-Task: the Counting Stroop and a single trial version of the Color-Word Stroop-Task.

In our fMRI study with 9 subjects, we used both the Counting Stroop test and a single-trial Color-Word Stroop-Task. The Color-Word-Task, compared to the Counting Stroop, showed a more pronounced interference effect on the basis of reaction times and imaging results. A similar fronto-parietal network, including structures along the borders of the posterior inferior frontal sulcus and the intraparietal sulcus, was activated for both tasks. The Color-Word version produced stronger hemodynamic responses then the Counting Stroop when contrasting the neutral versus the interference condition. But none of these two versions showed any substantial activation in the anterior cingulate cortex, neither in the left nor in the right hemisphere. Only the presupplementary motor area was activated, a region laying dorsal of the anterior cingulate cortex.

We argue that the anterior cingulate cortex, with its underdefined neuroanatomical structure, is not specifically involved in interference processes, but is rather a task unspecific arousal modulator. Further, we argue that the ventrolateral frontal cortex around the posterior inferior frontal sulcus is involved in solving interference problems, a concept that can be seen as a task management problem.

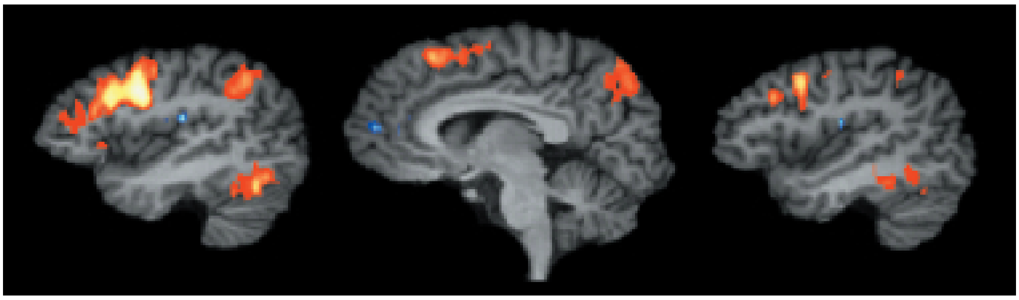

Figure 1. Color-Word Stroop: statistical Z-maps of the interference condition versus the neutral condition comparison mapped onto an individual brain ($z > 4$). Left graph: left lateral cortex; Middle graph: left medial surface; Right graph: right lateral cortex of the brain.

2.6.2 Learning rhythmic saccades: An fMRI-study on timing

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

The cerebral correlates of timing processes were investigated using rhythmically coordinated eye movements (saccades) during fMRI. Time perception and memory is often reflected by large activations in the *motor circuit* except the primary motor cortex, suggesting that tasks requiring timing skills even without any motoric implementation rely on those brain structures that normally serve motoric functions. The motor effectors, usually employed in timing studies, are one or more fingers of one or both hands (finger tapping paradigms). In contrast, the present study set out to investigate the eyes as the motor effector to be timed. To rule out that brain activation during perceptual timing is caused by (a) own movement or (b) perceptual attention to items in motion, the present study investigated cerebral activity during a rhythm-task employing sensory guided movements in both a rhythm and a control condition.

12 subjects participated in this experiment. Two tasks were presented to them visually in randomized order and announced by verbal cues. In both tasks, subjects had to fixate the currently marked item of eight circles arranged in two horizontal lines. Direction, number and length of saccades were kept equal between both tasks. In the *rhythm task*, the marking time changed between the first four items, thus presenting a short rhythm. The rhythm was presented four times in the learning phase and four times in the test phase of each trial, while the marking went from left to right in the upper row and from right back to left on the lower row. The subjects had to indicate changes in the rhythm (deviants) by button press. In the *control task*, the marking changed its position in randomized order and subjects had to indicate visually different items (targets) by button

press. The probabilities for deviant occurrence were 0.25 for 0 or 2 deviants and 0.5 for 1 deviant per trial. During the experiment echo planar images were acquired from 16 axial slices (TR=2.1 s).

As in former timing studies, all motor areas (except the primary motor cortex) were activated by the rhythm task (relative to the baseline task), including bilateral activations in the supplementary motor area (SMA), the promotor cortex (PMC), the lateral cerebellar cortex, the basal ganglia (left putamen, right caudate), and both the right and the left pars opercularis of the inferior frontalis gyrus (BA 44). As expected, the frontal eye field (FEF) was activated, too, but only in the right hemisphere. Moreover, there was a marked activation dominance for the left hemisphere during the learning phase and for the right hemisphere during the test phase, respectively, suggesting hemispheric preferences either for different processes (*left*/*encoding* vs. *right*/*recall*) or for different information format (*local, single elements/left* vs. *global, grouped information/right*).

2.6.3 Learning serial order of interval, spatial and object information: An fMRI-study on sequencing

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

Brain activations elicited by the processing of sequential rhythmical information were compared with those elicited by the processing of sequential spatial information (positions) and object-information (abstract symbols), respectively. The premotor cortex (PMC), the pre-supplementary motor area (pre-SMA), BA 44 and the cerebellum have shown to be bilaterally involved not only when motor output has to be ordered sequentially, but also when temporal sequential information has to be memorized and monitored for deviant rhythmical events. Thus, the present study addressed the question if there are distinct modulations of premotor, basal ganglia or cerebellar activation correlating to different informational domains when sequential information (position, object, duration) has to be memorized.

12 subjects participated in the experiment. Four tasks (rhythm, position, object, baseline) which presented visually in randomized order and announced by verbal cues were used. Each screen display showed two equal objects arranged on two opposite positions on a virtual circle. Within each trial, 12 of these pictures were shown successively. The first three pictures established the *set* to be memorized with regard to its temporal order (picture 1-2-3). The following 3 x 3 pictures were repetitions of the first set, but only with regard to the task relevant informational dimension. In the rhythm (position, object) task, subjects had to attend only to the display durations (positions, objects) of the set, and to indicate omissions (sequential deviants) of a duration (position, object) in subsequent repetitions, respectively (deviant probability 0.38). In the baseline task, subjects had to indicate by button press when the fixation sign changed in size out of turn, i.e., earlier or later than between picture 3/4, 6/7, or 9/10, respectively. During the experiment, echo planar images were acquired from 16 axial slices (TR=2 s).

Relative to the baseline activation, all tasks elicited brain activations in the pre-SMA, the left lateral PMC and the right and left lateral cerebellar hemispheres, suggesting that these areas are involved generally during sequencing. Additionally, all tasks elicited activations in the left inferior frontal sulcus. The BA 44, the SMA and the basal ganglia were only active during the *rhythm task*, as expected on the basis of former fMRI timing studies (Figure 2, panels a-d). Activations were seen in the motion area (MT) (panel f) and the medial inferior parietal sulcus (IPS) (panel e) only for the *position task*, whereas the fusiform gyrus and the lateral IPS (panel g) were activated due to the *object task* (see panel h, too, for direct contrast between *object* [positive] and *position* task [negative]). The precuneus was activated by both the *object* and the *position* task (panel c, negative contrast), probably reflecting a perceptual expectation of arranged visual information established during the tasks, which could be totally ignored in the rhythm-task. For the same reason, the superior PMC was activated in the region of the frontal eye field (FEF) only by these two tasks (panel d, negative contrast).

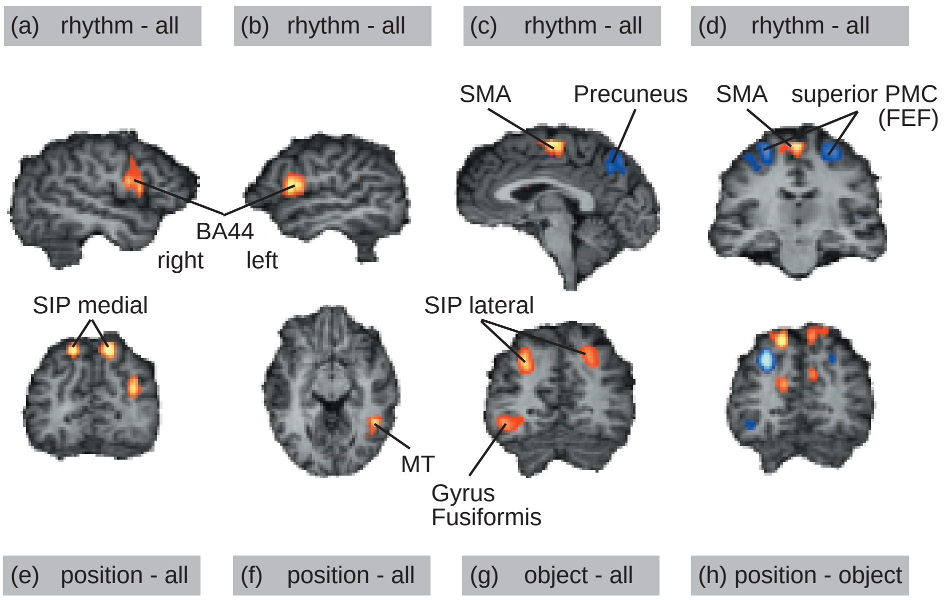

Figure 2.

Frontal lobe contributions to phonological working memory

2.6.4

Gruber, O.

'Active maintenance' has been defined as a memory process that enables (at least) humans and non-human primates to keep information on-line over a short time interval after its perceptual disappearance, thus bridging short temporal discontinuities between perception and action, and enhancing behavioral flexibility. Concerning verbal information the Baddeley and Hitch model of human working memory claims that this process is implemented by the phonological loop. The aim of the present investigations was to re-evaluate this model of verbal working memory by measuring brain activity during verbal short-term memory tasks with varying task conditions and, in particular, by looking into activity changes associated with the well-established behavioral effect of articulatory suppression. This effect refers to the observation that verbal short-term memory is reduced when humans have to simultaneously perform articulations, and is presumed to be caused by a disruption of the phonological loop. In a behavioral study aiming to validate the experimental approach, both the overt and silent articulatory suppression significantly reduced the performance in the memory task used for the functional neuroimaging experiments. During the latter, this task was performed under single- and different dual-task conditions. In accordance with numerous previous studies, the single-task condition revealed significant memory-related activations in brain regions that are regarded to be part of the phonological loop, i.e. Broca's area, lateral and medial (SMA) premotor cortex, and parietal regions (Figure 3). During articulatory suppression, by contrast, this pattern of brain activity largely disappeared and, instead, activations related to mnemonic performance showed up bilaterally in the anterior part of the intermediate frontal sulcus as well as in a number of additional brain areas (Figure 4).

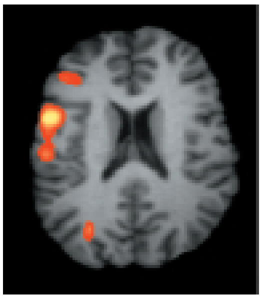

Figure 3.

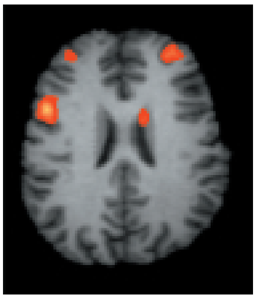

Figure 4.

In a second fMRI experiment, it could be confirmed that these frontopolar brain activations were related to a non-articulatory maintenance process distinguishable from visual working memory mechanisms. Altogether, the present results challenge current models of human working memory by demonstrating a dissociation between processes underlying explicit verbal rehearsal and other mechanisms for actively maintaining phonological information.

2.6.5 Error processing in patients with frontal lobe lesions

Ullsperger, M.[1], Müller, N.[2], von Cramon, D.Y.[1,2] & Mecklinger, A.[1]

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In several cognitive tasks, it could be demonstrated that erroneous responses elicit a negative ERP component, the error-related negativity (ERN; Falkenstein et al., 1990; Gehring et al., 1993), which has been interpreted as a correlate of error detection. It has recently been proposed that the anterior cingulate cortex (ACC) is part of a frontal lobe network that serves as the neural substrate for response selection and error detection and that the ERN could be generated in the ACC (Dehaene et al., 1994; Carter et al., 1998). It is conceivable that frontal lobe lesions could lead to a change in error detection abilities which are reflected in the ERN. The present study addresses the question whether measurement of the ERN in patients can be used as a tool to characterize the ability of error detection. Furthermore, it examines to which extend lesions of prefrontal and other brain regions influence error detection. So far, a group of 20 patients with brain lesions involving the frontal lobes has been examined in a modified Eriksen flankers-task. That group was divided into two age-matched groups according to the localization of the brain lesions: patients in Group A had isolated lesions restricted to the frontal lobes (sparing the ACC), patients in Group B had lesions in posterior parts of the brain, in addition to frontal lobe damage. All patients were able to perform the task, only two of them had to be excluded for insufficient numbers of erroneous responses. This result reflects the suitability of the task for patient ERP studies. Three more patients had to be excluded due to excessive artifacts in the EEG. Performance was better in Group A (n = 6; 85% hits, 10% errors, 5% misses) than in Group B (n = 9; 62% hits, 18% errors, 20% misses). Reaction times for hits were comparable in both groups and showed the typical compatibility effect usually observed in Eriksen flankers-tasks (cf. Figure 5). Reaction times for erroneous responses were about 20 ms shorter in Group A than in Group B. In contrast to the behavioral differences, the peak latency and amplitude of the ERN which was elicited after errors with a maximum amplitude at FCz in both groups did not differ (Figure 6), suggesting that frontal lobe damage sparing the ACC and also additional posterior brain lesions do not disrupt or modulate the ERN. The study will be continued in larger groups of patients with focal lesions and healthy controls in order to reveal the neuronal networks responsible for error detection and correction.

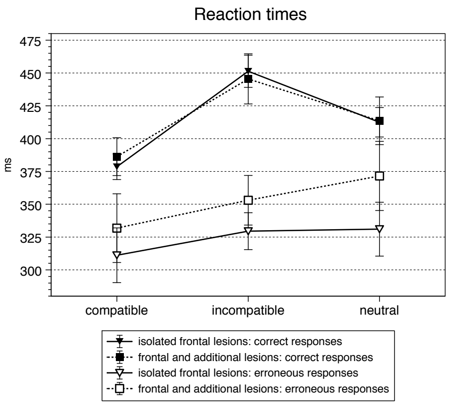

Figure 5. Reaction times in both groups for erroneous and correct responses to compatible, incompatible, and neutral stimuli.

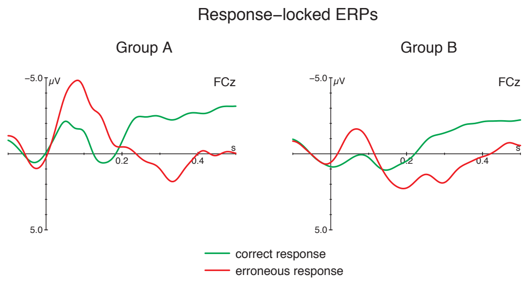

Figure 6. Response-locked grand average ERP waveforms for the Groups A and B elicited by correct and incorrect responses at FCz.

Recognition memory and frontal lobe damage: Combined performance and ERP results

2.6.6

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

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In this project, we investigated the subprocesses underlying true and illusory recognition memory after frontal lobe lesions of different etiologies. In a first step, a recognition memory paradigm adapted to the needs of brain injured patients was developed that allows to examine recognition judgments for studied words and for words that were categorically similar or dissimilar with studied words. To allow the examination of forgetting rates recognition memory was tested at two retention delays: 40 and 80 s. The recognition memory task comprised 24 study test trials, each of them was composed of 12 study words that were followed by 24 test words. The test words included studied words, new words and new words that were semantically related to the studied words (lures). For a group of 14 controls, the false memory effects (false alarm rate to lures minus base false alarm rate) were slightly larger with long delays (16.6%) than with short delays (13.4%). Moreover, the control group's ERPs showed reliable old/new effects between 400 and 700 ms in both retention delays at frontal and parietal recordings, suggesting that familiarity and recollection contributed similarly to recognition memory. While early ERP effects were not affected by the retention delay, a late post-decision slow wave with a right frontal maximum was more pronounced with long retention delays, suggesting higher post-decision monitoring demands. A medial frontal "illusory" familiarity effect (more positive ERPs for false alarms to lures than for correct rejection of lures) was obtained with short retention delays only. For the seven patients tested so far, the false memory effect amounted to 19% in the short delay and to 21% in the long delay condition. As the increase in false memories in the patients relative to controls was on the same level as the patients' general performance decrement, the data argue against a selective impairment in within-category recognition memory judgments. Furthermore, the forgetting rates were equivalent in patients and controls. The analysis of the patients ERPs is still in progress. The general pattern can be best described as a reduction of early old/new effects and a complete absence of late old/new effects.

2.6.7 Localization of deficits in multi-task performance: Parallel processing of stimuli in young and older subjects

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supported by BMBF / IZKF Leipzig

Deficits in different multi-tasking conditions have been described for patients with Parkinson's disease and patients with frontal lobe damage (e.g., Brown & Marsden, 1991; Malapani et. al., 1994), as well as for older subjects without any neurological disorder (e.g., McDowd & Craik, 1988). In order to explain these impairments beyond a mere description of deficits, a dissociation of processes underlying multi-tasking performance is necessary. We assume that the ability to process stimuli in parallel in a multi-task situation is one essential precondition to carry out multi-tasks successfully. Thus, an impairment of this ability can be seen as a source for multi-tasking deficits.

We used the *overlapping task paradigm* to examine the parallel processing of stimuli in a multi-task context. When two tasks have to be carried out with a variable interval between them (SOA), the reaction time for the second task (RT2) is prolonged compared with when the task is performed alone (Schubert, 1999). This prolongation of RT2 is determined by the *psychological refractory period* (PRP). We used the locus-of-slack technology (LST) to test whether the perceptual stages in two tasks can be processed in parallel in different subject groups. We manipulated the difficulty of the perception stage of Task 2 (e.g., Pashler & Johnston, 1989; De Jong, 1994). According to LST, a so-called *underadditive effect* should arise when the two tasks are processed in parallel: under short SOA-conditions, additional RT2 caused by a difficulty manipulation is absorbed in the PRP. First- and second-task processing stages before the PRP operate in parallel. Thus, underadditive effects in multi-tasking situations can prove whether individuals process early processing stages of both task in parallel.

During the first step, we tested whether this capability depends on age. Two groups of young (12 subjects per group, mean age M = 22,3 years) and two groups of older subjects (12 subjects per group, mean age M = 57,7 years) were asked to respond to dual-tasks consisting of two-choice reaction tasks separated by varying SOAs in two experiments. The difficulty of the perceptual stage of Task 2 was varied by a contrast manipulation (bright = easy, dark = hard). In the first experiment, very bright and salient stimuli were used in the easy second task condition.

The results showed significant intergroup differences: younger subjects produced the expected underadditive effect in the shortest SOA condition; a result that indicates parallel processing of the two tasks, whereas older subjects did not so. In the older group the RT2 for bright (easy) stimuli exceeded RT2 for dark (hard) stimuli under the shortest SOA condition, indicating impaired parallel processing. A second experiment showed that this impairment was caused by the high salience of the second stimulus which changed the task scheduling strategies of older subjects.

We conclude that the capability to process stimuli in parallel in a multi-tasking context depends on biological factors, such as age, and on environmental factors, such as salience of stimuli. Parallel processing of stimuli can be seen as a demanding requirement even for older individuals without any neurological impairments.

2.6.8 The locus of cohesion and coherence in text comprehension: An event-related fMRI study

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

Text processing requires inferences to bridge gaps between successive sentences. In neuropsychological studies and brain imaging studies, these coherence building processes have been ascribed to the right hemisphere (e.g., Brownell et al., 1986; Beeman, 1993). The goal of this study was to use an event-related, whole head fMRI methodology to describe in more detail the brain regions involved in inference processes.

For the fMRI experiment, we formulated 120 sentence pairs. The coherent pairs were pragmatically connected to minimal stories (e.g., *The earth trembled. The building collapsed.*). The incoherent trials were obtained by switching the first and second sentences of two pairs. As a second factor, we varied whether there was a lexical item signaling the connection between the sentences. In a behavioral pretest, these cohesive ties (e.g., pronouns, conjunctions) had been shown to be facilitative in the coherent trials, but misleading in the incoherent trials.

We scanned 12 participants while they read the sentence pairs and performed a coherence judgment. The control condition consisted of visually similar non-word trials in which a feature consistency judgment was required. Compared to this control condition, all language conditions yielded activation in left fronto-opercular and lateral temporal regions. In addition, we found left-lateralized activation in the fronto-median wall, the precuneus and the retrosplenial cortex. Contrasting coherent with incoherent trials, there was considerable activation in left fronto-median areas, as well as in the posterior hippocampal formation bilaterally. Incoherent trials, as compared to coherent trials, elicited bilateral activation along the banks of the inferior frontal sulcus. Cohesion had an impact on the lateralization of the latter activation.

These results are consistent with previous imaging studies on text processes (e.g., Fletcher et al., 1995; Mazoyer et al, 1995). However, we found no evidence for a special role of the right hemisphere for coherence processes (St. George et al., 1999).

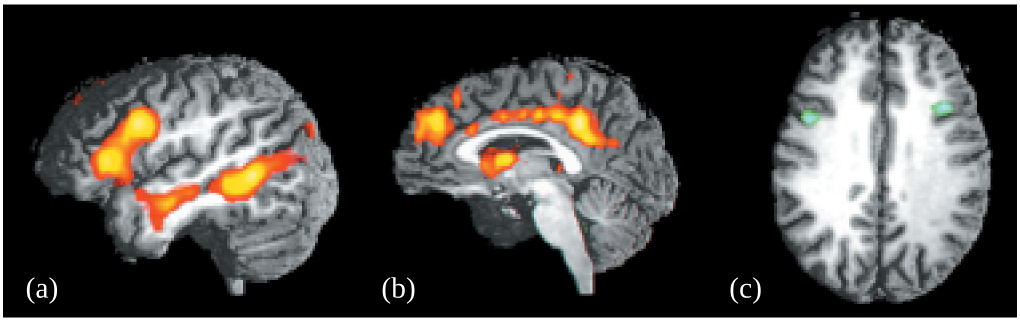

Figure 7. (a) Comparison of the language trials with the control condition ($Z > 7.0$).
(b) Regions more activated in the coherent condition than in the incoherent condition ($Z > 3.1$).
(c) Regions more activated in the incoherent condition than in the coherent condition ($Z > 3.1$).

2.6.9 Localization of prefrontal activation in dual-task processing

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In a dual-task paradigm, subjects have to perform two separated tasks simultaneously. Often this leads to dual-task costs (slowing of reaction times), due to some processing limitations. In order to manage these processing limitations, many authors (e.g., Meyer & Kieras, 1995) proposed that executive control functions, i.e. allocation and coordination of attention or scheduling of processing steps, are needed. D'Esposito et al. (1995) and Koechlin et al. (1999) suppose that these executive functions are localized in the dorsolateral prefrontal cortex (DLPFC). However, while these authors found dual-task specific activations in the DLPFC, others did not. (Klingberg [1998] as well as Goldberg et al. [1998] even found reduced DLPFC activation in the dual-task condition, compared to the single tasks.) In our study, we tested the assumptions that dual-task specific executive functions are located in the DLPFC and that these areas are more activated when dual-task specific coordination requirements are increased.

11 right-handed subjects were examined. In the first task, subjects had to respond to a visual stimulus presented at one of three possible spatial locations (with the right hand), in the second task to a tone, presented in one of three possible pitches (with the left hand). The stimuli were separated by varying intervals. In the dual-task conditions, subjects had to respond in the order of stimulus presentation. To investigate the hypotheses whether dual-task specific executive functions are localized in the DLPFC, we used the following conditions: (1) a resting baseline, (2) each single-task, and (3) an easy dual-task with fixed order of stimuli. To assess the hypothesis that these areas will be more strongly activated when the control demands are increased, we included a second (hard) dual-task condition with randomly varying order of stimuli. This task required subjects to recognize the stimulus order in each trial and to adapt the corresponding response order.

An extended interaction analysis of the appropriate contrasts showed dual-task specific activations in the left DLPFC in the easy dual-task condition and bilateral, but left lateralized DLPFC activations in the hard dual-task condition. Furthermore, a comparison of the hard and easy dual-task conditions indicated that the "strength" (intensity and spatial extent) of the DLPFC activation increased when the coordination demands in the dual-task situation were parametrically increased, too. However, comparisons of the activations in the single tasks against baseline showed also activations in the DLPFC, but they were smaller in extent and strength compared to the dual-task specific activation. Thus, these results confirm our hypothesis that executive processing during dual-task performance takes place in the DLPFC. However, the DLPFC seems not to be specialized for dual-task processing. On the contrary, our results indicate the existence of an executive network which is activated even when the single tasks have to be executed.

Localization of task switch processes using event-related fMRI

2.6.10

Dove, A.[1], Pollmann, S.[1], Schubert, T.[2], Norris, D.G.[1] & von Cramon, D.Y.[1]

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When a switch between two tasks has to be carried out, performance is slower than in trials where the same task is performed repeatedly (an effect called 'switch costs'). It has been shown that, with increasing advance preparation prior to presentation of the new task's target, switch costs declined. This was taken as evidence for deliberate, endogenously initiated control processes which can take place in advance of target presentation.

In an fMRI study, we wished to examine areas showing switch-related activation in (1) a condition with no advance preparation, and (2) a condition with a long preparation period where activation elicited during the preparation period could be separately assessed. Thus, condition (2) allowed to assess areas involved in deliberate control processes during the preparation period.

Eight subjects took part in the fMRI experiment. A cueing paradigm was used in which a cue indicated which task had to be performed next and in which targets (presented in a 2x2 grid) and responses (one arranged more 'up' and 'right' than the other) were either interpreted as being 'up' or 'down' ('vertical' task) or as 'left' or 'right' ('vertical' task). The presentation of switch / no switch trials and the cue-target-interval (CTI) was varied randomly (0, 0.2, 1, 2, 4 s).

As expected, behavioral results showed that switch costs declined with increasing CTI. This supported the hypothesis that switch related advance preparation took place. In the short CTI condition (CTI 0 s, 0.2 s) among other areas the left lateral prefrontal cortex, the pre-SMA/SMA region and the banks of the left intraparietal sulcus (IPS) were activated, as in a previous study by us. In addition, the left hand motor area was involved. In the long CTI condition (CTI 4 s) these regions were involved in the preparation period of task switch trials (compared to baseline activation) as well as in the execution period after target presentation. Additionally, the hand motor area showed switch-related activation in the preparation period. Thus, it could be shown that in this particular switch task the hand motor area was involved in advance preparation for a switch. This could be due to a hand movement of subjects in the preparation period of switch trials: it might be helpful to position the fingers in such a way that response ambiguity is lowered.

2.6.11 Role of executive functions and memory processes in delayed intentions after head injury

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Deficits in prospective memory performance are highly relevant for patients' autonomy in everyday life. These deficits may be due to memory loss for the content of future intentions, but may as well be based on a lack in self-initiated retrieval processes, i.e. a lack of executive functions. For event-based prospective memory tasks, the execution is prompted by more or less prominent cues in the environment. The success of an external cue depends on the demands of the concurrent task being executed while the cue occurs. Despite its impact on everyday life, only a few studies have addressed prospective memory performance in brain injured patients (Cockburn, 1996; Kinsella et al., 1996; Shapiro et al., 1998).

To further clarify the nature of processes involved in the retrieval of event based delayed intentions, we embedded a prospective memory task in a well established working memory paradigm (2-back task) and employed it in patients with deficits of the executive functions and/or deficits in retrospective memory.

As shown in Figure 8, the Low-Low group (deficits in executive functions and retrospective memory) answered significantly less prospective cues than either of the other two groups did. Thus, the execution of delayed intentions seems to rely on both retrospective memory *and* executive functions. This implies that prospective memory deficits could be observed in a variety of neurological patients, which might require different forms of neuropsychological interventions.

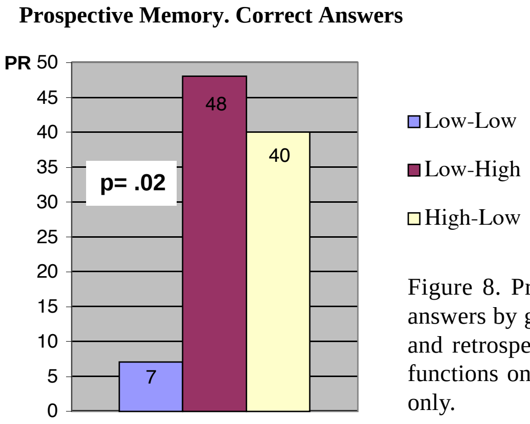

Figure 8. Prospective memory task. Percentage correct answers by group. Low-Low=deficits executive functions and retrospective memory, Low-High=deficits executive functions only, High-Low=deficits retrospective memory only.

During the course of the still ongoing statistical analyses, we will link individual task performance to neuroanatomical structures (i.e., hippocampal system and/or frontal lobes) and compare the behavioral data to the performance of a healthy control group that still had to be examined to reveal different patterns of task performance dependent on lesion side.

Furthermore, we are interested in learning how prospective memory and working memory capacity are related. Therefore, our patients examined an operation span-task (Turner & Engell, 1989). If the retention of delayed intentions is influenced by the demands of the ongoing activity, performance in the prospective memory task should be poor in patients with diminished working memory capacity.

This newly founded workgroup has the aim to investigate the involvement of posterior parietal cortex in tasks such as overt and covert spatial orienting and attentional selection in general.

This topic evolved out of previous studies which demonstrated that posterior parietal cortex was involved in a number of different paradigms, such as visual working memory, visual search, attentional weighting of visual dimensions and task switching, to name a few. In these studies, we observed both overlapping activations related to different cognitive processes and differential activation patterns which may be related to specific processes. We now aim to investigate the functional parcellation of posterior parietal cortex in a systematic way.

In the projects presented on the following pages, parietal cortex activation was investigated in relation to other areas of the brain which support high-level visual-attentional processing, with specific emphasis on prefrontal cortex. Differential activation patterns for visual working memory and visual search were observed along the intraparietal sulcus as well as the superior frontal sulcus (2.7.1). Zooming in on the network supporting visual search, we analyzed the contributions of specific brain areas by correlating the regional fMRI signal with the parameters of a mathematical reaction time model (2.7.3). A main finding was that two networks of brain areas could be separated, the activation pattern in one network correlating with the spatial movement of attention, whereas in the second network the activation correlated with the time subjects taken for featural analysis.

Attentional selection of visual dimensions, such as color and form, was the topic of a third study (2.7.2). Here we could show that changes in the target defining dimension led to transient signal changes in a fronto-posterior network subserving visual processing. These change-related activation changes went along with tonic increases in the dimension-specific visual areas when subjects searched within a given dimension. The data indicated a network of brain areas involved in shifts of attentional weight between visual dimensions, leading to attentional modulation of dimension-specific visual processing.

2.7.1 A direct comparison of visual working memory for objects and visuospatial orienting in an event-related fMRI study

Pollmann, S. &
von Cramon, D.Y.

Working memory can be subdivided into a memory component, holding information active for the current task, and a manipulation component, working on the activated information. It has been further subdivided according to the information it works on, into verbal versus nonverbal, into spatial versus nonspatial, or verbal versus object memory. In this paper, we compare the functional neuroanatomy associated with holding object information accessible with a specific manipulation component, attention-demanding visual search. Using event related functional magnetic resonance imaging, we investigated the time course of activation when an object was held accessible over a short delay, followed by visual search for a target object which had to be matched to the cue. The target object was hidden in a distractor-filled display, its location being indicated by a location cue that varied in salience. In this way, activations associated with holding object information accessible (activation following the variable delay duration) were discriminated from activations related to visuospatial orienting (easy versus difficult search).

Delayed object matching and visuospatial orienting involved a highly overlapping network of brain areas. Common areas were the frontal eye fields (FEF), the pre-SMA/SMA complex, the precentral gyri and the descending part of the intraparietal sulcus (IPS). Selective delay activation was observed anterior to the FEF and in the ascending part of the IPS. Selective orienting-related activation was seen in right middle frontal gyrus. Analysis of the BOLD signal time courses indicated stimulus-, delay-, and response-related activation in close proximity within the common network, especially along the IPS. Right dorsolateral prefrontal cortex was involved in the goal-directed control of visuospatial orienting, but not in maintenance of target information per se.

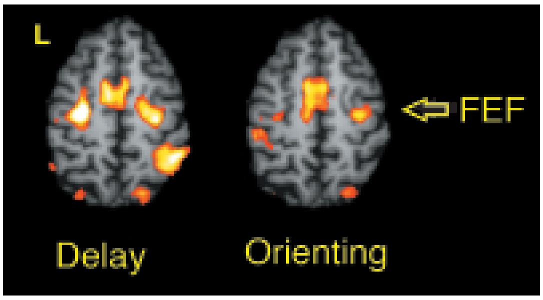

Figure 1. Visual orienting activated the frontal eye fields (FEF). Delay activity extended further anterior, along the superior frontal sulcus.

2.7.2 Attentional weighting of visual dimensions – An fMRI study

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von Cramon, D.Y.[1]

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Objects characterized by a unique visual feature may pop out of their environment. When participants have to search for such 'odd-one-out' targets, detection is facilitated when targets are consistently defined within the same feature dimension (e.g., color) compared with when the target dimension is uncertain (e.g., color or motion). Further, with dimensional uncertainty, there is a cost when a given target is defined in a different dimension to the preceding target, relative to when the critical dimension remains the same. Behavioral evidence suggests that a target dimension change involves a shift of attention to the new dimension.

We carried out an fMRI study to investigate the functional neuroanatomy of visual dimension weighting. Changes in the dimension defining singleton feature targets led to increased activation in a fronto-posterior network consisting of left frontopolar cortex and inferior frontal gyri, high-level visual processing areas in parietal and temporal cortex, and dorsal occipital visual areas. In addition, activation in primary visual cortex was transiently reduced.

When attentional weight was shifted to a new target-defining dimension, activation increased in the visual areas involved in processing features of this dimension – area V4 when attention was shifted to color, and human MT+ complex when attention was shifted to movement.

We hypothesize that the frontopolar cortex is involved in controlling attentional weight shifting and that inferior frontal gyri and high-level parietal and temporal areas mediate attentional weighting via feedback to extrastriate visual areas that process the features of the new target dimension. Reduced activation in striate cortex may indicate attentional selection by suppression of features of the old dimension.

2.7.3 Localizing subprocesses of visual search - A correlational fMRI-study

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In 1997 and 1998, we developed the reaction time model STRAVIS (STRAtegies of VIsual Search), which decomposes reaction times in visual search tasks into the durations of successive search steps (see Ann. Rep. 1998, pp. 84-85). In the present fMRI experiment, STRAVIS was used to investigate which brain areas are involved in which subprocesses of the search.

Five subjects performed a feature search task with graded difficulty in target-distractor-discrimination. By fitting STRAVIS to the reaction times, the following parameters were individually estimated: the size of the focus of attention, the dwell time of attention on each (group of) item(s), the movement time of attention, a 'basic time' for processes that are constant over all search-tasks (e.g., initial perception, motor response) and the number of dwells and movements. The estimated parameter values were related to the individual strengths of the BOLD-response in distinct brain areas.
We assumed that the activation of brain areas involved in the *target identification* (selective attention) correlate with the model parameter 'attentional dwell time' multiplied

with the number of dwells. This was the case for an area around the posterior part of the right inferior frontal sulcus, the horizontal segment of the intraparietal sulcus (IPS), extrastriate visual areas in the lingual and fusiform gyri and the pre-supplementary motor area (pre-SMA). In the extrastriate visual areas and the SIP, the activations showed a lateralisation pattern dependent on the estimated focus size: with a larger focus of attention, activations were stronger in the right hemisphere, while for smaller attentional foci, the activation center moved to the left hemisphere.

For brain areas involved in the *spatial movement of attention* (visuospatial attention), we assumed a correlation of the activation with the number of attentional movements. Such areas were the anterior part of the right inferior frontal sulcus, the anterior segment of the IPS and the anterior cingulate gyrus.

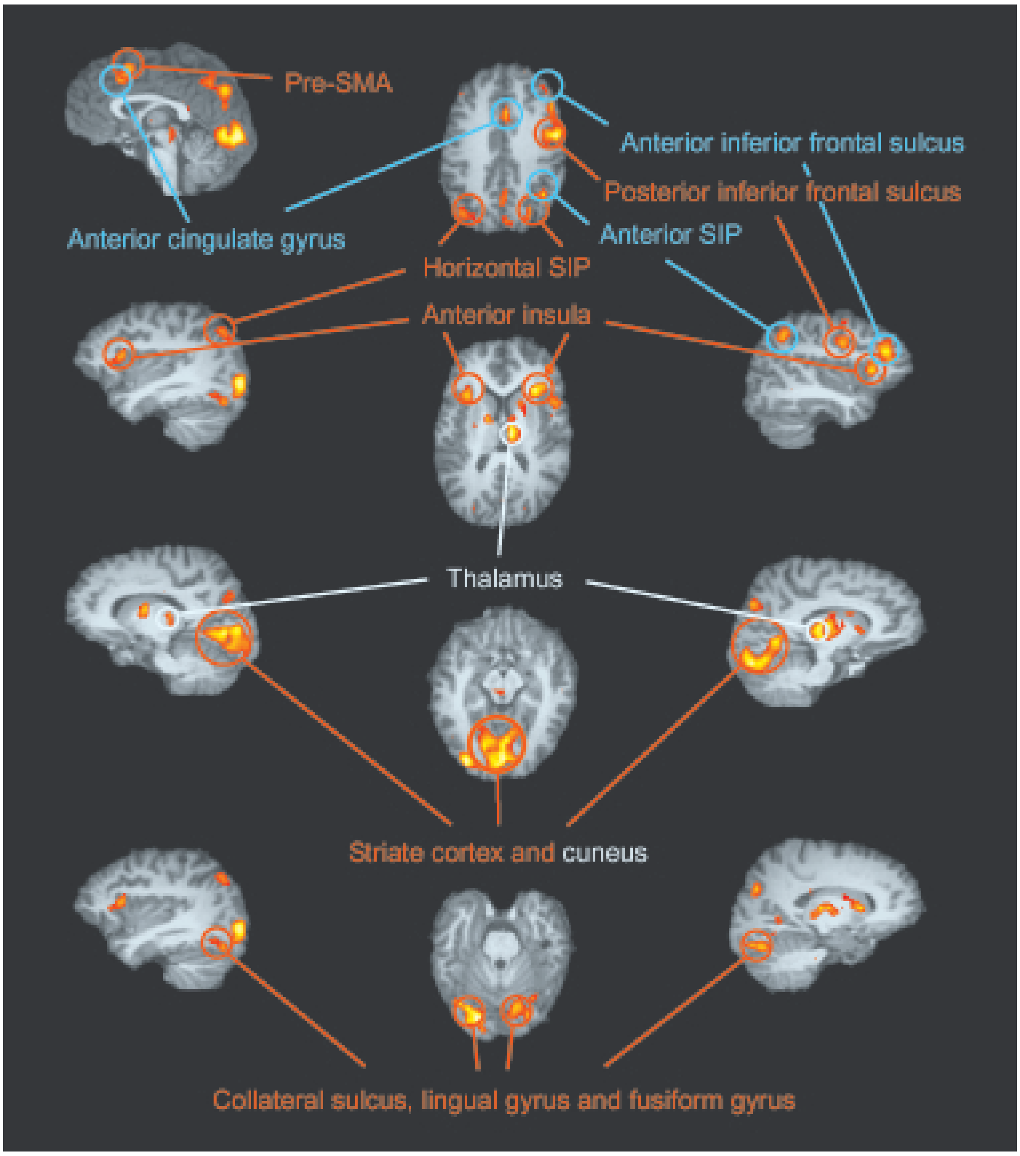

Figure 2. Localization of activations during the visual search task (most difficult target-distractor-discrimination). Brain structures labeled in red are associated with the subprocess 'item checking' (attention to features). Brain structures labeled in blue are associated with the subprocess 'spatial movement of attention'. White labeled structures showed no perfect correlation to either subprocess.

Further, we observed a strong activation in the cuneus and smaller activations in the thalamus, which increased with increasing discrimination difficulty in the search task but did not show perfect correlations with either model parameter.

Therefore, two presumably interconnected networks were identified, one involved in the attentional modulation of feature perception, the other in the application of this modulation to distinct spatial positions. The cuneus and/or the thalamus might contain an interface between the two networks. The changing lateralisation pattern with decreasing focus size is consistent with findings in the literature, in which the right hemisphere is specialized for a global stimulus processing while the left hemisphere concentrates more on local stimulus characteristics.

Like in the years before, there are some changes in composition of the group. Dr. T. Jiang (National Laboratory of Pattern Recognition, The Chinese Academy of Sciences, Beijing, China) joined our group. Dr. M. Pélégrini returned to her former group at CHU Salpetriere in Paris, France, and Dr. S.A. Hojjatoleslami left for UK to continue his career with the School of Computer Science at the University of Birmingham.

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. Funded by the "Tempus Project" of the European Community, we built up a cooperation with the University at Torun, Poland, with mutual short visits of scientists, and three Polish students performing on small-scale projects for introducing them to recent problems in medical imaging. A scientific collaboration with the Unite 494 at CHU Salpetriere in Paris was established in the form of common projects in functional MRI analysis, with one of them already finished.

We are also glad to announce that the SIP group will take part in a European collaboration project funded by the IST-V Programme of the European Community, which focuses on biomechanical simulations of the human head using Finite Element Models. This project is expected to strengthen the involvement of the group in a European research framework.

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 1999 onto the following projects:

- the segmentation of pathological MR images (4 sections),
- the analysis of functional MR images (4 sections),
- the spatio-temporal analysis of EEG/MEG data (2 sections),
- enhancements and additions to the BRIAN package (1 section.

In addition, some small-scale projects were taken on by students focusing on spatio-temporal filters for fMRI data, segmentation of the skull from MR tomograms and on the visualization of dense vector fields.

2.8.1 Segmentation of large brain lesions

Hojjatoleslami, S.A.[1] & Kruggel, F.[2]

[1]*School of Computer Science, University of Birmingham, UK,* [2]*Max Planck Institute of Cognitive Neuroscience*

High resolution T_1-weighted MR images of the brain are used in clinical practice to reveal focal lesions of the brain as consequences of head trauma, intracerebral hemorrhages or cerebral infarcts. Lesion properties (i.e., position, extent, density) are known to be related to cognitive handicaps of a patient. While a *semi-quantitative* analysis of MR tomograms based on visual inspection (i.e., rating scales) is common today in certain clinical protocols, tools for a *quantitative* analysis are still rare. One of the reasons for this deficiency is that building reliable tools to segment MR images with pathological findings is considered a non-trivial task.

We focused on the segmentation of focal brain lesions in their chronic stage. Such lesions are not necessarily complete, i.e. MR intensities of the lesion are found in the range between values of undamaged tissue and values similar to the CSF, indicating a completely damaged area. Lesions are generally not homogeneous, often with completely damaged core parts and minor damage in peripheral portions. In addition, the boundary between a cortical lesion and the CSF compartment is often hard to draw.

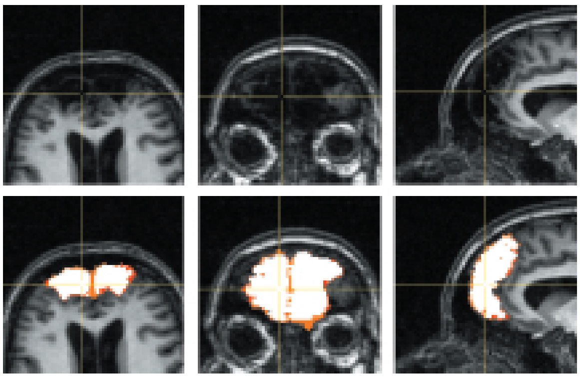

Figure 1. Sections from a 3D brain data set of a patient with a bifrontal lesion (top). The segmentation and annotation of left and right-hemispheric lesions overlaid on the original image (below).

A segmentation procedure was developed based on a region growing algorithm, which is governed by a global discontinuity measure to choose the highest gradient region from the set of evolving regions and by a size criterion to prevent from over-growing into other low-intensity compartments of the image (e.g., the CSF). It is resilient to local brightness changes of the image, which are often caused by inhomogeneities of the B_1 field of the scanner. Only a single MR weighting is needed.

Results in a series of pathological data sets showed a high reliability of the proposed algorithm. Size errors of detected lesions were in the same order as the inter-rater reliability. This method offers an efficient and reliable alternative to the tedious manual process of lesion segmentation.

2.8.2 Detection and classification of white matter lesions by combining pixons-based technique with Polya urn model

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Pixons are variable-sized cells which locally define the resolution of data. The size, shape and position of all pixons over an image are collected into a pixon map, which corresponds to a multi-resolution description of the image. Pixons are ideally suited to detect and quantify white matter lesions which occur with degenerative brain diseases. Mechanisms for the classification and qualification of such lesions will help in drawing diagnostic decisions.

We made an attempt to apply this powerful tool to segmentation of white matter lesions. For this purpose, we assumed the following *a priori* knowledge for white matter lesions: lesions are completely surrounded by white matter; lesions are small; lesions are hypo-intense in T_1-weighted images; lesions are spheres or ellipsoids of varying sizes.

First, lesion segmentation was implemented in 2D, where some related works existed for reference (see Ann. Rep. 1997, pp. 119-120). Then we extended our results to the 3D case, assuming that 3D structures are contiguous. Another attempt was made to process 3D MR data sets directly. In order to improve the efficacy of our segmentation, we extended the 2D Polya urn models (Banerjee, 1999) to 3D to process 3D MR data sets directly. This model - a stochastic analogue of relaxation labeling – was applied as a refinement procedure to improve the segmentation result. The performance of Polya urn process for 2D segmentation is attractive. Two alternative strategies may be suggested: (a) Use the region growing method to obtain a rough segmentation and then use the 3D urn model to refine the results. (b) Use pixon-based MRF models for segmentation and 3D urn models to refine it.

The second approach may be applied to find the white matter areas first, and then adopt region growing to find the lesions in these areas, because prior knowledge tells us that lesions lie in the WM. For a Polya urn model, a central problem is to determine a suitable neighborhood and sampling rule for urns. The performance of several different strategies were compared and evaluated quantitatively.

2.8.3 Mechanical forces induced by disease processes in the brain

Wollny, G. & Kruggel, F.

Changes introduced by pathological processes may be revealed by monitoring MR time series images (i.e., tumor growth, scarification, atrophies). To quantify the changes between images taken at different times, registration procedures must be applied to find the displacement field corresponding to forces induced by the disease process. This field is used to develop an individual template of the forces induced and to create a finite element model for further investigation (in order to predict the disease progress). Moreover, a general template of inner forces will be generated, which can then be used to estimate the course of the disease even if no history is known.

Beside the changes induced by the disease process, other differences are due to altered imaging conditions (i.e., different head positions). Since they are of no interest to us, a method of rigid registration, based on the maximization of mutual information was selected and implemented, to be able to eliminate them.

To model deformations the brain is assumed to be of viscous-fluid matter, which can be described by the equations of viscous-fluid mechanics. Registration of a source image to a reference image is then achieved by deforming the source so that either the mean square of the differences of intensity is minimized or mutual information is maximized.

First experiments showed promising results (see Figure 2), but its performance in terms of speed needs improvement. So, current work focuses on applying a multi-grid approach and restricting the computation to regions of interest. Our current solution of solving the linear PDE uses successive overrelaxation with checkerboard update. Alternatives to this time consuming step are under study. One candidate is the use of scale-space convolution. Other possible approaches are the use of a implicit finite element or finite difference methods.

Figure 2. Snapshot during non-linear registration: original (left), intermediate step (middle), final result (right).

2.8.4 Independent component analysis - Basics

Chojnowski, A.[1] & Kruggel, F.[2]

[1]Department of Computer Methods, Nicholas Copernicus University Torun, Poland, [2]Max Planck Institute of Cognitive Neuroscience

The goal of Independent Component Analysis (ICA) is to express a set of random variables as linear combinations of statistically independent components. Decomposition of observed signals into components without any prior knowledge is also called a "blind separation" problem. First, the algorithm requires to pre-whiten the data. Observed signals are then linearly transformed, such they are mutually uncorrelated using a Principal Component Analysis. Usually, only the few first components need to be included because they carry almost the all variance of data. The remaining components mostly represent noise. ICA uses a neural network with nonlinear Hebbian and Antihebbian learning rules to separate signals. As a criterion of signal separation, the kurtosis (fourth-order cumulant) is typically used, and extracted signals are made as "non-Gaussian" as possible. That explains why ICA cannot deal with Gaussian mixtures or Gaussian sources. A single neuron is enough to separate one component. Multiple Hebbian neurons are arranged into one ICA layer, and a feedback from outputs to inputs of neurons prevent neurons from converging to the same basis vectors. The convergence depends strongly on choosing the right learning rate. If this rate is too high, convergence is destroyed, too small learning rates are inefficient.

As an example, 5 grayscale images of 256^2 pixels were mixed. Data were rearranged as 5 random variables with 65536 samples each. The extended ICA algorithm by Lee, Girolami and Sejnowski was used to separate mixed images into separate components. The quality of extracted independent components is nearly perfect.

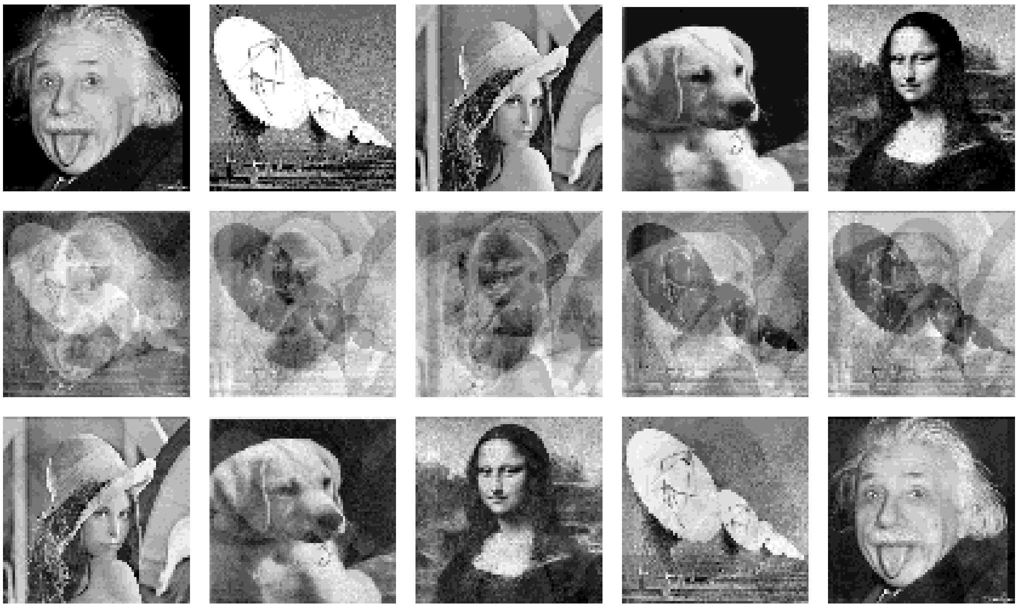


Figure 3. Example of ICA decomposition: original images (top row), mixed images (middle row), and decomposition results shown below.

Independent component analysis of event-related fMRI data

2.8.5

Svensen, M.

Recently, independent component analysis (ICA) was proposed as a method for exploratory analyses of functional Magnetic Resonance Imaging (fMRI) data. It was suggested that ICA would not only separate out signals originating from the stimulation, but also signals from other sources, such as baseline drift and subject movements. The underlying assumption is that such sources are statistically, mutually independent, i.e.

information about one source (e.g., baseline drift), will not convey any information about the other sources (e.g., stimulus induced signals or head movements). This technique was demonstrated using data from an fMRI experiment with a *block trial* design. We have investigated the use of ICA for analyzing event related, single trial design, fMRI data sets.

It is worth pointing out that ICA has already been applied in the analysis of EEG and MEG data, but the application to fMRI data is different. For EEG and MEG data, ICA is used to separate out statistically *independent time courses*, with associated spatial configurations, while for fMRI, it separates out spatially *independent images* and associated time courses (which may be correlated). The motivation is that spatial distribution of regions that respond to the stimuli should be independent of the spatial distribution of other signal sources, e.g. head movements or baseline drift.

We have implemented two widely used ICA algorithms and applied them to a number of data sets from fMRI experiments with single trial design. The results are somewhat inconclusive: as it is shown in Figure 4, there are examples where ICA successfully separates out the stimuli induced activation, but there are also examples where it does not. Regarding separation of other sources, ICA produces a range of images, some of which could be interpreted as representing, e.g. baseline drift. However, firm conclusions must wait until methods for reliably identifying such sources have been developed.

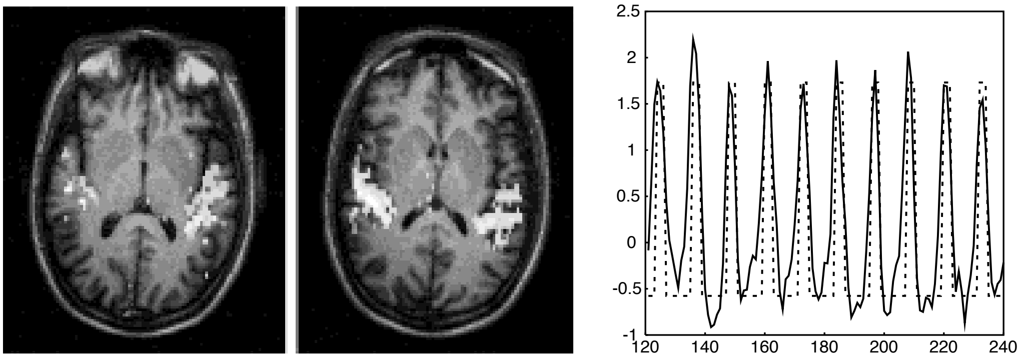


Figure 4. The two images to the left show two slices (2nd and 3rd) from the independent image whose associated time course showed the strongest correlation with the stimulus function. The images have been thresholded and overlaid on the corresponding anatomical images. The time course is shown right, plotted (solid) together with the stimulus function (dashed). Both the time course and the stimulus function have been normalized to zero mean and unit variance prior to plotting; for clarity, this plot only shows a period of 10 trials. This example comes from an fMRI study of sentence comprehension.

2.8.6 Modeling the hemodynamic response in functional MRI

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

Most functional MRI (fMRI) studies apply the blood-oxygen-level-dependent (BOLD) effect, where an indirect correlate of brain activation, the so-called hemodynamic response (HR) of the vascular system, is measured. Activations are found as stimulus-linked and time-dependent local intensity changes in the images. Data analysis is complicated by the following circumstances: the effect is rather small, data are noisy and overlaid by artifacts, the HR due to a brief stimulus is typically delayed by 3-5 s and dispersed by 1.5-2.5 s, and perhaps also displaced with respect to the activation site. So the question remained open, how much could be inferred from the HR shape characteristics about the underlying neuronal activation.

We proposed a flexible nonlinear regression context for modeling the HR in fMRI data (see Ann. Rep. 1998, pp. 91-92). Data are modeled as a sum of a deterministic function and a stochastic part. By adaptation of the model function to the observed HR, we obtain parameters which characterize the HR shape, such as the gain (height of the HR), the lag (time from stimulation onset to maximum) and dispersion (temporal width of the HR). These parameters are compared with the stimulation context in a regression model.

To prove this concept in a complex experiment, we conducted an fMRI study on an item recognition task. Subjects were shown a cue set of 3-6 letters. After a variable delay length (2.0-7.0 s) a probe letter appeared, and the subject was asked to respond via a button press whether the probe letter belonged to the previously presented set. An experimental run consisted of 48 different combinations, subjects completed 4 runs.
Because cue and probe phases were expected to elicit HRs, we used a sum of two Gaussian functions as a model function. Due to the HR dispersion, both responses merge for short delay times. Modeling each trial separately would lead to biased estimates, so we included the whole time series in the model. Parameters were directly set up as functions of the stimulation context of a given trial.

The cue phase response was found to depend on the set size only, with a gain increase of up to 15% per set item in activations along the inferior frontal sulcus. The lag of the probe phase response depended obviously on the delay time, but on the set size (+80 ms per item) and on the hit/foil manipulation (+200 ms). Responses in both phases decreased during experimental time by more than 50% in some focal activations, indicating an on-going parallel optimization of the task.

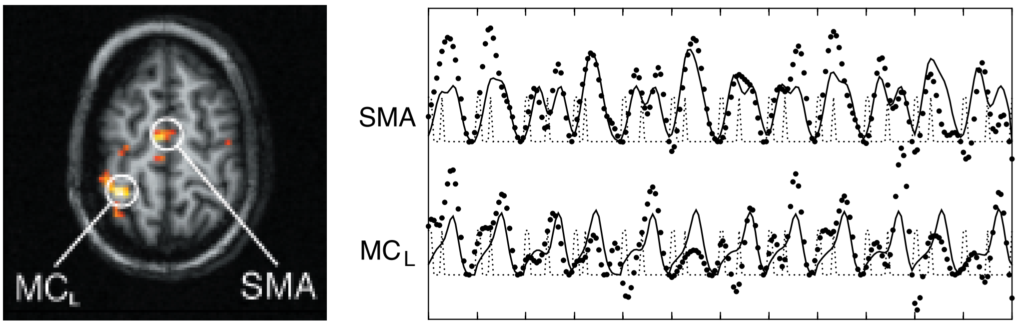


Figure 5. Activated brain regions in a fMRI experiment on working memory (left). A few trials from the (spatially averaged) time course of the signal in two sample regions are shown on the right. Dotted lines denote the visual stimulation. Note the variable delay time between cue and probe phase. The thick dots correspond to the measurements, and the black lines to the estimated waveforms.

2.8.7 Estimating the effective degrees of freedom in univariate multiple regression analysis

Kruggel, F.[1], *Pelegrini-Issac, M.*[2] *&* *Benali, H.*[2]

[1]*Max Planck Institute of Cognitive Neuroscience,* [2]*Unite 494 INSERM, CHU Pitie-Salpetriere Paris, France*

The general linear model provides the most widely applied statistical framework for analyzing fMRI data today. With increasing temporal resolution of recent scanning protocols and more elaborate data preprocessing schemes, data independence is no longer a valid assumption. Revising the statistical background of the general linear model in the presence of autocorrelations, an equation for correcting the effective number of degrees of freedom (DOF) was derived. The effective DOF was found to depend on the regressor matrix and on the correlation matrix of the residuals. The advantage of this interpretation is given by the fact that is data-driven, independent of any specific preprocessing method, and not linked to properties of a pre-defined smoothing matrix. We investigated different autocorrelation models by studying semi-synthetic fMRI data filtered by different preprocessing algorithms. For data from blocked designs, an AR(1) model was found as the most parsimonious model. For data from event-related experiments preprocessed by filters commonly applied for fMRI time-series, we proposed a "damped oscillator" function to model the correlation structure. Approximations were derived which avoid complex matrix calculations and dramatically reduced computation time. Efficient analytical expressions exist for both correlation models, so processing times were only slightly higher in comparison with the uncorrected linear regression method.

We consider an important result that the assumption of spatially isotropic correction for the effective degrees of freedom is invalid: numbers differed substantially between different brain regions and activated vs. non-activated sites. Residuals in unfiltered data may not be considered independent: unmodeled components (such as "physiological noise") contribute to the autocorrelation structure, so either filtering or modeling these components is advisable.

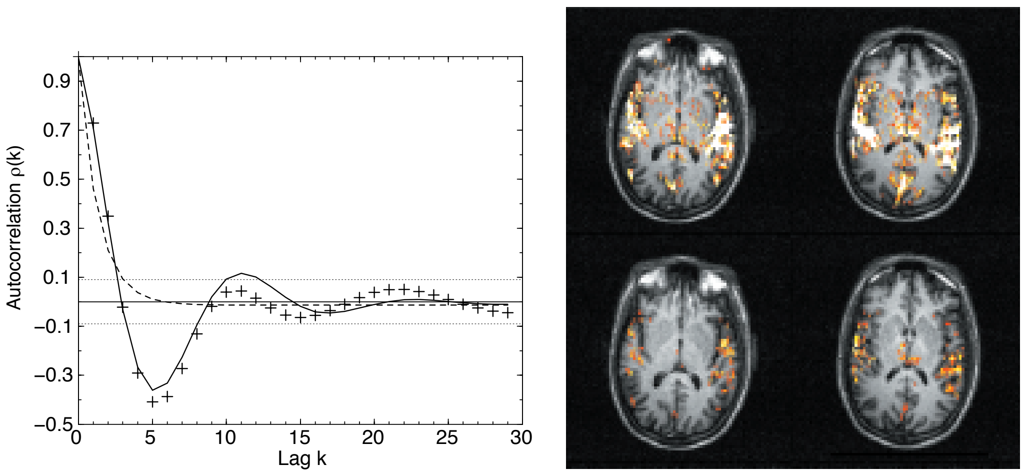


Figure 6. Left: Estimated autocorrelation coefficients (crosses), fitted autocorrelation functions (AR(1) model: dashed, damped oscillator model: continuos line) for a sample background voxel of a LP-filtered data set. Right: Two z-score maps, overlaid onto the corresponding anatomical slices, from an event-related fMRI experiment in language comprehension are shown. In the top row, z-scores were uncorrected, in the bottom row corrected by the correlation-based approach, using the "damped oscillator" function.

This DOF correction approach is easily integrated with any scheme for linear multiple regression analysis. The choice between the exact formulation and the approximation is based on the knowledge about correlation structures in the data and computational efficiency.

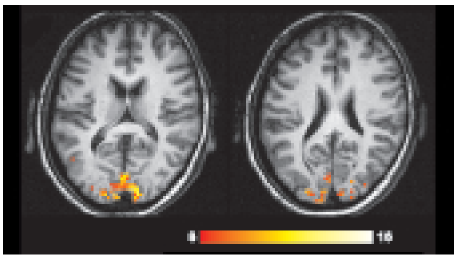
2.8.8 Recording of event-related potentials while functional MRI scanning: Experiences at 3.0 Tesla

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

Measurable correlates of neuronal activation in the brain are electromagnetic fields (by event-related potentials, ERP) and the hemodynamic response (by fMRI) of the vascular system. The first effect is a direct consequence of the electrical activity of neurons, and thus features the same millisecond time scale as the underlying cognitive process, while the second is only indirectly linked to the energy consumption of the neuronal population, and thus takes place on a time scale which is in the order of seconds. However, recent experiences in modeling the shape characteristics of the hemodynamic response have shown that responses are indeed modulated by the experimental stimulation and carry information about the underlying processes at least on a 100 ms time scale (see section above). Technically, due to the limited number of sensors, the localization of an activation by ERP source analysis is hard to achieve. Here, fMRI features a much easier access to a high spatial resolution.

It is obvious that a combination of both techniques is a very attractive aim in neuroscience. However, recording ERPs during fMRI scanning reveals a number of delicate technical problems: gradients applied during fMRI scanning induce currents which are much higher than the brain's response, and thus disturb electroencephalogram (EEG) acquisition. Electrodes and leads of the EEG setup interact with the fMRI scanning process. Head movements induced by heart action lead to small movements of the electrodes and cables in the magnetic field, and thus induce a current in the wires.

Using a careful experimental set up and *post-hoc* signal correction procedures, we were able to reliably record visually evoked potentials (VEP) while measuring the BOLD effect elicited by the visual stimulation simultaneously using a clustered echo-planar imaging (EPI) protocol. Mean and variance of latencies (in ms) for N2 and P3 components of the VEP corresponded well with published data, no noticeable influence of electrodes and wires on fMRI acquisition was found.



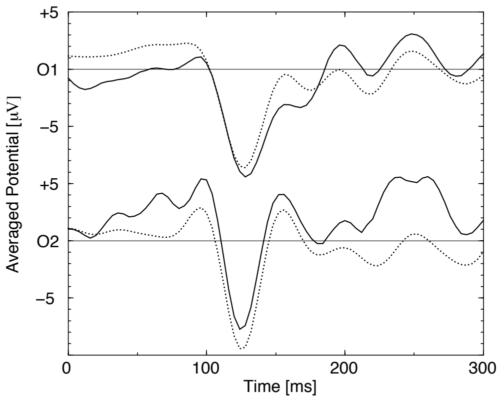


Figure 7. Example results from a single subject: BOLD activation (left) shown as a z-score map overlaid onto the corresponding anatomical slices and visually evoked potential (right).

2.8.9 Dynamical states in ERP-data sets

Hutt, A.[1], Uhl, C.[2] & Friedrich, R.[3]

[1]Max Planck Institute of Cognitive Neuroscience, [2]Philips Research Laboratories, Man-Machine Interfaces (MI), Aachen, Germany, [3]Institute for Theoretical Physics, University of Stuttgart, Germany

According to previous results (see Ann. Rep. 1997, pp. 121-124), a hypothesis about the connection between the theory of dynamical systems and cognitive neuroscience can be formulated. It connects dynamical states with components in ERP. To investigate this, a method is developed to determine dynamical states in ERP data. A comparison of detected states and the ERP components obtained by conventional methods indicates the hypothesis' validity.

Multi-channel ERP data form a trajectory whose dimension corresponds to the number of channels. One recognizes that there are regions in data space with a higher density of data points. In accordance with the idea of dynamical systems, such point clusters indicate dynamical states. They may be detected by a clustering algorithm, and characterized by their cluster centers. The Euclidean distance between each data point and a cluster center represents the degree of membership of a data point to a cluster. The smaller the distance from a data point to a cluster center, the more likely it is a member of this cluster. An example is shown in Figure 8 from an auditory experiment (see Ann. Rep. 1997, pp. 70-72).

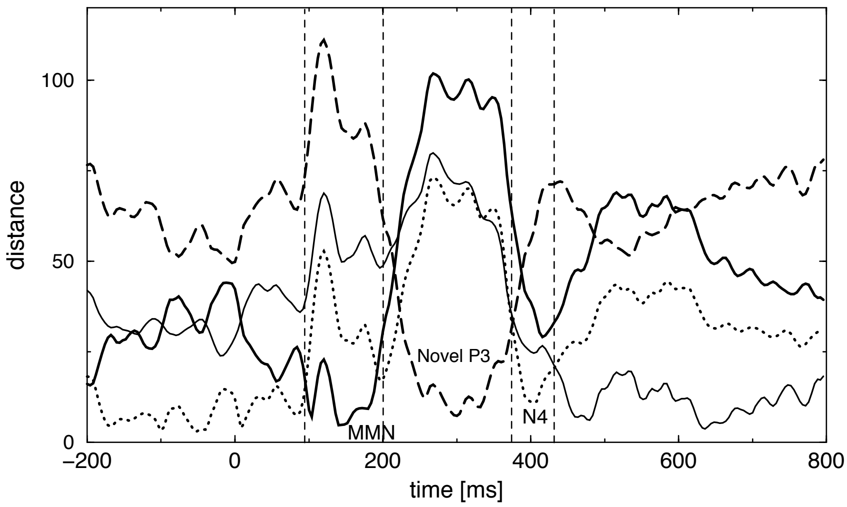


Figure 8. The smallest distance of a data point indicates the membership to a cluster. Here four clusters were found. One recognizes the signal's change between clusters. The solid cluster represent the mismatch negativity (MMN), the dashed the novel P300 component and the dotted cluster indicates the N400 component.

A new method for detection of dynamical states in ERP data is presented. The comparison between the results obtained by clustering and the neuropsychological results shows accordance of dynamical states and ERP components.

In the last year, the NMR group has continued to pursue the themes established in previous years and to develop and intensify collaborations with external laboratories. The latter have lead to publications and exchanges with Aberdeen, Berlin (Charité), Marseille, Minnesota, Nagoya, Ohio, and Taipei not to mention collaborative projects with the departments of Anesthetics and of Neurology at the University of Leipzig. This wealth of external contacts has given the group the opportunity to work on the world's first 8 T imaging system at Ohio-State University (2.9.1) and to participate in the development of radio-frequency coils for head imaging of up to 7 T (2.9.2). In the NMR world, in general the initial skepticism regarding the application of imaging systems with main magnetic field strengths of more than 4 T has been replaced by cautious optimism. The advantages of higher field strengths have been underlined by a study at our now modest 3 T field which shows that inflow effects for fast functional imaging are not significant at 3 T (2.9.3).

The mechanisms of fMR continue to provide plentiful scope for research with interesting results arising from investigations during anesthesia (2.9.4) and the lateral geniculate nucleus (2.9.5). More fundamental investigations aim to verify the 'balloon model', the only physiological model that attempts to explain the MR signal time course during activation (2.9.6).

There have also been methodological progress, especially the development of a method for the simultaneous detection of BOLD and perfusion changes (2.9.7). A low-distortion method for imaging the diffusion tensor which makes it possible to follow white-matter tract into the gyral crowns has also been developed (2.9.8).

2.9.1 Brain imaging at 8 T

Norris, D.G. & Schwarzbauer, C.

In Spring of 1999, we had the chance to perform some initial studies using the 8 T system at the Ohio State University. The experiments were performed primarily with two members of Prof. Robitaille's group (A. Kangarlu, and A.M. Abduljalil) with the aim of examining the T_1 and T_2 contrast available at 8 T. Although it is not expected that 8 T will offer significant advantages for simple anatomical imaging over standard 1.5 T systems it is important to be able to obtain such images as a basis for more complex studies.

It was possible to obtain T_1-weighted images of the human head obtained using the modified driven equilibrium Fourier transfer (MDEFT) pulse sequence T_2 images were also obtained using the RARE sequence.

The MDEFT sequence was implemented using a sech inversion followed by a three lobe sinc (sinc3) excitation pulse, which also acted as the excitation pulse for a gradient echo imaging sequence. All MDEFT images were acquired using a transverse electromagnetic (TEM) RF coil. The coil was tuned for ^{1}H imaging at 340.6 MHz. The MDEFT constituted of the following components. TE_{eff} = 20 ms, TI 900 ms, and FOV 22 cm. Typical parameters for RARE images for a 2 mm slice thickness were; TE_{eff} =160 ms, TR 5 s, echo train length (ETL) 16, echo train spacing (ETS) 20.3 ms, and FOV 22.4 cm.

Human brain images were acquired with high T_1 and T_2-weighted contrast. While the level of this contrast is a function of the pulse parameters, no optimization of sequence variables was performed. The MDEFT images obtained are shown in Figure 1.

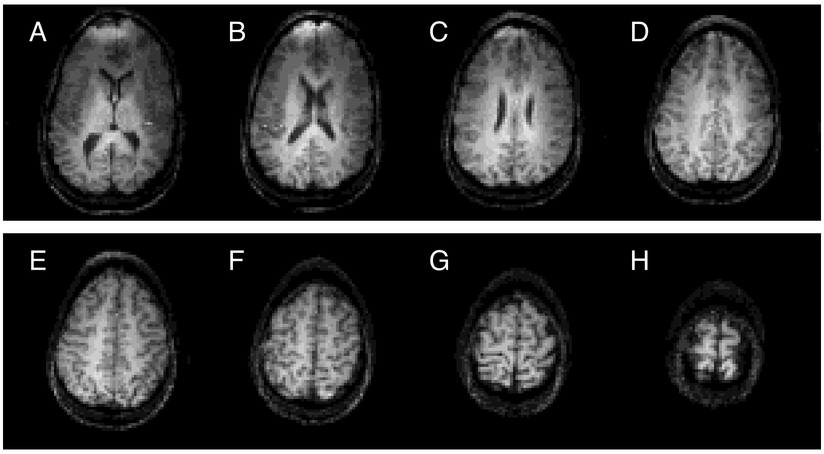


Figure 1.

2.9.2 Circular polarized RF coils for MRI / MRS studies at 3 and 7 Tesla

Driesel, W.[1] & Merkle, H.[2]

[1]Max Planck Institute of Cognitive Neuroscience, [2]Center for Magnetic Resonance Research, University of Minnesota Minneapolis, USA

In order to maximize the sensitivity of a surface coil as well as the homogeneity of the B_1 field, we redesigned a circular polarized RF coil structure (Merkle et al., 1991) based on an assembly of two coplanar dual-loop coils of the split-circle design which are arranged in a crossed fashion (see Figure 2).

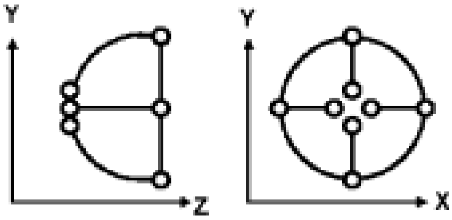
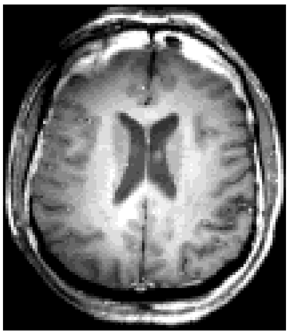


Figure 2. Structure of the coil and pathways of the RF current.

The coils were constructed from copper foil which are glued to the surface of a safety helmet. The conductor is broken along its length and capacitors added at these positions to shorten the wave-length. The geometry of the quadrature coil unit intrinsically decouples the two coils. RF currents in the conducting strips induce B_1 predominantly perpendicular to B_0 and the spokes are therefore NMR active over their full lengths. RF currents in the circular base induce B_1 parallel to B_0 which is NMR inactive. Due to the symmetry of the assembly a high degree of circularly polarized radio frequency within the volume of interest (e.g., a human brain) is expected.

The homogeneity and the degree of polarization of the surface coils was measured using a cylindrical phantom (diameter 18 cm; length 22 cm) filled with 60 mM saline and placed in the center of the coil. In the case where the coil was connected to a quadrature hybrid images in axial, coronal and sagital direction are obtained and compared with corresponding ones, taken, with the RF-polarization reversed. The ratio between the intensities obtained was about 55 indicating a very high degree of circular polarization within the sample (≈ 98%; filling factor ≈ 90%). The homogeneity obtained in the x-y-plane is excellent. Along the z-axis there is a moderate B_1 gradient.



In the human studies, images were obtained using either a modified turbo flash pulse sequence, or in those cases when we wanted to obtain information about the B_1 gradient with more sensitivity we used a spin echo sequence. For best contrast in the brain studies, an MDEFT based sequence was used (for an example, see Figure 3).

Figure 3. 7 Tesla axial MDEFT image of the human brain (256x256 voxel, slice thickness: 4 mm).

2.9.3 Absence of inflow effects in high time resolution fMRI at 3T

Wiggins, C.J.

Reducing the repetition time (TR) between successive image acquisitions in fMRI can be useful both in terms of modeling of the BOLD response and in trying to investigate small temporal shifts in activation in different brain areas. However, a possible drawback is the potential sensitivity to changes in blood flow. This arises due to the saturation of the signal from stationary tissue caused by repeated excitation. Flowing spins, however, may move from an area outside of the slice to inside the slice, and so will exhibit less saturation (i.e., increased signal) after the following excitation. In fact, just this process is often used to produce MR angiograms.

Such inflow effects can be reduced by decreasing the excitation flip angle, with consequent reduction in signal to noise (SNR). For this reason, a study was conducted to investigate whether larger flip angles can be used to give optimal SNR for short TR fMRI studies, without significant influence from task-related blood flow changes. An EPI sequence was implemented in which an additional gradient pulse was used to re-set the phase encoding to allow acquisition of several successive images following a single excitation. This allowed, with a TR of 200 ms, the collection of three images following the excitation pulse, with echo times of 17, 42, and 67 ms. The three echo images could then be used to create T_2* (a measure of the local field homogeneity) and M_0 (the basic signal intensity) maps for each timepoint. True activation, which results in field homogeneity changes through the BOLD effect, should appear only in the T_2* maps. Inflow effects, if present, should result in changes in M_0 that are correlated with the task.

A total of 5 subjects were investigated. The stimulation paradigm was 8 Hz flicker using GRASS goggles. A single slice was selected through the calcarine fissure, with 5 mm slice thickness, 19.2 cm FOV, 64x64 matrix and 100 kHz bandwidth. Six short-TR (200 ms) scans were performed, with pulse angles of 5°, 10°, 32°, 45°, 60°, and 90°.

Since the data was acquired with such short TR, the number of degrees of freedom used in the analysis has to be corrected due to the non-independence of successive data points. Using a regression analysis which includes this correction, it was found that, with a Z-score threshold of 2.0, no task-correlated M_0 changes were present, i.e. there was no significant inflow effect at any of the flip angles used. In contrast, analysis of the T_2* time courses, using a higher threshold of $Z>4.0$, showed extensive activation of the visual cortex as expected. The spatial extent of this activation was largest at flip angles between 32° and 60° for all subjects.

The results above indicate that inflow effects at 3 T do not appear to be a source of fMRI artefacts even at short TR. Thus, the optimal flip angle (in terms of SNR) can be used for excitation without significant effects from task-related flow changes.

2.9.4 The effect of subanesthetic isoflurane on BOLD signal changes during a visual search-task

Schwarzbauer, C.[1] & Heinke, W.[2]

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The effect of common anesthetic agents (e.g., isoflurane) on cerebral blood flow and metabolism has been studied extensively, whereas the effect on perception and cognition is less well established. Functional magnetic resonance imaging (fMRI) offers a very promising approach to investigate this phenomenon. In the present study, we investigated the effect of subanesthetic isoflurane on BOLD signal changes during a visual search-task.

Ten healthy volunteers were investigated with fMRI during different experimental conditions. In turns the subjects were breathing air (control experiment, CE), isoflurane in air (0,42 Vol% inspiratory, isoflurane experiment, IE) and air again (recovery experiment, RE) while performing a visual search task. Functional magnetic resonance images were acquired during the entire experimental session. In addition, reaction times and error rates were recorded during different conditions.

During the CE, large areas were activated in the occipital lobe (striate and extrastriate visual areas), the parietal lobe (medial and lateral posterior parietal cortex), and the frontal lobe (primary motor cortex, medial and lateral premotor cortex). Activation was also detectable in subcortical structures (lateral geniculate nucleus). Breathing of subanesthetic isoflurane resulted in a decreased fMRI response in most activated brain regions. Both cortical and subcortical structures were affected by subanesthetic isoflurane. The observed signal decrease exhibited a spatially highly heterogeneous pattern difficult to assign to specific anatomical or functional structures. Interestingly, two regions, one in the right inferior temporal lobe and the other in the right inferior frontal lobe opposed the general trend of signal decrease (cf. Figure 4).

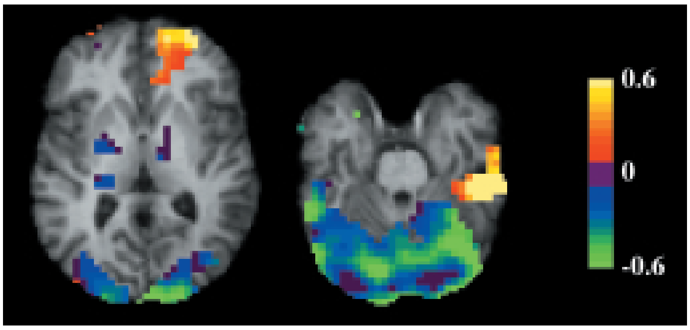

Figure 4. Maps of relative signal changes (given in %) between the control and the isoflurane experiment. Top of the images is anterior, and left is the left hemisphere of the subject.

Both regions were only activated during the IE. A regional comparison of the corresponding maps exhibited that relative signal changes between the CE and the IE are almost completely complementary to the relative signal changes between the IE and the RE. In comparison with the CE and the RE error rates were increased and the reaction times were prolonged during the IE ($p < 0.05$). All measured parameters indicated a recovery of the brain within five minutes.

2.9.5 Functional magnetic resonance imaging of low-frequency fluctuations in the primary visual pathway

Schwarzbauer, C. & von Cramon, D.Y.

Most functional magnetic resonance imaging (fMRI) studies are based on measuring task-induced changes in the blood oxygenation level dependent (BOLD) contrast. However, even if no specific task is performed, the BOLD signal exhibits characteristic low-frequency fluctuations of the order of 0.1 Hz as first described by Biswal and coworkers. The present study addressed the question whether neuronal connectivity within a functional network (such as the primary visual pathway) manifests itself in a high temporal correlation of low-frequency fluctuations.

Two different fMRI experiments were performed on each subject. During the first experiment, no specific stimulus was presented. First, the subjects performed no specific task. The room was completely darkened and the subjects were asked to keep their eyes closed during the experiment. Second, a visual stimulation experiment was performed. Signal fluctuations due to respiration and cardiac cycle were removed by applying a digital low-pass filter with a cut-off frequency of 0.1 Hz.

Figure 5a shows a representative functional correlation map calculated from the data of the second experiment. To investigate spatiotemporal signal fluctuations during the first experiment, regions of interest were selected in the left and right lateral geniculate nucleus (LGN), the left and right primary visual cortex (V1), as well as in two contralateral control regions. For each pair of pixels within the selected regions the correlation coefficient was calculated by correlating the corresponding signal time courses with each other. To obtain an index of spatiotemporal coincidence (ISC), the maximum correlation coefficient between each pair of the selected regions was calculated and averaged over all subjects (n = 8). The results are illustrated in Figure 5b. ISCs between regions belonging to the primary visual pathway are significantly greater than ISCs between these regions and the control regions. Despite the direct ipsilateral neuronal connection between LGN and V1, the corresponding ISCs are significantly smaller than with the corresponding contralateral IRCs. This finding clearly demonstrates that a direct neuronal connection within a functional network does not necessarily cause a maximum temporal correlation of low-frequency signal fluctuations.

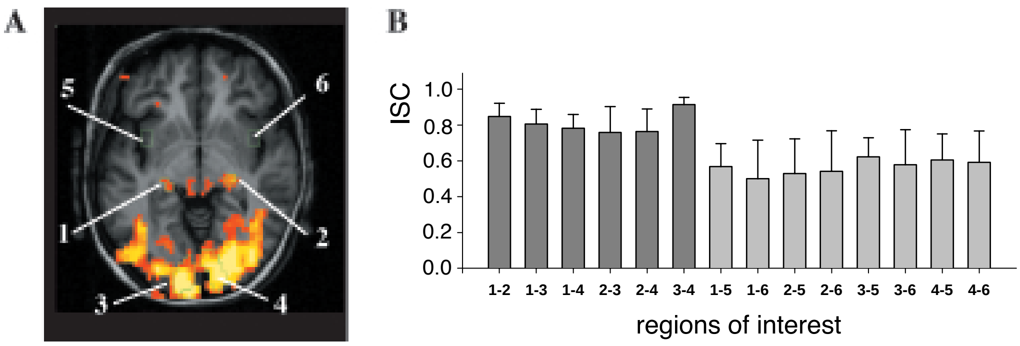

Figure 5. Selected regions of interest in a representative subject (a) and the calculated index of spatiotemporal coincidence (ISC) averaged over all (N = 8) subjects (b); LGN (1,2), V1 (3,4), control regions (5,6).

2.9.6 Investigating the influence of diffusion weighting on the BOLD signal

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

A mechanistic model of Buxton et al., the *Balloon Model*, can explain transient features of the BOLD signal, such as the *Fast Response* and the *Post-stimulus Undershoot*. The aim of this study was to verify the *Balloon Model*'s predictions for the intra- and extravascular signal contributions using DWI. In order to obtain the BOLD signal with and without diffusion weighting an EPI sequence with bipolar gradients was used. The interleaved use of these gradients creates two data sets belonging to the same stimulation time course. This significantly improves the ability to compare the signals with and without diffusion weighting. In addition, the use of template scans for each diffusion weighting for image reconstruction reduces the distortions due to eddy currents. Figure 6 shows the percent signal change during and after a 6 s visual stimulation of a subject. The overall repetition time was 0.5 s yielding 1 s time resolution for each data set. Ten stimulation cycles with a total duration of 36 s were recorded and then added to get the time-resolved BOLD signal. A b value of b = 200 s mm^{-2} was applied. At this gradient strength the signal of extravascular water falls by less than 20%, whereas the intravascular signal vanishes completely. It can be seen from Figure 6, that the relative signal change of the BOLD signal maximum falls significantly with diffusion weighting. This provides evidence for intravascular signal contributions to the BOLD signal. The *Post-stimulus Undershoot* shows approximately no change between the curves. This could support the prediction of the *Balloon Model*, that the *Post-stimulus Undershoot* is a purely extravascular effect.

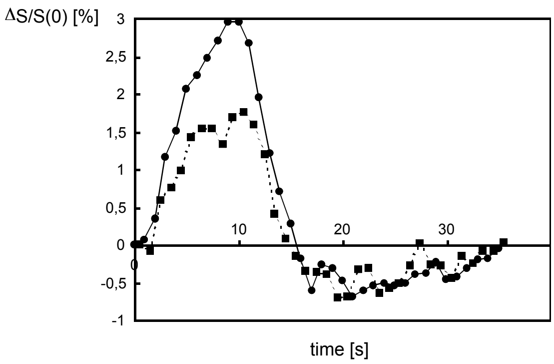

Figure 6. Time courses of the percent signal change during and after a 6 s checkerboard stimulation of a subject. The circles and squares correspond to the signal without and with a diffusion weighting with a b value of 200 s mm^{-2}, respectively.

Another prediction of the *Balloon Model* is the conflicting signal contribution of the intra- and extravascular water for the first few seconds of the stimulation period. Thus, diffusion weighting should emphasize the negative dip (*Fast Response*) of the functional signal. In order to separate intra- and extravascular contributions it was attempted to add the voxel time courses by their specific attenuation. This work is still in progress and could allow the verification or even improvement of the *Balloon Model*.

2.9.7 Simultaneous detection of changes in perfusion and BOLD contrast

Schwarzbauer, C.

A new functional Magnetic Resonance Imaging (fMRI) technique for *si*multaneous *de*tection (SIDE) of changes in perfusion and blood oxygenation level dependent (BOLD) contrast has been developed. Perfusion contrast is generated by using magnetically labeled endogenous water proton spins as a freely diffusible tracer. A single slice-selective inversion pulse is combined with dual echo echo-planar imaging to generate a spin-echo (SE) image sensitive to changes in perfusion and a gradient-echo (GE) image sensitive to changes in both perfusion and BOLD contrast. In the present study, the SIDE technique was applied to detect functional changes induced by a visual search task. Maps of the correlation coefficients (R_{se} and R_{ge}) were calculated from the SE and GE image time series on a pixel-by-pixel basis by correlating the corresponding time courses with a boxcar function representing the switching on and off of the stimulus. Maps of changes in cerebral blood flow (DCBF) and effective transverse relaxation time (DT_2*) were calculated on the basis of all pixels that exhibited a significant activation in both correlation maps ($R_{se} > 0.6$ and $R_{ge} > 0.6$). Representative results obtained in a single subject are shown in Figure 7.

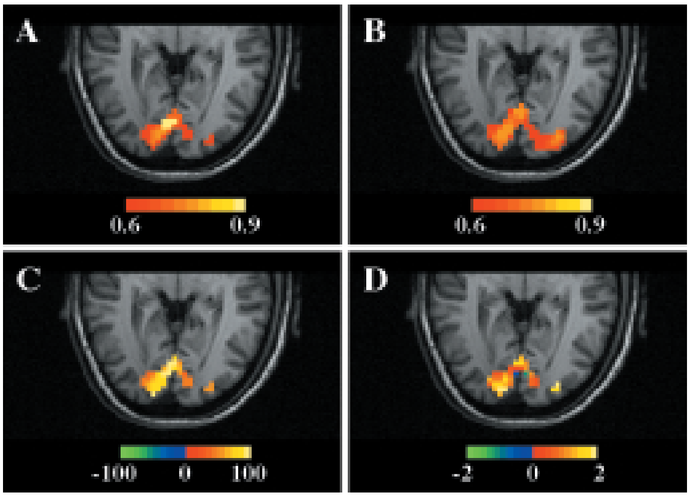

Figure 7. R_{se} and R_{ge} correlation maps (a, b), as well as DCBF and DT_2* parameter maps (c, d) of a single subject performing a visual search task. DCBF and DT_2* parameter maps were calculated for all pixels with a significant activation in both correlation maps. DCBF is given in units of ml / min / 100 g, DT_2* in unit of ms. Top of the images is anterior, and right is the left hemisphere of the subject.

In conclusion, this study has demonstrated the feasibility of simultaneous detection (SIDE) of changes in perfusion and BOLD contrast. Furthermore, it has been shown that quantitative changes in DCBF and DT_2* can be calculated from the acquired image data. Since perfusion and BOLD weighted images are generated from the same longitudinal magnetization, no errors due to spatial or temporal mismatch can arise.

2.9.8 Distortionless diffusion tensor imaging (DTI) with UFLARE

Koch, M. & Norris, D.G.

An important application of DTI is the characterization of association fibers between cortical areas. Since the degree of alignment (and thus the anisotropy of water diffusion) in association fibers is lower than in the large commissural fibers, such experiments require an imaging sequence with high SNR and resolution. Echo planar imaging which is most widely used for DTI suffers from distortion and shift artefacts induced by eddy currents, and the achievable resolution is often low. RF refocused sequences are free of image distortions due to B_0 inhomogeneities, and insensitive to eddy currents that are constant during the echo train.

A protocol was developed for diffusion tensor imaging based on a single-shot RF refocusing sequence, providing high resolution and low sensitivity to eddy currents.

The sequence consisted of a spin-echo magnetization preparation for diffusion weighting, and a displaced UFLARE imaging sequence. Diffusion weighting was provided by two strong gradient pulses (22 ms long, onset separated by 40 ms) before and after the refocusing pulse. 7 gradient directions and 4 amplitudes (b = 20 to 800 s/mm^2) were applied. The total experimental duration was 35 min for a single 5 mm axial slice, 15 averages for the lowest and 50 for the highest b value. Tensor elements were calculated by linear regression for each image pixel in IDL (Research Systems, Inc.). The measured data matrix was 128×54, including 6 lines beyond the center of k space. Half k space acquisition reduces the number of RF pulses and hence the power deposition. In order to minimize the effective echo time (TEeff) TIPE (template interactive phase encoding) was applied.

The reconstructed images did not show distortion or shift artefacts although eddy current induced shifts of the echoes in the acquisition window were present. Figure 8 shows a fiber orientation map, overlaid upon an anatomical T_1 image (MDEFT). The straight lines indicate the in-plane components of the calculated fiber direction. Only a 6.75×6.75 cm part of the full FOV is shown. The sulcus at the bottom is the right central sulcus.

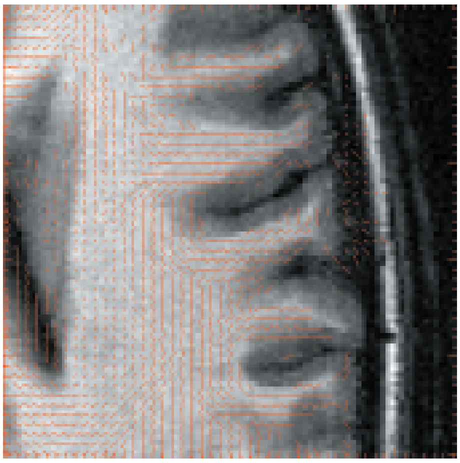

Figure 8.

LEIPZIG IMAGE PROCESSING AND STATISTICAL INFERENCE ALGORITHMS 2.10

The working group "LIPSIA" focuses on developing 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 1999, we have focused on two main areas of research:

- the methodology for the analysis of fMRI time series,
- the automatic analysis of T_1-weighted anatomical images.

At the heart of the methodology for the analysis of functional MRI data is our software package called *Lipsia* (Leipzig image processing and statistical inference algorithms).

Lipsia contains numerous algorithms for pre-processing, statistical analysis and visualization of fMRI time series. Its statistical basis is the general linear model described in (2.10.1). In addition to standard statistical inference mechanisms for performing group studies, it provides a new method of inter-subject averaging based on a Gaussian test across statistical parametric maps of several subjects (2.10.2).

A second area of our research focuses on the analysis of T_1-weighted anatomical MRI data. Of particular interest to us is to find ways for a better understanding of the high inter-personal variability of the cortical folding. In previous work, we have introduced the notion of "sulcal basins" that represents substructures of sulci. In addition to the sulcal basin model, we have developed a line representation model for cortical folds that we applied to MRI data of monozygotic twins. As expected, we found that the cortical folding of monozygotic twins is more similar than that of unrelated pairs of subjects. More importantly, we found out that the deepest parts of the neocortical sulci are even more similar. This result suggests that the deepest sulcal parts are more strongly genetically predetermined than the more shallow ones (2.10.3).

In our future work, we plan to develop more refined methods for the analysis of fMRI data. In particular, we want to find new approaches to modeling and detecting functional connectivity. We will also continue to work on our methods for the analysis of anatomical T_1-weighted MR images. Our main goal here is a further validation of our sulcal basin model through correlation with fMRI data.

2.10.1 Evaluation of fMRI data using the general linear model

Müller, K., Lohmann, G. & Mentzel, H.

For the evaluation of fMRI data, a software package called *Lipsia* (Leipzig image processing and statistical inference algorithms) has been developed. This software package includes programs for preprocessing, registration, visualization and statistical evaluation of fMRI data. The heart of this software package is the general linear model which is a widely used approach. In some sense, it is a generalization of various statistical tests like regression, variance and covariance analysis. Because of its generality, the general linear model provides the description of a large amount of experimental designs.

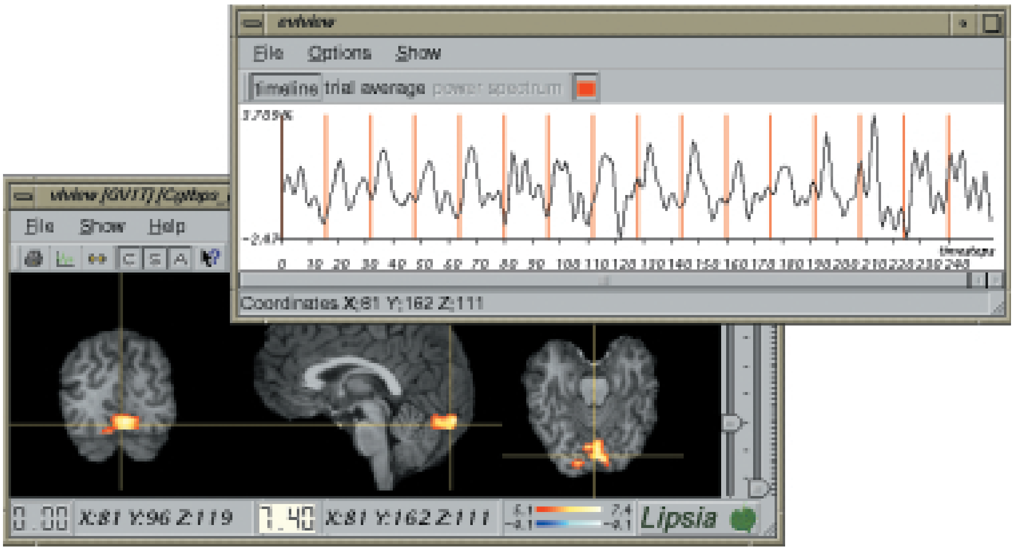

Figure 1. Visualization of fMRI data evaluated by Lipsia. The upper window shows the sequence of stimuli and the raw fMRI signal of the voxel selected in the main window.

The software can handle both epoch and event-related designs. In the last few years, event-related fMRI studies have become more and more popular. The hemodynamic response to each event is modeled to take regional differences in the response to different event types into account. The output of the program consists of a set of images that contains all estimated parameters indicating the slope of the regression. These parameters are obtained by the least-squares estimation and can be processed by computing contrasts that specify linear combinations of the parameter set. The results are statistical parametric maps of t-distributed values that can be transformed into standard normally distributed values.

The Lipsia package admits two kinds of intersubject analysis. The user can choose between (1) generating the design matrix for all subjects, and (2) performing the statistics for each subject separately followed by a group analysis that consists in either a Gaussian t-test over all statistical parametric maps or a one-sample t-test over all contrast images.

Statistical analysis of multi-subject fMRI data: Averaging z-maps and performing ANOVAs across focal activations

2.10.2

Bosch, V.

The most powerful way of analyzing multi-subject fMRI data statistically is to transform individual brains into a standardized 3D-space (e.g., Talairach & Tournoux, 1988) and to apply the General Linear Model (GLM) for further analysis on a single-voxel basis. However, the simultaneous handling of a large amount of data sets is restricted by computational limits. Furthermore, comparisons of focal activations located in different anatomical structures are not possible with that approach. In this work, the analysis of individual z-maps is proposed in order to overcome these problems (for a detailed description of the methods see Bosch, in press).

Using individual z-maps rather than raw data, a group analysis can be performed utilizing a "Gaussian test" that results in normally distributed t-values. These are simply the mean z-values multiplied by the square root of the number of subjects. The statistical power is thereby comparable to the power of a standard GLM procedure.

Whenever significantly activated areas ("blobs") are observed bilaterally, important questions may be: 'Is the pattern lateralized?' or 'Does the pattern obtained in condition A differ systematically from the pattern in condition B (an Area x Condition interaction)?' A common approach to this is to rely on blob-size, i.e., the size of blobs is determined for each subject and a non-parametric test is applied thereafter. However, the frequent absence of blobs in individual data sets that nevertheless show up in the group analysis render it difficult to derive valid statistics. Therefore, z-values within a blob rather than size are a promising way to analyze blob patterns. Regions of interest (ROIs) covering significant blobs of the group z-map are defined (e.g., spheres of a certain diameter) and mean z-scores within ROIs in individual data sets serve as the dependent variable entering an ANOVA. Most importantly, the power of this ANOVA is considerably higher than the power of a blob-size analysis.

In conclusion, the described methods offer simple and powerful ways to analyze fMRI-data obtained in more than one subject. Besides their simplicity, the definition of ROIs allows blob analyses that otherwise are difficult or impossible to perform.

Sulcal variability of twins

2.10.3

[1]Max Planck Institute of Cognitive Neuroscience, [2]Clinic for Neurology, Johann Wolfgang Goethe-University of Frankfurt, Germany

Lohmann, G.[1],
von Cramon, D.Y.[1] &
Steinmetz, H.[2]

We investigated three-dimensional depth-encoded line representations of neocortical sulci calculated from magnetic resonance image datasets of 19 pairs of normal monozygotic twins.

Monozygotic co-twins were significantly more alike than control pairs of unrelated twins matched from the same sample. Sulcal depth influenced sulcal similarity, with deeper sulci being more similar than superficial sulci. This was true both for the pairs of related co-twins and for the unrelated pairs, although the sulcal depth effect was stronger for the related twins.

Methodologically, these results were obtained by the representation of sulci as three-dimensional polygonal lines (termed "sulcal cuts") that are extracted automatically from MRI data sets using new image analysis techniques. Since sulcal depth is encoded in each vertex of a sulcal cut, we were able to study the degree to which sulcal variability is correlated with sulcal depth. Below, examples of sulcal cuts are shown.

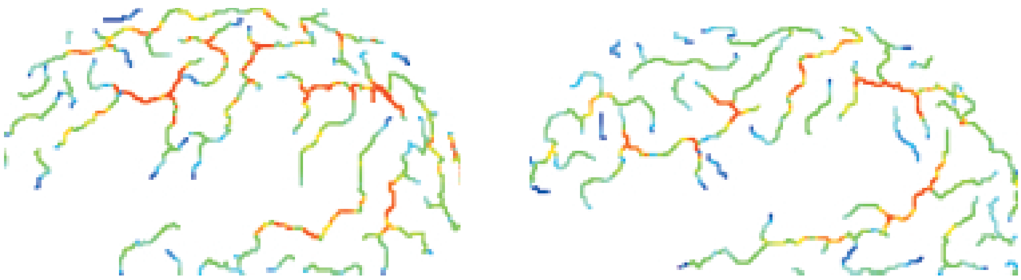

Figure 2. Sulcal cuts (left hemispheres of monozygotic twins). The colors encode sulcal depth.

We performed pairwise comparisons of these sulcal cuts using local proximity measurements.

The set of 19 twin pairs was contrasted with a set of 19 control pairs. The control pairs were obtained by "reshuffling" the twin pairs such that pairs of unrelated subjects resulted. The twin pairs showed significantly higher degrees of similarity at all levels of sulcal depth. However, the *difference* in similarity between the twin pairs and the unrelated pairs more than doubled from the most shallow sulci towards the deepest sulci. These results indicate that the shape of deep (ontogenetically early) sulci of the human brain is more strongly predetermined than that of superficial sulci. Details can be found in Lohmann et al. (1999).

In completion of the psychological and clinical goals of the institute, we have developed advanced methods for signal analysis and statistical evaluation of magnetoencephalographic and electroencephalographic recordings (MEG and EEG). While, on the one hand, these methods intended to incorporate new approaches for EEG signal analysis, they are on the other hand especially important to cope with the challenge of analyzing the 148 channels of MEG.

Among the advantages of using an MEG in neurocognitive experiments is the possibility of precise localization of neural activity. In order to achieve high-quality localization results, a head model is needed which closely resembles the real shape of a subject's head. Therefore, a method was developed which resizes the boundary element model (BEM) used for source space modeling to fit individual head shapes (2.11.1).

Even more realistic models of the head can be accomplished with finite element models. Inside the brain, conductivity along nerve fibers is considerably higher than perpendicular to them. This is accounted for by modeling the anisotropy of white matter with conductivity tensors for each element, approximated through measured whole-head water diffusion (2.11.2). Both the anisotropic and inhomogeneous skull conductivity also have a great effect on source localization and thus needs to be adequately represented. A first step in doing so is a multi-MR-protocol-based skull segmentation for an improved modeling of the inner skull surface (2.11.3). Since finite element models are computationally quite expensive, parallel sparse linear equation solvers have been tested with regard to appropriate solution times (2.11.4). Application of MEG source localization yielded the sources of dipolar activity during processing of syntactic violations in spoken sentences (2.1.1). In a music experiment, the neural correlates of syntactical violations of music were modeled by one dipole per hemisphere. Similar to early left anterior negativities (ELAN), which are evoked by syntactic violations of sentences, violations of music syntax results in early anterior negativities which are larger over the right hemisphere, called ERANm in MEG (2.2.6). By comparing the perception of spoken speech in silence and in noise, early sensory processing and subsequent linguistic processing were differentiated due to their different reaction to noise in another language experiment (2.11.5).

When interpreting MEG data, it is possible to either argue about the magnetic fields recorded in the sensors or about dipoles inside the brain which result from source localization. A third powerful alternative is offered by investigating the current density inside the skull computed by the so-called source current density (SCD) method. The

SCD was applied to EEG and MEG yielding an almost orthogonal relationship between the two (2.11.6). Interpretation of the SCD in an auditory experiment with musicians, revealed involuntary motor activity during music perception for piano players which was not found for non-piano players (2.11.7). By projecting the SCD activity onto three-dimensional reconstructions of individual MR scans, differences were found between the processing of nouns and verbs (2.1.12). In order to differentiate the neural activity of voluntary movements from those of externally triggered and passive movements, SCD was compared between the three conditions revealing a magnetic field prior to movement for active movements only (2.11.8). In a memory experiment, SCD was used to assess the effects of repetition onto magnetic brain responses showing that new visual stimuli evoked larger magnetic fields than repeated ones (2.4.10).

While the above methods all investigate the broad-band response (approx. 1-100 Hz) to sensory stimulation, a new approach of time-frequency analysis was used in two studies to investigate different frequency bands individually. A wavelet decomposition of EEG signals could show that early evoked gamma responses (40 Hz) are significantly higher for targets than for standard stimuli and thus reflect top-down processes (2.11.9). Applying the same approach to MEG data in two different experimental paradigms revealed that this activity is associated with the need to differentiate the features of a stimulus (2.11.10). When methods which are used for frequency analysis of EEG signals are combined with a subsequent rule-based analysis in an expert system, artefacts and rhythmic patterns can be automatically detected with a high hit rate (2.11.11). Automatic artefact detection and rejection was also the aim of a three-stage artefact rejection method which was applied to MEG (2.11.12).

2.11.1 Adjustment of a standard BEM-Model to the subject's head shape

Maess, B. & Oertel, U.

The accuracy of source localization is strongly influenced by the model of the head, which describes the conductive volume. The best accuracy can be achieved by models based on a subject's individual Magnetic Resonance Image (MRI). For most cognitive experiments it is important to learn in general which regions are activated at what time, when volunteers are solving a specific cognitive task rather than determining all activated regions of one single subject. Hence, a number of subjects (>16) should be tested and the localization results analyzed by statistical methods. The aim of this research is twofold. First, the localization accuracy of the volume conductor model should be comparable to that of individual MRI-based models. Second, a final statistical analysis of the localization results should be possible.

The adjusted BEM-model is derived from the standard model by applying linear scaling factors for the three spatial dimensions separately.

Simulations were carried out in order to compare the localization results of the different volume conductor models (sphere, standard BEM-model and adjusted BEM-model). Two series of five, vertically oriented dipoles at roughly 15 mm depth with respect to the inner skull surface were placed along virtual lines from anterior to posterior. A third series was created by using the dipole positions of the first series and orientating them horizontally. As a reference, forward solutions for each dipole in the different setups were computed using an individual MRI-based BEM model. The exact positions were used as seed points for all inverse calculations.

The adjusted models fit quite well to the individual head shapes. The outer shape of the subject's head is revealed with deviations less than 5 mm.

The localization accuracy of the different volume conductors varied as a function of the position and the orientation of the simulated current dipoles. In all cases, the results of the adjusted BEM model were equally accurate or even better than the solutions of the two others.

The application of the method is only slightly more complicated than the use of the sphere model. Additionally, this method allows inter-subject comparison because the transformation of the head model at the beginning of the procedure is reversible.

2.11.2 Improving FE-volume conductor modeling in EEG/MEG-source localization: Investigation of the influence of white matter conductivity anisotropy

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Localizing the current distribution in the human brain from extracranial EEG/MEG-measurements is an Inverse Problem whose solution requires the repeated simulation of the electric/magnetic propagation for a given dipolar source in the brain using a volume-conduction head model. In order to model the head most realistically, the different tissues first have to be segmented and then assigned individual conductivity tensor material parameters. This should also lead to better standard models for quantitative cognitive research. In current research two methods for determining conductivity parameters are under investigation. One is the Electrical Impedance Tomography (EIT), estimating conductivities through the solution of an inverse problem by means of current injections and potential measurements on the head surface (Vaukhonen et al., 1999). A second strategy, the DTI-EMA, has recently been described by Tuch et al. This method exploits the relation between the effective electrical conductivity tensor and the effective water diffusion tensor as measured by diffusion MRI. The goal of our study is to determine the influence of white matter anisotropic conductivity (AC), measured/calculated by DTI-EMA, to the different inverse EEG/MEG-source reconstruction algorithms and source locations. Diffusion tensor MR imaging was performed with a displaced U-FLARE protocol. Diffusion weighting was implemented as a Stejskal-Tanner spin-echo preparation experiment. U-FLARE was preferred to EPI in order to avoid spatial misregistration between the DTI and the anatomical 3D data sets due to magnetic field inhomogeneities. Whole-head tensor data were acquired in 8 sessions (4 axial slices per session, voxel size 2x2x5 mm^3, exp. duration 50 min). Each session included acquisition of T_1 weighted images for the registration of the DTI data on the 3D dataset. The diffusion tensors were calculated by multivariate linear regression.

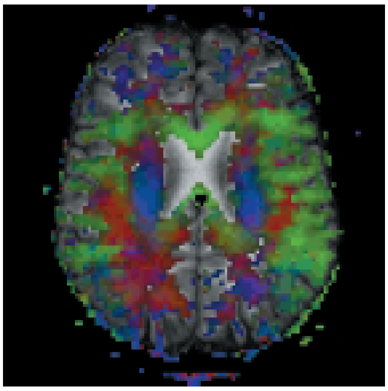

Figure 1. DTI-MRI.

Figure 1 shows an overlay of a T_1 weighted image and a color-coded map of the direction with the largest principal diffusivity (green=horizontal, red=vertical, blue=through-plane, coloring suppressed in voxels with low anisotropy). White matter fiber directions and low anisotropy of CSF and grey matter are correctly reproduced. Preliminary results concerning the influence of white matter AC on the EEG/MEG forward solution for focal sources (Haueisen et al., 1999) in different depths encourage us to systematically study the extent of the inverse mislocalization caused by the simplified white matter modeling. The influence seems to be strongest for deep sources. A further goal will be the validation of the DTI-EMA with a rabbit study using implanted physical sources.

2.11.3 Improving FE-volume conductor modeling in EEG/MEG-source localization: Multi-MR-protocol-based skull segmentation

Wolters, C.H.[1,2], Kruggel, F.[1], Burkhardt, S.[1,2] & Koch, M.[1]

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

It has been shown that the modeling of the anisotropic (ratio of about 1:10, radially:tangentially to the skull surface) and inhomogeneous (e.g., sutures) low-conducting properties of the human skull is of special importance for EEG/MEG-source localization. In a realistic finite element model of the head, the radial direction in a volume element of the skull can be defined as the normal to the triangular element of the internal or external skull surface that is the nearest to this volume element. The identification of the CSF–skull 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 CSF and skull, is most suitable for this problem. Therefore, multi-MR-imaging protocol (T_1-MRI and PD-MRI) acquisition, registration and segmentation should lead to an improved skull modeling. The 3D T_1-MRI was acquired using an inversion recovery MDEFT sequence. For the PD-MRI a 3D FLASH protocol was employed. The resolution was $1\times1\times1.5$ mm^3 in both acquisitions. To exploit both protocols, the PD-MRI has to be registered onto the T_1-MRI. We examined two registration techniques. The first is a linear non-rigid edge-based registration of the pre-segmented outer skull surfaces on both image protocols using genetic optimization. The second strategy is a voxel-similarity based rigid registration without any pre-segmentation using a cost function based on mutual information (MI) to measure the statistical dependence between the image intensities of corresponding voxels in both images.

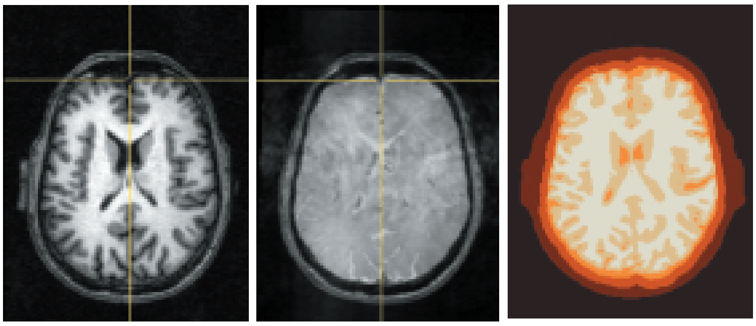

Figure 2. T_1-MRI (left), voxel-registered PD-MRI (middle), segmentation result exploiting edge-based registration (right).

The maximization of MI has been performed by means of Powell's direction set method. Segmentation of ventricles, white matter, gray matter, skull and scalp-tissues was then carried out using the toolkit BRIAN. Figure 2 shows the registration result of the PD-MRI onto the T_1-MRI using the voxel-similarity based rigid registration method (middle), and the 6-tissue-segmentation exploiting the edge-based registration method (right).

2.11.4 Accelerating FE-volume conductor modeling in EEG/MEG-source localization: Fast and parallelized iterative methods for sparse linear equation systems

Wolters, C.H.[1,2], Hartmann, U.[3] & Basermann, A.[3]

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In EEG/MEG-source localization a large, sparse (many entries are zero), symmetric and positive definite geometry matrix arises from the 3-D finite element (FE) modeling of the volume conductor head.

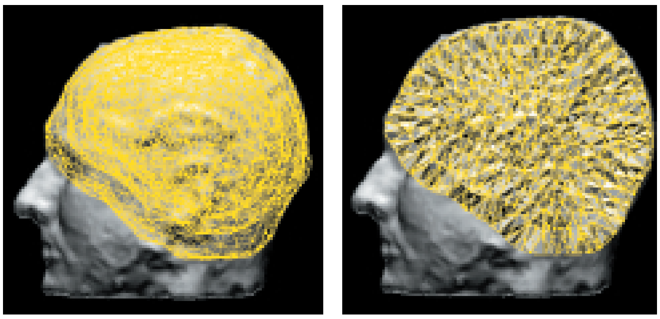

Figure 3. BE-Model (left) and FE-model (right).

The matrix used for our study, for example, has an order of 71,403, but within this only 1,402,157 non-zero entries to be stored in memory. The same number of multiplications is necessary for one sparse matrix-vector operation (S-MVO). The use of fast techniques to solve such equation systems is essential to obtain an appropriate solution time for the inverse source localization. To draw a comparison: the full and asymmetrical geometry matrix arising from a boundary element (BE) head model has an order of about 4000. After inverting this matrix just once using a direct method, the solution for every primary source needs one forward-back substitution (FBS) of 4000^2=16,000,000 mult. (plus about 1500^2 mult. for the numerically important isolated problem approach).

Three parallelized iterative linear equation solvers were tested for the FE-matrix and their execution times depending on the number of processors are depicted in Figure 4.

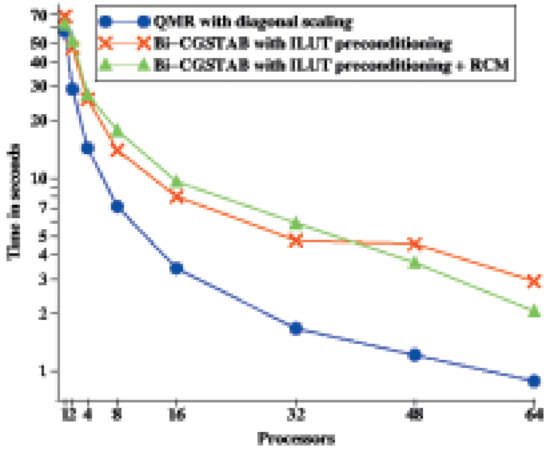

Figure 4. Solver performance.

The diagonally preconditioned Quasi-Minimum-Residual (QMR) method for symmetric matrices (one S-MVO per iteration) showed the best time and scaling behavior. In fact, on 64 processors the QMR speedup is slightly superlinear (i.e., 65) due to cache effects. We further tested the BI-CGSTAB algorithm (two S-MVO per iteration) exploiting Incomplete LU preconditioning with Threshold (10^2) (ILUT) (two S-FBS per iteration) with and without Reverse Cuthill-McKee (RCM) bandwidth reduction. All tested solvers are most appropriate for high-resolution modeling with great demand for memory or for forward modeling with a moderate number of dipoles (e.g., fMRI-constrained source reconstructions). However, in most applications the forward solution has to be calculated for many different sources during the inverse optimization procedures. Therefore, parallelization on the dipole level (every processor calculates a solution for one dipole to assemble the lead field matrix) is most efficient, but only practicable if the demand for memory is not beyond the available resources. In future investigations, we will couple iterative solvers and dipole level parallelization with the efficient preconditioning of the Incomplete Cholesky Factorization with Threshold (ICCT) or of Sparse Approximate Inverse techniques, which can be tuned for a maximal exploitation of the available memory resources and a minimal demand for subsequent iterations after preconditioning.

2.11.5 Noise affects auditory and linguistic processes differently

Herrmann, C.S., Oertel, U., Wang, Y., Maess, B. & Friederici, A.D.

We investigated the influence of noise on brain responses to spoken sentences in MEG. Sixteen subjects had to listen to acoustically presented sentences and to judge their syntactic correctness. Sentences were either presented in silent background or with noise recorded from an fMRI scanner. ANOVAs were calculated for the root mean square values of four regions of interest differentiating anterior/posterior and left/right. Noise had differential effects on early auditory and syntactic processes. While noise affected early auditory processes only in the right hemisphere, noise had a general effect on syntactical processes. Early auditory responses (20..120 ms) were significantly suppressed by noise only over the right hemisphere but not over the left. In a later time interval (120..200 ms), responses to syntactic violations were significantly higher compared to correct sentences (cf. Figure 5). This effect is known from EEG as an early left anterior negativity (ELAN). The bilateral magnetic correlate of the ELAN was significantly suppressed when noise was present. The noise suppression effect, however, was not lateralized. This indicates a functional dissociation of the early auditory and the subsequent linguistic processes which are reflected by the two investigated components.

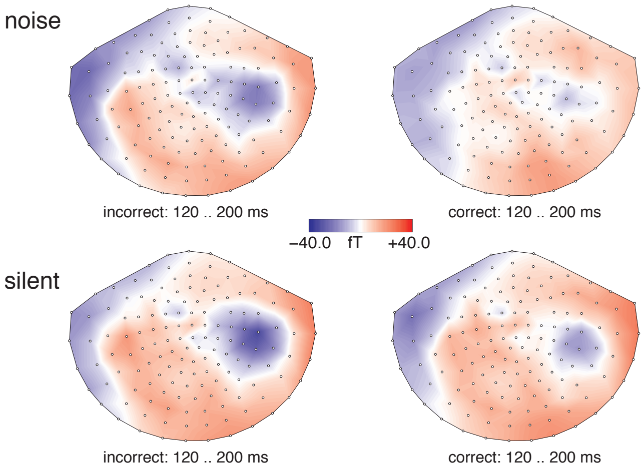

Figure 5. Topographical distribution of the event related fields in the time interval of linguistic processing (120..200 ms). A main effect of condition is reflected by fields being larger for incorrect (left column) than correct (right column) sentences. In addition, the main effect of noise is reflected by fields being suppressed for noisy (top row) as compared to silent (bottom row) background.

2.11.6 Electrically/Magnetically silent sources in current density estimation from EEG/MEG

Wang, Y.

Interpreting EEG/MEG always involves speculation as to the possible neural current sources in the brain which can account for the EEG/MEG recordings. In recent years, in order to image the electrical sources for complex brain activities, a fair amount of attention has been given to the distributed current density estimation approach. Such an approach tries to estimate the source current density (SCD) everywhere in a 3 dimensional volume or on a 3 dimensional surface. From the methodological point of view, the SCD methods are equally applicable to both EEG and MEG. Such equal applicability very likely leads to the misunderstanding that the SCD result from EEG would be similar, if not identical, to that from MEG (for tangential sources). However, there are essential differences between the SCD results estimated from different modalities, which have not been elaborately addressed in the literature yet.

To demonstrate the difference, computer simulations were carried out with tangential dipoles located at different depths as the test brain sources. Three-shell sphere model was used as the volume conductor. 148 channel whole-head MEG data and 90 channel EEG data were simulated. For the same source, SCDs over a sphere surface within and concentric to the sphere model were estimated from the simulated EEG and MEG respectively. The results show that the SCD from EEG is magnetically silent and that from MEG is electrically silent. Further theoretical analyses reveal that such a property comes from the quasi-orthogonal relationship between different lead field matrices. Because of such an essential difference, combining EEG and MEG measurements for a SCD solution would be equivalent to a simple addition of the individual results estimated from different modalities separately. This problem should be taken into consideration in any attempt to combine EEG and MEG for a SCD approach.

2.11.7 Motor activity during music perception in piano players and non-piano players

Knoesche, T.R.[1] & Haueisen, J.[2]

[1]Max Planck Institute of Cognitive Neuropsychology, [2]Biomagnetic Center, Friedrich Schiller-University, Jena

Musicians often report that listening to a well trained piece of music can trigger the associated movements. We designed an MEG experiment to compare the motor activation related to musical stimuli in pianist and non-pianist. The study was carried out on 20 subjects, 10 of them with a history of piano playing at least for 7 years, the others with a comparable experience with producing music, but not involving fingers of the dominant hand. The stimulus material consisted of sequences of well-known piano pieces, which were purely instrumental without any singing tradition. Filler items with notes deviating from the music piece were inserted into the randomized stimulus sequence. Their detection served as task. The tangential derivative of the MEG was statistically compared between the groups. We found a clear difference above the region of the contra-lateral motor cortex (see Figure 6).

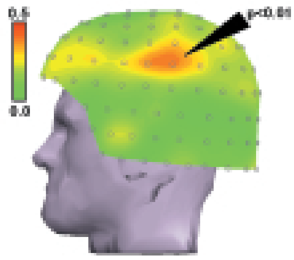

Figure 6. Relative difference of MEG tangential derivative between pianists and non-pianists, averaged over a time window of -300 to 0 ms before the onsets of the notes.

In order to make sure that the differential activity really originates from the motor cortex, separate averages were computed for notes preferably played by little finger and thumb. Brain surface current density plots were computed to establish a spatial dissociation between the two types of notes according to the somato-motor homunculus (Figure 7).

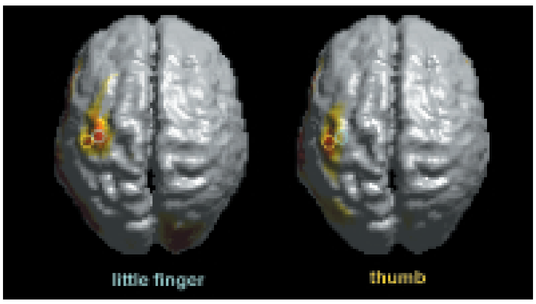

Figure 7. Group differences of the brain surface current density plots, overlaid to the standard MRI, integrated over -300 to 0 ms before stimulus onset. The peak for the thumb (yellow) is about 8 mm more lateral than the one for the little finger (turquoise).

Hence, we could demonstrate that pianists, when presented with a well-trained piece of piano music, exhibit involuntary activity in the contra-lateral motor cortex. Our results strongly support an auditory-motor co-activation in musicians.

Movement-related cortical magnetic fields in healthy subjects and patients after stroke

2.11.8

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

Conscious movements cannot be executed without participation of the cerebral cortex. Voluntary or externally triggered movements involve numerous brain regions. Characteristics of cortical processes involved in voluntary movements have been demonstrated in primates by single cell and field potential recordings. Movement-related cortical potentials (MRCPs) and ERPs in humans have been classified into premovement and postmovement activity (Kornhuber & Deecke, 1965; Shibasaki et al., 1980; Barret et al., 1986; Tarkka & Hallett, 1991; Schubert et al., 1998). This study examined these processes using the MEG's high spatial and temporal resolution. In previous studies of movement with MEG, only selected brain areas have been studied at the same time (Deecke et al., 1982; Antervo et al., 1983; Hari et al., 1983; Cheyne & Weinberg, 1989; Chiarenza et al., 1991; Kristeva et al., 1991; Nagamine et al., 1994). Whole-head neuromagnetometers allow to investigate in detail how the somatomotor areas and the supplementary motor area (SMA) work during movement execution (Deecke et al., 1999). The aim of this study is to compare the functional cortical processes in voluntary, externally triggered and passive movements, especially in respect to neurological rehabilitation after stroke. In a first step, neuromagnetic data were recorded from 20 healthy individuals. Subjects were positioned on a bed inside a magnetically shielded room and their body was stabilized by a vacuum mattress. In the experimental task, subjects had to execute an externally triggered active right hand movement in the direction of an arrow presented on a screen. In a second step, data were recorded in 10 cases in passive movements. Active movements were preceded by a slow magnetic field about 300 ms prior to EMG onset and reaching peak amplitude of 200-400 fT at or immediately prior to EMG onset. These fields are not seen in the case of passive hand movement. The localization results for the externally triggered movement indicate an activation in the contralateral precentral cortex while the SMA remains silent (Figure 8).

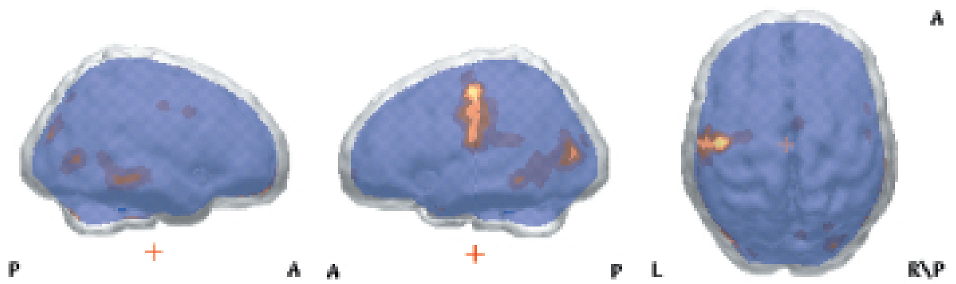

Figure 8. Current density map; subject 8978; time range: -250 to -10 ms prior EMG-onset; right view, left view, top view.

2.11.9 Target gamma response in visual ERPs

Herrmann, C.S. & Mecklinger, A.

We examined event-related potentials (ERPs) and gamma range EEG activity in two experiments in which subjects performed a visual classification task. Subjects silently counted the occurrence of rare targets embedded in frequent standards. We used four triangular and square stimuli, one of which was defined to be a target. The stimuli were two Kanizsa figures composed of either three or four pac-men and two non-Kanizsa figures composed of the same pac-men with different orientation such that no illusory figure was visible (cf. Figure 9, middle column). In Experiment 1, the Kanizsa square (top row) served as target. In Experiment 2, it was the non-Kanizsa square (third row).

In both experiments, the N170 was largest for the Kanizsa square. The second largest N170 was evoked by the Kanizsa triangle and the non-Kanizsa square was larger than the N170 for the non-Kanizsa triangle, which was smallest. This did not change between experiments. In Experiment 1 the target evoked a clear P300. In the second experiment the target P300 was delayed for 50 ms and suppressed compared to Experiment 1. We found two different types of gamma responses to Kanizsa figures: an early phase-locked gamma response at 40 Hz in the N100 time range and a late phase-locked gamma activity (200-300 ms) at 40 Hz (cf. red blob around 100 ms in Figure 9). In Experiment 1, the early gamma response was largest for the target stimulus while the late gamma response was more pronounced for both Kanizsa figures than the non-Kanizsa figures. In Experiment 2, we found an early phase-locked gamma response which was higher for the target and the two target-like stimuli which share one feature with the target. In addition, there was a late gamma response which was larger for Kanizsa figures than non-Kanizsa figures. The topography of the early and late gamma response was very distributed with a frontal maximum in Experiment 1.

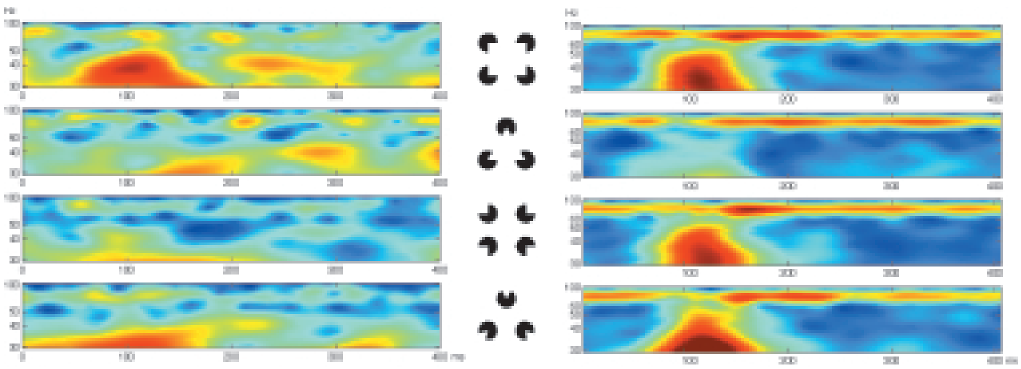

Figure 9. Time-frequency representations in response to four different stimulations as indicated by the stimuli in the middle column.

The fact that, independent of targetness, Kanizsa figures evoke higher N170s than non-Kanizsa figures, could indicate that Kanizsa figures are more salient. The delayed P300 component in Experiment 2 seems to show that it is harder to detect those stimuli which are less salient and evoke smaller primary components.

While the N170 was unaffected by the change of target between Experiment 1 and 2, the early gamma response was clearly influenced. This shows that there is object-based attention in a very early time interval that is associated with evoked gamma activity.

Evoked gamma responses in MEG reflect top-down processing

2.11.10

Herrmann, C.S. & Mecklinger, A.

We examined broad-band and gamma activity of evoked and induced responses in event-related fields in the magnetoencephalogram (MEG) during a visual classification task. The objective was to investigate the effects of target classification and the different levels of discrimination between certain stimulus features. We performed two experiments which differed only in the task of the subjects while the stimuli were kept identical. In Experiment 1, subjects had to respond with a button-press to rare Kanizsa squares (targets) among Kanizsa triangles and non-Kanizsa figures (standards). All stimuli are shown in the top row of Figure 10. In this experiment, the two features of which the presented stimuli were comprised (shape and collinearity) had to be discriminated for adequate task performance. In Experiment 2, the occurrence of a rare and highly salient red fixation cross had to be detected and reported with a button-press (go/no-go task). Therefore, discrimination of shape and collinearity was not necessarily required for task performance. We applied a wavelet-based time-frequency analysis to the data and calculated topographical maps of the 40 Hz activity. The early evoked gamma activity (100..200 ms) in Experiment 1 was higher for targets (cf. Figure 10). In Experiment 2, no significant differences were found in the gamma responses to the figural stimuli. This pattern of results suggests that early evoked gamma activity in response to visual stimuli is affected by the targetness of a stimulus. In addition, early evoked gamma activity was only present over frontal areas in Experiment 1 but not in Experiment 2, while it was present over occipital areas in both experiments. This seems to indicate that frontal evoked gamma activity is associated with the need to discriminate between the features of a stimulus.

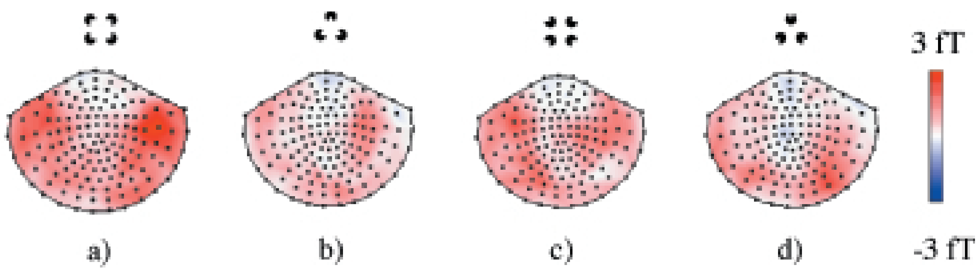

Figure 10. Topography of the early phase-locked gamma activity for the conditions Kanizsa square (a), Kanizsa triangle (b), non-Kanizsa square (c) and non-Kanizsa triangle averaged over ten subjects. Activity is larger for the target (a) than the standards (b, c and d).

2.11.11 An expert system for focus detection in EEG

Herrmann, C.S. & Arnold, T.

For the purpose of finding focal slow activity in human EEG, we developed a new approach that applies an expert system for rule-based analysis of EEG time-frequency data. As a preprocessing step, the EEG raw data is transformed into the time-frequency domain by the Adaptive Frequency Decomposition. This allows to extract those frequency components which physicians normally use to verbally describe EEG phenomena (cf. Figure 11).

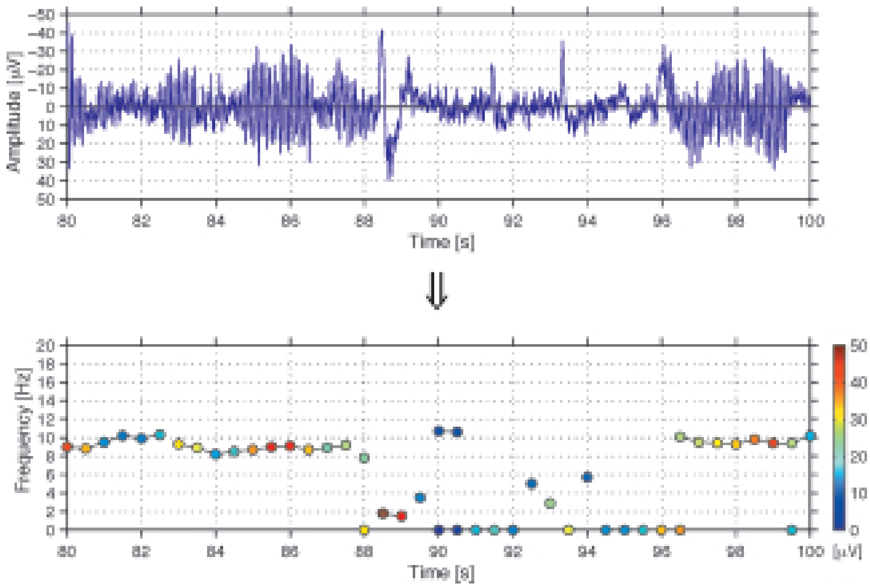

Figure 11. Ten seconds of raw data (left) and the resulting frequency components (right).

The components are brought then into a pseudo-linguistic representation via fuzzy-logic. The expert system carries out its analysis of these facts based on a knowledge that was formulated by a neurologist. At first, a set of rules searches each electrode for any slow activity. Second, after thresholding with the previously detected alpha-activity, the system infers electrode and eye-movement artefacts and excludes them from further analysis. Third, in a final step, maps of the temporal extent of the remaining slow activities are generated (cf. Figure 12) and classified into focal or generalized slowings according to another set of rules.

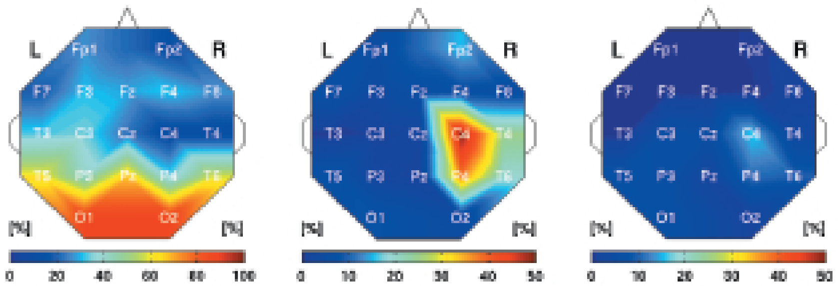

Figure 12. Temporal extent of α- (left) , δ- (middle) and υ-activity (right) in the same patient.

Evaluation of 20 EEG recordings showed a correspondence between automatic and visual analysis in the classification of slow activity of 95%. The system provides an integrative analysis of routine EEG, taking into account a broad variety of EEG patterns. The use of an expert system together with a linguistic representation of rules and facts make system supervision easy and intuitive and allows modifications by the user. The system proved to be a useful assistant tool for the clinical neurologist.

Automatic artefact rejection for MEG data

2.11.12

Herrmann, C.S., Oertel, U., Wang, Y. & Maess, B.

For long recordings of MEG and EEG data, an automatic artefact detection method is desirable. We implemented a new three-stage method for the detection of artefactual data in MEG which can also be applied to EEG signals. In a first stage, we computed the standard deviation in a moving time window and epochs were rejected if a threshold was exceeded. EOG electrodes were checked with a threshold of 30 µV in a window of 200 ms to find eye-movement artefacts. MEG channels were checked with a threshold of 1100 fT with window size 3 s to detect slow artefacts. In a second stage, we tested if the min-max value of any sensor exceeded a threshold of 3000 fT. If this was the case, we assumed extra-cerebral sources and rejected those epochs. Due to the volume conduction effect in the head, adjacent sensors or electrodes will have temporal dynamics which are closely related. If this is not the case, an artefactual noise source most probably is the reason. Therefore, in a third stage, we rejected epochs in case adjacent sensors (distance < 40 mm) showed mean absolute correlations of the magnetic field strengths of less than 0.7. This method can also be used for EEG artefact rejection if the parameters are adapted.

Technical development for the BRIAN package

2.12.1

Härtwig, J. & Kruggel, F.

The software package BRIAN (BRain Image ANalysis) developed by the MPI provides facilities for visualization, editing and processing 3D volume data sets, 2D signal data sets and surfaces represented as polygon meshes (see Ann. Rep. 1996, pp. 118-123). After 5 years of software development, the need for a global revision became urgent. The first focus was given on the visualization tool *ipe* (image processing environment). The main point was to enhance the stability of the system and to improve the ergonomic behavior by providing a common look and feel. The user may now customize the program by setting preferences. A HTML browser was integrated within *ipe* for the display of help pages, which removed the need for an external browser (e.g., Netscape). A stereo viewing mode may now be switched on if the necessary hardware (eyewear, emitter) is provided (Schoepp, 1999).

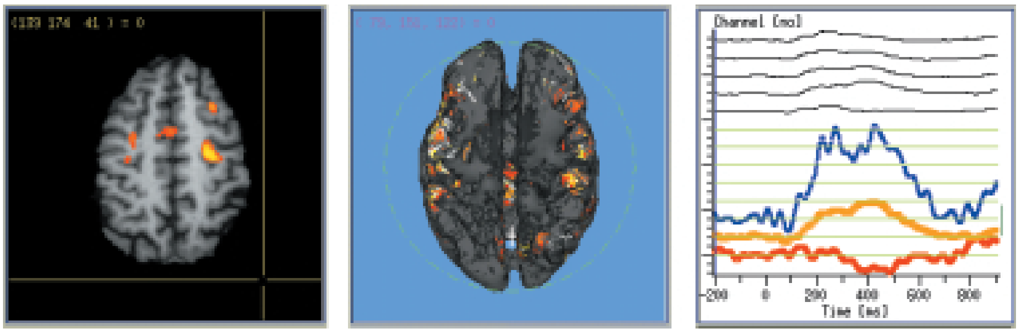

Figure 1. Example 3D functional data set (left), surface representation (middle) and signal data set (right).

For the upcoming release the following changes are planned:

- combining the libraries *libvista.a* and *libvcontrib.a* into *libBRIAN.a* . The aim is to provide a single-system library and revising to create a shared object library.

- integrating related 2D and 3D modules in a single module in order to reduce the number of modules and to provide a more consistent interface,

- removing obsolete modules. Users determine whether a module will be retained in the next release,

- streamlining the development environment. The egcs compiler is used for the whole software package on all platforms (Linux, SGI, Alpha, SUN).

Vista data sets may contain a date attribute, which is saved and reread as a string. Transformation and time calculations are unnecessary and therefore not implemented. Due to the fact that various modules reread the system time, the operating system has to be checked (BIOS, RTC, OS). Hence, the BRIAN software is considered as not affected by the year 2000 problem.

2.12.2 Clinical NMR spectroscopy

Riemer, T.[1], Norris, D.G.[2] & Hund-Georgiadis, M.[2]

[1]Interdisciplinary Center for Clinical Research, University of Leipzig, [2]Max Planck Institute of Cognitive Neuroscience

This project's aim is the evaluation and development of modern NMR spectroscopic methods with respect to clinical applications. The special focus herein lays on the quantitative determination of metabolites in the human brain by in vivo proton NMR spectroscopy.

A volume selective spectroscopic method (^{1}H) based on the PRESS sequence was implemented on the Bruker 3 T MRT system using the MPIL parameter interface. Figure 2 shows a typical spectrum for a 1.5x1.5x1.5 cm voxel using 64 accumulations, an echo time of 50 ms and a repetition time of 2 s. The proton signals from NAA, (P)Cr and Cho can clearly be distinguished. The quantification of these metabolites is straight forward, and established (Saunders et al., 1999). It is more challenging to get information for other important metabolites like Glu/Gln (Glx) and mIno. All of these, as well as Cho, show resonances in the range of 3.4 to 3.9 ppm leading to the broad unresolved peak shown in the insert of Figure 1. In order to allow for the quantification of those spectral contributions, one may try to separate the overlapping contributions by means of a 2D J-resolved NMR experiment.

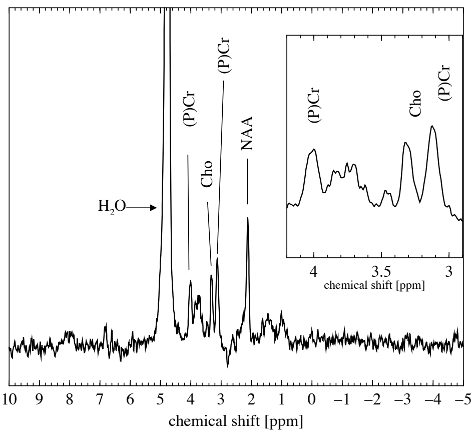

Figure 2. Typical 1.5x1.5x1.5 cm single voxel 1H NMR spectrum of the human brain, showing signals of NAA, (P)Cr and Cho; 64 accumulations were used; TE = 50ms, TR = 2s.

Beside the implementation of a 2D-J-resolved NMR method and a chemical shift imaging method (SESI), the release of a "Fast Automatic Shimming Technique Along Projections" (FASTMAP) will be the next targets. Especially the FASTMAP method will help in the clinical routine application of the MRS methods, since it makes the shimming of a volume element independent from starting conditions and operator skills.

Library Report

3.1

Lewin, G.

The expansion and completion of our library stock over the past four years has made it increasingly attractive to internal and external users alike. It is especially important to emphasize that 1/3 of our 185 current journal are now available from the first edition (59 titles from the first issue). Compared to last year, inter-library lending has decreased. This year, a total of 1500 article and inter-library loan requests were made.

The possibility of using electronic journals via the Electronic Journals Library (EZB) has been available since November 1999. The EZB includes the MPG-wide licenced e-journals as well as scientific journals that are free of charge and freely accessible on the Internet.

In coming months our library will have print version and the electronic version of many journals at the scientists' disposal.
The price increase for this additional service will be significantly below 15% for the year 2000.
The well known and heavily used bibliographic databases under the uniform surface of OVID technologies are also at the scientists' disposal.

Current Contents/All Ed	1995 to Wk 47 1999
INSPEC	1969 to Oct 1999
BIOSIS Previews	1985 to Oct 1999
Medline	1966 to Dec 1999
EMBASE: Drugs & Pharma	1980 to Sept 1999
PsycINFO	1887 to Nov 1999
Dissertation Abstracts	1861 to Oct 1999

The cross-retrievals feature that became possible in WOS (Web of Science) this summer was of great interest to users. This feature provides citation matches of own papers and details about connected relevant subject areas in as little time as possible. Especially in the last two years, there has been a change in library services because of the rapid speed of information creation on the Internet and the change of communication paths. These new developments were discussed at the "1st Autumn conference of the Bio-medial-section" which was organized and hosted by our library.
Our library is prepared for these new targets and will improve the retrieval possibilities of the homepage.

The entire stock of the library now comprises over 7500 media units :

3310	monographs
185	current journal titles
3700	bound volumes of journals
2	CD-ROM data bases
10	data bases with access via Internet

3.2 Teaching

S O M M E R S E M E S T E R 1 9 9 9

Ausgewählte Kapitel der Klinischen Neuropsychologie
Universität Leipzig
von Cramon, D.Y. mit MitarbeiterInnen der Tagesklinik für kognitive Neurologie und des MPI für neuropsychologische Forschung

Electrophysiological Investigations of Language
Universität Potsdam, LOT Summer School
Friederici, A.D., Saddy, D. (Institut für Linguistik, Universität Potsdam)

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

Analyse neurophysiologischer Daten aus kognitionspsychologischen Experimenten - Seminar (Forschungsorientierte Vertiefungsrichtung "Kognition" im Hauptstudium Psychologie)
Universität Leipzig
Herrmann, C.S., Maess, B., Friederici, A.D.

Klassische Befunde der Neuropsychologie (2SWS)
Universität Leipzig
Mecklinger, A.

W I N T E R S E M E S T E R 1 9 9 9 / 2 0 0 0

Ausgewählte Themen der Klinischen Neuropsychologie und neurologischen Rehabilitation
Universität Leipzig
von Cramon, D.Y., Opitz, B., Thöne, A.I.T. (Tagesklinik für kognitive Neurologie), Hummelsheim, H. mit MitarbeiterInnen des Neurologischen Rehabilitationszentrums (NRZ) Bennewitz

Forschungsorientierte Vertiefungsrichtung "Kognition" im Hauptstudium Psychologie
Universität Leipzig
Friederici, A.D., Mecklinger, A.,
Müller, H. mit MitarbeiterInnen der Fakultät für Biowissenschaften der Universität Leipzig

Neuropsychologie der Sprachproduktion und des Sprachverstehens
Universität Leipzig
Friederici, A.D., Jescheniak, J.D.

Streßkonzepte
Universität Leipzig
Mecklinger, A.

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

Wahrnehmung - experimentalpsychologische und kognitiv-neurowissenschaftliche Aspekte
Freie Universität Berlin
Pollmann, S.

Intonation und Sprachsynthese
Universität Wien, Austria
Alter, K.

Intonation
Universität Leipzig
Alter, K.

Phonetik
Universität Leipzig
Alter, K.

Neuropsychologische Gedächtnisforschung
Universität Eichstätt
Hahne, A.

3.3 Committees and memberships

Prof. Dr. Angela D. Friederici

Deutsche Forschungsgemeinschaft / German Research Foundation
Member of the Senate

State of Brandenburg
Member of the Landeshochschulrat

University of Leipzig

- *Zentrum für Kognitionswissenschaften / Center for Cognitive Science*
  Director
- *Zentrum für Höhere Studien / Center for Advanced Studies*
  Speaker of the Board of Directors
- Member of the DFG Research Group "Arbeitsgedächtnis"
- Member of the DFG Graduiertenkolleg "Universalität und Diversität"
- Member of the DFG Schwerpunktprogramm "Zentrale auditorische Systeme"
- *Nomination Committees*
  Neuropediatrics
  Neurology, Psychiatry, Psychology
  Phonology
- *Doctorate Committee*
  Psychology

University of Potsdam

- Member of the DFG Research Group "Konfligierende Regeln"
- Member of the Organization Committee "Potsdam Lectures"

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"*

University of Leipzig

- *Day Care Clinic of Cognitive Neuroscience*
  Director
- *Interdisziplinäres Zentrum für Klinische Forschung (Interdisciplinary Center for Clinical Research)*
  Member of the Board
  Coordinator of the "Schwerpunkt Neurowissenschaften"
- *Zentrum für Kognitionswissenschaften (Center for Cognitive Science)*
  Member of the Board
- *Committee of Computer Recources*
  Member of the Board
- *Koordinierungszentrum für Klinische Forschung (Coordination Center for Clinical Research), Leipzig*
  Member of the Board
- *Nomination Committees*
  Cognitive Neurology
  Cognitive Psychology
  Experimental Physics
  Neurology
  Neuropediatrics
  Membran and Cellbiophysics
- *Doctorate Committee*
  Neurology, Neuropathology and Neurosciences

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

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

Forschungszentrum Jülich
Scientific Board of Biomedicine

LURIJA INSTITUT für Rehabilitationswissenschaften und Gesundheitsforschung an der Universität Konstanz
Member of the Board

Editorial Activities

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

3.4 Visitors

Prof. Stefano Cappa, Medical School, University of Brescia, Italy
11-16 Jan 1999, 5-11 July 1999

Michael Fink, Department of Psychology, The Hebrew University of Jerusalem, Jerusalem, Israel
19 Jan - 8 Feb 1999

Arthur Liu, MGH-NMR Center, Charlestown, MA, USA
24-31 Jan 1999

David Tuch, MGH-NMR Center, Charlestown, MA, USA
24-31 Jan 1999

Prof. Michael E. Goldberg, National Institutes of Health, Laboratory of Sensorimotor Research, Bethesda, MD, USA
3-7 Feb 1999

Prof. Shlomo Bentin, Department of Psychology, The Hebrew University of Jerusalem, Jerusalem, Israel
25 Feb - 6 March 1999

Prof. Carlo A. Marzi, Department of Neurology, University of Verona, Italy
10-12 March 1999

Prof. Karen Emmorey, Salk Institute for Biological Studies, La Jolla, CA, USA
28 March - 1 April 1999

Prof. Douglas Saddy, Institute for Linguistics, University of Potsdam, Germany
1 April -30 Sept 1999

Dr. Dirk Vandermeulen, Medical Image Computing Radiology / ESAT, University Hospital Gasthuisberg, Leven, Belgium
8-11 April 1999

Dr. Edith Kaan, Utrecht Institute for Linguistics OTS, Utrecht, The Netherlands
14 April -12 May 1999

Dr. Mireille Besson, CNRS, Centre de Recherche en Neurosciences Cognitives, Marseille, France
28 April - 7 May 1999

Prof. Jean Saint-Cyr, Toronto Western Hospital, University of Toronto, Canada
15 May -12 June 1999

Prof. Harald Clahsen, Department of Language and Linguistics, University of Essex, Colchester, UK
17-30 May 1999

Dr. Laurie Stowe, Department of Linguistics, University of Groningen, The Netherlands
31 May - 6 June 1999

Dr. Amy Schafer, Department of Linguistics, UCLA, Los Angeles, CA, USA
1-30 June 1999

Prof. Shari R. Speer, Speech-Language-Hearing & Psychology Department, University of Kansas, Lawrence, KS, USA
13-18 June 1999

Prof. Randy L. Buckner, Massachusetts General Hospital, Nuclear Magnetic Resonance Center, Charlestown, MA, USA
18 June1999

Prof. John Kounios, Department of Psychology, University of Pennsylvania, Philadelphia, PA, USA
28 June - 2 July 1999

Prof. Egbert de Boer, Academical Medical Center, University of Amsterdam, The Netherlands
2-8 July 1999

Dr. Seana M. Coulson, Department of Cognitive Science, University of California, San Diego, CA, USA
5-8 July 1999

Ing. Paola Scifo, Hospitale San Raffaele, University of Milano, Italy
8-11 July 1999

Dr. Daniel Strüber, Institute for Psychology and Cognitive Research, University of Bremen, Germany
19-30 July 1999

Dr. Matthias Schlesewsky, Institute for Linguistics, University of Potsdam, Germany
1-31 Aug 1999

Dr. Esther Grabe, Department of Linguistics, University of Cambridge, UK
5 Sept - 9 Oct 1999

Dr. Adrian M. Owen, Cognition and Brain Sciences Unit, Cambridge, UK
7-9 Sept 1999

Prof. Nachshon Meiran, Department of Behavioral Science, Ben Gurion University of the Negev, Beer Sheva, Israel
10-13 Oct 1999

Markus Damian, MPI for Psycholinguistics, Nijmegen, The Netherlands
30 Nov - 3 Dec 1999

Prof. Glyn Humphreys, School of Psychology, University of Birmingham, UK
9-12 Dec 1999

3.5 Guest lectures

Prof. Ferruccio Fazio, San Raffaele Hospital, University of Milano, Italy
PET studies in neurophysiopathology
13 Jan 1999

Prof. Glyn Humphreys, School of Psychology, University of Birmingham, UK
Analyzing disorders of everyday action: Goal structures and working memory
27 Jan 1999

Prof. Michael E. Goldberg, National Institutes of Health, Laboratory of Sensorimotor Research, Bethesda, MD, USA
Beyond the receptive field: Mechanisms for spatial accuracy in the visual system
4 Feb 1999

Dr. Christoph Braun, MEG-Zentrum, Universität Tübingen, Germany
Kortikale Reorganisation, Bedingungen für einen zuverlässigen Nachweis
17 Feb 1999

Dr. Bertram Scharf, CNRS, Centre de Recherche en Neurosciences Cognitives, Marseille, France
Evidence for attentional modulation of cochlear mechanisms
10 March 1999

Prof. John Gabrieli, Department of Psychology, University of Stanford, CA, USA
FMRI visualization of memory processes
24 March 1999

Dr. Dirk Vandermeulen, Medical Image Computing Radiology / ESAT, University Hospital Gasthuisberg, Leuven, Belgium
MRI-based brain analysis in MS and Schizophrenia
8 April 1999

Dr. Edith Kaan, Utrecht Institute of Linguistics OTS, Utrecht, The Netherlands
The P600 as an index of syntactic integration difficulty
21 April 1999

Prof. Carlo A. Marzi, Department of Neurology, University of Verona, Italy
What kind of attention is impaired in contralateral extinction following parietal-temporal damage?
28 April 1999

Dr. Christo Pantev, Institut für Experimentelle Audiologie, Universität Münster, Germany
Musik und kortikale Plastizität
10 May 1999

Prof. Hans-Joachim Markowitsch, Institut für Psychologie und Sportwissenschaften, Universität Bielefeld, Germany
Organische und psychische Komponenten von Gedächtnisstörungen
12 May 1999

Prof. Reinhard Grebe, Dépt. Génie Biologique, UTC Compiègne, France
A maxillo-facial surgery environment
21 May 1999

Dr. Harald Clahsen, Department of Language and Linguistics, University of Essex, Colchester, UK
Empty categories in sentence processing: evidence from cross-modal priming and ERP studies
26 May 1999

Dr. Laurie Stowe, Department of Linguistics, University of Groningen, The Netherlands
Sentence comprehension: Localizing components of a complex task
1 June 1999

Prof. Jean A. Saint-Cyr, Toronto Western Hospital, University of Toronto, Canada
What can we learn about basal ganglia functioning from pallidotomy and deep brain stimulation?
2 June 1999

Dr. Amy Schafer, Department of Linguistics, University of Los Angeles, CA, USA
Prosodic disambiguation of prepositional phrase attachment
14 June 1999

Dr. Carsten Eulitz, Sozialwissenschaftliche Fakultät, Fachgruppe Psychologie, Universität Konstanz, Germany
Raumzeitliche Aspekte der Sprachverarbeitung im MEG und EEG: Studien zur phonologischen Verarbeitung bei Legasthenie und Wortproduktion
16 June 1999

Dr. John Kounios, Department of Psychology, University of Pennsylvania, Philadelphia, PA, USA
Neurocognitive modules revealed by event-related brain potentials
29 June 1999

Prof. Eckart Altenmüller, Hochschule für Musik und Theater, Hannover, Germany
Apollos einzigartig vielfältige Gabe: Neuronale Grundlagen der Musikwahrnehmung
7 July 1999

Dr. David Kemmerer, Division of Cognitive Neuroscience, University of Iowa, IO, USA
A double dissociation between linguistic and perceptual representations of spatial relationships
8 July 1999

Dr. Peter Hagoort, Max Planck Institute for Psycholinguistics, Nijmegen, The Netherlands
A few thoughts on the neurocognition of sentence processing
14 July 1999

Dr. Daniel Strüber, Institut für Psychologie und Sozialforschung, Universität Bremen, Germany
Electrophysiological studies of multistable visual perception
21 July 1999

Dr. Matthias Schlesewsky, Institut für Linguistik, Universität Potsdam, Germany
(and *Stefan Frisch*, MPI staff member)
The specifity of diagnosis of case ungrammaticalities: ERP and grammaticality judgment evidence from argument doubling in German - Part I
18 Aug 1999

Dr. Matthias Schlesewsky, Institut für Linguistik, Universität Potsdam, Germany
(and *Stefan Frisch*, MPI staff member)
The specifity of diagnosis of case ungrammaticalities: ERP and grammaticality judgment evidence from argument doubling in German - Part II
19 Aug 1999

Prof. Karl Heinz Höhne, Institut für Mathematik und Datenverarbeitung in der Medizin, Universität Hamburg, Germany
Digitale Modelle des menschlichen Körpers
1 Sept 1999

Dr. Adrian Owen, MRC Cognition and Brain Sciences Unit, University of Cambridge, UK
The role of the lateral frontal cortex in working memory: The contribution of functional neuroimaging
8 Sept 1999

Dr. Ester Grabe, Department of Linguistics, University of Cambridge, UK
Prosodic resolution of anaphoric reference ambiguities
22 Sept 1999

Dr. Warren Meck, Department of Psychology: Experimental, Duke University, Durham, NC, USA
Coincidence-detection models of interval timing: Evidence from fMRI studies of cortico-striatal circuits
28 Sept 1999

Dr. Minna Huotilainen, Cognitive Brain Research, University of Helsinki, Finland
Intracranial and MEG recordings of auditory mismatch response (MMN)
29 Sept 1999

Dr. Olaf Sporns, The Neuroscience Institute, San Diego, CA, USA
Relating anatomical and functional connectivity in the cerebral cortex
5 Oct 1999

Dr. Rainer Goebel, Max-Planck-Institut für Hirnforschung, Frankfurt, Germany
Visualizing constructive brain processes: New insights from fMRI studies of adaptation to inverting spectacles, blindsight, mental imagery and auditory hallucinations
6 Oct 1999

Dr. Ghislaine Dehaene-Lambertz, Laboratoire de Sciences Cognitives et Psycholinguistique, Paris, France
Electrophysiological correlates of native language phonology
11 Oct 1999

Prof. Nachshon Meiran, Department of Behavioral Science, Ben Gurion University of the Negev, Beer Sheva, Israel
Component processes in task switching: A tentative model
12 Oct 1999

Dr. Emrah Düzel, Klinik für Neurophysiologie, Universität Magdeburg, Germany
Die funktionelle Organisation expliziter Wiedererkennung bei Gesunden und Patienten mit hippokampalen Läsionen
24 Nov 1999

Dr. Michael Falkenstein, Institut für Arbeitsphysiologie, Universität Dortmund, Germany
Zentralnervöse Korrelate der Fehlerverarbeitung
15 Dec 1999

Lüst Lecture

Prof. Leslie Ungerleider, Laboratory of Brain and Cognition, NIMH NIH, Bethesda, MD, USA
7 April 1999

3.6 Congresses, workshops and colloquia

Congresses

41.Tagung expermentell arbeitender Psychologen (*'TeaP99'*)
Friederici, A.D. & Mecklinger, A., and
von Collani, G., Geissler, H.-G., Müller, H.J. & Schröger, E. (University of Leipzig),
Tomasello, M. (MPI for Evolutionary Anthropology, Leipzig)
University of Leipzig, Leipzig, Germany, March-April 1999.

International Conference *'Basic Mechanisms of Language and Language Disorders'*
Friederici, A.D., and
Witruk, E., Müller, H., Stachowiak, F.-J. (University of Leipzig),
Tomasello, M. (MPI for Evolutionary Anthropology, Leipzig)
University of Leipzig, Leipzig, Germany, September 1999.

Workshops and colloquia

Workshop *'Textverstehen und Textproduktion bei Aphasie: Diagnostik und Therapie'*
Ferstl, E.C. & Engell, B.
2. Würzburger Aphasie-Tage, Würzburg, Germany, January 1999.

Workshop *'Versuchsplanung, –programmierung und statistische Auswertung'*
Jescheniak, J.D.
University of Leipzig, Leipzig, Germany, January 1999.

Workshop *'Interaktion zwischen pharmakologischen und übenden Behandlungs-verfahren in der neuropsychologischen Rehabilitation'*
Müller, U.
1. Gemeinsame Jahrestagung der Deutschen Gesellschaft für Neurotraumatologie und Klinische Neuropsychologie (DGNKN) und der Deutschen Gesellschaft für Neurologische Rehabilitation (DGNR), Hamburg, Germany, March 1999.

Workshop *'Gamma activity in the human brain'*
Herrmann, C.S. & Mecklinger, A.
MPI, Leipzig, Germany, March 1999.

Workshop 'Erstes Doktorandentraining der Deutschen Sektion der ISMRM'
Norris, D.G., Pollmann, S., Schwarzbauer, C., Wiggins, C.
MPI, Leipzig, Germany, April 1999.

Workshop *'Neuropsychopharmakologie 1'*
Müller, U. & Ullsperger, M.
Center of Neuropsychology, Würzburg, Germany, May 1999.
Workshop *'Neuropsychopharmakologie 2 + 3'*
Müller, U. & Ullsperger, M.
Center of Neuropsychology, Würzburg, Germany, June 1999.

GNP Workshop *'Einführung in die Psychopharmakologie und Neuropsychiatrie'*
Müller, U.
MPI, Leipzig, Germany, October 1999.

GNP Workshop *'Funktionelle Bildgebung in der Neurologie'*
Hund-Georgiadis, M.
University of Cologne, Germany, November 1999.

Degrees 4.1

Habilitations

Dr. Gabriele Lohmann	Habilitation in Praktischer Informatik, PD Dr. rer. nat. habil. Technische Universität München Verleihung der Lehrbefugnis Institut für Informatik der Universität Leipzig

Doctoral Degrees

Peter Bublak	Doktor der Philosophie, Dr. phil. Universität Leipzig
Rosemary C. Dymond	Doktor der Naturwissenschaften, Dr. rer. nat. Universität Leipzig
Ulrich Hartmann	Doktor der Naturwissenschaften, Dr. rer. nat. Universität Leipzig
Jorge Jovicich	Doktor der Naturwissenschaften, Dr. rer. nat. Universität Leipzig
Gisela Müller-Plath	Doktor der Naturwissenschaften, Dr. rer. nat. Universität Leipzig
Bertram Opitz	Doktor der Naturwissenschaften, Dr. rer. nat. Universität Leipzig
Sandra H. Vos	Doctor for Social Sciences, Ph.D. University of Nijmegen, The Netherlands
Stefan Zysset	Doktor der Naturwissenschaften, Dr. rer. nat. Universität Leipzig

4.2 Awards

Angela D. Friederici	Award "Daimler-Chrysler Fellowship at the Center of Advanced Studies in Berlin"
Axel Mecklinger	"Distinguished Scientific Award for Early Career Contributions to Psychophysiology of the Society for Psychophysiological Research"
Toshiya Murai	"Young Investigators Award 2000 of the American Neuropsychiatric Association"

PUBLISHED BOOKS AND BOOKCHAPTERS 5.1

Bungert, P., Dörrscheidt, G.J. & Rübsamen, R. (1999).
The perception of prephonematic acoustic signals alters with age.
In T. Dau, V. Hohmann & B. Kolmeier (Eds.), *Psychophysics, Physiology and Models of Hearing* (pp. 69-72), Singapore: World Scientific Publishing.

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

Cramon, D.Y. von & Markowitsch, H.J. (1999) [2000].
Human memory dysfunctions due to septal lesions.
In R. Numan (Ed.), *The Behavioral Neuroscience of the Septal Region* (pp. 380-413), New York/Berlin/Heidelberg: Springer.

Dymond, R.C. (1999).
Spatial specificity and temporal accuracy in functional magnetic resonance investigations.
In Max Planck Institute of Cognitive Neuroscience (Ed.), *MPI Series in Cognitive Neuroscience,* vol. 5, Leipzig.

Ferstl, E.C. & Flores d'Arcais, G.B. (1999).
The reading of words and sentences.
In A.D. Friederici (Ed.), *Language Comprehension. A Biological Perspective,* 2nd Edition (pp. 175-210), Berlin: Springer.

Ferstl, E.C. & Flores d'Arcais, G.B. (1999).
Das Lesen von Wörtern und Sätzen.
In N. Birbaumer, D. Frey, J. Kuhl, W. Prinz & F. Weinert (Eds.), *Enzyklopädie der Psychologie,* vol. C/ III/ 2: A.D. Friederici (Ed.), *Sprachrezeption* (pp. 203-242), Göttingen: Hogrefe.

Ferstl, E.C. & Guthke, T. (1998) [1999].
Diskursanalyse als Hilfsmittel zur klinischen Evaluation von nicht-aphasischen Sprachstörungen.
In I.M. Ohlendorf, W. Widdig & J.-P. Malin (Eds.), *Arbeiten mit Texten in der Aphasietherapie, Bonn-Bochumer Beiträge zur Neuropsychologie und Neurolinguistik (BBB),* vol. 5 (pp. 113-143), Freiburg: HochschulVerlag.

Ferstl, E.C. & Kintsch, W. (1999).
Learning from text: Structural knowledge assessment in the study of discourse comprehension.
In H. van Oostendorp & S.R. Goldman (Eds.), *The construction of mental representations during reading* (pp. 247-277), Mahwah, NJ: Lawrence Erlbaum.

Friederici, A.D. (Ed.) (1998), 2nd Edition (1999).
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Berlin/Heidelberg/New York: Springer.

Friederici, A.D. (1999).
The neurobiology of language comprehension.
In A.D. Friederici (Ed.), *Language Comprehension: A Biological Perspective,* 2nd Edition (pp. 265-304), Berlin/Heidelberg/New York: Springer.

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In N. Birbaumer, D. Frey, J. Kuhl, W. Prinz & F. Weinert (Eds.), *Enzyklopädie der Psychologie,* vol. C/ III/ 2, Göttingen: Hogrefe.

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

Friederici, A.D. & von Cramon, D.Y. (1999).
Neurobiologische Grundlagen des Sprachverstehens.
In N. Birbaumer, D. Frey, J. Kuhl, W. Prinz & F. Weinert (Eds.), *Enzyklopädie der Psychologie,* vol. C/ III/ 2: A.D. Friederici (Ed.), *Sprachrezeption* (pp. 307-349), Göttingen: Hogrefe.

Friederici, A.D., Garrett, M.F. & Jacobsen, T. (Eds.) (1999).
Processing of Grammatical Gender, Part 1.
Special Issue: *Journal of Psycholinguistic Research, 28 (5),* New York: Kluwer Academic/Plenum Publishers.

Friederici, A.D. Garrett, M.F. & Jacobsen, T. (Eds.) (1999).
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Special Issue: *Journal of Psycholinguistic Research, 28 (6),* New York: Kluwer Academic/Plenum Publishers.

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: Phonological, syntactic and neurophysiological aspects of early language acquisition*, Amsterdam/Philadelphia: John Benjamins.

Friederici, A.D. & Hahne, A. (1999) [2000].
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In H. Grimm (Ed.), *Enzyklopädie der Psychologie: Sprache.* vol. 3: *Sprachentwicklung*. Göttingen: Hogrefe.

Friederici, A.D., Maess, B. & Scharfenberg, C.D. (in press).
Event-related neuromagnetic responses to semantic and syntactic parameters during auditory sentence perception.
In T.F. Münte, H.J. Heinze & G.R. Mangun (Eds.), *Mapping Cognition in Time and Space: Combining EEG, MEG with functional Imaging,* Boston: Birkhäuser.

Friederici, A.D. & Menzel, R. (Eds.) (1999).
Learning: Rule Extraction and Representation.
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Gunter, Th.C., Vos, S.H. & Friederici, A.D. (1999).
Memory or aging ? That's the question: An electrophysiological perspective on language.
In S. Kemper & R. Kliegl (Eds.), *Constraints on language: Aging, Grammar and Memory* (pp. 249-282), Boston: Kluwer.

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In G. Diller, V. Gall, C. von Ilberg & J. Kiefer (Eds.), *Hören - Verstehen - Kommunizieren* (pp. 14-30), Friedberg: CIC Rhein - Main.

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Rule-application during language comprehension in the adult and the child.
In A.D. Friederici & R. Menzel (Eds.), *Learning: Rule Extraction and Representation* (pp. 71-88), Berlin/ New York: Walter de Gruyter.

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Hayd, H. & Müller, J.A. (1999).
Konzeption und Realisierung eines Gigabit-Institutsnetzwerkes.
In F. Kaspar & H.U. Zimmermann (Eds.), *Internet- und Intranet-Technologien in der wissenschaftlichen Datenverarbeitung: GWDG-Bericht,* vol. 53 (pp. 55-66), Göttingen: Gesellschaft für wissenschaftliche Datenverarbeitung mbH Göttingen.

Hayd, H. & Schlieder, T. (1999).
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In F. Kaspar & H.U. Zimmermann (Eds.), *Internet- und Intranet-Technologien in der wissenschaftlichen Datenverarbeitung: GWDG-Bericht,* vol. 53 (pp. 35-45), Göttingen: Gesellschaft für wissenschaftliche Datenverarbeitung mbH Göttingen.

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AI and cognitive science: Feedback leads to a new neural concept.
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Mecklinger, A. (Ed.) (1999).
Das Erinnern von Orten und Objekten. Zur Neurobiologie des visuellen Arbeitsgedächtnisses.
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In A.D. Friederici & R. Menzel (Eds.), *Learning: Rule Extraction and Representation* (pp. 187-214), Berlin: Walter de Gruyter.

Müller, N., Mecklinger, A. & Friederici, A.D. (in press).
Memory for object identity and spatial location: An ERP analysis of encoding and retention of information in working memory.
In T.F. Münte, H.J. Heinze & G.R. Mangun (Eds.), *Mapping Cognition in Time and Space*: *Combining EEG, MEG with functional Imaging,* Boston: Birkhäuser.

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Pharmakologie.
In P. Frommelt & H. Grötzbach (Eds.), *Neuro-Rehabilitation: Grundlagen, Praxis, Dokumentation* (pp. 541-551), Berlin: Blackwell.

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MAO-Hemmer - Indikationen.
In P. Riederer, G. Laux & W. Pöldinger (Eds.), *Neuropsychopharmaka,* vol. 4*: Antidepressiva und Stimmungsstabilisierer*, Wien: Springer.

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Pharmakologische Interventionen in der neuropsychologischen Rehabilitation.
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Murai, T. & Hadano, K. (1999).
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Murai, T., Hadano, K. & Hamanaka, T. (in press).
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Cramon, D.Y. von
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Cramon, D.Y. von
Geht es auch ohne Stirnhirn?
4-Jahres-Kongreß des Gesamtverbandes Deutscher Nervenärzte (GDN), Berlin, Germany, April 1999.

Cramon, D.Y. von
Executivfunktionen und ihre Störungen.
Jahrestagung der Deutschen Gesellschaft für Neurologie (DGN), Magdeburg, Germany, October 1999.

Engell, B. & Kotz, S.A.
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26. Jahrestagung der Arbeitsgemeinschaft für Aphasieforschung und -behandlung, Konstanz, Germany, November 1999.

Ferstl, E.C.
Syntactic ambiguity resolution in German: Evidence from event-related potentials.
7th International Conference on Cognitive Neuroscience (ICON VII), Budapest, Hungary, June/July 1999.

Ferstl, E.C., Guthke, T. & von Cramon, D.Y.
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Fiebach, C.J., Schlesewsky, M. & Friederici, A.D.
Separating effects of parsing and working memory during the processing of embedded wh-questions in German.
AMLaP99 — Conference on Architectures and Mechanisms for Language Processing, Edinburgh, Scotland, September 1999.

Friederici, A.D.
Language processing.
5th International Conference on Functional Mapping of the Human Brain, Düsseldorf, Germany, June 1999.

Friederici, A.D.
Neural dynamics of auditory language processing.
International Neuropsychological Symposium, Arcachon, France, June 1999.

Friederici, A.D.
Zum Ablauf und zur Repräsentation kognitiver Prozesse: EEG und MEG als Fenster zum Gehirn.
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Friederici, A.D.
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Guthke, T. & Ferstl, E.C.
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Der Einfluß von Textkontext und semantischer Kategorisierung auf die verbale Lern- und Gedächtnisleistung von Patienten mit Hirnschädigung.
Jahrestagung der Gesellschaft für Neuropsychologie, Köln, Germany, November 1999.

Hahne, A.
Auditory sentence comprehension: Evidence from event-related brain potential studies.
Symposium 'Progress in Experimental Psychology', Universität Regensburg, Regensburg, Germany, July 1999.

Hahne, A. & Kiefer, J.
Sprachverstehen bei Cochlea-Implant Trägern gemessen mittels ereigniskorrelierter Hirnpotentiale.
5. Friedberger Cochlear-Implant-Symposium, Bad Nauheim, Germany, June 1999.

Herrmann, C.S.
Gamma-oscillations in human pain.
Workshop on basic and clinical application of human brain mapping: Effective use of EEG/ERP neuroinformatics, Aalborg, Denmark, January 1999.

Herrmann, C.S.
Evoked EEG and MEG responses in a visual classification task.
European Workshop on MEG (EUWOMEG), Erlangen, Germany, June 1999.

Herrmann, C.S. & Mecklinger, A.
Gamma oscillations in the human EEG: Visual binding or attention?
Workshop on Gamma Activity in the Human Brain, Leipzig, Germany, March 1999.

Jescheniak, J.D.
Prosodische Aspekte des Sprachverstehens.
Klausurtagung des Graduiertenkollegs 'Universalität und Diversität', Großbothen, Germany, July 1999.

Koelsch, S. & Gunter, Th.C.
Distinguishing ERAN, MMN, and N5: ERPs of tonal modulations.
7th International Conference on Cognitive Neuroscience (ICON VII), Budapest, Hungary, June/July 1999.

Kotz, S.A.
Brain electrophysiology of linguistic elaboration.
Satellite Symposium 'Neurophysiology of Cognitive Processes', European Congress of Biological Psychiatry, Brescia, Naples, Italy, April 1999.

Kruggel, F.
Nonlinear regression analysis of functional MRI experiments.
52nd Conference on Imaging and Statistics, Uppsala, Sweden, August 1999.

Maess, B., Koelsch, S., Gunter, Th.C., Friederici, A.D. & Schröger, E.
Music processing reflected in EEG and MEG data.
European Workshop on MEG (EUWOMEG), Erlangen, Germany, June 1999.

Mecklinger, A.
Factes of memory retrieval.
(Award for Distinguished Early Career Contribution to Psychophysiology),
39th Annual Meeting of the Society for Psychophysiological Research, Granada, Spain, October 1999.

Mecklinger, A.
FMRI-constraint source analysis: A new approach to the brain dynamics underlying deviancy and novelty processing.
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Mecklinger, A. & Opitz, B.
FMRI and ERP indices of deviancy and novelty processing.
7th International Conference on Cognitive Neuroscience (ICON VII), Budapest, Hungary, June/July 1999.

Mecklinger, A., Nessler, D. & Penney, T.B.
Dissociation of true and false memories: FMRI and ERP evidence.
7th International Conference on Cognitive Neuroscience (ICON VII), Budapest, Hungary, June/July 1999.

Meyer, M., Alter, K., Friederici, A.D. & Cramon, D.Y. von
When the brain is listening to someone next door.
AMLaP99 — Conference on Architectures and Mechanisms for Language Processing, Edinburgh, Scotland, September 1999.

Müller, U.
Katecholaminerge Modulation präfrontaler Funktionen: Neuropharmakologische und klinische Studien.
4-Jahres-Kongreß des Gesamtverbandes Deutscher Nervenärzte (GDN), Berlin, Germany, April 1999.

Müller, U.
Klinische Forschung und informiertes Einverständnis.
Jahrestagung der Akademie für Ethik in der Medizin (AEM), Leipzig, Germany, September 1999.

Nessler, D., Mecklinger, A. & Penney, T.B.
Dissociable ERP responses for true and false recognition memory .
Tutorials in Behavioral and Brain Sciences (TuBBS), Summer School, Ohlstadt, Germany, July 1999.

Nessler, D., Schueller, A. & Mecklinger, A.
Do false memories depend on different retrieval strategies?
Conference on Cognitive Neuroscience, Bremen, Germany, November 1999.

Norris, D.G.
Funktionelle NMR-Bildgebung aus physikalischer Sicht.
Jahrestagung der Deutschen Gesellschaft für Biophysik, Ulm, Germany, October 1999.

Opitz, B. & Mecklinger, A.
Attention in time and space.
25. Arbeitstagung 'Psychophysiologische Methodik', Universität Trier, Germany, June 1999.

Opitz, B., Mecklinger, A. & Cramon, D.Y. von
FMRI localization of target and novel P300 neural generators.
39th Annual Meeting of the Society for Psychophysiological Research, Granada, Spain, October 1999.

Schirmer, A.
Prosodic phrasing and accentuation in speech production of patients with right hemisphere lesions.
6th European Conference on Speech Communication and Technology, Budapest, Hungary, September 1999.

Schlesewsky, M., Frisch, S., Friederici, A.D. & Fanselow, G.
The specificity of diagnosis of case ungrammaticalities: ERP and grammaticality judgment evidence from argument doubling in German.
AMLaP99 — Conference on Architectures and Mechanisms for Language Processing, Edinburgh, Scotland, September 1999.

Steinhauer, K. & Alter, K.
Written prosodic boundaries?
The 12th Annual CUNY Conference on Human Sentence Processing, CUNY Graduate School and University Center, New York City, NY, USA, March 1999.

Steinhauer, K., Alter, K. & Friederici, A.D.
Prosodic on-line effects on sentence processing: Parameters and ERP correlates of prosodic phrasing and a prosody-induced garden path.
41. Tagung experimentell arbeitender Psychologen (TeaP'99), Universität Leipzig, Germany, March/April 1999.

Steinhauer, K., Alter, K. & Friederici, A.D.
Prosodic properties, perception, and brain activity.
14th International Congress of Phonetic Sciences (ICPhC), San Francisco CA, USA, August 1999.

Steinhauer, K., Alter, K. & Friederici, A.D.
Are commas equivalent to prosodic boundaries? - Evidence from brain potentials.
European Conference on Cognitive Science (ECCS), Siena, Italy, October 1999.

Steinhauer, K., Alter, K., Meyer, M. & Friederici, A.D.
Prosodic processing during speech perception and reading: Evidence from event-related brain potentials.
6th International Cognitive Linguistics Conference (ICLC)), Stockholm, Sweden, July 1999.

Steinhauer, K. & Frisch, S.
When syntax guides semantics: Evidence from event-related potentials.
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Ullsperger, M., Müller, U. & Mecklinger, A.
An electrophysiological test of directed forgetting: Differential encoding or retrieval inhibition?
7th International Conference on Cognitive Neuroscience (ICON VII), Budapest, Hungary, June/July 1999.

Winkler, D., Szelenyi, A., Schön, H., Goldammer, A., Hund-Georgiadis, M. & Seifert, V.
Combination of fMRI, neuronavigation and electrophysiology - Technical overkill or useful investigation?
11th European Congress of Neurosurgery, European Association of Neurosurgical Societies (EANS), Copenhagen, Denmark, September 1999.

Winkler, D., Trantakis, C., Schön, H., Goldammer, A., Hund-Georgiadis, M. & Vitzthum, H.E.
Integration of functional data in neuronavigation of extra- and intracerebral lesions in eloquent regions.
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Wolters, C.H.
Influence of head tissue conductivities on EEG/MEG-source localisation.
European Workshop on MEG (EUWOMEG), Erlangen, Germany, June 1999.

5.5 PAPERS PRESENTED AT COLLOQUIA

Alter, K.
Prosodische Verarbeitung im Gehirn.
Forschungskolloquium der Universität Innsbruck, Austria, April 1999.

Cramon, D.Y. von
Sprachlateralisierung bei hirngesunden Probanden und neurologischen Patienten.
Neurologische Seminare, Neurologische Klinik des Universitätsklinikums Mannheim, Germany, January 1999.

Ferstl, E.C.
Qualitative Unterschiede von Textverständnisprozessen nach Frontalhirnschädigung.
Neuropsychologisches Kolloquium, Krankenhaus München Bogenhausen & Entwicklungsgruppe Klinische Neuropsychologie, München, Germany, January 1999.

Friederici, A.D.
Neuronale Dynamik des Sprachverstehens.
Institut für Psychologie, Johann-Wolfgang-Goethe-Universität, Frankfurt a.M., Germany, January 1999.

Friederici, A.D.
Prozesse des Sprachverstehens und ihre Abbildung im Gehirn.
Vortragsreihe 'Mehr Wissen-weiter Denken', 'Studium-Integrale-Programm' der Universität Kaiserslautern, Germany, January 1999.

Friederici, A.D.
Neuronale Dynamik des Sprachverstehens.
Institut für Psychologie, Johann-Wolfgang-Goethe-Universität, Frankfurt a.M., Germany, May 1999.

Friederici, A.D.
Sprache im Kopf.
Studium Universale, Universität Leipzig, Germany, November 1999.

Friederici, A.D.
Sprache und Gehirn.
'Medizin - An der Schwelle zum 3. Jahrtausend', Medizinisch-Naturwissenschaftliche Gesellschaft Wuppertal, Germany, November 1999.

Friederici, A.D.
Sprache und Gehirn: Zur Neurobiologie der Sprachverarbeitung.
Öffentliche Vorlesungsreihe 'Das Gehirn und sein Geist', Georg-August-Universität Göttingen und Akademie der Wissenschaften zu Göttingen, Germany, November 1999.

Hahne, A.
Mechanismen des auditiven Sprachverstehens: Evidenz aus EKP-Studien.
Fachbereich Psychologie der Philipps-Universität Marburg, Marburg, Germany, April 1999.

Hahne, A.
Hirnphysiologische Aspekte der Sprachverarbeitung.
Klinik für Kinder- und Jugendmedizin Lindenhof, Berlin-Lichtenberg, Germany, May 1999.

Hahne, A.
Hirnelektrische Untersuchungen zur Satzverarbeitung.
Universität Potsdam, Institut für Linguistik/Allgemeine Sprachwissenschaft, Potsdam, Germany, June 1999.

Hahne, A.
How the brain processes spoken sentences.
University of Essex, Department of Language and Linguistics, Colchester, UK, October 1999.

Hutt, A., Uhl, C. & Friedrich, R.
Analyse raumzeitlicher Signale: Störungstheoretischer Ansatz.
Institut für Theoretische Physik derUniversität Cottbus, Germany, July 1999.

Jescheniak, J.D.
Der Abruf von Wörtern aus dem mentalen Lexikon bei der Sprachproduktion.
Psychologische Institute I-IV, Westfälische Wilhelms-Universität Münster, Germany, December 1999.

Kruggel, F.
Temporal properties of the hemodynamic response in functional MRI.
Centre Hospitalier Universitaire Pitie-Salpetriere, Paris, France, February 1999.

Kruggel, F.
Short course in medical image processing: Analysis of structure-function relationships in the brain by MR imaging (2 lectures).
Institute for Physics, University of Torun, Poland, May 1999.

Kruggel, F.
Current aspects of functional MRI data analysis.
Forschungszentrum Jülich, Medizinisches Zentrum, Jülich, Germany, June 1999.

Kruggel, F.
Using image processing in neuroscience.
Forschungskolloquium des Lehrstuhls für Bildanalyse und Computergraphik, Universität Leipzig, Germany, July 1999.

Kruggel, F.
Analysis of structure-function relationships in the brain by MR imaging.
University of Granada, Spain, October 1999.

Kruggel, F.
Preprocessing of functional and anatomical MRI images (2 lectures).
CNRS School: L'Imagierie par Resonance Magnetique fonctionelle, Marseille, France, November 1999.

Lohmann, G.
Analysis of magnetic resonance image data: Segmentation and morphological analysis.
Institute for Physics, University of Torun, Poland, May 1999.

Lohmann, G.
Automatische Bildanalyse in der Hirnforschung.
Institut für Mathematik, Universität Leipzig, Germany, October 1999.

Lohmann, G.
Topological methods for the automatic analysis of volumetric images.
Institut für Techno- und Wirtschaftsmathematik, Kaiserslautern, Germany, December 1999.

Mecklinger, A.
Elektrische und hemodynamische Korrelate menschlicher Gedächtnisfunktionen.
Fakultät für Allgemeine Psychologie der Humboldt-Universität, Berlin, Germany, January 1999.

Mecklinger, A.
Gedächtnisspuren: Funktionale und neuronale Mechanismen des Erinnerns.
Psychologisches Institut der Universität Kiel, Germany, April 1999.

Mecklinger, A.
Arbeitsgedächtnis in Raum und Zeit: FMRI- und EKP-Befunde.
Zentralinstitut für Seelische Gesundheit, Mannheim, Germany, May 1999.

Mecklinger, A.
Arbeitsgedächtnis in Raum und Zeit.
Institut für Psychologie der Rheinisch-Westfälischen Technischen Hochschule Aachen, Germany, June 1999.

Mecklinger, A.
Gedächtnis und Gehirn.
Schulvortrag im Rahmen der Hauptversammlung der Max-Planck-Gesellschaft, Märkische Schule, Bochum & Freiherr-von-Stein Gymnasium Lünen, Germany, June 1999.

Mecklinger, A.
Weniger ist mehr: Zur Rolle der Arbeitsgedächtniskapazität bei der Sprachverarbeitung.
Institut für Psychologie, Universität Leipzig, Germany, July 1999.

Mecklinger, A.
Elektrophysiologische Korrelate des Erinnerns.
Institut für Psychologie, Universität des Saarlands, Saarbrücken, Germany, November 1999.

Norris, D.G.
Safety issues and the regulatory environment in Germany.
Institute of Physics and Engineering in Medicine, Current Safety Issues in Magnetic Resonance, London, UK, January 1999.

Norris, D.G.
Alternative methods to EPI for functional magnetic resonance imaging.
Opening Seminar, Veterans General Hospital, Taipei, Taiwan, March 1999.

Norris, D.G.
Diffusion: Methoden und Anwendungen.
Erstes Doktorandentraining der Deutschen Sektion der ISMRM, Leipzig, Germany, April 1999.

Norris, D.G.
Theorie der Diffusion.
Erstes Doktorandentraining der Deutschen Sektion der ISMRM, Leipzig, Germany, April 1999.

Norris, D.G.
RARE und GRASE.
Erstes Doktorandentraining der Deutschen Sektion der ISMRM, Leipzig, Germany, April 1999.

Norris, D.G.
Schnelle MR-Bildgebung.
DFG Seminar, Technische Universität Aachen, Germany, November 1999.

Penney, T.B.
Memory representation of visual objects: Evidence from event-related potentials (ERPs).
Psychology Department, Simon Fraser University, Vancouver, Canada, March 1999.

Penney, T.B.
Visual object representation in memory: The view from the brain.
Psychology Department, Duke University, Durham NC, USA, April 1999.

Schubotz, R.I.
Kognitive Modelle von Exekutivfunktionen.
Reihe 'Ausgewählte Kapitel der Klinischen Neuropsychologie', Tagesklinik für kognitive Neurologie der Universität Leipzig, Germany, May 1999.

Schwarzbauer, C.
Functional magnetic resonance imaging: principles, methods, applications.
University of Nagoya, Medical Center, Nagoya, Japan, September 1999.

Schwarzbauer, C.
Perfusion: Grundlagen, Methoden und Anwendungen.
Erstes Doktorandentraining der Deutschen Sektion der ISMRM, Leipzig, Germany, April 1999.

Steinhauer, K.

Ohne Pause auf dem Holzweg? - Das Gehirn und seine prosodischen Grenzen.
Forschungsseminar 'Allgemeine und Biologische Psychologie', Universität Leipzig, Germany, January 1999.

Steinhauer, K.

Event-related brain potentials (ERPs) and the prosodic processing of natural speech.
CUNY Graduate School and University Center, New York, NY, USA, March 1999.

Szameitat, A.

Lokalisation von exekutiven Funktionen in Doppelaufgaben mit fMRT.
Kolloquium am Institut für Allgemeine Psychologie, Technische Universität Braunschweig, Germany, December 1999.

Vos, S.H.

ERPs and language processing: Another vision of the brain?
4th Summer School in Behavioral and Cognitive Neurosciences, Groningen, The Netherlands, June/July 1999.

Wiggins, C.J.

Embedded single trial designs for fMRI.
Opening Seminar, Veterans General Hospital, Taipei, Taiwan, March 1999.

Wiggins, C.J.

EPI.
Erstes Doktorandentraining der Deutschen Sektion der ISMRM, Leipzig, Germany, April 1999.