MAX-PLANCK-INSTITUTE OF COGNITIVE NEUROSCIENCE

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PREFACE

1997 was characterized by a considerable amount of joint projects between the different work groups at our institute. Cognitive fMRI experiments were conducted successfully. New psychological protocols and new tools for mathematical-statistical data analyses were developed in close cooperation between the work groups. However, the enterprise of conducting an MEG experiment was routinely hampered by the fact that the high sensitivity of the MEG equipment picks up environmental noise to a large degree. Thus, options to locate the system outside the city of Leipzig are currently investigated.

During this last year,our the collaboration with the University of Leipzig was strengthened. In addition to already standing cooperation between the Day-Care Clinic for Cognitive Rehabilitation and our institute, several further links were established.

Due to a project on working memory and sentence comprehension in idiopathic Parkinson's disease, members of the institute are more closely associated with the interdisciplinary center for clinical research (IZKF), an institution unique in Eastern Germany and financed by the Federal Research Ministry and the Länder.

Moreover, our institute is involved in a newly founded "Graduiertenkolleg on Language Structure and Processes" at the University's Center of Cognitive Science in a proposed "Forschergruppe" on Working Memory, which will be part of the center as well as a "Schwerpunktprogramm". All of these programs, which are supported by the German Research Foundation, will help establish joint projects between the different scientific institutions in Leipzig.

The present report gives testimony of the collaborative and fruitful work conducted during 1997. We hope to demonstrate the synergy between different scientific domains and methods which characterize the interdisciplinary work at the MPI of Cognitive Neuroscience in Leipzig.

Angela D. Friederici
D. Yves von Cramon

Leipzig, January 1998

TABLE OF CONTENTS

PREFACE

1 ORGANIZATION OF THE INSTITUTE 17

2 STRUCTURE OF THE INSTITUTE 21

3 RESEARCH 23

3.1 NEUROCOGNITION OF LANGUAGE 23

3.1.1 Autonomous first-pass parsing processes in auditory language comprehension: Electrophysiological evidence 24
Hahne, A. & Friederici, A.D.

3.1.2 Prosodic influences on syntactic parsing processes: An ERP study 24
Jescheniak, J.D., Hahne, A. & Friederici, A.D.

3.1.3 The influence of visual contrast on early syntactic evidence from ERPs 26
Gunter, Th.C., Friederici, A.D. & Hahne, A.

3.1.4 Gender violations, semantic expectancy and ERPs 27
Gunter, Th.C., Schriefers, H. & Friederici, A.D.

3.1.5 Effects of case information on the processing of clause final verbs 28
Jacobsen, T. & Friederici, A.D.

3.1.6 Specifying the processing of verb argument structure information 29
Frisch, S. & Friederici, A.D.

3.1.7 Electrophysiological correlates of syntax parsing: Effects of violations in artificial grammar sentences 31
Pfeifer, E. & Friederici, A.D.

3.1.8 The neuronal networks involved in the processing of syntactic and semantic information: Evidence from ERPs recorded in the medio-basal temporal lobes 33
Mecklinger, A., Friederici, A.D., Grunwald, T., Pezer, N., Lehnertz, K., Penney, T.B. & Elger, C.

3.1.9 Auditory sentence comprehension as revealed by fMRI: Judging a sentence's grammaticality 33
Meyer, M., Friederici, A.D., von Cramon, D.Y., Kruggel, F., Wiggins, C.J. & Niendorf, T.

3.1.10 Processing syntactic violations as revealed by fMRI: Judgment vs repair 35
Friederici, A.D., Meyer, M., von Cramon, D.Y., Kruggel, F., Wiggins, C.J. & Niendorf, T.

3.1.11 Multiple conjunctions: Syntactic ambiguity resolution by case information 36
Gunter, Th.C., Gorrell, P. & Urban, S.

3.1.12 Parsing preferences driven by prosodic cues: Evidence from event-related brain potentials 37
Friederici, A.D., Alter, K. & Steinhauer, K.

3.1.13 A cross modal lexical priming study explores relative clauses 40
Urban, S., Friederici, A.D., Swinney, D. & Nicol, J.

3.1.14 A high density auditory ERP study: The processing of words, pseudowords and non-words 42
Maeß, B., Eulitz, C. & Friederici, A.D.

3.1.15 Lateralization effects of motor function and speech studied with fMRI 43
Hund, M., Lex, U., Friederici, A.D. & von Cramon, D.Y.

3.1.16 A modality comparison of the sequential semantic priming paradigm: Behavioral and event-related potential evidence 46
Kotz, S.A.

3.1.17 The influence of first language word ambiguity during second language word access 47
Kotz, S.A. & Wagner, S.

3.1.18 Effects of grammatical gender on picture and word naming: Evidence from German 48
Jacobsen, T., Bates, E.A. & Friederici, A.D.

3.2 NEUROCOGNITION OF MEMORY 51

3.2.1 Inhibition and rehearsal in directed forgetting: Behavioral and pharmacological investigations 52
Müller, U. & Mecklinger, A.

3.2.2 Cognitive correlates of slow cortical potentials during retention of visually coded information in working memory 54
Bosch, V., Mecklinger, A. & Friederici, A.D.

3.2.3 Event-related potentials dissociate visual memory processes under categorial and identical matching conditions 56
Berti, S., Mecklinger, A., Geissler, H.-G. & Lachmann, T.

3.2.4 Insight out: Intracranial and scalp recorded ERPs correlates of visual working memory 57
Mecklinger, A., Grunwald, T., Pezer, N., Lehnertz, K., Penney, T.B. & Elger, C.

3.2.5 Coordinating information in working memory: An investigation of the coordination process using the memory coordination paradigm 58
Bublak, P., Schubert, T. & von Cramon, D.Y.

3.2.6 Subcomponents of executive control: Dynamic aspects 59
Bublak, P., Mecklinger, A., von Cramon, D.Y., Göritz, A. & Springer, A.

3.2.7 Backward inhibition contributes to the costs of task set reconfiguration 61
Mecklinger, A. & Borrmann, K.

3.2.8 Is irrelevant input to working memory actively inhibited ? 61
Ungerer, C., Mecklinger, A. & Bublak, P.

3.2.9 Event-related brain potentials dissociate image-based and verbal representations in recognition memory 62
Mecklinger, A. & Bosch, V.

3.2.10 Perceptual and conceptual processing of pictures and words: Evidence from event-related potentials 63
Mecklinger, A. & Busch, A.

3.2.11 An ERP study of object representation: Implicit and explicit memory for 3D possible and 3D impossible line drawings 64
Penney, T.B., Mecklinger, A., Hilton, J. & Cooper, L.A.

3.2.12 Event-related potential indices of auditory sensory memory 65
Kaernbach, C., Schröger, E. & Gunter, Th.C.

3.2.13 Below the surface: fMRI and ERP analyses of human auditory memory 67
Opitz, B., Mecklinger, A., Kruggel, F. & Wiggins, C.J.

3.3 CLINICAL NEUROPSYCHOLOGY 69

3.3.1 Working memory in patients suffering from severe closed head injury: An investigation of storage and executive functions using the memory coordination paradigm 70
Bublak, P., Schubert, T. & von Cramon, D.Y.

3.3.2 A clinical test of executive functions during task-set reconfigurations 71
Mecklinger, A., von Cramon, D.Y., Springer, A. & Matthes-von Cramon, G.

3.3.3 Visual recognition memory in patients with cerebral hypoxia: A combined behavioral and event-related potential analysis 72
Mecklinger, A, von Cramon, D.Y. & Matthes-von Cramon, G.

3.3.4 Investigations on memory retrieval processes with brain injured patients 73
Thöne, A. & Zysset, S.

3.3.5 Implicit serial learning in brain injured patients 74
Thöne, A. & Andersen, B.

3.3.6 The role of basal ganglia in language comprehension 76
Friederici, A.D., von Cramon, D.Y. & Kotz, S.A.

3.3.7 Semantic and syntactic processing during auditory and visual sentence comprehension in an aphasic patient: An ERP case study 76
Kotz, S.A. & von Cramon, D.Y.

3.3.8 Agrammatic comprehension and theta-role asignment: A theoretical perspective 78
Friederici, A.D. & Gorrell, P.

3.3.9 Procedural learning in Broca's aphasia: Dissociation between the acquisition of spatio-motor and phoneme sequences 80
Goschke, T., Friederici, A.D., van Kampen, A. & Kotz, S.A.

3.3.10 Sentence comprehension and working memory in Parkinson's disease 82
Saupe, N., Müller, U. & Friederici, A.D.

3.3.11 Phonological discrimination in aphasia: Perception and short-term memory 83
Kotz, S.A., Lagotzki, A. & Friederici, A.D.

3.3.12 Text comprehension after brain-injury: Encoding and retrieval processes 84
Ferstl, E.C., Guthke, T. & von Cramon, D.Y.

3.3.13 Multilevel representation of text information in brain-damaged patients 86
Guthke, T. & Ferstl, E.C.

3.3.14 Neurolinguistic assessment of discourse comprehension deficits 88
Ferstl, E.C., Walther, K. & Guthke, T.

3.3.15 Dynamic changes of motor learning in normal controls visualized by fMRI 90
Hund, M. & von Cramon, D.Y

3.3.16 Characterization of small vessel disease by means of proton spectroscopy and structural 3-Tesla NMR 92
Hund, M., Norris, D.G., Guthke, T. & von Cramon, D.Y.

3.3.17 Response selection and deep brain stimulation 93
Schubert, T., Volkmann, J. & Müller, U.

3.3.18 A first clinical study with a mechanical finite element model of the human head 95
Hartmann, U. & Kruggel, F.

3.4 PSYCHOLOGICAL METHODS IN NEUROIMAGING 99

3.4.1 Use of short inter-trial intervals in 'single-trial' fMRI-experiments 100
Pollmann, S., Wiggins, C.J. & von Cramon, D.Y.

3.4.2 Embedded single trial design for fMRI 101
Dove, A., Pollmann, S., Wiggins, C.J. & von Cramon, D.Y.

3.4.3 Dynamics of working memory and long term memory: An fMRI study 102
Zysset, S., Pollmann, S., Wiggins, C.J. & von Cramon, D.Y.

3.4.4 Cortical areas and the control of self-determined finger movements 104
Schubert, T., Niendorf, T. & von Cramon, D.Y.

3.4.5 Determination of visual search strategies with a mathematical reaction time model 106
Müller-Plath, G.

3.4.6 Factors contributing to the enhanced bilateral redundancy gain in commissurotomy patients 107
Pollmann, S. & Zaidel, E.

3.4.7 The importance of interhemispheric visual transfer for spatial orienting 108
Pollmann, S. & Zaidel, E.

3.5 SIGNAL IMAGE PROCESSING 111

3.5.1 Invariances in sulcal patterns of the human brain 112
Lohmann, G. & von Cramon, D.Y.

3.5.2 Segmentation of structural MRI 114
Palubinskas, G. & Rajapakse, J.C.

3.5.3 Functional MRI analysis 116
Kruggel, F., Descombes, X. & Rajapakse, J.C.

3.5.4 A new concept for EEG/MEG - Signal analysis: Detection of interacting spatial modes 121
Uhl, C.

3.5.5 Implementation of a multimodal renderer for biomedical datasets 125
Dörr, M. & Kruggel, F.

3.6 NUCLEAR MAGNETIC RESONANCE 127

3.6.1 The application of double voxel fMRS to single trial cognitive experiments 128
Dymond, R.C., Zysset, S., Norris, D.G. & Pollmann, S.

3.6.2 Measurement of the fast response 130
Dymond, R.C. & Norris, D.G.

3.6.3 Template interactive phase encoding (TIPE): An application to brain imaging with GRASE 130
Jovicich, J. & Norris, D.G.

3.6.4 FMRI with GRASE : Initial evaluation using split echo technique at 3 Tesla 132
Jovicich, J. & Norris, D.G.

3.6.5 Origins of BOLD contrast - Diffusion and MTC weighted functional imaging of the human brain 134
Koch, M., Niendorf, T. & Norris, D.G.

3.6.6 Functional imaging with ultra-falst low angle RARE (U-FLARE) 136
Niendorf, T.

3.6.7 Monitoring of location-dependent visual cortex activation: Comparison between MUSIC and FLASH 137
Niendorf, T. & Pollmann, S.

3.6.8 Strategies for neurological imaging at high magnetic field strength 138
Norris, D.G., Hund, M. & von Cramon, D.Y.

3.6.9 0° slice-selective RF pulses: MT-equivalence for multi-slice perfusion imaging 139
Norris, D.G.

3.6.10 BASE perfusion imaging 142
Schwarzbauer, C.

3.6.11 Dependence of the BOLD contrast on oxygen consumption 143
Schwarzbauer, C. & Heinke, W.

3.6.12 Echo planar imaging - development of enhanced EPI methods 144
Wiggins, C.J. & Norris, D.G.

3.7 MEG AND EEG: SIGNAL ANALYSIS AND MODELING 147

3.7.1 Magnetic brain activation during auditory sentence perception recorded by a 148 channel whole head magnetometer system 148
Knösche, T.R., Maeß, B., Oertel, U. & Friederici, A.D.

3.7.2 Transformation of MEG recordings between different sensor positions 149
Knösche, T.R.

3.7.3 Information criteria determine the number of independent sources in EEG/MEG 149
Knösche, T.R., Berends, E.M., Jagers, B. & Peters, M.J.

3.7.4 Accuracy of single dipole localization from MEG recordings of a phantom head 150
Knösche, T.R.

3.7.5 Three-dimensional reconstruction from EEG - the performance of linear algorithms 152
Knösche, T.R.

3.7.6 Time-frequency analysis of event-related electrophysiological data 153
Herrmann, C., Pfeifer, E. & Mecklinger, A.

4 TECHNICAL DEVELOPMENT 157

4.1 A T2* phantom for testing of fMRI techniques 157
Dymond, R.C., Köhler, R. & Norris, D.G.

4.2 Measurement of the diffusion tensor of water 158
Koch, M. & Norris, D.G.

4.3 Development of an automated permutation program 'balance' 160
Schubert, T. & Sturm, P.

4.4 EEG recording during MR scanning 161
Wiggins, C.J. & Kruggel, F.

4.5 Installation of the MAGNEX head gradient set 161
Wiggins, C.J. & Weder, M.

4.6 Increased flexibility in statistical analysis of ERP data 162
Jacobsen, T., Maeß, B., Nowagk, R. & Oertel, U.

4.7 Improvement of the auditory presentation system for fMRI experiments 163
Opitz, B., Meyer, M., Kruggel, F. & Pfeifer, E.

4.8 Visual stimulation system 164
Oertel, U. & Maeß, B.

4.9 Library and scientific documentation 164
Lewin, G.

5 OTHER ACTIVITIES 167

5.1 Teaching 167
5.2 Committees and Memberships 168
5.3 Visitors 170
5.4 Guest Lectures 170
5.5 Congresses, Workshops and Colloquia 175

6 DEGREES, HONORS AND AWARDS 177

6.1 Degrees 177
6.2 Honors and Awards 177

7 PUBLICATIONS 179

7.1 Published books, papers & bookchapters 179
7.2 Technical reports 187
7.3 Published abstracts 188
7.4 Papers presented at conferences 193
7.5 Papers presented at colloquia 201

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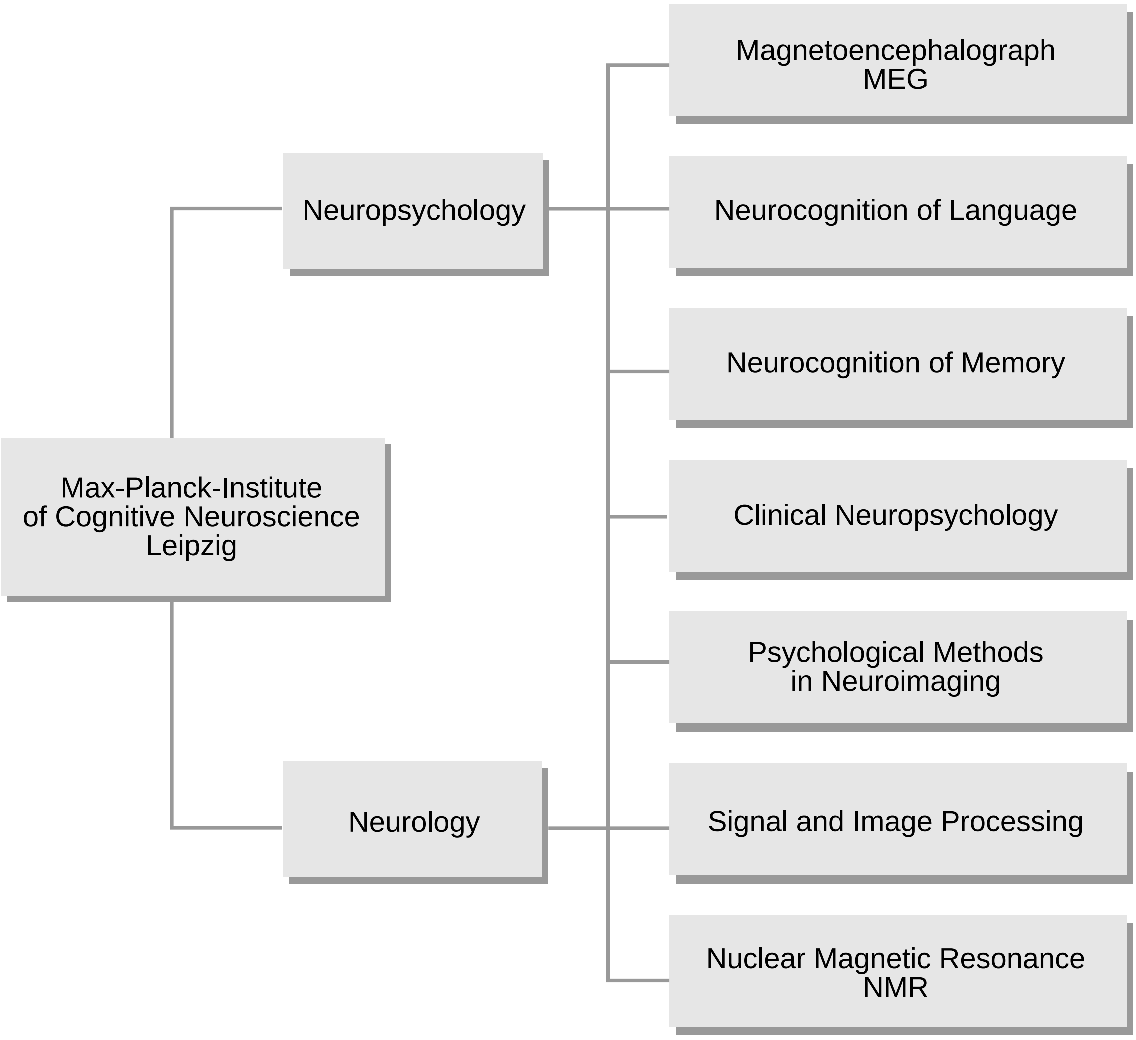
2

STRUCTURE OF THE INSTITUTE



RESEARCH 3

NEUROCOGNITION OF LANGUAGE 3.1

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

This year's research focuss on the specification of temporal and neuroanatomical aspects of early and late syntactic processes, of lexical processes and of their possible interdependence. The background for this research is a model which assumes three phases during comprehension to be correlated with three different ERP components: (1) an early syntactic phase of initial structure building reflected by an (early) left anterior negativity (ELAN, LAN), (2) a phase of lexical-semantic integration reflected by the N400 component, and (3) a final phase during which syntactic and semantic information are mapped onto each other (P600). Three studies tried to specify the nature of the early and the late syntactic processes by investigating their dependence/independence of non-syntactic factors, such as: lexical-semantic aspects (3.1.1), prosodic aspects in an auditory experiment (3.1.2), and visual contrast in a reading experiment (3.1.3). The processing of gender information during reading was investigated in (3.1.4), and the processing of verb argument structure and case information relevant for the identification of arguments in 3.1.5 and 3.1.6. Electrophysiological correlates for the processing of syntactic information of artificial grammar are reported in 3.1.7. Using depth electrodes (3.1.8) and fMRI (3.1.9 and 3.1.10), we tried to specify the neuroanatomical aspects of syntactic processing and repair. Three studies were designed to investigate parsing preferences, one evaluating the influence of case information (3.1.11), one evaluating the influence of prosodic cues on parsing preferences (3.1.12), and a third one evaluating filler-gap constructions (3.1.13). Four studies focussed on the processing of nouns either presented as single words investigating their lexical status (3.1.14), their syntactic status (3.1.15) or semantic status (3.1.16 and 3.1.17), or presented in minimal syntactic context evaluating the processing of grammatical gender (3.1.18).

3.1.1 Autonomous first-pass parsing processes in auditory language comprehension: Electrophysiological evidence

Hahne, A. & Friederici, A.D.

We investigated the time course and possible interactions of semantic and syntactic processes in language comprehension. Previous studies had frequently shown an early left anterior negativity (ELAN) and a late parietal positivity (P600) in correlation with phrase structure violations, whereas semantic integration processes are correlated with an N400. The aim of the present study was to find out whether, or how, these different processes might interact.

Four types of sentences were presented auditorily. The sentences ended with a target word that was either (a) correct, (b) semantically incorrect, i.e. violating the selectional restriction of the verb, (c) syntactically incorrect, i.e. violating the phrase structure, or (d) semantically and syntactically incorrect, i.e. violating both the selectional restriction and the phrase structure. In the first experiment subjects were asked to judge the overall correctness of a sentence. The ERP-results with regard to conditions (b) and (c) replicated earlier results: we observed an N400 for semantic violations and an ELAN component followed by a P600 for phrase structure violations. The combined violation (d), however, elicited the same result pattern as the pure syntactic condition, i.e. ELAN and P600. Interestingly, there was no N400 despite the clear selectional restriction error. This indicates that the semantic integration of a word in a sentence may only be initiated in case of a successful prior integration of the element into the phrase structure of the sentence.

In a second experiment we presented the same sentences but changed the instruction to the subjects. In this experiment they were asked to judge exclusively the "semantic coherence" of the sentences thereby ignoring syntactic aspects of the sentence. That is, participants had to classify sentences containing only a phrase structure error as being correct. The ERP-results were clear-cut: even when focusing on semantic aspects of the sentence an ELAN component was elicited in the pure syntactic condition (c) as well as in the combined semantic-syntactic condition (d). This illustrates the highly autonomous character of first-pass parsing processes in auditory language comprehension. Interestingly, under the "semantic coherence" there was no P600 for phrase structure violations which suggests that the processes reflected in this component are of a fairly controlled nature. A further important result of this experiment was that in contrast to Experiment 1 an N400 component was elicited also in the combined condition (d). The fact that the N400 was dependent on the instruction suggests that the underlying processes are also under the participants' strategic control.

3.1.2 Prosodic influences on syntactic parsing processes: An ERP study

Jescheniak, J.D., Hahne, A. & Friederici, A.D.

Our study addresses the question of how syntactic and prosodic factors interact during auditory language comprehension. Previous studies using event-related brain potentials have revealed that syntactic word category errors elicit an early negativity most pronounced at left anterior sites (ELAN) followed by a widely distributed late positivity at posterior sites (P600). These two components are assumed to reflect first-pass parsing processes (ELAN) and more general processes of repair and integration (P600), respectively. In our experiments we investigate whether this is the case, and if so, to which extent prosodic information, in particular word stress, can modulate the syntactic processes underlying the two ERP-components. Our first experiment included sentences spoken with a standard intonation but containing a phrase structure error as in (1a), as well as control sentences not containing such an error (1b, 1c; literal translation in square brackets).

(1a) *Die Gans wurde im gefüttert.*
[The goose was in the fed.]
(1b) *Die Gans wurde gefüttert.*
[The goose was fed.]
(1c) *Die Gans wurde im Stall gefüttert.*
[The goose was in the barn fed.]

Relative to the control sentences, both ERP-components (ELAN, P600) were obtained for the sentence final participle ("gefüttert") in case of a phrase structure error. Our first experiment also included a version of (1a) spoken in a non-canonical prosodic form. In this version, our speaker strongly stressed the preposition ("im"); stressing the closed class word is clearly anomalous when the sentence is presented in isolation, outside of a contrastive context. Interestingly, both ERP-components now disappeared suggesting that the prosodic anomaly blocked further syntactic processing.

In a second experiment, we included the same sentences which were, however, preceded by introductory questions putting the focus on the preposition such as (2a).

(2a) *Wurde die Gans vorm Stall gefüttert?*
[Was the goose in front of the barn fed?]

The context of the focusing question "normalizes" the stressed preposition. The prosodic pattern is not anomalous any longer: Rather, it appears contextually appropriate. As to the ERP-data, we then observed the standard ERP-pattern elicited by a phrase structure error (ELAN followed by P600) for sentences containing a stressed preposition as well, although the topography of the ELAN component was slightly different.
These data suggest that prosodic parameters of spoken language can effectively influence early syntactic parsing processes as reflected in the ELAN component. It seems that the initiation of first-pass parsing processes critically depends on the prosodic well-formedness of the sentence.

3.1.3 The influence of visual contrast on early syntactic evidence from ERPs

Gunter, Th.C., Friederici, A.D. & Hahne, A.

In this experiment we determined the impact of visual word discrimination difficulty on syntactic and semantic processing. Discrimination was easy in the high contrast condition where black words were presented on a light gray background whereas discrimination was difficult in the low contrast condition where black words were presented on a much darker background. We assumed that a more difficult discrimination situation results in a less automatic and slower processing mode. We expected automatic first-pass parsing processes to suffer from this manipulation.

Sixteen native German speaking students were presented with German sentences which could be divided into 3 experimental types:

correct:	*Die Tür wurde geschlossen* (The door was closed)
semantic violation:	*Das Dach wurde gewürzt* (The roof was spiced)
syntactic violation:	*Der Kanzler wurde am gewählt* (The president was in elected)

The sentences were presented word-by-word. The experiment was conducted in 2 sessions of approximately 3 hours. The EEG was recorded with 28 tin electrodes. Average ERPs were computed for each electrode position for each of the 4 conditions.

Recent ERP-research has correlated the processing of syntactic information processing with a late positivity (P600) which is often preceded by a left anterior negativity either present around 150 ms (ELAN) or around 400 ms (LAN). With the exception of one study, which found both these negativities followed by a P600 (Neville et al., 1991), all studies using word-by-word visual presentation observed the LAN whereas all studies using auditory presentation found an ELAN. As the ELAN-component is viewed to reflect fast automatic first-pass parsing processes, it may be primarily observable when the input can be processed fast. This is usually the case when sentences are presented via a headphone in an experimental setting. Processing visually presented input with a high visual contrast might also favour first pass-parsing even when words are presented one at the time.

The behavioral data revealed effects of violation type (better performance for syntactic violations) and contrast (better performance for high contrast).

ERPs: Semantic violations
Compared to the correct sentences, the semantic violations gave rise to a larger N400 component. This N400-effect had a duration of 300 ms. The onset of the N400-effect was delayed by approximately 100 ms in the low contrast presentation condition. In order to explore whether or not this delay in N400-effect was already present at an earlier stage of processing (e.g. at a P2 level), a peak picking procedure was carried out on both P2 and N4 peaks. Highly significant main effects of both contrast and component indicate that P2 and N4 differed in latency. The P2 was delayed by 44 ms in the low contrast condition. Thus, the slowing of the N400 effect is at least partially due to

a slowing of earlier components. In sum, the N400 effect was affected by the low contrast condition in that its onset was delayed by 100 ms and its duration was longer.

ERPs: Syntactic violations
In this section we concentrate on three ERP-components namely: The ELAN, the LAN and the P600. It was found that the ELAN disappears in the low contrast. Instead we observed a LAN followed by the P600 which seems to be reduced. These observations, with the exzeption of the reduction of the P600, were confirmed by statistical analyses.

Taken together, when the discrimination of the visual input during word processing is difficult, readers appear to use a more elaborated route of word access. This leads to a delay in the ERP-components in the low contrast condition. The finding that the effect of a word category violation seems to change from an ELAN (high contrast) to a LAN (low contrast) may suggest that both components reflect similar processes which are elicited, however, in a different time frame.

Gender violations, semantic expectancy and ERPs

3.1.4

Gunter, Th.C., Schriefers, H. & Friederici, A.D.

If native speakers are aware of gender at all, it is most likely that they are aware of biological gender (boy being male & girl being female etc.). However, the grammatical gender of a word is often independent of biological gender. The word 'house', for instance, is masculine in Russian, feminine in French and neuter in German (Corbett, 1991). There are several theories which try to explain differences in gender systems or why gender exists. It has been argued, for instance, that gender can be used for backtracking references in a complex discourse (Bates & MacWhinney, 1989). Gender may also play a facilitory role in sentence processing because: (a) gender cues may facilitate the recognition of words (Bates, 1994), or (b) gender can sometimes disambiguate homonyms (Van Berkum, 1996).

In two behavioral studies (Friederici et al., 1994 & Schriefers et al., in press) it was shown that in sentences like *'Er trinkt das Bier'*, the priming between the verb and the noun can be diminished/removed by a gender violation on the article. Thus in *'Er trinkt den Bier'* there is no facilitation in the recognition of the noun. Whether gender information comes into play at a pre-lexical or post-lexical level still remains to be solved.

In this study we used event-related brain potentials (ERPs) in order to explore the effects of gender violations onto lexical integration because of their on-line properties and their sensitivity to semantic and syntactic information. If, as suggested by Schriefers et al., semantic priming is indeed affected by gender violations, one would expect this to be particularly reflected in N400 effects which are typically interpreted as reflecting semantic integration. The three available ERP-studies which investigated gender violation (reflective-antecedent gender violation: Osterhout and Mobley, 1995; gender related social stereotypes: Osterhout, Bersick and McLaughlin, 1997; combination of gender and semantic violations: Hagoort and Brown, 1997) show a P600 -a response-which is typically found in syntactic violations and during the processing of syntactically infrequent sentence structures.

First, a rating study was carried out in which students had to complete 210 sentences which contained a personal pronoun, a verb and the neuter article (i.e. *Er/Sie trinkt das..... He/She drinks the*$_{neuter}$ ..). From this list the 40 highest expected sentences were chosen (close %>56%, mean: 74.2). For each of these sentences, a low close counterpart sentence was chosen (close %< 25%, mean: 15.3) such that the noun of the high close sentence was semantically acceptable (but not expected). Thus, a total of 160 eight-word sentences were constructed. All sentences were presented word-by-word. Half of them contained a gender violation (examples 2 & 4).

CLOSE %	GENDER	SENTENCE
high	ok	(1) Sie bereist *das* Land (She travels the$_{neuter}$ land$_{neuter}$)
high	Nok	(2) Sie bereist *den* Land (the$_{male}$)
low	ok	(3) Sie erkennt *das* Land (She recognizes the$_{neuter}$ land$_{neuter}$)
low	Nok	(4) Sie erkennt *den* Land (the$_{male}$)

The EEG was recorded with 28 tin electrodes. Preliminary data analysis of 32 native German speaking participants revealed the following ERP-patterns for the critical noun:

1. The low close nouns had a larger N400 than the high close nouns.
2. Gender violations elicited a left anterior negativity around 300-600 ms (i.e. LAN).
3. Gender violations also elicited a P600, although only for the high close nouns.
4. No N400 effect was found for the nouns in the gender violation conditions.

In this experiment gender violations elicited a LAN, a component typically found in syntactic incorrect sentences. The reflection of close probability (i.e. semantic processes) was reflected in the N400. The impact of close probability on gender violations was not reflected in N400 effects but in a P600-effect instead. On the one hand, it is clear that the major impact of the gender violation was in the highly expected noun. This is exactly the situation where Schriefers et al. would expect the largest effects of gender violations to occur. On the other hand, there are some reasons to believe that the P600 is influenced by semantic processes (cf. Gunter et. al., 1997). If this is true, the P600-finding would confirm Schriefers et al.'s behavioral finding using electrophysiology.

3.1.5 Effects of case information on the processing of clause final verbs

Jacobsen, T. & Friederici, A.D.

Jacobsen and Friederici continued their work on effects of case-marking. In contrast to English, morphological case is overtly marked in German. The present event-related brain potential (ERP) study investigated effects of case information on the processing of verbs. Accusative and dative case-marked wh-pronouns were used to constrain processing of the verb. The main verb was presented in clause-final position, realizing a violation between the case information given by the pronoun and the argument structure of the verb in half of the sentences. The other half consisted of correct sentences. The following types of sentences were used.

(1) AccCor *Er wußte, wen Nina gesehen hat, bevor sie ging.*
(He knew, whom Nina seen has, before she left.)
(2) AccInc **Er wußte, wem Nina gesehen hat, bevor sie ging.*
(He knew, *to whom Nina seen has, before she left.)
(3) DatCor *Er wußte, wem Nina geholfen hat, bevor sie ging.*
(He knew, to whom Nina helped has, before she left.)
(4) DatInc **Er wußte, wen Nina geholfen hat, bevor sie ging.*
(He knew, *whom Nina helped has, before she left.)

A 120 channel EEG was recorded while participants (N=16) read the 200 sentences in a word-by-word RSVP setting at 500 ms per word. Grammatical acceptability judgments were used to ensure sentence reading. The ERPs for the clause final past participles revealed effects of case and correctness. Incorrect case marking led to a more negative N400-like wave form for both case violation conditions compared to correct sentences in the time range of 450 to 600 ms after onset of the verb. This finding indicates that case information available during sentence processing affects the processing of sentence final verbs. Within the correct sentences, accusative verbs showed a more negative going wave than dative verbs. This result may reflect the fact that there are only few dative verbs in German allowing the reduction of possible verb candidates once dative-case information is available. The combined ERP effects suggest that case marking provided by prior sentential context guides the lexical integration of verbs.

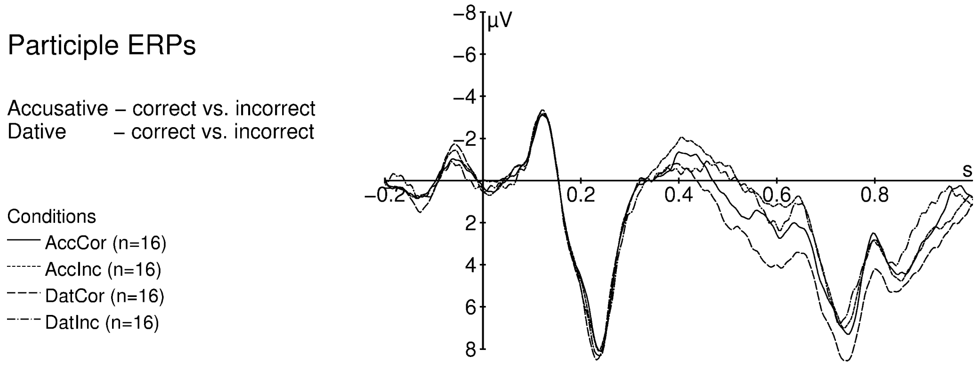


Figure 1. electrode 36 all four conditions

3.1.6

Specifying the processing of verb argument structure information

Frisch, S. &
Friederici, A.D.

The processing of semantic information, argument structure information and case marking information of verbs was investigated in two ERP studies. Earlier work had identified a negativity with a posterior maximum at about 400 ms evoked by semantic anomalies, the *N400* (Kutas & Hillyard, 1980). The N400 has been replicated in a number of studies which varied the type of semantic anomaly as well as the language. ERP findings for verb argument structure violations are less clear-cut: Rösler, Friederici, Pütz & Hahne (1993) reported a negativity within the N400 time window, but with a left anterior maximum. Osterhout, Holcomb & Swinney (1994) reported an N400-like negativity with a posterior maximum preceding a late positivity (P600). Hagoort, Brown & Groothusen (1993), in contrast, did not find any significant ERP component correlated with subcategorization violations.

In the first experiment, we presented sentences in which the sentence final verb either created a semantic violation, an argument structure violation, or both. In comparison to a correct condition, all three violation conditions elicited negativities between 400 and 600 ms with a posterior bilateral maximum (N400) differing, however, in their amplitudes. N400 amplitudes for sentences with only semantic or semantic plus argument structure violations were significantly more negative than those for argument structure violations alone, which were, in turn, more negative than those for the correct sentences. No significant N400 amplitude differences between sentences with only semantic violations and non with both types of violations were found. These findings suggest that lexical integration of a verb is not additively affected by semantic and argument structure information.

The absence of topographic differences between the ERP patterns for semantic and for argument structure violations seems to indicate that these two types of information are processed by the same brain systems. It is, however, also possible that this topographic correspondence is due to the materials used in this study: it might be explained by a general *semantic* constraint restricting the general possibility of adding a noun phrase with a thematic role "benefactive" (dative object) to nominative-accusative verbs in German (cf. Wegener, 1991; Wunderlich, 1985). Therefore, in a second study we constructed sentences with incorrect argument structure in a different manner, and contrasted them with sentences containing semantic and case marking violations. All types of violation elicited N400-like components with a posterior maximum in a time window between 300-500 ms. Again, no topographic differences were found. Unlike sentences containing semantic anomalies, sentences with argument structure violations, as well as sentences with case marking violations not only elicited an N400 but additionally a late posterior positivity (P600). The absence of topographic differences between the semantic and the argument structure condition in the N400 time window again raises the question if the processing of these types of information is supported by the same brain systems. Before drawing this conclusion a third experiment is being conducted in order to further evaluate whether these different types of information encoded in the verb, namely its semantic aspects (i.e., semantic features and thematic grid) and its syntactic aspects (i.e., number and form of arguments), are processed by the same or different neuronal structures.

Electrophysiological correlates of syntax parsing: Effects of violations in artificial grammar sentences

3.1.7

Pfeifer, E. & Friederici, A.D.

In previous ERP studies (Friederici, Pfeifer & Hahne, 1993; Friederici, Hahne & Mecklinger, 1996), we found an early left anterior negativity followed by a late positivity in response to syntactic violations in natural language stimulus material. The present study focused on the early negativity which is thought to reflect automatic first pass parsing processes specifically, the detection of word category errors (Friederici, 1995). Is this component natural language specific, or can it also be found with a well-trained artificial grammar? Does it only appear when language acquisition has taken place within a critical period of age and when learning went on for many years, as for the native language?

To empirically answer these questions subjects underwent an intense training procedure to learn the syntactic rules of a simple artificial language by speaking and listening to word sequences. The words were chosen to be non-words in languages known to the subjects, and the vocabulary was divided into word classes like verbs, nouns, modifiers and determiners. The syntax allowed 1 to 3-word noun- and verb-phrases that were concatenated to subject-verb[-object] structured sentences with a length of up to 8 words. A pilot study indicated that pure syntax is hard to learn and that practicable training durations can only be achieved when the sentences carry meaning and when the training environment keeps the subjects motivated for the time required to reach the predefined performance criterion (which usually took two or three 4-hour sessions). With this in mind we developed a computer game in which two subjects play against each other. The words of the artificial language referred to actions and objects in the game so that each sentence described a specific move. The rules of the game were independent of the syntactic rules, however, the language was embedded instrumentally by having subjects verbally inform each other of their current moves. In short, learning how to communicate in the new language improved their chances to win.

The subjects' mastery of the language was measured by tests that were inserted between the playing sessions. In each test the subjects heard 96 statements for which they had to specify what they had understood (using a couple of mouse clicks). The percentage of correctly comprehended sentences and the improvement in speed indicated when subjects were ready to enter the ERP experiment, which was always scheduled within one week after training. In the ERP session both correct and syntactically incorrect sentences were presented auditorily. To assure attentive listening the subjects had to perform a probe detection or grammaticality judgment task (randomly mixed), without knowing the type of task while hearing the sentence. This dual task situation was chosen to avoid problems that appeared in the pilot experiment when using either task alone.

Various types of syntactic violations were realized (word class, agreement, phrase level, etc.) but only the overall effects will be reported here. For each incorrect sentence there was a matched correct one that was identical up to the point of violation. This way each item had its own control, which turned out to be an advantage compared to natural language material where it is usually not possible to have exactly matched trial versions. Word repetition effects were considered irrelevant here as they can be assumed to have already been driven into saturation (words generally had to be repeated many times due to the limited vocabulary). At the sentence level, a behavioral pre-test revealed that subjects are not able to detect repeated sentences when they appear at sufficient distance from each other, with many interfering sentences in between.

ERPs were time-locked to the onset of the violation (and the respective point in the correct sentences). A comparison of both conditions shows highly significant differences: a negative component from 100 to 200 ms with a fronto-central distribution, a partially overlapping negativity peaking at 300 ms at parietal and occipital sites, and a broad positivity starting at 400 ms. The existence of the early negativity suggests that this component not only occurs in native natural language contexts, but more generally reflects activity of neural systems involved in processing language related structured sequences. However, in contrast to similar natural language studies, the effect is not left lateralized, possibly indicating the coactivation of other cortical areas.

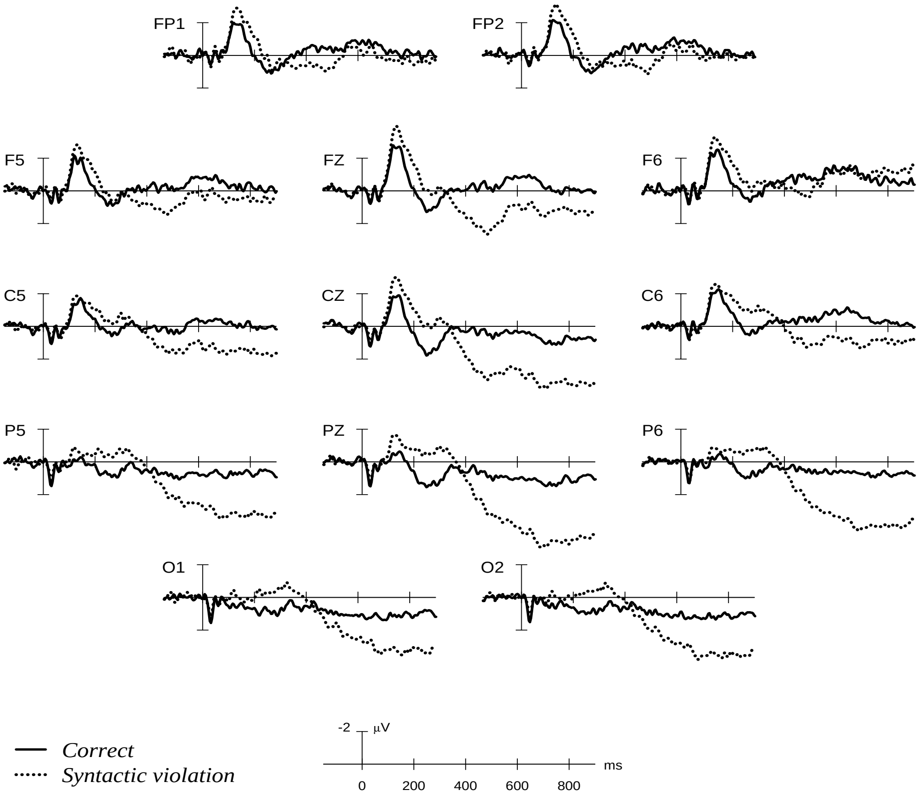


Figure 2. Grand average over 28 subjects with approx. 180 trials per subject and condition. ERPs are time-locked to the onset of the violation and the respective point in time in the correct sentences (denoted as 0 ms in the figure).

To provide additional evidence for the language specificity of these results, data are currently being collected in a follow-up experiment in which subjects get no training at all before they take part in an ERP session that is kept as comparable as possible to the one outlined above. Here we would predict to find some P3-related unspecific effects, but no early negativity. A second follow-up study will address the question of whether the above findings rely on a partial reuse of neural circuitry normally involved in parsing natural language syntax. Due to the similarity of the artificial grammar with languages like German and English, one cannot tell whether these neural systems also serve as sequence processors in a wider sense. A different grammar maximally dissimilar to languages spoken by the subjects will help to resolve this issue.

3.1.8

The neuronal networks involved in the processing of syntactic and semantic information: Evidence from ERPs recorded in the medio-basal temporal lobes

Mecklinger, A.,
Friederici, A.D.,
Grunwald, T.,
Pezer, N.,
Lehnertz, K.,
Penney, T.B. &
Elger, C.

In cooperation with the Department of Epileptology at the University of Bonn we are currently examining the neuronal networks underlying language comprehension by means of ERP recording from the medial temporal lobes in epileptic patients. The patients listened to auditorily presented sentences that were syntactically and semantically correct or contained either a syntactic violation, i.e. word category error or a semantic violation, i.e. selectional restriction error. Both types of violations can be dissociated electrophysiologically with scalp recorded ERPs. That is, syntactic violations evoke an early left anterior negativity peaking around 200 ms (ELAN), followed by a parietally distributed positivity (P600), whereas semantic violations give rise to a posterior distributed N400 component (cf. Friederici et al., 1993). As a control condition a second task, requiring the detection of tonal and atonal (novels) deviants in an auditory stimulus sequence was employed. The presence of a novel effect in the control condition was used as a selection criteria for the inclusion in the analysis of the language ERPs. Bilateral depth electrodes were implanted in the medio-basal temporal lobes along the longitudinal axis with the amygdala as the target of the most anterior electrode. Electrode distance was 4 mm and electrode placements were verified by post-implant CT and MRI. So far, the data from the non-epileptic temporal lobes of three patients have been examined. One patient showed no novel effect in the control condition. The two patients displaying this effect entered the analysis of the language task. For both patients no effect was found in the semantic violation condition. For both patients, however, a biphasic response to syntactic violations was obtained with a first peak at around 300 ms and a second peak at around 600 ms in the medial temporal lobe. These preliminary findings suggest the involvement of medial temporal structures in processing syntactic violations.

3.1.9

Auditory sentence comprehension as revealed by fMRI: Judging a sentence's grammaticality

Meyer, M.,
Friederici, A.D.,
von Cramon, D.Y.,
Kruggel, F.,
Wiggins, C.J. &
Niendorf, T.

Recent brain imaging studies investigating different aspects of sentence processing during visual presentation (Stromswold et al., 1996; Just et al., 1996; Bavelier et al., 1997) found increased activation in Broca's region, Wernicke's region and in remaining parts of temporal lobe, more prominent in left than in right hemisphere.
In order to identify the cortical and subcortical brain regions engaged in processing grammatical information during auditory sentence comprehension we designe an fMRI-experiment, containing correct and syntactically incorrect German sentences.

In this first experiment 64 sentences were presented which were either grammatically correct (1a, 1b) or contained word category errors (2). Note that the preposition *im* requires a noun instead of a verb form to follow.

(1a) *Das Mädchen wurde gesucht und gefunden.*
The girl was searched for and found.
(1b) *Der Seemann wurde im Sturm gerettet.*
The sailor was rescued in the storm.
(2) * *Der Bürgermeister wurde im geschätzt durch.*
* The mayor was in respected through.

Subjects were required to perform a grammaticality judgment after each sentence.
We expected participants to show more difficulties in processing incorrect sentences which would be reflected by stronger activation (signal intensity of hemodynamic response and spatial extent of clustered pixels) in language related-areas.

In addition to functional scans, a high T1 contrast 3D-MRI (MDEFT, cf. Norris, Annual Report 1996) of each participant was recorded to improve spatial description of the functional activation by registering the 2D functional slice to the individual three-dimensional anatomical image.

Methodologically the current study establishes a 'single-trial' design by applying a pseudorandomized order of correct and incorrect sentence presentation with a 24 second stimulus-onset-asynchrony (SOA). This approach excludes the drawbacks of classical 'blocked designs' (high predictability, decay of subject's engagement in following the instructions) which have been used in most functional imaging studies up to now. The present procedure allows computation of the hemodynamic response for each trial. The application and standardization of a 'single trial' based data acquisition design is a decisive step toward making fMRI- and ERP-experiments comparable.

This experiment was recorded with MR-sequences MUSIC and EPI (cf. Annual Report 1996).
Initial data evaluation of individual subjects revealed a pattern of significant BOLD-activation in primary auditory cortex (transverse temporal gyrus) and in 'classical' posterior language related areas bilaterally, more prominent in the left compared to the right hemisphere. Moreover, activation in the thalamus was also found to be significant in most participants. An increase in signal intensity and number of pixels found for incorrect relative to correct structures indicated the involvement of similar brain structures in processing grammaticality correct and incorrect structures. Further analyses will reveal areas in which the intensity increase is most dominant.

Processing syntactic violations as revealed by fMRI: Judgment vs. repair

3.1.10

Friederici, A.D.,
Meyer, M.,
von Cramon, D.Y.,
Kruggel, F.,
Wiggins, C.J. &
Niendorf, T.

To further specify brain regions involved in processing grammatical information during auditory sentence comprehension, we conducted a second fMRI experiment, containing correct (1) and syntactically incorrect sentences.

In this experiment a total of 76 sentences was presented auditorily. Incorrect sentences carried violations of inflectional morphology with respect to number agreement (2a), gender agreement (2b) or case agreement (2c). Note that in contrast to English, gender and case are marked overtly in German by morphological inflections either in the article and/or the noun.

(1) *Das Mädchen wurde in dem Wald gefunden.*
The girl was found in the forest.
(2a) * *Der Seemann wurde in dem Stürme gerettet.*
The sailor was rescued in the storms.
(2b) * *Der Seemann wurde in der Sturm gerettet.*
The sailor was rescued in the storm.
(2c) * *Der Seemann wurde in dem Sturmes gerettet.*
The sailor was rescued in the storm.

In this experiment one half of the participants was asked to perform a grammaticality judgment, the other half was asked to repair the incorrect sentences mentally on-line (covert speech) in addition to the judgment task.

This experiment was recorded with MR-sequences MUSIC and EPI (cf. Annual report 1996).
Initial evaluation of 13 participants showed significant BOLD activation in primary auditory cortex and the language related cortex bilaterally. Activation was also found in the thalamus. The anterior part of the supramarginal gyrus as well as the inferior frontal gyrus appeared to be particularly active in the right hemisphere during the sentence repair condition.

A detailed analysis of the task effect is currently under way.

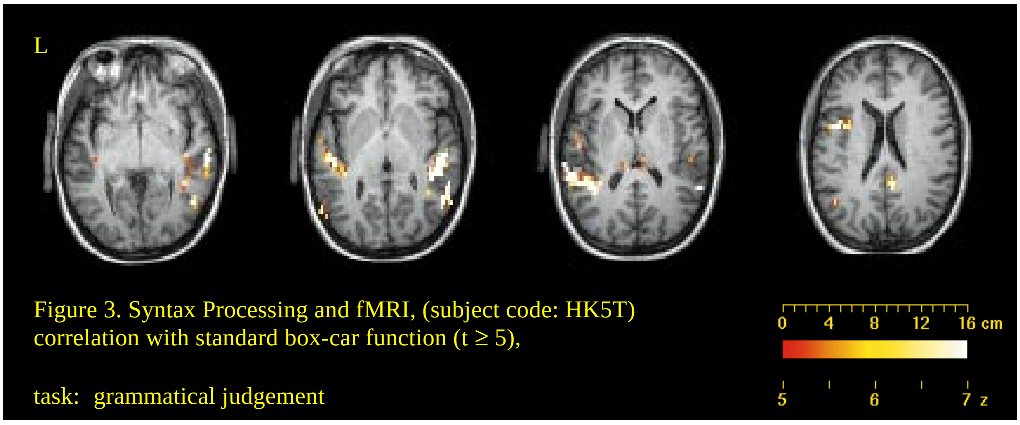


Figure 3. Syntax Processing and fMRI, (subject code: HK5T)
correlation with standard box-car function ($t \geq 5$),

task: grammatical judgement

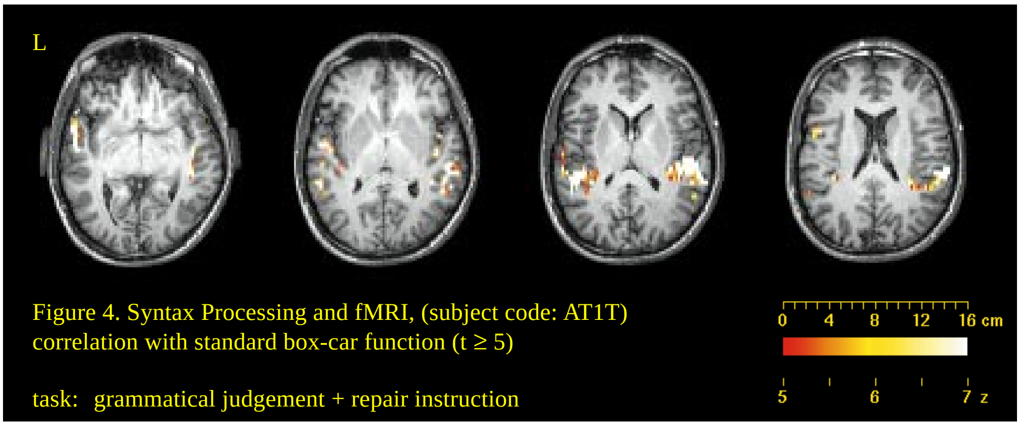


Figure 4. Syntax Processing and fMRI, (subject code: AT1T)
correlation with standard box-car function (t ≥ 5)

task: grammatical judgement + repair instruction

3.1.11 Multiple conjunctions: Syntactic ambiguity resolution by case information

Gunter, Th.C., Gorrell, P. & Urban, S.

This experiment used ERPs to explore types of multiple conjunction ambiguity (MCA). In these types of ambiguities, a case-ambiguous noun phrase (i.e. 'die Trainerin', in the examples below) can be attached either as second object of the verb (1d) or as the first noun-phrase of a new clause (1b). The unambiguous NPs are presented in 1a and 1c.

(1) *Der Dirigent besucht den Apotheker,*
the conductor visits the pharmacist,

a. ***der** Trainer besucht den Bruder, und der Beamte besucht den Arzt.*
the trainer visits the brother, and the official visits the doctor

b. ***die** Traine**rin** besucht den Bruder, und der Beamte besucht den Arzt.*
the trainer visits the brother, and the official visits the doctor

c. ***den** Trainer und den Bruder auch gerne im Sommer.*
the trainer and the brother especially in summer.

d. ***die** Traine**rin** und den Bruder auch gerne im Sommer.*
the trainer and the brother especially in summer.

Thus, in (1a), the nominative NP *der Trainer* indicates the beginning of a new clause (i.e. a coordinated sentence), whereas the accusative NP *den Trainer* in (1c) signals a NP- conjunction. We can address the question of on-line preferences (with minimal lexical variance) by considering case-ambiguous NPs, such as the case-ambiguous, feminine NP, *die Trainerin* in (1b, d). If we compare the coordinations (1a, b), we see that (1b) is ambiguous until the appearance of the verb following *die Trainerin*. In contrast, the disambiguation in (1a) occurs prior to the verb: the unambiguously nominative *der Trainer*. Now we are in a position to address the question of how the parser incrementally structures the NP which signals conjunction. We will refer to this NP ('the trainer' in (1)) as the *critical* NP. The advantage of testing MCAs in German is that the comma is ambiguous, and the case-marking properties allow us to compare the ERPs for the disambiguating verb in (1b) with its counterpart in the unambiguous (1a) sentence, as well as the conjunctions in both the ambiguous and unambiguous sentences (1d&c).

Because data collection is ongoing, we discuss the data of half of the subjects. Sixteen right-handed, native German speaking students (8 female, mean 23.3 years, age range 19 to 28 years) were presented with 48 quadruples like 1a-d. The stimuli were presented in 4 blocks of 48 sentences which had a word-by-word presentation format (300 ms/word).

The EEG was recorded with 28 tin electrodes. Average ERPs, starting 200 msec before and lasting 1000 msec after the presentation of the verb and conjunction following the ambiguous critical NP were computed for each electrode position for each of the 4 conditions. The ERPs elicited at the determiner of the critical NP were more negative for the unambiguous then for the ambiguous conditions. The main difference between the conjunctions and verbs following the critical NP was a much more positive waveform for the verbs. This positivity probably does not represent a word class difference as such, since in the literature on open and closed class words it is typically found that open class items (e.g. verbs) show a negativity at more posterior electrodes and a positivity in the same time range more frontally. The ERP-effects of ambiguity, as found at the verb/conjunction following the critical NP showed 2 main effects. The verbs in the ambiguous conjoined clause showed an N400-like negativity. Whereas the ambiguous conjunctions showed a P600-like positivity. These findings might be interpreted as follows. When, in the ambiguous sentence the verb is parsed, it is clear that a coordinated sentence is read and the word has to be integrated into second sentential clause. This integration is more difficult in the ambiguous case (larger N400). In the case of a conjunction, however, the parser needs to track back into the matrix clause (i.e. the verb) in order to carry out some syntactic reanalysis (fits the critical NP for instance the verb). This back-tracking possibly starting the syntactic reanalysis is reflected by the found P600.

3.1.12

Parsing preferences driven by prosodic cues: Evidence from event-related brain potentials

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

It is generally maintained that prosody fulfills a demarcative function in speech processing. In addition to pitch variations, durational cues such as prefinal lengthening or the position and length of pauses are also used to signal the presence of a prosodic boundary in running speech. Two ERP studies were carried out to examine the influence of prosodic boundaries on parsing processes. We used the material originally introduced by Höhle, Hofmann and Friederici (1995) in a reaction time study. The first two conditions consisted of 48 pairs of correct sentences each containing a first verb (e.g., *'versprechen' /'to promise'*) which could either take a subsequent noun phrase (NP) as its optional indirect object (sentence 1), or not (sentence 2). In sentence (1), the second verb, i.e., the non-finite verb *'arbeiten'* (*'to work'*) is intransitive and the second NP *'Anna'* must thus be the object of the first verb. In sentence (2) in contrast, the second verb *'besuchen'* (*'to visit'*) is transitive and the second NP *'Anna'* becomes the object of this verb.

(1) *[[Peter verspricht Anna zu arbeiten]*$_{IP}$ *[und die Wäsche zu waschen]*$_{IP}$*]*$_{utt}$
Peter promises Anna to work and to wash the linen
(2) *[[Peter verspricht]*$_{IP}$ *# [Anna zu besuchen]*$_{IP}$ *[und die Wäsche zu waschen]*$_{IP}$*]*$_{utt}$
Peter promises to visit Anna and to wash the linen

Prosodic cues like pause insertion, rhythmical variations, and tonal patterns indicate prosodic phrasing as illustrated in (1) and (2) via bracketing where 'IP' means Intonational Phrase and 'utt' means Utterance (cf. Nespor & Vogel ,1986). Note that '#' in sentence (2) marks the presence of a phonetically significant pause signaling the prosodic boundary. In sentence (1), on the other hand, no pause preceding the second NP is detectable in the acoustic time signal. There are also differences in the tonal behavior: In sentence (1) the critical word '*Anna'* is embedded in a larger prosodic domain (i.e., the first Intonational Phrase) and does not carry a pitch accent. In sentence (2), however, the tonal pattern on '*Anna'* marks the beginning of a new prosodic domain (i.e., the second IP) by means of a rise-fall sequence and an increased pitch range.

The third sentence type was obtained by cross-splicing the first part of (2) and the second part of (1) [position marked by ↑] resulting in a false prosodic boundary:

(3)***** *[[Peter verspricht]*$_{IP}$ *# [Anna zu arbeiten]*$_{IP}$ *[und die Wäsche zu waschen]*$_{IP}$*]*$_{utt}$
Peter promises Anna to work and to wash the linen

If the prosodic cues are used on-line to guide first pass parsing processes, the prosodic boundary *'#'* in (2) and (3) can be assumed to prevent the hearer from attaching *'Anna'* to the first verb *'verspricht'* ('*promises*'). Instead, the NP should initially be attached to the second verb causing an argument structure violation at the obligatorily intransitive verb *'arbeiten'* (*'to work'*) in (3). The conflict between first analysis and syntactic requirements should occur when the verb *'arbeiten'* has to be integrated in the sentence structure. Furthermore, in order to obtain the correct interpretation, the hearer should be forced to revise the initial analysis.

ERP components reflecting both argument structure violations and subsequent reanalyzes should then be detectable during the auditive processing in sentence (3) as compared to sentence (2). This prediction is of particular interest since the parser normally (i.e., without prosodic cues) prefers to initially attach an NP to the *preceding* verb.[1]

This preference has comprehensively been discussed and explained by means of the principles of 'Late Closure' and 'Minimal attachment' in the framework of Frazier and colleagues (1978, 1995). It is not unlikely that this preference during reading results from a subvocal intonation strategy avoiding unnecessary pauses (i.e., increasing reading speed).

That is, in a reading study, one would expect sentence (2) to require a reanalysis and to be more difficult than sentences (1) and (3), respectively.

Experiment 1: 48 experimental sentences in each of the 3 conditions plus 144 filler sentences were presented auditorily in a pseudo-randomized sequence. 19 participants were asked to listen carefully and to answer comprehension questions in 20 % of the trials. EEG was recorded continuously from 25 electrode sites.
Error rates of the comprehension task varied between 5.7 and 7.6 % across conditions and did not differ significantly. The ERPs reflect both the intonational patterns per se and their adequacy with respect to syntactic requirements (i.e., the argument structure of the second verb).
Figure 5a shows the grand average ERPs of the three conditions from sentence onset until 4 seconds thereafter. Whereas the waveforms for conditions 2 and 3 are very similar, condition 1 shows a more negative potential between 1 and 2 sec, followed by a positivity between 2 and 2.7 sec, then by a second relative negativity from 2.7 to 3.3 sec and finally by a late positive component between 3 and 4 sec. These differences reflect the deviant prosodic phrasing and associated processing in condition 1 as compared to the other two conditions.

Due to their identical prosody, conditions 2 and 3 display the same ERP patterns until the second verb has been encountered. At about 2 sec after sentence onset, the intransitive verb in condition 3 elicits an N400-like negative component followed by a positivity (P600). These effects are also illustrated in figure 5b from onset of the second noun phrase until 3 seconds thereafter. (Note that the onset of the critical verb in figure 5b is at about 500 ms.)

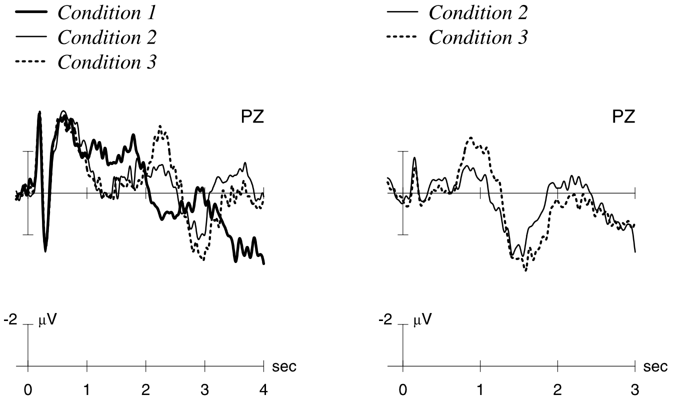


Figure 5a

Figure 5b

Figure 5. Grand average ERPs of 19 subjects at PZ. 5a shows the ERPs of all 3 conditions after sentence onset. 5b shows a comparison between conditions 2 and 3 after onset of NP2.

Similar ERP components have repeatedly been reported for violations of verb argument structure (Rösler et al., 1993; Osterhout et al., 1994; Frisch & Friederici, this annual report; Jacobsen & Friederici, this annual report). The N400 can be assumed to reflect the detection of the violation whereas the P600 might reflect subsequent processes of reanalysis. The data of the present study suggest that prosodic information is immediately used to guide parsing processes and can determine initial preferences of the structural analysis.

Experiment 2: An open question concerning ERP correlates of language processing is to what extent the components are influenced by the task employed in the experiment. For example, Hahne & Friederici (this annual report) found that a semantic task enhanced N400 effects whereas a grammaticality judgment enhanced P600 effects of words that violated both semantic and syntactic constraints.
A second ERP study has been conducted in order to examine the influence of task on the effects obtained in the first experiment. The sentence material was the same as in Experiment 1. However, the 16 new subjects had to judge each sentence with respect to prosodic adequacy. In 20 % of the trials the judgment task was followed by an additional comprehension question as it was in Experiment 1.

The prosody judgment data clearly demonstrate that condition 3 was perceived as prosodically inconsistent. Conditions 1 and 2 were judged as acceptable in 88 % and 81 % of the trials, respectively. In contrast, only 6 % of the trials in condition 3 were accepted.

Preliminary ERP data suggest that the critical verb in condition 3 again elicited an N400 component which was followed, however, by a large late positive waveform with a duration of several hundreds of milliseconds which had not been observed in the first experiment. The late positivity can be taken as further evidence for task effects in the time domain of the P600.

3.1.13 A cross modal lexical priming study explores filler-gap processing in German in relative clauses

Urban, S.,
Friederici, A.D.,
Swinney, D. &
Nicol, J.

Major linguistic (cf. Chomsky, 1981, 1986) or psycholinguistic theories (Frazier, 1995; Gorrell, 1995) assume an underlying sentence structure (or deep structure) from which each heard or read sentence is derived. This structure is a fixed word order postulated in order to describe several linguistic phenomena such as movement. Languages differ with respect to their underlying syntactic structure: i.e., for English, there is clear agreement that the deep structure is S-V-O whereas the underlying word order for German has the order S-O-V. Taking these assumptions into consideration, a specific construction such as an object relative clause contains an element moved overtly from its base position (indicated by *t* for trace) in deep structure. Consider the following example of an object relative clause:

D-structure:	*subject*	*object*	*verb*
	der Pilot	den	unterstützte
	the pilot	who	supported
S-structure:	*object*	*subject*	*verb*
	den	der Pilot	unterstützte
	who	the pilot	supported

Comparison of D- and S-structure reveals that these configurations contain a moved element (or, *filler*). A filler has a dependency relation to the vacated position (or, *gap*). This is indicated by indexation (i): *den*$_i$ *der Pilot t*$_i$ *unterstützte.* As documented in previous studies (cf. Nicol et al., 1989) dependencies between a moved element and its vacant position can be demonstrated by using a cross-modal lexical decision task. It has been shown for English that a semantic activation of a noun phrase is evoked at its potential gap location. This phenomenon, known as *antecedent reactivation,* occurs if: a) the semantic activation is reduced or eliminated prior to the gap site and b) an interaction can be postulated between different target types and the position in a sentence at which they are presented.

An additional fact of the experiment was whether processing differences could be found in previous experiments in English and similar German constructions. Two pre-tests (an RT-based item selection and a semantic priming study) had to be performed in order to prepare the appropriate stimulus material for the main experiment. This was designed to test whether semantic activation originating from the direct object of the main clause can be evoked at the gap position of the relative pronoun, as in:

1. sample sentence containing an object relative clause:
Die Lehrerin erhört den Piloten, den *^{1} der Klempner an besagtem gestrigen Abend *^{2} unterstützte *^{3}, ...
The teacher$_{\text{(fem)}}$ hears the pilot, who *^{1} the plumber on the mentioned yesterday evening *^{2} supported *^{3}, ...
(The teacher$_{\text{(fem)}}$ hears the pilot, who the plumber supported on (the already mentioned) yesterday evening, ...)

2. control sentence containing a subject relative clause:
Die Lehrerin erhört den Piloten, der *^{1} den Klempner an besagtem gestrigen Abend *^{2} unterstützte *^{3}, ...
The teacher$_{\text{(fem)}}$ hears the pilot, who *^{1} the plumber on the mentioned yesterday evening *^{2} supported *^{3}, ...
(The teacher$_{\text{(fem)}}$ hears the pilot, who supported the plumber on (the already mentioned) yesterday evening, ...)

Asterisks in the examples above indicate the points in time at which participants were confronted with visually presented targets while listening to an auditorily presented sentence. It was hypothesized that RTs for semantically related targets at test position 3 are significantly facilitated compared to test point 2, at which semantic activation should have declined. Participants had to perform a lexical decision task and a sentence verification task. The experimental stimulus set contained a total of 180 auditorily presented sentences (of which were 60 filler sentences).

The results showed two main effects: (1) a main effect of target type differences and (2) a main effect of test position of targets. The interaction between target type and test position of targets needed to demonstrate antecedent reactivation was not found. This finding differs from studies for the English language which could be due to the different D-structures for both languages. It may be that, in a verb-final language like German, a reduction of semantic activation of the object NP does not occur before the verb because of the base position of this NP.

3.1.14 A high density auditory ERP study: The processing of words, pseudowords and non-words

Maeß, B., Eulitz, C. & Friederici, A.D.

There is a recent discussion as to whether the cortical and subcortical networks involved in word, pseudoword and non-word processing are the same or not (1). It may be possible that the same structures are involved in both processes, but vary in degree of activation only (2). The presented experiment was designed to disentangle lexical, sublexical and non-lexical auditory processing.

Three different classes of auditory stimuli, matched in loudness, number of syllables and duration were presented: (1) "word" stimuli chosen from German content words with two syllables and a cvcv pattern, (2) "pseudoword" stimuli containing also two syllables and which are mainly derived from the word stimuli by altering one letter, (3) "inverted" word stimuli, constructed by replaying the word stimuli backwards.
For each stimulus class, 42 items were created. From all of these stimuli, targets were derived by superimposing the stimulus partly by a beep lasting 60 ms. Superposition was allowed only within a time window from 100 to 400 ms after stimulus onset. The subject's task was to detect the targets and to respond by pressing a button as quickly and accurately as possible. The probability of a target to appear was 15% for all stimulus conditions.
The experiment consisted of 3 blocks. Within each block, two of the three experimental conditions were presented in a randomized order with a varying inter stimulus interval of 2000 ms ± 200 ms. A training block was presented in advance without recording EEG data in order to familiarize the subject with the task and the stimuli. After passing the training block, all subjects identified the targets with an accuracy of 100%.
Measurements were carried out in an electromagnetically shielded room with a 128 channel EEG amplifier system. Electrode positions were given by a 120 channel cap and digitized by a 3D tracker system. All channels were referenced against the nose. Continuous data were recorded at a sampling rate of 250 Hz with a bandpass from 0.1 Hz to 30 Hz. Averaged waveforms for non-targets were calculated for each stimulus class of each block across epochs of 1200 ms including a 200 ms prestimulus baseline.

26 right-handed subjects (13 female), aged 19 to 27 years, participated in the experiment. Two subjects were excluded from further analysis because of their high blink rates (only 20% of the epochs was not contaminated by eye activity).

The time domain analysis shows an onset response (0 ... 200 ms) which is nearly independent of the stimulus class in signal shape but not in amplitude. It can be described as a broad central negativity peaking at 180 ms and starting to rise at about 100 ms post stimulus onset.

Between 250 and 300 ms there is a smaller frontal positivity elicited by the conditions "word" and "pseudoword". The response to the "inverted" stimuli is much weaker and differs in spatial distribution. "Word" and "pseudoword" cause a central negative peak at 400 ms. There is no significant difference in amplitude between the conditions "word" and "pseudoword". "Inverted" does not show a peak at 400 ms. The spatial potential distribution of the "inverted" stimuli is weaker and frontally shifted in comparison to the others. "Word" and "pseudoword" elicit a second negative peak between 550 and 600 ms. They differ only slightly in amplitude at some electrodes. But, a comparison of the potential distributions yields similarities between all non-language stimuli on one side and both "word" stimuli on the other.
From the N550 peak to the end of the epoch (1000 ms) there is no significant difference between "word" and "pseudoword" responses. At 550ms, it reaches approximately the same level as in all other conditions, excepting the occipital electrodes. The frontal, not lateralized negativity, peaking at 600 ms, is observed. On some electrodes, activity remains until the end of the averaged epoch at 1200 ms.

Our findings show, that at an upperlimit of approximately 450 ms the processing of "word" and "pseudoword" stimuli elicits an almost identical potential distribution on the scalp. The evoked responses of these two conditions differentiate at a point later than 500 ms. At about 580 ms the responses to the "inverted" and "pseudoword" stimuli are comparable but differ from those to "word" stimuli. Because of the same potential distribution, the 400 ms peak and 580 ms peak can probably be identified as the known N400. The question arises as to whether or not the two peaks reflect two subprocesses of lexical processing. The observed ERP pattern may be caused by at least two different subprocesses: one of which could be defined as lexical search, and one of which may be involved in creation of associations. "Pseudowords" may have to pass the former but not the latter subprocesses.

Lateralization effects of motor function and speech studied with fMRI

3.1.15

Hund, M.,
Lex, U.,
Friederici, A.D. &
von Cramon, D.Y.

The aim of this study was to determine hemispheric lateralization effects of speech and language function by means of functional fMRI related to behavioral tests. The activation in the inferior prefrontal gyrus (Brodmann Area 45, 46, 47) during lexical and semantic encoding tasks may reflect hemispheric dominance for speech (Desmond et al., 1995). Self paced random finger tapping of the right and left hand as well as bilaterally was applied to assess the dominance of primary motor cortex and SMA. Finally we addressed the question, whether lateralization effects of motor and language functions agree with each other and whether they can be reproduced by means of other behavioral tests.

Recent studies, based on the method of Wada-testing (intracarotid injection of sodium amytal), showed correlations between handedness and speech dominance. Risse et al. (1997) reported among 87% of studied right handers but only in 62 % of left handers speech representation in the left hemisphere. Bilateral organization and right hemispheric language dominance appeared in 9% and 4% of right-handed but in 20% and 18% of left-handed subjects. Knowledge about the localization of cortical speech functions is useful for several clinical and rehabilitative aspects. Preoperative neurosurgical interventions in patients with epilepsy and the reorganization of speech functions in patients with aphasia and motor paresis are important issues.

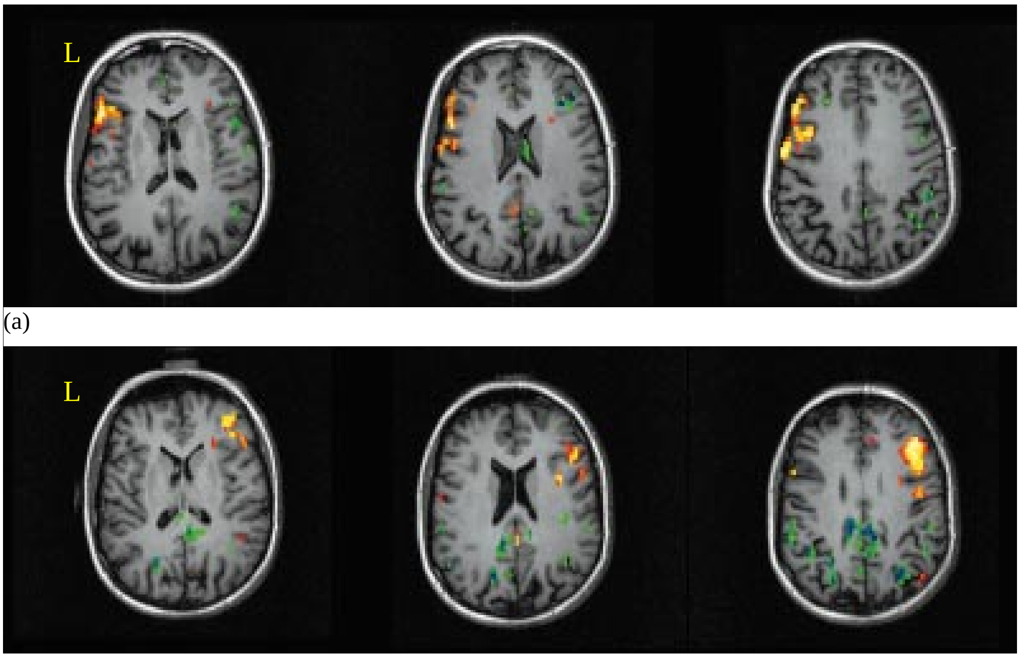
We included 22 normal subjects, half left- and half right-handed, in our study (age x_{mean} = 23.73, 11 men and 11 women). Each person performed the Edinburgh-Handedness-Inventory (EHI) and the Hand-Dominance-Test to assess the degree of handedness. Speech lateralization was determined in behavioral terms using an auditory dichotic listening test (Haettig and Disch, 1997). In the task 10 monosyllabic pairs of rhyme words were aurally presented, simultaneously to the left and the right ear. The subject had to name the word, he understood clearest. The dichotic listening is based on the principle that, whenever two auditory signals are put in conflict, the contralateral input is suppressing the ipsilateral signal. The ear, contralateral to the dominant language cortex, should thus project stronger than the ipsilateral ear.

During the fMRI-experiment 640 German common words composed of two syllables (length: 4–7 letters) were presented visually every two seconds in a word classification task. The words were half and half nouns or verbs and abstract or concrete and divided in eight blocks per 20 words with a pseudorandom presentation order. In four different categorization tasks the subjects had to judge whether the presented words were a) nouns or verb: lexical encoding; b) abstract or concrete: semantic encoding; c) written in upper or lower case: structural encoding and d) whether the words were written with spaces in between or not: structural encoding. The baseline condition was either one of the two structural encoding conditions or a resting condition (dark desktop with five white x for 40 sec. duration).

Functional MRI-recording was performed using echo planar imaging (seven axial slices, 7 mm slice thickness, TR=30 msec., TR=2 sec., matrix 128 x 64). FMRI data evaluation was performed with the Brain-Software (Kruggel et al., 1995). Functional images were created by generating statistical zmaps with z-values >5 on as a single pixel level. The regions of interest were characterized in size, volume and intensity of activity.

Behavioral tests. EHI-evaluation showed a mean value of 82.8% (SD=16.28) in the group of right-handed subjects and a mean value of – 69.1 % (SD=21.55) in the group of left-handed subjects (positive values indicating left hemispheric dominance). In the dichotic listening test we found mean lateralization indices of 1.81 (SD=0.92) for right and – 0.71 (SD=1.30) for left handers. The correlation between EHI and the dichotic listening test was 0.77.

fMR-experiment. Preliminary fMRI data analysis showed extended activation of the inferior frontal gyrus (pars triangularis and pars orbitalis) in all studied subjects during the semantic and lexical encoding conditions. The most prominent activations of primary speech cortex were seen in the semantic encoding task with the resting condition used as baseline. However, the best lateralization effects could be detected in the semantic decision task applying the structural condition as baseline. Right-handed subjects showed clearer lateralization effects than left-handed ones. Left hemispheric language dominance was assessed in 10 out of 11 studied right handers. In the group of left handers, four were left dominant, four bilateral and four right dominant for speech, based on fMR-activation criteria.



(a)

(b)

Figure 6. Activations in the primary speech cortex of a right handed (a) and a left handed control subject (b).

Prominent activations were also observed in almost all subjects in the middle frontal gyrus, in the thalamus, and caudate nucleus. Additionally the lexical encoding paradigm also disclosed areas of increased activation in the precentral gyrus, transverse temporal gyrus and in the intraparietal gyrus.

Thus, fMR-imaging technique can detect lateralization effects of primary language cortices applying word classification tasks. The preliminary fMR-data evaluation showed the best agreement of fMR-based functional lateralization effects with behavioral indices gained from the dichotic listening test. To a lesser extent, EHI and fMRI-based hemispheric speech dominance deliver comparable results. To address the question of cortical speech reorganization following brain lesions in the chronic stage: After establishing the paradigms in a normal control group data acquisition in patients with chronic aphasia is ongoing,

3.1.16 A modality comparison of the sequential semantic priming paradigm: Behavioral and event-related potential evidence

Kotz, S.A.

Numerous behavioral and event-related potential studies (Holcomb & Anderson, 1993; Neely, 1991) have shown that the processing of a word is facilitated when it is preceded by a semantically related word (*word pair priming*). However, the debate is still ongoing as to whether automatic or controlled processing mechanisms underlie the priming effect.

Some priming research has focused on whether *types of semantic information* and *type of presentation* (word pair or word list) can influence automatic or controlled processes (Fischler, 1977; Moss et al., 1995; Shelton & Martin, 1992). Shelton & Martin (1992) reported associative (e.g., *dog-cat*) and semantic (e.g., *horse-cow*) priming effects using a visual paired lexical decision task (LDT), but only associative priming when prime and target words were presented in a word list. In contrast, Kotz & Holcomb (1996) reported comparable behavioral results for the visual word list LDT, but ERP priming effects (N400) for associative and non-associative semantic relations. In addition, there were latency and distributional differences of the ERP priming effects for the two types of semantic information.

The current experiment set out to replicate and specify the effects from the earlier visual ERP study. We also extended the examination of priming effects to the auditory domain in order to determine whether the priming mechanism(s) operate in a modality specific way. We were specifically interested in onset latency difference and topographic differences in associative and non-associative semantic relations. It has been argued (Sabol & DeRosa, 1976) that an early onset of priming suggests lexical access. Furthermore, there is fMRI evidence (Beeman, 1996) that shows activation in right frontal regions for non-associative semantic relations.

Subjects listened to or saw 640 items in two blocks (320 items each) of a word list. Blocks were used to examine whether types of semantic information were evaluated differently at the beginning and end of a word list. Types of semantic information were normed according to associative and semantic strength level and familiarity that defined 'relatedness' between critical targets and primes. Critical target words were also matched for word length and frequency. Word list presentation was balanced across subjects and response hand in both modalities. Subjects responded to every item in the word list. A total of 32 subjects (16 per modality) participated in the visual and auditory version of the ERP/RT LDT experiment. ERPs were measured from 74 electrode sites and RT and accuracy rates recorded.

Reaction time results showed a significant interaction between type of semantic information and relatedness in the auditory modality. These data indicate that in word list LDTs only associative priming occurs. Similar to the previous visual study, the critical interaction was weak in the visual modality. However, an interaction of type of semantic information and block showed that type of semantic information was significantly different in the second half of the visual word list. The accuracy data was comparable across types of semantic information in both modalities. Overall, subjects made more mistakes for unrelated than related targets.

A first tentative conclusion is that subjects evaluate types of semantic information differently at the beginning than at the end of a visual word list, but not in the auditory word list. Therefore, the main effect of type of semantic information in the second block of the visual word list might indicate a learning effect.

The analysis of the ERP data and statistical procedures are currently in progress. Preliminary visual inspection shows latency and topographic differences for type of semantic information in both modalities.

The influence of first language word ambiguity during second language word access

3.1.17

Kotz, S.A. &
Wagner, S.

There has been a long-standing debate about whether first (L1) and second (L2) language word recognition is interactive or not. More specifically, there is evidence for mediated lexical access, while conceptual activation is assumed to be a modal (Keatley, 1992). Support for mediated lexical access comes from naming and translation studies (e.g., Kroll & Steward, 1994). However, some cross-language priming studies (e.g., Altarriba, 1991) do not fully support mediated lexical access. At most, the controversial results in the literature indicate that mediated lexical access can be subject to degrees of language fluency.

The current study investigated the degree of L2 fluency on lexical access using the cross-modal priming paradigm. Cross-modal priming shows that even in a biasing context all meanings of an ambiguous word are activated at the time of the critical word presentation. Along these lines we assumed that L1 word ambiguity should result in a prolonged reaction time for the unambiguous L2 translations. If lexical access in L2 is mediated by L1, then L1 word ambiguity should result in an 'inhibition 'effect during L2 lexical access.

In a first step, two norming procedures were applied to a list of English words with ambiguous German word meaning, and to a list of German words with ambiguous English word meaning. Norms were used to select those English items as test material that had a strong, medium or weak ambiguous German translation. Subjects were native speakers of German who had either spent more than 50 weeks or less than 50 weeks in an English speaking country. Subjects answered a bilingual questionnaire that evaluated their second language fluency. All of the selected speakers evaluated their second language skills as fluent.

In the experimental task, subjects listened to English sentences with embedded unambiguous target words. 250 ms after target word offset an English probe was visually presented. The meaning of the probe word was equivalent to one of the ambiguous

German meanings of the English target word. Sentences followed by unrelated probes, pseudoprobes and filler sentences were included. The subject's task was to decide whether the visually presented word was an English word or not. Reaction time and % Correct measures were taken. The following example illustrates the critical experimental sentences. In this sentence the words '*jaw'* and '*pine'* are unrelated English translations of the ambiguous German word '*Kiefer'*.

> *Cederic broke his* ***jaw*** *by running into a post on his bicycle —* ***pine.***

Results indicate that subjects with less than 50 weeks of L2 experience show a diverse cross-modal priming picture of the three levels of word ambiguities. Subjects with more than 50 weeks of second language experience showed a similar and consistent 'inhibition' effect for the strongly, medially and weakly ambiguous German meaning equivalents of the English target words.

This evidence further supports a model of mediated L2 lexical access. However, the exact timing shift of mediated L2 lexical access as a function of L2 fluency remains to be further explored. Work is underway to address this question.

3.1.18 Effects of grammatical gender on picture and word naming: Evidence from German

Jacobsen, T.,
Bates, E.A. &
Friederici, A.D.

In collaboration with Bates from the University of California, San Diego, Jacobsen and Friederici set out to investigate the effect of prior gender information on picture and word naming latencies. Named targets were nouns or pictures of concepts with names that feature masculine, feminine and neuter grammatical gender in German. Simple sentence fragments, which were either gender congruent (1a) or incongruent (1b) with the target or provided a gender-neutral baseline (2) were presented auditorily as primes prior to the pictures (a modified replication of Hillert & Bates, 1996) or words in a completely counterbalanced design.

(1a) *Dies ist der / die / das ...* <gender-congruent target>
This is the$_{\text{masc}}$ / the$_{\text{fem}}$ / the$_{\text{neut}}$ ...
(1b) *Dies ist der / die / das ...* <gender-incongruent target>
(2) *"Bitte sage jetzt ..."* */"Sage jetzt bitte ..."*

Relative to baseline, reliable facilitation and inhibition effects were observed for the picture naming latencies. For the word naming latencies only inhibition effects were obtained. The table shows mean picture and word naming latencies (mean), standard deviations (stddev) and standard errors (stderr) aggregated over subject means (N = 24) for the gender congruent, baseline, and gender incongruent conditions of Experiment 1 (picture naming) and Experiment 2 (word naming).

	picture naming			word naming		
	mean	stddev	stderr	mean	stddev	stderr
congruent	644	49	10	479	32	7
baseline	657	48	10	479	30	6
incongruent	685	77	10	493	40	8

The results suggest that gender information differentially affects picture and word naming. The data can be accounted for by a serial model in which a postlexical syntactic integration and congruency check affects pronunciation latencies, but also by a fully interactive model of lexical processing.

This research program examines memory systems and processes and their functional representation in the brain. In accordance with recent developments in memory research, memory is regarded as process specific, that is memory performance is examined in terms of specified processes such as encoding, storage and retrieval. Additionally, memory is considered to be comprised of multiple systems, such as working memory, semantic and episodic memory. 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 information specific maintenance functions that enable storage of information.

The ongoing research focused on the functional characteristics and neuronal correlates of rehearsal processes in working memory by means of neuropharmacological measures (3.2.1) and ERPs recorded from the scalp (3.2.2)(3.2.3) and from medio-basal temporal lobe recording sites (3.2.4). We furthermore try to specify the interaction of executive control and active maintenance functions in working memory using memory coordination (3.2.5)(3.2.6), task switching (3.2.7) and interference (3.2.8) experimental paradigms.

Another research focus is on the neurocognitive systems underlying recognition memory. We study the memory processes (explicit or implicit) and the representational systems (image-based vs. verbal) that enable recognition memory performance. ERP measures are taken in direct (3.2.9) and indirect tests (3.2.10) of recognition memory for pictures and words as well as in a combination of both tests (3.2.11). Last but not least, we evaluate auditory memory functions and their neuronal correlates by means of ERP measures (3.2.12) and by a combination of ERP and fMRI measures (3.2.13).

3.2.1 Inhibition and rehearsal in directed forgetting: Behavioral and pharmacological investigations

Müller, U. & Mecklinger, A.

In every-day life it is beneficial to forget information that turned out to be wrong or that is no longer relevant. To further characterize the neurocognitive nature of memory-related inhibitory processes we used a modified version of the item method directed forgetting (DF) paradigm (Basden et al., 1993). The DF method investigates the ability to forget items that one has recently attended to while at the same time remembering other items presented in the same context. In a behavioral experiment we tried to separate the contribution of differential encoding versus retrieval inhibition to recognition differences between to-be-remembered (TBR) and to-be-forgotten (TBF) items. The finding of impaired inhibitory mechanisms in older adults (Zacks & Hasher, 1994) stimulated the idea to test the dopaminergic modulation of inhibitory processes in normal volunteers.

The first step in establishing a German version of the DF paradigm was a *categorial noun generation* experiment performed with 139 undergraduate students (107 female, mean age 22.2 [18-34]) in order to normalize the stimuli (categorial-related nouns) in terms of word frequency and typicality. The DF method described by Zacks et al. (1996) was then modified in several ways to make it more difficult and memory specific: (1) Instead of lists with 24 words we presented 30 words, five per category. (2) A 2500 msec delay was introduced between item and cue ("remember"/"forget") presentation to activate memory in addition to attentional processing. (3) The immediate recall was time limited. The delayed recognition task had two levels, (4) a forced-choice "old"/ "new" distinction that allows measure ment of *reaction times*, and (5) a "*recollect*"/ "*know*" decision for items that have been classified as "old", a procedure that is claimed to dissociate recognition judgments based on conscious recollection from those based on familiarity (Tulving 1976, Basden & Basden, 1996). Table 1 shows the results of the *validation experiment* with 16 young adults. There were significant directed forgetting effects (poorer performance for TBR items) in all recognition tasks. In the immediate recall there was also a category specific effect, namely increasing performance with decreasing numbers of interfering "forget" items within a given category.

		remember items	forget items	lures
immediate recall	%	55.4 ± 5.7	4.3 ± 3.1	
item recognition	%	82.6 ± 12.2	54.5 ± 9.8	23.7 ±12.0
	Pr	59.8 ± 15.6	32.5 ±13.2	
	RT [msec]	730 ± 133	802 ± 134	856 ± 120
recollection rate	%	55.5 ± 14.1	21.8 ± 8.1	6.8 ± 6.2
	Pr	57.7 ± 15.2	20.5 ± 7.8	
list recognition	%	71.0 ± 7.6	46.1 ±12.9	32.9 ±14.4
	Pr	46.9 ± 6.9	-27.0 ±14.2	

Table 1. Immediate recall and differential recognition after directed forgetting (mean±SD)

Our next behavioral experiment (n = 24) investigated the effect of rehearsal time, i.e. the time from cue onset until presentation of the next item, on directed forgetting. The main results can be interpreted in the light of levels of processing and neuropsychological theories of memory consolidation (Rugg et al. 1997). Reducing the time that can be used to selectively rehearse the task-relevant information significantly impaired memory performance (recall, recognition, and recollection) for TBR items. The recognition of TBF items was equal in all conditions, whereas the number of recollection responses significantly increased with decreasing rehearsal time (Figure 1).

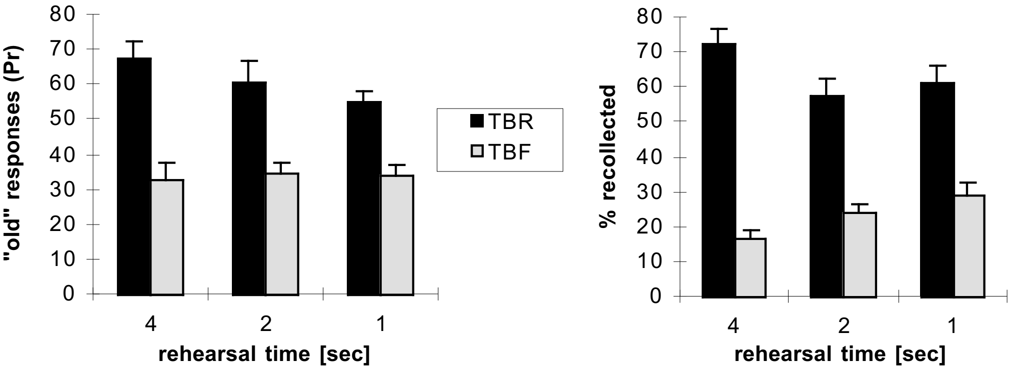


Figure 1. Influence of decreasing rehearsal time on recognition (left) and recollection (right) after directed forgetting (mean±SE).

The last experiment was a placebo-controlled pharmacological cross-over study of young volunteers (n = 16) using pergolide, a D1/D2 dopamine agonist, in a dosage of 0.1 mg that had been shown to facilitate visuo-spatial short-term memory in a previous study (Müller et al., in press). We wanted to test the hypothesis that dopaminergic activation does improve memory-related inhibition of "forget" items, presumably by increasing cognitive signal-to-noise ratio via prefrontal mechanisms (Servan-Schreiber et al., 1990). The 4 sec version of the DF paradigm was chosen because it produced the most stable semantic interference effects in immediate recall. In contrast to our predictions pergolide showed no significant effects. It did not facilitate memory performance for TBR items or inhibit recognition or recollection of TBF items. Post-hoc data analysis revealed trends (p<0.1) toward poorer immediate recall, especially for those categories that included "remember" and interfering "forget" items,

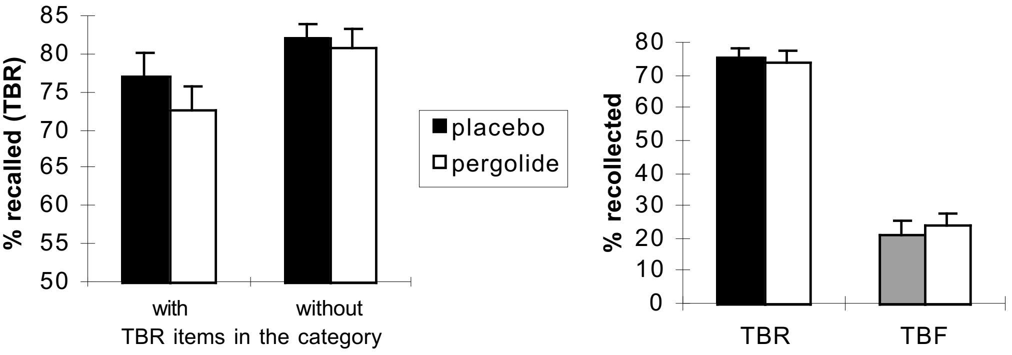


Figure 2. Effects of pergolide on immediate recall (left) and recollection (right) after directed forgetting (mean±SE).

and of slightly improved recollection of TBF items (Table 2). These unpredicted effects have to be replicated and should be interpreted cautiously. Based on these preliminary observations and our previous findings of slowing of information decay after dopaminergic stimulation (Müller et al., in press) we conclude that pergolide might favor deeper encoding of "forget" items and impair the recollection of "remember" items. In young healthy volunteers, however, inhibitory processes seem to function quite optimally. Further pharmacological studies will have to be performed with aged subjects or prefrontal patients in order to show an improvement of memory-related inhibition by dopaminergic stimulation.

3.2.2 Cognitive correlates of slow cortical potentials during retention of visually coded information in working memory

Bosch, V.,
Mecklinger, A. &
Friederici, A. D.

In 1996 (MPI Annual Report) we reported several EEG-experiments which used the S1-S2 cueing paradigm to examine object and spatial working memory. Subjects were required to retain object and spatial information in working memory across a 5s S1-S2 delay. S1 consisted of two distinct geometrical objects at two positions in a three-dimensional space. In one half of the trials S1 and S2 were figural (figural condition), whereas in the remaining half of the trials S1 was figural but S2 consisted of objects and their positions presented as written words (verbal condition). Subjects had to decide if either object or spatial information in S2 was the same as S1 ("old") or not ("new"). Whether the required comparison was of object or spatial information was indicated by a cue presented midway through the S1-S2 delay. Because these conditions were blocked and the subject knew the format of S2, this experimental manipulation was assumed to induce either verbally or figurally based rehearsal.

We demonstrated that retention of spatial information evoked a parietally (Pz) focused negative slow potential (SP) and a left lateralized negative SP at frontal recording sites. Furthermore, retention of object information led to a posteriorly (POz) focused positive SP and a negative SP at frontal recording sites which was similar, although more negative, to the one obtained in the spatial condition. These patterns where highly similar in both the verbal and the figural condition. A possible interpretation is that parietal negative SPs reflect spatial operations (corroborated by the literature) whereas the frontal SP is a correlate of verbal rehearsal. Because positive SPs probably reflect inhibitory-like processes (see e.g. McCallum & Curry, 1993) the posterior positive SP may reflect inhibition of higher cortical visual areas in favor of verbal rehearsal in the object task.

This year we tested this interpretation in two experiments which used difficult-to-name objects ('Klingon Letters') and spatial locations. The stimuli consisted of two objects presented on a virtual three-dimensional horizontal plane. In the first experiment the amount of verbalization during retention was tested utilizing articulatory suppression in exactly the same way as in Experiment 1 from '96. Unlike the '96 result, recognition performance was the same in the suppression condition and the non-suppression condition for both the object and the spatial task, indicating that verbal rehearsal did not occur.

Experiment 2 was similar to Experiment 4 from '96 with the exception that the Klingon Letter stimuli were used and the verbal condition was omitted. In both the object and the spatial task a frontal negative SP emerged during the retention phase. These SPs were highly similar to those obtained in the previous experiments. Moreover, in the object task a pronounced posterior positive SP was observed, whereas in the spatial task the parietally focused negative SP appeared to be absent. A subsequent analysis showed that the apparent absence of the parietal negative SP was due to an overlap with a posterior positive SP that stemmed from the partial retention of object information in the spatial task.

The absence of verbal rehearsal strategies in Experiment 2 has two implications. First, the frontal negative SP-pattern is not a correlate of verbal rehearsal and instead may reflect general control operations of working memory. Second, it is quite unlikely that the posterior positive SP reflects inhibition of higher cortical visual areas. We attempted to determine the cognitive correlate of the posterior positive SP by testing the possibility that this potential has its origin in the basal part of the temporal lobe, namely the mid-anterior fusiform gyrus. In a recent fMRI study this area has been shown to play a crucial role in the perception of faces but a minor role in retention (Courtney, Ungerleider, Keil & Haxby, 1996; 1997). Negative SPs generated in this cortical area produce a positive voltage at parieto-occipital electrode sites. In a forward computation for dipolar sources, two hypothetical dipoles, highly constrained in location and direction by the findings of Courtney et al., were placed bilaterally. Additionally, one dipolar source's location was estimated in the posterior cingulate gyrus. It accounts for the Contingent Negative Variation (CNV) prior to S2. Another source was placed in the superior frontal gyrus to account for the left frontal negative slow potential (Figure 3).

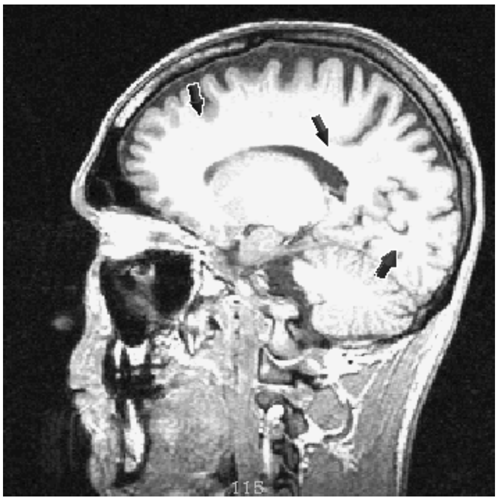


Figure 3. Placement of the sources in the dipole model.

The resulting scalp topography of the forward solution was nearly identical to that observed in the EEG-experiments. In a backward computation with dipole activation strength serving as the only degree of freedom, the model accounted for about 90% of the variance in the data at each time step in the time interval from 1000 to 2500 ms after cue onset. These results strongly suggests that the mid-anterior fusiform gyrus is involved in retention of visually coded object information in addition to perception. They are also consistent with those models of working memory that assume that prefrontal cortical areas mediate general control functions, whereas posterior cortical regions are more engaged in active maintenance of information.

3.2.3 Event-related potentials dissociate visual memory processes under categorial and identical matching conditions

Berti, S., Mecklinger, A., Geissler, H.-G. & Lachmann, T.

Event-related potentials (ERPs) have been successfully employed to examine the functional and neuronal characteristics of working memory processes. Negative slow waves in the ERP were found to be specific for the attributes and the amount of information held in working memory during retention intervals. In the present study we examined ERP waveforms in a Posner-like matching task with structured 5-point patterns as stimulus materials. S1 and S2 were separated by a 1500 ms retention interval and upon presentation of S2 either categorial or physical identity judgments were required.

Based on transformation rules (rotation in 90° steps and mirroring) the 5-point patterns can be divided into 17 equivalent classes (EC) of different sizes (1, 4, 8), that are assumed to differ in complexity. For category judgments (CM) S1 and S2 had to be from the same EC-set whereas for physical judgments (IM) S1 and S2 had to be identical. In prior studies using behavioral measures it was shown that RT covaries with the size of the equivalent class in the CM condition but not in the IM condition. These results have been taken to support the guided inference model (Geissler, 1994), that assumes that in CM conditions the complete set is activated and that decisions are made after locating the actual pattern in the activated set. In the present experiment 10 subjects performed two blocks of 576 trials each in either the CM or IM condition. S1 and S2 were presented with 150 ms duration. ERPs were recorded from 19 electrodes equally spaced across the scalp and were analyzed for the (S1-S2) retention interval and the S2 response intervals.

Subjects made more errors in the CM (6%) as compared to the IM (3.7%) condition. Consistent with prior studies employing these stimulus materials, same responses were faster in the ES-4 than in the ES-8 condition in the IM condition (498 ms vs. 537 ms) and the CM condition (583 ms vs. 676 ms). Moreover, same responses in the CM condition were faster for physical than for categorical matches in both ES conditions. For the ERPs recorded in the retention interval the following pattern of results was obtained: Stimuli in the CM condition elicited larger P300 components at around 400 ms than in the IM condition. In the IM condition the P300 was followed by a broadly distributed negative slow wave that extended until the end of the S1 interval. Both effects were unaffected by the ES-factor. Moreover, patterns of ES-8 elicited a posteriorly distributed negativity at 350 ms (N350) that was of comparable magnitude in both judgment conditions.

In parallel to the RT results, the P300s evoked by S2 had longer peak latencies for ES-8 than for ES-4 during categorial judgments but not during physical judgments. Notably, in contrast to RTs, no differences in P300 latency were found between physical and categorial matches in the CM condition.

The enhanced P300 components evoked by S1 in the CM condition support the view that S1 was more elaborately processed in the more demanding (CM) judgment condition. Based on the early onset and the long temporal extension of the negative slow wave in the IM condition it can be assumed that for identity comparisons sensory input is directly transferred to a visual retention buffer and maintained in this buffer until the end of the retention interval. The N350 effect that was observed in both judgment conditions might suggest that subjects classify the visual patterns according to their complexity, irrespective of the judgment condition. The P300 latency results replicated the RT pattern and were thus consistent with the guided inference model proposed by Geissler (1994). The ERP pattern evoked in the retention interval provides a detailed picture of the cognitive processes enabling memory-based comparison and judgment processes.

3.2.4

Insight out: Intracranial and scalp recorded ERPs correlates of visual working memory

Mecklinger, A., Grunwald, T., Pezer, N., Lehnertz, K., Penney, T.B. & Elger, C.

Recordings of intracranial event-related potentials (ERPs) from depth electrodes in patients with temporal lobe epilepsy are a valuable tool for identifying the contribution of the medial temporal lobe to a variety of memory demanding cognitive processes. Moreover, the simultaneous recording of intracranial and scalp recorded ERPs during cognitive tasks reveals important insights about the neuronal mechanisms contributing to scalp recorded ERPs. In cooperation with the Department of Epileptology at the University of Bonn we examined scalp recorded and intracranial ERPs evoked by visual target stimuli in two tasks typically used to elicit P300s. P300 elicitation depends on the contents of a memory buffer and is assumed to reflect the updating of working memory. Two versions of a visual oddball paradigm were used in which subjects were required to identify either target objects or target locations within a 4 x 4 spatial matrix (see Mecklinger et al., in press). Bilateral depth electrodes were implanted in the medial temporal lobes along the longitudinal axis with the amygdala as the target of the most anterior electrode. Electrode distance was 4 mm and electrode placements were verified by post-implant CT and MRI. Scalp recordings were taken from Fz, Cz and Pz and bilateral frontal and parietal electrodes. To date, ERPs from 15 subjects have been obtained. Target objects evoke a pronounced parietal maximum P300 component at the scalp. For target locations this P300 was delayed and also smaller in amplitude. Analyses of the ERP in the non-epileptic temporal lobe revealed a negative potential peaking at around 600 ms at hippocampal recording sites (MTL-P300). It was largest in amplitude for target objects that also revealed pronounced scalp recorded P300. Conversely, for target locations the MTL-P300 was virtually absent. These initial results have two implications: First, they support those models of P300 generation that assume that the major part of the neuronal network involved in P300 generation and thus the updating of working memory is located in neocortical brain regions. Second, they also suggest that the MTL-P300 and the scalp recorded P300 to some extent reflect dissociable processing functions.

3.2.5 Coordinating information in working memory: An investigation of the coordination process using the memory coordination paradigm

Bublak, P., Schubert, T. & von Cramon, D.Y.

According to Yee, Hunt & Pellegrino (1991), coordination can be defined as the establishment of a goal-directed correspondence between two types of information. Carlson, Wenger & Sullivan (1993) have shown that coordination of information from two different working memory subsets leads to an increase in response times and a decrease of accuracy compared to a control condition where no coordination is demanded. These authors assume that such coordination costs arise during the response phase, when an appropriate response strategy has to be generated. This strategy is an economic way of corresponding two activities, namely readout and report.

This interpretation implies two hypotheses concerning the coordination process. First, it should be possible to plan a strategy in advance if information concerning the action goal is provided earlier during task progression, i.e. well before the response phase. Second, it could be assumed that the response strategy has to be adapted to a specific motor output program and, hence, that different programs require different coordination strategies. We examined these two questions by using a memory coordination paradigm, in which two subsets of items have to be integrated with each other prior to recall. This task is assumed to be a representative working memory task because it has two basic demands: (1) a storage demand and (2) an executive demand to manipulate memorized items.

The first question was investigated by manipulating the time at which information about the demand to perform a coordination task was provided to subjects during task progression. Subjects had to encode a list of four digits, presented successively at the center of the screen. The first two digits were shown in green, the last two digits in red color. A cue was shown either before encoding (condition "*v*"), or before (condition "*m*") or after (condition "*n*") a memorizing period. The color of the cue determined the mental operation to be executed by the subject. A black cue (condition "*short term memory*") indicated, that recall was demanded in the same order as the digits were presented (e.g. digits 3 6 7 5 had to be recalled in that order). A green cue (condition "*easy working memory*") indicated, that subjects had to reorganize the digits prior to recall, so that the first green digit is followed by the first red one, then the second green digit and the second red digit (hence 3 6 7 5 becomes 3 7 6 5). Finally, a red cue (condition "*difficult working memory*") indicated, that recall was demanded in the order "first red digit, first green digit, second red digit, second green digit" (i.e. 3 6 7 5 becomes 7 3 5 6). For recall, a two-alternative forced choice mode was used. Four pairs of digits were successively presented, one digit to the left, the other to the right of center. Each digit was part of the memory list, but, according to the task determined by the cue color, only one digit per pair was appropriate for response. Subjects had to press the left/right response button, if the left/right digit was the correct answer.

The results indicate that coordination costs are diminished, but by no means abolished, when information concerning coordination is presented earlier during task progression. A subgroup of subjects was able to carry out coordination prior to recall in cue condition "*v*". Even this group, however, showed coordination costs as soon as the cue was presented after encoding (condition "*m*"). Thus, coordination costs can be divided into at least two different subcomponents: one component is due to the need to carry out coordination within working memory, the second component was depends on the degree to which a coordinated new sequence can be practiced prior to recall. Both components contribute to coordination costs in cue condition "*n*".

The second assumption was that a coordination strategy is adapted to the specific motor program demanded during recall. To test this hypothesis we manipulated the motor program to be carried out during recall. It was hypothesized, that this would influence the coordination strategy. We used the "*short term memory condition*" and "*difficult working memory condition*" described above. Two *motor program conditions* were realized. In the *first* condition, the first two items had to be reproduced by using one hand (e.g. the left one), the last two items by using the other hand (e.g. the right one). In the *second* condition, the responding hand changed with every item to be reproduced. As expected, response time curves for the *difficult working memory* condition (with coordination) were different depending on the motor condition. This result corroborates a close relationship between working memory representation and motor programming for recall. More precisely, information stored in working memory is used to guide action, but specific motor demands of the action system influence the way stored information is organized. Thus, working memory storage has to be regarded as a dynamic, not a static representation.

Subcomponents of executive control: Dynamic aspects

3.2.6

Bublak, P.,
Mecklinger, A.,
von Cramon, D.Y.,
Göritz, A. &
Springer, A.

The concept of executive control is central to theories of cognitive psychology. Executive control is assumed to operate from the highest level within the cognitive architecture, a position that allows organization of lower level cognitive functions in guiding goal-directed action. In working memory models executive processes are regarded as those functions that go beyond the aspect of simple storage of information. They rather denote the capacity to transform and manipulate stored information in accordance with a subjects' intentional actions.

There are at least three questions concerning executive functions which are currently under debate. Their solution is considered as one important task of current cognitive psychological research. The *first question* refers to the division of executive functions into subcomponents. While it is widely accepted that "central executive" is too global a concept as to provide much explanatory value, there is less agreement about which elementary constituents should be regarded as the essential ones. The *second question* is concerned with the relationship between these constituents. They could only be regarded as separate if a functional segregation between them is demonstrable. The *third question* is related to the hierarchical status of executive functions. A continuum can be assumed between controlled and automatic processes. Controlled processes require executive functions, whereas with increasing task repetition executive functions are less involved and finally a completely automatized process runs without executive control

(Schneider et al., 1994). The implication is that executive control processes mediate automatization, but cannot be automatized themselves. In other words, a controlled process should be separable from the controlling authority.

The current project is aimed to investigate these questions in more detail. To that end, we focus on two experimental tasks which are assumed to realize two separate executive functions: a task switch paradigm (see 3.2.7) and a memory coordination paradigm (see 3.2.5). Duncan et al. (1996), for example, made the basic assumption that executive control is involved everytime a subject faces novel stimuli or situations, i.e. when there is absence of familiarity. Furthermore, they consider executive control to be necessary to prepare a sequence of actions for achieving a prespecified goal. These concepts can be operationalized and experimentally investigated. Within this context, a prespecified goal is determined by the instructions a subject has to obey to perform an experimental task successfully. Control is involved when a shift between instructions has to occur, i.e. when a currently running action has to be interrupted and another action has to be executed. These kinds of experiments are known as "task-switch" experiments (Allport et al., 1994; Rogers & Monsell, 1995).

The requirement to prepare a sequence of actions by using information stored in working memory can be realized by a coordination paradigm. For example, Carlson et al. (1993) introduced a task where a number of memory items had to be integrated with each other before a new sequence of the items could be reported. This paradigm stresses active processing and manipulation of temporarily stored information to guide a sequence of actions. Both paradigms provide a measurement of costs caused by the executive processes necessary to perform the tasks. Hence, switch costs result from the difference between the experimental condition (switch) and a control condition (no switch). Similarly, coordination costs result from the difference between the experimental task (coordination) and a control condition (no coordination).

We used two such paradigms in a training procedure in which subjects receive practice in only one task. Thereby, we wanted to examine (i) whether task switch and memory coordination are true executive functions, and (ii) whether these functions are dissociable.

In a pilot study, two groups of four subjects each were trained during eight sessions. In the first session (baseline) subjects performed both the task switch and the memory coordination paradigm. Sessions two to seven were training sessions, where one group of subjects practiced only the task switch, while the other group practiced only memory coordination. In session eight (evaluation), again both tasks were performed. A comparison within tasks between sessions one and eight allows assessment of task-specific practice effects, whereas a comparison between tasks assesses effects of transfer. The absence of transfer effects would indicate involvement of functionally dissociable executive processes in the two different tasks. The existence of costs in the experimental conditions compared to the control condition even after practice could be expected if a true executive function is under investigation.

The results so far obtained support essentially both kinds of hypotheses. Costs remain even after six practice sessions in the switching task as well as in the coordination task. A dissociation between response time and cost function was observed: reductions of response times are less than the relative reductions of switch costs and coordination costs, respectively. As to transfer effects, a slight transfer in both directions was observed, but more so from coordination to switch than vice versa.

These are only hints given the small number of subjects which does not allow strong statistical testing. Nevertheless, the pattern of results in single subjects is promising and justifies future investigations.

Backward inhibition contributes to the costs of task set reconfiguration

3.2.7

Mecklinger, A. & Borrmann, K.

Switching between task sets is associated with considerable costs. These switch costs are usually obtained when contrasting situations in which a task set is repeated or alternated over consecutive trials. It is generally assumed that task set reconfigurations are under voluntary control, i.e. they can be initiated endogenously. However, an exogenous trigger, such as a stimulus attribute associated with the task, is required to complete the reconfiguration process. In this project we aimed at identifying a potential source of switch costs, namely the inhibition of a previously executed task set (see also Mayr & Keele, in preparation). Subjects performed a task-switching experiment in which they had to switch between three visual discrimination tasks on every second trial (e.g. AA-BB-CC). On each trial a task cue (background screen color) was provided 200 ms prior to the task stimuli. By systematically controlling task order, each task could either be repeated with a lag = 1 (e.g. **AA**-BB-**AA**) or with a lag > 1 (e.g. **AA**-BB-CC-**AA**). For all three tasks reliable switch costs were obtained. That is, reaction times were longer for task alternations than for task repetitions. Interestingly for all three tasks these switch costs were systematically affected by the lag manipulation: They were larger when a task was repeated with lag 1 (243 ms) than with lag > 1. When the lag > 1 condition was further divided in to a medium lag (lag=2) and a large lag (lag > 2) condition, switch costs were smaller (but not eliminated) for the large lag (133 ms) than the medium lag (208 ms) condition. Similar results were also obtained when the time between task cues and task stimuli was increased to 1200 ms. The results are consistent with the view that in task situations that require the alternation of different task sets a recently executed task set is selectively inhibited, and that this task-specific backward inhibition mechanism is a substantial source of residual switch costs.

Is irrelevant input to working memory actively inhibited ?

3.2.8

Ungerer, C., Mecklinger, A. & Bublack, P.

Traditionally, working memory has been divided into two types of processes: executive control and active maintenance. It has been proposed that these processes are mediated by different brain regions, with the prefrontal cortex being more engaged in executive control and posterior cortical areas mediating maintenance processes. To achieve efficient working memory functioning goal-irrelevant information within working memory or from external sources has to be inhibited. To examine the mechanisms and neuronal processes underlying the inhibitory control of irrelevant input to working memory a S1-S2 paradigm with intervening task-irrelevant stimuli was developed.

In the first experiment we used three letters from an unknown alphabet (Klingon letters) as study items. They were followed either by three interference letters or by random dot patterns. Upon presentation of S2 an old/new decision was required. The results showed item specific effects, i.e. subject generated preferences for some of the letters and also tended to verbalize the study items. Therefore, a second experiment was designed in which the stimuli were of equivalent complexity (Walker et al., 1993) and rehearsal strategies were controlled for by using interference stimuli from either the same or from a different categorial set as S1 and S2. In this experiment S1 and S2 were always taken from the same categorial set and the interference stimuli consisted either of a mask (m), or of stimuli from different (d) or same categorial sets (s). The results revealed shorter reaction times and lower error rates in the mask condition (m) than in the two conditions with structured interference stimuli (m, d). However, no ignored repetition effects were obtained. That is, performance was not different when interference stimuli or completely new stimuli were presented as S2 probes. This absence of ignored repetition effects might suggest that subjects either did not actively attend to the distractor stimuli or only processed global stimulus characteristics. The latter issue is currently under investigation in an experiment in which subjects have to perform a visual discrimination task with the distractor stimuli. In order to examine the generalizablity of the observed mechanisms, as a next step the same interference paradigm will be employed in the auditory domain, using phonemes as stimulus materials.

3.2.9 Event-related brain potentials dissociate image-based and verbal representations in recognition memory

Mecklinger, A. &
Bosch, V.

This project aims at identifying the functional subsystems involved in processing image-based and verbal information. In contrast to project 3.2.10, direct tests of recognition memory were employed in which ERP repetition effects can be directly related to the subjects' performance. In the first experiment the representational codes for object forms (image-based or verbal) were manipulated by presenting line drawings of familiar objects as study stimuli and either pictures or words as test stimuli in a study-test paradigm. ERP repetition effects for pictures were most pronounced around 350 ms and showed a fronto-central scalp topography, whereas for words these effects were largest around 500 ms and yielded a centro-parietal scalp topography. The temporal aspects of these repetition effects parallel the RT data obtained for both kinds of judgments. Experiment 2 examined whether a similar topographical dissociation is also obtained with identical test stimuli that allow the generation of image-based or verbal representational codes. We used letters from an unknown alphabet (Klingon letters) as stimulus materials. Based on the outcome of post-experimental debriefing the ERPs for two groups of subjects that can be assumed to have generated either visual images (visualizers) or verbal labels (verbalizers) for the Klingon letters were contrasted. For the visualizers, the repetition effects were frontally distributed and most pronounced around 450 ms. Conversely, verbalizers displayed centro-parietally focused effects, most pronounced at 550 ms. These results parallel those of Experiment 1 and indicate that the representational systems for image-based and verbal information underlying direct tests of recognition memory can electrophysiologically be dissociated. In both Experiments the repetition effects reflect the modulation of a negative N400-like ERP component evoked by new objects and words. Based on this latter observation it is tempting to speculate that both representational systems enable the generation of context or meaning against which new information can matched

3.2.10

Perceptual and conceptual processing of pictures and words: Evidence from event-related potentials

Mecklinger, A. &
Busch, A.

Recent functional imaging studies and studies with intracranial event-related potentials in epileptic patients indicate that there are functionally and neuroanatomically distinct subsystems in the ventral pathway mediating the processing of faces, colors, words and numbers. Despite this growing evidence for a modular, category-specific organization of the ventral pathway only recently has the functional anatomy of processing of pictures and words been examined using neuroimaging techniques. Vanderberghe et al.(1996) found word and picture specific processing regions, however, there was considerable overlap in the brain regions that were activated by different semantic tasks irrespective of the input modality. These results argue against word or picture specific semantic subsystems and rather suggest that a common semantic system operates on picture and word specific input systems. Conversely, a variety of ERP studies found differential N400 scalp topographies for semantically processed pictures and words.

In the present study the functional and neuronal correlates of picture and word processing was addressed in more detail by means of high density ERP recordings. In 1996 (see 1996 Annual Report) an experiment was performed in which nonsense words and nonsense pictures (p=.20) had to be detected in a series of legal pictures and words. The pictures and words were from a standardized set of line drawings (Snodgrass & Vanderwart, 1980). To enable the examination of perceptual and conceptual aspects in picture and word processing there were four different repetition conditions: A picture or word could be followed by the same picture (PI-PI) or word (WO-WO) (perceptual repetition conditions). Analogously, a picture could be followed by a word denoting this picture (PI-WO) or words could be followed by a picture denoting the meaning of the word (WO-PI) (conceptual repetition conditions). This procedure can be considered as an indirect memory test. Although in the perceptual priming conditions ERP repetition effects (i.e. more positive-going ERP waveforms for repeated as compared to not-repeated items) started as early as 250 ms, the corresponding effects in the conceptual priming condition did not start before 400 ms. Consistent with previous ERP studies the repetition effects evoked by pictures and words could topographically be dissociated with picture-evoked effects yielding a fronto-central scalp distribution and word-evoked effects yielding a centro-parietal scalp distribution.

In 1997 two additional experiments were performed: In one study it was shown that the above mentioned effects are also obtained when not only the overall probabilities of pictures and words but also the probabilities for pictures (words) being followed by either a picture or word were controlled for. Thus, the differential scalp topographies did not arise from differential expectancies built up during the experiment. The second study was designed to investigate the temporal characteristics of the repetition effects. To this end the same four repetition conditions as in the 96' experiment were employed but there were two intervening items between the first and second exposure of the stimuli. Reliable effects were found for all four repetition conditions. Similar to the two previous experiments the perceptual effects had an earlier onset than the conceptual effects and picture-evoked effects had a more anterior scalp distribution than word-evoked effects. The effects were similar in magnitude to the '96 Experiment except for the condition in which words were followed by pictures denoting the meaning of the word (WO-PI), here only small amplitude repetition effects were obtained.

These results suggest that the brain systems engaged in picture and word processing on both perceptual and conceptual levels can be dissociated electrophysiologically. Currently, we are conducting a spatio-temporal dipole analysis to estimate the neuronal sources that contribute to the scalp-recorded repetition effects.

3.2.11 An ERP study of object representation: Implicit and explicit memory for 3D possible and 3D impossible line drawings

Penney, T.B.,
Mecklinger, A.,
Hilton, J. &
Cooper, L.A.

In collaboration with Lynn Cooper and John Hilton of Columbia University in New York City we have begun to examine the neuro-cognitive substrate of visual object representation. Behavioral and brain imaging (PET) data suggest that the brain encodes information from line drawings of possible and impossible 3D objects differently. Possible objects may be represented as a holistic unit in a low level perceptual representation system (PRS) whereas impossible objects are not. Information about both types of object, however, is available to the recognition memory system. The major behavioral evidence for this view is that priming is obtained for possible items but not impossible items in the object decision task. This means that prior exposure to possible objects facilitates possible/impossible classification accuracy and reduces reaction time relative to novel possible items whereas prior exposure to impossible objects does not enhance classification accuracy and reaction time relative to novel impossible objects.

We are going to utilize the object decision task to determine if the ERP waveforms are different for possible and impossible items as a function of prior exposure (repetition effect). In addition, we will compare the ERP response to possible and impossible objects in a recognition task that includes a source memory component.

The adaptation of the object decision task to an ERP design required the creation of additional stimulus materials. These new materials (94 line drawings of impossible items) and material used in prior studies (184 line drawings of both possible and impossible items) were tested for intersubject agreement on possible/impossible classification under conditions of unlimited viewing time. A set of 113 possible and 113 impossible items met the criterion of at least 85% agreement among subjects. In addition, we have completed a second experiment to determine baseline error rates in object classification at a presentation duration of 50 ms.

The planned EEG experiment consists of three stages: implicit encoding, object decision, and recognition. *Implicit Encoding:* Subjects will classify each member of a subset of the items as facing predominately toward the left or the right. Half of the items will be presented against a blue background and half against a red background. *Object Decision:* Subjects will classify each member of the entire set of items as possible or impossible in the real world. *Recognition and Source Memory:* Each member of the entire set of items will be presented against a gray background. Subjects will indicate if the object was seen in stage one (old judgment) and if so, whether the background color was red or blue.

Event-related potential indices of auditory sensory memory

3.2.12

Kaernbach, C., Schröger, E. & Gunter, Th.C.

Periodic noise as an auditory stimulus has been used in psychophysical studies to investigate the lower limit of auditory periodicity analysis. Subjects were presented with periodically recurring iterations of a segment of white noise that were seamlessly connected to each other. For cycle lengths of two seconds or more this sounded exactly like homogenous nonrepeating white noise. For cycle lengths of one second or less subjects easily noticed the periodic nature of the stimulus due to the perception of recurring faint events such as clanks and beeps.

This stimulus is of indubitable value to the study of sensory auditory memory (echoic memory). It has served in numerous psychophysical studies estimating phase sensitivity or time-constants of echoic memory. The present study aimed at determining the event related potentials (ERPs) elicited by periodic noise. A modified version of periodic noise was used with only a small part of the sound wave recurring in order to permit interpretation of the ERP components relative to the onset of the recurring segment. Omissions of the noise (white noise at 60 dB HL) were included, allowing the investigation of ERP components which should only be present if a subject was able to detect such an omission. After each task block subjects were asked how many omissions (probability of 25%) occurred in the foregoing block. The counting task was made difficult so that subjects (N=20) could be graded according to their behavioral performance.

Behavioral performance was determined by calculating the correlation coefficient r of the number n_s entered by the subject and the real number n_r of omissions in a specific block. In order to estimate the signal-detection criterion employed by the subject, the ratio n_s/n_r of the entered and the real count was determined. The average correlation was 0.24, and the average ratio n_s/n_r was 0.9, i.e. the subjects counted on the average 10% fewer omissions than were presented. For the ERP-analysis subjects were classified as good performers (r > 0.2, 7 subjects) and bad performers (r < 0.1, 5 subjects) .

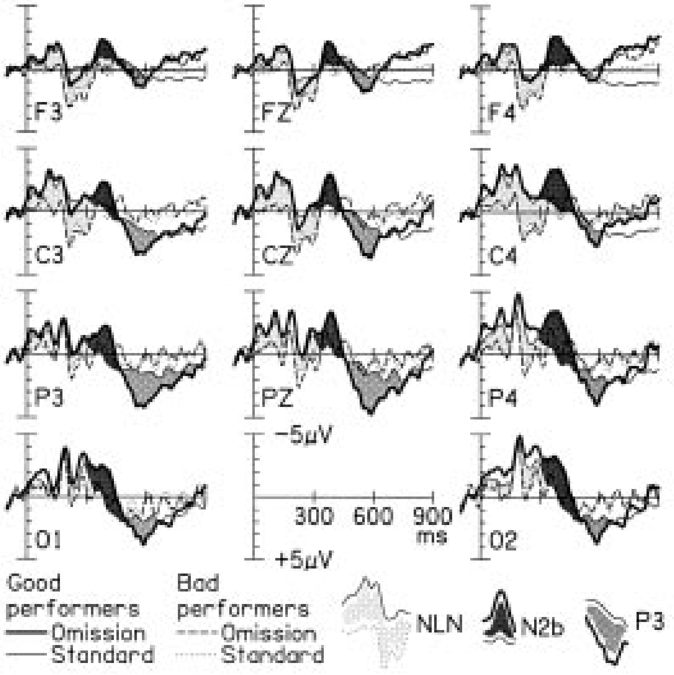


Figure 4. ERPs to periodic noise.

The figure shows the ERPs elicited by standard stimuli (i.e. when the segment was present) and the omissions. For the bad performers it made no difference whether the segment was presented or not. The good performers showed a marked negativity during the first 200 to 300 ms and in the case of an omission there is an additional negativity at about 395 ms and a positivity around 590 ms. Thus, it seems that a difficult task involving echoic memory can only be solved by those subjects that show an early negativity locked on the relevant part of the stimulus. This negativity might reflect a process which is a prerequisite for the recognition of the recurring sound segment by echoic memory. Subjects that show this negativity can solve the task and show the corresponding ERPs (N2b, P3).

The present data may be seen as an indication that echoic memory acts on sensory stages to produce the percepts audible in periodic noise. It is conceivable that this activity is due to a top-down tuning of auditory feature detectors. Given this, it can be assumed that the feature detectors tuned by the echoic memory deal with complex features and not with simple onsets, offsets, or energy peaks.

Below the surface: fMRI and ERP analyses of human auditory memory

3.2.13

Opitz, B.,
Mecklinger, A.,
Kruggel, F. &
Wiggins, C.J.

In 1996 (MPI Annual Report) we presented the results of a dipole analysis suggesting that similar neuronal networks including the auditory cortices and more superior and medial cortical regions are involved in early processing of deviant and novel stimuli. Furthermore, we obtained equivalent current dipole (ECD) models, providing evidence for the view that different neuronal structures are engaged in later processing of deviant and novel sounds. For the deviants, two medial dipoles, roughly located in thalamic structures were found. In contrast, the sources of the novel P3 have been estimated in hippocampal structures. The goal of the present study was to resolve the ambiguity related to precise location of activated brain structures which is inherent in the dipole modeling approach by combining this approach with structural and functional imaging techniques that provide neuroanatomical constraints for the inverse solution. Therefore, we developed an experiment allowing the investigation of electrophysiological as well as hemodynamic brain responses to deviant and novel stimuli with exactly the same experimental settings. Due to fMRI-requirements a design slightly different from the one used in the experiment described last year was employed. First, we increased the standard-deviant distance from 60 Hz to 400 Hz in order to get a pronounced mismatch activation. Prior studies have shown that such a manipulation leads to a higher amplitude and shorter latency of the mismatch negativity (MMN) in the ERP. Second, based on ERP-studies that have shown that the amplitude and the latency of the MMN is unaffected by the predictability of the occurrence of a deviant we used a block design with resting blocks, comprised of standard tones, and activation blocks, comprised of standards and either novels or deviants. The stimulus train consisted of alternating resting and activation blocks. To control attentional aspects of task performance subjects were either required to carefully watch a cartoon (unattend condition) or to silently count the deviants (attend condition). The EEG-recordings were carried out using 128-channel system. Functional images were acquired at a rate of 2 sec per image using EPI-sequence (128 x 64 matrix). Data were collected from seven axial slices, parallel to AC-PC line with a slice thickness of 6 mm and spacing of 8 mm.

The results of the current EEG experiment replicated and extended those of the earlier experiment (cf. Annual Report 1996). Compared to the '96 experiment the MMN was larger in amplitude and had an earlier onset and the P3b component showed a more central scalp distribution. The analyses of the fMRI experiment is still in progress and uses a pixel-wise correlation of the BOLD-response with a box-car-function to model the resting and activation blocks. Preliminary results suggest that different neuronal networks are involved in generating the activation pattern for deviants and novels. For the deviants this network probably includes the Heschl's gyrus and the posterior part of the middle temporal gyrus bilateral, the posterior part of the superior temporal gyrus with a right hemisphere dominance and subcortical structures such as the putamen. The intraparietal sulcus was also found to be engaged in deviant processing.

Parahippocampal regions were bilaterally activated during the processing of novel sounds. Additionally, for identifiable novels, in contrast to nonidentifiable, a pronounced right hemisphere activation of the inferior frontal gyrus was obtained. Conversely, the anterior cingulate and the putamen were more activated during the processing of nonidentifiable sounds. These differences in brain activation for identifiable and nonidentifiable novel sounds might indicate that episodic memory traces are activated by identifiable but not nonidentifiable sounds.

A combined analysis of the ERP as well as the fMRI data will be performed to obtain more detailed structural and temporal information of auditory processing of different stimulus types.

In its second year of existence the clinical and scientific management of our Day-Care Clinic at the University of Leipzig was substantially improved. On the basis of individually tailored rehabilition programmes offered to 131 neurological patients this year, we found a majority of them (87%) willing to give us their informed consent to take part in one or several studies presented in this chapter. About 40% of the patients participated in studies even after having been discharged from the Day-Care Clinic.

According to the framework we outlined last year we completed several patient studies, the purpose of which had been the development of clinically applicable tools for the assessment of so-called *executive dysfunctions*. In patients with severe closed head injury (CHI) a "memory coordination paradigm" (3.3.1) and a "task switching paradigm" (3.3.2) were investigated which, in the meantime have become part of routine clinical testing.

In the *memory* domain we completed a combined clinical and ERP study on "visual recognition memory" in patients with global ischemia due to cardiac arrest (3.3.3). Other studies examined to memory retrieval processes and implicit serial learning (3.3.4, 3.3.5).

Language dysfunctions on several levels of complexity occupied a large part of our clinically oriented work. At first, we finished two ERP studies on sentence comprehension in aphasic subjects, (3.3.6, 3.3.7) a more theoretical study dealt with the question whether agrammatic aphasics rely on a structure-based strategy when committing thematic reversals (3.3.8). In Broca's aphasics potential dissociations in procedural learning abilities (i.e. in phoneme and spatio-motor sequences) were studied (3.3.9). A study investigated the possible relationship between phonological discrimination and memory load (3.3.11). Three related projects of substantial significance for our cognitive remediation programme examined text and discourse comprehension deficits in brain-injured patients (3.3.12-3.3.14).

Finally, some projects prepared *future developments.* An fMRI study on dynamic changes of motor learning in healthy subjects will be completed in the near future by patients suffering from mild to moderate motor impairment (3.3.15). A first study combining MR-spectroscopy and neuropsychological measures focused on neurological patients with small vessel disease (3.3.16). In cooperation with the Department of Neurology at the University of Düsseldorf, deep brain stimulation (DBS) was employed in Parkinson patients with the goal of studying how DBS manipulation affects performance in (simple/choice) reaction tasks (3.3.17). Finally, a mechanical finite element model was designed to study the contre-coup phenomenon in CHI patients (3.3.18).

3.3.1 Working memory in patients suffering from severe closed head injury: An investigation of storage and executive functions using the memory coordination paradigm

Bublak, P.,
von Cramon, D.Y. &
Schubert, T.

One subgroup of brain damaged patients known to suffer from executive deficits are patients with severe closed head injury (CHI). This may be due either to frontal lobe contusions or diffuse axonal injury. On the other hand, because cerebral hypoxia is a frequent complication in CHI patients, afflicted memory functions may contribute to executive problems as well. After all, experimental psychological studies in normal subjects have shown that performance on a test of executive capacity deteriorates when a list of items close to a subject's memory span has to be stored simultaneously (Baddeley & Hitch, 1974). It may also be the case, however, that executive problems depend on the complexity of control functions even though only a relatively small amount of information has to be stored in memory. More specifically, it is assumed that performing a complex working memory task, for example, calls for executive resources to a greater degree than an easy working memory task. A greater demand should reduce executive resources that can be set up to influence automatically scheduled behavior (Norman & Shallice, 1986; Roberts et al., 1994). That is, subjects would be rendered more prone to get caught by predominant response tendencies. As to patients suffering from severe closed head injury, it is hypothesized that they have to use more executive resources to perform a complex working memory task, compared to normal controls, whereas they should have much less difficulty to manage a short term memory condition. Therefore, these patients should be less able to inhibit predominant response tendencies, when facing a complex working memory task.

We used the memory coordination paradigm as one possible approach to assess this possibility and to gain a better understanding of the cognitive difficulties CHI patients face in managing complex cognitive tasks in real life situations. The task demands integration of two memory subsets with each other, i.e. the transposition of the original temporal order of memorized items into a different one. Therefore, it has a storage component (keeping the subsets in memory) and a control component (manipulation of stored items).

Subjects have to encode a list of four digits presented successively at the centre of the screen. The first two digits are shown in green, the last two digits in red colour. After a delay period, a cue is shown to indicate the beginning of the response phase, which starts after a random time interval. Three conditions were realized. In the baseline *short-term memory condition* ("STM"), recall is demanded in the same order as the digits were presented (e.g. the digits 3 6 7 5 have to be recalled in that order). In the *easy working memory condition* ("WM 1"), recall is demanded in the order first green digit, first red digit, second green digit and second red digit (i.e. 3 6 7 5 becomes 3 7 6 5). In the *difficult working memory condition* ("WM 2"), recall is demanded in the order first red digit, first green, second red and second green digit (i.e. 3 6 7 5 becomes 7 3 5 6). For recall, four pairs of digits are successively presented, one digit to the left, the other to the right of centre. Each digit was part of the list, but due to the temporal order of the items demanded by a given task condition, only one digit per pair is appropriate for response. The subject has to press the left/right response key, if the left/right digit is the correct answer. The three conditions were presented block-wise and with ascending difficulty (STM, WM 1, WM 2) to a group of subjects suffering from severe CHI and to a normal control group, matched for sex, age, and education.

Within the response phase, a congruent and an incongruent condition was realized. In the *congruent condition*, the two items of the third pair were the same as in the fourth pair and also had an identical spatial position. In the *incongruent condition*, item identity was also preserved, but the spatial position of the items was reversed. In the incongruent condition, an inhibition of return effect is assumed to induce a predominant tendency to press the key corresponding to the spatial position opposite to the target item. This should cause the need to actively inhibit the prepotent tendency, leading to elevated response times compared to the congruent condition.

In accord with the hypotheses, the decisive prediction is a group x task interaction for response times as well as for accuracy in the memory tasks. That is, the difference between patients and controls should increase with increasing task difficulty. If patients are suffering from a short-term memory deficit, worse performance than controls should also be evident in the baseline condition (STM). The increasing amount of control processes necessary to perform the coordination tasks should lead to the aforementioned interaction and a significant performance deterioration in WM 2 compared to WM 1. Concerning the ability to inhibit the prepotent response tendency in the incongruent condition, the difference between the congruent and the incongruent condition should be more pronounced in WM 1 and 2 than in STM, and more pronounced in patients than in controls.

These predictions are corroborated by the data. CHI patients differ significantly from controls in all three task conditions (regarding response times, for accuracy, there is no difference in STM), but the difference increases with increasing task difficulty. Congruent and incongruent conditions differ from each other, this difference being more pronounced in task condition WM 2, and more so in patients than in controls.

A clinical test of executive functions during task-set reconfigurations

3.3.2

Mecklinger, A.,
von Cramon, D.Y.,
Springer, A. &
Matthes-von Cramon, G.

Executive control processes are assumed to operate on the highest level of the cognitive architecture and play an essential role in guiding goal directed behavior in a large variety of daily-life activities. However, the functional architecture as well as the neuronal basis of these control processes is poorly understood. In '96 (see MPI Annual Report) we developed a task switching paradigm that allows us to examine the executive mechanisms required to voluntarily shift between two simple cognitive tasks. Two experimental conditions were examined: In a neutral condition, the irrelevant attributes (those to which the subjects had to respond in the other task) were not present, whereas in the crosstalk condition, the irrelevant attributes were either mapped to the same response (congruent trials) or to the other response (incongruent trials). In this study reliable *switch costs* were obtained, i.e. reaction times were longer when subjects had to switch to another task, as compared to the repeated performance of the same task. Moreover, pronounced *interference effects* were found. That is, performance was poorer in the crosstalk conditions than in the neutral condition. These results are consistent with the view that task set reconfigurations can be initiated endogenously, but an exogenous stimulus attribute associated with the new task is required to complete the reconfiguration process.

Thirty-seven brain damaged patients have been examined with a clinically adapted version of the task-switching paradigm. In order to examine the temporal extension of switch costs, a subgroup of patients also performed a modified task version in which task switches were required only on every fifth trial. Based on performance characteristics, three subgroups could be differentiated: (1) patients with normal switch costs and high interference effects (n=10), (2) patients with high switch costs and normal interference effects (n=9) and (3) patients with high switch costs and high interference effects (n=5). A fourth group with normal interference effects and switch costs (n=13) served as a clinical control group. In group (2) but not in the other two groups there was a high proportion of patients with left hemisphere brain damage, supporting the idea that integrity of the left hemisphere brain regions is particularly important for the voluntary initiation of task set reconfigurations. In addition to left hemisphere brain damaged patients, patients with traumatic brain injury also showed increased switch costs and preserved interference effects. Data analyses of the modified switch task suggest that all except two patients show a normal time course of switch costs, i.e. performance improved immediately when the first trial of the new task was performed.

3.3.3 Visual recognition memory in patients with global ischemia: A combined behavioral and event-related potential analysis

Mecklinger, A,
von Cramon, D.Y. &
Matthes-von Cramon, G.

Transient global ischemia due to cardiac arrest may lead to profound neuropsychological disorders. Recent research indicates that memory processes are particularly impaired after cerebral hypoxia. In 1996 (see MPI Annual Report) we examined visual recognition memory functions in six chronic hypoxic patients and age-matched controls by means of event-related potential (ERP) and performance data. All subjects performed a visual recognition memory task requiring recognition judgments for either object forms or spatial locations and a visual classification (i.e. oddball) task, that imposes negligible memory demands. Reliable P300 oddball effects were obtained for patients and controls, whereas both groups differed in P300 latency and scalp topography. For all six patients under investigation the P300 maximum was shifted from parietal to central recording sites. It is conceivable that this parietal attenuation of P300 arose from neuronal cortical alterations along the cortical arterial boundary zones in the posterior cortex that are typically found in cerebral hypoxia.

In the memory task old/new effects (i.e., larger ERP waveforms for previously studied than for unstudied items) were found for the controls. In contrast, these old/new effects in patients were absent or even inverted in polarity while recognition performance was well above chance level, except for one patient. These results suggest that recognition based on the retrieval of an item's study episode is degraded in hypoxic patients. In light of the patients' above chance recognition performance and the outcome of a post hoc analyses of practice related changes in recognition performance it is argued that hypoxic memory disorders are best characterized as a degradation of explicit memory functions (i.e. episodic retrieval) and intact implicit functions, such as the assessment of an item's familiarity.

In '97 a variety of patients suffering from cerebral hypoxia as a secondary disorder (e.g. traumatic brain injury) were investigated using the same tasks and recording procedures. In contrast to patients with global ischemia due to cardiac arrest, these patients' recognition memory performance is similar to the age-matched controls and the corresponding ERP old/new effects do not differ in magnitude, latency or scalp topography from the controls. Interestingly secondary order hypoxic patients show a similar parietal attenuation of the visual P300 component, suggesting that P300 scalp topography might have some predictive power for the diagnoses of hypoxic conditions from a variety of diseases.

Memory retrieval processes in brain injured patients

3.3.4

Thöne, A. &
Zysset, S.

The purpose of this study was to investigate memory retrieval processes in patients with brain lesions of different etiologies. A modification of Sternberg's paradigm was designed to investigate the role of the prefrontal cortex in retrieval from long term memory on the one hand and scanning processes in working memory on the other. We investigated whether the necessary information processes in patients are generally slowed compared to normal subjects and if there are qualitative differences in addition.

In a typical Sternberg task, the subjects must decide whether or not a probe item belongs to a previously seen stimulus set. According to Sternberg's additive-factors logic (Sternberg, 1969) a serial sequence of components or stages makes up the process that is necessary to accomplish the task: (1) stimulus encoding, (2) memory scanning, (3) response selection, and (4) response execution. The slope of the regression function can be used as a measure of running stage 2, that is, as a measure of the speed of memory scanning. Since this component reflects the internal processes bridging the afferent and efferent stages of information processing, it is interpreted as a measure of cognitive slowing. The intercept of the regression curve reflects the time consumed by stages 1, 3 and 4.

Experiments with the Sternberg item recognition task suggests that patients with closed head injury (CHI) are slower than controls in their ability to rapidly scan for information in working memory (Haut, Petros, Frank & Lamberty, 1990). The data also suggested slower encoding of information into working memory following CHI.

A modified version of the paradigm proposed by Conway & Engle (1994) was used in this study. Patients learned three different sets of letters to criterion. In the actual experiment, a cue for the set and a letter were presented on the screen. The patient had to decide whether this letter was a member of the indicated set or not. Retrieving the set from long term memory and memory scanning both contribute to the reaction time when the cue and letter appear simultaneously. By introducing a sufficiently long delay between cue and letter, retrieval from long term memory can be assumed to be completed by the time the letter appears. In this case, only memory scanning contributes to reaction time. The difference in reaction time between the two delay conditions represents the time to retrieve the set. The slope of the regression curve represents the speed of memory scanning. The intercept reflects the time consumed by the above mentioned stages 1, 3, and 4. In a control task, only stimulus encoding and motor response were measured.

In a pilot study, an unselected sample of 12 patients and a group of 10 matched controls were examined. Preliminary results: As expected patients were generally slower in their reaction times than controls. In addition to general slowing, the difference between trials with and without delay, i.e. retrieval from secondary memory, was delayed in contrast to control subjects (300 vs. 500 ms). Due to varying individual response patterns it was not possible to decide a posteriori, what contributes to this prolongation of retrieval processes in patients. Patients and controls did not differ on error rates

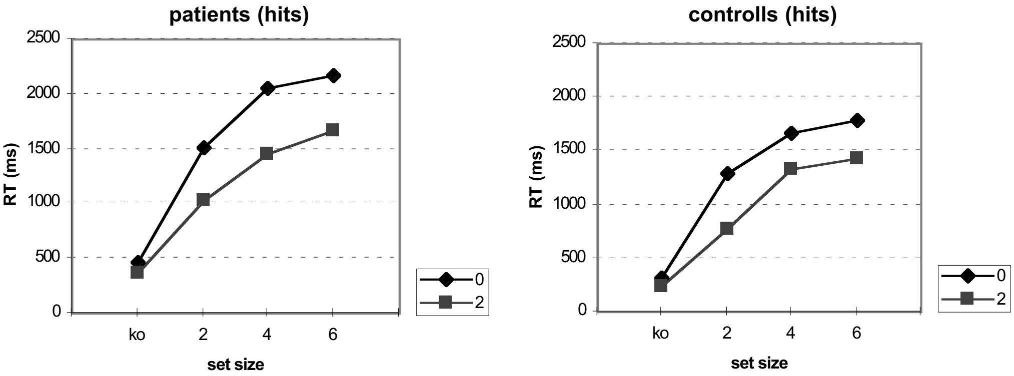


Figure 1. Mean reaction times for patients and controls as a function of set size and delay. 0, rsp. 2 stand for the delay, *ko* for the control condition.

3.3.5 Implicit serial learning in brain injured patients

Thöne, A. &
Andersen, B.

According to the literature on serial learning (e.g. Cohen, Ivry, & Keele, 1990; Nissen & Bullemer, 1987 and Willingham, Greenley & Bardone, 1993), a sequence of visually presented stimuli can be learned implicitly by normal subjects. An unintentional way of learning and recall without consciousness was derived from the fact that subjects were not able to recall the sequence explicitly, despite an improvement of reaction time over trials. Although various paradigms of implicit memory (e.g. perceptual priming or procedural learning of motor skills) have been studied extensively in brain injured patients, implicit serial learning has hardly been examined in this population. Thus, the purpose of this project was to find out if intact implicit serial learning can be observed in brain injured patients. In addition, patients with brain injuries due to different etiologies were compared in order to examine differences in learning. A special interest lay in the question of whether or not an explicit learning instruction can improve learning.

A modified version of the implicit serial learning paradigm used by Nissen & Bullemer (1987) developed by Frensch (1996) was used in this study. Colored targets, (red, green or blue), were presented on a computer screen. Each color matched a predefined key, which had to be pressed when the respective color appeared on the screen. Subjects performed a three-choice serial reaction time task in which the order of the stimuli followed a repeating sequence of six elements. Ten such sequences were presented without interruption so that the beginning and the end of the sequence could not be detected. Trials with repeating sequences were alternated with trials with random order.

An unselected group of 31 patients took part in the study. Patients had brain lesions of different etiologies. Twenty-one male and 10 female subjects with a mean age of 40.3 years (sd = 11.4) took part in the project.

Subjects were tested individually on two occasions with an inter-test interval of about two weeks. Patients did not get any information about the sequence of the stimuli when tested for the first time, but they were informed about the repeating order on the second occasion. Thus the effect of an explicit learning instruction could be determined.

Indirect measures of learning:

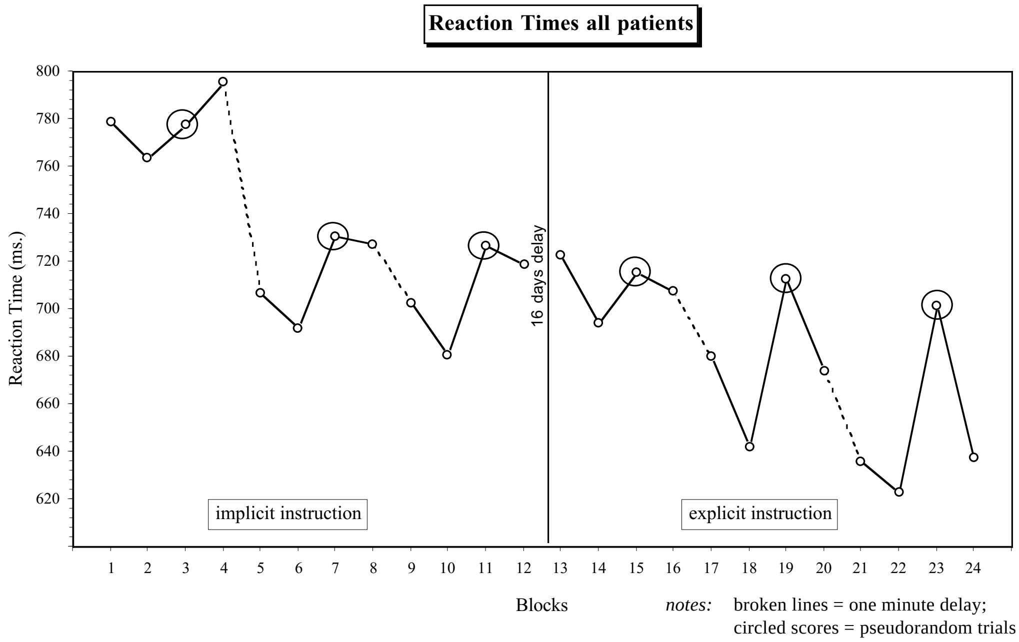
- comparison of reaction times for trials of fixed versus random order
- errors during trials of fixed vs. random order

Direct measures of learning:

- interview concerning awareness of a fixed sequence occurring repeatedly
- overlap of a sequence generation task and the learned sequence

Results

Looking at the data of the patient group as a whole there is a highly significant difference between sequential and random trials. The sequential patterns can already be detected after a few trials (block 6-8), i.e. it takes only a short time to learn the sequence implicitly. Reaction times at the beginning of testing on occasion 2 hardly differ from those of the last trials on occasion 1, i.e. implicit serial learning seems to be a long lasting effect.



notes: broken lines = one minute delay;
circled scores = pseudorandom trials

Figure 2.

When given an implicit learning instruction 32% of the patients showed the expected effect. These patients did not differ on any neuropsychological or neuroanatomical variable from other patients. With an explicit learning instruction the percentage of learners in the sample increased significantly (61,3%). 79% of these learners, however, also met criteria for explicit learning in the interview or generating task. Therefore the explicit learning instruction had significant effect.

Our results indicate that brain injured patients with lesions due to different etiologies and with various functional disabilities are able to learn an implicit sequence. In addition, an explicit learning instruction improves this learning process significantly, even in densely amnesic patients.

3.3.6 The role of basal ganglia in language comprehension

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

The role of the basal ganglia in language processing is currently a matter of discussion. Therefore, three patients with left frontal cortical and four patients with subcortical lesions involving the basal ganglia as well as fourteen normal controls were investigated in a language comprehension paradigm. Semantically incorrect (*selectional restriction violation*), syntactically incorrect (*word category violation*) and correct sentences were presented auditorily. Subjects were required to listen to the sentences and to judge whether a sentence was grammatically correct or not. Event-related potentials were recorded while subjects heard the sentences. Normal participants showed the expected N400 component for semantically incorrect sentences, and an early left anterior negativity (ELAN) followed by a late positivity (P600) for syntactically incorrect sentences. Patients with left frontal cortical lesions displayed an attenuated N400 component in the semantic condition, while the syntactic condition elicited no ELAN but a late positivity. Patients with lesions of the basal ganglia showed an N400 to semantic violations, and an ELAN component related to fast first-pass parsing procedures followed by a P600 assumed to reflect controlled second-pass processes. That is, these patients showed an ERP pattern in the syntactic and the semantic condition similar to the normal controls. The present results suggest that the left frontal cortex supports first-pass parsing and, indicate that the basal ganglia are not necessarily involved in first-pass processes during comprehension.

3.3.7 Semantic and syntactic processing during auditory and visual sentence comprehension in an aphasic patient: An ERP case study

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

There is an ongoing debate about the underlying deficits related to syntactic processes in Broca's aphasia. While some researchers assume reduced memory capacities (Kolk & van Grunsven, 1985), others indicate that the deficit is a reflection of altered temporal dynamics of either the access or integration of syntactic information (Friederici, 1988 and Hagoort, 1992). While this discussion has mostly focused on syntactic processes there has been evidence that deficits related to semantic processes might also reflect altered temporal patterns of access or integration of semantic information (Hagoort, 1993 & Schwab, Brown, & Hagoort, 1997).

Previous ERP evidence from normal populations has identified an early left anterior negativity that was correlated with first-pass syntactic parsing processes, while a late centro-parietal positivity has been observed with secondary syntactic processes (Friederici, 1995). A centro-parietal negativity around 400 ms post-stimulus onset (N400) has been associated with lexical-semantic processes (Kutas & Hillyard, 1980).

The goal of this study was to investigate the ERP activity in a subject with circumscribed brain lesions. The patient had suffered a posterior lesion that involved the left Heschl gyrus, the posterior part of the superior temporal gyrus, the supramarginal gyrus and the lateral occipital gyri. There was also a small lesion involving the middle part of the precentral gyrus and the adjacent part of the middle frontal gyrus. According to a standard aphasic measure (AAT) the patient was diagnosed as a Broca's aphasic. This was based on extremely low scores for naming and repeating items. While it could be assumed that phonological mistakes in the patient's speech production could reflect a problem in the 'phonological loop' (Baddeley & Hitch, 1974), results of a phonological discrimination test indicated that rehearsal processes were intact. This is compatible with the fact that the anterior lesion did not involve the cortical areas of the inferior frontal gyrus which are functionally engaged in rehearsal mechanisms. While a deficit for processes involved in verbal working memory can not be excluded, it is possible that an overall information processing delay could play a role in the speech production and perception of the patient. This was confirmed by anamnestic information by the patient and the speech and language therapist.

Based on the functional and neurotopographic specifications of language-related ERP components, the current experiment therefore set out to investigate the temporal pattern of language-related brain activity in this aphasic patient. A previously tested auditiory and visual sentence paradigm was used (Hahne, 1997 unpublished dissertation; Gunter, Friederici, Hahne, annual report). Event-related potentials were recorded from 19 electrode sites while the patient listened to or read sentences that were either correct, contained a semantic selectional restriction violation or a syntactic phrase structure violation. The subject's task was to judge whether a sentence was grammatically correct or not. In the auditory version the SOA was 500 ms (300 ms stimulus presentation time (SPT), ISI 200 ms). There were also a total of four visual sessions with short and long SOAs (VIS 1: SPT 300 ms, ISI 200 ms; VIS 2: SPT 600 ms, ISI 500 ms; VIS 3: SPT 300 ms, ISI 500 ms; VIS 4: SPT 300 ms, ISI 800 ms).

While the accuracy data was high in both the auditory and the visual sentence paradigms (above 92 %), the ERP data displayed differences as a function of the timing parameters of presentation in a non-modality-specific pattern. Only in the two long visual SOAs manipulations did a semantic violation elicit an N400 with a mean latency of 400 ms. Furthermore, the P600 was elicited as a function of ISI. In the SOA versions that used ISIs between 500 ms and 800 ms there was a P600 with an onset latency of 1000 ms.

In conclusion, it appears that syntactic and semantic processes during speech perception are influenced by different timing parameters of the stimulus input in this aphasic patient. These data give further evidence for the view that normal processing and integration of syntactic and semantic information during language comprehension critically depend upon a given temporal structure. An impairment of the normal temporal course may cause an aphasic breakdown. The finding that the present patient shows a normal N400 or slightly delayed P600 ERP pattern once the temporal structure of the input is adjusted clearly indicates that the underlying deficit must be defined in computational terms rather than in representational terms.

3.3.8 Agrammatic comprehension and theta-role assignment: A theoretical perspective

Friederici, A.D. & Gorrell, P.

In studies with speakers of English, agrammatic aphasics display a tendency toward thematic reversals in comprehension, i.e. a tendency to assign a preposed object the subject role. In act-out or picture-matching tasks, (1a) is often interpreted as (1b), and (2a) as (2b). [e.g. Caplan & Hildebrandt, 1988; Hickok & Avrutin, 1996]

(1) a. *It was the tiger that the lion chased*. (2) a. *Which horse did the giraffe chase?*
(1) b. *It was the tiger that chased the lion*. (2) b. *Which horse chased the giraffe?*

The tendency toward thematic reversals has led many researchers to suggest that agrammatics rely on a linear, rather than a structure-based, strategy of theta-role assignment. We argue that consideration of a broader range of languages shows that agrammatic aphasics (and presumably other aphasics as well) in fact rely on a structure-based strategy when committing thematic reversals.

Grodzinsky (1990, 1995) and others have proposed a linear strategy that uses verb position to heuristically assign theta roles not grammatically assigned. The data from Bates et al. for VNN sequences and Hagiwara & Caplan's (1990) data from Japanese show that a linear strategy is inadequate. The latter propose that direction of theta-role assignment is an important factor, with theta-role assignment to internal arguments taking priority. This is a language-specific version of a strategy which relies on the relation of NPs to the verb. But the data from Dutch and German show that verb position is not a factor in theta-role assignment. Although it is clearly possible to formulate different strategies for each language, this would miss an important cross-linguistic generalization. Stating this generalization requires abandoning linear accounts and turning to structural factors.

Consider the normal assignment of the theta roles in a verb's argument structure to syntactic positions. For example, if a verb has two roles to assign, agent and theme, why is it that the subject receives the agent role and the object the theme role? Recent work by Grimshaw (1990) links argument structure and syntactic structure in the following way. A verb's argument structure is hierarchically organized such that agent is more prominent than theme. The mapping to syntactic structure reflects this relation such that the agent role is assigned to the more-prominent syntactic position. If the verb is *chase* and the agent is *the lion* and the theme *the tiger*, then it is the agent that occupies the subject position in the structure, i.e. the most-prominent argument position.

One property common to all accounts of theta-role assignment by aphasics is that they make reference to the relations among lexical items, disregarding empty categories. Empty categories may be seen as one form of purely grammatical elements in a tree. Given this, the comparative insensitivity to the information carried by empty categories is not surprising. Given this, we can now state our proposal in (3).

(3) The Structural Prominence Hypothesis [SPH]

Agrammatic comprehension displays a tendency to use the relative structural prominence of lexical (argument) NPs as a guide to theta-role assignment.

Our proposal makes use of the connection between argument structure and syntactic structure. When argument structure is directly linked to syntactic structure, the most prominent argument in a verb's argument structure fills the most-prominent syntactic position.

Cross-linguistic evidence supports the SPH as a structure-based alternative to comprehension strategies which rely on linear relations (either among NPs, or between an NP and a verb). An investigation of experimental results in English, Japanese, Dutch and German shows that the position of the verb does not affect interpretation. Further, the relative linear positions of the argument NPs does not adequately account for the cross-linguistic results concerning theta-role assignment. Rather, relative structural prominence appears to provide the best account of the observed tendency. In referring to a tendency, we wish to indicate that the SPH is not the sole factor which may influence agrammatic (or, more generally, aphasic) comprehension. For example, we do not exclude features such as [human] or [animate] from affecting interpretation, especially when the candidate nouns are differently marked for such features.

The SPH will interact in still unexplored ways with the parsing of more complex structures, such as sentences with more than one clause. In the sentences, the manner in which the input string is segmented into clauses (i.e. the recognition of clause boundaries) will greatly affect the SPH application. We have considered only simple structures here. The SPH must be understood within the context of a more-fully articulated parsing theory (cf. Friederici & Frazier, 1992). Finally, we note that we do not need to assume that agrammatic comprehenders compute more structure than is commonly assumed in the literature. One advantage of the SPH is that, unlike linear strategies, it does not require that this computed information be ignored in comprehension. Rather, agrammatic comprehenders, like their normal counterparts, use structure to guide interpretation, albeit with a decreased ability to exploit the purely grammatical vocabulary.

3.3.9 Procedural learning in Broca's aphasia: Dissociation between the acquisition of spatio-motor and phoneme sequences

Goschke, T., Friederici, A.D., van Kampen, A. & Kotz, S.A.

Several studies indicate that procedural knowledge of sequential structures can be acquired in an *implicit* manner, that is, without an intention to learn and even though the knowledge is difficult, if not impossible, to verbalize. Implicit sequence learning has been investigated with a *serial reaction task*: in each trial a stimulus appears at one of several locations and participants respond to the location of the stimulus by pressing one out of several response keys mapped to the different locations. When the sequence of locations follows a regular or repeating pattern reaction times decrease with practice faster as compared to a random sequence, whereas response times increase again when the repeating sequence is switched to a random sequence after practice.

Previous research has primarily focused on whether implicit and explicit sequence learning can be dissociated and whether implicit learning is independent from brain structures necessary for declarative memory. For instance, intact sequence learning was observed for participants showing little explicit knowledge and for amnesic patients with impairments of declarative memory. Far less attention has been paid, however, to the question of whether sequence learning itself is a unitary phenomenon, or whether separable, domain-specific brain systems underlie the acquisition of different types of sequential structures. In order to investigate this question we compared learning of *spatio-motor* sequences and *phoneme* sequences in neurological patients suffering from strokes in the left frontal cortex including Broca's area. From recent brain-imaging studies suggesting that Broca's area is involved in the processing of phonological sequences, we derived the hypothesis that such patients would be selectively impaired with respect to the learning of phoneme sequences. In contrast, we expected intact learning of spatio-motor sequences, which has been shown to involve a cortico-striatal network related to motor control.

In an initial experiment, we tested 6 patients suffering from left frontal cortical lesions (hereafter Broca's aphasics), 6 patients with lesions in the left temporal cortex (hereafter Wernicke's aphasics), and a group of 11 age-matched control subjects with the standard serial reaction task in which a repeating sequence of stimulus locations had to be responded to with a repeating sequence of key presses. Patients were selected according to classification (Aachen Aphasia Test) and CT lesion information (left anterior versus left posterior lesions). Both Broca's and Wernicke's aphasics showed intact learning of the spatio-motor sequence, as indicated by reliably faster response times for a repeating as compared to a random sequence. This was true for *unique* sequences composed of simple pairwise associations, and *ambiguous* 10-element sequences containing higher-order sequential dependencies. There were no reliable differences between patients and age-matched control participants.

In a second experiment, we used a new *serial search task* which allowed us to investigate learning of a phoneme sequence independently from a spatio-motor sequence (Goschke, 1997). On each trial participants were presented with a visual display consisting of four letters, followed by an auditorily presented letter. The task was to press one out of four response keys corresponding to the *location* of the auditory letter in the visual display. The locations of the four letters in the visual display were changed from trial to trial such that either the sequence of responses followed a repeating 8-element pattern while the sequence of auditory letters was random (*response sequence*), or the sequence of auditory letters followed a repeating pattern while the location-response sequence was random (*phoneme sequence*). Previous research has shown that healthy participants do learn both the response and the phoneme sequence, and that performance increments are of equal magnitude for the two types of sequences (Goschke, 1997).

Six patients with left-anterior lesions classified as Broca's aphasics according to the Aachen Aphasia Test served as participants. All participants performed the serial search task with a response and a phoneme sequence. The order of the two conditions was counterbalanced across participants. In each condition, participants performed 7 blocks consisting of 10 repetitions of the structured sequence, followed by an 80-trial-block with a random sequence, and a final block with the structured sequence.

As in our first experiment, patients learned the manual response sequence: response times reliably decreased over the training blocks and increased when the repeating sequence was switched to a random sequence (see Figure 3). In marked contrast, the patients showed no evidence of learning in the phoneme sequence condition. Neither did response times decrease across blocks, nor did they increase in the random block.

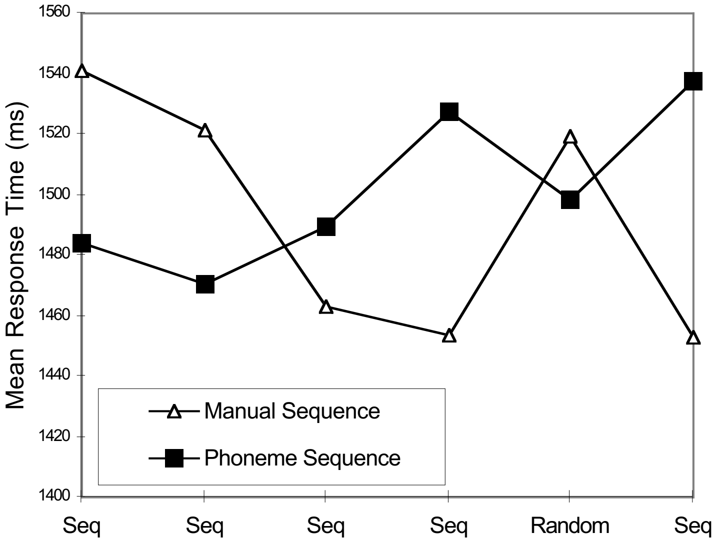


Figure 3.

These findings are evidence for a dissociation in Broca's aphasics with respect to procedural learning of phoneme and spatio-motor sequences. The finding that patients showed intact learning of a sequence of manual responses is consistent with studies of sequence learning in Parkinson and Huntington patients as well as brain imaging studies, which indicate that implicit motor-sequence learning involves a cortico-striatal network related to motor control. To the degree that this network is spared in our patients, intact learning of spatio-motor sequences is to be expected. By contrast, Broca's aphasics did not learn a sequence of phonemes when the response sequence was random. This was the case even though the task requirements and the structure and complexity of the sequences in the two conditions were identical in all other respects. This dissociation is consistent with a modular view of implicit learning according to which separable brain systems are involved in procedural learning of different types of sequential structures.

3.3.10 Sentence comprehension and working memory in Parkinson's disease

Saupe, N.,
Müller, U. &
Friederici, A.D.

Cognitive deficits in patients with Parkinson's disease (PD) without dementia are similar to those reported in patients with frontal lobe lesions and have been attributed to dysfunctional cortico-striato-thalamic loops. Neurolinguistic examinations of PD patients revealed language comprehension deficits when syntactically complex sentences had to be processed. Since most comprehension tests used sentences with embedded relative clauses the syntactically complex sentences were usually longer or semantic complexity was not varied within the same sentences (Lieberman et al., 1990, Natsopoulos et al., 1991 and Grossman et al., 1992).

In our study 18 patients with idiopathic PD (mean age 55.7 [32-78] years, duration 55.1 [1-156] months) and two groups of age-matched and young controls were investigated with a new off-line comprehension task that was carefully controlled for sentence length (Mecklinger et al., 1995). Main exclusion criteria were dementia (MMS < 27) and depression (HRSD < 8). The sentence processing task consisted of 64 target

Subject-relative clauses***, biased-verb / neutral verb*** **(SRB/SRN)**	
	Das ist die Professorin, die die Studentinnen *geprüft hat.* [This is the professor that the students *examined has*.]
	Das ist die Professorin, die die Studentinnen *gesucht hat*. [This is the professor that the students *sought has*.]
Object-relative clauses***, biased-verb / neutral verb*** **(ORB/ORN)**	
	Das sind die Studentinnen, die die Professorin *geprüft hat.* [These are the students that the professors *examined has*.]
	Das sind die Studentinnen, die die Professorin *gesucht hat*. [These are the students that the professor *sought has.*]
Question:	**Wurde/n die Professorin/Studentinnen geprüft/gesucht?** [Was/were the professor/students examined/sought?]

Table 1. Examples of Target Sentences and Probes with Literal English Translations

sentences with relative clauses varying on syntactic and semantic dimensions. Each sentence was presented on a separate chart and had to be read aloud. After a short delay a simple probe question had to be answered with yes or no (table 1). The neuropsychological test battery also included tests for verbal working memory (digit span, word span, reading span), declarative memory, attention and executive functions.

A 3 (group) x 2 (semantic variation) x 2 (syntactic variation) ANOVA revealed significant main effects for group ($p<0.05$), semantics ($p<0.01$), and syntax ($p<0.01$), but only a significant group by syntax interaction ($p<0.05$) (Figure 4). Syntactic deficits correlated with poor performance in the digit and reading spans.

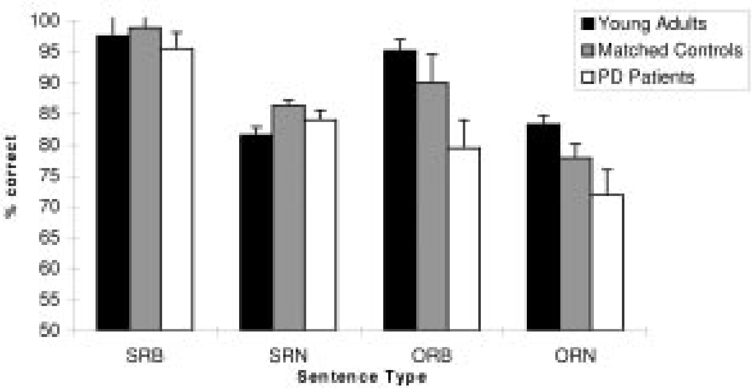


Figure 4. Comprehension of sentences with different syntactic (subject relative [SR] or object relative [OR] sentences) and semantic (final verb biased [B] or neutral [N]) complexity (mean±SE).

We conclude that both aging and PD impair verbal working memory as well as the ability to (re-) analyze and understand syntactically complex sentences.

Phonological discrimination in aphasia: Perception and short-term memory

3.3.11

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

The question as to whether language deficits are correlated with memory deficits or vice versa is still unanswered. Vallar, Corno & Basso (1992) reported that aphasic patients often show a reduced auditory verbal memory span but have no problems with phonological discrimination. In contrast, Martin & Breedin (1992) showed that aphasics can have problems with phonological discrimination while displaying no verbal memory deficits. Lastly, Blumstein (1995) claimed that most aphasics have some problems with phonological discrimination.

Since none of these studies give sufficient evidence to reject a possible correlation between phonological discrimination and verbal memory, the current experiment set out to investigate this possible relationship by manipulating both phonological discrimination and memory load. If there is in fact a relationship between the two factors, then phonologically similar items in a high memory load condition should have an effect on the overall performance. More specifically, patients with specific phonological discrimination or memory deficits should show qualitatively different response patterns under these conditions.

Word-initial phonological discrimination (same, similar, different) was tested with one and two syllable words in two memory conditions (low, high). Three aphasic patients and eight age- and gender-matched controls were tested in a same-different decision paradigm. Patient A suffered from a stroke in the left temporo-parietal cortex involving the left angular gyrus and the left supramarginal gyrus and was classified as an amnestic aphasic. Patient B has a lesion in the left fronto-parietal cortical area and was diagnosed as a Wenicke's aphasic. Patient C suffered a stroke in the left frontal cortex involving the left frontal inferior gyrus and left frontal cortical areas and was diagnosed as non-aphasic.

Results of two aphasic patients showed an interaction of phonological discrimination and memory load, even though by standard measures they had qualitatively different deficits. The data of the third non-aphasic patient were comparable with control data, though overall reaction times were slower than in controls.

In conclusion, these data provide evidence for an interaction between phonological discrimination and short-term memory processes. Based on these results procedures to refine diagnostic and therapeutic tools are under way.

3.3.12 Text comprehension after brain-injury: Encoding and retrieval processes

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

The distinction between micro-processes (which encode linguistic information), and macro-processes (which allow for a representation of the main ideas; vanDijk & Kintsch, 1983) in text comprehension seems to map on to the neurolinguistic distinction between aphasic and non-aphasic language deficits (e.g., Prigatano et al., 1986; MacDonald, 1993 and Glindemann & von Cramon, 1995). While in aphasic patient, the macrolevel and the use of general world knowledge seem to be relatively intact, patients with non-aphasic language deficits seem to show difficulties in these areas. For instance, patients with frontal lesions after closed-head injury (CHI) have difficulties organizing their discourse and establishing coherence between ideas. However, the empirical evidence available to date is mostly concerned with language production (e.g., Kazcmarek, 1987 and Hartley & Jensen, 1991). The few studies investigating comprehension processes in CHI patients showed that, like control subjects, they are able to identify main ideas in narratives, and that they remember explicit information better than implicit information (Nicholas & Brookshire, 1995 and Haut, Petros & Frank, 1991). We take this qualitatively similar pattern of performance to suggest that encoding processes are relatively intact in patients with non-aphasic language deficits. The hypothesis of the present study was that prefrontal brain lesions impair the active use of the resulting text representation.

In testing this hypothesis, it is crucial to be able to distinguish encoding and retrieval processes, interacting with both general world knowledge and text information. These interactions were studied in a seminal paper by Anderson and Pichert (1978). They showed that adopting a certain perspective during reading, which requires the activation of the appropriate general world knowledge, yielded better recall of perspective relevant ideas. More interestingly, providing subjects with an alternative perspective before a second recall attempt improved recall for items relevant to this new perspective.

In the present study with brain-injured patients we adopted this paradigm. Two stories were written which could be read under two distinct perspectives. The first uses the scenario of Anderson and Pichert (1978), in which two children take a tour of a house and describe what they see. The information in this story can be relevant either to a homebuyer (e.g., a leaky roof), or to a burglar (e.g., jewelry). The second text was about two children walking through a city, and could be read either from a tourist's point of view, or from an inhabitant's. The procedure was slightly modified, to take into account the special needs of brain-injured patients. Before encoding, the subjects were instructed to adopt one of the two perspectives. To facilitate comprehension, the story was presented both auditorily and visually. Subjects were asked to retell the story, and their recall was tape recorded. After the first recall, the experimenter gave instructions to now consider the alternative perspective, and to retell the story a second time.

Thirty patients' results have been analyzed. We classified the patients according to whether their lesions involved left prefrontal cortical areas or not. Twenty-five patients could be unambiguously assigned to one of the resulting two groups. The results show that both patient groups used the encoding perspective, i.e., they recalled more information from the relevant perspective during the first recall attempt. In addition, for patients without left prefrontal lesions we replicated Anderson's & Pichert's (1978) finding. After instructions to switch the perspective, these patients recalled less neutral information and less information from the first perspective than in the first recall, but the same amount of information from the second perspective. As hypothesized, this

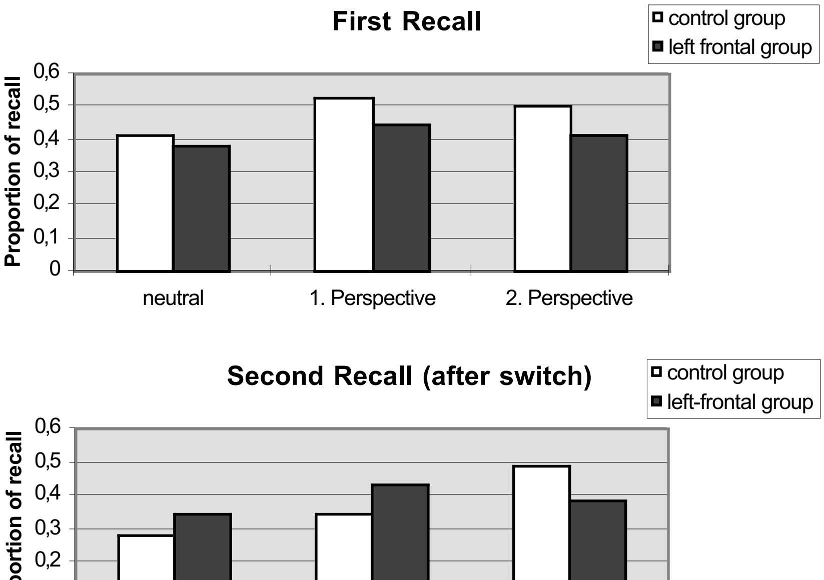


Figure 5.

perspective effect was *not* observed for the patients with left prefrontal lesions. More interestingly, when looking only at the information added during the second recall, the same interaction between perspective and patient groups was obtained. Control subjects recalled significantly more information from the second perspective during the second recall, while patients with left frontal lesions did not show this perspective effect.

These results are consistent with our hypotheses. First, in line with previous studies, the pattern of the first recall provided evidence for intact encoding processes in patients with left-frontal lesions. Second, the pattern of the second recall provided evidence for difficulties with the flexible application of general world knowledge during recall.

3.3.13 Multilevel representation of text information in brain-damaged patients

Guthke, T. & Ferstl, E.C.

The investigation of text comprehension in brain damaged patients is important for theoretical and clinical reasons. Following theories of text comprehension (van Dijk & Kintsch, 1983; Kintsch 1988, 1992) and empirical studies (Kintsch et al., 1990; Guthke & Beyer, 1995) we assume that during the processing of text a multilevel representation is built. We can distinguish three levels of text representation: the linguistic surface structure, the propositional textbase, and the situation model.

In this study, we were interested in whether brain damaged patients with various etiologies and neuropsychological syndromes are also able to build such a multilevel representation of a text. In particular, we attempt to establish a relationship between the patients' specific brain injury, their neuropsychological deficits, and the level of representation at which text comprehension deficits emerge.

To empirically differentiate the levels of representation, we adopted a word recognition paradigm (cf. Welsh et al., 1991). In this paradigm, subjects have to decide for a number of test words whether the word was mentioned in a text previously read. Beside old words from the text and unrelated new words, three different categories of related words are used: synonyms (or paraphrases) - which are in the propositional textbase; inference words - which tap an elaborated textbase; and contextually appropriate words - which are part of the situation model. Accuracy and reaction times for the recognition responses are measured. The variable of interest is how difficult it is to reject new words, as a function of the word type. With normal subjects, Guthke and Beyer (1995) confirmed that false alarm rates for synonyms were highest, followed by those for inferences and for context appropriate words.

We tested patients receiving treatment after brain injury. Three groups were of particular interest: aphasic patients, amnestic patients, and patients with deficits of executive functions.

Evidence from the literature on cognition and discourse processing in brain-damaged patients suggests differences between these groups of patients. For example the work by Ulatowska & Chapman (1994) suggests that in aphasic patients the ability to derive a situation model of a text is more preserved than the ability to remember the exact words and phrases of the text. Thus, we expect similar performance on inference and context appropriate words, while the distinction between old words and paraphrase words is expected to be more difficult. Research on semantic memory in amnestic patients (Tulving, 1994) is the basis for our assumption that amnestic patients are able to use their prior knowledge to build a situation model of the text. Following work by Baddeley & Wilson (1994) on amnesia and the problem of error elimination we predict difficulties in deciding whether a test word had been part of the text or is part of the activated prior knowledge. Thus, we expect to find a pattern similar to that of aphasic patients. In contrast, patients with executive dysfunction should have a preserved textbase, but more problems building the situation model of a text (see for example the description of nonaphasic communication disorder in Glindemann & von Cramon, 1995). Thus, we hypothesize that these patients have equal false alarm rates for inference words and context appropriate words.

At this time we have collected data of twenty brain-damaged patients. The comparison of the patients' performance with the performance of students (from Guthke & Beyer, 1995) shows no differences in rejecting inappropriate, unrelated test words. Similarly, patients performed as well as controls on test words mentioned in the text. These results suggest that the patients comprehended the texts, and that the recognition task is appropriate for use with brain damaged patients. The major difference was observed for the three crucial new word types. Across the patient group, all three categories yielded higher false alarm rates than for control subjects. This suggests that after brain injury the levels of representation are not as clearly separated. Further analyses, which are currently being conducted, include the evaluation of reaction times, as well as a classification of patients according to the aforementioned subgroups.

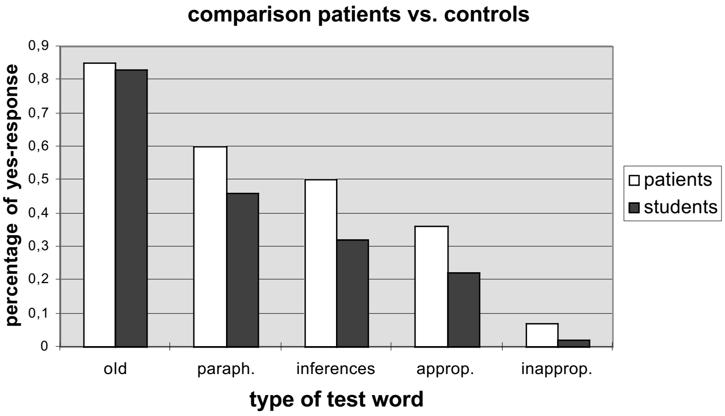


Figure 6.

From a clinical viewpoint our results may contribute to the process of making a differential diagnosis. It is important to attempt to unravel which structures and processes on which levels of text representation are more or less preserved in order to develop and evaluate appropriate intervention.

3.3.14 Neurolinguistic assessment of discourse comprehension deficits

Ferstl, E.C., Walther, K. & Guthke, T.

The assessment of cognitive deficits after brain injury is an important prerequesite for clinical rehabilitation. Only if we accurately understand which processes are intact, and which processes pose problems for a patient, can we design an appropriate rehabilitation programme. In the domain of language, a variety of standardized tests are available for the evaluation of aphasic symptoms (e.g., Token Test; AAT - the Aachener Aphasie Test; Huber et al., 1983).

However, there are patients whose communicative abilities and text processing seem to be impaired although they perform flawlessly on tests involving syntactic or semantic processes. These patients have difficulties with establishing coherence in discourse, in sequencing and organizing their ideas, in understanding non-literal language, such as irony, or in taking into account the situative context in which communication takes place. Empirical studies on various aspects of these deficits are accumulating (for reviews see MacDonald, 1993; Glindemann & von Cramon, 1995; Nicholas & Brookshire, 1995, among others), and a variety of diagnostic tools for the analysis of discourse *production* have been proposed.

In contrast, for the clinical assessment of non-aphasic *comprehension* deficits there are no standardized materials available that cover the whole range of symptoms. In German, the AAT contains a supplement which tests the comprehension of idiomatic expressions in the context of short scenarios. For comprehension of expository texts, a screening test has been developed (Salinas, 1993). Material for the assessment of narrative comprehension is lacking. The present project aims to be a first step in filling this gap.

Brookshire & Nicholas (1993) developed the DCT (Discourse Comprehension Test) for their North American patients. This test contains 10 easy, short stories (about 200 words long) describing humorous situations from familiar domains. After each story, eight yes/no - questions are used for testing comprehension. The questions crossed two factors. They either asked about main ideas of the text or about details, and they asked about explicitly stated information or about implicit information that needed to be inferred by the reader. With control subjects, as well as with brain injured patients (aphasic, right-hemisphere damage, and closed-head injury), Nicholas & Brookshire (1995) confirmed the expected pattern of performance: Main ideas are easier than details, and explicit information is easier than implicit information. In addition, there was an interaction between explicitness and salience; explicitness had a stronger effect on the comprehension of details than on main ideas.

We adopted one of the DCT stories for use in the outpatient clinic. We observed that the yes/no-questions were not sufficient for diagnosing language deficits. For most patients we obtained a ceiling effect, with a majority of the questions being answered correctly. Thus, we wanted to design similar, but more difficult materials.

Following a similar approach we then wrote two new stories, one about a hiking trip, and the other about going shopping. These stories were longer than the original text, and each was written in two versions. One version followed the story grammar and contained a complicating event and a resolution. In the more difficult version, this complication was replaced by an episode that was only temporally related to the preceding context. For each story, 48 questions were written. Twenty-four of these were appropriate for both versions, and 8 only for one version. These 32 questions were classified according to explicitness and salience. In addition, 16 questions were not assigned a priori to one of these conditions.

We tested these intuitive categories with 20 students and colleagues. Each participant read one story in the complicating version, and the other in the temporal version. The order was counterbalanced. After reading each story, subjects rated how interesting the story was on a 7-point scale. The results confirmed the differences in the versions. The complicating versions were rated significantly more interesting than the temporal versions.

One day later, (this delay was introduced to make the task more difficult for this population), the subjects answered the 48 questions for each of the two texts. After each question, they rated how important this question was, and how sure they were of their answer. Ratings for main ideas were reliably higher than for details. In addition, confidence ratings were higher for correctly answered questions than for errors. Again, these rating results confirmed the intuitive classification of the questions.
The performance on the yes/no questions showed the following effects. Overall, subjects made errors on 20% of the questions, and the hiking story was slightly easier than the shopping story. The interest level of the story did not influence accuracy on those questions which were the same for both versions. However, the eight questions specific to the complicated versions were easier than those for the temporal versions. Finally, the analysis using the different question types only partly confirmed the classification. There was a main effect of salience, with main ideas responded to more accurately than details (12% errors vs. 30%). However, no corresponding effect was observed for the factor explicitness (21% errors for both explicit and implicit information), and the interaction was not reliable.

To summarize, the pretest showed that the stories had a difficulty level which allows for a wider range of performance. The ratings confirmed the design choices with respect to interest level and salience of the questions. However, the failure to find differences in performance between explicitly stated information and inferred information makes it necessary to re-evaluate each of the questions, and to modify or replace some of them. This analysis by items is currently in progress.

3.3.15 Dynamic changes of motor learning in normal controls visualized by fMRI

Hund, M. &
von Cramon, D.Y

New imaging techniques such as fMR, PET and MEG have widened the possibilities to study the dynamics of new motor learning and continuous performance of a motor sequence. Motor learning processes have been associated with contributions of the premotor, supplementary motor and motor as well as sensorimotor and cerebellar cortices (Seitz et al., 1990 and Karni et al., 1995). In this fMRI-study, we investigated the neural changes and the time course underlying short-term motor learning and studied the effect of advanced motor skills in musicians on the functional patterns of motor learning. The activation patterns were analyzed in relation to the subjects' performance. Recent PET and fMRI-studies suggest a decrease or increase of activity (i.e. oxygen utilization or bold-effect) of certain contributors in the motor systems as a correlate of a short term-learning process. Whether the dynamic changes reflect pure habituation effects or indicate functional correlates of motor learning and how the performance influences the underlying neural network still remains unclear.

Thirty-three healthy subjects (18 females and 15 males, mean age: 27.3, stdev: 4.1, 4 left-handed, 29 right-handed) were included in the study. Nine of the 33 controls were piano players. Daily training of more than one hour for more than ten years was the inclusion criterion. The Edingburgh handedness inventory was performed to determine the degree of hand dominance. All subjects were instructed to perform a motor sequence with their dominant hand without visually controlling the movement, immediately before fMRI-recording. The sequence consisted of a rapid and repetitive finger tapping opposed to the thumb: 1-3, 1-5, 1-2, 1-4, 1-2, 1-2. Each subject executed a behavioral test of this sequence before and after motor training in the scanner. The tapping frequency and the number of errors were evaluated. The fMRI-experiment started with a motor control task consisting of rapid flexions and extensions of all fingers, followed by a tapping-learning block of 35 minutes in five consecutive runs performed with the dominant hand. FMR-data acquisition finished with one run of finger tapping of the non-dominant hand using the same just learned sequence.

A FLASH sequence was chosen in all subjects, using TE=40 ms and TR=80 ms with a 128 x 64 matrix. Sixty-four consecutive images were acquired per scan alternating between four images of rest and four images of motor training. Slice thickness was 5 mm with 2 mm interslice gap. Three axial slices through the SMA-field and the primary motor cortex were chosen.

Raw data were preprocessed, further evaluation was performed with the routines of the BRIAN software (F. Kruggel) using t-test. Functional images were created by generating statistical zmaps with z-values > 3.5 on a single pixel level. For further analysis regions of interest were selected and characterized in size, volume, and intensity of activity during the course of motor learning.

Behavioral task. All subjects profited significantly from the training session: The mean frequency prior to training was 33/min (6 errors) and post training 58/min (5 errors), (p

< 0.001). Piano players tapped significantly quicker than all other subjects (pre-training: 52 versus 26, post-training: 72 versus 53, $p < 0.001$). The number of errors did not differ significantly pre and post training within the groups.

fMRI-study. The activation patterns throughout the learning stage showed dynamic changes in all subjects and disclosed differences between the piano players and the non-musicians.

Primary motor cortex (M1): M1-activation was more prominent in the control task (=rapid finger flexion) than in the tapping task and showed higher activation levels in the non-musicians than in the piano players (2.2 versus 2.0 %, group means). In the more complex tapping task, however, M1 was slighty more activated in the musicians (Figure 7). This was especially true for the contralateral M1, when the non-dominant hand was performing the tapping task (group mean activations - musicians versus non-musicians: 2.3 versus 1.54 %, $p > 0.05$). Motor learning (Figure 8) showed habituation effects for M1 only in the non-musicians with activation levels of 1.8 % in the first seven minutes of training and 1.4 % after 35 minutes of training. The piano players, however, showed sustained M1-activation with a slight increase in activated pixels (1.9 % in the first seven minutes and 2.4 % after 35 minutes of training).

SMA. The SMA region was involved to a lesser extent in the piano players than in the non-musicians. This was true thoughout the course of motor leaning of the dominant hand, in the less complex control task and as well in the tapping task performed with the non-dominant hand (Figures 7 and 8). Both groups disclosed decreases in activation during motor learning (piano players 0.7 to 0.26 %, non-musicians 0.93 to 0.48 %).

In conclusion, dynamic changes during motor learning disclose different patterns of activation in musicians and non-musicians: Piano players showed little involvement of the SMA and sustained activation of M1 whereas untrained subjects showed considerable changes of all activated areas during the time course of motor learning. We found lateralization effects only in the non-musicians with higher activation levels in the dominant motor cortex.

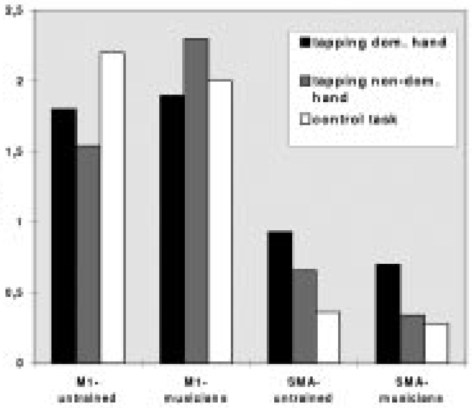


Figure 7. Standardized mean group activations in the different conditions are shown

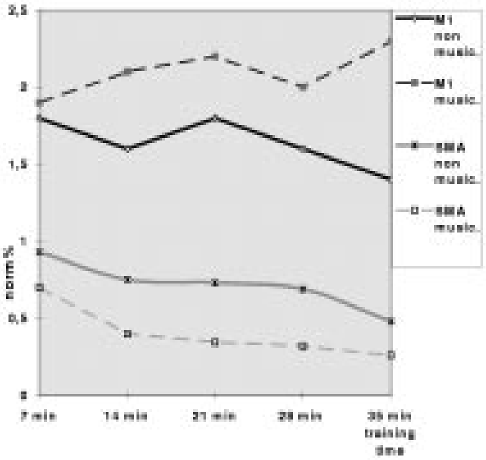


Figure 8. Group means of activation changes during motor learning in M1 and SMA

3.3.16 Characterization of small vessel disease by means of proton spectroscopy and structural 3 Tesla-NMR

Hund, M., Norris, D.G., Guthke, T. & von Cramon, D.Y.

The aim of this study was the characterization of cerebral small vessel disease (CSVD) by means of proton spectroscopy (^{1}H-MRS) and high resolution MR-Imaging. CSVD is the common pathological feature of a series of different subtypes of cerebral microangiopathy varying in clinical symptoms, neuropsychological abnormalities and MR-imaging characteristics (Constans et al., 1995 and Oppenheimer et al., 1995). Despite profoundly improved MR-imaging techniques applied to the patient population a corresponding clinical characterization of the disease via imaging criteria is still missing. In particular, the prevalence of cognitive disorders in this inhomogeneous patient group seems to be far from predictable. In this study two different MR-techniques were applied in an attempt to relate the findings to clinical and neuropsychological data.

Ten patients with cerebral microangiopathy underwent single voxel-^{1}H-MRS and high resolution structural T2- and T1-weighted-imaging. All investigations were performed using a Bruker 3 T/100 Medspec, whole-body system. Signal transmission and reception were performed using a 28 cm id. quadrature birdcage resonator. Either a whole-body gradient set (30 mT/m switchable within 500 ms) or a head gradient insert (Magnex: 40 cm id., 35 mT/m, 150 ms switching time) were employed. Spectra were obtained from the parietal white matter and the occipital cortex in all patients and in an age-matched control group (TR 3 sec, TE 135 ms, voxel-size 2 x 2 x 2 cm). The spectra obtained were analyzed in terms of NAA/Cr,PCr-, NAA/Cho- and Cho/Cr-ratios. The results were compared to the spectroscopic data obtained from an age-matched normal control group of 15 subjects. In addition, a detailed clinical and neuropsychological examination completed the patients' study. The latter consisted of an evaluation of attention and memory. Simple reaction times in tonic alertness testing were used to summarize the degree of attentional impairment.

Significant differences in regional metabolite levels were found in the patient group as compared to the control subjects (Figure 9). This was especially true for NAA/Cho- (patients: 1.4, SD±0.2, control: 1.8, SD±0.3, $p < 0.001$) and NAA/Cr ratios (patients: 1.5, SD±0.2, control: 1.8, SD±0.2, $p < 0.009$) obtained in the parietal white matter. Even more pronounced were the deviations in NAA/Cho levels obtained from occipital cortices (patients: 1.6, SD±0.4, control: 2.2, SD±0.1, $p < 0.018$). The patient group showed less homogeneous metabolic NAA-concentrations and more variation than were seen in the parietal white matter. Significantly elevated Cho/Cr-levels also indicated the pathological state (patients: 0.8, SD±0.1, control: 0.6, SD±0.04, $p < 0.002$).

Preliminary evaluation of neuropsychological and spectroscopic data seem to indicate a close relation between impairment of tonic alertness (vigilance) and decreases in NAA/Cho. Three patients showed normal metabolic NAA/Cho levels and also had normal reaction times (mean 228±42 ms) in the tonic alertness task. Selective and divided attention testing revealed normal results, too. The remaining seven patients with decreased NAA/Cho levels, however, showed prolonged reaction times (mean 310±45 ms) in the tonic alertness task.

Structural high resolution MR-imaging at 3 T especially in the T2-weighted sequence allowed the characterization of detailed white matter-abnormalities in the patient group. These ranged from periventricular hyperintensities (leucoaraiosis) and lacunar infarction to small hyperintense signals in the vicinity of white matter arterioles without obvious signal changes in other subcortical structures. The degree of abnormalities found in structural MR did not correlate with the severeness of CSVD as defined by focal neurological signs and neuropsychological deficits.

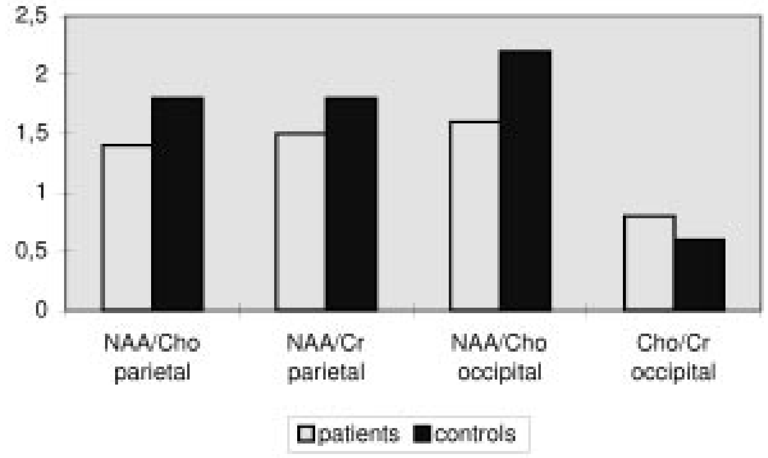


Figure 9. Distribution of metabolic levels in patients and controls

Single voxel ^{1}H-MRS allowed a clear discrimination of patients and age-matched controls. Moreover, preliminary comparisons of ^{1}H-MRS and neuropsychological data could introduce NAA-metabolic levels as a predictor of the severeness of attentional impairment. Hence, combined neuropsychological testing and ^{1}H-MRS could be of use in the characterization and prognosis of CSVD.

Response selection and deep brain stimulation

3.3.17

Schubert, T., Volkmann, J. & Müller, U.

Recent models (Alexander et al., 1986) of basal ganglia circuits suggest an involvement of basal ganglia in the mechanism of response selection. However, research on patients with Parkinson's disease (PDs), a well known basal ganglia dysfunction, reported contradicting evidence concerning the involvement of basal ganglia in tasks requiring different degrees of response selection. For example, Pullman et al. (1988) showed evidence for a selective involvement of basal ganglia in the response selection. The authors investigated the influence of levodopa on performance in a choice reaction task (CRT) and a simple reaction task (SRT). Since in a CRT subjects have to respond to different stimuli with distinct reactions a CRT is assumed to involve the response selection stage. On the contrary, in a SRT only one stimulus is presented repeatedly to subjects requiring one and the same motor response. Therefore, it is assumed not to require the response selection stage. PDs performance in a SRT and a CRT was investigated with a so called on-off paradigm. In that paradigm, the dopamine antagonist levodopa, assumed to compensate deficits in basal ganglia processing, was manipulated in different steps (optimum-dose, mid-dose, off-state). The results showed an influence of levodopa on CRT performance, but not on SRT performance. The authors concluded that the basal ganglia circuits are involved in CRT processing but not in SRT processing. The different involvement of basal ganglia circuits is explained by the different involvement of a response selection stage in the investigated tasks. In a CRT the basal ganglia are needed since a response selection is involved, whereas in a SRT due to the lack of the response selection stage the basal ganglia can be bypassed. On this background, Pullman et al. (1988) concluded that CRT and SRT are based on different independent neural circuits and therefore can be carried out independently each from other.

However, serious objections have been raised in literature concerning the conclusions of these authors. In contrast to Pullman et al. (1988) the results of Goodrich, Henderson & Kennard (1989) imply that in a SRT the same neural systems are involved as in the CRT. However, in addition to CRT a special prefrontal system is involved in the SRT maintaining a certain stage of attentional arousal and preparing all neural systems for stimulus processing in advance. According to these assumptions the results of Pullman et al. (1988) should be regarded as an artifact. To further elucidate the possibility of a selective involvement of the basal ganglia in the response selection we investigated two predictions of Pullman et al.'s conclusions in two studies:
1st prediction: If CRT and SRT are based on independent neural systems they should not interfere each other if carried out together in a dual-task situation. This prediction only holds if CRT and SRT do not share the same input and output systems.
2nd prediction: A direct manipulation of the basal ganglia circuits should influence SRT and CRT performance differently. To test this assumptions a deep brain stimulation (DBS) of the Globus Pallidus internus in the basal ganglia (Davis et al., 1997) was employed in cooperation with Jens Volkmann, Department of Neurology of the Heinrich-Heine University in Düsseldorf, Germany. It was asked how this manipulation affects performance in a CRT and a SRT.

To test the first prediction of the Pullman et al. model we used a dual-task paradigm. In different conditions subjects carried out different tasks together. Situation A required an auditory CRT together with a visual SRT. Situation B required an auditory CRT with a visual CRT. An important manipulation in both situations concerned the time interval between both tasks. Time interval 1 amounted to 50 ms between onset of both tasks. Thus, it required a large overlap between both tasks and should lead to a large interference between both tasks. Time interval 2 (800 ms between onset of both tasks) induced no overlap between both tasks. Therefore in this situation task processing in both tasks should not interfere each other. The difference between task performance in situation 1 (maximal overlap) and situation 2 (no overlap) should reveal dual-task costs due to task interference. The results yielded significant and equal dual-task costs in situation A and situation B suggesting dual-task interference between a CRT and a SRT similar to dual-task interference between two CRTs. Thus, the first Pullman et al. prediction about independent processing of CRT and SRT was not supported. These results of course do not rule out conclusively the possibility of differential involvement of basal ganglia in CRT and SRT processing.

Therefore, the second experiment was conducted to directly test this possibility. In cooperation with Jens Volkmann,Düsseldorf, Germany, neural processing in basal ganglia circuits was directly manipulated by DBS. DBS induces a reversible lesion of the Globus Pallidus internus and leads to an improved information flow through intrinsic basal ganglia loops in patients with PD. According to the Pullman hypothesis DBS should influence performance in CRT but not in SRT. In a pilot study one 38 year old patient with juvenile onset Parkinson's disease was investigated. The data revealed an influence of DBS on reaction times in CRT as well as on reaction time in SRT. Thus, the second prediction of independent processing in CRT and SRT was not supported by empirical testing. Although not conclusive, the data reveal that even in a situation without response selection, information needed for motor programming needs to be processed by the basal ganglia. Thus, there is no suggestion of for a bypass of the basal ganglia in the information processing stream if no response selection is needed. Further research is needed to support this conclusion.

A first clinical study with a mechanical finite element model of the human head

3.3.18

Hartmann, U. & Kruggel, F.

About twenty years ago the finite element method (FEM) was first applied to head impact modelling which allowed the geometrical restrictions imposed by analytical continuum models to be overcome. With FEM the different material properties and the complex geometry of internal brain structures can be taken into account. Within the past 20 years only about ten mechanical FEM-models have been developed. Most of them are two-dimensional with the brain geometry taken from an anatomical atlas or from anthropometric data. Because of the simplifications made in modelling brain anatomy, many of these models are not able to explain injury mechanisms.

In contrast, our model is designed to help investigate brain damage of individual subjects due to external (i.e. impact) and internal forces (i.e. space-consuming lesions). In order to take the patient's individual brain anatomy into account we base the geometry description of our model on MR tomograms. Starting from a segmented MRI dataset a 3D finite element mesh of the object (i.e. the head and internal structures) is produced by our fully automated mesh generator that was specially designed for medical image data. Figure 10 shows as a typical output of our mesh generator a cross section through a finite element head mesh consisting of bricks with 2 mm edge length. We are able to

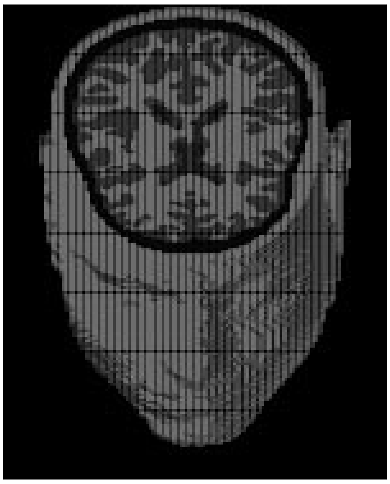


Figure 10. 3D finite element mesh consisting of bricks with 2 mm edge length. This mesh was generated automatically on the basis of a segmented MRI dataset.

perform simulations with a up to 400 000 elements thus reaching a ten times higher spatial resolution than prior models. The advantages are a very precise description of brain structures with highly complex shape (e.g ventricles) and a high numerical reliability of the obtained results.

As a first clinically relevant application we studied the coup-contrecoup phenomenon. This phenomenon occurs when the whole head is subject to an acceleration caused by a focal impact. At the end of the first phase of the coup-contrecoup phenomenon the brain hits the interior of the skull according to the rule of inertia. This process leads to a pressure increase in the region where the brain hits against the skull and a suction effect in the opposite head area. Measurements from cadaver experiments are available for comparison with results from our model. We simulated an impact to the forehead in the fronto-occipital direction and performed a dynamical FE analysis on the mesh shown in Figure 10 covering 15 ms in steps of 0.2 ms. Figure 11 shows the development of the stress component in the fronto-occipital direction for a sample slice. Within the first ms a pressure wave propagates through the skull. An area of negative stress becomes apparent and as this spreads out there is a simultaneous development of a region of positive stress originating from the occipital skull. The simulated pressure values that can be calculated with the help of the stress values compare satisfactorily with the published data. Their correspondence shows that our model yields qualitatively and quantitatively reasonable results.

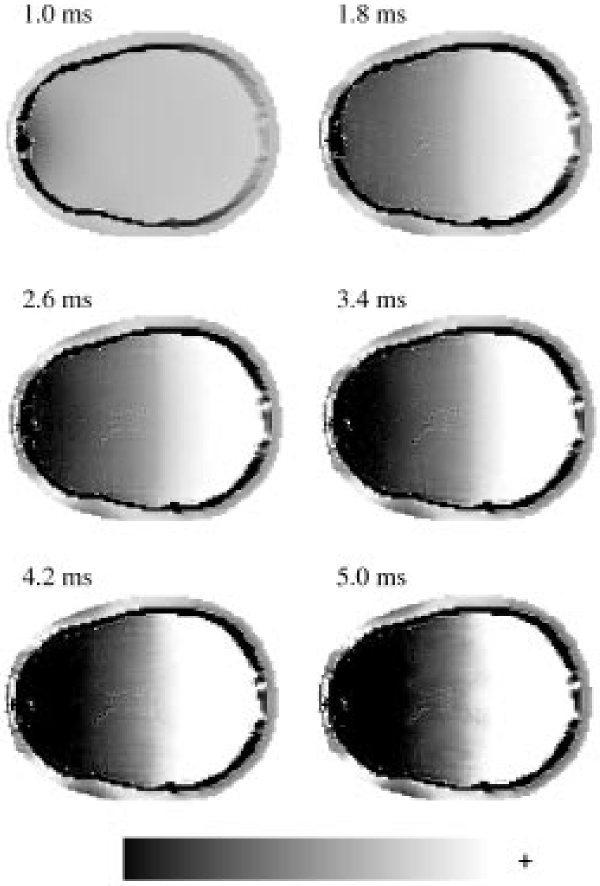


Figure 11. Simulation of an impact to the forehead in the fronto-occipital direction by a dynamical FE analysis on the mesh shown in Figure 10. Within the first ms a pressure wave propagates through the skull. An area of negative stress becomes apparent and as this spreads out there is a simultaneous development of a region of positive stress originating from the occipital skull.

This first successful application encourages us to further develop our model by adding mathematical and anatomical features. Within the mathematical domain, a modal FE analysis yielding the eigenvalues and eigenmodes of our head model has recently been accomplished. Measurements of the eigenfrequencies have been determined in volunteers, so a modal analysis may be used as a second method of model validation. Finally, it may serve to examine other brain injury mechanisms such as diffuse axonal injury (DAI).

Experimental designs have developed rapidly in the short history of fMRI. We started with simple block designs and have introduced more recently socalled 'single-trial' experiments which allow an event-related analysis of the fMRI signal. When EPI became available in the summer of 1997, we started a number of projects with the common aim to investigate methodological aspects of single-trial designs and to apply them to the analysis of specific cognitive processes. We began with a systematic analysis of short intertrial intervals (3.4.1). The finding of this particular study was that substantially shorter intervals can be used than have been reported so far in the literature. This finding will be quite significant for further studies since it allows many psychological experiments to be administered in an almost indentical manner as the were administered traditionally. A second line of research investigated changes of the BOLD-response towards critical trials presented in isolation, or embedded in a rapid sequence of trials (3.4.2). Beyond demonstrating that signal changes can be measured in a rapid succession of trials, the goal of this project was to search for sources of signal loss that may accompany rapid single trial experiments. In a third project, we looked for signal changes that occured at defined timepoints within a trial. The behavioral paradigm allowed us to distinguish the temporal onset of processes related to retrieval from primary and secondary memory, among others (3.4.3). Results showed analogous shifts in the BOLD-response time curves in specific brain areas. Other projects prepared future methodological developments. Before EPI became available, a study of random sequence generation was run to investigate the principal brain areas involved in this task (3.4.4). A follow-up experiment, which allows a parametric analysis of the component processes will soon be conducted. In the context of our visual search experiments, a mathematical model for visual search was developed which will, among other applications, be useful for the investigation of individual differences in future fMRI-experiments (3.4.5). In cooperation with Prof. E. Zaidel, two projects on interhemispheric transfer in commissurotomy patients could be completed (3.4.6, 3.4.7).

3.4.1 Use of short inter-trial intervals in 'single-trial' fMRI-experiments

Pollmann, S., Wiggins, C.J. & von Cramon, D.Y.

Recently, single trial designs have been used as an alternative to the conventional blocked designs for fMRI-experiments. Single-trial designs have major advantages over blocked designs. However, so far they had a major drawback in the long inter-trial intervals (ITIs) that were applied to allow the BOLD-response to return to baseline before the next trial is presented. The use of interval durations of 14 s and longer, limits the total number of trials that can be run in a given experimental session, reducing statistical power. Moreover, control over subjects' mental activity during the long ITI is poor. This has prompted us to investigate whether shorter ITIs can be used for single-trial designs in spite of the overlap of BOLD-responses elicited by temporally contiguous trials.

Twenty-two subjects were scanned in visual search experiments with varying ITIs between 12 s and 4 s.

Seven AC-PC oriented slices were acquired using a two-shot EPI sequence with a TR of 2 s for a complete image. A gradient recalled echo, with TE = 40 ms, was used with an RF flip angle of 40 degrees. Data were collected at 3T using a Bruker 30/100 Medspec (Bruker Medizintechnik GmbH, Ettlingen, Germany).

We observed a gradual decline of signal amplitude with shortening of ITIs. However, in the cortical ROI, the effect size, i.e. the ratio between task-related signal changes and noise remained approximately the same between ITIs of 12 s down to 6 s. Only at ITI = 4s

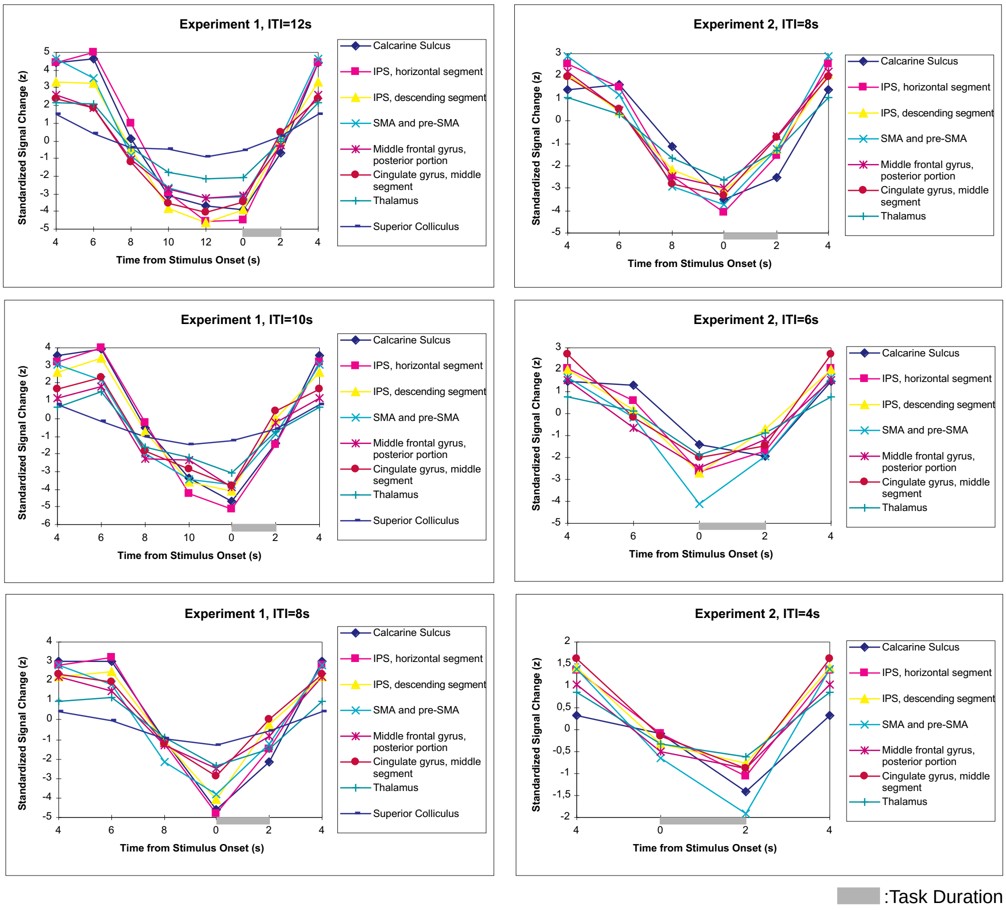


Figure 1. Timecurves of the BOLD-response for eight ROI

was effect size reduced by about 50% in all cortical ROI. In the two subcortical ROI, effect size was already reduced at longer ITIs. Since effect size determines the statistical power needed for a test this means that averaged 'single-trial'-experiments can be run with ITIs as short as 6 s without overlooking activations that may have become significant at longer ITIs. If one takes into account the fact that reduction of ITI allows the experimenter to run more trials in a given duration of an experimental session, short ITIs may even lead to better results than long. However, our data imply that caution is needed if subcortical areas are to be investigated. At ITI = 4 s, the shape of the BOLD-response changes in a qualitative way. Therefore, it appears as if data analysis of experiments with such extremely short ITI could profit from timecurve modeling methods.

Embedded single trial design for fMRI

3.4.2

Dove, A.,
Pollmann, S.,
Wiggins, C.J. &
von Cramon, D.Y.

To overcome drawbacks of the conventional block design used for PET and fMRI studies, averaged 'single trial' designs were recently introduced. Individual trials were spaced approximately 15 s apart to allow the BOLD signal to return to baseline. For most psychological questions it is desirable to use shorter intertrial intervals (ITI). However, when short ITIs are used, the BOLD responses of contiguous trials overlap. We investigated: 1. whether it is possible to detect activation elicited by critical trials in designs with overlap, and, 2. whether critical trials elicit comparable signal changes in a condition with an overlap of trials as well as in a condition without overlap. To address these questions, critical trials were embedded pseudorandomly in an continuously presented basic task with a trial duration of two seconds (ITI=1s). BOLD-signals elicited by these 'embedded' trials were compared to those elicited in a standard 'single trial' experiment (ST) with an ITI of 15 seconds. Critical trials differed from basic task trials in an additional task component. Since the critical trials in the embedded single trial (EST)-experiment were spaced a minimum of 15 s apart, comparable to the ST-experiment, we expected the activation associated with the additional task component to be comparable in the 'embedded' as well as the 'standard' experiments.

For data-acquisition a two-shot EPI sequence was used (TR = 2 s, TE = 40 ms, FOV = 25 cm). In the basic task a green plus or minus sign was presented, and the subject reacted by pressing the right (+) or left (-) button of a response board. In the critical trial the stimulus color was changed to red and the required response was reversed (right: - / left: +). Behavioral pretests showed, as is consistent with the literature (see Rogers & Monsell, 1995), significantly longer reaction times in these switch- compared to no-switch-trials in both experiments. The data of 6 subjects were analyzed. They performed both the EST- and the ST-experiment in the tomograph on two different days.

Both experiments led to comparable results: The critical trials elicited activation in the same cortical areas in the EST- and the ST-experiments. This shows that it is possible to detect activation elicited by critical trials even if the ITI is very short. This is a significant result, because it confirms that psychological experiments may be run in their natural fashion as fMRI experiments. To examine further whether the variation of the

ITI caused changes of the timecourse of the BOLD signal, ROIs were chosen based on the functional maps. The data of one normal right-handed female subject are presented below. An area in the left superior parietal cortex, which was activated during the basic and critical tasks, was examined in both experiments, as well as an area in the left middle frontal gyrus, where significant activation was observed in the critical condition of both experiments, but not in the basic task. Figure 2 shows the timecourses for two ROI averaged over the timepoints shortly before (r-1), during (red) and after the presentation of the critical trial in the EST experiment (r+1 to r+7) and the averaged timecourses of the same ROI as measured in the ST experiment.

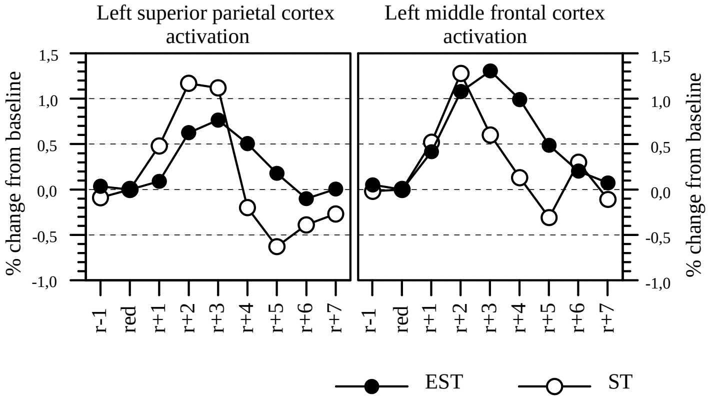


Figure 2. Timecourses of two ROI in percent change from baseline (EST: embedded single trial experiment; ST: single trial experiment, see text).

As can be seen in both cases, the latency of the time course is different in both experiments. This might be due to the fact that in only the EST experiment, the subject has to switch tasks when the embedded single trial is presented, as well as switching back to the basic task in the next trial. No undershoot was observed in the BOLD response timecourses in the EST condition, which is probably due to the fact that the basic task continued after the presentation of the embedded task. While the amplitude of both curves obtained in the middle frontal region is comparable, the amplitude of the timecourse of the superior parietal ROI was smaller in the EST experiment than in the ST experiment. This might indicate that in regions already activated, an additional activation does not linearly add up, although, it may be reduced.

3.4.3 Dynamics of working memory and long term memory: An fMRI study

Zysset, S.,
Pollmann, S.,
Wiggins, C.J. &
von Cramon, D.Y.

The primary aim of this study was to determine the neuronal correlates of areas involved in retrieving stored information and in utilizing or manipulating this information. Previous work has shown that retrieval from secondary memory and from primary (working) memory can be dissociated by behavioural measures (Conway & Engle, 1994). Retrieval from secondary memory is independent of set size, whereas retrieval from primary memory is set size dependent. A modified version of the Sternberg (1966) paradigm, in which subjects learned three different sets of letters to criterion, was used. In each trial of the experimental tasks, a cue for the set and a letter were presented on a screen. The subject had to decide whether or not this letter was a member of the indicated set. The main processes involved in solving this task are: encoding of the cue and probe item, retrieval from secondary memory, scanning of primary memory, response selection and response execution. By introducing a sufficiently long delay between the presentation of the cue and the probe item, scanning of primary memory, response selection and the response execution are postponed. Brain areas specifically involved in scanning and decision making process should show delayed activation timecourses compared to areas involved in retrieval and perceptual processes. Additional processes, such as subvocal rehearsal to bridge the delay, come into play or are prolonged in the delay condition. Furthermore, in the delay condition, the retrieved set has to be kept active in primary memory for a longer time than in the absence of a delay.

Using fMRI, we were able to locate the anatomical structures involved and to analyze the time course of the different regions of interest. The comparison of the two delay conditions will allow us to investigate the association of memory processes and brain structures.

Using the above mentioned paradigm, we conducted a series of fMRI experiments using an EPI sequence. The comparably short repetition times with EPI and the single trial design allowed us to investigate the time course of different activated areas.

Trials were presented every 15.3 seconds and one scan consisted of 24 trials. For every condition (delay, no delay), two scans were measured. The experiment was conducted with 18 subjects, none of whom had participated in a similar experiment before.

Functional MR images were acquired at 3T using a Bruker Medspec 30/100 system. 14 slices were aquired (19.2 cm FOV, 5 mm thick, 2 mm spacing, 128 x 64 matrix), using single shot, gradient recalled EPI (TE 46 ms, TR 1700 ms).

Strong bilateral activation was found in both conditions in the inferior precentral sulcus (pCSinf), in the pars opercularis of the inferior frontal gyrus (F3op), and in the posterior middle frontal gyrus (F2p). The intraparietal sulcus (SIP) and SMA were active bilaterally. Additionally, extended activations in the lingual gyrus and fusiform gyrus were found. In the delay condition, a more anterior part of F2p was additionally activated.

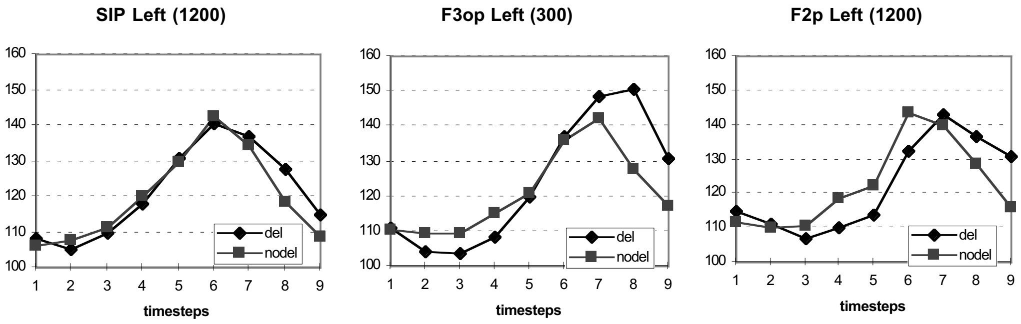


Figure 3. Averaged time course of the activation in the SIP, F3op and F2p for one subject. The trial starts during timestep 4, the probe item in the delay condition appeared during timestep 5.

The activation time course for the left intraparietal sulcus (SIP) is similar for both conditions. It seems that the underlying process is not affected by the introduction of a delay. Activation in the left opercular pars of the inferior frontal gyrus (F3op) is prolonged by the delay, thus supporting the findings that this area is involved in subvocal rehearsal and phonological sequencing. This process is needed for bridging the delay and scanning the set. Activation in the left posterior middle frontal gyrus (F2p) is postponed due to the delay. The underlying process seems to be dependent on the presentation of the probe item, being involved in the matching component of the retrieval process.

3.4.4 Cortical areas and the control of self-determined finger movements: An fMRI study

Schubert, T.,
von Cramon, D.Y. &
Niendorf, T.

Introduction. The aim of this study was to investigate the cortical areas involved in the control of self-determined finger movements. In the past, cortical activation during this control process was often investigated with tasks requiring subjects to generate actions in random order. This forces subjects to select actions by an inner criterion reflecting randomness and to control the order of executed actions compared to this criterion. However, PET studies about the cortical areas in the control of such self-determined actions did not report homogeneous results. For example, results of a PET study by Frith et al. (1991b, Exp. 2) indicated that a region in the prefrontal cortex (PFC), the dorsolateral PFC, and regions in the higher order parietal association area, e.g. the angular gyrus (GA), play a major role in the generation of self-determined finger movements. Concerning the role of prefrontal activation in movement control, Frith et al. (1991b) suggest a supervisory control concerning the selection of action. However, different hypotheses concerning prefrontal activation in the control process are reported in the literature. Petrides et al. (1993) reported a PET study where subjects had to generate digits verbally in self-determined order. Although the results indicated an involvement of dorsolateral PFC in this task, the authors were able to show that this prefrontal activation is not associated with the process of controlling the action selection. The results imply an activation of dorsolateral PFC due to high working memory load while manipulating and maintaining the sequences of generated digits in working memory. The different assumptions concerning the role of different brain regions in the control of self-determined actions require further investigation. We used fMRI to investigate the involvement of brain areas during the control of self-determined finger movements. We were especially interested in examining the role of higher order parietal association areas in the process of movement control. In our view, this area, due to its multimodal processing character, seems to serve as an area integrating sensory, motor and sensorimotor information used for local movement control. The role of this area for control of self-determined finger movements was hitherto underestimated compared to the large emphasis on control processes associated with prefrontal activity.

Methods. In contrast to the studies of Frith et al. (1991) and Petrides et al. (1993) we used a parametric design (Braver, 1997) and manipulated the difficulty of control by increasing movement frequency (low versus high). An increase of movement frequency does not increase memory load per se (Baddeley, 1966). However, it should lead to a higher processing rate in regions which are involved in the integration of feed-back information from the moved effectors with motor information about the next movements to be executed. In the activation task subjects should tap with different tapping frequency in two different movement conditions (predetermined versus self-determined movements). It was asked whether movement frequency and movement condition affect the activation associated with movement control. Measurement of blood-oxygen-level-related signal intensity changes was conducted by the MUSIC approach, which facilitates the acquisition of multi slice data sets within the same time as it is necessary for a standard single slice FLASH-experiment (Loenneker et al., 1996 and Niendorf et al., 1997). Functional MR images were acquired using a 3 Tesla whole body system (Medspec 30/100, Bruker, Ettlingen, Germany). For the T_2*-weighted scanning procedure an HF spoiled version of the MUSIC technique (1,2) (TE=40 ms, TR=70 ms, $\alpha=20^0$, 128 x 64 data matrix) was employed.

Results. Several areas were identified as being activated in all tapping tasks. Activation in left and right hemisphere was located in the areas surrounding the ascending and horizontal segments of the intraparietal sulcus (IPS). However, only in the area surrounding the horizontal segment of the left IPS number of subjects with significant activation differs between the self-determined and predetermined tapping conditions. Independently of frequency condition number of subjects with significant activation was higher in the self-determined condition than in the predetermined condition. Other activated areas were around the central sulcus, superior precentral sulcus and the supplementary motor area (SMA). Decreases of activation were located in the left and right hemisphere in the superior frontal gyrus, middle frontal gyrus and posterior cingulate gyrus. In the superior frontal gyrus, as well as in the posterior cingulate gyrus, a number of subjects with significant decreases of activation was higher in the self-determined conditions than in the predetermined conditions. Thus, this analysis indicates the horizontal segment of IPS, the superior frontal gyrus and the posterior cingulate gyrus to be task-relevant in generating self-determined actions. After having established this the influence of frequency on intensity of activation change was assessed. It revealed that only in the horizontal segment of IPS extent of activated voxels was influenced by movement frequency indicating a major role of IPS in the control of generating self-determined movement sequences. Thus, the results of this experiment provide evidence that, while generating self-determined finger movements, the brain needs sensorimotor information which is probably delivered by regions surrounding the ascending segment of the IPS. The horizontal segment of IPS is involved selectively when the sequence of movements has to be controlled according to the randomness criterion. For this task, the brain needs continuous on-line information about which finger was moved during the preceding taps. This requires information about the identity of fingers and their spatial position. The decisive role of the regions surrounding the horizontal segment of the IPS in this task is probably due to its vicinity to posterior parietal areas involved in the processing of finger identity (angular gyrus) and control of spatial motor processing (superior parietal lobule). Most likely, the lack of prefrontal activation in our study is due to low memory load while controlling the finger sequences. Currently, this hypothesis is being assessed by a follow-up study where a tapping task is combined with a working memory task.

3.4.5 Determination of visual search strategies with a mathematical reaction time model

Müller-Plath, G.

The purpose of this research is to create a mathematical reaction time model for visual search tasks. This model will be able to be applied to determine search strategies and to estimate the time duration of attentional subprocesses.

The visual search literature mostly relies on a dichotomy of search strategies: the display size independent 'pop out search', and the display size dependent 'serial search'. These two strategies are traced back to two subsequent processing stages of visual attention: the preattentive and the attentive stage (Neisser, 1967 and Treisman, 1980). The search strategy is determined by analyzing the slope of the reaction time function with increasing display size. This approach contains several problems. First, the dichotomy of flat versus linearly increasing reaction time functions seems to be a gross oversimplification of many different reaction time courses. Therefore, the dichotomy of search strategies (pop out search vs. strictly serial search) is doubtable (Müller, Heller & Ziegler, 1995). Second, there is some evidence that the search strategy not only depends on the target and the distractor qualities, but also on the display size (Wolfe, 1994). Therefore the slope of the function 'reaction time by display size' is not a valid indicator to determine the search strategy. We tried to find evidence for the proposed continuum of search efficiencies and to generate an alternative approach to determine the search strategy.

This alternative approach is to consider the total reaction time a sum of the time duration of single search steps. The number and duration of these steps depend partly on task parameters (e.g., target and distractor features, number and arrangement of items in the visual field) and partly on processing parameters of the subject (e.g., times for attention dwell, for attention shift, and for the motor response). The interaction of these parameters is modelled as a set of mathematical equations based on the model 'Guided search 2.0' (Wolfe, 1994). A fit of the modelled reaction times to empirical reaction times yields numerical estimations of the parameters and an exact determination of the search strategy of the subject in the given task.

A simple visual search task was used to obtain empirical reaction times under suitable experimental variations: subjects had to search for a target that differed from the homogeneous distractors in only one basic feature (brightness, spatial frequency, size or shape). Two factors were varied: the difference between target and distractors in the relevant basic feature, and the number of items in the display.

Figure 4. Example of the visual search task: The subject had to search for a darker grating. The difference between the target and the distractor grating contrast and the number of items in the display were varied.

The experiment was conducted with three subjects. A numerical algorithm was programmed to fit the model equations to the empirical data. Figures 5 a - b give an exemplary overview of the results for one subject and one stimulus dimension. The other subjects and dimensions showed similar characteristics.

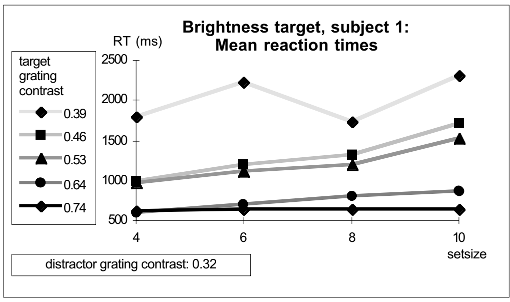


Figure 5a. Mean reaction times of subject 1 in the brightness dimension (target present trials only)

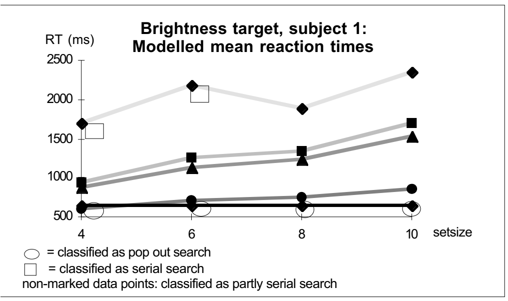


Figure 5b. Model fit and strategy classifications

The results confirm that the often claimed dichotomy between a flat time course (interpreted as pop-out-search) and a linearly increasing time course (interpreted as serial search) can not be maintained. There must exist a third class of search strategies, a so-called "partly serial search", between the two poles "pop-out-search" and "strictly serial scanning". Additionally, the search strategy seems to depend not only on the target-distractor-contrast, but also on the display size.

The model achieves a good fit to the empirical data: In all cases more than 99% of the variance of the mean reaction times are explained. Because of the high number of free parameters this indicator may be of limited use. However, at the two poles, "pop out search" and "serial search", the strategy classifications of the model agree with those of the traditional method. The estimated parameter values show a good psychological validity (relations to each other regarding the experimental conditions). In particular, the estimated durations of attentional subprocesses are compatible with the values discussed in the current literature (Egeth & Yantis, 1997).

Subsequent experiments will be performed to test the model more thoroughly: experimental variations of certain stimulus attributes should lead to the change of certain parameter values (the task dependent ones) while leaving others unaffected (the subject dependent ones).

Factors contributing to the enhanced bilateral redundancy gain in commissurotomy patients

3.4.6

Pollmann, S. &
Zaidel, E.

When commissurotomy patients are asked to respond to visual targets, they show a redundancy gain, i.e., a reduction of response latencies when two targets are presented instead of one. As long as the redundant targets are presented within one hemifield, the size of the redundancy gain is comparable to that of normals. However, if the two targets are presented, one in each hemifield, the redundant targets' effect (RTE) was enhanced over that of normals. This counterintuitive finding was first reported by Reuter-

Lorenz et al. (1995) but has since been replicated in two other commissurotomy patients. In the patient that we studied previously, L.B., response latencies were strongly reduced in tachistoscopic visual search tasks that differed in their attentional demand characteristics. Using the same task, we investigated another commissurotomy patient, N.G. The crucial difference between L.B. and N.G. was that N.G. has previously demonstrated, in spite of complete commissurotomy, an ability to cross-match visual stimuli of moderate complexity, e.g., letter forms and Vanderplas shapes. N.G. showed comparable RTE effects within and between hemifields, lacking an enhancement of the bilateral RTE. This confirms earlier data that disruption of stimulus input to one hemisphere is crucial for the development of the bilateral RTE after complete commissurotomy.

In addition, it turned out that slow crossed responses of commissurotomy subjects contributed to the enhancement of the bilateral RTE. When this source of artefacts was removed by comparing the redundant target responses only to unilateral uncrossed responses, the enhancement of the bilateral RTE was much stronger for inefficient than for pop-out search conditions.

Reuter-Lorenz et al. (1995) have argued that the locus of the RTE enhancement lies in the motor domain. Their argument was backed by the finding that stimulus variations in intensity or eccentricity did not affect the size of the bilateral RTE. However, our data imply that early attentional visual processes contribute, possibly in concert with later response-related processes, to the RTE enhancement in splits. This finding is compatible with recent findings which relate redundant target effects to changes of the N1 ERP-component which, in turn, have been attributed to sources in extrastriate cortex.

3.4.7 The importance of interhemispheric visual transfer for spatial orienting

Pollmann, S. & Zaidel, E.

Disorders of spatial orienting are common after a variety of, mostly right hemispheric, brain lesions. For instance, after a lesion of right posterior parietal cortex, neglect and extinction are often apparent. Obviously, the analogous regions in the left hemisphere are, in these patients, not sufficient to guide attention to ipsilateral hemispace.

Previously, we had the opportunity to test a complete commissurotomy patient, L.B., who had demonstrated an inability to transfer simple visual form information between the hemispheres. In L.B., we had found a laterality reversal of an extinction-like effect that we had found earlier in normal subjects. Normals have greater difficulty in detecting a target in the left visual hemifield (LVF) when a pop-out distractor is presented in the right hemifield (RVF), than vice versa. In L.B., the laterality was reversed. Distractors in the LVF slowed contralateral target search more than RVF-distractors.

We explained this reversal under the assumption that the right hemisphere is better at directing attention to ipsilateral hemispace than the left hemisphere. Given this assumption, we have shown that that the laterality reversal can be explained by the disruption of ipsilateral visual input to the RH. However, there are alternative explanations. In particular, commissurotomy interrupts inhibitory callosal fibers which may serve to balance the left- and right hemispheric orienting systems. Testing a second complete commissurotomy subject, N.G., who differs from L.B. in her capacity of interhemispheric visual transfer, enabled us to differentiate between these hypotheses. In contrast to L.B., N.G. has demonstrated an intact ability to crossmatch simple geometric or letter shapes between the visual hemifields. Thus, testing her enabled us to investigate the contribution of disruption of nonvisual interhemispheric pathways to the extinction-like effect.

We found that N.G. showed a 'normal' extinction-like effect: RVF-distractors slowed LVF-target search significantly, while LVF-distractors did not affect search for RVF-targets. When we compare the data of L.B. and N.G., we can conclude that the lack of interhemispheric visual transfer was decisive for the reversal of the extinction-like effect in L.B. Taken together, the data support a dominant role of the right hemisphere in the bilateral allocation of spatial attention. The data also explain why spatial orienting is, at least in their everyday behavior, intact in commissurotomy patients. Both hemispheres process contralateral input, and the balance between the hemispheric orienting systems is kept via subcortical commissures.

Cognitive processes in man are usually studied by stimulation experiments. Responses are recorded by methods such as functional MRI, EEG, MEG, SPECT and PET - all of which map different aspects of the underlying cognitive process. Because these different methods yield complimentary information about the anatomical, metabolical and neurophysiological states of the brain, integrated data evaluation is highly desirable and will lead to results unobtainable with only one modality.

The workgroup on signal and image processing (SIP) focuses on the following aims:

- to develop and install new algorithms so that the information yielded from these experiments is improved upon
- to allow a combination of results from different modalities
- to achieve a precise anatomical description and quantification of the functional activity
- to build structural and functional models of the brain.

These long-term goals were mapped in 1996 onto the following projects:

- the analysis of the individual neocortical structure of the human brain
- the segmentation of structural MR images
- the detection and analysis of functional MR images
- a spatio-temporal analysis of EEG/MEG data.

In addition, one Ph.D. project, covering the visualization of complex biomedical datasets, is currently underway.

Program modules developed in these projects were integrated into the BRIAN processing environment (see Annual Report 1996), which now serves as a standard data evaluation platform for structural and functional data in our institute.

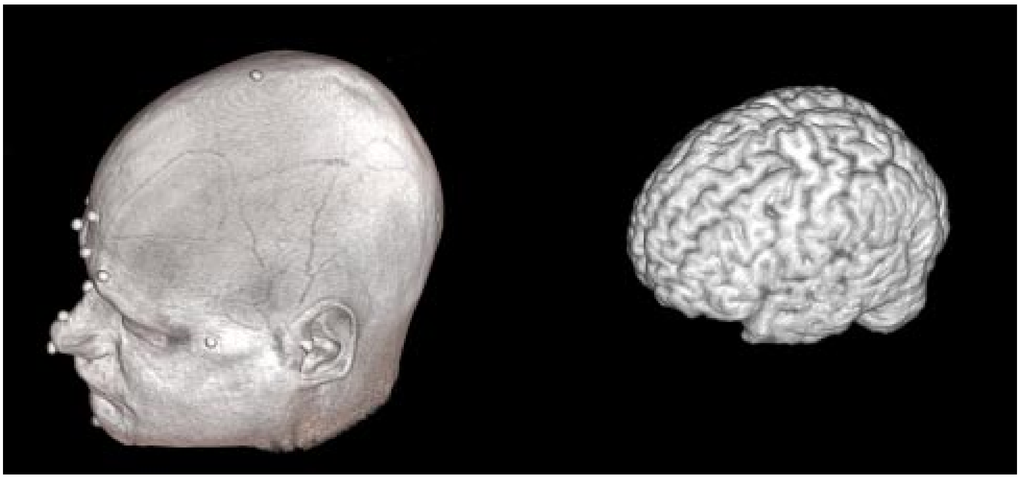


Figure 1. Reconstruction of a human head from a 3D high resolution MR dataset (left). The beads serve for later reference with the SQUID system in our MEG scanner. The brain (right) is extracted and aligned with the stereotactical coordinate system by an automatical procedure.

3.5.1 Invariances in sulcal patterns of the human brain

Lohmann, G. & von Cramon, D.Y.

The folding of the cortical surface of the human brain varies dramatically from person to person. Figure 2 illustrates this fact: the foldings patterns of the three brains shown here are quite different.

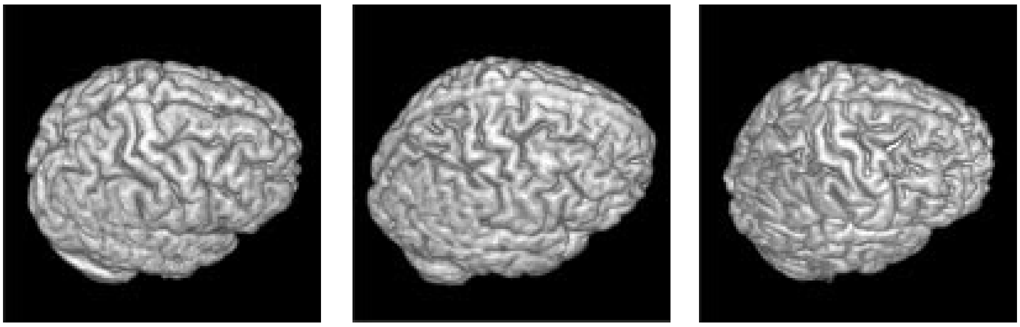


Figure 2. Reconstructions of 3D high resolution MR datasets of three different persons. A considerable interindividual variability of the neocortical surface is apparent.

Nevertheless, the folding pattern is not arbitrary. Our research has shown that there are some clearly definable regions within the cortical surface for which the folding pattern has a low degree of inter-personal variability. This result was obtained from a probability map which shows the probability of the occurrence of a fold. We found that the most invariant regions are located in a regular pattern across the cortical surface consisting of two strings of regions- one of which is aligned with the inter-hemispheric cleft, and one of which surrounds the Sylvian fissure. Although interhemispheric differences are evident from the map, we found remarkable inter-hemispheric similarities supporting the notion that anatomical asymmetries - related to functional lateralization - superimpose basically homologous hemispheres.

Our input data consisted of T1-weighted MRI scans of 50 healthy volunteers, of whom 21 were female and 29 were male. All data sets were subjected to a standard preprocessing routine which ensured that all data sets were rotated and scaled into a standard coordinate system and with an isotropical resolution of 1mm.

The basic idea underlying our investigations is as follows: we automatically extract the sulcal patterns from every MR data set using new image analysis procedures, explained below. We then merge the sulcal patterns from all data sets into a single combined data set, such that each location in the combined data set receives a frequency count which denotes the number of different sulcal patterns found at that location. Locations where sulci from many different data sets are found receive a high count; locations where sulcal patterns from only a few data sets are found receive a low count. Thus, regions of invariability can be identified by their high frequency count. To give an unbiased estimate of the frequency of sulcal patterns, we restrict our investigation to one particular level of depth. In order to focus on the more relevant primary and secondary sulcal structures, we used a depth level of 10 mm.

Figure 3 illustrates the sequence of image analysis steps required to extract the sulcal cuts. Figure 3a shows one vertical (coronal) slice of an input MR data set. The input data set is first subjected to a white matter segmentation (Figure 3b) which separates

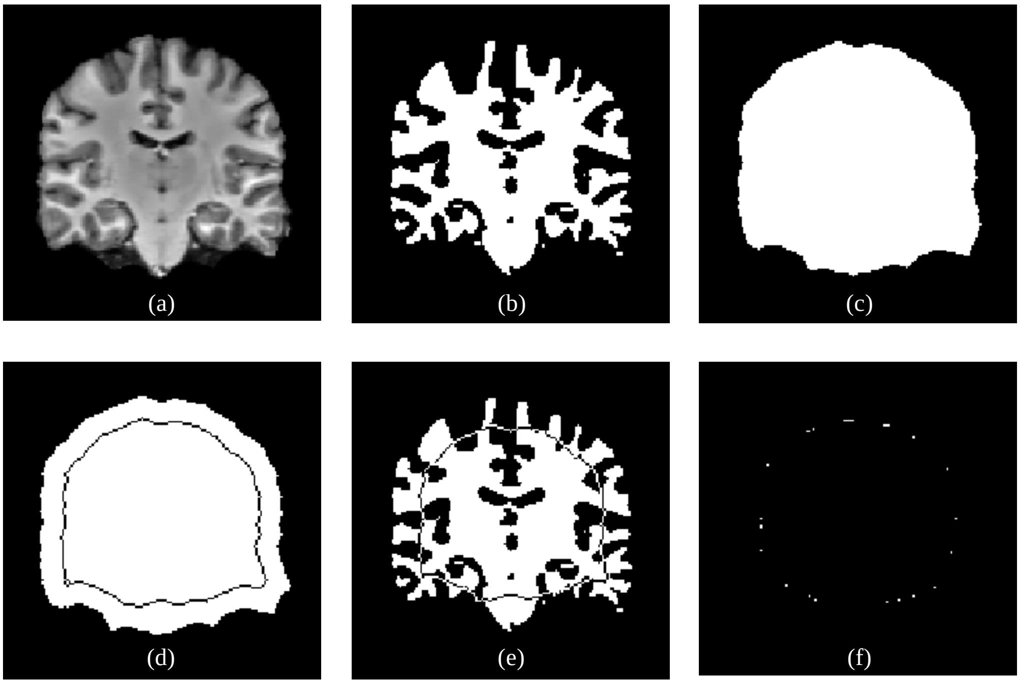


Figure 3. Sequence of image analysis steps required to extract the sulcal cuts: a coronal slice of an input MR data set (a), white matter segmentation (b), closing the sulci to obtain an idealized smoothed surface (c), depth level of 10 mm (d), level superimposed on the white matter (e) and, finally, the sulcal cuts (f).

white matter from other tissue classes. This step helps to ensure that the sulcal indentations are more pronounced and thus more easily identifiable. We then close the sulci using a morphological closing filter (Figure 3c) to obtain an idealized, smoothed surface. The depth level is computed with respect to this surface using a distance transform. Figure 3d shows a depth level of 10 mm as is displayed superimposed on the white matter in figure 3e. Finally, we perform a 3D thinning which reduces the sulcal interiors to a thin medial surface residing in the center of the sulcus. Intersecting the medial surface with the depth level yields the sulcal cuts shown in figure 3f. For ease of presentation, only one two-dimensional slice through the data set is shown, despite the fact that the procedure is entirely three-dimensional and produces a three-dimensional output.

The resulting sulcal cuts from all 50 data sets were subsequently assembled into a single combined data set from which a probability map was compiled. The maps of both the left and the right hemispheres (Figure 4) reveal that there exist a number of regions of particularly high probability which we may interpret as regions of high interpersonal invariance. They show up as grey spots in the probability maps. For brevity, we will call them ROI (region of invariance). Note that the ROIs are grouped in regular patterns across the cortical surface. There is one string of ROIs which is grouped around the Sylvian fissure consisting of the following structures: the inferior frontal sulcus (ifs), the lower parts of the central (cs (inf.)) and postcentral/intra-parietal sulcus (poc/ips), and a posterior and anterior component of the superior temporal sulcus (sts (post.) and sts (ant.)). The left hemisphere also has a local probability maximum at the middle temporal sulcus (mts) which is not present in the right. The right hemisphere has an ROI at the inferior pre-central sulcus (ipc) which is not as pronounced in the left hemisphere.

A second string of ROIs is aligned with the inter-hemispheric cleft and consists of an anterior and a posterior component of the superior frontal sulcus (sfs (ant.) and sfs (post.)), the upper part of the central sulcus (cs (sup.)), and the horizontal and descending part of the intra-parietal sulcus (ips (hor.) and ips(desc.)). The central sulcus has an additional maximum at Broca's knee (cs (Broca)).

In comparing the left and right probability maps, we found that the left hemisphere generally has a higher degree of invariance. In fact, there are more than twice as many voxels with a probability count of more than 70 percent in the left hemisphere map than in the right (311 vs. 141). We found that structures pertaining to the sts (post.), mts and the ips (hor. and desc.) are clearly left-dominant, a finding that fits in with the fact that language related cognition show dominance on the left side. However, we could not confirm that visuo-spatial processing makes up for it on the right. Thus, caution must be used when trying to interpret the functional significance of anatomical asymmetries.

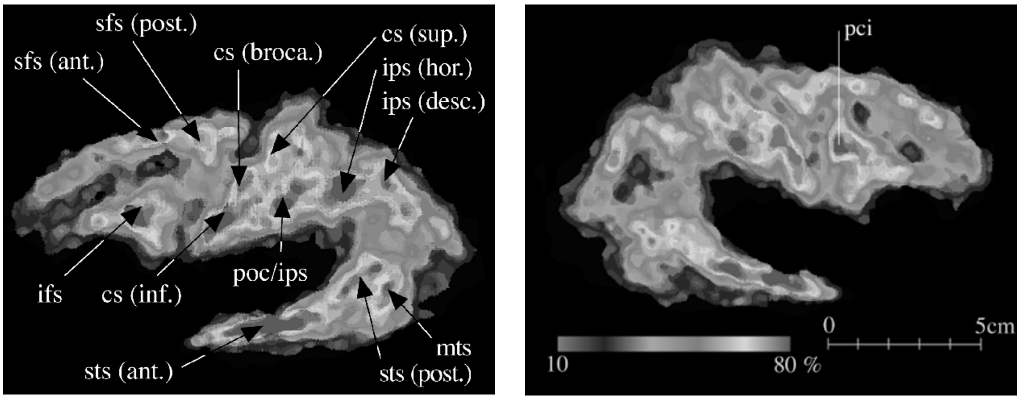


Figure 4. Probability maps of the left and the right hemisphere reveal that there exist a number of regions of particularly high probability which we may interpret as regions of high interpersonal invariance.

3.5.2 Segmentation of structural MRI

Palubinskas, G. & Rajapakse, J.C.

Image segmentation is a basic problem in "low level" image processing. A low level task consists in extracting information from a set of data without any semantic interpretation. It can be compared to the first level of human vision - perception without interpretation. In the case of image processing, a segmentation algorithm consists in labelling a given scene, namely, a label referring to a specific class or area is associated with each voxel. So the problem can be divided into three parts: information extraction, classification and regularization. The aim of this process is to obtain a symbolic description of the image.

Before classifying the data, we first have to define the relevant feature to be classified and extracted. Given the set of relevant features, we have to divide it into different clusters. Finding the number of these clusters and their localisation in the feature space is the problem of classifying the data. The last part of the problem consists in adding some *a priori* knowledge to the classification. When classifying voxels, some errors arise due to noise, inhomogeneities, partial volume effects, etc. Regularization and statistical methods (MRF, maximum entropy, etc.) are thus used to enforce constraints on the solution such as spatial homogeneity.

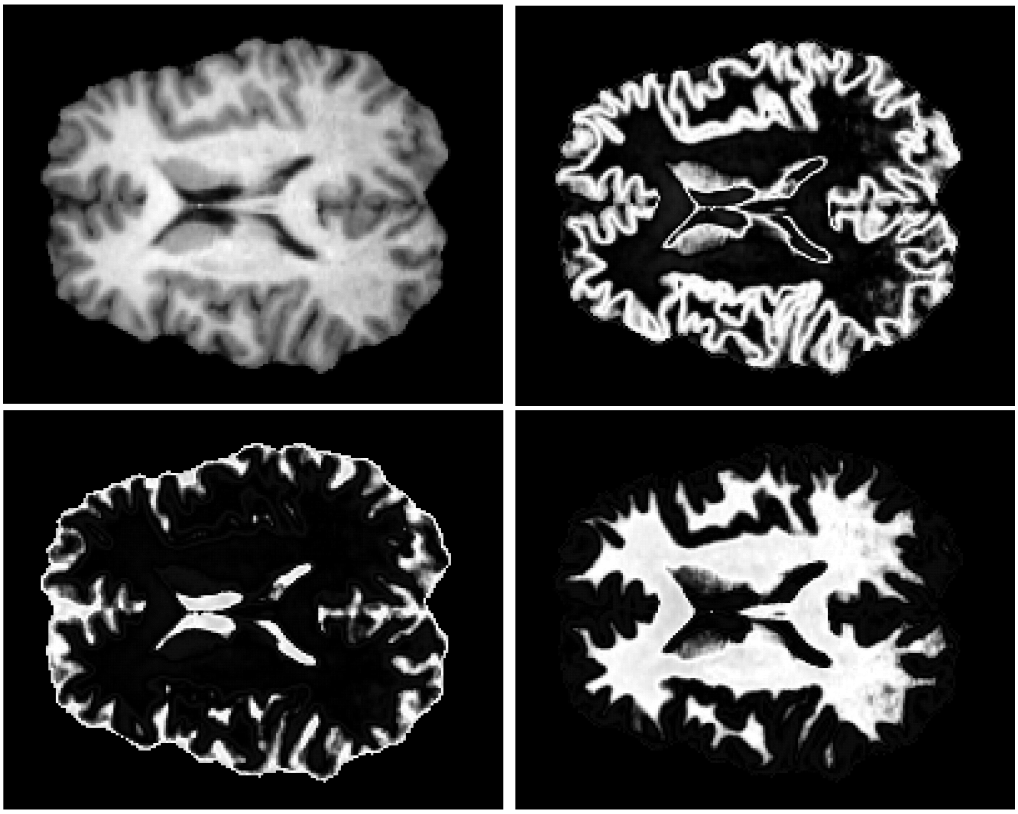


Figure 5. Example of clustering using the fuzzy k-means algorithm in ist ML-EM variant. Top left is a sample slice from a high resolution 3D MR dataset, top right the "cortical" class, bottom left the "CSF" class, bottom right the "white matter" class.

We have studied the most common clustering algorithms which employ global criteria, including k-means, fuzzy k-means and maximum likelihood with expectation maximization (ML-EM). Algorithms are investigated on T_1 images in comparison with a manual segmentation. The influence of cluster initialization and stopping criteria on the accuracy of clustering algorithms were studied. As a result, we extended the k-means algorithm to use variances and a priori probabilities of classes by using a Bayesian framework and entropy minimization. This extension allows a better adaptation of clustering algorithm to data and an automatic detection of the number of clusters.

Intensity inhomogeneities and partial volume effects have a great influence on the accuracy of a clustering result for MRI. In addition to the AMAP and BMAP approaches developed last year, we have studied fuzzy clustering techniques. The result of a fuzzy clustering algorithm is a fuzzy image, where each pixel contains membership values for all clusters (Figure 5). During the hardening of a fuzzy image, a pixel is assigned to a cluster with a highest membership value, which means that we are sure about a given label of a cluster. We can construct a reject cluster by introducing a threshold (e.g. 0.9) for a membership value. For pixels from a reject cluster we can perform additional clustering or segmentation by introducing some a priori information. These could be operations on labels of a clustered image (voting in a window, MRF), or operations on memberships of a fuzzy image (summation in window, MRF). Results of the various approaches are compiled in figure 6.

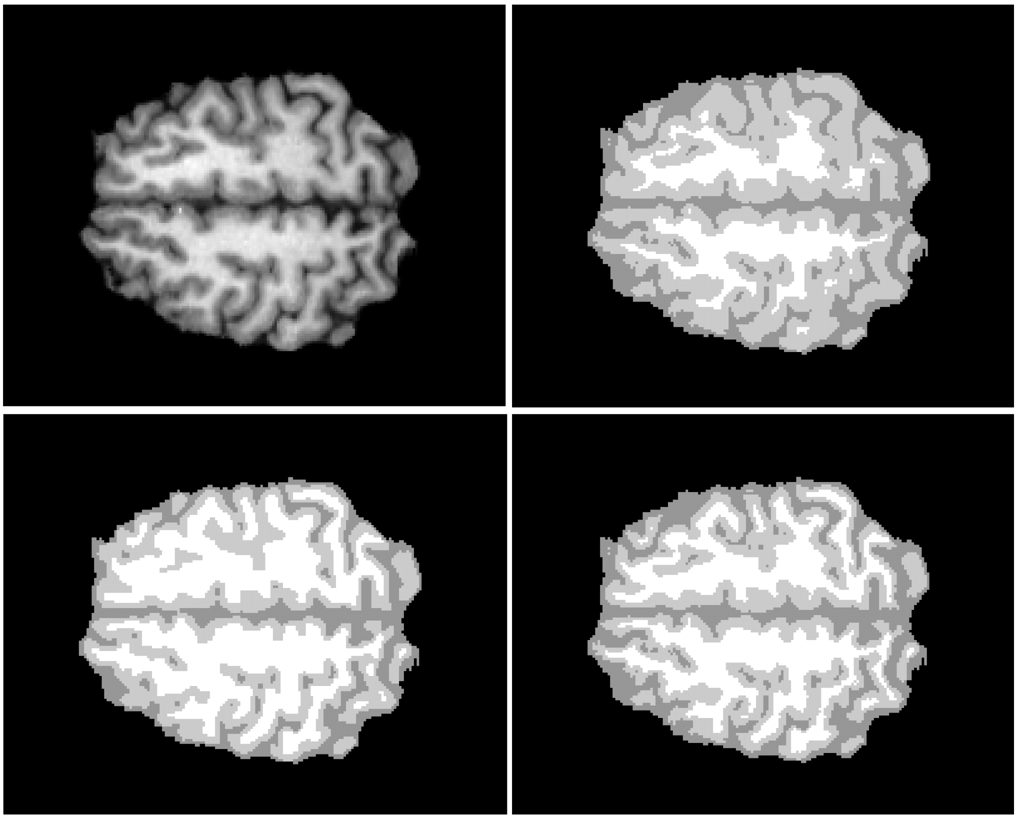


Figure 6. Comparison of the currently available "advanced" clustering techniques. Top left is a sample slice from a high resolution 3D MR dataset, top right the result of a standard k-means technique using 3 classes, bottom left the output of an AMAP clustering, bottom right the output of the k-means ML-EM variant.

3.5.3 Functional MRI analysis

Kruggel, F., Descombes, X. & Rajapakse, J.C.

Functional image analysis needs to address the following questions:

- Which functional activation is correlated with the experimental task?
- At which anatomical location is an activation center located?
- How much activation is there?
- Are there common activation patterns in a group?
- How do activated brain regions interact?

As a result of a functional study, we have a time series of 2D or 3D images and a set of stimulus functions which represent the experimental design. The problem of detecting functional activity from these data is determined by the following factors:

- the underlying T_2*-weighted image
- uncorrelated intensity changes due to noise, scanner instabilities, etc.
- localized intensity changes correlated with a stimulus in time-series which are (i) delayed and (ii) dispersed
- uncorrelated intensity changes due to other cognitive processes.

Besides these problems, we also have to deal with spatial distortions of the image and with areas of signal void.

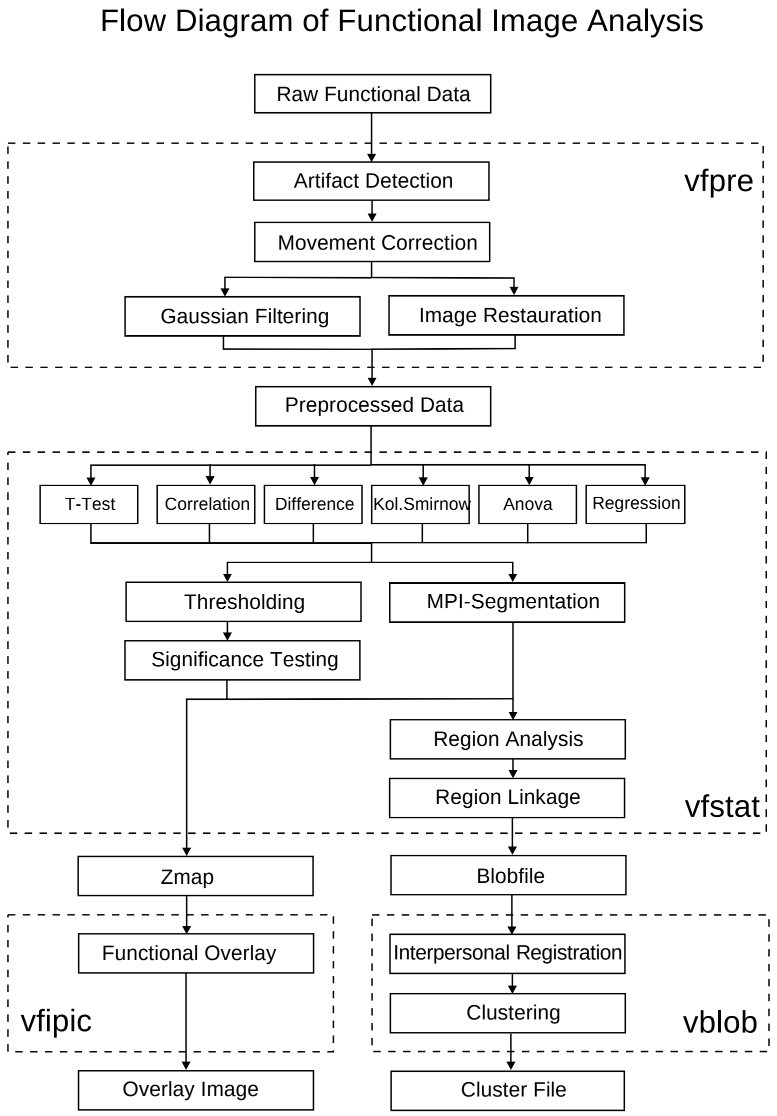


Figure 7. Flow diagram of the processing steps to analyze functional MR data: preprocessing (vfpre), statistical analysis (vfstat), visualization (vfipic) and interpersonal registration (vblob).

Figure 7 contains an overview of the process structure to evaluate functional data as are currently implemented within the BRIAN package. Basically, four steps are necessary to evaluate the data: (1) a preprocessing stage, (2) signal detection, (3) data visualization, and (4) quantification and interpersonal comparison of functional activation. These steps will now be explained in more detail.

The *preprocessing stage* improves the signal quality before signal detection. Included within this stage are: artifact detection, baseline correction, movement correction, and image restoration.

Gaussian filtering is commonly applied to increase the signal to noise ratio in fMRI preprocessing. However, this filter spoils the signal and introduces artifacts (loss of fine objects, blurring of edges, fusion of neighboring objects, displacement of objects). Several alternatives have been proposed for signal restoration. Markov Random Fields are very popular in this context because statistical tools to estimate parameters and to

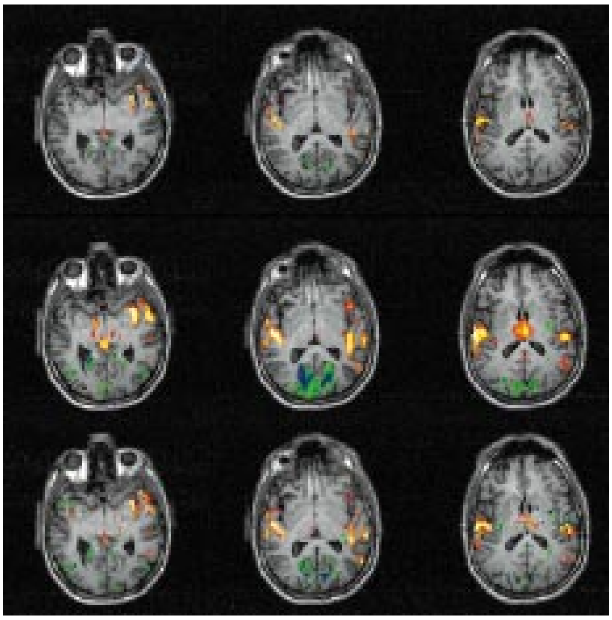


Figure 8. Comparison of standard evaluation (left), Gaussian filtering (center) and image restoration (right) on the results of a statistical evaluation of the same fMRI experiment.

optimize the model are well defined and efficient. A priori properties are modeled by interactions between neighboring pixels in time and space. Using well-adapted interactions, we can reduce noise without introducing blurring.

We have developed a spatio-temporal MRF to restore fMRI time series. Expected activated areas are very fine structures and consist of a few voxels. Therefore we pay particular attention to preserve edges in the spatial domain. In the time dimension, we have smoothed the data to avoid false alarms during the analysis step. As we will study the derivative of the signal, this smoothing can be quite strong. The results show that the noise has been considerably reduced without spoiling the signal of the activated voxels.

The *detection of significantly activated areas* is commonly achieved by application of a test statistic. In this stage, a statistical parameter map (referred to as zmap) is calculated, which represents the amount of correlation of the data with a given stimulus function. The Pearson correlation coefficient and its multivariate extension, the multiple regression, have been found to be most sensitive and useful here.

The introduction of a model for the hemodynamic response in the BOLD effect allows us to enhance the detection specifity. We have developed a novel approach to determine hemodynamic responses from fast fMRI time-series. This hemodynamic response is delayed, dispersed, habituated, and transient at the onset and offset of the stimulus condition. Our attempt is to quantify these aspects of fMRI time-series using a simplified mathematical model.

We presume a Gaussian function as a hemodynamic modulation function. Parameters of this function are considered to be space-variant and stimulus-dependent. We determine these parameters using frequency- and time-domain analyses of fMR time-series with least square estimations. The general linear model (or regression equation) for a time-series y in response to an experiment with design matrix X, which consists of $x_1 ... x_q$ stimulus conditions and $x_{q+1} .. x_{q+p}$ dummy covariates, is given by:

(1) $$\mathbf{y} = \mathbf{MX}\beta + \varepsilon$$

where β denotes the regression coefficients and ε is uncorrelated noise. The modulation matrix M is given by:

$$\mathbf{M} = \left[\frac{\gamma_i}{\sqrt{2\pi\sigma^2}} \exp\left(-\frac{(i-j-\mu)^2}{2\sigma^2} \right) \right]_{i \times j} \qquad (2)$$

where μ is called the lag, σ the dispersion, and γ the gain of the hemodynamic response. Introduction of hemodynamic correction significantly improved the analyses in all fMRI experiments studied so far (see table 1 for a comparison). The comparison of intrasubject and intersubject hemodynamic parameters supported our conjecture of space-variance and stimulus-dependence of parameters. Also, the values of lag and dispersion of fMRI time-series obtained in the experiments were close to those previously reported, thus validating our model.

Model	Regression	Poisson	Gamma	Gauss
Location	(68, 92)	(67, 93)	(67, 93)	(67, 94)
Size (Voxel)	48	44	39	43
z-score	3.46	4.45	4.34	5.00
Gain	0.03	0.05	0.05	0.05
Lag (s)	-	3.35	3.18	4.50
Dispersion (s^2)	-	3.35	20.87	4.72
Square Error	0.05	0.05	0.06	0.05
SNR (dB)	16.68	18.23	17.92	19.53

Table 1. Characteristics of the largets activated region on a selected slice in a visual stimulation experiment obtained without hemodynamic correction (regression) and with hemodynamic correction using Poisson, Gamma and Gaussian modulation functions.

The final signal detection is usually performed by thresholding the statistical map converted into a z-map. A z-map is modeled by a zero mean unit variance Gaussian Random Field of which the smoothness parameter can be estimated using different approximations. Clusters above a given threshold are then analyzed with respect to their size, their maximum value, or both. Most commonly, the Friston-Worseley formula, which is based on Adler's theory of excursion sets, is applied here. In the theoretical foundations as well as in practice, we have found a number of problems with this approach such that a re-evaluation of this problem is necessary.

Besides the Friston-Worseley approach, one can use image processing techniques to segment the z-map so that activated areas can be delineated. Here, the "MPI model" has been developed and has been seen to improve the detection sensitivity. We consider a stochastic model embedded in a Bayesian framework and describe the z-map by three maps referred to as the restored image, the segmented image and the pixon-map. The pixon-map represents the local scale of the description. The restored image is obtained by locally convolving the pixon-map and the segmented image. The segmented image is interpreted as a classification of the original image using contextual information. We model local interactions of neighboring pixels by a Markov Random Field. Because we expect some fine structures delineating the edges of functional activation in the pixon

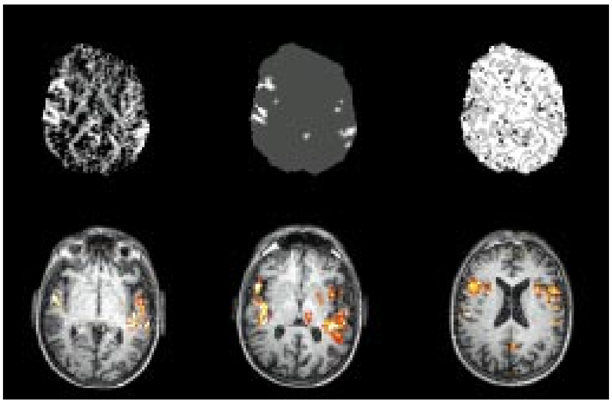


Figure 9. MPI segementation of z-maps: the restored image (top left), the segmented image (top center) and the pixon-map (top right). In the bottom row, a resulting segmented z-map is overlaid onto the corresponding anatomical slices. In addition to cortical areas, activation is indicated clearly in the thalamus and putamen on the left body side (corresponding to the right part of the image).

map, we select the Chien model as a fine structures preserving model. This completes a low level description of the image which is referred to as the MPI model (Markov Pixon Information model). We have applied this approach to analyse z-maps, where the segmented image provides the detection of the activated areas and the restored image gives a description of these areas (see Figure 9). On EPI data we have detected a low activation spread over different regions of the left hemisphere and a thalamic activation in the same hemisphere. These activated areas were not detected by a simple threshold. Therefore, the MPI approach provides a refined tool to analyse z-maps.

The next step consists of the *visualization* of the results. The simplest way of visualization is to overlay the zmap onto the anatomical (T_1- weighted) images recorded at the same location. As an alternative, one can register the zmaps with a 3D anatomical dataset of the same person to obtain a better relationship between the extent of a functional activation to the underlying individual neuroanatomy.

Finally, a *quantification and interpersonal comparison* of functional activity is performed. To address the question of how much activation is found at a given region, the region size, its maximum z-score, the norm (activation integral) and the mean signal rise (in percent) have been analyzed within and across a number of functional studies. The most sensitive measure is found with the activation integral. The region size is related to the activation norm: first, an activation center appears to spread out (increase in size), then to enhance the activation (increase in z-score). When comparing the same activated cortical area between persons, an individual factor (a proportionality constant) links the strength of the hemodynamic response to neuronal activation. The histogram of maximum z-scores in a group study suggest (at least) a bimodal distribution of functional activation centers: a few big, highly activated areas are found exclusively in primary cortices while a larger number of small activation centers are found in secondary areas. A third, currently subliminal group may be found within deep brain structures like the basal ganglia.

We have found a way to parcellate the neocortical surface into substructures which may be described on a symbolic level and thus are more easily comparable between persons. Functional activation centers registered with a 3D dataset may thus be attributed to neuroanatomical structures and referenced in a symbolic notation. Interpersonal comparisons are then performed on the basis of this neuroanatomical description. This approach is currently under study in our group.

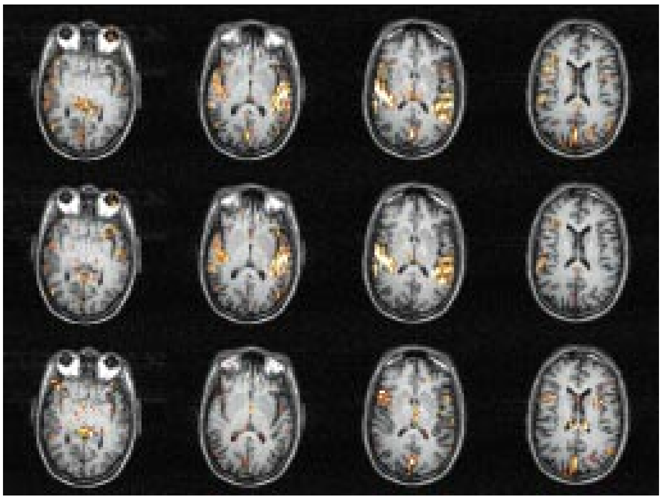


Figure 10. Analysis of the time-course of the BOLD effect in a language-related fMRI experiment. A standard evaluation using a box-car function (top row) is shown in contrast with a separation of early ("cortical") responses (middle row) and late ("venous") responses (bottom row).

We can also study the time-course of the BOLD response. Flow changes for a contrast medium from the empty (cortical) phase to the late (venous) phase occur, as can be deduced from cerebral angiography, in the order of 4-5 seconds. A comparable transit time can be expected for desoxygenated blood (which gives rise to the BOLD effect in fMRI) to move from its capillary (cortical) bed into the draining veins. Standard fMRI protocols based on echoplanar imaging (EPI) exhibit a sufficiently high temporal resolution to separate the BOLD effect in the cortical and venous compartment. By focusing on certain time windows after a stimulation, we can classify "early" and "late" responses. Regions with early reponses within a time window of 4-6 s seem to correspond neatly to *cortical areas*, while regions with a later response (10 s) correspond largely to *cerebral veins*. The very late intraventricular activity (16 s), although in a way task-related, remains anatomically as well as functionally obscure. The proposed classification procedure allows us to better separate the brain´s complex hemodynamic responses to (cognitive) stimulation by utilizing the temporal information attributed to a given activation focus.

The last question, to find the amount of interaction between brain regions, will be a subject of research in the next year.

3.5.4

A new concept for EEG/MEG - signal analysis: Detection of interacting spatial modes

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

The analysis of EEG/MEG-datasets of an experiment seeks to answer which regions in the brain interact and how they interact. Thus, an interpretation of the spatio-temporal signal by means of interacting processing units of the human brain must be obtained.

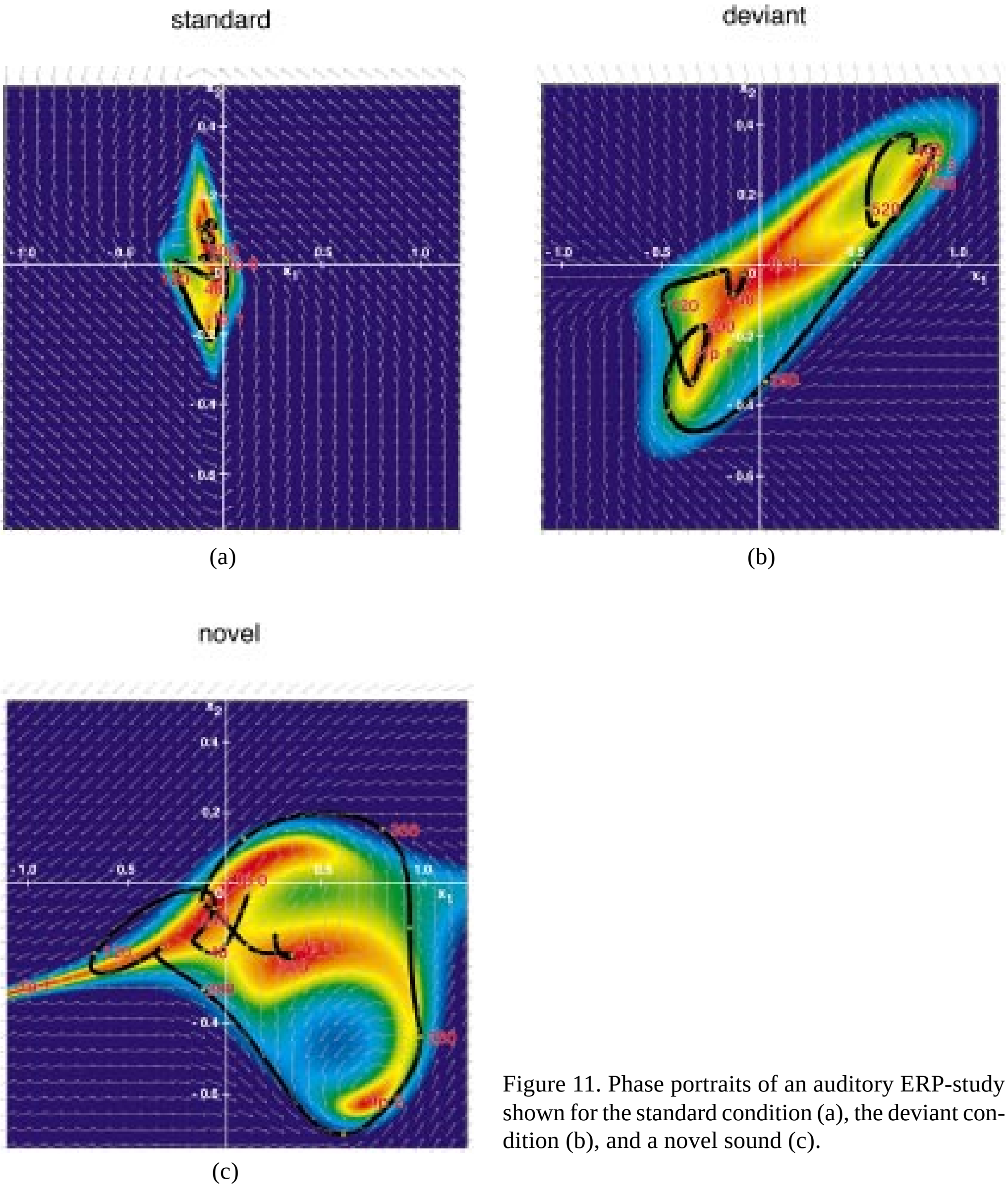
In mathematical terms, the signal can be described as a time-dependent vector q(t) with vector components $q_i(t)$ representing the time series of electrode or squid i of EEG/MEG-data obtained from an experiment. A possible answer to the above quoted questions is to find a signal representation:

$$\mathbf{q}(t) = \sum_i x_i(t)\ \mathbf{v}_i \tag{3}$$

and a model for the corresponding different dynamics, $dx_i/dt = d_i[\{x_j\}]$, which can be expressed as a polynomial function:

$$d_i\left[\{x_j\}\right] = \sum_{j=0}^{N} a_{i,j}\, x_j + \sum_{j=0}^{N}\sum_{k=j}^{N} a_{i,jk}\, x_j x_k + \sum_{j=0}^{N}\sum_{k=j}^{N}\sum_{l=k}^{N} a_{i,jkl}\, x_j x_k x_l \tag{4}$$

The analysis of the dynamics then yields features which correspond to interacting brain functions. Our approach consists of two steps: first, identifying spatial modes v_i and the underlying dynamics d_i and second, an interpretation of the obtained model.
To obtain the coefficients $a_{i,j}$, $a_{i,jk}$, $a_{i,jkl}$ and the spatial distributions v_i, we define a cost function and search for the global minimum which represents the best choice of the parameters. Constraints are introduced to avoid ambiguities. We solve this problem by a genetic algorithm. The global minimum of the cost function leads to a description of the signal in terms of a representation and a model for the underlying dynamical system. Dynamical systems can be characterized by fixed points, which attract or repel



(a)

(b)

(c)

Figure 11. Phase portraits of an auditory ERP-study shown for the standard condition (a), the deviant condition (b), and a novel sound (c).

trajectories in the phase space. The fixed points y_j are the points in phase space which do not evolve with time, i.e. they can be obtained by solving the non-linear set of equations, $d_i [\{ y_j \}] = 0$.

These fixed points of the obtained dynamical system can be of great interest in terms of psychological interpretation: the spatial mode belonging to occurring attractive fixed points may be identified as a field representation on the scalp surface of processing units in the brain. Different stimuli can yield different fixed points due to different brain functions. Identifying these fixed points and observing the trajectory in phase space being attracted in the course of time by different fixed points leads to a description of the brain dynamics in terms of successive processing. This can be conceived as an analogy to spatial microstate analysis, but instead of stepping from one state into the next one, our analysis leads to brain dynamics which is determined by changing attractions of different states. This also leads to an impact on current dipole analyses: we may simply fit dipoles to the stationary field belonging to the fixed point representing a certain brain function. The time interval corresponding to these "states" can be obtained by studying the phase portrait. Of course the length of the time intervals belonging to the same fixed point for different stimuli is not necessarily of the same size and reflects different durations of the "same" brain function in different tasks.

We have chosen an auditory ERP-study as an example for the application of our algorithm, which was performed to examine the neuronal and functional characteristics of processing deviancy and novelty in auditory stimuli. Three different stimuli were presented (a standard tone of 600 Hz (s), a deviant tone of 660 Hz (d), and a novel sound selected from a class of unique sounds (n)). The deviant tones had to be counted (attend condition).

Spatio-temporal analysis: To allow a transparent comparison of the different cases, the same spatial field distributions v_i were fitted simultaneously to the different datasets. A signal representation of 80-90 % was already obtained by fitting two spatial modes to the data. The number of modes was not increased to allow a clear presentation of our concept interpreting the dynamics in a two-dimensional phase space.

Figure 11 (top row) shows graphical representations of the obtained dynamics. The axes represent the amplitudes of the corresponding spatial modes v_i. Each point in that space represents a different spatial field distribution: a linear combination of v_1 and v_2, weighted by the corresponding x_1 and x_2 values. The solid thick line represents the spatio-temporal signal in that space. The line is marked every 40 ms to obtain a correspondence with the time series. The obtained set of differential equations predicts for each point in phase space the development of a trajectory in that point. The direction is illustrated by little arrows in Figure 11 (top row), the absolute value is indicated by color (red represents a small value: the trajectory remains longer in that region compared to the blue areas - large value). Finally we have plotted the fixed points (fp) calculated from the set of differential equations.

Temporal interpretation: In all three conditions (standard, deviant and novel) the trajectory is first repelled by fixed point 0 (fp 0) and then influenced by fixed point 1 (fp 1, fp 1', fp 1''). The time range of the influence of fp 1 (fp 1', fp 1'') varies from 0 - 160 ms (novel condition) up to 0 - 240 ms (deviant condition). The influence of fp 1 and the

resulting trajectory is similar for all three conditions, and reveals the N100 component. After 200 ms for the standard condition the trajectory is influenced by a number of additional fixed points. Most likely they correspond to artifacts and may be neglected, since the signal in that time domain does not represent significant changes.
In the cases of deviant and novel conditions the trajectories behave different: they show both a strong attraction by different fixed points leading to P300 components. In the case of the deviant condition the trajectory after 240 ms leaves the region of fp 1 and is strongly attracted by fp 3. This region is reached after 340 ms and the trajectory stays there up to 520 ms. The trajectory of the novel condition shows a different behavior: After 160 ms the trajectory is attracted by fp 2, reaches the region of that fixed point in the interval 230 - 270 ms, passes at 360 ms fp 3 of the deviant condition and is finally attracted by fp 4 at 480 - 520 ms.

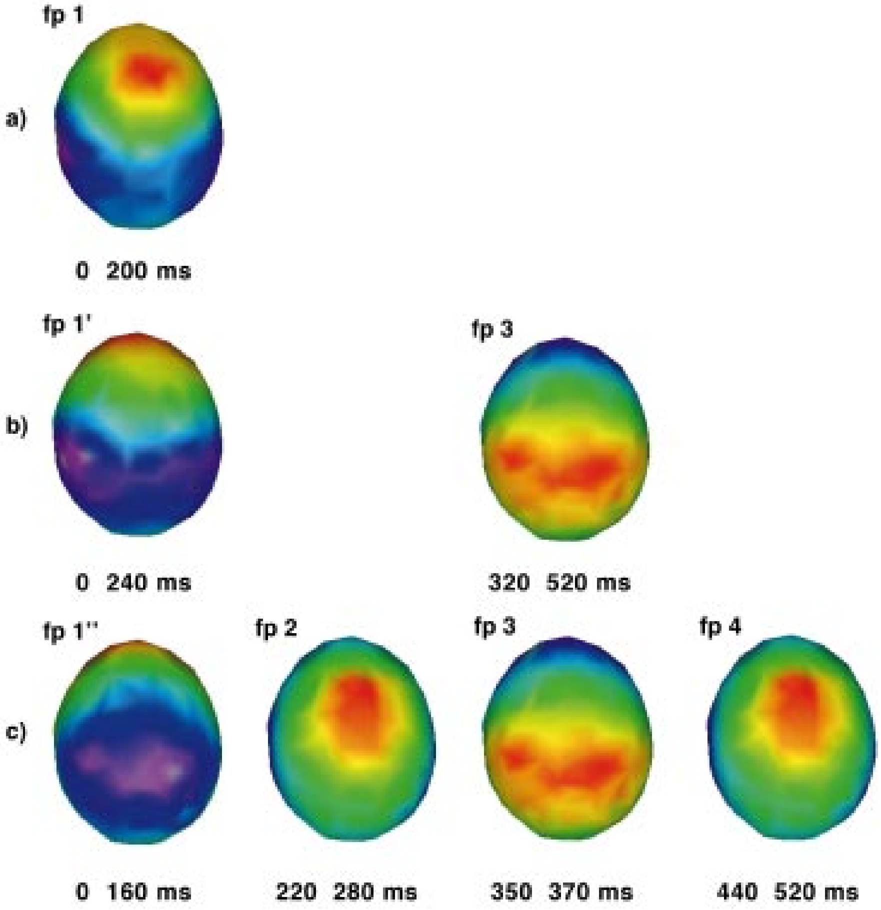


Figure 12. Spatial field distributions corresponding to the occurring fixed points of the auditory ERP experiment.

Spatial interpretation: Figure 12 presents the spatial field distributions corresponding to the occurring fixed points. The amplitude of these distributions is given by the distance of the fixed point to the origin. Therefore the spatial information given by fp 0 can be neglected, the amplitude is zero. Fp 1 and fp 1' differ slightly but show similar field distributions corresponding to the N100 field maps. Fp 1'' of the novel condition differs more but by taking the trajectory into account one observes that fp 1' of the deviant condition also seems to influence the novel case.

Fp 2 and fp 3 differ clearly, indicating that different brain regions may be active. Such information - confirms findings of a dipole analysis where different active cortical regions between 250 - 420 ms were found. The potential maps of these dipoles coincide with our findings of potential maps corresponding to fp 2 and fp 3. Fp 3 represents a fixed point of the deviant condition but is also passed by the trajectory of the novel condition at the same time as in the deviant case. This observation suggests that also in the novel condition brain functions represented by fp 3 play a role in human brain information processing, but are less important than in the deviant case. The final "processing unit" of the novel case (fp 4) shows a similar distribution like fp 2. The strength however is decreased.

Summarizing these findings, figure 12 shows spatial field distributions ordered in the way of occurrence for the different stimuli: after the N100 component (fp 1), fp 3 in the deviant case becomes active, and in the novel case a processing unit represented by fp 2 is first activated before fp 3 and finally fp 4 are involved.

A method was sketched which allows a projection of spatio-temporal EEG/MEG signals in a relevant subspace (relevant, in terms of both dynamics and signal representation). The analysis of the dynamics in that subspace (the phase space) allows an objective and quantitative interpretation of the occurring phenomena in terms of attracting and repelling fixed points. This interaction of fixed points leads to an observation of potential field maps corresponding to different brain "states" with changing influence on the information processing in the human brain. In contrast to spatial microstates these states are not really occupied, they are "centers of attraction" with changing influence on brain dynamics.

This new concept of interpretation of EEG/MEG-signals enables new quantitative approaches to obtain a better understanding of information processing in the human brain:

- Fitting dipoles to EEG/MEG-signals does not rely on chosen time intervals.
- Inter individual differences can be investigated in terms of different values of attraction of fixed points.
- Averaging could be improved by classifying different trials to categories discriminating different dynamics.

Implementation of a multimodal renderer for biomedical datasets

3.5.5

Dörr, M. &
Kruggel, F.

Visualization is the last step in the data processing chain for neuroimaging experiments. Functional datasets have different characteristics which have to be considered within the visualization routines:

- modalities with time-dependent data (i.e., EEG and MEG datasets)
- modalities with spatially varying data (i.e., MRT, SPECT and PET)
- modalities with time- and spatially varying data (i.e., fMRI).

To aid the interpretation of data, a special kind of rendering system had to be designed to handle the specific characteristics of various datasets. This rendering system combines the different modalities in a single image to allow a simultaneous inspection. While a renderer transforms a 3D dataset into a 2D image, a multimodal renderer has to combine and project more than one dataset (modality) together onto a single image plane.

This system was split into two parts: an interactive viewing environment which is executed locally on a workstation, and a computation module which resides on a parallel computer. It is designed as a rendering server to handle requests from multiple interactive clients. The core part of the computation module consists of the management unit for the different modalities, which interprets the display settings sent from the interactive environment and compiles a rendering. Data from different modalities are rendered separately and in an overlay buffer. The modality manager calculates the final image step by step through the overlay buffers. Using the HSV color model, the brightness coefficient V is used to preserve the anatomical structure of the image, and the color components are combined with respect to their display parameters. The final image is sent back to the local viewing environment for display.

Figure 15. Results of a functional MRI experiment registered and overlaid onto a 3D dataset of the same person. The relation between neuroanatomical structures and functional activity is readily apparent.

The progress made by the NMR group within the last year has generally been encouraging. At year's start, all staff members were engaged in setting up infrastructure and developing experiments, modeled from those already present in the existing literature. By the year's end, all were persuing research projects the most of which can be expected to lead to publications. The main focus of activity was functional MR, and both the quality of fMR data and the confidence with which it is handled have improved markedly in the course of 1997. The contribution of the NMR group to this multidisciplinary effort has been: the establishment and refinement of already existing experiments such as EPI and MUSIC, the considerable effort expended on the addition of a head gradient-set, and the development of, sometimes, novel methods for fMR. The last of which should see functional GRASE, U-FLARE and multi-voxel functional spectroscopy available for cognitive experiments 1998. Refinements of the EPI experiment and progress in establishing perfusion as a complementary examination to fMR have been made as well. Despite some technical difficulties sufficient advancement has been made with diffusion tensor imaging such that it should be shortly available for anatomical studies. The work with the Day-Care Clinic for Cognitive Neurology centres around now well established protocols for T_1 and T_2- weighted imaging as well as basic proton spectroscopy.

Such a colorful and optimistic picture is paled only by the enforced exchange of our magnet which was consistently outside the specification for helium consumption. At the time of writing (December 1997), however, the new magnet is already in place, and it seems highly probable that we shall be operational in January 1998.

3.6.1 The application of double voxel fMRS to single trial cognitive experiments

Dymond, R.C.,
Zysset, S.,
Norris, D.G. &
Pollmann, S.

In order to examine the processing of a given cognitive task, it is desirable to adopt a single trial stimulation strategy (Buckner et al., 1996), rather than the blocked trial approach which is more typical in functional imaging studies. The use of single trials presents much greater demands in terms of sensitivity and time resolution which may not be attainable with standard imaging techniques. Hennig et al. (1994) have demonstrated the detection of functional activation using oxygenation-sensitive functional spectroscopy (fMRS), which involves examining the timecourse of the water signal from a given voxel of interest. In this project we investigated the feasibility of using fMRS with acquisition alternating rapidly between two voxels to compare activations in distinct cortical regions and to measure small time offsets in the BOLD response within these regions.

The method adopted was a standard PRESS experiment (TE/TR = 30/300 ms) with water suppression omitted. One experiment comprised 12 single trials, each having duration 25.2 s, during which 42 FIDs were acquired from each 15 x 15 x 15 mm voxel. Voxels were localized using data from a blocked trial EPI experiment (120 repetitions, TR = 2 s, matrix 128 x 64) overlayed on 512 x 512 anatomical RARE images. Volume selective shimming was performed for each voxel independently and the linear shims required were stored and converted to gradient trim values. In this way it was possible to switch repeatedly between the first and second voxel - giving a potential time resolution within each voxel of 600 ms.

For the purposes of assessment of the two voxel fMRS approach, a stimulation paradigm was adopted into which known delays in processing could be introduced. The subject was first given a cue comprising an 'L' shape of a given orientation. After a delay of 3.6s, a 10x10 array of randomly oriented flickering 'L's was presented for a period of 2s. After a further 0, 600 or 1200 ms (the 'pre-search delay'), four of these shapes became stationary while the remainder continued to flicker. At this point, the subject was to determine whether the orientation of any one of the stationary shapes matched that of the cue and to give a yes/no response using a two button key pad. The flicker stimulation was aimed at producing occipital activation in V1and V2 and the eye movement during search at producing activation in the supplementary motor area (SMA) (Marsden et al., 1996). The voxels were located in these two regions and the fMRS technique evaluated by examining the timecourses of the response curves and the changes in these timecourses between experiments having different pre-search delays.

Figure 1 presents typical examples of the timecourses obtained from both voxels for a single subject. Averaging was performed over 24 single trials. The SMA results demonstrate a smaller initial BOLD signal change arising from eye movement related to the the appearance of the preliminary shape cue. The maxima of both visual and SMA responses are seen to shift forward by 600 ms or 1200 ms in correspondence with the introduced delay. While this effect was anticipated for the SMA voxel on account of the change in stimulation, it is not immediately apparent why such a time shift should also appear in the visual timecourse. A possibility is a longer rise time in the visual region but this requires further investigation.

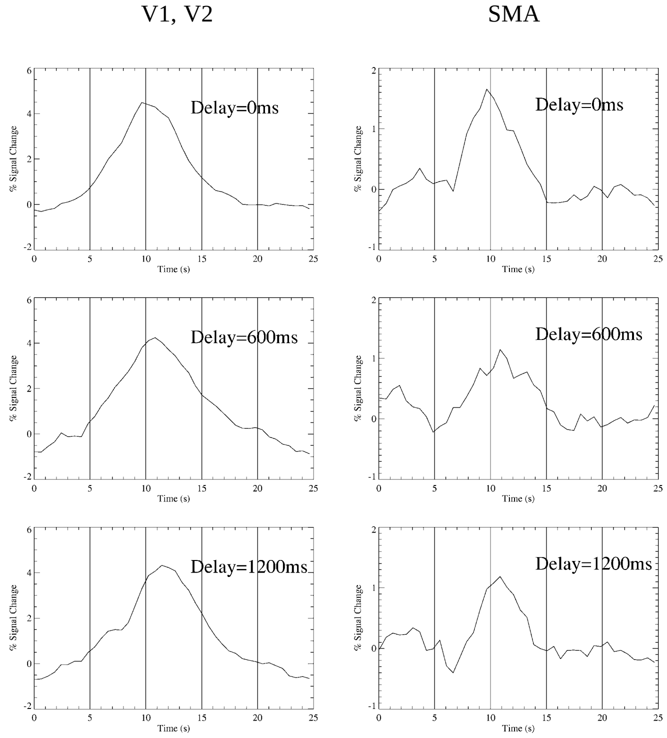


Figure 1.

The two voxel technique has been shown capable of producing well-defined activation traces and also of detecting time shifts of as little as 600 ms. Since only a single FID is required per functional time point, it should be possible to improve the time resolution still further to a level approaching that attainable from ERP experiments, but nevertheless retaining the distinct advantage over EEG techniques of being able to achieve precise spatial location.

Advantages of the fMRS technique over single trial experiments using fMRI are the superior SNR and the fact that, since the full FID is collected, the T2* weighting can be varied at will as a postprocessing step, in order to introduce the optimum contrast to noise ratio. However, on account of the requirement for a priori knowledge of the location of an activation, the fMRS method will always need to be used in conjunction with anatomical and/or functional scout scans.

This study has demonstrated the feasibility of double voxel fMRS as an approach for examining the timecourse of activations in distinct cortical regions. Given its specific advantages over other modalities, it would seem to hold significant potential for use in cognitive investigations.

3.6.2 Measurement of the fast response

Dymond, R.C. & Norris, D.G.

The fast response (Ernst et al. 1995) is a small negative dip in the fMR signal obtained from the visual cortex which is evident as early as 400 ms after the onset of stimulation. We have previously performed Monte Carlo simulations of the mechanism of the effect which demonstrate that its echo time characteristics are consistent with the occurrence of a highly localized early increase in deoxyhaemoglobin concentration. If the negative signal change can be reliably observed and quantified in different regions of the cortex, it may be possible to obtain improved temporal resolution in fMRI experiments. With this aim in mind, we are now in the process of developing an optimized method for fast response measurement.

Initial EPI experiments were performed using low flip angles and short repetition times with single slice acquisition. However, the influence of physiological artifacts on the signal timecourse was such that, while the development of the conventional BOLD signal increase and post stimulation undershoot could be readily identified, the smaller early negative signal change was largely obscured. For this reason we decided to undertake physiological monitoring and retrospective correction of k-space data using the method of Hu et al (1995). We are now able to monitor and record both ECG and respiration signals and carry out the necessary post-processing of the fMRI data. Physiological monitoring is being used in a volunteer study involving both visual and motor stimulation in an attempt to address the question of how the activations differ between different cortical locations and, more specifically, to establish whether an early response can be identified in regions outside the visual cortex.

3.6.3 Template interactive phase encoding (TIPE): An application to brain imaging with GRASE

Jovicich, J. & Norris, D.G.

Introduction. We present a novel method for interactively calculating the phase encoding order from the signal decay of a template scan (i.e. a scan without phase encoding). This method (TIPE) is aimed at obtaining a phase encoding order that gives a smooth amplitude modulation of the signal in the phase encode direction in experiments where the signal decay along the echo train is not known *a priori*.

The TIPE method can be applied to GRASE (Johnson et al., 1996) where the amplitude modulation of the signal along the echo train depends on T_2 and T_2* and does not always decrease monotonically . Therefore, a conventional centric phase encoding order will not always give a smooth amplitude modulation. In addition, most phase encoding orders proposed for GRASE aim at minimizing the phase modulation (resulting from frequency offsets) and give strong amplitude modulations.

The advantage of TIPE is that if the signal decay from a template scan is known, then a smooth amplitude modulation can be obtained by properly reordering the echoes in k-space. The disadvantage is that there is a resulting phase modulation. However, if a perfect phase correction were performed prior to image reconstruction then the phase errors would be corrected and the smoother amplitude modulation would lead to reduced artifacts.

A short effective TE (TE_{eff}) application of the TIPE method was implemented (centric TIPE) and compared with other short TE_{eff} phase encoding schemes proposed for GRASE (Johnson et al., 1996).

Methods. A computer simulation was performed in which the point spread functions (PSFs) of the centric GRASE, kb-centric GRASE, conventional centric and centric TIPE methods were calculated and compared. Two cases were considered: T_2* short compared to T_2 (strong main field inhomogeneities), and T_2* tending to T_2 (weak field inhomogeneities).

GRASE with the different phase encoding methods were implemented on a 3.0 T whole body imaging system (Bruker MEDSPEC 30/100, Ettlingen, Germany). Brain images were acquired from 10 normal volunteers with a TE_{eff} of 23ms. Slices far from and slices incorporating the frontal sinuses were acquired to investigate artifacts with imaging regions with weak and strong susceptibility-induced field inhomogeneities, respectively. The whole of k-space was sampled in 380 ms following one excitation and 99 phase encoding steps. Three gradient echoes per RF refocusing pulse were used. Data were zero filled to form 128×128 image matrices. Slice thickness was 5 mm and the FOV was $25 \times 25 cm^2$. The phase-encode direction was vertical. For the TIPE experiment a template scan was first acquired, which was then processed off-line with IDL (Research Systems, Inc. Colorado). The 1D profiles in the read-out direction were calculated and the maxima of the profiles were ordered in k-space to give a smooth, centred amplitude modulation. Each echo was assigned a phase encoding step number which allowed the calculation of a table of phase encoding gradient strengths used for the image scan.

Results and Discussion. The simulation shows, if is assumed perfect phase correction (i.e. artifacts arising from amplitude modulation alone): a) When $T_2^* << T_2$, centric and kb-centric GRASE give strong side lobes in their PSFs, conventional centric gives much smaller well separated side lobes (resulting from a high frequency low amplitude modulation), and centric TIPE gives no side lobes; b) As T_2* tends to T_2 , both conventional centric and centric TIPE give a smooth amplitude modulation and therefore no side lobes, whereas artifacts remain for centric and kb-centric GRASE.

The brain images showed the artifacts predicted by the simulated PSFs: diffuse artifacts for centric GRASE and more structured artifacts for kb-centric GRASE images. In regions with weak field inhomogeneities conventional centric and centric TIPE (Figure 2) gave similar results and less artifacts than centric and kb-centric GRASE. In regions

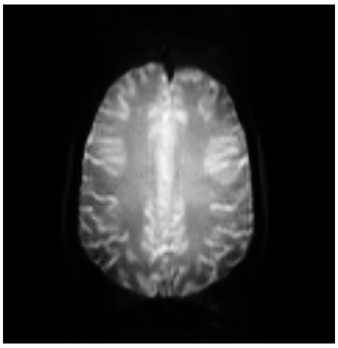


Figure 2.

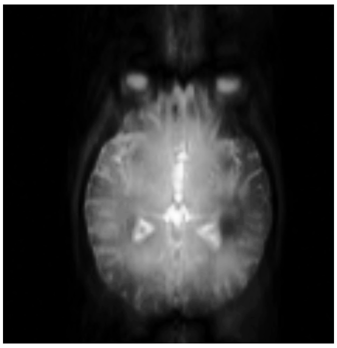


Figure 3.

with strong field inhomogeneities centric TIPE (Figure 3) showed less artifacts than the other methods. In particular to conventional centric, the strong amplitude modulation produced low frequency artifacts which interfered, giving rise to dark areas in the image.

Conclusions. This work confirms the possibility of obtaining images from a template interactive phase encoding order. The method was implemented and tested using a GRASE sequence at 3 Tesla. The imaging results agree well with the simulations. Centric TIPE does not give artifact free images but generates less artifacts than the other methods considered, particularly when a good average phase correction can be achieved.

3.6.4 fMRI with GRASE : Initial evaluation using split echo technique at 3 Tesla

Jovicich, J. & Norris, D.G.

Purpose. To investigate the reliability of T_2* weighted GRASE imaging for detecting brain activation during visual stimulation.

Introduction. GRASE (Johnson et al., 1996) is a fast imaging method that combines advantages of EPI and RARE imaging and is therefore an attractive alternative for fMRI, particularly at high fields (Annual Report 1996, 3.6.1). EPI is, however, the main modality used in fMRI and to our knowledge there are no reports of fMRI GRASE studies.
In this report a method for obtaining phase insensitive T_2* weighted GRASE images is described. The method is based on the split echo technique (Norris et al., 1992) and was used to acquire images during a conventional visual stimulation fMRI study.

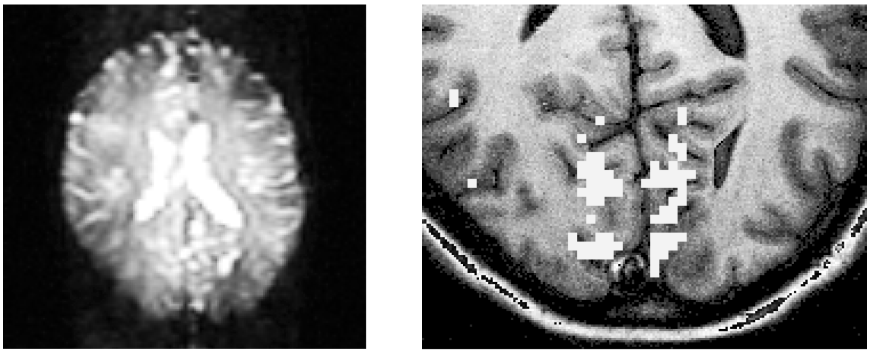
Materials and Methods.
Instrumentation: Our Bruker 3.0 T whole body imaging system equipped with a transmit/receive quadrature birdcage head coil.
Imaging: In a conventional single shot GRASE sequence the read dephase gradient was imbalanced in order to split odd and even echoes under each acquisition window. Both echo groups were simultaneously phase encoded allowing reconstruction of one image for each echo group after a single excitation. The two magnitude images were added to get a final image. The T_2* weighting was incorporated by use of an additional delay τ between the 90° and the first 180° pulse. The whole of k-space was sampled in 380 ms following one excitation and 99 phase encoding steps. Three gradient echoes per RF refocusing pulse were used (TE=11.5 ms). Each split echo was sampled with 64 points and data were zero filled to form 128×128 image matrices. Images were acquired from a single slice along the calcarine sulcus. Slice thickness was 5 mm and the FOV was $25 \times 25 \text{cm}^2$. The centric GRASE, kb-centric GRASE, conventional centric and centric TIPE phase encoding methods (Johnson et al., 1996, Jovicich & Norris, submitted) were considered to investigate the image quality of the split echo GRASE technique. The TIPE method was implemented so that it produced a centre-out amplitude modulation in k-space of the echo group with higher signal intensity.
Paradigm: Four normal volunteers were investigated. Visual stimulation was generated using LED goggles (Grass, W. & Warwick, R.I.) and consisted of a full field of red check-

erboard pattern (8 Hz) during stimulus, and a black field during rest. A time series of 56 single slice images was acquired at 6 second intervals in 7 epochs of equal duration which alternated between rest and stimulus conditions. No averaging was performed.

Data Analysis: Cross correlation maps of the pixels' time series with an ideal waveform were generated using AFNI Software from the Medicinal College of Wisconsin.

Results and Discussion. T_2* weighted split echo GRASE images using the different phase encoding methods considered, showed that the TIPE images have less artifacts, particularly for a low number of dummy cycles. As the number of dummy cycles increases both conventional centric and TIPE give similar results and less artifacts than centric GRASE and kb-centric GRASE. It is important to keep the number of dummy cycles to a minimum to minimize power deposition and maximize SNR. For this reason the TIPE phase encoding method with two dummy cycles (Figure 4a, τ=30 ms) was chosen for the fMRI experiments.

Figure 4b shows an activation map superimposed on an high resolution anatomic image. Only pixels with cross correlation coefficients over 0.6 are shown. The activated brain regions correspond well with the primary visual cortex. Figure 4c shows the unsmoothed time series of an activated pixel from Figure 4b. In activated pixels the average signal change between baseline and stimulation was approximately 8 %.


a) Split echo TIPE GRASE

b) GRASE fMRI map

c) Time course

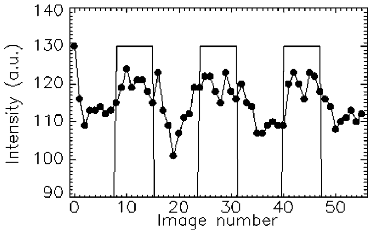


Figure 4. a) Split echo TIPE GRASE. b) Activation map given by split echo TIPE GRASE (c > 0.6). τ=30 ms for both. c) Unsmoothed time course of an activated pixel superimposed on the ideal waveform.

Conclusions. Our preliminary results show that: a) it is possible to acquire acceptable single shot T_2* weighted GRASE images with the split echo method; b) brain activity during visual stimulation is detectable in the primary visual cortex by T_2* weighted GRASE at 3 Tesla.

3.6.5 Origins of BOLD contrast - diffusion and MTC weighted functional imaging of the human brain

Koch, M., Niendorf, T. & Norris, D.G.

Magnetic resonance imaging based on blood oxygenation level dependent (BOLD; Ogawa et al., 1990) contrast is established as a method to image brain activity. It relies upon a decrease of the deoxyhemoglobin concentration in the blood that is related to neuronal activity. The reduction of microscopic magnetic field gradients that are caused by the paramagnetic deoxyhemoglobin in red blood cells results in a signal increase. Both intra- and extravascular protons may be subjected to these field gradients. Their relative contribution to the observed signal change is not known. Using diffusion weighting (DW), it is possible to suppress the signal from protons in capillaries selectively. By magnetization transfer contrast (MTC), the signal from protons in the extravascular tissue and, through water exchange between tissue and blood, in the capillary bed can be suppressed (Zhang et al., 1997; and Balaban et al., 1992). These two methods have been applied to obtain information on which pool of protons is mainly responsible for the signal change observed during stimulation.

BOLD contrast images were obtained with T_2* sensitized UFLARE (Norris et al., 1993). The sequence was modified to incorporate diffusion weighting and MTC sensitization. Macroscopic blood vessels were localized by FLASH based 2d inflow angiography. Flashing LED goggles were used for visual stimulation. The image slice (5 mm thickness) was positioned along the calcarine sulcus.
A bipolar gradient pulse pair (δ=15 ms, Δ=15.5 ms) on each gradient axis just after the excitation RF pulse provided diffusion weighting. Magnetization transfer sensitization was achieved by the application of a set of consecutive pre-irradiation pulses before excitation. ECG gating was applied in the MTC experiments.

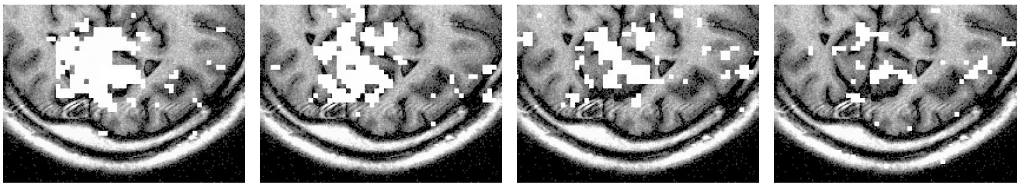


Figure 5. Effect of diffusion weighting on functional data. White areas exhibit high correlation of signal with timecourse of stimulus (Correlation coefficient > 0.6). Diffusion weighting is b = 0, 20, 50, 120 s/mm^2 from left to right.

Figure 5 shows the areas of stimulation-induced signal intensity changes for an individual volunteer. For all data sets the relative signal change during stimulation decreased with increasing diffusion sensitization. With the strongest applied diffusion weighting (b = 120 s/mm^2), only a few pixels with a correlation coefficient above 0.6 remained visible. At this b value the total signal attenuation in grey matter was approximately 10 %.

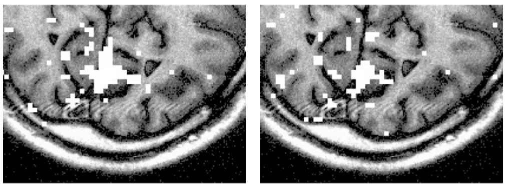


Figure 6. Effect of magnetization transfer on functional data (left image without MTC). White areas exhibit high correlation of signal with timecourse of stimulus (correlation coefficient > 0.6).

The application of MTC weighting also reduced the number of activated pixels (see Figure 6, same volunteer). Although signal from grey matter was attenuated by about 40 %, the number of pixels that exhibit a correlation coefficient above 0.6 was only reduced by a factor of about 2. All data sets acquired showed this behaviour.

It has been suggested (a) that the stimulation related signal intensity changes arise predominantly from extravascular protons that experience the local field gradients around blood vessels and from larger scale vessels (Song et al., 1996). Other authors have come to the conclusion (b) that the main contribution is due to intravascular protons experiencing local field gradients in the vicinity of red blood cells (Menon et al., 1995 and Boxerman et al., 1995).

By diffusion weighting, the signal amplitude is being reduced due to incoherent motion of water molecules. In vivo this can be related either to true diffusion of water molecules or to the flow of blood in the capillaries. The motion of water molecules in a network of randomly oriented small vessels can be seen as a random walk process similar to diffusional motion but on a different scale (pseudo-diffusion or IVIM; Le Bihan et al., 1988). The high velocities of flowing blood result in a pseudo-diffusion coefficient $D^* \approx 60 \cdot 10^{-9}$ m^2/s which is considerably larger than the diffusion coefficient of water in tissue ($D \approx 1 \cdot 10^{-9}$ m^2/s). Therefore the signal contribution of the flowing blood in the capillary network that contains less than 5 % of the total water in brain (Neil et al., 1994) can be selectively suppressed by weak diffusion weighting. The signal from protons in the capillary bed is expected to be completely attenuated at b=100 s/mm^2. The measured decrease in relative signal change during stimulation periods by diffusion weighting indicates that intravascular protons dominate the functional signal.

MTC damps contributions from tissue with a high concentration of macromolecules while it does not affect signal arising from blood or CSF. However, due to the high proton exchange rate between the capillary bed and extravascular tissue ($\tau \approx 300$ ms, Schwarzbauer et al., 1997). MTC attenuates the signal arising from capillaries as well. Those pools of protons that are affected by MTC or DW attenuation are indicated below.

large vessels, arterioles, venules	capillaries	extravascular tissue
DW ↓	DW ↓ MTC ↓	MTC ↓

With MTC, protons in vessels of sizes down to arterioles and venules remain unaffected. These vessels are too small to be visible in angiograms. On the basis of the conclusions above, the MTC experiments suggest that the functional signal arises from *both* larger vessels *and* capillaries.

We thus conclude that in these experiments protons within the capillary network and in larger scale vessels account for the majority of the stimulation-correlated signal changes. The use of MTC images may be of value in detecting signal changes arising from the vicinity of blood vessels larger than capillaries.

3.6.6 Functional imaging with ultra-falst low angle RARE (U-FLARE)

Niendorf, T.

Introduction. The dominant fMRI sequence is EPI, which allows low spatial resolution imaging of the brain in multi-slice mode. The acquisition time per image is typically less than 100 ms, and the repetition time for a given slice of the order of seconds. One of the main difficulties with EPI is that it is prone to susceptibility artefacts. These are particularly pronounced in regions adjacent to the sinuses, and manifest themselves as image distortion and signal loss. Pulse sequences such as RARE that are based on spin-echo sequences do not suffer as acutely from susceptibility effects, but, especially at higher field strengths, are limited in the number of slices per unit time by considerations of energy deposition. In this project the application of the U-FLARE imaging method to fMRI is examined.

Implementation. The sequence was implemented as follows: FOV 250 mm, slice 5 mm, Refocusing pulse angle 60°, evolution time 20-30 ms, scan time 300 ms. Three variants were implemented: displaced, split-echo and phase-cycled. In the first and last of these the data matrix was 128 by 64, in the split-echo technique it was 64 by 64. A number of applications of this experiment were examined:

Visual Stimulation. Studies were performed on ten volunteers. Stimulation was generated by Grass goggles. The paradigm consisted of 7 rest/stimulation periods each of 48 ms. Eight images per slice and cycle were obtained giving a temporal resolution of 6 s. All three paradigms were employed, results are shown in figure 7. The split-echo technique gave the higher functional sensitivity due to the coarser matrix and, in comparison to displaced U-FLARE the conservation of echo groups of both parities.

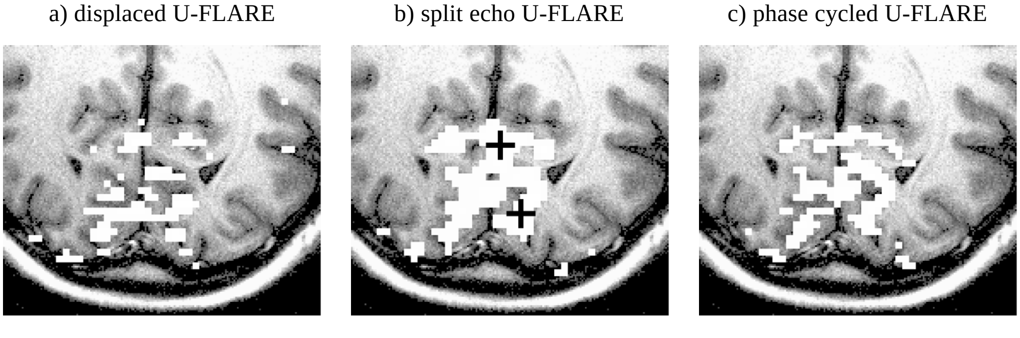


Figure 7. Comparison of activation maps derived from experiments with a) displaced (effective data matrix (edm) 128 x 64) b) split-echo (edm: 64 x 64) and c) phase-cycled (edm: 128 x 64) U-FLARE overlaid on an anatomical image located along the calcarine sulcus.

Motor Stimulation. Four volunteers were examined. The 'on' condition was a regular tapping of thumb and index finger. Slices were aligned parallel to the AC-PC line through the central gyrus and supplementary motor area. Only the split-echo variant was employed. The block design was the same as for visual stimulation. Signal changes of 5 - 10% were found in the primary motor cortex as illustrated in figure 8.

Quantitative T_2^* Mapping. The ability to vary the evolution time in U-FLARE from zero upwards makes it possible to quantify changes in T_2^* This was performed for the viusual stimulation experiment described above using evolution times spaced between 0 and 55 ms. For grey matter, the initial T_2*=(31.2 ± 1.5) ms increased to 33.0 ± 1.5 ms during periods of visual stimulation. A significant increase in T_2* from 42.3 ± 2.5 ms to 46.7 ± 2.5 ms was observed for voxels containing not only grey matter but also larger scale vessels.

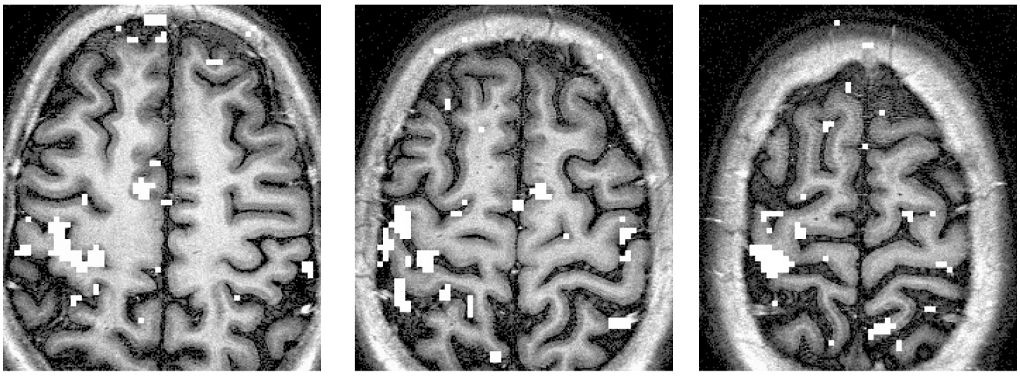


Figure 8. Motor task activation maps obtained from multi slice split-echo U-FLARE experiments overlaid on an anatomical image. Only pixels with cross correlation over 0.65 are shown.

3.6.7

Monitoring of location-dependent visual cortex activation: Comparison between MUSIC and FLASH

Niendorf, T. & Pollmann, S.

Introduction. MUSIC is a FLASH variant which enables the acquisition of a multi-slice data set of about 5 slices within the same time as a conventional FLASH experiment. This study scrutinizes the application of MUSIC to the precise localization of activation in anatomically adjacent brain areas and examines its reliability compared to FLASH experiment. It focuses on the detection and tracking of visual retinotopic activation which is important for the investigation of visual field defects.

Methods. Three contiguous slices placed perpendicular to the calcarine sulcus into the posterior third of the area striata were investigated (slice thickness= 5 mm).
For the T_2*-sensitized experiments, RF spoiled versions of the MUSIC and FLASH technique (*TE*=40 ms, *TR*=70 ms, a=20^0, 128 x 64 data matrix) were employed. The periodic stimulus consisted of a rotating windmill containing four areas of high contrast flickering checkerboard patterns (45° angular width, n=8 Hz, stepwidth=3.75°) projected by an LCD projector system onto a translucent screen placed inside the magnet bore.
The experimental protocol involved two different groups of experiments: (i) the continuous acquisition of 96 multi slice data sets using the MUSIC sequence and (ii) single slice FLASH data sets for those slices investigated with MUSIC. In each set of experiments, one cycle of the rotating stimulation pattern was simultaneously applied leading to four stimulation periods.
Functional activation maps were computed by cross correlation between the experimental time course and a set of 24 ideal response functions to cover all phase shifts (rotating windmill positions) of one activation period.

Results. For both FLASH and MUSIC experiments, correlation coefficient maps showed stimulation-associated signal intensity changes within the visual cortex for all three slices investigated. The areas of retinotopic activation progressed over striate cortex in a circular manner in the direction of stimulus rotation and were displaced between single steps in the stimulation cycle. The correlation coefficient maps revealed a good agreement between the location and spatial extension of the activated brain regions obtained by the MUSIC- and FLASH experiments (Figure 9). However, the dynamic range of the stimulation-induced signal intensity changes derived from the MUSIC experiments was slightly less than that observed in the single slice FLASH experiments.

Conclusions. The MUSIC experiment has been shown to give comparable results to FLASH, the remaining differences may be accounted for by the higher motion sensitivity of MUSIC. Further work shall examine methods of eliminating this.

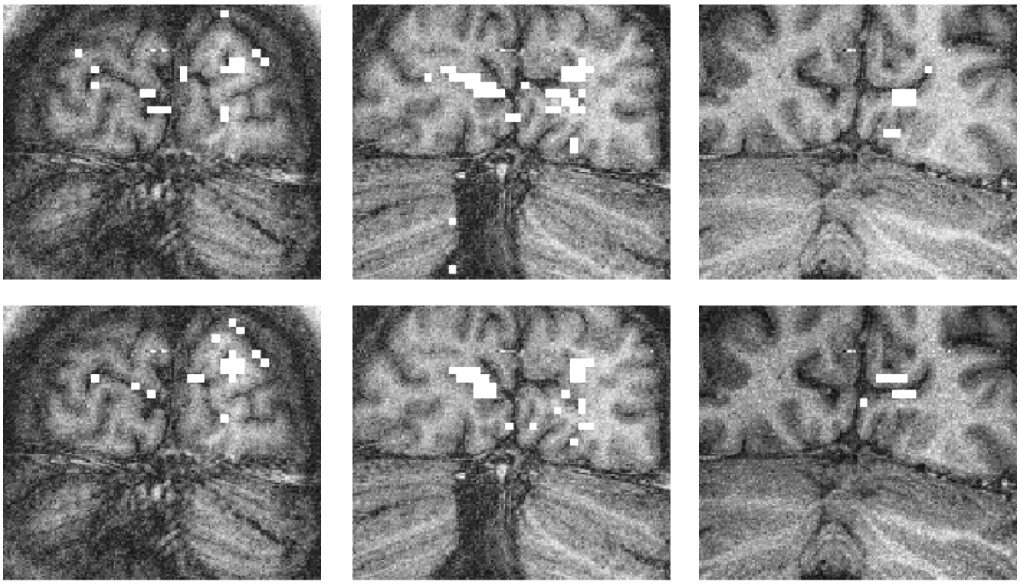


Figure 9. Activated regions for a certain position of the rotating windmill derived from the MUSIC (bottom) and FLASH-experiment (top) overlaid in grayscaled intensities on an anatomical image located perpendicular to the calcarine sulcus.

3.6.8 Strategies for neurological imaging at high magnetic field strength

Norris, D.G.,
Hund, M. &
von Cramon, D.Y.

Introduction. The benefits of high main magnetic field strengths for fMRI and spectroscopy are broadly accepted, with the result that an increasing number of such systems are being used both for these established applications and increasingly for routine diagnostic imaging. For T_1 and T_2 imaging the main advantage of high field systems is a superior SNR, disadvantages are the lengthening and convergence of T_1 values, the shortening of T_2, increased SAR, and increased susceptibility effects. Images of diagnostic quality can be obtained by developing strategies to deal with these problems.

Methods.

T_1 Imaging: Clinically it is desirable to have a multi-slice protocol capable of simultaneously acquiring about 20 slices. In this situation, sequential slice selective inversion

produces problems of power deposition. At high field strengths inflow effects are more pronounced owing to the longer T_1 values. These can become significant if slice selective inversion is used. Hence, 3D imaging sequences are attractive because global inversion can be employed, reducing both SAR and flow effects. We have found two 3D strategies to be efficacious:

(i) 3D segmented MDEFT. In this sequence the $90°–\tau$-$180°$-τ preparation is followed by 64 FLASH readouts. This makes it possible to generate a 256 x 256 x1 28 matrix within about 15 min. The data are acquired in sagittal section to minimize motion artefacts from the eyes.

(ii) 3D Multi-slab MDEFT FLARE. In this, the MDEFT sequence is accelerated by using RARE imaging. The total energy is kept within SAR limits by reducing the refocusing pulse angle, making this a FLARE sequence. The RF pulse scheme is $180°$-τ-$90°$-TE/2-$[\alpha\text{-TE}]_n$ $90°$-τ-...

where the last 90° pulse saturates the magnetization, ensuring that the MDEFT sequence is effectively only interrupted by the FLARE part. This sequence can collect a 256 x 256 x 16 data set in about 12 min using a RARE factor of 8.

T_2 Imaging: The general appearance of T_2 images at 3 T differs from that at lower field strengths mainly in the high spatial resolution of white matter structures. Even in healthy subjects small vessels such as arterioles appear as small hyperintense zones. Multislice imaging with RARE is again often limited by SAR constraints, but these can be overcome by reducing the refocusing pulse angle to about 120°.

Experimental. Signal transmission and reception were performed using a 28cm id. quadrature birdcage resonator. Either the whole-body gradient set (30mT/m switchable within 500 μs) or the head gradient insert (Magnex: 40 cm id., 35mT/m, 150 μs switching time) were employed.

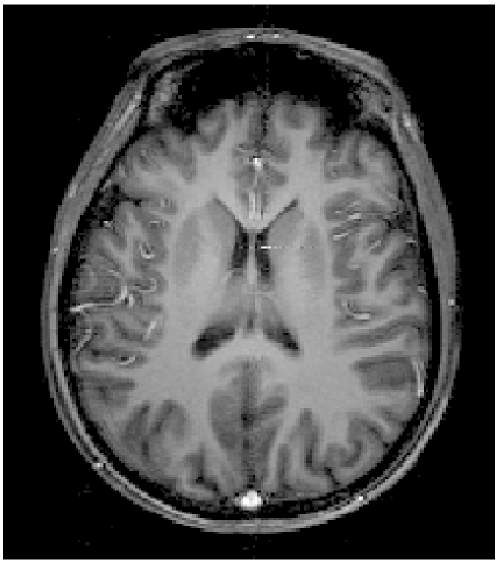


Figure 10. 2D MDEFT: axial plane through the basalganglia. Data matrix 256x256, FOV 25 cm, slice 5 mm. TI 650 ms. Experimental duration 6 min. Slice selective excitation with a sech pulse was employed. Flow effects are pronounced.

Figure 11. Sagittal MDEFT image through midline structures taken from a segmented 3D acquisition. The data matrix was 256x256x128. Slice 1.5 mm. Excitation angle in FLASH sequence 20°.

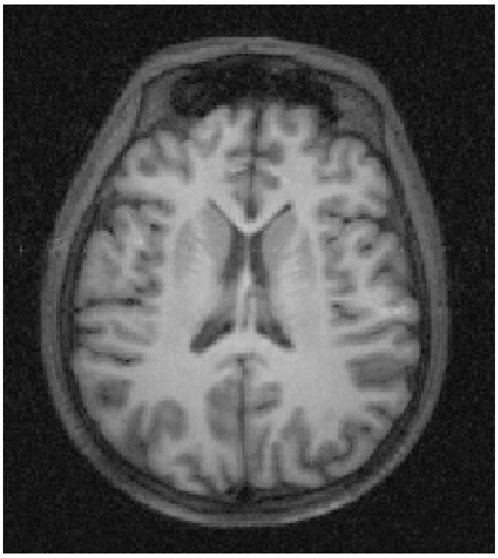


Figure 12. Axial 3D-MDEFT FLARE image with fat suppression achieved by the application of 3 10 ms Gaussian pulses. FOV, 25 cm, slice 3 mm, TI=650 ms, TE=22 ms, RARE factor 8, refocusing pulse angle 120°.

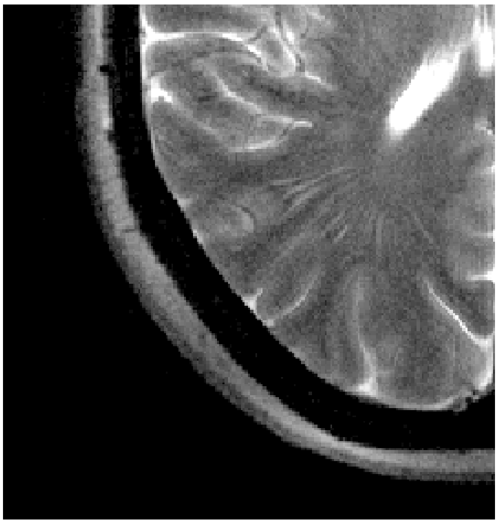


Figure 13. Part of a FLARE image in the axial plane: The parietal white matter shows very small vessels with a hyperintense signal. This is one of a data set of 20 slices acquired within 5 min. FOV, 25 cm, *slice, 5 mm, TR=8.5 s, TE=22 ms, RARE factor 16, refocusing angle 120°, data matrix* 512^2.

Conclusions. Clinical neurological imaging at 3 T is possible provided that the methods employed are specifically designed for high field strengths and that the image interpretation takes into account the variation in contrast with field strength.

3.6.9 0° slice-selective RF pulses: MT-equivalence for multi-slice perfusion imaging

Norris, D.G.

Introduction. Widespread application of NMR perfusion imaging is, in many instances, hampered by the lack of multi-slice capability. In particular, the family of methods based on the FAIR experiment are difficult to implement in multi-slice mode. Their requirement is for one experiment in which muti-slice inversion takes place, and another in which a global inversion occurs. In the two experiments, are two basic confounds to multi-slice perfusion measurement: first, 'crosstalk' - i.e., the flow of magnetically labelled blood between the slices and second, unequal magnetization transfer (MT). It will be shown here how to generate pulses which have the same MT effect as commonly used inversion and saturation pulses but generate no net excitation.

Theory. The excitation angle of an RF pulse with a symmetrical time domain envelope may be made to be zero on-resonance by simply reversing the phase of the pulse at its mid-point. Off-resonance, this will not give zero excitation because the effective B_1 field contains a term $(\Delta\omega/\gamma)k$ that is not reversed with the pulse phase. The general solution is thus to reverse both the phase of the RF pulse and that of the vector $(\Delta\omega/\gamma)k$. If the frequency offset is due to main field inhomogeneity or chemical shift this is impossible, but not if it is due to magnetic field gradients. As most pulses used for saturation or inversion, such as the sinc or sech pulse, are time-symmetric this approach is of general applicability. In terms of the k-space representation of selective excitation the k-vector starts at the origin, moves out to its maximum displacement and then returns to the origin after the sign-reversal of the gradient field. The excitation profile is the Fourier transform of the k-space trajectory weighted by the B_1 field strength. After the gradient is reversed, the sign of the B_1 field is also reversed, so that at each coordinate in k-space the B_1 field during the second half of the pulse is equal and opposite to that during the first half, resulting in zero excitation. It should be noted that the technique is valid both for adiabatic and non-adiabatic pulses.

The MT equivalence of the pulses is based on the mirror symmetry of the MT effect about resonance. Two half pulses at frequency offsets of plus and minus *x* Hz are hence equivalent to a whole pulse at plus or minus the same offset.

Experimental. Signal transmission and reception were performed using a 28 cm id. quadrature birdcage resonator. The whole-body gradient set (30 mT/m switchable within 500 μs) was employed. A sech pulse was divided in half, and the phase of the second half reversed. The slice selection gradient was reversed in polarity between the pulses and trimmed so that the net integral was zero between the end of the first half pulse and the start of the second.

Initial experiments on water filled phantoms gave the expected behaviour, namely that at a pulse gain identical to that required for inversion the excitation profile was the same as in the absence of the pulse. The 0° pulses were then incorporated into a simple FLASH imaging sequence, so that each line of acquisition could be preceded by a 0° pulse. On a well shimmed water phantom the SNR was reduced to about 90% of its value in the absence of the 0° pulse. In an *in vivo* experiment on a healthy volunteer (FLASH, TR=400 ms, TE=8 ms, α=30°, matrix 256^2, FOV 25 cm, slice 5 mm) the SNR reduction was 75% in CSF and 70% in NAWM for a 0° sech pulse of total 10 ms duration. The images obtained in this experiment are shown in the figure: left with 0° pulse, right without. Some of the difference in performance may be due to MT but the main part is more likely caused by the effects of main field inhomogeneities.

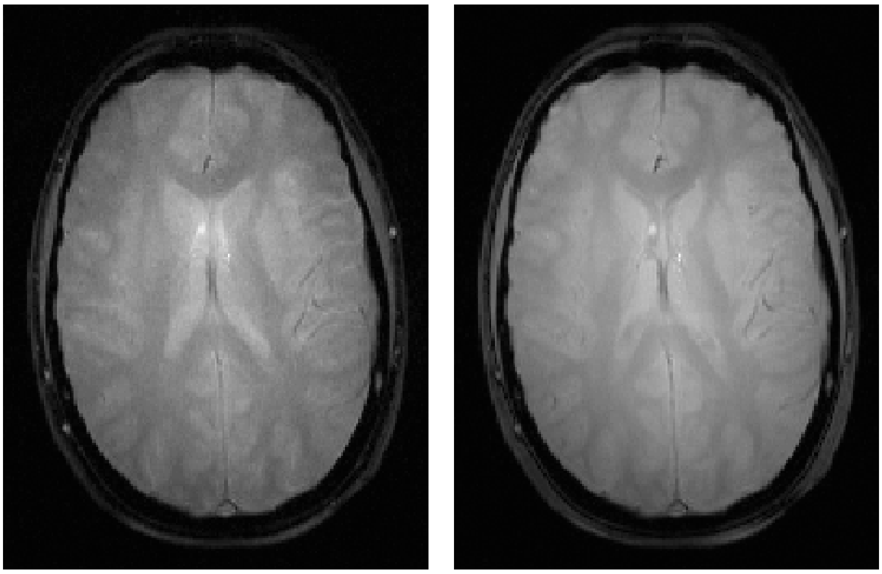


Figure 14.

Conclusion. The scheme outlined above has the advantage that optimal inversion/saturation pulses can be employed, and their corresponding 0° pulses generated and used in a non slice-selective experiment.

3.6.10 BASE perfusion imaging

Schwarzbauer, C.

BASE is a new technique for magnetic resonance imaging of absolute perfusion changes which uses magnetically labeled tissue water proton spins as a freely diffusible tracer. It consists of basis (BA) images which are acquired without any spin preparation experiment and selective (SE) inversion prepared images. Unlike the FAIR technique (1-3), the BASE technique does not require nonselective spin inversion. It can therefore be applied in combination with small transmit/receive head coils (e.g. surface coils). Furthermore, no error correction is required to account for different longitudinal relaxation times of tissue and blood (3).

Absolute changes in the cerebral blood flow can be calculated from the signal intensities of the BA and SE images obtained during periods of control (co) and stimulation (st)

$$\Delta CBF = \frac{\lambda}{TI} \ln\left(\frac{1 - SE_{co} / BA_{co}}{1 - SE_{st} / BA_{st}} \right),$$

where λ is the tissue/blood partition coefficient for water and TI is the inversion time.

Five healthy volunteers were investigated on a 3 Tesla whole body system (Medspec 30/100, Bruker, Ettlingen, Germany). Visual stimulation was achieved with a full-field checkerboard flickering at a frequency of 8 Hz. The stimulation protocol consisted of 5 blocks of control interleaved with 4 blocks of visual stimulation. During each block, BASE experiments were performed in three intervals of 30 seconds. BA and SE images were separated by a recovery delay of 6 s. The inversion time was TI = 1.4 s. Images were acquired by means of an RF spoiled Snapshot FLASH sequence (4). Imaging parameters were flip angle, $\alpha = 7°$; echo time, 5 ms; image acquisition time, 0.465 s; matrix size, 64 x 64; field of view, 25 cm; slice thickness, 5 mm. A Gaussian-shaped excitation pulse was used in combination with a hyperbolic secant inversion pulse which exhibits an approximately rectangular slice profile. The thickness of the inversion slice was 18 mm.

Image time series were corrected for bulk motion using the AFNI 2.0 software package and a linear baseline correction was applied to remove baseline drifts. ΔCBF maps were calculated on the basis of a t-test ($p > 0.999$) assuming a brain/blood partition coefficient for water of $\lambda = 0.9$ ml/g (5). The number of activated pixels in the calculated ΔCBF maps varied from 12 to 26. The individual mean ΔCBF values, obtained by averaging over all activated pixels, ranged from 69 ±18 to 99 ± 26 ml / min / 100g. The average value over all subjects (n = 5) was calculated to give 86 ± 13 ml / min / 100g. A representative example for the time courses of ΔCBF averaged over all activated pixels in a single subject is given in Figure 15. The measured perfusion changes exhibit an excellent correlation with the visual stimulation paradigm.

The BASE technique was implemented with Snapshot FLASH imaging which implies that the longitudinal relaxation process is perturbed during the acquisition of an image.

For the imaging parameters specified above, the resulting systematic error in ΔCBF was calculated to be less than 2 %. Systematic errors of that kind can be completely avoided by implementing the BASE technique with a single-shot imaging technique (e.g. EPI, GRASE, U-FLARE).

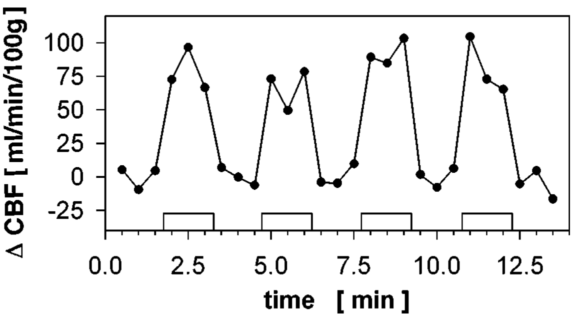


Figure 15. Time course of ΔCBF in a single volunteer.

Dependence of the BOLD contrast on oxygen consumption

3.6.11

Schwarzbauer, C. & Heinke, W.

Functional activation results in an increase in oxygen consumption which gives rise to a higher deoxyhemoglobin concentration. The brain reacts with a local increase of perfusion which causes a decrease of the deoxyhemoglobin concentration below its normal level. Due to the paramagnetic properties of deoxyhemoglobin, the effective transverse relaxation time (T2*) increases, giving rise to an increase in the BOLD (blood oxygenation level dependent) contrast (1). The BOLD contrast therefore depends on changes in both oxygen consumption and perfusion, where the later is the dominant effect.
In the present study we addressed the question of whether information on oxygen consumption can be obtained from a combined measurement of BOLD contrast and perfusion. For this purpose we used two different stimuli: visual stimulation (VS) and hypercapnia (HC). During VS both oxygen consumption and perfusion are increased, whereas during HC only perfusion is increased and oxygen consumption can be considered constant (2,3). A comparison of the corresponding changes in BOLD contrast and perfusion should therefore reveal whether oxygen consumption significantly contributes to the BOLD contrast.

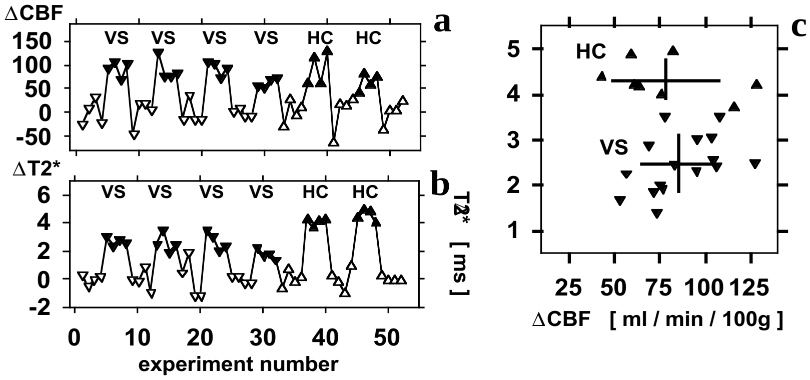


Figure 16. Mean time courses of ΔCBF (a) and ΔT2* (b) measured in a single volunteer; correlation plot (c).

The mean time courses of perfusion (ΔCBF) and BOLD contrast (ΔT2*) measured in a single volunteer are depicted in Figure 16a and b. The corresponding mean values were calculated only for pixels that exhibited a significant increase in both perfusion and BOLD contrast during VS. The difference between VS and HC is evident in the correlation plot (Figure 16c) which shows ΔT2* versus ΔCBF. The upwards and downwards pointing triangles refer to HC and VS, respectively. The corresponding mean values and standard deviations are represented by black crosses. ΔT2* is significantly lower during VS than during HC, whereas the corresponding DCBF values do not differ significantly from each other. This means, however, that for the same CBF the deoxyhemoglobin concentration during VS is higher than during HC. From the assumption that oxygen consumption remains constant under HC, it follows that there was a significant increase in oxygen consumption under VS. Similar results were obtained in 6 of the 8 volunteers investigated. In two volunteers ΔCBF values were significantly higher during VS than during HC. Therefore, a direct comparison of the corresponding ΔT2* values was not possible.

By applying this analysis on a pixel-by-pixel basis we were able to identify pixels with a significant increase in oxygen consumption. However, due to the prerequisite of a non significant difference in the ΔCBF values between VS and HC, the analysis was not applicable to all pixels. We are currently investigating, whether this problem can be solved by applying different concentrations of CO_2.

Using hypercapnia as a reference stimulus, we were able to show that the increased oxygen consumption under visual stimulation significantly reduces the BOLD contrast. Applying this technique on a pixel-by-pixel basis offers the possibility of identifying pixels with a significant increase in oxygen consumption.

3.6.12 Echo planar imaging - development of enhanced EPI methods

Wiggins, C.J. & Norris, D.G.

One important issue in EPI is the decrease in signal intensity (shortened T_2^*) and increase in image distortion (due to slightly altered MR frequency) associated with regions of poor magnet field homogeneity. The most crucial area in which this is a problem is in the inferior part of the frontal lobes where the magnetic subsceptibility differences between brain tissue and the air cavities in the sinuses cause strong local magnetic field gradients. Since this region is also an area of great interest for the Institute, it is of interest to examine variations of EPI that may be less sensitive to local field inhomogeneities.

The sensitivity of EPI to field homogeneity is a consequence of the fact that the central phase-encoding lines are necessarily offset from the start of the acquisition train, and that phase errors accumulate throughout the echo-train. This can most easily be reduced by making the train more rapid, but a limit is set by hardware performance. Two different approaches to reducing these effects have been implemented:

Ultrafast segmentation: Susceptity artefacts in EPI can be reduced by collecting the data in two (or more) excitations (or 'segments'), with consequent reduction in image distortion. In standard segmented EPI, the first segment for a given slice is acquired, followed by the first segment for the other slices in a multislice set. Only then are the second segments acquired for each slice. Subject motion during the time between the acquisition of the two segments can cause image artefacts. If the two segments for one slice are collected in quick succession motion effects can be eliminated. This can be achieved by adjusting the excitation angle for each segment so that each pulse reads out an equal amount of magnetization. Up to 16 segments can be acquired.

Multiple echo time imaging: The echo time (TE) generally used for the fMRI studies is 40 ms, which should maximize the signal change (due to the BOLD effect) in activated regions. However, the shortened T_2^* in parts of the frontal lobes is severe enough to completely dephase the MR signal by this echo time, and thus no signal is observed in these regions. It would be of interest, then, to collect a shorter TE image to detect signal from these areas, while simultaneously being able to collect an image at the normal TE for areas of the brain where the field is more uniform. With a suitable image matrix, and either some degree of segmentation or very fast and strong gradients, collection of two (or more) images in succession following a single MR excitation is easily possible. As a demonstration, fMRI was performed with a visual stimulus, initially with a normal, homogeneous field to locate the activation. The magnetic field was then deliberately spoiled and a dual echo sequence run. As can be seen in the accompanying figure, while the disrupted magnetic field has caused severe signal loss in the visual cortex in the long echo time image, clear functional activity can be seen in the short echo time data.

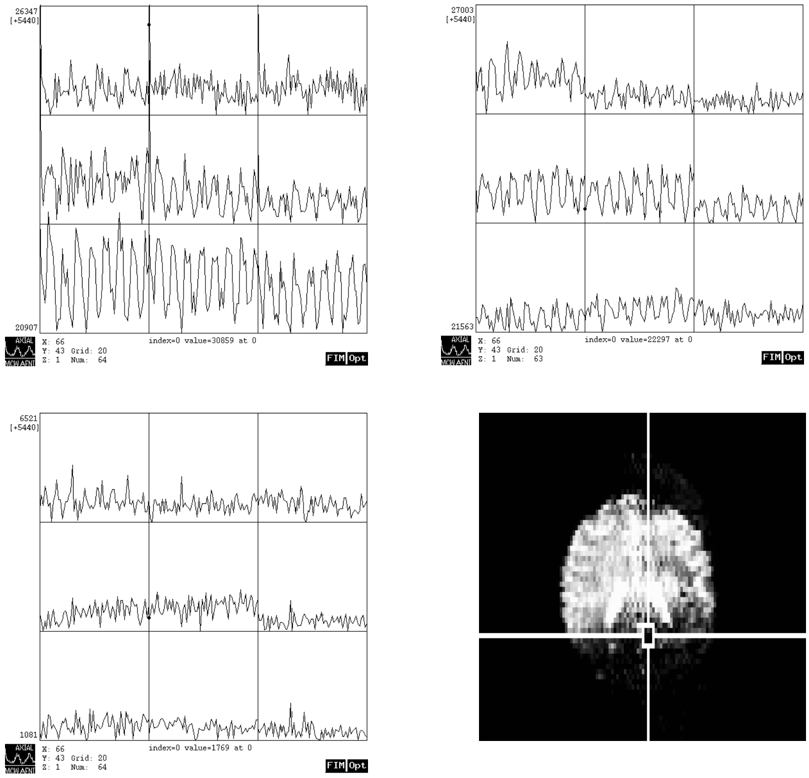


Figure 17.

Multiple echo time imaging. The fMRI timecourse from a standard scan (TE=40 ms) with a homogeneous field (upper left) is also seen in the first echo image (upper right) at TE=15 ms. At TE=50ms the signal had decayed due to the poor shim, as seen in the timcourse plot (lower left) and the corresponding image (lower right).

Last year's activity was marked by endeavors to increase the quality of the MEG data by compensating for environmental noise. MEG measures on weekends and late at night revealed that the quality of data was dramatically influenced by the absence / presence of the city's traffic.

A series of experiments showed that cognition and language related magnetic fields were particularly affected by environmental noise. After further deliberations, it became clear that additional passive and active noise can cellation systems allow for only insufficient noise reduction. Given this discovery, a new location for the MEG system was considered.

The work reported here reflects the group's activities in analyzing first data from the 148 channel MEG and EEG data to test models concerning dipole localization (3.7.2, 3.7.3, 3.7.4 and 3.7.5), as well as in developing a specific time-frequency analysis (3.7.6).

3.7.1 Magnetic brain activation during auditory sentence perception recorded by a 148 channel whole head magnetometer system

Knösche, T.R.,
Maeß, B.,
Oertel, U. &
Friederici, A.D.

Event-related magnetic fields were recorded during auditory perception of both correct and sematically or syntactically incorrect sentences. Earlier ERP studies have shown for syntactically incorrect sentences an early left anterior negativity (ELAN, 200 - 300 ms) and a late centro-parietal positivity (P600, 500 – 800 ms) (Annual Report 1995/ 1996). For semantically incorrect sentences, a centro-parietal negativity (N400, around 400 ms) was found (Annual Report 1995/1996). The ELAN was also seen in MEG using a dual 37-channel magnetometer system (see Annual Report 1996). However, because of the placement of the two clusters above the temporal parts of the brain, the other two effects could not be shown. Therefore, the experiment was repeated with a 148-channel whole-head magnetometer system (MAGNES WHS 2500, BTi).

Twenty right handed female volunteers, who were native speakers of German (mean age 23.3 years, 19 – 29 years) participated in the study. The sentences were presented as connected speech, including 50 % correct, 25 % syntactically incorrect, and 25 % semantically incorrect ones. Altogether 520 stimuli were presented to each subject. Semantic incorrectness was realised as selectional restriction error, syntactic incorrectness was realised as word category error. Because strong low-frequency noise was present in the data, two alternative filterings were applied: a low-pass filter at 25 Hz, and a bandpass filter from 2 Hz to 25 Hz. The data were averaged with respect to the onset of the critical word (underlined), resulting in three data sets (correct, syntactically incorrect, sematically incorrect), and to the sentence beginnings, yielding a fourth average. The average of the sentence beginnings was used to rate the subjects according to their signal-to-noise ratio, which was defined by the amplitude of the primary auditory response (M100) and the standard deviation of a 200 ms baseline before the stimulus onset. High environmental noise and small amplitudes of the effects made a selection of subjects necessary. Only the 10 subjects with an SNR greater 4 in both hemispheres and both filter conditions were selected for further analysis.

For statistical analysis, 4 time intervals (25 .. 75 ms; 100 .. 200 ms; 300 .. 600 ms; 600 .. 900 ms) and 12 regions of interest (ROI) were defined, each containing approximately the same number of sensors (11 or 12). For each time window and for both filtering conditions, an ANOVA (condition times ROI) was computed. For the low-pass filtered data, significant differences between the syntactically incorrect and the correct condition were found in the first two time windows for 4 temporal ROIs (p=0.06 .. 0.005), and in the last time window for one right temporal ROI (p=0.01). If the band pass filtered data were used, the early effects became even more pronounced (7 ROIs, p=0.04 .. 0.0005), while the late effect vanished.

Significant differences between the semantically incorrect and the correct condition could only be found for the low-pass filtered data, in the third time window in two ROIs (p=0.004 .. 0.002).

Hence, it can be concluded that all three targeted effects (ELAN and P600 for syntactic violation, N400 for semantic violation) could be found in the data. The two long latency components were only present in the low-pass filtered data, while the ELAN was more pronounced in the band-pass versions. It was therefore shown that the whole-head magnetometer system is capable of detecting these effects. Further analysis of the data, including source modelling, is in progress.

Transformation of MEG recordings between different sensor positions

3.7.2

Knösche, T.R.

With MEG recordings, the positions of the sensors are always constant with respect to each other, but not with respect to the head. In order to average the data of different subjects or of different recording sessions of the same subject, it is necessary to project all recordings onto one target sensor array. Since this is not a unique procedure, it seems sensible to use an interpolation function that is based on intracranial currents. Such an algorithm was developed and tested using both simulations and phantom measurements.

In order to explore the accuracy of the algorithm, computer simulations were carried out. Using a realistically shaped head model, 148 channel whole head MEG data were simulated. Three positions of the sensor array were considered, differing up to 10 mm by translation and 10 degrees by angle. Four different dipoles, located deep, central, lateral, and frontal, were used to simulate MEG data for all 3 sensor arrays. The proposed algorithm was used to transform the MEG data for the first sensor to the two other sensor arrays. The results were compared to the directly (from the sources) calculated data sets by means of correlation. For all superficial dipoles the accuracy is very high, expressed by correlations above 98 %. For the deep dipole, the error was larger (correlation 68 %), most likely due to volume conductor mismatch.

The next step was the application of the routine to single dipole localisation from measured data. A saline filled sphere (diameter 80 mm) was placed in the sensor array of a 148 channel MAGNES© WH 2500 system of BTi. Three tangetial current dipoles were placed along the z-axis inside the sphere. Three different relative positions of sphere and dewar were tested. The dipoles were localised under wrong dewar position assumptions, with and without applying the proposed transformation. It was found that in all cases the corrected (transformed) data sets yield much smaller errors than the uncorrected ones, and that these results are close to the ones computed with the correct dewar positions. The results were also satisfactory for the deep dipole.

It can be concluded that the proposed procedure is usable as long as the volume conductor mismatch is not too strong. This goes for all superficial sources. For deep sources, it might be necessary to employ realistically shaped head models.

Information criteria determine the number of independent sources in EEG/MEG

3.7.3

Knösche, T.R.,
Berends, E.M.,
Jagers, B. &
Peters, M.J.

Regarding the application of many methods for the reconstruction of sources of EEG or MEG, the number of independent source components is a vital input parameter, e.g., spatio-temporal dipole analysis (e.g. Scherg & von Cramon, 1986). Information criteria can be applied to make a decision on the basis of a statistical model of the data, which takes into account the properties of the noise (as represented by the estimated noise covariance matrix). Such information criterion is represented by a function of the number of independent source components, which depends upon the data and additional information about the noise (covariance matrices). We are looking for the true number of components, at which the function has a minimum. For details, see: Uijen and van Oosterom (1992), or Knösche (1997). In order to assess the performance of such criteria, and to quantify the parameters that influence this performance, 18 different information criteria have been used (summarized by Knösche, 1997) to analyze computer simulated EEG data. Different dipole combinations were assumed as sources. Gaussian, spatially correlated, and uncorrelated noise was added to the data. The noise level, the relative inaccuracy of the noise covariance matrix, and the numbers of channels and time samples were varied. The main aim of the study was to determine which criteria to use under which conditions.

The results of the simulations showed very different tolerances of the various information criteria towards the investigated parameters. On the one hand, the criteria's tolerance towards higher noise levels increased, if more channel and/or more time steps were used. On the other hand, the criteria's stability against inaccuracy of the estimated noise covariance matrix declined, if more channels/time steps were employed.

Two of the investigated criteria can be recommended. Both use the assumption of spatially correlated noise in their statistical models (many others apply a so-called pre-whitening procedure and then assume uncorrelated noise), and both apply the Akaike correction term (Akaike, 1974). We believe that these specific information criteria can play an important role in supplying extra information to the inverse procedure by making a more accurate distinction between phenomena which are stable over epochs (signal), and phenomena that are stochastic (noise). Moreover, these criteria might introduce a greater degree of objectivity and reproducability into dipole EEG/MEG data analysis.

3.7.4 Accuracy of single dipole localization from MEG recordings of a phantom head

Knösche, T.R.

In order to determine the minimum signal-to-noise ratio (SNR), which is necessary for reliable dipole localisations from 148-channel MEG data (MAGNES© 2500 WH of BTi), a series of phantom experiments was carried out. As phantom, a saline filled sphere provided by the manufacturer of the MEG equipment was used. Five current dipoles at different depth within the phantom were used to generate artificial signals and three different dewar positions were investigated (see Figure 1).

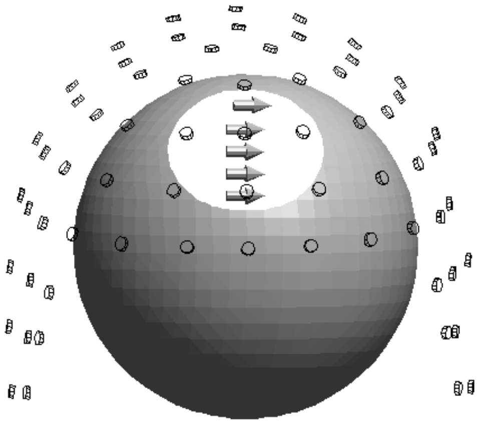


Figure 1. Dipole positions with volume conductor model and sensor positions.

The current through the dipoles was varied in order to obtain different signal-to-noise ratios. For each recording, 100 epochs were created, consisting of 150 ms signal-free data and 100 ms of a 10 Hz sine wave. After averaging, the signal to noise ratio was computed as ratio of the variances over all channels and all latencies between 150 and 250 ms (signal + noise), and over all channels and all latencies between 0 and 149 ms (noise). The software package ASA© was used to carry out rotating dipole fits on a time window from 150 to 250 milliseconds. A single sphere model accounted for the volume conduction effects (see Sarvas, 1987).

First, the relationship between the SNR and the localisation error was investigated. Figure 2 shows the result.

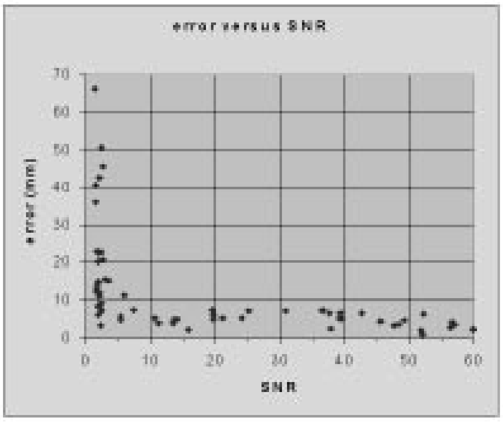


Figure 2. Relationship between SNR and localisation error.

Below a critical SNR of about 6, errors can be very high, indicating that the fit is unstable. Above the value, the errors vary between 1 and 8 mm, regardless of the SNR (at least below an SNR of 20).

Second, it was investigated, as to whether a relationship exists between dipole depth and SNR. As is obvious from Figure 3a, none is present. This result is not due to different SNRs in different depths, as shown in Figure 3b.

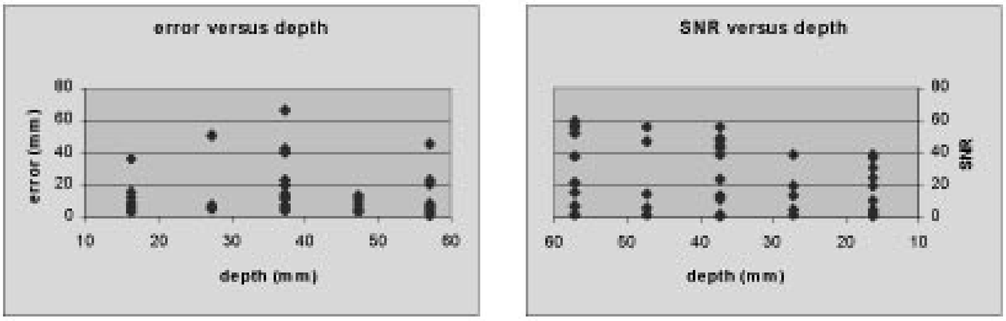


Figure 3. Relationship between dipole depth and localisation error (left panel). The right panel shows that there is no clear depth dependence of the SNR.

3.7.5 Three-dimensional reconstruction from EEG - the performance of linear algorithms

Knösche, T.R.

If one could construct a three-dimensional image of the intracranial currents at any given instant in time from EEG or MEG measurements, this would be the ultimate functional imaging method. However, it is known from theory that this goal cannot be reached for principle reasons. Nevertheless, there have been numerous attempts to design algorithms that can at least construct certain aspects of the three-dimensional current distribution within the head. Such algorithms have been proposed, e.g., by Sekihara and Scholz (1995, 1996), van Drongelen et al. (1996), Smith et al. (1990), and Pascual-Marqui et al. (1994). Each of these methods has to cope with both the principle non-uniqueness of the problem and additional instability in the presence of noise. Therefore, regularization has to take place, i.e., the selection of one of the possible solutions as a representative which should reflect as much of the signal and as little of the noise as possible. Regularization against principal non-uniqueness is done, for example, by assuming mutual independence of the current elements (e.g., Sekihara & Scholz, 1996) by demanding a solution with minimum norm (e.g., Sekihara & Scholz, 1995; Smith et al., 1990; Graumann, 1991), or by picking the solution with maximum smoothness (or minimum second spatial derivative), as introduced by Pascual-Marqui et al. (1994). The effect of noise on the solution is combatted by Tikhonov regularization (e.g., Graumann, 1991) or the Wiener-Helstrom filter principle (e.g., Smith et al., 1990; Sekihara & Scholz, 1995).

All methods have been validated by computer simulations using very different and sometimes quite unrealistic settings. In order to find out what the relative merits and drawbacks are and which tradeoffs have been made in order to achieve three-dimensional images, a set of computer simulations was designed. Eleven different simulated focal and extended sources were used to simulate measurements with 98 EEG electrodes employing a spherical model of the head. Gaussian noise of different levels was added and then different methods were used to reconstruct the sources. The study is still going on. So far, three algorithms have been evaluated: (1) a modified Wiener filter according to Sekihara and Scholz (1995), (2) a spatial filter according to Sekihara and Scholz (1996), (3) linear estimation with lead field normalization and Tikhonov regularization (see e.g. Graumann, 1991).

The results show that only the spatial filter by Sekihara and Scholz (1996) was capable of estimating the three-dimensional position of the source, at the expense of the recovery of shape and extent of the generator. All sources where reconstructed as focal generators at the approximate centre-of-mass. For an example, see Figure 4. The other two methods were, within certain limits, sensitive to the extent of the active area, but had a strong bias towards the surface of the reconstruction area.

In the future, this evaluation will be extended to the LORETA method, proposed by Pascual-Marqui et al. (1994), and the modified Backus-Gilbert approach as presented by Grave de Peralta Menendez et al. (1997). Furthermore, the performance of the algorithms with simulated magnetic data will be evaluated. The approach with the best performance will then be used to analyse event-related magnetic fields due to syntactic and semantic violations in connected speech (see 3.7.1 in this anual report).

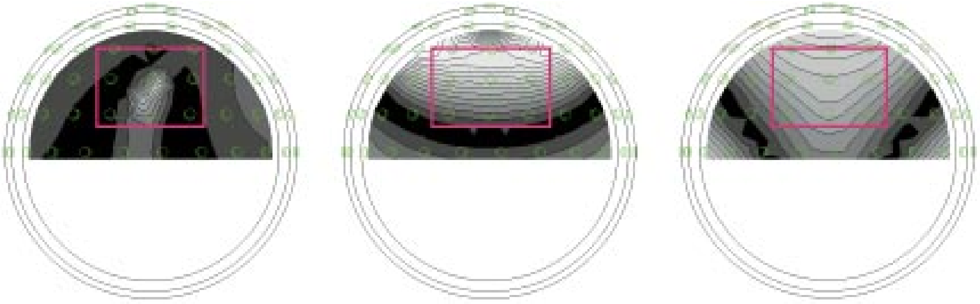


Figure 4. Reconstruction of a cylindrical generator with upward orientation. A cross-section of the interior of the skull through the centre of the sphere is displayed. The pink rectangle outlines the original source, the grey-shaded map represents the reconstructed current density (white – maximum, black – zero). The volume conductor model (black circles) and the electrodes (green circlets) are indicated as well. The simulated data were contaminated with Gaussian noise (variance 10 % of the signal) prior to reconstruction. The left panel shows the result for the spatial filter according to Sekihara and Scholz (1996), the middle panel for the modified Wiener-Helstrom filter according to Sekihara and Scholz (1995) and the right panel for linear estimation according to Graumann (1991).

3.7.6

Time-frequency analysis of event-related electrophysiological data

Herrmann, C.,
Pfeifer, E. &
Mecklinger, A.

When analyzing event-related electrophysiological data, it is often desirable to obtain information about the frequency-domain in addition to the mere time-domain signal. The Fourier-transform (FT) has been used in many variations to achieve this goal. Unfortunately, the FT is not suited for all types of time-domain signals. Two main drawbacks are to be considered when using the FT:

The FT is only appropriate for the analysis of pseudo-stationary signals with continuous frequency components. Short and sudden bursts, so-called transients, are hard to detect with this method. A spectrum computed via an FT yields frequency information only about a whole interval of time(not about certain points of time within the interval.

Due to the Heisenberg-Gabor inequality all FTs (including short time FT) bear a trade-off between temporal and frequency resolution. I.e. the frequency resolution is inversely related to the bandwidth of the analysis window while the temporal resolution is determined by the duration of the window.

Especially when searching for Gamma-band frequency changes, which are assumed to be associated with the feature binding mechanism, it is important to detect short burst as well as their time of appearance.

For the above reasons, we employed so-called time-frequency methods in order to obtain representations of our signals in two-dimensional time-frequency maps. Wavelets were used for this task. They have proven to be very efficient for the detection of transients in the EEG and overcome the limitations of FTs by offering a constant ratio of bandwidth to frequency. By compressing and stretching one type of waveform (the wavelet) a short window is used at high frequencies and a longer window at lower frequencies.

A wavelet (literally: small wave) is a complex wave that can be calculated according to different formulas. In the case of the so-called Gauß-wavelet calculations are as follows

$$g_a(t) = e^{-\frac{1}{2}\cdot\left(\frac{t}{a}\right)^2 + j2\pi\frac{t}{a}}$$

where a is the parameter to manipulate the wavelet frequency which is proportional to the window duration ($|a| > 1$ dilates the wavelet while $|a| < 1$ compresses the wavelet). The effective frequency v of a dilated wavelet can be determined by dividing the mother wavelet's frequency v_0 by a. The result of the above equation is a waveshape depicted in Figure 5 where only the real part of the complex wave is represented.

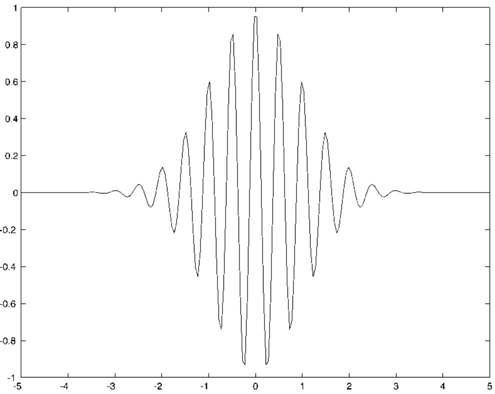


Figure 5. The real part of a basic (unshifted and undilated) Gauß-wavelet $Real(g_1(t))$.

Having such a wavelet $g_a(t)$, different new signals $s_a(b)$ can be derived by a convolution of the EEG signal eeg(t) with the wavelet (is the wavelet dilation and the time scale of the convolved signal). The resulting signal $s_a(b)$ can be regarded as a measure of similarity between the EEG signal and the shape of the wavelet $g_a(t)$. Convolving multiple, differently dilated wavelets with the time-signal results in a representation as shown in Figure 6 (c).

Figure 6 (a) shows an evoked response potential (ERP) with a negative and positive component peaking at 200 ms (N200) and 300 ms (P300), respectively. In the frequency-domain the low-frequency potentials are easily detectable, but no inferences may be drawn about their temporal characteristics (Figure 6 (b)). In contrast, both components can be localized adequately in the time-frequency representation (Figure 6 (c)) being the absolute wavelet transform (WT) of the signal. The brightness at a point in the map specifies the amplitude of the frequency component occurring at that point in time. Note that the logarithmic scaling of the y-axis reflects the actual focus of interest in electrophysiological data where frequency differences must be regarded with respect to the frequency itself (i.e., a change of 1 Hz matters a lot when regarding a 1 Hz component, but is negligible at 40 Hz).

When averaging single trials before applying the WT, frequency components that are not synchronized with the stimuli will average out. To detect such components it is necessary to apply the WT to each single trial epoch. When averaging the resulting WT spectra non-synchronous activity will be retained.

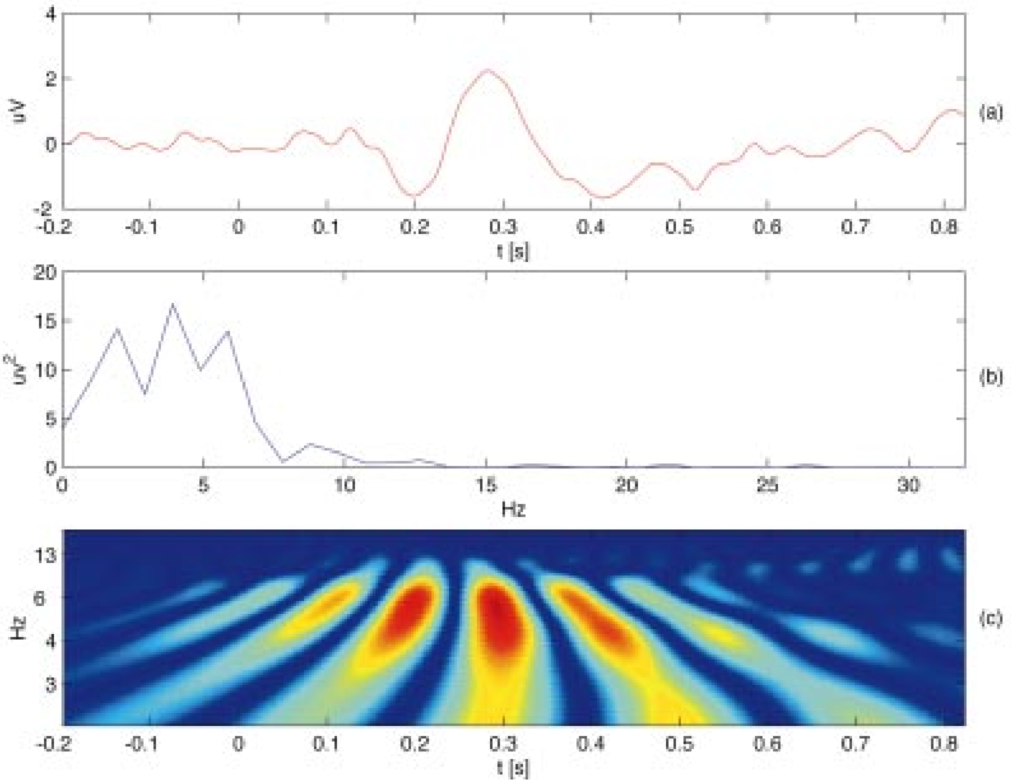


Figure 6. The averaged ERP of a language experiment in its time-domain (a), frequency-domain (b) and time-frequency representation (c).

A T2* phantom for testing of fMRI techniques

4.1

Dymond, R.C.,
Köhler, R. &
Norris, D.G.

The in vivo evaluation of functional imaging methods is clearly unsatisfactory due to the large number of possible reasons for a lack of observed activation. While the method itself may be at fault, the problem may also arise from physiological motion artefacts, from a failure in the stimulation equipment, from subject habituation to stimulation, from inappropriate data processing assumptions or from a general degradation of the system SNR. The aim of this work was the development of a dynamic T2* phantom with which it is possible to generate a realistic functional timecourse and which can be used to make an objective in vitro assessment of a given functional imaging sequence, to compare one sequence with another or to check methods of analysis.

In order to simulate fMRI signal changes, a true T2* contrast is required and this is generated using a suspension of superparamagnetic iron-oxide particles (SPIOs) in argarose gel. The SPIOs give rise to local susceptibility gradients which are comparable with those produced by paramagnetic deoxyhaemoglobin in blood. Varying the concentration of argarose primarily affects the T2 of the sample and additional doping with nickel chloride can be carried out to attain a desired reduction in T1. For the purposes of this phantom, relaxation parameters were chosen to approximate to those measured in grey matter at 3T (T1=1300 ms, T2=70 ms).

The phantom assembly comprises a perspex cylinder and axle resting on two semi-circular supports which are fixed to the patient head rest within the RF head coil. Rotation is effected via a 5 m drive shaft by a stepper motor outside the magnet chamber. A functional timecourse is 'pre-programmed' by dividing the cylinder into 10 compartments having differing T2* values. Stepping of the motor is triggered by a logic signal from the spectrometer which is defined within the imaging pulse program. A single trigger pulse causes the motor to rotate by 36°, corresponding to an advancement from one sector of the phantom to the next.

In vivo measurements in occipital grey matter have shown T2* to be 31.2 ± 1.5 ms during rest periods and 33.0 ms ±1.5 ms during stimulation. For the purposes of the phantom, a comparable T2* of 31.37 ± 2.32 ms was obtained using an 0.02 mM concentration of SPIOs in a 1% solution of argarose in distilled water. This was used as the 'baseline' sample in the timecourse detailed below.

In addition to the well-known BOLD response which forms the basis of the contrast in fMRI experiments, various groups have reported an early negative signal dip produced by a localized increase in deoxyhaemoglobin concentration (Ernst et al., 1994) and a larger negative undershoot arising after the cessation of stimulation (Davis et al., 1994).

These features were incorporated into a set of 10 samples as follows: 1-4. Baseline (0.02 mM Fe), 5. Negative Dip (0.025 mM Fe), 6-8. BOLD (0.005 mM Fe), 9. Undershoot 1 (0.03 mM Fe), 10. Undershoot 2 (0.025 mM Fe). Figure 1 presents the results of a functional experiment performed using the phantom. 64 consecutive FLASH images were collected with TE/TR=40/80.5 ms and matrix 128 x 64. Any misregistration of the latter images in the functional dataset (typically found to be $\pm 3^o$ on account of a slight instability in the drive shaft) was eliminated using a simple motion correction procedure.

The functional data were evaluated using the AFNI software package. Figure 1(a) shows the correlation coefficient map (r=0.75) overlayed on a T2-weighted image of the phantom. As expected, one test tube demonstrates a timecourse which is exactly in phase with the ideal waveform (upper trace in Figure 1(b)). Examination of the lower trace of Figure 1(b), which is the timecourse for a representative pixel within the 'activated' region, reveals the desired features of the functional signal change.

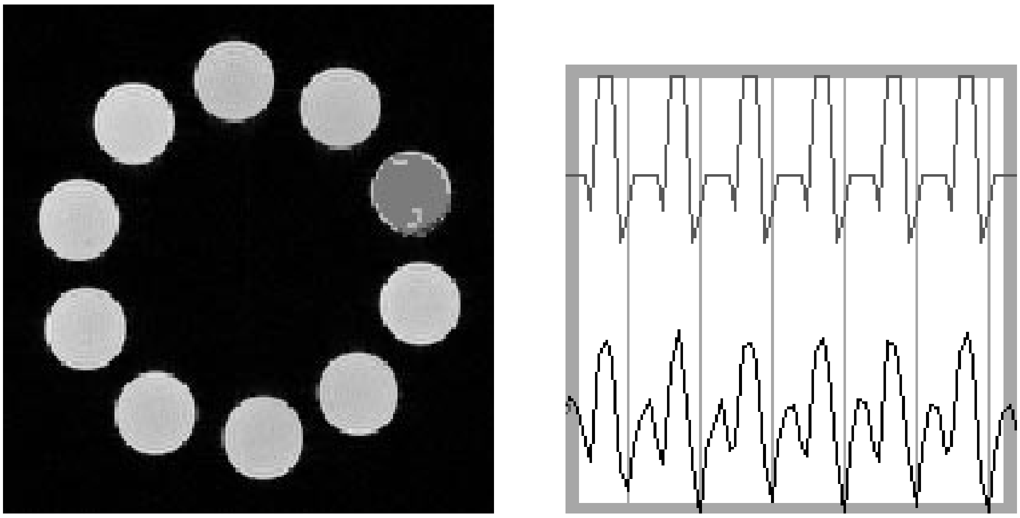

(a) (b)

Figure 1.

An imaging phantom has been proposed with which it is possible to generate realistic T2* contrast and any desired fMRI timecourse. It is expected that this design will find a wide range of applications in the evaluation and assessment of dynamic imaging techniques.

4.2 Measurement of the diffusion tensor of water

Koch, M. &
Norris, D.G.

In anisotropic media diffusional displacements of water in a given time are not necessarily the same for all directions. The apparent diffusion coefficients in all spatial directions can be described by a symmetric 3 × 3 matrix of real non-negative numbers, the diffusion tensor, $\underline{\underline{D}}$.

1. Since water molecules diffuse more rapidly in the direction parallel to a nerve fibre, it is possible to image myelin fibre orientation in brain white matter by measuring the anisotropy of water diffusion.

2. The electrical conductivity tensor is believed to be coaxial with the diffusion tensor. Results from diffusion tensor imaging (DTI; Basser et al., 1994) could thus help in developing improved algorithms for EEG/MEG reconstruction.

Magnetic resonance experiments can be made sensitive to diffusional motion by the application of magnetic field gradients. The signal attenuation by diffusion gradient pulses is given by

$$\frac{S}{S_0} = \exp\left[-\underline{\underline{b}}:\underline{\underline{D}}\right], \quad \underline{\underline{b}}:\underline{\underline{D}} = \sum_{i=1}^{3}\sum_{j=1}^{3} b_{ij} D_{ij} \in \mathrm{R}$$

$$\ln S = \ln S_0 - b_{11}D_{11} - b_{22}D_{22} - b_{33}D_{33} - 2b_{12}D_{12} - 2b_{23}D_{23} - 2b_{13}D_{13}$$

where the matrix $\underline{\underline{b}}$ accounts for direction, strength and timing of all field gradients in the pulse sequence. S_0 is the signal amplitude at $\underline{\underline{b}} = 0$. In order to calculate the 6 independent elements of the diffusion tensor the signal amplitude is measured as a function of the $\underline{\underline{b}}$ matrix. S_0 and the 6 independent tensor elements D_{ij} are then determined by multivariate linear regression. This means that at least 28 images must be acquired: 7 different diffusion gradient directions, and 4 to 8 different attenuation factors (e.g. gradient strengths) per gradient direction are necessary. The gradient directions have to be chosen in such a way that the $\underline{\underline{b}}$ matrices span the vector space of symmetric 3 × 3 matrices. The large number of measurements requires the application of rapid imaging methods to keep the total measuring time reasonably low. The data processing software for the tensor calculation from measured image data has been written in IDL. Since diffusion weighting renders a measuring sequence sensitive to coherent (e.g. subject motion) and incoherent (diffusion) motion, in non-single-shot in vivo experiments some type of motion correction has to be applied. A further complication is the contribution of the imaging gradients to the diffusion weighting. The computation of the exact b matrix that contains information about all gradient pulses in the sequence requires large computational resources.

Diffusion weighted spin-echo experiments were performed on a water phantom. The diffusion tensor of a water sample is proportional to the identity matrix. However, the measured tensor was not isotropic (diffusion coefficients *D* differed by a factor of 1.5). The measured diffusion anisotropy was not reproducible quantitatively over days or weeks. Further control experiments showed that these problems arise from eddy currents that produce additional field gradients, and from instabilities in the probe temperature (a temperature difference of 2 K causes a change in *D* of about 0.12 10^{-9} m^2/s). The measured anisotropy was less severe in *spatially resolved* experiments on a *thermally insulated* phantom (diffusion coefficients in x, y, and z direction differ by about 8%). Using a head gradient set delivered by Magnex Scientific Ltd. the coefficients agreed within 4 % accuracy. In the table below diffusion coefficients measured with the Bruker and Magnex gradient sets on an insulated water phantom are shown.

	T	D/10^{-9} m^2s^{-1}			
		x	y	z	Lit.
Bruker gradients, spin-echo image, xyz=RePhSl	17.9°C	**2.07**	**2.15**	**2.23**	1.94
Magnex gradients, spin-echo image, xyz=RePhSl		**2.19**	**2.18**	**2.19**	

A first diffusion weighted rapid imaging sequence has been implemented: the diffusion sensitizing gradient pulses have been incorporated into an EPI sequence. The sequence is about to be tested in vivo. Some results from phantom measurements are shown below.

1. Mean diffusion tensor, measured with diffusion weighted spin-echo EPI on a water phantom (5 cm diameter), expressed in xyz coordinate system, xyz = PhReSl, TR = 6 s, TE = 200 ms, matrix size = 128 × 128 pixels, FOV = 27 cm × 27 cm, slice thickness = 5 mm, *b* values = {20, 147, 273, 400} 10^6 s/m^2 (imaging gradients not being accounted for), 7 gradient directions, Bruker gradient set, at 19.6°C room temperature:

$$\underline{\underline{D}} = \left[\begin{pmatrix} 2.090 & -0.025 & 0.039 \\ -0.025 & 2.438 & -0.021 \\ 0.039 & -0.021 & 2.316 \end{pmatrix} \pm \begin{pmatrix} 0.024 & 0.000 & 0.004 \\ 0.000 & 0.038 & 0.004 \\ 0.004 & 0.004 & 0.053 \end{pmatrix}\right] \cdot 10^{-9}\ \mathrm{m}^2/\mathrm{s}$$

   (Error is standard deviation of pixel values from mean over all pixels.)

2. Mean diffusion tensor, measured with diffusion weighted spin-echo EPI on a gel phantom (15 cm diameter), expressed in xyz coordinate system, xyz = PhReSl, TR = 3 s, TE = 200 ms, matrix size = 128 × 128 pixels, FOV = 25 cm × 25 cm, slice thickness = 5 mm, *b* values = {10, 140, 270, 400} 10^6 s/m^2 (imaging gradients not being accounted for), 8 gradient directions, Bruker gradient set:

$$\underline{\underline{D}} = \left[\begin{pmatrix} 1.927 & -0.000 & 0.019 \\ -0.000 & 2.183 & -0.025 \\ 0.019 & -0.025 & 2.125 \end{pmatrix} \pm \begin{pmatrix} 0.061 & 0.052 & 0.057 \\ 0.052 & 0.056 & 0.059 \\ 0.057 & 0.059 & 0.074 \end{pmatrix}\right] \cdot 10^{-9}\ \mathrm{m}^2/\mathrm{s}$$

4.3 Development of an automated permutation program 'balance'

Schubert, T. & Sturm, P.

Planning of psychological experiments often requires the careful construction of triallists consisting of different kinds of trials (called trial-types). This process is often realized by means of a randomization procedure of the computer used for experimentation. However, this randomization procedure does not necessarily lead to optimally permutated tirallists since the computer's random generator does not exclude systematic contingencies between separate events in shorter lists. Another possibility would be to permutate the trial-types in the triallist manually. This is a very timeconsuming process especially if the triallist and the number of different trial-types are large. Therefore, the computer-aided system 'balance' was developed which automates the process of trial-permutation to some extent.

Up to now two different permutation problems in triallists (1, 2) can be solved by the balance program. A third application (3) has been under development.

1. Different trial-types (e.g., trial -type A and trial-type B) in one triallist: the program solves the permutation problem for at least two criteria: the transition probabilities

between all possible trial-type combinations (p(A following A), p(A following B), p(B following B), p(B following A)) are equalized. Furthermore, the presentation probabilities of different trial-types are also equalized (p(A)= 0.5 versus p(B)=0.5)

2. Different trial-types in two or more related triallists are permutated by the criterions of point 2
3. An experiment requires non equal presentation probabilities of different trial-types (A, B) in the triallist (p(A)=0.8 versus p(B)=0.2). For this variant, it is planned to develop a tool which allows the determination of the transition probabilities between A and B in advance.

The system requires a PC with at least an i386 processor or, even better, an i486 processor and 16-Bit-Windows. Developed object oriented C++ programming was used to realize the system on Windows3.1. This allows us to add new components to the system if required. The program uses a stochastic algorithm which finds with high confidence, one solution of the permutation problem.

EEG recording during MR scanning

4.4

Wiggins, C.J. &
Kruggel, F.

The development of an EEG recording device for use within the MR scanner has been somewhat sidelined during 1997. This has been mainly in favour of developing suitable fMRI protocols (in particular EPI) that will allow sufficient 'quiet time' during which the EEG can be recorded undisturbed. Some development of the electronics has taken place, in particular, the interfacing of the EEG preamplifier to the acquisition board. The initial setup used simple electrical connections, but it was found that the extreme length of the cabling involved (ca. 20 m) resulted in the pickup of large amounts of extraneous noise. For this reason, an optical coupling system was developed, which both eliminates the noise pickup problems and allows for complete electrical isolation of the preamplifier. In the initial configuration, however, this has been found to have a low frequency cutoff at about 8 Hz, which impinges greatly on the range of frequencies we desire to measure. This cutoff can be directly attributed to frequency dependent transmission properties of the optical components. For this reason a revised configuration is presently under development using FM modulation.

Installation of the MAGNEX head gradient set

4.5

Wiggins, C.J. &
Weder, M.

Various MRI techniques being used in the Institute, such as EPI and diffusion weighted imaging, benefit greatly from increases in available gradient strength and decreases in switching time. In general, simply decreasing the diameter of the gradient bore acts to improve both parameters. For this reason, the Institute ordered and, in May 1997, took possession of a gradient set dedicated to head imaging. While the absolute gradient strength achievable is not greatly different from the existing whole body set (38 mT/m vs. 30 mT/m), the difference in switching time to maximum strength is considerable (150 µs vs. 500 µs).

Having purchased the head gradient set, various aspects of the present hardware had to be altered to allow its use, both in terms of simply providing the necessary connection and in incorporating sufficient safety mechanisms to satisfy TUV inspection. To this end, Bruker was contracted to alter the gradient cabling to incorporate a robust plug and socket arrangement, suitable to handle the current (600 A) and voltage (presently 350 V, but soon to be upgraded to 1 kV) involved, as well as modifications to the temperature monitoring and gradient amplifier matching to handle switching between gradient sets.

Many other components of the new system were constructed in-house. Not least of these was the installation gantry. Since different experiments may require one or the other of the gradient sets, it was desireable to have a system that would allow the head gradient set to be removed and installed relatively easily. Considering the weight of the gradient set (approximately 300 kgs) this is no small task, especially as no ferromagnetic components could be used. For this purpose a gantry and roller arrangement has been constructed out of aluminium and stainless steel, which allows the gradient to be rolled in and out of the magnet relatively easily.

Another major component was concerned with the electrical connection of the gradient. While it is possible to connect to the head gradient terminals with normal, heavy duty electrical cable, it becomes more difficult to hold these cables firmly in place when strong currents are passed through them while they are in the magnet field. As a more robust arrangement, a 'bus bar' system has been constructed consisting of solid metal rods embedded in epoxy. These run from the gradient terminals out of the magnet and then down under the double flooring. Under the double floor the bus bars are then connected to the gradient current leads.

Other components constructed and altered include: modifications to the patient couch and RF coil support, various tools to aid gradient installation and removal and re-routing of cooling tubing, and modifications to the visual stimulation screen.

Despite the many components that need to be changed, and the sheer weight of some components, it is now possible for two people to install the gradient set in less than 1.5 hours. Removal is somewhat less complicated, and can thus be performed in less than an hour.

4.6 Increased flexibility in statistical analysis of ERP data

Jacobsen, T., Maeß, B., Nowagk, R. & Oertel, U.

Quantifying ERP effects, either derived from EEG or MEG data, requires a complex procedure that naturally involves multiple levels of analysis such as the experimental conditions, different time windows, recording channels or regions of interest (ROI).

For this purpose, a new, more flexible, and thus more powerful analysis procedure has been designed. By using a data file format consisting of columns of classifying parameters and electrical potential or magnetic field strength values, analyses of varying degrees of aggregation can conveniently be computed. This includes the processing of standardized values and different configurations of ROIs. A new output format for the EEP avraverage module (see Annual Report 1996) was created. Codes for participants, conditions, windows and channels classify each value. Within EEP, switches [SAS output] and [SAS command file] should be set to 'Window Averages' and 'none' respectively and [SAS output format] is set to 'natural'. A z-standardization of values, e.g. for assessing topographical effects, may be done within SAS and is controlled considerably more transparently compared to the previous analysis procedure. ROI definitions can be added using an external program.

The PERL script and sample SAS script are available from the authors/on the WWW server.

Improvement of the auditory presentation system for fMRI experiments

4.7

Opitz, B.,
Meyer, M.,
Kruggel, F. &
Pfeifer, E.

An improved stimulation equipment was developed for auditory presentation of tonal and verbal stimulus material in the magnet for fMRI purposes. Two major problems had been faced when testing auditory stimulation under real measurement conditions.

First, in a pilot study using verbal material (words and non-words), a left/right asymmetry in headphone channels due to a microphone cable embedded in the right sound conduction tube was noted as yielding an attenuation of the right side's loudness. This microphone cable was placed separately in an additional tube. Furthermore, we found that the amplifier output did not reach a sufficient volume to maintain unblurred presentation, thus, new amplifier was constructed and installed by Frank Meyer. This not only improved the output quality, but also allowed us to control the left-right balance.

Second, the signal to noise ratio of the auditory stimulus stream was heavily influenced by the sound of the scanner (especially EPI-sequence) which led to insufficient task performance. To reduce the perceived scanning noise we considered earplugs as their use in tympanometric measurements was helpful. Therefore, we ordered from a company (MEDSERV GmbH), special reusable ear plugs in five different sizes and a sterilisator to meet hygienical standards. A connector to the headphones to optimize the sound conduction through the earplugs was also developed.

A further test study to evaluate the stimulus equipment under real conditions was designed. As a criterion for sufficient functioning, we aimed to localize fine grained BOLD activation in primary auditory cortex (gyrus transversalis) bilaterally by presenting complex artificial stimuli as proposed by Rübsamen (1992). Subjects were asked to listen carefully to a stimulus track consisting of continuous sinus tones, varying in frequency (500 - 4000 Hz), intensity (70 - 85 dB/SPL), and duration (20 - 100 ms) - the so called "random walk". Such activation blocks lasting 20 s were alternated with rest (silent) blocks. We used the FLASH sequence (TE = 40 ms and TR = 80 ms) to acquire functional images on axial slices oriented along the sylvian fissure. In seven out of eight subjects an activation of both Heschl's gyri was obtained.

The results were considered to show the efficiency resulting from the improvement of the auditory stimulation.

4.8 Visual stimulation system

Oertel, U. &
Maeß, B.

Since November the optical stimulation system has been operational. It consists of an LCD-projector positioned outside the Magnetic Shielding Room (MSR), a system of mirrors and a projection screen.

The LCD-projector (Epson) has a resolution of 600x800 pixels. Its original lens was replaced (Fa. Wenzel, Jena) due to the long optical way and the small image needed. The projector is placed outside of the MSR in front of the upper right ventilation opening. This ventilation opening was replaced by a specially designed tube system to get an acceptable image quality and avoid additional electromagnetic noise. An increasing of the magnetic flux caused by the new projection opening was not detectable.

The image passes the projection opening and is back projected onto a screen by means of a system of three mirrors. The screensize is 40 by 30 cm so that comparable conditions can be obtained in our EEG-labs.

4.9 Library and scientific documentation

Lewin, G.

The research in our Institute is supported by an in-house library whose classification system reflects current themes and research issues in cognitive neuroscience, and is revised when necessary.

The entire stock of our library has grown to 4,000 media units; they are

1,376	monographs
130	running numbers of journals
2,500	bound volumes of journals
10	CD-ROM data bases in our library
4	data bases with access via Internet.

In order to have efficient and technically current library software, an Internet based program was developed. This software system enables the librarian to process book loans and book / journal orders in an efficient way, and can also be used by the employees to obtain information about the availability of particular media units. All documents collected in our library and other locations of our Institute can be searched using different bibliographic parameters such as subject headings or full text database.
In the future, the search engine of the software will be available for Internet users in general, which is particularly important for journal requests.

A newly established library will always be characterized by the lack of a historically grown stock. Due to the provision of additional funds, however, it was possible to add back issues from 1980-1994 (or even earlier) of high priority journals.

The primary tasks of a library include various services in addition to the acquisition and indexing of relevant literature. Five thousand copies of articles were ordered from throughout Germany in the past year using inter-library lending and document delivery services.
This is an increase of approximately two thousand copies compared to last year. This higher demand was due to an increase in employees and the initiation of new research projects.

To date, book lending is done in a "self-service" manner. Next year the library will change to an automatized barcode based lending system, which will make the lending procedure more transparent and better documented.

The library is operated as a One-Person-Library (OPL) under the management of a full-time librarian. During the past year, one medical documentalist, Ms. Mareike Bromnitz, was trained. At the end of her training she wrote a thesis, called: "The use of medical data bases at the MPI of Cognitive Neuroscience".

Plans have been made for the library in the new building. These are aimed at efficiency, stock security, and a good working atmosphere.

Teaching

5.1

SOMMERSEMESTER 1997

Seminar Kognitive Neurowissenschaften
Universität Leipzig
Hund, M., Müller, U., Pollmann, S. & Schubert, T.

Komplexkurs 'Einführung in die Prosodie / Akustik'
MPI für neuropsychologische Forschung
Alter, K.

Klinische Neuropsychologie - Ausgewählte Kapitel
Universität Leipzig
von Cramon, D.Y. mit Mitarbeiterinnen/Mitarbeitern der Tagesklinik für kognitive Neurologie und des MPI für neuropsychologische Forschung

Methoden der biomedizinischen Kernspinresonanz-Bildgebung und Spektroskopie
Universität Leipzig
Norris, D.G.

WINTERSEMESTER 1997 / 98

Aktuelle Themen der Kognitionspsychologie
[a]Universität Leipzig in Kooperation mit dem [b]MPI für neuropsychologische Forschung
Kaernbach, C.[a], *Müller, H.*[a], *Sommerfeld, E.*[a], *Schröger, E.*[a]
Friederici, A.D.[b], *Gunter, Th.C.*[b], *Mecklinger, A.*[b]

Neuropsychologische Falldemonstrationen
Universität Leipzig
von Cramon, D.Y. mit Mitarbeiterinnen/Mitarbeitern der Tagesklinik für kognitive Neurologie und des MPI für neuropsychologische Forschung

Seminar Kognitive Neurowissenschaften
Universität Leipzig
Hund, M., Müller, U., Pollmann, S. & Schubert, T.

Fakultative Vorlesung Neuroanatomie und Sinnesorgane: Funktionell-bildgebende Verfahren in der kognitiven Neurowissenschaft
Universität Leipzig
Hund, M.

Methoden der biomedizinischen Kernspinresonanz-Bildgebung und Spektroskopie
Universität Leipzig
Norris, D.G.

Prosodie / Phonologie II
Universität Leipzig
Alter, K.

5.2 Committees and Memberships

Prof. Dr. Angela D. Friederici

Deutsche Forschungsgemeinschaft
Member of the Senat

Berlin-Brandenburgische Akademie der Wissenschaften
1. Member of the board der Berlin-Brandenburgischen Akademie der Wissenschaften
2. Head of the Working Group "Regelwissen und Regellernen in biologischen Systemen"

Wissenschaftsrat
Member of the committee "Naturwissenschaften in Sachsen-Anhalt"

University of Leipzig
1. Director of the Zentrum für Kognitionswissenschaften (Center of Cognitive Science)
2. Member of the board of directors of the Zentrum für Höhere Studien (Center of Advanced Studies)
3. Head of the Research Group "Arbeitsgedächtnis" at the Center of Cognitive Science
4. Member of the Graduiertenkolleg "Universalität und Diversität"

University of Potsdam
Member of the "Initiativkreis Potsdamer Naturwissenschaftliche Vorträge / Potsdam Lectures"

Max-Planck-Society

1. Nomination Committee: MPI für Bildungsforschung
2. Nomination Committee: MPI für psychologische Forschung

Editorial Activities

1. Editor-in Chief of the *"Zeitschrift für Experimentelle Psychologie"*
2. Member of the Editorial Board of the *"Journal of Psycholinguistic Research"*
3. Member of the Advisory Board of the *"Neurolinguistik"*

Prof. Dr. med. D. Yves von Cramon

University of Leipzig

Director of the Day Care Clinic of Cognitive Neurology

Nomination Committees (University of Leipzig)

1. Neurological Rehabilitation
2. Computer Network and Distributed Systems
3. Signal and Image Processing
4. Nuclear Medicine
5. Junior Research Group for MR-Spectroscopy

Interdisziplinäres Zentrum für Klinische Forschung (IZKF) Leipzig

1. Member of the board
2. Coordinator of the "Schwerpunkt Neurowissenschaften" (Center of Neuroscience)

Zentrum für Kognitionswissenschaften (Center of Cognitive Science)

Member of the board

Other Committees (University of Leipzig)

1. Committee for Computer Resources
2. Doctorate Committee: Neurology, Neuropathology and Neurosciences

Deutsche Gesellschaft für Neurologie

Chairman of the DGN-Committee 1.08 (Behavioural Neurology)

Editorial Activities

Member of the Editorial Board of the *"Cortex"*
Member of the Editorial Board of the *"Journal of Neuropsychological Rehabilitation"*
Member of the Advisory Board of the *"Nervenarzt"*

5.3 Visitors

Dr. Mireille Besson, University of Marseille, France
01.-28.02.1997

Ms. Stanislava Antonievic, Filozofski Fakultet Novi Sad, Jugoslavija
01.-22.05.1997

Prof. Dr. Eran Zaidel, University of California, Los Angeles, USA
30.06.-03.07.1997

Dr. Graham Hole, University of Sussex, UK
02.-04.09.1997

Prof. Dr. Jim V. Haxby, National Institute of Health, Bethesda, USA
18.-24.09.1997

Prof. Dr. Ken Kwong, Massachusetts General Hospital, Boston, USA
21.-26.09.1997

Prof. Dr. Herbert Schriefers, Nijmegen Institute for Cognition and Information (NICI), Nijmegen, The Netherlands
19.-25.10.1997

Dr. John Hilton, Columbia University, USA
28.11.-10.12.1997

Sandra Vos, University of Nijmegen, The Netherlands
01.01.-30.04.1997

5.4 Guest Lectures

Dr. Leun Otten, University of Illionois, USA
Processing the ignored: Implications from a modulation of event-related potentials by the repetition of unattended words
08.01.1997

Prof. Dr. Olaf Breidbach, Universität Jena, Biologisch-Pharmazeutische Fakultät, Jena
Interne Repräsentation: Bausteine zu einer Neurosemantik
10.01.1997

Dr. Jean François Mangin, Service Hopitalier Frederic Joliot, Orsay, France
Towards a better management of cortical anatomy in brain functional studies
22.01.1997

Dr. Bruno Laeng, Harvard University, Cambridge, USA
Spatial and facial categories: The role of the left hemisphere
28.01.1997

Dr. Hermann J. Müller, Birkbeck College, University of London, UK
Visuelle Suche über mehrere Dimensionen: Evidenz für parallele Aufmerksamkeitsgewichtung
29.01.1997

Dr. Mark Elliott, Birbeck College, University of London, UK
Flicker sensitivity within the gamma bandwidth enhances Kanizsa figure coding
29.01.1997

Dr. Thomas Grunwald, Universitätsklinik für Epileptologie, Bonn
Elektrophysiologische Untersuchungen des Gedächtnisses ohne Ratten: Der Hippokampus außerhalb der Labyrinthe
05.02.1997

Prof. Dr. Dirk Vorberg, TU Braunschweig, Institut für Psychologie, Braunschweig
Aufmerksamkeitswechsel zwischen visuellen Objekten
11.02.1997

Dr. Hermann Kolk, University of Nijmegen, The Netherlands
Agrammatic aphasia and language capacity
12.02.1997

Dr. Peter König, Neuroscience Institute, San Diego, USA
Top-down and bottom-up processing in the visual system. A study in behaving cats
18.02.1997

Dr. Christian Kaernbach, Universität Leipzig, Institut für Allgemeine Psychologie
Temporale Tonhöhenwahrnehmung
26.02.1997

Dr. Gereon Fink, Wellcome Department of Cognitive Neurology, University of London, UK
Visuelle Wahrnehmung: Interaktion von 'top-down' und 'bottom-up' Prozessen
26.02.1997

Dr. Ulrich Mayr, Universität Potsdam, Institut für Psychologie
Endogene Kontrolle sequentiellen Denkens und Handelns: Dissoziationen und Prozesse
19.03.1997

Prof. Dr. Johannes Dichgans, Universität Tübingen, Neurologische Klinik
Was weiß das Neugeborene von der Physik?
02.04.1997

Prof. Dr. Hans-Joachim Freund, Universität Düsseldorf, Neurologische Klinik
Funktionelle Organisation der SMA und des prämotorischen Kortex beim Menschen
09.04.1997

Prof. Dr. Cornelius Weiller, Universität Jena, Klinik für Neurologie
PET- und fMRI-Studien zur Restitution motorischer und sprachlicher Funktionen nach Hirninfarkt
16.04.1997

PD Dr. Lutz Jäncke, Forschungszentrum Jülich GmbH
FMRI-Experimente zur auditorischen Informationsverarbeitung
23.04.1997

Dr. Dorothee Auer, Max-Planck-Institut für Psychiatrie, München
Protonenspektroskopie des Gehirns bei klinischer Feldstärke
07.05.1997

Dr. Ralph-Axel Mueller, PET-Center, Wayne State University, Detroit, USA
Functional mapping of language and movement in patients with early lesion and developmental disorders: An approach to developmental plasticity
13.05.1997

Dr. Tomás Paus, McGill University, Montreal, Canada
Functional connectivity in the human brain
28.05.1997

Dr. Werner X. Schneider, Universität München, Institut für Psychologie
Kontrollprozesse im visuellen Arbeitsgedächtnis: Eine neuro-kognitive Theorie
11.06.1997

Dr. Trevor Penney, Columbia University, USA
Modality differences in duration bisection: Clock speed, memory or both?
17.06.1997

Dr. John Polich, Scripps Research Institute, La Jolla, USA
Brain potentials and cognition: Electric thoughts in basic and clinical research
18.06.1997

Dr. Takashi Yamauchi, Columbia University, USA
Category learning by inference and classification
19.06.1997

PD Dr. Peter Bartenstein, Universität München, Nuklearmedizin, Klinikum Rechts der Isar
Erfahrungen beim Aufbau eines neurologischen PET-Zentrums - Klinische und Aktivierungsstudien
20.06.1997

Prof. Dr. Eran Zaidel, University of California, Los Angeles, USA
Hemispheric independence: Degrees of modularity in interhemispheric relations
02.07.1997

Prof. Dr. Lyn Frazier, University of Amherst, USA
Syntactic processing
09.07.1997

Dr. Mari Tervaniemi, University of Helsinki, Finland
Pre-attentive processing of complex auditory information in the human brain
20.08.1997

Dr. Graham Hole, University of Sussex, UK
Decay and interference effects in visuospatial short-term memory as measured with parameter estimation by sequential testing (PEST)
03.09.1997

Dr. Chrit Moonen, University of Bordeaux, France
Rapid imaging with PRESTO: Its application to functional studies
10.09.1997

Prof. Dr. Helmuth Steinmetz, Universität Düsseldorf, Neurologische Klinik
"Kognitive Neuroanatomie": Beiträge der MR-Morphometrie
17.09.1997

Dr. Matthias Schlesewsky, Universität Potsdam
"Er verwandelt sich in den Eselshuf, den zu sein er verdient hatte" - Kasusattraktion und ihre Folgen für Sprachverarbeitungstheorien
18.09.1997

Prof. Dr. Stefano F. Cappa, University of Brescia, Italy
PET studies of semantic memory
22.09.1997

Prof. Dr. Jim V. Haxby, National Institute of Health, Bethesda, USA
Functional brain imaging studies of visual cognition
23.09.1997

Prof. Dr. Ken Kwong, Massasuchetts General Hospital, Boston, USA
Perspectives in functional MRI
25.09.1997

Dr. Vasili Kovalev, Fraunhofer Institut, Darmstadt
Non-linear registration of 3D images
06.11.1997

Dr. Paul Corbalis, Center for Cognitive Neuroscience, Dartmouth College, USA
Non-invasive optical measures of human brain function
20.11.1997

Prof. Dr. M. Rugg, St. Andrews University, UK
The functional and neural bases of memory retrieval: Evidence from brain potentials and neuroimaging
26.11.1997

Dr. Habib Benali, INSERM Paris, France
Space-time statistical model for fMRI and invariant properties of task-induced activation
03.12.1997

Prof. Dr. Graham Hitch, University of Lancaster, UK
Working memory in complex tasks: How do processing and storage interact?
04.12.1997

Dr. John Hilton, Columbia University, USA
The structural representation of objects
08.12.1997

PD Dr. Gebhard Sammer, Universität Hamburg
Priming in einer expliziten Gedächtnissuchaufgabe: Effekte auf ereigniskorrelierte Potentiale
10.12.1997

Workshops

Workshop *'Case and Case marking in European Languages'*
K. Steinhauer & A.D. Friederici, Leipzig, 17-18 July 1997.

Workshop *'Concept-to-Speech Generation Systems'* in conjunction with 35th Annual Meeting of the Association for Computational Linguistics,
K. Alter (co-organizer), Madrid, Spain, 8-13 July 1997.

Workshop *'Language and Music Processing'*
funded by the Max-Planck-Institute of Cognitive Neuroscience, Leipzig, and Centre National de la Recherche Scientifique, Departments of Human and Social Sciences and of Life Sciences,
M. Besson & A.D. Friederici, Marseille, France, 28-30 September 1997.

GNP workshop *'Neuropsychologie der Sprache'*
E. Ferstl & T. Guthke, Leipzig, November 1997.

Workshop *'Einführung in die Neuropsychiatrie und Psychopharmakologie'*
Müller, U. & Bauer-Wittmund, T., Leipzig, 12 April 1997.

Workshop *'Alltagsorientierte Gedächtnisdiagnostik und -therapie'*
Thöne, A., Guthke, T. & Ferstl, E., Leipzig, 26-27 April 1997.

Workshop *'Einführung in die Interpretation kernspintomographischer Befunde aus neuropsychologischer Sicht'*
von Cramon, D.Y., Leipzig, 12 July 1997.

Workshop *'Neuropsychologische Grundlagen der Sprache'*
Kotz, S., Ferstl, E. & Guthke, T., Leipzig, 4-5 October 1997.

Workshop *'Klinische MR-Spektroskopie'*
von Cramon, D.Y. & Norris, D.G., Leipzig, 11 November 1997.

Workshop *'Approaches to symbolic representations of brain structures'*
Kruggel, F. & Lohmann, G., Leipzig, 1-3 December 1997.

Workshop *'Model-based analysis of neurophysiological brain functioning'*
Uhl, C. & Kruggel, F., von Cramon, D.Y., Leipzig, 12-13 December 1997.

Degrees 6.1

Dr. Axel Mecklinger	Habilitation in Psychologie, Dr. phil. habil., University of Leipzig
Anja Hahne	Doktor der Philosophie, Dr. phil., Free University of Berlin
Thomas R. Knösche	Ph.D., University of Twente, The Netherlands
Stefan Frisch	Diplom in Psychologie, Free University of Berlin
Axel Hutt	Diplom in Physik, University of Stuttgart
Annegret Lagotzki	Diplom in Rehabilitationswissenschaften, Humboldt-University of Berlin
Gisela Müller-Plath	Diplom in Psychologie, Christian-Albrechts-University of Kiel
Silke Urban	Master of Science in Linguistics, University of Leipzig
Carsten Wolters	Diplom in Mathematik, Rheinisch-Westfälische Technische Highschool of Aachen

Honors and Awards 6.2

Prof. Dr. A.D. Friederici	Honorary Professorship at the University of Potsdam

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