MAX-PLANCK-INSTITUTE OF COGNITIVE NEUROSCIENCE

ANNUAL REPORT 1996

Editors: Angela D. Friederici
D. Yves von Cramon

Max-Planck-Institute of Cognitive Neuroscience
Inselstraße 22 - 26
D-04103 Leipzig
Germany
Tel: ++49 (0)3 41 / 99 40-112 / 220
Fax: ++49 (0)3 41 / 99 40-113 / 221
e-mail: angelafr@cns.mpg.de
cramon@cns.mpg.de

Annual Report 1996

PREFACE

In its second year of existence, the work of our institute has been determined and, to some extent, burdened by the considerably delayed delivery of both the 3-Tesla nuclear magnetic resonance tomograph (MRT) and the 150-channel magnet-encephalograph (MEG).

The MRT has been at our disposal since July so that in the following two months an extensive quality control of the system could be performed. Later in the year, we faced a multitude of technical and experimental problems on our way to both high-resolution anatomical imaging and fMRI (functional magnetic resonance imaging) studies. This laborious work ranged from adapting and optimizing the (visual and acoustic) stimulation equipment to the development and installation of various NMR sequences appropriate to the 3-Tesla environment. It has taken particular effort to optimize sequences for high resolution anatomical images. Currently, initial fMRI experiments are being conducted in order to test the entire “experimental chain” from the psychological protocol to the mathematical-statistical data processing and postprocessing.

In October, the MEG equipment was finally delivered. Here we were in a position to immediately start calibration measures. After resolving some initial technical problems we launched a series of combined EEG-MEG experiments.

Finally we should mention that substantial progress was made with the building of the future permanent quarters of our institute in the “Stephanstraße”. In June, we were able to move into a first section housing the MRT and the associated NMR working group. Since then the second phase of construction, including further laboratories (EEG and reaction time) and offices, has been started.

In the last year, the MPI of Cognitive Neuroscience in Leipzig made good headway and we are looking forward to a still better year in 1997 granting us a more internally controllable development of the laboratories. We are now eager to present results that shall demonstrate both the synergetic effects of close scientific partnerships within and across our working groups and the usefulness of complementary technical equipment and “know-how”.

We would appreciate any comments or suggestions our readers may provide for our present and future work.

Angela D. Friederici
D. Yves von Cramon

Leipzig, January 1997

PREFACE

1 ORGANIZATION OF THE INSTITUTE 13

2 STRUCTURE OF THE INSTITUTE 17

3 RESEARCH 19

3.1 NEUROCOGNITION OF LANGUAGE 19

3.1.1 Syntax processing: The involvement of cortical and deep areas 20
Friederici, A.D., Maeß, B., Knösche, T.R. & von Cramon, D.Y.

3.1.1.1 Electrical recordings during auditory sentence perception 20
Maeß, B. & Friederici, A.D.

3.1.1.2 Localization of the sources of the ELAN from EEG and MEG data 21
Knösche T.R., Maeß B., Friederici A.D. & von Cramon, D.Y.

3.1.2 Specifying the processing of grammatical incongruencies of different types 23
Friederici, A.D., Meyer, M., Gunter, Th.C. & Weissenborn, J.

3.1.3 Processing of syntactic violations in artificial grammars: In-depth acquisition of the artificial language as a prerequisite 25
Pfeifer, E.

3.1.4 Syntactic processing: Early automatic and late controlled processes 28
Hahne, A., Friederici, A.D. & Frisch, S.

3.1.5 Processing syntactic and semantic information during aging: Automatic versus controlled aspects 29
Friederici, A.D. & Hahne, A.

3.1.6 The effect of prior processing load on the P600 30
Gunter, Th.C. & Friederici, A.D.

3.1.7 Processing of subject and object relative sentences under different working memory loads 32
Vos, S., Gunter, Th.C., Schriefers, H. & Friederici, A.D.

3.1.8 Inter-sentential context effects on parsing preferences: A study using event-related potentials 34
Ferstl, E. & Friederici, A.D.

3.1.9 The effect of animacy specification on the processing of German relative clauses 37
Gorrell, P. & Gunter, Th.C.

3.1.10 Prepositional phrase attachment: Is it a syntactic ambiguity? 38
Ferstl, E.

3.1.11 Noun phrase-attachment ambiguities in German: The impact of lexical and semantic information 41
Steinhauer, K., van Kampen, A., Schriefers, H. & Friederici, A.D.

3.1.11.1 A sentence completion study 42
Steinhauer, K., Schriefers, H. & Friederici, A.D.

3.1.11.2 A self-paced reading study 43
van Kampen, A., Schriefers, H. & Friederici, A.D.

3.1.12 Complement ambiguities 49
Gorrell, P. & Gunter, Th.C.

3.1.13 Multiple-conjunction ambiguities: Parsing preferences and the effects of manner of disambiguation 51
Gorrell, P. & Gunter, Th.C.

3.1.14 On the use of case information for verb processing 53
Jacobsen, Th. & Friederici, A.D.

3.1.15 Parsing theory and structural ambiguity in German 55
Gorrell, P.

3.2 NEUROCOGNITION OF MEMORY 59

3.2.1 The neurocognitive systems underlying recognition memory for object forms and object locations 60
Mecklinger, A.

3.2.2 Dopaminergic modulation of visuo-spatial working memory with bromocriptine and pergolide 62
Müller, U., Pollmann, S. & von Cramon, D.Y.

3.2.3 Rehearsal processes in working memory: Effects of information type and coding formats as revealed by high density ERP recordings 63
Bosch, V., Mecklinger, A. & Friederici, A.D.

3.2.4 Perceptual and conceptual processing of pictures and words: Evidence from event-related potentials 65
Mecklinger, A. & Busch, A.

3.2.5 Functional and topographical dissociation in the processing of spatial and temporal information in working memory 66
Schubotz, R. & Friederici, A.D.

3.2.6 Rehearsing object forms, object location and temporal duration: A combined SPECT and ERP study of information specific working memory processes 68
Mecklinger, A., Friederici, A.D., Knapp, W. & Schedel, U.

3.2.7 Exploring sequential processing in visuospatial working memory 69
Bublak, P.

3.2.8 Processing novel and deviant auditory stimuli: An event-related potential and dipole-model analysis 70
Opitz, B. & Mecklinger, A.

3.2.9 Subprocesses underlying predictable switches between cognitive tasks 72
Mecklinger, A., Springer, A., Matthes-von Cramon, G. & von Cramon, D.Y.

3.3 CLINICAL NEUROPSYCHOLOGY 73

3.3.1 Day-Care Clinic 73

3.3.1.1 A clinical test of executive function 74
Bublak, P., Matthes-von Cramon, G. & Schubert, T.

3.3.1.2 Visual recognition memory performance in patients with cerebral hypoxia: A combined behavioral and event-related potential (ERP) analysis 75
Matthes-von Cramon, G., Mecklinger, A. & von Cramon, D.Y.

3.3.1.3 Working memory in patients with Parkinson’s disease 76
Müller, U., Bublak, P. & Schubert, T.

3.3.1.4 Syntax processing: The involvement of mediobasal temporal structures as indicated by focal brain lesions 77
von Cramon, D.Y., Friederici, A.D. & Kotz, S.

3.3.1.5 Multilevel representation of text information in brain-injured patients 78
Guthke, Th. & Ferstl, E.

3.3.1.6 Change of perspective as a retrieval aid for brain-injured patients 79
Ferstl, E. & Guthke, Th.

3.3.2 External Cooperation 82

3.3.2.1 Redundant targets effects in a commissurotomy subject 82
Pollmann, S. & Zaidel, E.

3.3.2.2 A receptive-field based gradient for spatial orienting: Evidence from commissurotomy 86
Pollmann, S. & Zaidel, E.

3.3.2.3 Evaluation of brain diseases by quantitative magnetic resonance metabolic, perfusion, and diffusion imaging 88
Norris, D.

3.4 PSYCHOLOGICAL METHODS IN NEUROIMAGING 89

3.4.1 Involvement of prefrontal cortex in dual task processing 91
Schubert, T.

3.4.2 Working memory and long term memory 92
Zysset, S. & Pollmann, S.

3.5 SIGNAL AND IMAGE PROCESSING 95

3.5.1 Analysis of individual neuroanatomy from MR tomograms 96
Lohmann, G., von Cramon, D.Y. & Kruggel, F.

3.5.2 Removal of non-brain parts in MR tomograms of the head 99
Palubinskas, G.

3.5.3 Segmentation of structural MR images 101
Descombes, X., Palubinskas, G., Rajapakse, J., Kruggel, F. & von Cramon, D.Y.

3.5.4 Inhomogeneity correction of MR data sets 102
Rajapakse, J., Descombes, X. & Kruggel, F.

3.5.5 Statistical analysis of fMRI data 105
Descombes, X. & Rajapakse, J.

3.5.6 Spatio-temporal analysis of EEG - data 106
Uhl, C.

3.5.7 A finite element model of the human brain 109
Hartmann, U. & Kruggel, F.

3.6 NUCLEAR MAGNETIC RESONANCE 112

3.6.1 Fast functional imaging: GRASE 113
Jovicich, J. & Norris, D.

3.6.2 Mechanism of the fast response 114
Dymond, R. & Norris, D.

3.6.3 Perfusion imaging 116
Schwarzbauer, C.

4 TECHNICAL DEVELOPMENT 118

4.1 Image and signal processing environment 118
Kruggel, F. & Lohmann, G.

4.2 Design and implementation of a multimodal viewer for biomedical datasets 122
Dörr, M. & Kruggel, F.

4.3 Whole head MEG system 123
Maeß, B., Oertel, U. & Knösche, T.

4.4 Unix implementation of the ERP evaluation package (EEP 3.0) 124
Nowagk, R. & Pfeifer, E.

4.5 Medspec 3T/100 system: Quality control 126
NMR-group

4.6 Development of a visual projection system for fMRI experiments 127
Pollmann, S.

4.7 First fMRI results 127
Wiggins, C.J., Niendorf, T., Pollmann, S. & Hund, M.

4.8 Implementation of a multislice FLASH technique (MUSIC) 129
Niendorf, T.

4.9 EEG recording during MRI scanning 131
Wiggins, C.J. & Kruggel, F.

4.10 Navigator echoes: Correction of motion artefacts in diffusion weighted MR images 133
Koch, M., Redpath, T.W. & Norris, D.

4.11 High *T*1 contrast 3D MRI of the brain 136
Norris, D.

5 OTHER ACTIVITIES 138

5.1 Teaching 138
5.2 Committees and Memberships 139
5.3 Visitors 141
5.4 Guest Lectures 142
5.5 Congresses, Workshops and Colloquia 146
5.6 Exhibitions 147

6 DEGREES, HONORS AND AWARDS 148

6.1 Degrees 148
6.2 Honors and Awards 148

7 PUBLICATIONS 149

7.1 Published books, papers & bookchapters 151
7.2 Published abstracts 159
7.3 Papers presented at conferences 163
7.4 Papers presented at colloquia 169

Directors:

Friederici, Angela D.
von Cramon, D. Yves

Scientific research staff:

Bublak, Peter
Ferstl, Evelyn
Gorrell, Paul
Gunter, Thomas
Hayd, Helmut
Hund, Margret
Knösche, Thomas
Kotz, Sonja
Kruggel, Frithjof
Lohmann, Gabriele
Maeß, Burkhard
Mecklinger, Axel
Müller, Ulrich
Niendorf, Thoralf
Norris, David
Pfeifer, Erdmut
Pollmann, Stefan
Schubert, Torsten
Schwarzbauer, Christian
Uhl, Christian
Wiggins, Christopher
Zanow, Frank
Zimmermann, Roger

Visiting Research Fellows:

Bardinet, Eric (France)
Descombes, Xavier (France)
Palubinskas, Gintautas (Lithuania)
Rajapakse, Jagath (Sri Lanka)

PhD. Students:

Bosch, Volker
Dillmann, Jennifer
Dörr, Michael
Dymond, Rosemary
Groß, Joachim [c]
Hahne, Anja [d]
Hartmann, Ulrich
Held, Patric [e]
Jacobsen, Thomas
Jovicich, Jorge
Koch, Martin
Meyer, Martin
Opitz, Bertram
Schubotz, Ricarda [b]
Steinhauer, Karsten [a]
van Kampen, Anja [d]
Zysset, Stefan

M. Sc. Students:

Andersen, Björn	Nitzel, Almut
Busch, Astrid [b]	Reimann, Brit
Drietchen, Nadine [a]	Sabisch, Beate
Frisch, Stefan [d]	Saupe, Nadja
Hofmann, Monika [b]	Schmidt, Björn-Helmer
Ihle, Daniel [a]	Seltmann, Ina
Just, Viola	Springer, Anne-Kristin
Kotz, Daniel	Stolterfoht, Britta [a]
Meinshausen, Raik-Michael [a,b]	Urban, Silke
Müller, Notger	Wächter, Tobias
Naumann, Peter [b]	Wagner, Susanne
Neubauer, Catrin	Weber, Manfred
Nikolajewska, Malgoziata [b]	

Technical Staff:

Böthel, Heike	Pitzmaus, Anke
Busker-Rössig, Sabine	Riegel, Jacqueline
Koch, Ina	Sandmann, Andrea
Korsawe, Heiko	Schmidt-Duderstedt, Heike
Liebig, Stephan	Struensee, Mike
Meyer, Frank	Weder, Manfred
Nowagk, Rainer	Wenge, Grit
Oertel, Ulrich	Wiese, Joachim

Administration and Other Services:

Schmude, Ingrid, Head	Landis, Beate
Blank, René	Müller, Adelheid
Gabler, Elke	Werner, Tilo
Junghanns, Berndt	Zimmermann, Astrid

supported by

[a] Deutsche Forschungsgemeinschaft
[b] Berlin-Brandenburgische Akademie der Wissenschaften
[c] Forschungszentrum Jülich
[d] Freie Universität Berlin
[e] Universität Leipzig

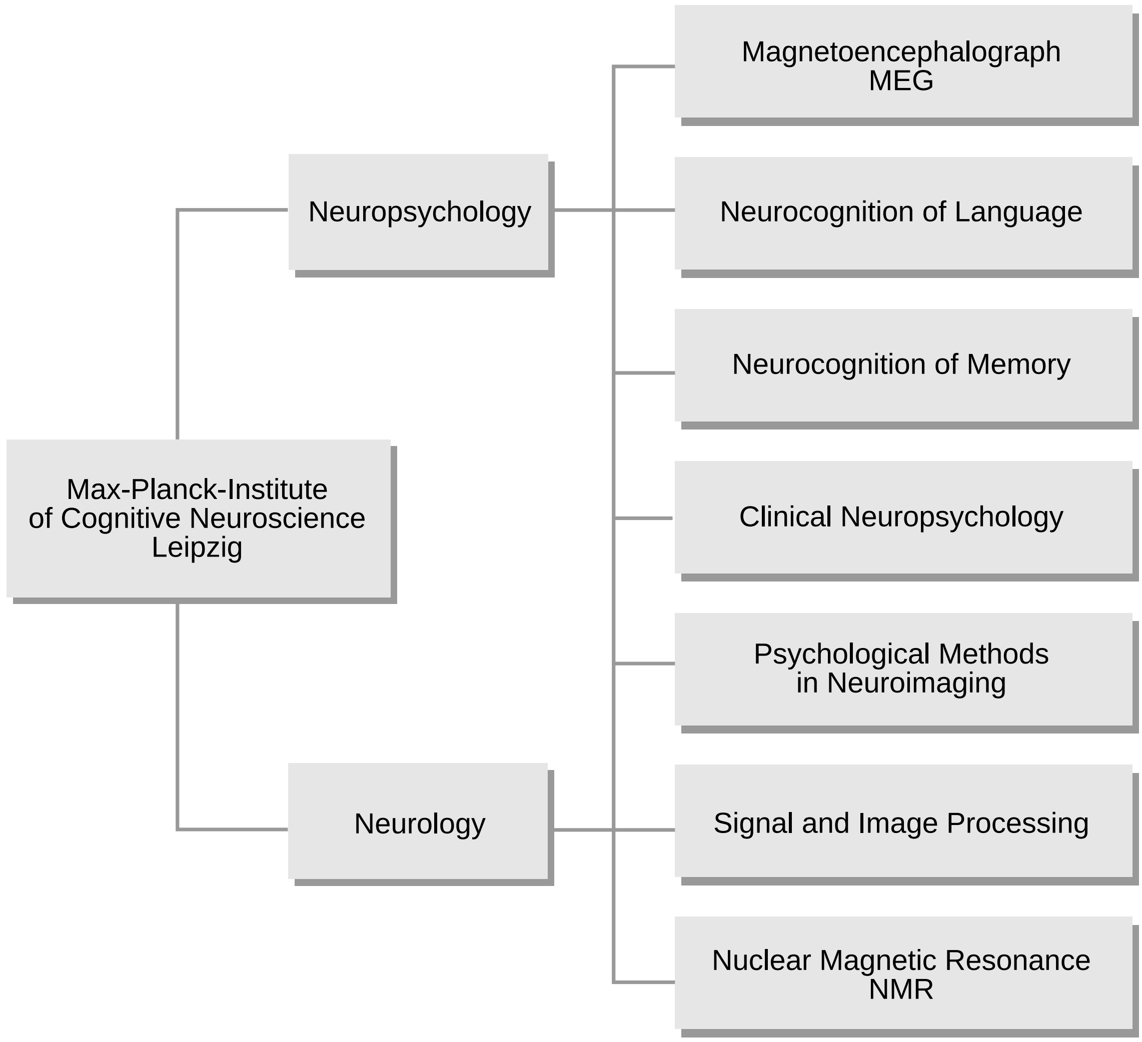
Secretaries:

Blumberg, Marion
Gertz, Ines-Kristin
Koßack, Corinna
Orendi-Fischer, Sabine
Rudisch, Karin

Library:

Lewin, Gerlinde

Board of trustees:


Max-Planck-Institute
of Cognitive Neuroscience
Leipzig
Neuropsychology
Neurology
Magnetoencephalograph
MEG
Neurocognition of Language
Neurocognition of Memory
Clinical Neuropsychology
Psychological Methods
in Neuroimaging
Signal and Image Processing
Nuclear Magnetic Resonance
NMR

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 modelling, 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. The focus of on-going research is the relation between syntax, syntactic processing (parsing), and sentence comprehension in general. That is, we isolate structural factors in sentence comprehension and inquire into their relation to other factors such as lexical, semantic, and discourse information.

The ongoing research focused on the processes of early syntactic parsing as well as processes of syntactic reanalysis within a framework of a two stage parsing model. We study the temporal and neurotopological parameters of early and late syntactic processes investigating natural language (3.1.1 & 3.1.2) and artificial language (3.1.3). We, furthermore, try to specify the nature of these processes with respect to their automaticity and controlledness (3.1.4 & 3.1.5). Two projects evaluate the influence of sentence internal (3.1.6) and sentence external (3.1.7) memory load upon late syntactic processes. The influence of sentence external syntactic context information (3.1.8) and sentence internal semantic information (3.1.9) upon parsing preferences is investigated as well. The incidence of syntactic ambiguous structures is used to further specify parsing preferences during first-pass parsing. The influence of lexical information upon parsing preferences is investigated for the processing of prepositional phrases (3.1.11). The processing of structural ambiguities is, furthermore, studied in its dependence of argument structure information provided by the verb (3.1.12) and of case marking information provided by the article (3.1.13). Last not least we evaluate the use of case information for the processing of the verb itself (3.1.14). Section 3.1.15 provides a theoretical perspective upon first-pass parsing processes and processes of reanalysis.

3.1.1 Syntax processing: The involvement of cortical and deep areas

Friederici, A.D., Maeß, B., Knösche, T. & von Cramon, D.Y.

Recent neuropsychological studies in language processing have identified different components in the event-related brain potentials (ERPs) for semantic and syntactic processes. In the syntactic domain two different ERP components were observed in correlation with different aspects of structural processes. First, an early left anterior negativity (ELAN) was found in correlation with phrase structure violations probably reflecting first-pass parsing processes. Second, a late centro-parietal positivity (P600) was found in correlation with violations of syntactic structure as well as with violations of structural expectancies. The goal of the current investigation was to identify the brain areas involved in the generation of the ELAN. The stimulus material used was similar to that used in an earlier study (Friederici, Pfeifer & Hahne, 1993). The critical sentences included a phrase structure violation realized as a word category error. Sentences carrying this structural violation were presented auditorily as running speech together with correct sentences (and sentences carrying a semantic violation). Four male subjects participated in the study consisting of one magnetic resonance imaging session, one experimental session during which the auditory stimulus material was presented while magnetic fields were recorded using a 2 x 37 magneto-encephalograph (MEG) and one experimental session during which ERPs were recorded. The magnetic measurements had been carried out in close colaboration with the Institute of Medicine (Research Center Jülich) and are described in the Annual Report 1995, section 3.1.4. For a more detailed treatment of the ERP recordings, see section 3.1.1.1 this Annual Report. Two of the subjects showed a clear ELAN component in response to the phrase structure violation between 150 - 200 msec post onset of the critical word compared to the correct condition. Dipole modelling on the basis of the MEG data suggested two sources for this component in each of the subjects: one cortical source located in area 44 (Broca's area) and one deep source. The location of the latter source was less precise and did not allow to pinpoint any particular brain structure. The data are taken to suggest that first-pass parsing syntactic processes are supported not only by Broca's area but also by deep structures that are to be specified by further experiments. For a more detailed account of the modelling aspects of this study see section 3.3.1.4, this Annual Report.

3.1.1.1 Electrical recordings during auditory sentence perception

Maeß, B. & Friederici, A.D.

Four normal right handed male volunteers which German as their mother tongue participated in the study. The stimuli were presented as connected speech consisting of correct sentences (50%), as semantically incorrect (25%) and as syntactically incorrect sentences (25%). Semantic incorrectness was realized as a selectional restriction error and syntactic incorrectness was realized as a word category error. Subjects listened to 540 sentences presented in four blocks in randomized order. 1000 ms after the offset of each sentence a single probe word was presented and subjects were required to indicate whether the word had appeared in the previous sentence or not.

The subjects were identical to the first experiment (see 3.1.1 this Annual Report).

Bioelectric activity was recorded with a 128 channel EEG system (SynAmps by Neuroscan, Inc.). The sampling rate was 1000 Hz (frequency band DC to 250 Hz). EOG and EMG signals were recorded to detect artifacts.

Time domain analysis starts with a low pass filtering (f_l = 20 Hz) and a downsampling to 250 Hz.

An artifact rejection scheme was applied and averaged data sets were generated. Different baselines were tested: the beginning of the critical word itself, the beginning of the auxiliary as the last region all sentences have in common, the whole epoch of the critical word (done by a detrending algorithm) and strong high pass filtering. High pass filtering yields averages with the smallest spatial noise. Therefore these averages were used for source localization of early syntactic effects.

For the discussion of all time domain results the detrended averages were used. One subject showed intensive alpha activity, rendering any reliable analysis impossible. Two of the remaining subjects showed a long lasting negativity around 500 ms after onset of the critical word within the comparison of the semantically incorrect and the correct condition. The comparison between responses to syntactically incorrect and correct sentences displays two effects: an early negativity between 150 ms and 180 ms and a late positivity around 600 ms to 700 ms.

This is in full agreement with an other EEG study conducted by Hahne and Friederici (see Annual Report 1995, 3.1.7) using the same stimulus material but another task. Comparing the EEG and the MEG results, only the early deflection about 170 ms appears in both modalities. The MEG finding of no difference between semantically incorrect and the correct condition supports the hypothesis that either deep sources or sources not covered by the MEG sensor arrays were responsible for the appearance of the N400.

Localization of the sources of the ELAN from EEG and MEG data

3.1.1.2

Knösche, T.,
Maeß, B.,
Friederici, A.D.
& von Cramon, D.Y.

When normal subjects are confronted with sentences containing phrase structure violations, event-related potentials exhibit a negativity with a left anterior or frontal distribution. Its latency ranges between 130 and 200 ms after onset of the critical word. This effect, called the early left anterior negativity (ELAN), has been described by e.g. Friederici (1995).

Corresponding effects can be observed with MEG measurements (For a description, see Annual Report 1995, 3.1.4). The observed pattern above the left hemisphere shows an anterio-inferior negativity (magnetic field lines pointing into the head) and a posterio-superior positivity. Above the right hemisphere the patterns do not display any recognizable common features. Unfortunately, the poor coverage of the head by the 2 x 37 channel twin-cluster magnetometer system leaves the possibility of missing larger, more global features in magnetic field distribution around the head.

In this study, we undertook to localize the sources of the ELAN from 128 channel EEG and 2 x 37 channel MEG recordings from two normal subjects (named 08 and 36 from now on). The difficulties which had to be overcome were different for the two modalities.

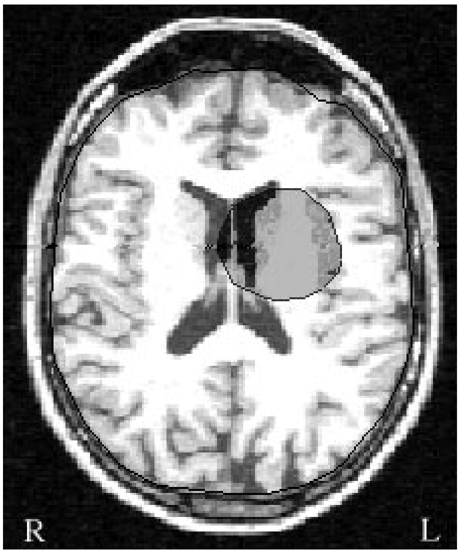


Figure 1: 95 % confidence region for sub-cortical source as found from EEG for subject 08.

EEG random shifts in many electrode potentials were observed. This effect can be described as high frequency spatial noise. On the other hand, the temporal frequencies of the disturbances were very low (slow waves and trends). This gave us the opportunity to combat the effect by using a high-quality high pass filter. Localizations using the single rotating dipole model yielded positions in various sub-cortical regions. Subsequently, goal function scans using the same source model were carried out. Taking into account the noise level, the result suggested that sub-cortical structures are involved in the generation of the ELAN. It appears, however, impossible to name the precise structure involved. Moreover, because of spatial noise, it cannot be decided whether any cortical structures are active as well. Figure 1 shows a section through the region of 95 % confidence for the sub-cortical source in subject 08. For subject 36, the result is very similar. In comparison to the EEG data, the problem of spatial noise is far less important for MEG. This has, of course, been expected because reference problems and electrode potentials play no role here.

Figure 2: Position of the cortical source in subject 08, as found from MEG.

On the other hand, only a small portion of the actual magnetic field distribution around the head is captured by the twin-cluster magnetometer array. This leaves room for ambiguity in dipole localization. Nevertheless, it was possible to construct a meaningful source configuration that explains the measured data. The source model again involves a sub-cortical generator. This time, however, the location is even less clear than the one found from EEG. This may have to do with the lower sensitivity of the MEG to deeper sources (However, it could be shown by simulations that the sensors were sufficiently sensitive to *detec*t activity of realistic strength (> 10 nAm) anywhere in the head). The second source belonging to the source model lies in the Broca area of the left hemisphere.

Figure 2 depicts its position in subject 08. It is rather weak compared to the sub-cortical generator.

The presented localization demonstrate the possibility to gain insight into the processing of syntactic information and provides a hypothesis on the possible generation of the ELAN. In order to achieve a more accurate and reliable source model, more subjects have to be investigated. Moreover, certain changes concerning the data acquisition are necessary. First, EEG measurements should be performed with online high pass filters in order to obtain smoother distributions. Second, the MEG should be recorded with a whole-head magnetometer system. Fortately, such a system is just getting operational at our institute.

3.1.2 Specifying the processing of grammatical incongruencies of different types

Friederici, A.D., Meyer, M., Gunter, Th.C. & Weissenborn, J.

The processing of syntactic anomalies was found to be correlated with an early left anterior negativity (ELAN) and/or a late centro-parietal positivity (P600) in the ERP. The general picture emerging from a number of studies suggests that phrase structure violations, in particular, elicit an early left anterior negativity (Neville et al., 1991; Friederici, Pfeifer & Hahne, 1993; Friederici, Hahne & Mecklinger, 1996). Processes of reanalysis seem to be correlated with a late centro-parietal positivity (Osterhout & Holcomb, 1992, 1993). However, a late positive component has also been seen in correlation with agreement violations (Hagoort et al., 1993; Osterhout & Mobley, 1995; but see Friederici, Pfeifer & Hahne, 1993), verb subcategorization violations (Osterhout, Holcomb & Swinney, 1994; but see Rösler et al., 1993) and word order violations (Hagoort et al., 1993 but see Rösler et al., in preparation). The majority, but certainly not all data that accumulated over the last years is compatible with a model that views the left anterior negativity to reflect first-pass parsing processes and the late centro-parietal positivity to reflect second-pass parsing processes including reanalysis and repair (Friederici, 1995).

The finding that agreement violations do not elicit a left anterior negativity is comparable with this proposal in so far as the specific information of an inflection carrying e.g., number information is not used during initial structure building during first-pass parsing. At this stage the information (INFLection) is sufficient to build a verb phrase (also called INFLphrase). Interestingly, agreement violations, that is the lexical realization of the required inflection, are in some studies correlated with a biphasic ERP pattern, a positivity preceeded by a negativity which either appeared to be more central (Friederici, Pfeifer & Hahne, 1993) or more frontal (Gunter et al., in press).

The findings for verb argument structure violations are very mixed. Hagoort et al. (1993) do not find any significant component. Rösler et al. (1993) report a negativity around 400 ms with a left anterior maximum followed by a positivity in correlation with verb subcategorization violations (transitive/intransitive) in German, and Osterhout et al. (1994) report a negativity around 400 ms with a posterior maximum followed by a positivity for the same type of violation in English.

The observation that word order violations in Dutch (Hagoort et al., 1993, they call it phrase structure violation) seem to elicit a late positivity only, may be viewed to be more critical for the proposed model. In their sentence material they used adjective-adverb-noun sequences as the violation condition. As adjective-adverb combinations, however, are grammatical as part of a possible but infrequent adjective-adverb-adjective-noun sequence the critical word to signal the incorrectness is the noun. They, however, found a positivity already for the adverb carring over into noun. As parsing preferences have been found to correlate with a late positivity this finding is compatible with the above made proposal.

To test how the brain reacts to different types of grammatical incongruencies we designed an experiment including (a) word order violations and compared those with (b) agreement violations.

(a) Word order violation:

(1) *Er meinte, dass Vera Ruhm erlangt.*
He thought that Vera credit gains.

(2) **Er meinte, dass Vera erlangt Ruhm.*
He thought that Vera gains credit.

(3) *Er meinte, auch Vera erlangt Ruhm.*
He thought also Vera gains credit.

(4) **Er meinte, auch Vera Ruhm erlangt.*
He thought also Vera credit gains.

In principle the grammar of German requires the finite verb in subordinate clauses introduced by the complementizer "*dass*" to be in clause final position (1), whereas the finite verb in subordinate clauses without complementizer obligatorily is in second position (3). A change in verb placement causes ungrammaticality, e.g. sentences (2) and (4). However, given the left-to-right processing sentence type (2) could be judged as being incorrect at the verb due to either argument structure (missing argument) or due to selectional restriction information (animacy of the prior NP) as sentences like (2') are possible.

(2') *Er meinte, dass Ruhm erlangt wurde.*
He thought that credit was gained.

(b) Agreement violation:

The correct sentence in this condition was identical to (1) and (3); whereas, the incorrect sentences contained a subject-verb number agreement error.

(5) *Er meinte, dass Vera Ruhm erlangen.*
He thought that Vera credit gain.

(6) *Er meinte, auch Vera erlangen Ruhm.*
He thought also Vera gain credit.

(7) *Er meinte, dass Piloten Ruhm erlangt.*
He thought that pilots credit gains.

(8) *Er meinte, auch Piloten erlangt Ruhm.*
He thought also pilots gains credit.

Half of all sentences in condition (a) and (b) contained subordinate clauses with singular marked subjects (proper names) and half contain plural marked subjects (names of professions), counterbalancing for number.

There were 64 sentences in each of the different conditions: 4 word order conditions and 4 agreement conditions resulting in 512 test sentences.

The sentences were presented visually word-by-word successively with a presentation time of 500 ms and no inter-word-interval. 500 ms after the offset of the sentence subjects were required to indicate the sentence's grammaticality by pressing a push button.

Preliminary data analysis suggest the following ERP pattern: all violation types were found to evoke a biphasic pattern consisting of a negativity and a positivity. The amplitude of each of the subcomponents as well as the distribution of negativity varied as a function of violation type. The violation of argument structure/selectional restriction as in sentence (2) appeared to correlate primarily with a broadly distributed negativity around 400 ms suggesting the involvement of lexical aspects such as animacy. The agreement violation conditions mainly evoked a strong centro-parietal positivity peaking around 800 ms indicating the prominence for second pass parsing processes. The data indicate that the brain reacts quite specifically to different grammatical incongruencies involving lexical and syntactic processes to different degrees.

3.1.3 Processing of syntactic violations in artificial grammars: In-depth acquisition of the artificial language as a prerequisite

Pfeifer, E.

Friederici (1995) proposed a model of syntactic processing during language comprehension, which assumes automatic first-pass parsing to be subserved by left anterior parts of the brain. The objective of the artificial grammar project is to further elucidate the role of Broca's area in syntax and sequence processing. Is it language-specific or is it involved in sequence processing in the widest sense? How does parsing differ in native language, second languages and artificial languages? For the latter, what is the influence of complexity, similarity to natural languages, training/exposure duration and the related degree of automaticity?

The electrophysiological approach has been chosen to assess fast on-line processes while being able to roughly localize sources. The findings can be compared with results from natural language ERP studies, one of which is an early left anterior negativity appearing when a syntactic violation is encountered (Friederici, Pfeifer & Hahne, 1993).

One substantial problem to solve when trying to investigate effects of violations in an artificial syntax is how to have the subjects acquire the grammar to a sufficient level of competence. A survey of the literature for experiences on artificial grammar learning/ training reveals procedures resulting in moderate or low degrees of mastery. Mostly, the researchers are interested in implicit learning and are thus satisfied with just-above-chance performances (usually below 60% correct in various tasks). For the present purpose this degree of mastery is far from being adequate. Considering the fact that potential ERP effects of violations are small in magnitude even for native natural language stimuli, one is well advised to assure efficient training to avoid having potential effects be buried in noise.

Two behavioral pilot experiments were run to examine the feasibility of training subjects to the required level of perfection by means of conventional procedures. Both experiments consisted of alternate learning and test phases. For the learning phases the subjects were instructed to monitor for any regularities occuring in the stimuli presented, which were all grammatically correct sentences (i.e. being generated by the specific grammar). The test phases consisted of randomly mixed correct and incorrect sentence trials (50% each), the task being grammaticality judgement. Approximately 500 learning and 300 test trials were presented to each subject.

The first experiment was carried out to find the maximal complexity of the grammar that allows to achieve the envisaged level of mastery within a reasonable period of time. This was done on the grounds that more complex grammars also allow more interesting types of violations. The initially chosen complexity turned out to be too hard to acquire, so, the syntax was simplified step by step, leaving the following structure of rules:

S: NP VP
NP VP NP

NP: d N
D M N

VP: v
v m

N: *plox*
tok
gum
trul

M: *böke*
füne

v: *pel*
prez
glif
rix

m: *nöri*
rüfi

d: *aaf*
D: *aak*

example sentense: *aak füne trul rix rüfi aak böke tok*

(Notes: Each colum specifies a rule, with alternative symbol sequences to substitute being listed on the right, one each line. Terminal symbols (i.e. the vocabulary) are printed in italics.)

The second experiment mainly served to test the influence of different introductory hints on the training outcome. The hints were intended to bias the subjects into specific modes of performing the task. Three conditions were realized, the first of which was meant to induce a “syntactic mode” by employing the following introductory procedure. The subjects were given detailed information on the specific grammar used in the experiment after having been made familiar with a formal notation commonly used to represent phrase structure grammars. Even though the generating grammar was being explicated most clearly, it was not mentioned to the subjects that the resulting strings of tokens might convey any meaning nor that they comprised vocabulary items such as nouns and verbs.

The second condition was supposed to induce a “semantic mode”. Subjects were informed that each trial is a statement that can be “understood” in terms of abstract concepts such as agent, action, object (e.g. “someone is doing something”) with the concrete vocabulary being unknown. By reducing the complexity down to the word class level, this was expected to be beneficial for finding out the syntactic structure necessary to parse the sentences.

In the third condition subjects were given no additional information; they were simply confronted with the stimulus material to find out structural regularities (note that this, too, is not an implicit learning task, as subjects are being aware of the task itself).

With additional information the performance for both conditions improved significantly from 65% in the “no hint”-condition to about 80% correct (50% chance level). Obviously, subjects found it very difficult to acquire a purely syntactic structure without being supplied a semantic reference system as it exists for any natural language. However, a formal explication of the artificial syntax can also lead to performances comparable to those achieved by subjects trying to parse the sentences primarily to extract meaning. Yet, it remains questionable, whether such an explication is a suitable means to improve the training efficiency. As a side effect, it might lead to strategies that no longer have much in common with highly automatic syntax parsing (as assumed to occur during natural language comprehension).

In summary, the results of the pilot study indicate that conventional training methods similar to the one outlined above do not suffice to bring about the necessary grasp of the language, except with impracticably long training durations. Also, subjects often perceive the given task as a problem solving issue, which can hardly be expected to foster fast on-line processing of the syntax. Thus, it seemed promising to devise a more natural learning environment by embedding the artificial language into some game context and also having the subjects actively speak phrases to communicate with their game partner. The relatively uninteresting language no longer has to be acquired for its own sake, as it has been integrated instrumentally into a more attractive context to get the subjects more involved and motivated.

With this in mind a suitable game was designed and implemented as a computer program. As every sentence being generated by the grammar should map onto some relevant game semantics and vice versa, a board game seemed to fit the requirements best. The verbs, nouns and modifiers in the grammar reference actions and objects in the game so that each valid sentence corresponds to a specific move. Two subjects are playing against each other, having the artificial language as the only means of communicating which move they made and to inform each other of how the game is proceeding. The game is set up such that in order to win the game one will have to engage in learning the language. The game incorporates aspects of both speech perception and speech production to improve on training speed and persistance of acquirements. To keep the training and ERP session in the same modality, subjects get into contact with the language purely auditorily, i.e. the words never appear written.

To assess the progress in acquiring the language each game session is followed by a comprehension test block. A combined measure of performance and reaction time improvement is used as the criterion indicating when subjects are ready to enter the actual ERP experiment.

Currently, the evaluation of this new training tool is under way.

3.1.4 Syntactic processing: Early automatic and late controlled processes

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

In earlier work we have identified two ERP-components correlated with syntactic word category processing: an early anterior negativity and a late posterior positivity (Friederici, Pfeifer & Hahne 1993; Friederici, Hahne & Mecklinger 1996). These two components are thought to reflect two phases of syntactic processing during sentence comprehension. The early negativity is interpreted as reflecting a first-pass parse defined as the assignment of the initial phrase structure. The late positivity, by contrast, seems to be related to processes of structural reanalysis which may become necessary when the initially build syntactic structure cannot be successfully mapped onto the semantic information and argument information provided by the lexical elements.

We assume that the early negativity reflects a highly automatic process. The present study further examines this aspect of automaticity. We tested this hypothesis by systematically varying the proportion of syntactically incorrect sentences containing a phrase structure error (1).

(1) *Der Fisch wurde im geangelt.*
The fish was in the catched.

If this component reflects an automatic process, it should be relatively independent of conscious expectancies and strategic behavior on behalf of the participants.

In our experiment participants listened to auditorily presented sentences. In one experimental condition 20% of those sentences contained a word category violation while in another experimental condition 80% of the sentences contained a word category violation.

To the extent that the early negativity is highly automatic and independent of conscious expectancies and strategies (as induced by our proportion manipulation), this early ERP-component should be roughly equivalent across proportion conditions. By contrast, to the extent that the late positivity reflects consciously controlled processing, it should vary across the two proportion conditions.

Results showed that the early negativity was present and equally pronounced under both proportion conditions, while the late positivity was observed only for the 20% violation condition, but not for the condition in which participants listened to 80% word category violations.

This pattern clearly supports the assumption that the early structure building process as reflected in the anterior negativity is highly automatic. The fact that the late positivity could not be observed in the case of a high proportion of incorrect sentences suggests that this process of syntactic reanalysis is much more controlled. This finding is also in agreement with a study by Gunter et al. (see Annual Report 1995, 3.1.6).

3.1.5 Processing syntactic and semantic information during aging: Automatic versus controlled aspects

Friederici, A.D. & Hahne, A.

The influence of age on the processing of semantic and syntactic information was investigated in an ERP study in which correct and semantically or syntactically incorrect sentences were presented to adult subjects of different age groups. Earlier studies investigating the influence of age upon semantic processes found the N400 component which indicates lexical processes to be reduced in amplitude and delayed in older age (Harbin, Marsh & Harvey, 1984; Gunter, Jackson & Mulder, 1992, 1995; Woodword, Ford & Hammett, 1993). No age-related differences behavioral studies are using a semantic priming paradigm (Burke & Vee, 1984; Burke, White & Diaz, 1987; Balota & Duchek, 1988; Madden, Pierce & Allen, 1993). Thus the reduced N400 component seems to reflect lexical integration processes rather than semantic processes per se. It is an open question whether and to what extent age influences syntactic processes. Age related processing effects in the syntactic domain are reported for the processing of filler-gap constructions presumably involving working memory (Zurif et al., 1995), and most recently for some aspect of syntactic priming (Friederici, Schriefers & Lindenberger, Annual Report 1995). In this study, it was found that the inhibitory component of the syntactic priming effect was enlarged by age; whereas, the facilatory component remained uneffected by age. It was argued that the facilatory component might represent automatic aspects of the priming effect while the inhibitory component might rather reflect controlled aspects of the semantic priming effect. Under the assumption that the early left anterior negativity reflects automatic first-pass parsing processes and the late positivity second-pass parsing processes (Friederici, 1995) and under the hypothesis that automatic processes are quite uneffected by age (Hasher & Zacks, 1979), we predict the early anterior negativity to be uninfluenced by age.

The experiment presented a total of 192 sentences half of which were correct (1) and (3) and half of which were either (2) semantically incorrect containing a selectional restriction error or (4) syntactically incorrect containing a phrase structure error.

(1)	*Der*	*Fisch*	*wurde*	*geangelt.*	
	The	fish	was	angled.	
(2)	*Die*	*Schule*	*wurde*	*geangelt.*	
	The	school	was	angled.	
(3)	*Der*	*Fisch*	*wurde*	*im See*	*geangelt.*
	The	fish	was	in the lake	angled.
(4)	*Der*	*Fisch*	*wurde*	*im*	*geangelt.*
	The	fish	was	in the	angled.

Five age groups 20 - 30, 30 - 40, 40 - 50, 50 - 60 and 60 - 70 years were included in the study. Up to now there are 6 subjects in each group. It is planned to enlarge each group up to 10 subjects, half female and half male.

Preliminary ERP results for the sentence final critical word, as expected, show a reduction in the N400 component for semantically incorrect sentences (2) by age. For the syntactically incorrect sentences (4) we found the early negativity and the late positivity to be unaffected by age in amplitude and latency up to the age of 50 - 60 years. The oldest age group 60 - 70 years did not show an early negativity, although a late positivity.

These preliminary findings may suggest that automatic syntactic processes in contrast to semantic integration processes remain stable during adult development, although not unaffected by old age.

3.1.6 The effect of prior processing load on the P600

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

Earlier research has shown that the so-called P600 component, a late centro-parietal positivity, is correlated with the processing of syntactic anomalies, being outright errors or violations of syntactic preferences. In a study investigating the processing of syntactic preferences in German, less preferred object relative clauses were found to elicit a more positive-going wave at the point of disambiguation than the preferred subject relative clauses (Mecklinger et. al., 1995): in this case the sentence final word. In the present ERP-study we explored the processing of German subject (SR) and object relative (OR) clauses which were either disambiguated early in the sentence through case information (early) or late through subject verb agreement information (late). It was hypothesized that particularly the late disambiguated sentences would give subjects a greater working memory burden, which was expected to lead to a larger processing load at the sentence-final verb, belonging to the main clause.

Example: *Das leckere Müsli wurde von ......*
The tasty muesli was by ......

Early SR	*dem Sportler,*	der *die Trainerinnen*	*gesucht hatte,*	*gegessen.* *essen.*
	the sportsman,	who$_{[nom]}$ the trainers$_{[fem]}$	sought had$_{[sing]}$,	eaten. [to] eat.
Early OR	*dem Sportler,*	den *die Trainerinnen*	*gesucht hatten,*	*gegessen.* essen.
	the sportsman,	whom$_{[acc]}$ the trainers$_{[fem]}$	sought had$_{[plu]}$,	eaten. [to] eat.
Late SR	*den Sportlern,*	*die die Trainerin*	*gesucht* hatten,	*gegessen.* *essen.*
	the sportsmen,	who$_{[amb]}$ the trainer$_{[fem]}$	sought had$_{[plu]}$,	eaten. [to] eat.
Late OR	*den Sportlern,*	*die die Trainerin*	*gesucht* hatte,	*gegessen.* *essen.*
	the sportsmen,	who$_{[amb]}$ the trainer$_{[fem]}$	sought had$_{[sing]}$,	eaten. [to] eat

The sentence-final verb was either correctly inflected (*gegessen*/eaten) or not (*essen*/[to] eat) (i.e. a morpho-syntactic violation). The morpho-syntactic violation should evoke a P600 component, and a major issue in this experiment was to explore the effect of prior processing load on this component. On the basis of Gunter et al. (in press) it was hypothesized that a larger processing load should lead to a smaller P600, particularly in the late disambiguated sentences, since in these sentences the disambiguation of the subclause and the sentence final verb follow each other immediately. This is a highly demanding situation compared to the early disambiguation, where the number information at the auxilliary ("*hatte*/hatten") is only a confirmation of already known information (SR or OR clause).

A total of 256 sentences were presented in 8 blocks to each subject. Half of the sentences were fillers and half were experimental sentences. In the experimental sentences, all categories described above (i.e. 8, depending on late/early disambiguation, SR/OR and sentence final correct/not inflected) were equally divided across the experiment making a total of 16 trials per category. All factors were also balanced across items by making 16 different versions of each particular block.

After a sentence was read, subjects had to answer a question related to its content (e.g. The question for the first example could have been: "Wurden die Trainerinnen von dem Sportler gesucht?" [Were the trainers sought by the sportsman?]; answer: "Yes").

A total of 32 out of 39 subjects participated in the actual ERP-study. The 7 subjects which were excluded from the experiment did not fulfill the criterion of having a

performance above 60% correct at the end of the training. Working memory score was measured using a German version of the Daneman and Carpenter reading span test (1980). Interestingly enough, reading span was always 3 or above with a mean value of 3.8 (Sd: .9) for the subjects entering the experimental group. Subjects with a lower score did not reach the performance criterion.
In general, the subjects used in the experiment had a mean percentage correct of 85%. ERPs were analyzed for correctly answered items only. ERPs were measured from 64 electrodes equally distributed over the scalp.

As the data analysis is still in progress, the ERP results presented are preliminary and statistically untested. It was found that the P600 difference between the violation and correct sentence ending was larger and started earlier in the early disambiguated sentences. The most straightforward explanation is that the P600 is sensitive not only to the processing of the violation itself, but also to the complexity of the foregoing sentence context. ERP effects related to the early disambiguation were found at the relative pronoun in the early disambiguating conditions (i.e. *der* vs. *den*). The ERPs for the early disambiguated SR condition showed a more positive waveform compared to all other conditions. This positivity lasted across the whole subclause. In order to explore the dependency of this effect to WM-capacity, two subgroups of 12 subjects each were formed on the basis of the span test (mean WM score: High span group:4.7; Low span group:3.0). Inspection of the data for each span group give reasons to believe that the positivity depends on WM-capacity. The high span group showed the positivity very clearly, whereas the effect was not present for the low span group.

3.1.7 Processing of subject and object relative sentences under different working memory loads

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

Earlier studies in English on the processing of subject and object relative clauses have shown that subject relative clauses are easier to process than computationally more demanding object relative clauses and that this is related to individual differences in working memory capacity (King & Just, 1991; King & Kutas, 1995). Recent studies in German showed that subjects initially prefer a subject relative reading (as shown in (1)) to an object relative reading (as shown in (2)) (Mecklinger, Schriefers, Steinhauer & Friederici, 1995; Schriefers, Friederici & Kühn, 1995).

(1) Subject relative sentence (SR):

Das	*ist*	*die*	*Managerin,*	*die*	*die*	*Arbeiterinnen*	*gesehen*	*hat.*
This	is	the	manager,	who	the	workers	seen	has.

(2) Object relative sentence (OR):

Das	*ist*	*die*	*Managerin,*	*die*	*die*	*Arbeiterinnen*	*gesehen*	*haben.*
This	is	the	manager,	who	the	workers	seen	have.

An important feature of the German sentences is that until the presentation of the final auxiliary, the sentences are completely ambiguous for a SR or an OR reading. The disambiguation at the final auxiliary was reflected in longer (self paced) reading times (Schriefers et al., 1995) and in a positive ERP component (Mecklinger et al., 1995) for the unpreferred OR structures compared to the preferred SR structures. In addition, both studies showed that the OR sentences were harder to process because subjects made more errors on questions about thematic roles. The Mecklinger et al. (1995) study also indicated that individual differences in working memory capacity can account for differences in parsing processes, because a post-hoc reading span test revealed that the positive ERP-component was only present in high span subjects.

The present experiment was designed to further examine this relation between working memory capacity and parsing processes. Therefore, we used SR and OR structures like the ones presented in Table 1. In addition to these different relative clause structures, we employed an additional working memory load (Vos, Kolk, Gunter & Mulder, 1996). For this aim a word-monitoring task was used. In such a task, a subject has to monitor for a given target-word during sentence presentation and to press a button whenever it is presented in the sentence. We designed the task such that subjects had to monitor for either one target-word (e.g., *"gang"*) or for three possible target-words (e.g., *"gang, murder, spy"*) during sentence presentation (see Table 1). In half of the sentences, there was no target-noun presented that originated from the given working memory set (i.e., a so-called nogo sentence). Finally, we looked at individual differences in working memory capacity. From the MPI database, 32 subjects were selected on the basis of individual span scores on a translated Daneman and Carpenter (1980) span task. A low span group (N=16) with individual span scores lower than 3.0 was compared with a high span group (N=16) with individual span scores higher than 4.5.

Table 1 gives an example of the different syntactic structures in combination with the additional working memory load.

(1) Subject relative sentence (SR)

Das ist die Detektivin, die die Polizistinnen aufgeklärt <u>*hat*</u>*, um den* Gauner *zu stellen.*
This is the detective, who the police officers informed <u>has</u>, in order to arrest the *swindler*.

(2) Object relative sentence (OR)

Das ist die Detektivin, die die Polizistinnen aufgeklärt <u>*haben*</u>*, um den* Gauner *zu stellen.*
This is the detective, who the police officers informed <u>have</u>, in order to arrest the *swindler*.

Targets to monitor for:
low working memory load: *agent* or (*gang*)
high working memory load: *Agent, Mörder, Spion* or (*gang, murder, spy*)

A total of 128 experimental sentences were constructed that varied both on syntactic complexity and the number of words subjects had to monitor for (see Table 1). Each trial began with the presentation of a memory set (1 or 3 words) for 1500 ms, followed by a word by word presentation of the experimental sentence (300 ms visual presentation, 200 ms ISI). After every experimental sentence a second sentence was given, whose meaning had to be verified with the meaning of the previously presented experimental sentence (i.e, if the meaning was the same than the right button had to be pressed, else the left button). The subjects were instructed to prefer accuracy to speed, and to avoid eyeblinks during the presentation of the experimental sentence.

EEG (from 32 Sn electrodes (electrocap)), word-monitoring times on target detection and sentence-verification performance were measured. The ERP data is still under consideration, but the first behavioral data showed that there is a large difference in performance data for the two span groups. Both the word-monitoring performance and the sentence-verification performance was better (fewer errors and faster RTs) for the high span subjects than for the low span subjects. Moreover, only the low span subjects were affected by the additional load manipulation and the syntactic complexity manipulation. They made more misses when they had to monitor for three words than for one word and had worse comprehension performance on OR than SR sentences. Interestingly, we found that in neither of the two spangroups the comprehension performance was influenced by the additional working memory load.

3.1.8 Inter-sentential context effects on parsing preferences: A study using event-related potentials

Ferstl, E. & Friederici, A.D.

The question of whether pragmatic or contextual information can override syntactic preferences is crucial for distinguishing modular theories of language processing from constraint-based accounts (cf. Frazier, 1995; MacDonald et al., 1994). Psycholinguistic experiments using behavioral measures have not yet provided a conclusive answer. Recently, event-related brain potentials have been established as a powerful tool to dissociate non-syntactic from syntactic language comprehension processes. However, no ERP data have been collected to date to study context effects on parsing.

We conducted an ERP study in which German relative clause ambiguities were presented after biasing context questions. The preferred subject relative (SR) structure (e.g., *"It is the students who saw the professor"*) was preceded by the question *"Who saw the professor?"*. If the readers follow usual rules of discourse, they will presuppose that a professor exists who was seen. Furthermore, the answer to the question is felicitous only if it provides information on the agent of the seeing (Kaan, 1996; Blok, 1990). Analogously, the unpreferred object relative (OR) sentence *"It is the students who the professor saw"* was preceded by the question *"Whom did the professor see?"*. In German, both relative clauses have the same word order, so that the structure is disambiguated on the sentence final verb by subject-verb agreement (e.g. *"Es waren die Studentinnen* (plural), *die die Professorin* (singular) *gesehen hat* (singular) / *haben* (plural)"). The context questions provided syntactic information as to the case of the relative pronoun (nominative vs. accusative), as well as information about the thematic role of the noun phrase *"the professor"* (theme vs. agent).

Question type was crossed with sentence structure, yielding the two biasing context conditions just described, as well as two inconsistent conditions, in which the question-answer pair was infelicitous. In addition, a neutral context condition (*"Which students were there?"*) was included, in order to confirm the previously reported preference for subject-relative structures (Schriefers et al., 1995; Mecklinger et al., 1995). Examples for the six conditions are:

Neutral context
no bias, SR sentence

Welche Studentinnen waren da?
Es waren die Studentinnen, die die Professorin gesehen haben.

Which students were there?
It were the students who saw the professor.

no bias, OR sentence

Welche Studentinnen waren da?
Es waren die Studentinnen, die die Professorin gesehen hat.

Which students were there?
It were the students who the professor saw.

Biasing context
SR bias, SR sentence

Wer hat die Professorin gesehen?
Es waren die Studentinnen, die die Professorin gesehen haben.

Who saw the professor?
It were the students who saw the professor.

OR bias, OR sentence

Wen hat die Professorin gesehen?
Es waren die Studentinnen, die die Professorin gesehen hat.

Whom did the professor see?
It were the students who the professor saw.

Inconsistent context
OR bias, SR sentence

Wen hat die Professorin gesehen?
Es waren die Studentinnen, die die Professorin gesehen haben.

Whom did the professor see?
It were the students who saw the professor.

SR bias, OR sentence

Wer hat die Professorin gesehen?
Es waren die Studentinnen, die die Professorin gesehen hat.

Who saw the professor?
It were the students who the professor saw.

To verify the efficacy of the bias, a sentence completion task was conducted. For this experiment, the relative clause sentences were presented up to the second noun phrase (e.g., "*die Professorin*"), after one of five contexts. In addition to the three context questions of Table 1, we also included the isolation condition, in which no context question preceded the fragment, and another neutral question, in which the second noun phrase was mentioned (e.g., "*Who was there except for the professor?*"). For each context condition, 12 sentences were used. The total of 60 trials was randomly interleaved with 72 fragments from an unrelated experiment which did not contain relative clause structures. Seventeen students completed each of the resulting 132 fragment with a sensible verb phrase. Without bias, 69% of the completions were subject-relative clauses, and there was no difference between the three neutral conditions. After the subject-bias question, this proportion increased significantly to 90%, while after the object-bias questions only 39% of the sentences were subject-relatives. Note that the instructions did not require to repeat the verb of the context question. In most of the subject-relative completions after object-bias questions, subjects selected a different verb, and were thus not violating discourse based constraints.

For the ERP experiment, 240 trials with 40 trials in each of the six conditions were used. 29 subjects read the sentences word by word, while EEG was recorded continuously from 64 electrodes. Function words were presented for 250 ms each, and content words for 350 ms, with an inter-stimulus interval of 300 ms. To ensure that the crucial wh-pronoun at the beginning of the trial was read, this word was left on the screen for 450 ms. 1500 ms after presentation of the final auxiliary, a comprehension question appeared. It required subjects to decide whether the context question and the target sentence were consistent with each other, and, in case they were, to indicate the object of the relative clause.

Accuracy and reaction time data showed significant interactions between sentence type and context type, indicating that the garden-path for object-relative clauses in the neutral context condition was reduced (errors) or eliminated (reaction times) after the felicitous bias. In the neutral and the biasing context conditions, the ERP data for the sentence final auxiliary showed a late positivity (P600) for object relative sentences, indicating syntactic processing costs (Osterhout & Holcomb, 1992). In the inconsistent context condition, we observed a late positivity for the object-relative sentences in the same time window. However, this late positivity had a different scalp distribution, being more pronounced at the anterior electrodes. In addition, context relevance had an effect in an earlier time window, independent of syntactic structure. A sharp, pronounced positivity with a peak at around 350 ms was larger for the inconsistent trials than for biasing trials. This P300 effect might be related to the violation of contextual expectations. Thus, inter-sentential context information was available immediately, but it did not override the structural preference for a subject-relative reading.

The effect of animacy specification on the processing of German relative clauses

3.1.9

Gorrell, P. & Gunter, Th.C.

Previous experimental work using event-related potentials (Mecklinger, Schriefers, Steinhauer & Friederici 1995) and a self-paced reading task (Schriefers, Friederici & Kühn 1995) yielded results consistent with first-pass attachment preferences being governed by a syntactic processing strategy (the "Active Filler Strategy" of Frazier & Flores d'Arcais 1989) rather than by information concerning semantic plausibility. However, other experimental studies using different structures and a different language (English) suggest that plausibility information can influence first-pass operations. It may be that, as Schriefers et al. (1995) suggest, this is due to the fact that, unlike the English studies, in the German relative clause structures tested by Schriefers et al. (1995) and Mecklinger et al. (1995), the relevant semantic information occurred late in the sentence or clause, after the point at which an incremental, serial parser is forced to make structural commitments.

An experiment was designed and run to test the hypothesis that semantic plausibility information can influence first-pass operations, provided that it is available prior to the parser making an attachment decision based on structural factors. In the prior studies with German relative clauses, the head of the relative was always [+ animate]. In the present experiment this factor was manipulated such that the head of the relative was either [+ animate] or [- animate]. As in the prior studies, disambiguation was by the number specification of the sentence-final auxiliary. Sentences were presented word-by-word, centered on a computer screen, with rate of presentation controlled by the subject. After each sentence, subjects answered a comprehension question. Example stimuli are given in (1).

(1) a. subject relative, animate head
Das ist die Intendantin, die die Schauspielerinnen gesehen hat.
This is the director that has seen the actresses.

b. object relative, animate head
Das sind die Intendantinnen, die die Schauspielerin amüsiert hat.
These are the directors that the actress has seen.

c. subject relative, inanimate head
Das ist die Komödie, die die Schauspielerinnen amüsiert hat.
This is the comedy that has amused the actresses.

d. object relative, inanimate head
Das sind die Komödien, die die Schauspielerin gesehen hat.
These are the comedies that the actress has seen.

For relative clauses with animate heads, question-answering accuracy reveals a clear processing advantage for subject relative clauses, with subject relatives yielding 90% accuracy and object relatives 63% accuracy. A non-significant trend in the same direction was found with relative clauses with inanimate heads, with subject relatives producing 97% accuracy and the object relatives 88% accuracy. For subject relatives, clauses with inanimate heads were answered more accurately than clauses with animate heads. This difference (97% to 90%) is significant and may be due to the fact that processing two noun phrases before the appearance of the verb is easier when these phrases are more clearly distinguished, as in the case in the inanimate condition where one animate and one inanimate noun phrase precede the verb (in the animate condition, two feminine, animate noun phrases precede the verb).

Unlike the Schriefers et al. (1995) self-paced reading study, reading times for the disambiguating, sentence-final, auxiliary did not reveal a subject advantage in the animate condition. There were no significant reading time differences at the final auxiliary in either the animate or inanimate condition. One possibility for the difference between the two experiments is that subjects in the present experiment were simply reading quickly through the sentence, with processing difficulty becoming evident after the end of the sentence and reflected in question-answering. This possibility is supported by the fact that reading times for the sentence-final auxiliary averaged about 485 msec in the present study, but over 1300 msec in the Schriefers et al study. Further, word-by-word reading times in the Schriefers et al. (1995) experiment averaged 200 msec slower than in the present study. For question answering times, object relatives in the Schriefers et al. (1995) study produced 90% accuracy, compared with 63% in the present study.

In general, an examination of post-sentence question answering times in the present study support the conclusion of Schriefers et al. (1995) and Mecklinger et al. (1995) that the subject analysis is the preferred interpretation for ambiguous structures with an animate head. Further, this advantage for the subject reading is not found in the inanimate condition. Yet there was no evidence of an object preference in the inanimate condition, suggesting that an inanimate head fails to simply switch the preference from subject to object relative clause. Further experiments are required to determine more precisely the nature of the interaction between the subject preference and non-structural sources of information.

3.1.10 Prepositional phrase attachment: Is it a syntactic ambiguity?

Ferstl, E.

Modular parsing theories, such as the garden-path model (Frazier, 1978), postulate that semantic, pragmatic, and contextual information is only taken into account after the initial syntactic analysis has been carried out. If the resulting structure is inconsistent with non-syntactic information, a reanalysis process takes place. Interactive theories, on the other hand, consider language comprehension a constraint-satisfaction process in which multiple information sources are used in parallel (e.g., McClelland, 1987; Marslen-Wilson, 1975). Empirically distinguishing these two classes of theories requires linguistic structures for whose interpretation non-syntactic information is needed. An example for such an ambiguity is the prepositional phrase attachment. Consider the sentence pair (1).

(1) *The cleaning lady swept the floor with the broom.*
The cleaning lady swept the floor with the tiles.

In the first example, *broom* is the instrument of the action *sweeping*, and thus, the prepositional phrase must be attached to the verb phrase. In the second example, *tiles* are a feature of the object, so that the prepositional phrase must be attached to the noun phrase *the floor*.

For sentences of this type, a verb attachment preference has been repeatedly reported. Depending on the theoretical background, a variety of explanations have been suggested. Syntactic complexity (Frazier & Rayner, 1982), argument structure of the verb (Clifton, Speer & Abney, 1991), sentence context or thematic role information (Taraban & McClelland, 1988), discourse information (Altmann & Steedman, 1988), and verb type (Spivey-Knowlton & Sedivy, 1994) are among the candidates - and there is some empirical support for all of these explanations. Common to these studies is the assumption that the prepositional phrase is a constituent already fully assembled at the point of attachment into the phrase marker. I have argued that it is necessary to more closely examine the interactions between local parsing processes, such as building a constituent phrase, and global attachment (Ferstl, 1994).

The goal of the present study was to provide further off-line evidence for the sensitivity of attachment preferences to information within the prepositional phrase. Two sentence completion experiments were conducted. The first was intended to obtain for a large sample of sentences cloze probabilities for different attachment types, i.e. the probability with which structure the particular sentence beginning is completed. Furthermore, it tested the hypothesis that the preposition *with* (which is used for a large majority of experimental materials in this domain) induces a stronger verb attachment preference than other prepositions. The second experiment tested the hypothesis that it is crucial whether the noun phrase within the prepositional phrase is definite (see also Spivey-Knowlton & Sedivy, 1994).

130 sentences of the aforementioned form were written. For each sentence, two noun fillers yielding different attachments were selected, so that both readings were semantically acceptable. 68 of the prepositional phrases contained the preposition *with* (*mit*), the remaining 62 other prepositions (e.g., *vor, zu, an, für, ohne*). In both sets, there were 15 psychological state verbs. The noun phrase within the prepositional phrase (e.g., *the broom*) was then deleted, and the resulting sentence fragments typed in four different random orders. Due to the large number of sentences, no filler items were used. In the first experiment, 69 students completed the sentences with the first continuation that came to mind. The answers were first scored according to the syntactic structure. Ambiguous attachments were then discarded (about 15% of the data), and the verb attachments classified according to their thematic role. Of particular interest were adverbial continuations (*with patience*), and instrumental continuations.

Since there were no differences between the psychological state verbs and the action verbs, the data, shown below, are collapsed across verb types. For *with*-sentences, there was a strong verb attachment preference, with a majority of these attachments expressing instrumental roles. In contrast, for the sentences with other prepositions, this preference was reversed. Furthermore, among the verb attachments, more completions realized adverbial roles than instrumental ones.

		Noun attachment	Verb attachment	VA adverbial	VA instrumental
Experiment 1	(n = 69)				
	preposition with	19	81	30	48
	other prepositions	62	37	14	4
Experiment 2	(n = 227)				
	without article	16	84	34	46
	with article	43	57	3	50

Percentages of unambiguous Cloze completions. Since there were other thematic roles besides adverbial and instrumental roles, these two scores do not sum to the total percentage of verb attachments.

The second sentence completion task was designed to first exclude the possibility that presenting the fragments without fillers might have drawn attention to the sentence structure (each fragment ended in a preposition). Secondly, the study included a condition in which a definite article immediately followed the preposition. This manipulation made adverbial continuations less likely (but not impossible; e.g., *with the greatest excitement*). The question of interest was whether this would affect the overall preference for verb attachment.

64 of the previously used *with*-sentences were randomly selected. Each sentence was presented in each of four conditions (two of which used verb-final clauses, but are not discussed here). 227 students participated in the study and completed 32 experimental sentences embedded in 110 filler sentences. Each sentence was thus seen by approximately 26 subjects who took about 35 minutes to complete the 142 sentences.

Since data analysis is still in progress, only preliminary results for the verb-second sentences are available. Although in this study filler items employing different structures were included, the results for the condition without article closely resemble those of Experiment 1. Once more, a strong verb attachment preference was found, which was realized in both adverbial and instrumental continuations. Including an article after the preposition changed this pattern considerably. Half of the continuations were still instrumental verb attachments, but adverbials were used seldom in this condition. Instead, subjects chose noun attachments much more frequently.

These data suggest that single factors such as syntactic structure, verb information or sentence context alone are not sufficient to account for attachment preferences. Further experiments are planned to confirm and specify these findings using on-line measurements.

Noun phrase-attachment ambiguities in German: The impact of lexical and semantic information

3.1.11

Steinhauer, K., van Kampen, A., Schriefers, H. & Friederici, A.D.

One of the best known structural ambiguities concerns the prepositional phrase (PP) attachment in sentences like (1) where the PP can either be attached to the verb phrase (VP) (*to observe with something*) or to the noun phrase (NP) (*the cop with something*).

(1) The spy observed the cop with binoculars/with a revolver.

In German there is a very similar ambiguity with respect to the attachment of feminine singular NPs which are case ambiguous between genitive and dative reading. In (2) the ambiguous NP2 *"der Sängerin"* (the singer) functions as the indirect dative object of the ditransitive verb *"gab"* (gave) and has to be attached to the VP whereas in (3) NP2 modifies the preceding NP1 *"der Arzt"* (the doctor) and requires a genitive reading.

NP-VP attachment - dative reading:

(2) Er wußte, daß der Arzt der Sängerin ein neues Medikament gab.
He knew that the doctor gave a new medicine to the singer.

NP-NP attachment - genitive reading:

(3) Er wußte, daß der Arzt der Sängerin ein neues Medikament entwickelte.
He knew that the doctor of the singer developed a new medicine.

In contrast to English, disambiguating verb information is encountered only in the clause final position. The "minimal attachment principle" (Frazier, 1978) generally predicts an initial preference for NP-VP attachment. According to the "head attachment principle" suggested by Hemforth, Konieczny, Scheepers, and Strube (1994), however, NP2 should initially only be attached to NP1 since the lexical head of the VP is not yet available. Hemforth et al.'s (1994) predictions were confirmed by data of their self-paced reading and eye-tracking studies. Schriefers, Friederici, and Scharfenberg (1995), however, found a weak preference for dative reading and a significant ambiguity effect for feminine NPs as compared to case marked non-ambiguous masculine NPs (see Annual Report 1995, 3.1.10).

These contradictory results might be due to differences in the linguistic material. Even in the absence of verb information certain pairs of NPs may show a stronger bias towards genitive reading compared to others, particularly, if the NP1 offers a kind of 'argument slot' with respect to NP2 as in kindred relations or in case of nouns which were derived from transitive verbs (e.g., *the father of the girl*; *the admirer of the movie star*). As post-hoc analyses revealed, such NP combinations were indeed more frequent in the Hemforth et al. (1995) study than in the Schriefers et al. (1995) study and could have led to the observed genitive bias.

3.1.11.1 A sentence completion study

Steinhauer, K., Schriefers, H. & Friederici, A.D.

The assumed impact of lexical and semantic differences on the processing of case ambiguous NP pairs was examined in a first step by means of a paper-and-pencil sentence completion test. Four types of potential genitive bias conditions were constructed and tested against non-biasing control conditions :

1. The first condition comprised an NP1 derived from a transitive verb together with an NP2 that could serve as object of the verb. In the control condition NP1 was substituted.
   <u>Bias:</u> *the admirer* - *the movie star* <u>Control:</u> *the camera man* - *the movie star*

2. In the second condition kindred relations served as genitive bias. Each kinship can be expressed by two complementary relationships ("*the father of the girl*" / "*the daughter of the man*"). Their tautological combination ("*the father of the daughter*") is therefore less common in German and was used as control.
   <u>Bias</u>: *the father* - *the biologist* <u>Control:</u> *the father* - *the daughter*

3. In the third condition the impact of world knowledge was tested. We made use of the fact that some professions are more or less restricted to serve the upper class, e.g. a cleaning woman is more likely to be found in an executive's than in a beggar's household.
   <u>Bias:</u> *the cleaning woman* - *the executive* <u>Control:</u> *the cleaning woman* - *the beggar*

4. The fourth bias condition consisted of names of professions as NP1 and related inanimate objects as NP2 which could modify NP1. NP2 was substituted by related animate nouns in the control condition.
   <u>Bias:</u> *the captain* - *the fregate* <u>Control:</u> *the captain* - *the surfer*

A total of 100 biased NP pairs and 100 corresponding controls was used to construct sentence fragments like (4), which had to be completed.

(4) Er wußte, daß der Arzt <u>der Sängerin</u> _______________ .

The 200 fragments were equally distributed over 8 versions each of which also included 50 sentence fragments of other experiments and 70 irrelevant filler fragments. NP repetitions were avoided. 200 students (22-31 per version) participated in the test. Only unambiguous dative or genitive completions entered the statistical analyses (one-tailed Wilcoxon Tests).

Figure 3 illustrates the results. For each bias type the number of genitive completions was significantly larger in the bias conditions as compared to the controls (p-values between .002 and $1.7*10^{-8}$). Only 6 out of 20 NP pairs in the third condition (world knowledge) did not show this pattern. In further studies more sensitive on-line methods will be applied in order to investigate the time course in which lexical information of the NPs influences reading (see also section 3.1.11.2).

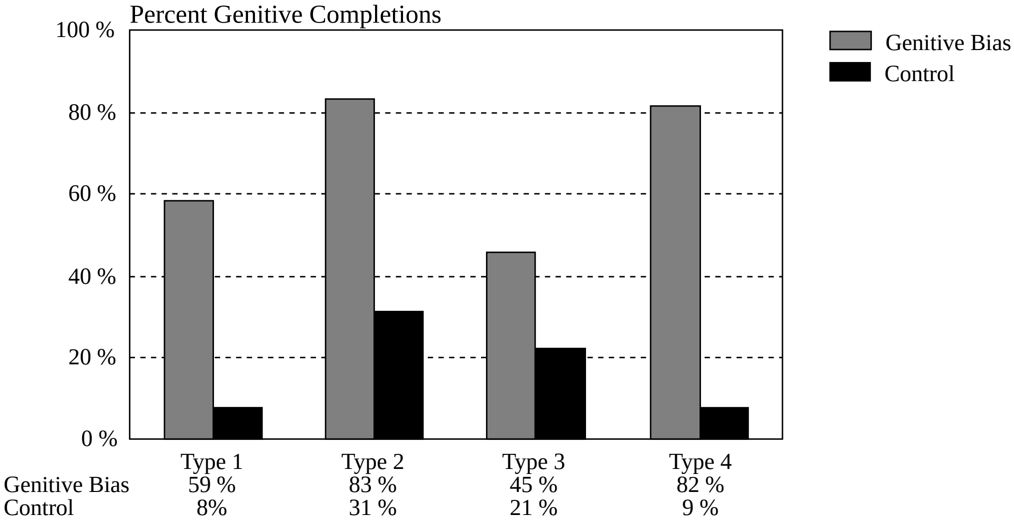


Figure 3. Impact of the 4 types of genitive bias on the sentence completion: Biased NP pairs versus controls.

A self-paced reading study

3.1.11.2

van Kampen, A., Schriefers, H. & Friederici, A.D.

This study was designed to investigate the influence of semantic aspects upon (noun phrase (NP) attachment) preferences in locally ambiguous sentences during reading. The particular type of syntactic structures under investigation makes use of a particular type of ambiguity in German case marking system: the definite article for feminine singular nouns like *der Studentin* either marks a genitive or dative.

In a first step we replicated the self-paced-reading experiment of Schriefers, Friederici & Scharfenberg (see Annual Report 1995, 3.1.10).

Experiment 1:

In our interpretation we will concentrate on four experimental conditions, for which the pattern of results was replicated in general. The only difference we found was a general decrease of the reaction times in comparison to the prior study, which we attributed to a slight modification in the experimental procedure: the delay between the sentence and the following question (every sentence was followed by a question to force the subjects to really interpret the sentences) was prolonged, from 700 to 1200 ms.

We compared the processing of locally ambiguous structures like (1) and (3) with corresponding sentences not containing an ambiguous case marking like (2) and (4), which contained the masculine form of the singular noun, e.g. *des Studenten*.

(1) Er wußte, daß	*die Professorin*	*der Studentin*	*dem Mitarbeiter*	*den Scheck*	*gab.*
He knew that	the professor	the student	the coworker	the cheque	gave.

(2)	*Er wußte, daß*	*die Professorin*	*des Studenten*	*dem Mitarbeiter*	*den Scheck*	*gab*
	He knew that	the professor	the student	the coworker	the cheque	gave
(3)	*Er wußte, daß*	*die Professorin*	*der Studentin*		*den Scheck*	*gab*
	He knew that	the professor	the student		the cheque	gave
(4)	*Er wußte, daß*	*die Professorin*	*dem Studenten*		*den Scheck*	*gab*
	He knew that	the professor	the student		the cheque	gave

In the sentences (1) and (3) the NP *der Studentin* is ambiguous between a genitive attribute of the NP *die Professorin* and an indirect object (dative) of the verb. Assuming a first-instance interpretation of the NP *der Studentin* as an indirect object, as should be predicted by the parsing principle "minimal attachment", in (1), this analysis will turn out to be incorrect when reading the NP *dem Mitarbeiter* which is unambiguously marked as a dative object. In (3), this first analysis as an indirect dative object is not undermined because the following NP *den Scheck* is clearly marked as an direct (accusative) object.

Subjects read the sentences in a word-by-word self-paced-reading paradigm. By pressing a push-button, the subjects requested the first word of the sentence. The second press on the push button replaced the first word by the second word and so on until the last word of the sentence. After the last word two question marks appeared on the screen which lasted for 1200 ms (in the experiment of Schriefers, Friederici & Scharfenberg (1995) they only stayed for 700 ms). A yes/no-question concerning the preceding sentence appeared on the screen, which the subject should answer by pressing the corresponding push-buttons.

Table 1 gives the reading times per word for sentences with a correct answer to the subsequent question:

Table 1:

	Er	wußte,	daß	die	Prof.	der	Stud.	dem	Mitarb.	den	Scheck	gab.
(1)	364	294	306	298	389	386	410	420	505**	529**	518**	638**
(2)	408	314	312	324	402	387	399	427	467	450	448	583
(3)	388	308	310	314	393	393	419	41o			450	625*
(4)	400	324	318	323	406	394	421	416			438	589

* the mean reading-time for this word differs significantly from the reading-time of the same word in the non-ambiguous condition (1%-niveau)

** the mean reading-time for this word differs significantly from the reading-time of the same word in the non-ambiguous condition (5%-niveau)

We found a general effect of ambiguity. The genitive condition showed longer reading-times for the ambiguous version while and after the sentence becomes unambiguous as being predicted by the principle of minimal attachment. There was also an effect of ambiguity for the dative condition, though it was restricted to the last word of the sentence and did not expand, as in the genitive case over the last four words.

The data seem to favor a model, in which both possible interpretations for the ambiguous NP remain available while reading the sentence. However, there is a cost of processing capacity which can be seen in longer reading times for the ambiguous versions of the sentences. There also seems to be an advantage for sentences in which the ambiguity is solved as a dative object.

These results are not only in conflict with the predictions of the principle of minimal attachment, but also clearly differ from results found by Scheepers et al. (1990). In their study, they found no differences in the reading times for both the genitive conditions but clearly slower reading times in the ambiguous compared to the unambiguous dative condition.

Experiment 2:

These data lead to the idea that there might have been an influence of semantic aspects in the sentences used, i.e., that the subject of the sentence and the ambiguous NP are related in a special way, favoring the dative- or the genitive reading. A sentence like

(5)	*Er wußte, daß*	*die Tochter*	*der Biologin....*
	He knew that	the daughter	(of) the biologist....

may favor the genitive reading, whereas the sentence

(6)	*Er wußte, daß*	*die Wissenschaftlerin*	*der Biologin...*
	He knew that	the scientist	the biologist...

may force an interpretation of the ambiguous NP as an indirect object to the verb.

This hypothesis was tested in an off-line experiment by Steinhauer, Schriefers, Friederici, and van Kampen (this Annual Report).

The results showed, that in an off-line paradigm semantic aspects had a clear effect on interpreting those ambiguous structures. Sentence pairs like (5) and (6) were taken out of the testmaterial, which fulfilled the demands of three conditions integrated in

Experiment 3:

Three types of bias NP-NP pairs were constructed from the material of Experiment 2:

Type A: This type strictly favors a genitive interpretation in one version and shows a clear preference for the dative reading in the other version (not containing familiar relationships)

(a)	*Er wußte, daß*	*der Freund*		*der Friseurin.....*
	He knew that	the friend	(of)	the hairdresser...

(b)	*Er wußte, daß*	*der Urlauber*		*der Friseurin...*
	He knew that	the vacationist		the hairdresser...

Type B: This type contain NP-NP pairs which about one half of the subjects interpreted as dative and the other half as genitive in one version. The other version again showed a preference of the dative reading (not containing family relationships)

(a)	*Er wußte, daß*	*der Mitarbeiter*		*der Forscherin...*
	He knew that	the coworker	(of)	the researcher...

(b)	*Er wußte, daß*	*der Tourist*		*der Forscherin...*
	He knew that	the tourist		the researcher...

Type C: This type contains family relationships showing a strong bias for the genitive reading

(a)	*Er wußte, daß*	*die Tochter*		*der Biologin*
	He knew that	the daughter	(of)	the biologist...

The subjects saw sentences belonging to Type A (a), B (a) and C (a) in four conditions:

Condition 1: Ambiguous genitive construction

Er wußte, daß	*der Freund*	*der Friseurin*	*dem Mitarbeiter*	*den Scheck*	*gab.*
	der Mitarbeiter	*der Forscherin*	*dem Laboranten*		
	die Tochter	*der Biologin*	*dem Studenten*		

He knew that	the friend	the hairdresser	the coworker	the cheque	gave.
	the coworker	the researcher	the technician		
	the daughter	the biologist	the student		

Condition 2: non-ambiguous genitive construction

Er wußte, daß	*der Freund*	*des Friseurs*	*dem Mitarbeiter*	*den Scheck*	*gab.*
	der Mitarbeiter	*des Forschers*	*dem Laboranten*		
	die Tochter	*des Biologen*	*dem Studenten*		

He knew that	the friend	the hairdresser	the coworker	the cheque	gave.
	the coworker	the researcher	the technician		
	the daughter	the biologist	the student		

Condition 3: ambiguous dative construction

Er wußte, daß	*der Freund*	*der Friseurin*		*den Scheck*	*gab.*
	der Mitarbeiter	*der Forscherin*			
	die Tochter	*der Biologin*			

He knew that	the friend the coworker the daughter	the hairdresser the researcher the biologist	the cheque	gave.

Condition 4: non-ambiguous dative construction

Er wußte, daß	*der Freund* *der Mitarbeiter* die Tochter	*dem Friseur* *dem Forscher* dem Biologen	*den Scheck*	*gab.*

He knew that	the friend the coworker the daughter	the hairdresser the researcher the biologist	the cheque	gave.

Sentences belonging to Type A(b) and Type B(b) were only presented in condition 3 and 4, for a genitive construction would have resulted in a meaningless sentence. The experiment contained 8 sentences belonging to the Type A, 8 sentences belonging to Type B, and 12 sentences belonging to Type C.

The subjects were tested in the same way as described above. Again a self-paced-reading paradigm was used. The design of the experiment was slightly modified: only 1/5 of the sentence was followed by a question and filler material was used, i.e. one half of the sentences were filler-sentences.

Again (as in Experiment 1) we found an effect of ambiguity which differed between the three bias-types:

Table 2-4 show the reaction times for every word of the sentences in the genitive conditions:

Table 2:

<u>Type A:</u>	Er	wußte,	daß	der	Freund	der des	Friseurs Friseurin	dem	Mitarb	den	Scheck	gab.
(a)Cond.1	288	267	290	278	268	289	312*	331*	338*	328	305	324
(a)Cond.2	286	265	279	279	290	291	286	314	313	322	299	334

<u>Type A:</u>	Er	wußte,	daß	der dem	Freund Friseurin	der	Friseur	den	Scheck	gab.
(a)Cond.3	283	254	281	270	290	294**	299	326*	323*	345*
(a)Cond.4	284	269	274	269	285	272	293	307	293	311

* the mean reading-time for this word differs significantly from the reading-time of the same word in the non-ambiguous condition (1%-niveau)

** the mean reading-time for this word differs significantly from the reading-time of the same word in the non-ambiguous condition (5%-niveau)

Table 3:

<u>Type B:</u>	Er	wußte,	daß	der	Mitarb.	der des	Forschers Forscherin	dem	Mitarb.	den	Scheck	gab.
(a)Cond.1	285	262	275	266	278	289	304	338	365**	361**	333**	367*
(a)Cond.2	293	263	281	275	290	281	292	319	320	333	309	334

<u>Type B:</u>	Er	wußte,	daß	der	Mitarb.	der dem	Forscher Forscherin	den	Scheck	gab.
(a)Cond.3	293	252	275	269	275	284	298*	320(*)	321**	337*
(a)Cond.4	293	261	271	273	271	289	278	306	294	310

* the mean reading-time for this word differs significantly from the reading-time of the same word in the non-ambiguous condition (1%-niveau)

** the mean reading-time for this word differs significantly from the reading-time of the same word in the non-ambiguous condition (5%-niveau)

Table 4:

<u>Type C:</u>	Er	wußte,	daß	die	Tochter	der des	Biologen Biologin	dem	Mitarb	den	Scheck	gab.
(a)Cond.1	286	256	274	269	271	277	293	327(*)	312	331	306	321
(a)Cond.2	297	253	260	268	276	287	289	308	318	320	299	326

<u>Type C:</u>	Er	wußte,	daß	die	Tochter	der dem	Biologen Biologin	den	Scheck	gab.
(a)Cond.3	291	257	271	270	276	284	297(*)	326**	307(*)	347*
(a)Cond.4	288	261	271	273	276	279	284	298	296	316

* the mean reading-time for this word differs significantly from the reading-time of the same word in the non-ambiguous condition (1%-niveau)

** the mean reading-time for this word differs significantly from the reading-time of the same word in the non-ambiguous condition (5%-niveau)

For the dative-bias type A (b) and B (b) there also was clear effect of ambiguity.

The effect of ambiguity in the genitive conditions differed between the different bias types, in type B it concerned the last 4 words of the sentence, in type A it only involved three words and in type C only one word showed an effect which failed significance (p=0.08).

Comparing the ambiguous genitive conditions of the three bias types, a clear facilitation effect for the bias types with a stronger genitive bias (A and C) compared to type B was seen, which reached statistical significance on the last four words of the sentence for both the comparisons (type A/type B and type C/type B).

Table 5 shows the reaction-times for every word for the ambiguous genitive conditions (1) in type A-C.

Table 5:

	Er	wußte,	daß	der der die	Freund Mitarb. Tochter	der der der	Friseurin Forscherin Biologin	dem	Mitarb.	den	Scheck	gab.
Type A	288	267	290	278	268	289	312	331	338*	328*	305**	324**
Type B	285	262	275	266	278	289	304	338	365	361	333	367
Type C	286	256	274	269	271	277	293	327	312**	331**	306**	321**

* the mean reading-time for this word in type A or C differs significantly from the reading-time of the same word in type B (1%-niveau)

** the mean reading-time for this word in type A or C differs significantly from the reading-time of the same word in type B (5%-niveau)

Comparing the ambiguous dative to the ambiguous genitive condition for each bias type, there were also clear differences between the bias types: In type B the reading of the last three words was significantly slower in the genitive condition than in the dative condition. In types A and C there was no difference between the reading times for the last three words of the sentences in the same comparison.

The combined data can be interpreted as follows:
The local bias built up between the subject and the ambiguous noun phrase affects the interpretation of the sentence not only off-line, but also on-line. In the on-line study there still was a general effect of ambiguity in all conditions. These results seem to favor a model of sentence-analysis assuming multiple activation. In the ambiguous case subjects did not seem to build up one single structure only but considered multiple interpretations. Semantic aspects, moreover, seem to affect reading times possibly reducing cognitive load on some structures.
Another explanation for this pattern of results may be, that subjects handled those sentences differently depending on their memory capacities. There are some hints that a high reading span enables the subject to keep both possible interpretations active while a low reading span leads to an early decision.

Further investigation of these phenomena currently entails experiment in which a "global context" is introduced. The material described above is now being tested with a preceding neutral or biasing context-sentence.

Complement ambiguities 3.1.12

Gorrell, P. & Gunter, Th.C.

A number of parsing theories incorporate some form of preference for minimal structure. One ambiguity that has been investigated in a number of studies involves verbs which permit either a nominal or clausal object (Rayner & Frazier 1987; Trueswell, Tanehaus & Kello 1993). Most of these studies have used English stimuli such as those in (1). In (1a) and (1b) the verb "*know*" takes a clausal object. In (1c) the object is simply a noun phrase. In (1b, c), at the point at which the postverbal noun phrase is processed, attachment as an object is the minimal attachment.

(1) a. The man knew that the boy was intelligent.
b. The man knew the boy was intelligent.
c. The man knew the boy very well.

In English, the ambiguity in (1b) stems from the fact that the grammar of English generally allows the complementizer "*that*" to optionally delete. There is at present a debate as to whether there is a general structural preference for the minimal structure, or whether the preference depends on the type of verb. As a preliminary study of this ambiguity in German, sentences such as (2) were tested in a self-paced reading study. In German, unlike English, the omission of the complementizer ("*daß*") is always dependent on the particular verb.

(2) a. Der Masseur sah, daß die Sportler laufen, obwohl das Wetter schlecht war.
The masseur saw that the athletes ran, although the weather was bad.

b. Der Masseur sah die Sportler laufen, obwohl das Wetter schlecht war.
The masseur saw the athletes run, although the weather was bad.

c. Der Masseur sah die Sportler und winkte, obwohl das Wetter schlecht war.
The masseur saw the athletes and waved, although the weather was bad.

d. Der Masseur grüßte die Sportler und winkte, obwohl das Wetter schlecht war.
The masseur greeted the athletes and waved, although the weather was bad.

In (2a), a clausal object for "*sehen*" is unambiguously signaled by the complementizer. In (2d), the verb *"grüßen"* does not permit a clausal object, so a following noun phrase is unambiguously a nominal object. In (2b) and (2c), attachment of the postverbal noun phrase may either be as the object of the verb, or as subject of a following clause. If there is a preference for the minimal structure, then reading times for the verb following this phrase will be longer in (2b) than in (2a). Further, reading times for the conjunction and verb following this noun phrase in (2c) and (2d) should not differ, as they are consistent with the simple nominal object analysis.

Preliminary analysis of the data for 32 subjects shows that reading times for the disambiguating verb in (2b) were significantly longer than its counterpart in the unambiguous (2a). Further analysis of the effects of specific verbs is required. Subjects (who completed a post-experiment questionnaire) display considerable individual variation in judging the acceptability of structures such as (2b) with different verbs. Also, reading times for the conjunction and verb following the ambiguous phrase in (2c, d) did not differ, consistent with an object analysis of the prior noun phrase.

Multiple-conjunction ambiguities: Parsing preferences and the effects of manner of disambiguation

3.1.13

Gorrell, P. & Gunter, Th.C.

This self-paced reading experiment investigated the processing of multiple-conjunction ambiguities due to ambiguous case marking, illustrated in (1)

(1) *Der Dirigent besucht den Apotheker, die Trainerin...*

(2) a. *Der Dirigent besucht den Apotheker, die Trainerin* [NOM, ACC] *besucht den Bruder und der Beamte besucht den Arzt.*
The conductor visits the pharmacist, the trainer visits the brother and the official visits the doctor.

b. *Der Dirigent besucht den Apotheker, der Trainer* [NOM] *besucht den Bruder und der Beamte besucht den Arzt.*

c. *Der Dirigent besucht den Apotheker, die Trainerin* [NOM, ACC] *und den Bruder auch gerne im Sommer.*
The conductor (likes to) visit the pharmacist, the trainer and the brother also in the summer.

d. *Der Dirigent besucht den Apotheker, den Trainer* [ACC] *und den Bruder auch gerne im Sommer.*

In this type of ambiguity, a case-ambiguous phrase (e.g. *die Trainerin* NOMinative and ACCusative) may be attached as either a second object of the verb (as shown in (2a, b)) or as the first phrase of a new clause (as shown in (2c, d). The first option is referred to as NP conjunction; the second option is called clause conjunction. Previous work with simple conjunction ambiguities in English and Dutch (Frazier 1978, 1993) has demonstrated a preference for NP conjunction. One problem with work on simple conjunction is that a potentially disambiguating comma must be omitted from the stimuli to preserve the ambiguity (a comma signals clause conjunction). An advantage of multiple-conjunction structures is that the comma preceding the ambiguous phrase is itself ambiguous. It is required for both NP and clause conjunction.

It was hypothesized that the experiment would reveal a preference for NP conjunction as follows: the verb following the ambiguous phrase due to case marking in (2a) will produce longer reading times than the verb following an unambiguous counterpart (e.g. *"der Trainer"*) in (2b). From the structure-based perspective, this preference can be viewed as following from a preference for minimal structure, or as preference to attach new material to more-recently computed parts of the syntactic representation. In either case, it is a general, structural, preference as there is no lexical item in the sentence which might produce either a NP or clause conjunction bias. More specifically, such a preference to analyze an ambiguous phrase as a second object could not be interpreted as a verb-based preference. That is, the verb has already had its object requirement satisfied by the preceding noun phrase (*"den Apotheker"* in (1) and (2)). At the point at which the ambiguous phrase is processed, the prior clause is functionally complete, with all lexical and syntactic requirements satisfied. Therefore, an attachment preference for the ambiguous phrase cannot be due to properties of the material in the computed clause. Further, in multiple-conjunction structures, there is a prosodic break between the first and second noun phrases following the verb in both possible analyses of the ambiguity. This is of interest because work by Bader (1996) suggests that prosodic breaks are computed in reading as part of the phonological coding of the input and may serve to affect subsequent processing operations.

A further prediction is that reading times for the conjunction "*und*" in (2b) and (2c) will not differ because, in both versions, it is consistent with NP conjunction. NP conjunction is unambiguously signaled by the accusative-marked phrase following the verb in (2d), and is the hypothesized preferred analysis in (2c).

Thirty-two subjects participated in the experiment. Words were individually presented in the center of a computer screen, with rate of presentation controlled by the subject. To insure that subjects read for comprehension, each sentence was followed by a Yes/No comprehension question (e.g. "*Besucht der Dirigent den Apotheker?*" "Did the conductor visit the pharmacist?"). The reading-time results show that the verb following the ambiguous phrase in the (a) version produced significantly longer reading times than their counterparts in the (b) version. Reading times for the preceding noun phrase (feminine in (a); masculine in (b)) did not differ (This was true both for the determiner and the noun). Reading times for the conjunction in the (c) and (d) versions did not differ, nor did reading times for the determiner and noun of the preceding noun phrase. The longer reading times for the verb following the ambiguous phrase in the (a) versions is consistent with the hypothesis that this phrase was analyzed as an object of the first verb. That is, longer reading times reflect the cost of reanalyzing the computed structure so that the ambiguous phrase can function as subject of a new clause, which is signaled by the appearance of the verb.

Reading times for the noun phrase immediately following the verb did not reflect case differences. This is not unexpected, given recent reports that self-paced reading is less sensitive to disambiguation by nominal case marking than by disambiguation at the verb (Meng, 1996). It may be the case that the nominative noun phrase which forced the computation of a new clause (e.g. *"der Trainer"* in (b)) failed to show an effect of dispreferred disambiguation because there was no expectation of any particular continuation (prior to this noun phrase, there was only a complete clause). Given this, a nominative noun phrase does not violate an expectation of the parser's. In contrast, when the verb following *"die Trainerin"* is processed, there is an expectation of structure compatible with the NP conjunction analysis, and the verb violates this expectation. An ERP experiment will investigate the potential differential effects of disambiguation by case marking and by verb in multiple-conjunction ambiguities.

On the use of case information for verb processing **3.1.14**

Jacobsen, Th. & Friederici, A.D.

The question how linguistic case information is used during sentence processing is the focus of the present study. Jacobsen and Friederici set out to investigate the processing characteristics of morphological case marking in a cross-linguistic comparison between English and German. In particular the influences of sentential morphological case marking on lexical access of verbs are being studied. Interesting cross-linguistic effects can be expected, since the English language marks case primarily by word order and makes very scarce use of overt case marking, whereas in German morphological case marking is an omnipresent feature.

In cooperation with Prof. Bates and Prof. Swinney, both at the University of California, San Diego, USA, a set of experiments was designed in English in order to address this issue using wh-question constructions as stimulus material in a cross-modal on-line task.

As a pilot, off-line experiment, grammaticality judgments were gathered to establish which variant of morphological case marking in English wh-question constructions would be accepted as grammatically correct by American college students. Interestingly, no homogenous pattern of judgments was found. Interindividual differences were reflected in bimodal distributions of grammaticality judgments. Subjects, however, showed intraindividual consistency, indicating that the native speakers' usage of the English case marking system is in flux.

Verbs that do allow an accusative object but do not allow a dative object were selected. It was decided to use sentences of the following type as stimulus material, because it was the most accepted variant of a dative wh-question construction:

Whom has Pete |grabbed at the party when he was drunk?
* *To whom has Pete |grabbed at the party when he was drunk?*
|*<u>tribute</u>*

Three experiments with English speaking subjects, using cross-modal repetition naming and lexical decision techniques, combined with unrelated nouns as targets (underlined) presented in the vicinity of the main verb, were conducted. Sentences were presented auditorily and continously; targets were presented visually. A total of 48 experimental sentences was used. The results showed that the case marking violation had no influence on the lexical processing of the verb (e.g. *grabbed*), as indicated by the cross-modal naming latencies of the unrelated noun target (e.g. *tribute*). Two interpretations are possible: First, it could be that case-marking information is not used to guide verb processing in English (as compared to a heavily case marked language such as German), be it on-line or off-line. Second, it may be that case marking is not used to guide verb processing in general, be it in English or in German.

To further investigate these two possibilities two off-line and one on-line experiment were conducted with German sentence material. Two experiments investigated the relevance of accusative and dative case information for verb processing in German using a sentence completion task. Note that, in German the accusative and the dative case feature are in a prominent asymmetry. Linguistically, accusative is viewed as the default case. Accusative verbs are more frequent in German than dative verbs, with 3-argument-dative-verbs being more frequent than 2-argument-dative-verbs. Hence the former can be considered the default for the dative case.

72 sentence beginnings were constructed. 18 common female first names and 18 common male first names were combined with the auxiliary "*haben*" (have). Each of these 36 pairs was combined with an accusative (1) and a dative (2) question pronoun to form a sentence beginning. Subjects' task was to complete each sentence with a single word that formed a syntactically-correct sentence.

(1) *Wen hat Meike ...*
Whom has Meike ...

(2) *Wem hat Meike ...*
To whom has Meike ...

In the first experiment, 40 subjects were presented with a questionnaire that contained the 72 sentence beginnings in pseudo-randomized order. Results showed that subjects processed the case information correctly. The completions of the dative sentences, however, featured significantly more errors than those of the accusative sentences. Most of these errors were due to the subjects' using 3-argument-dative-verbs in a 2-argument sentence frame.

In a second experiment, 24 subjects were auditorily presented with the 72 sentence beginnings in pseudo-randomized order. Subjects were asked to enter sentence completions using a computer keyboard. Besides this difference, instructions equaled those of Experiment 1. Results showed that subjects processed the case information correctly. Response latencies and error rates were significantly higher for dative verbs. As in Experiment 1, most of the errors were due to the subjects' using 3-argument-dative-verbs in a 2-argument sentence frame.

Both experiments clearly showed that German subjects process case information to guide verb processing in this off-line verb generation paradigm. Moreover, they indicate that the access of accusative case is easier than the access of dative case during verb processing. An analysis of errors showed that the violation of verb-argument-structure occurred by far more often than a violation of case information.

An additional experiment using the same type of German sentence material was conducted using a cross-modal naming technique. This experiment failed to show an influence of morphological case marking on the lexical processing verbs.

The observed difference in the sensitivity to case marking information upon verb processing in the on-line and the off-line paradigm leads to the following consideration.

German subjects are sensitive to case marking information, however, either they are not able to use this information on-line or lexical information provided by the verb overrides initially processed case information. Further experiments using ERP measures are planned to disentangle lexical and morphological processes during verb processing.

Parsing theory and structural ambiguity in German

3.1.15

Gorrell, P.

The process of language comprehension involves the rapid integration of various types of information (e.g. phonetic, lexical, morphological, structural, prosodic, semantic). The study of language processing investigates the precise manner in which these different information types are accessed and utilized incrementally in real time. One focus of this research is syntactic processing (parsing): the on-line computation of a structural representation for the input. A necessary precondition for the study of syntactic processing is the specification of the properties of the structural representation computed by the parser. Gorrell (1996) proposes that, in German verb-second clauses, the observed preference for canonical word-order follows from a general preference for the simplest structural analysis consistent with the input (cf. the Minimal Attachment strategy of Frazier 1978).
Crucial for this proposal is a syntactic analysis in which subject-initial, verb-second, clauses are structurally less-complex than clauses with initial non-subject phrases (e.g. an object noun phrase or an adverbial phrase). Although it has been a common assumption in generative syntax that the sentences in (1) both involve a filler-gap relation (in which the initial noun phrase occurs in a pre-clausal position, having been displaced from a clause-internal position), recent work in syntactic theory points to the conclusion that this is only true of structures in which a non-subject is in first position, such as (1b).

(1) a. *Der Student sah den Mann.*
The student saw the man.

b. Den *Mann sah der Student.*
The student saw the man.

Adapting work of Travis (1991) and Grimshaw (1993), it is possible to outline a theory of the structure of German verb-second clauses which is consistent with observed parsing preferences. For example, a fully ambiguous structure such as (2) produces a strong preference for the subject-verb-object order.

(2) *Die Frau sah das Kind.*
The woman saw the child. (given the preferred reading)

Important for this approach to the processing of such ambiguities is that the proposed syntactic analysis not only offers the necessary distinction with respect to global structural complexity, but also that the complexity difference is evident precisely at the point in the parse sequence where the processor must compute either one structure or the other.

In general, the approach adopted here aims to make syntactic theory more responsive to processing concerns (by taking processing phenomena as valid data for syntactic theory construction) and theories of language comprehension more responsive to precise analyses of linguistic structure.

It is further argued that the observed preference for the type of ambiguity illustrated in (2) is problematic for parsing theories (e.g. Pritchett, 1992) in which the preference for one structure over another is ascribed to properties of verb-argument relations. A central property of such theories is that the parser prefers to structure a noun phrase as the argument of a verb already processed, rather than wait for a verb in subsequent input. For English, where the subject precedes the verb, but an object follows it, this type of approach is capable of accounting for a number of ambiguities in which an object analysis is preferred to a subject analysis. But, in German, phrase-order variation, as illustrated in (1), shows that the proposed argument-based strategies must be modified or made response to structural complexity. For example, in (2) whether the initial noun phrase is analyzed as a subject or as an object, it functions as an argument of the verb. Argument-based theories simply make no predictions concerning such ambiguities. This type of ambiguity provides an important test case for choosing between structure-based and theta-theoretic (or, semantic role) accounts of parsing preferences.
This approach can be extended to verb-final clauses and wh-structures (Gorrell, in press a.). Additional motivation for the proposal that subject-before-object clauses are structurally simpler than object-first clauses comes from research into the relation between argument structure and syntactic structure. Argument structure is an internally-structured listing of a verb's arguments which is sensitive to various thematic and aspectual properties (Grimshaw, 1991). In general, noun phrases which have high argument-structure prominence appear in a syntactic position superior to phrases with less prominence. Given the nature of a syntactic representation, the highest syntactic position is the leftmost. Subjects are the noun phrase with highest argument-structure prominence. The mapping from argument structure to syntactic structure yields a canonical subject-before-object order. Deviations from this order must be justified by other requirements (e.g. wh-phrases must be in initial position; focus requirements). The similarity between the preferences for declarative and wh-structures is illustrated in (3).

(3) a. *Die Frau sah das Kind*
The woman saw the child.

b. *Welche Frau sah das Kind*
Which woman saw the child. or Which woman did the child see.

Experimental investigations reveal that there is a processing preference to take the first noun phrase in both these examples as the subject of the sentence (e.g. Konieczny, 1996; Meng 1996; Schlesewsky et al., in press). The effect is more subtle (and less persistent) in (3b) than (3a), but a number of experiments in the literature reveal such a preference. An extension of this approach to wh-subject structures (also commonly assumed to involve a filler-gap construction) allows for a unification of the explanation for the preference observed in processing. As noted, this subject-before-object preference is stronger in (3a) than (3b), at least for sentences in isolation. This appears to follow from the fact that the sentence-level grammar requires a wh-object to be in initial position, whereas a non-wh-object requires some sentence-external justification (e.g. focus) to appear in initial position.

This preference for the minimal structure is also evident in verb-final clauses such as those in (4).

(4) a. ... *daß der Student den Mann sah.*
that the student saw the man

b. ... *daß den Mann der Student sah.*
that the student saw the man

c. ... *daß die Frau das Kind sah.*
that the woman saw the child

Also discussed is the relation between the general, initial, preference for comparatively simple structures in syntactic processing and the need to keep short-term memory load to a minimum. A number of different approaches exist in the literature. Specifically discussed is the proposal of Schlesewsky et al. (in press) which attributes the subject preference, not to a general preference for minimal structure, but to the particular manner in which nodes in a syntactic structure are computed and stored. A number of empirical problems with this approach are noted, and it is argued that the general preference for minimal structure is to be preferred on both empirical and conceptual grounds.

In recent years there has been renewed interest in the process of reanalysis required when the initial structural analysis of linguistic input is disconfirmed by subsequent information. A theory of syntactic reanalysis is connected in numerous ways to a theory of first-pass analysis. For example, the representational properties of the output of first-pass operations are important determinants of the properties of reanalysis. Given this, there must be close links between first-pass analysis and reanalysis operations. One common assumption concerning syntactic representation is that it is a phrase-structure tree. A tree has certain specific properties. One central property is that any two nodes in the structure must be in either a dominance or a precedence relation. From the perspective of incremental processing, this means that input is being structured such that dominance and precedence relations are being computed on-line.

An important property of both first-pass and reanalysis operations is Structural Determinism, which proposes that a parse sequence in which dominance or precedence relations must be altered is more costly than sequences in which preserve these primary relations (Gorrell 1995, in press b.). If the parser is initially building the simplest structure possible, then incorporating new input will involve additions to the computed representation (which preserve dominance and precedence relations), rather than alterations (which restructure the tree). For example, if a case-ambiguous noun phrase in first position is initially analyzed as a subject (the simpler structure), reanalyzing it as an object will involve only structure addition, not structure alteration. This is not the case for a hypothetical object-to-subject reanalysis. In general, there appears to be a well-designed fit between the initial preference for the simplest structure and Structural Determinism. If the minimal structure is initially computed, then changes to the structure are most likely to involve structure addition.

This approach also allows for a unification of apparently distinct parsing preferences. For example, the initial subject preference for ambiguous wh-phrases has been argued to follow from a preference for certain filler-gap configurations over others (roughly, a preference for the leftmost gap site). But this preference has been difficult to demonstrate in cases where there is no complexity difference (e.g. an ambiguity in which an initial wh-phrase may be analyzed as either the first or second object of a dative verb). It is argued that the best analysis involves a general preference for the simpler structure (wh-subjects preferred to wh-objects), with the processing of object-object ambiguities affected by other factors (e.g. a particular verb's lexical preferences).

This research program examines working memory processes and their functional representation in the brain. Working memory refers to a brain system that provides temporary storage and manipulation of information necessary for a large variety of cognitive tasks. In this research program working memory is not only specified in terms of the different types of information to be processed like visual, spatial or temporal information but also in terms of specific memory processes like encoding, storage and retrieval. Behavioral and neuropharmacological measures as well as electrophysiological measures (EEG) and functional imaging techniques (SPECT) from normal subjects are used to make inferences about the functional architecture of working memory processes as well as the brain structures subserving these processes. The on-going research focuses on storage and retrieval processes for visuo-spatial information (3.2.1 & 3.2.2) as well as visuo-spatial and verbal information (3.2.3. & 3.2.4). Three other projects examine rehearsal processes for temporal and visuo-spatial information (3.2.5 & 3.2.6) and for sequential information (3.2.7). Moreover the role of attentional controll processes in working memory are invesigated in 3.2.8 and 3.2.9.

3.2.1 The neurocognitive systems underlying recognition memory for object forms and object locations

Mecklinger, A.

Recent research suggests that the processing of object and spatial information in the primate's visual system involves functionally and anatomically different systems, a "what" and a "where" system, respectively. An important question on the neuroanatomical basis of memory is whether the functional and anatomical dissociation in the visual processing of "what" and "where" information can be extended to memory processes. For example, recent models of recognition memory assume that the same neuronal pathways involved in perceptual processing of these two types of information are also active during storage and retrieval of these information types. In studies in which recognition judgements were monitored by ERPs, correctly identified old items were found to elicit more positive going waveforms than correctly identified new items. These old/new effects in the ERP waveforms are assumed to reflect the sucessfull retrieval of memory information.

In 1995 a paradigm was developed which allows to examine retrieval operations for object forms and object locations using identical study phases and test phases for both information types (see Annual Report 1995). Subjects memorized object forms (i.e. abstract geometrical objects) and their spatial positions within a 3 x 4 spatial matrix. Prior to the test phase a task-cue informs the subjects whether they have to make recognition judgements based on object forms or object locations. This paradigm enables us to examine ERP activity in the preparatory phases after cue presentation as well as old-new differences as a function of recognition task. In two ERP experiments task specific topographies of the old/new effects were obtained, with these effects being anteriorly distributed during object recognition and posteriorly distributed in the spatial recognition task. These results have been taken as evidence that different neuronal systems are engaged when object forms or object locations are retrieved from working memory. In 1996 two further experiments were conducted. Experiment 1 addressed the issue whether visual or verbal representational formats are used to rehearse object forms and object locations in this paradigm. Using the dual task interference approach, three interfernce tasks, a visual, a verbal and a non-interference task were interpolated between the study in the test phase of the two recognition tasks. The assumption was that if verbal labels (i.e. object names and verbaly recorded positions) are used to rehearse both types of information, recognition memory should be selectively impaired by the verbal interference task. The results indicate that object and spatial recognition memory were selectively impaired by the visual interference task relative to the non-interfernce task but not by the verbal interference task. This pattern of results supports the notion that visual representation formats are used to rehearse object forms and object locations in this recognition memory paradigm.

The major goal of the second experiment was to estimate the neuronal systems contributing to the scalp recorded old/new differences. ERPs were recorded from 64 channels while subjects made recognition judgements on object forms (familiar objects with low complexity) or object locations. As in the previous studies the old/new differences in the 300 to 600 ms time range were anteriorly distributed for object forms and posteriorly distributed for object locations. These results are displayed in Figure 1. Employing a spatio-temporal dipole modelling approach the neuronal generators for the old/new effects were found in the medio-basal temporal lobe. Interestingly these dipoles were located approxiomatelly 4 cm more anterior for object-based as compared to spatial-based old/new effects. These results are taken to tentatively support the view that anterior parts of the medio-basal temporal lobe mediate the retrieval of visuo-semantic object information whereas posterior portions of the medio-basal tempral lobes are engaged to a larger extent in the retrieval of more percept-like spatial information

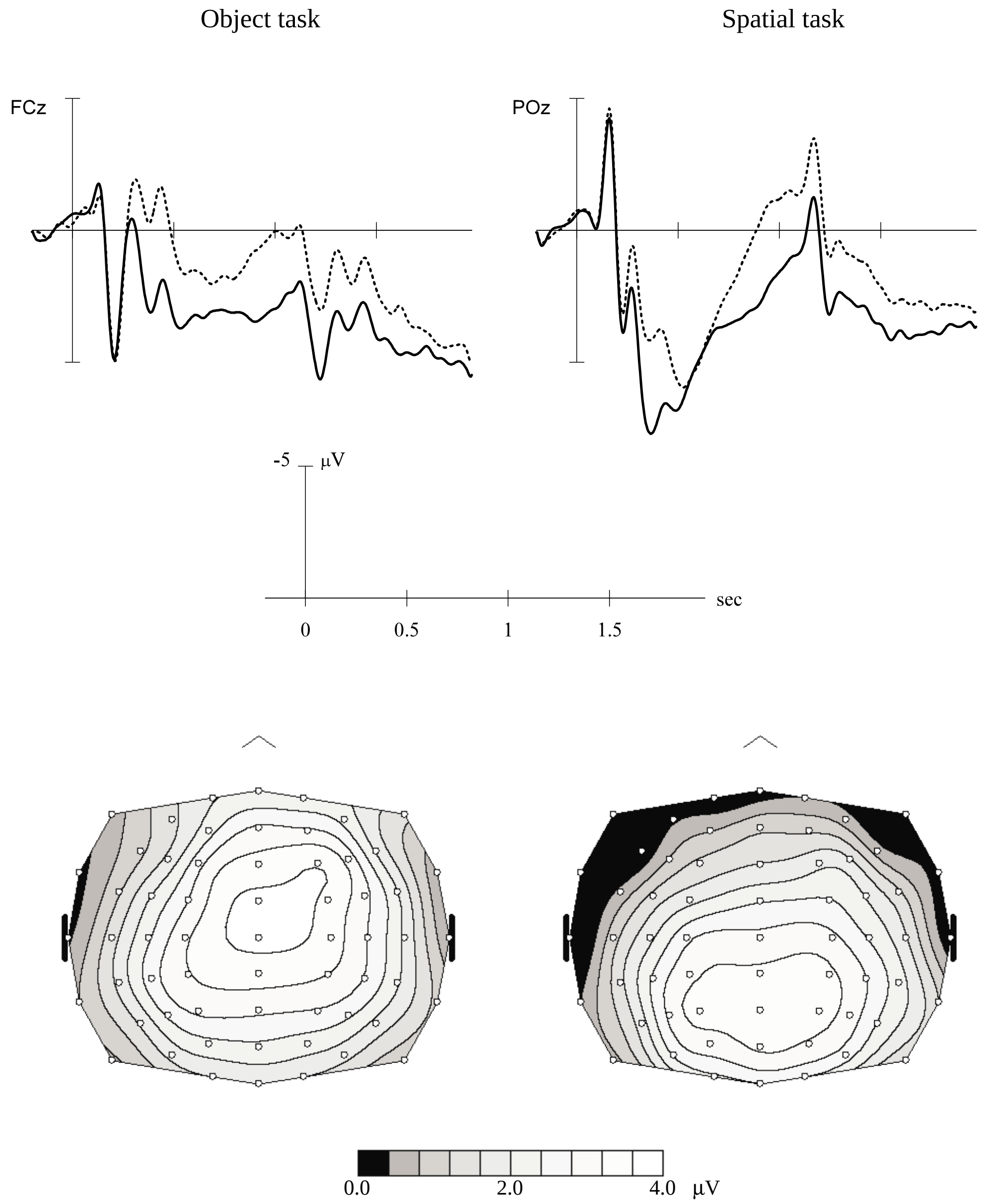


Figure 1. ERPs evoked by old (solid line) and new responses (dotted lines) in the object and spatial recognition task at an anterior (object task) and a posterior recording site (spatial task). The corresponding topographic distributions of the differences between old and new responses, 400 ms after stimulus onset are displayed in the lower part of the figure.

3.2.2 Dopaminergic modulation of visuo-spatial working memory with bromocriptine and pergolide

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

Studies with single-cell recording in monkeys and functional neuroimaging methods in man have shown that the prefrontal cortex plays an important role in mediating working memory, i.e. the short-term maintainance of information that is necessary for on-going decision-making (Fuster, 1995; Goldman-Rakic, 1995). The performance of monkeys in visuo-spatial delay-tasks can be specifically modulated by dopamine agonists and antagonists (Goldmann-Rakic, 1992). Therefore a special "dopamine link" of working memory mechanisms within the prefrontal cortex has been proposed (Desimone, 1995). Studies with intracerebral application of dopaminergic agents claim a particular role of the D1 receptor subtype for the modulation of delay-related neuronal activity (Williams & Goldman-Rakic, 1995). This finding is in accordance with the tenfold higher cortical density of D1 receptors as compared to D2 receptors. The functional role of other dopamine receptor subtypes and of D2/D1 receptor interactions still remains unclear.

In order to further investigate the dopamine link of working memory in man, and to look for differential D1 versus D2 receptor contributions, we assessed the effects of bromocriptine, a specific D2 receptor agonist, and pergolide, a mixed D1/D2 receptor agonist, in a visuo-spatial delayed matching task. In a first experiment 12 male volunteers received either 0, 2.5 or 5 mg of bromocriptine on three separate days in a balanced double-blind design. 16 volunteers completed our second experiment and received either placebo or 0.1 mg (per 80 kg body weight) of pergolide. To reduce side-effects we administered a pretreatment with domperidone, a peripherally active D2 antagonist. Our third experiment is an extension of experiment one. In order to compare the two substances we administered 2.5 mg (per 80 kg) of bromocriptine or placebo to another 8 male volunteers. Regular blood samples were taken to measure prolactin levels. The intra- and inter-individual comparison of prolactin inhibition makes it possible to monitor biological effectivity and the individual time-course of action.

Our working memory paradigm was a visuo-spatial delayed matching task implemented on a personal computer. The subjects had to memorize the location of a random-generated 7-point pattern (sample) and to compare it after 2, 8 or 16 sec. with a second pattern (match) that was either equal or slightly shifted within the frame. The task was designed with the intention to present unique stimuli at each trial and to require minimal motor demands. The main task consisted of 180 balanced trials and lasted about 50 minutes. To further monitor the effects of drugs on arousal and mood, pencil-paper tasks of attention (d2-Test, ZVT) and psychological ratings (BfS, STAI) were performed.

As predicted from pilot studies the paradigm showed significant ($p<0.01$) increases of errors with longer delays. Bromocriptine did not significantly reduce the error rate or reaction times in neither of the three conditions. For pergolide there was a trend ($p=0.083$; drug by delay) to improve visuo-spatial working memory (Fig. 2), this facilitation was significant ($p<0.05$) when relative error increases (error $\text{rate}_{16\ sec}$ - error $\text{rate}_{2\ sec}$) were calculated. Error increases were not due to faster reaction times, i.e. there was no speed-accuracy effect (Fig. 3). No significant effects of the two dopamine agonists on conventional measures of attention and mood were seen.

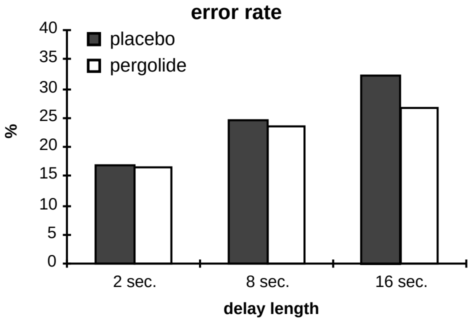


Figure 2.

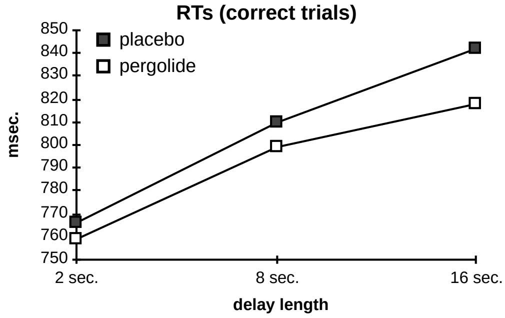


Figure 3.

In our first experiment we could not replicate the findings of Luciana et al. (1992) who showed a facilitation of working memory by 2.5 mg of bromocriptine in a somewhat different visuo-spatial delayed response task. The divergent results might be explained by minimal motor demands in our delayed matching paradigm (button press) as compared to the delayed response paradigm (pointing movement). D2 agonists might rather improve the preparation and release of motor programs on the level of the basal ganglia than act on delay neurons via cortical receptors. Our findings in the pergolide and pergolide versus bromocriptine experiments are, however, in good accordance with the monkey literature. This is the first study in man that shows a preferential role of the D1 receptor in working memory modulation.

To further investigate the effects of D1 receptor stimulation on working memory processes the approach will be extended to studies with more sophisticated pharmacological manipulations and to experimental designs with verbal and visual working memory paradigms including inhibitory processes (directed forgetting). Combined pharmacological and neuro-imaging (ERPs, fMRI) studies are planned to investigate the temporal and topological characteristics of interactions between neurotransmitters and the neuronal networks of cognition.

3.2.3 Rehearsal processes in working memory: Effects of information type and coding formats as revealed by high density ERP recordings

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

There are two fundamental dichotomies with respect to the information processed in working memory. First, there are verbal and figural formats. Second, there is object and spatial information. A large amount of experimental research indicates that object and spatial information is processed separately in both visual perception and visual working memory, but it is less clear whether there is a corresponding functional separation in the verbal domain. To investigate this issue, the electrophysiological approach, i.e. the measurement of event-related-potentials (ERPs), is promising. For example, Mecklinger and Pfeifer (1996) showed that during the retention of object forms or spatial locations in visual working memory, task specific slow wave patterns emerge. Retention of object forms is associated with frontal negative slow waves whereas retention of spatial locations elicits parieto-occipitally focused negative slow wave patterns. It can thus be assumed that rehearsal of object forms and spatial locations can electrophysiologically be dissociated, with the scalp topography of negative slow waves reflecting the type of information retained in working memory.

To address the issue of coding formats, a modified S1-S2-paradigm was developed. In S1 the subjects saw two geometrical objects at two positions in a simulated three-dimensional space. This object and spatial information had to be retained for later comparison with S2. The S1-S2-interval lasted five seconds and midway through this interval a cue was presented indicating if either object or spatial information needs to be compared at S2. Upon presentation of S2 an old-new decision was required. In one half of the trials S2 was figural, as was S1 (figural condition), whereas in the remaining half of the trials the objects and their respective positions at S2 were presented as written words (verbal condition). The verbal and the figural conditions were blocked and this experimental manipulation was assumed to induce either verbally or figurally based rehearsal.

Experiment 1:
To examine the extent to which figural or verbal rehearsal is induced by this paradigm, a behavioral experiment was performed in which the memory tasks were combined with an articulatory suppression task, i.e., in one half of the trials subjects had to count backwards during the entire rehearsal interval. Analysis of error rates indicates that subjects used verbal formats in the verbal condition. It also revealed a tendency for objects to be coded verbally in the figural condition which was not the case for spatial locations.

Experiment 2:
In this experiment the EEG was recorded from 72 channels while subjects performed the S1-S2 memory task described above. Prior to the cue for both conditions negative slow wave activity was right lateralized at posterior recordings and also more pronounced in the verbal condition. When the cue indicated that object information is relevant for the S2 comparison, in both the figural and verbal condition a frontally focused negative slow wave, starting at 700 ms and extending for several hundred ms, was obtained. For spatial information, a parietally focused negative slow wave with a similar time course was found in the verbal task and less pronounced in the figural task. For both object and position comparisons, cues in the figural condition but not in the verbal condition evoked a negative component at around 500 ms which was most pronounced at the frontal recordings.
These results replicate those reported by Mecklinger & Pfeiffer (1996). Moreover they suggest that the ERP pattern correlated with the rehearsal of object forms and spatial locations are highly similar for figural and verbally recoded stimuli. In addition, in the figural but not in the verbal condition a frontally focused, phasic ERP component was found. It may either reflect attentional shifts towards figural representations per se or an attentional shift within the figural domain towards the relevant type of information. The latter hypothesis implies that the corresponding shift in the verbal domain is less effortfull and therefore does not produce a related ERP component.

Experiment 3
In order to investigate the functional significance of the frontal component, the design of Experiment 2 has been cut down on the object task with the cue now indicating whether S2 is verbal or figural. The EEG was recorded from 120 channels. All slow wave patterns related to the object task in Experiment 2 were replicated in this experiment but the frontal component was absent. This result rules out the first hypothesis stated above and provides some evidence for the second interpretation.

Experiment 4
In Experiment 2, the slow wave patterns could only be quantified as relative differences between the object and the spatial memory tasks. In order to get a more precise picture about the timing and the scalp topography of the task-related slow wave pattern obtained in Experiment 2, a third memory-unspecific task was added to the S1-S2 paradigm. This task serves as a baseline for the quantification of task-specific slow wave patterns. The results indicate that parieto-occipital negative slow wave activity was present in both the figural and verbal spatial task between 700 and 1500 ms. In contrast, in the two object tasks, dipolar slow wave patterns (i.e., frontally focused negativities and parieto-occipitally focused positivities) were obtained in this time period. After 1500 ms negative slow wave activity was most pronounced at left frontal recordings in all four task conditions relative to the baseline task.
In summary, there are two possibilities to explain the data obtained so far: First, the results might indicate that different cortical areas are involved when object and spatial information are rehearsed in working memory, with these areas being highly similar for figural and verbally recoded stimuli. Another, more likely interpretation would be, that posteriorly distributed negative (and positive) slow potentials reflect the temporary activation (and inhibition) of a visuo-spatial rehearsal system whereas the (left) frontally distributed negative slow wave patterns are correlated with the engagement of a more elaborated rehearsal system being based on abstract, verbal codes. The time course of the slow wave pattern obtained in Experiment 4 suggest that the former system is engaged earlier and shows and earlier decay whereas the latter system is not engaged before 1000 ms and holds information in a more durable form.

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

Mecklinger, A. & Busch, A.

Recent functional imaging studies and studies of patients with brain lesions indicate that the ventral pathway, connecting the occipital lobe with the inferior temporal lobe is differentially engaged in the processing of different objects features. While it is well established that different parts of the inferior temporal lobe mediate the processing of faces and objects, not much is known about the brain systems engaged in processing objects and words. The major goal of the present study was to investigate the brain activation related to perceptual and conceptual processing of objects and words in the visual domain. More specifically the analysis focused on the differences between the ERPs evoked by repeated (i.e. old) and unrepeated (i.e., new) pictures and words.

20 subjects performed a semantic classification task in which nonsense words and nonsense pictures had to be detected in a series of legal pictures and words. The pictures and words were from a standardized set of line drawings (Snodgras & Vanderwart, 1980). Nonsense words were pronounceable non-words whereas the nonsense pictures were constructed by interchanging parts of the line drawings between and within pictures. These target stimuli occurred with a probability of 20%. To examine perceptual and conceptual aspects in the processing of pictures and words, four different repetition conditions were constructed: A picture could be followed by the same picture (PI-PI) or by the word denoting this picture (PI-WO). Analogously words could either be followed by the same word (WO-WO) or by a picture denoting the meaning of the word (WO-PI). The EEG was recorded from 64 channels and ERPs were calculated for each of the four repetition conditions.

Analysis of performance data indicate that subjects classified nonwords and nonpictures with an accuracy of more than 98% with these classifications being about 20 ms faster for non-pictures than for non-words. For all four repetition conditions reliable old/new effects were found. Repeated pictures evoked more positive going ERPs than not repeated pictures. This old/new effect for pictures started around 350 ms and was most pronounced at the frontal recordings. The old/new effect for words (WO-WO) had about the same onset but was largest at the central recording sites. Moreover repeated words in contrast to not repeated words evoked an additional broadly distributed negative peak at about 200 ms. In contrast to these within-domain repetition effects, across-domain repetition effects (PI-WO; WO-PI) did not emerge before 380 ms. Similar to the within-domain repetition effects the across domain repetition effect for pictures was more frontally distributed than for words.

These preliminary results suggest that the brain systems engaged in processing pictures and words can electrophysiologically be dissociated. Additional analyses will focus on perceptual and conceptual repetition effects for both, pictures and words. In addition, spatio-temporal dipole analyses will be performed to estimate the neuronal sources contributing to the scalp-recorded old/new effects in each of the repetition conditions.

3.2.5 Functional and topographical dissociation in the processing of spatial and temporal information in working memory

Schubotz, R. & Friederici, A.D.

Recent research suggests that the storage and manipulation of basic types of information (e.g. spatial information, object information) is subserved by functionally and neuroanatomically dissociable subsystems of working memory. There is converging evidence for a "what"-system, specialized for the processing of object information, and a "where"-system specialized for the processing of dynamic and static spatial information. Based on neuropsychological studies indicating the importance of frontal lobe structures for the processing of temporal information in particular, we set out to investigate if the modularity assumption holds as well for the processing of temporal information.

On the assumption that two cognitive processes interfere to the extent to which they make simultaneous demands on the same processing systems, we used the selective interference paradigm to find further behavioral evidence for a functional dissociation of spatial and temporal information processing in working memory.
According to the selective interference paradigm, the performance in a spatial memory task should be selectively impaired by a secondary spatial task (because both tasks rely on the same cortical areas), but not by parallel processing of temporal information. In analogy, performance of a temporal task should be selectively degraded by parallel processing of temporal information (but not by processing of spatial information), because both tasks might rely on the same neuronal structures.

In order to test these assumptions, we therefore combined temporal information tasks and spatial information tasks with each other as primary and secondary tasks in a simple dual-task-paradigm in a set of three behavioral experiments.
In the first experiments, 18 subjects (mean age 25.1) performed three memory tasks which were completely crossed with each other as primary and secondary tasks and a non-interference control condition. Subjects were required to indicate whether two stimuli were the same with regard to (a) the duration of presentation, (b) the spatial location, or (c) the spatial relation.
In the second experiment 16 other subjects (mean age 23.7) performed (beside further tasks which will not be reported here) the same tasks like in the first experiment, slightly modified in difficulty.
In the third experiment, four memory tasks (two static, two moving stimuli tasks) were combined with two secondary tasks and a non-interference condition. 16 subjects (mean age 22.6) were required to indicate whether two stimuli were the same with regard to (a) the duration of presentation, (b) the spatial location, (c) the speed of rotation, or (d) the distance of rotation.

The results of the three experiments confirmed that a combination of tasks with identical type of information (time/duration or space/location) yield a significantly higher error rate than the combination of different information-type tasks.
The spatial relation task (second experiment), involving mental rotation, displayed an interference effect in combination with both types of secondary tasks. Giving evidence to the assumption that mental rotation as a movement requires spatial as well as temporal coordination.
In contrast to the actively imagined movement of mental rotation, the passively perceived movement in the movement memory tasks (distance of rotation and speed of rotation, third experiment) did not interfere with temporal but with spatial secondary tasks. This effect was explained by the assumption that the processing of combined information (temporal and spatial components) relies on spatial features, if possible.
The result of all three experiments support the hypothesis, that temporal and spatial information processing can be functionally dissociated.

In a current event-related potential (ERP) study we investigated the question whether and how the behaviorally-established functional dissociation of temporal and spatial information processing is realized in terms of neuronal structure and organization.

Two S1-S2 memory tasks were employed in both the auditory and visual modality. Subjects were required to indicate whether two stimuli were the same with regard to (a) duration of presentation or (b) spatial location. They had to perform a visuo-spatial task (position of a visually presented square), a visuo-temporal task (duration of the visual presentation of a square) and two different auditory temporal tasks (duration of an auditory presented tone or an auditory presented phonem).
ERPs were recorded from 64 channels of the 10-20-system during the S1-S2 interval.

For the visual tasks there was a parietally focused positivity from 200 to 600 ms post-stimulus onset (S1). Auditory stimuli elicited a frontally maximal negativity between 280 and 700 ms, a parietal positivity between 600 to 1000 and a second positivity between 1200 to 6000 ms (end of the S1-S2 interval). Independent of modality, temporal memory tasks dispayed a frontal negativity between 1000 and 2000 ms, whereas the spatial memory task shows a parietal negative going shift between 700 and 3000 ms post-stimulus onset.
The data suggest the distinction of three processing phases: modality-specific encoding, additional information-specific encoding, and modality-specific pre-response decoding. We conclude that processing of temporal and spatial information (as well as modality-specific processing) is not only functionally dissociated, but also realized in topographically distinct neuronal structures.

3.2.6 Rehearsing object forms, object location and temporal duration: A combined SPECT and ERP study of information specific working memory processes

Mecklinger, A., Friederici, A.D., Knapp, W. & Schedel, U.

Recent functional imaging studies suggest that different cortical and subcortical brain areas are engaged when different types of information have to be retained in working memory for a period of several seconds. While functional imaging techniques like PET, SPECT or fMRI provide a reasonable spatial resolution to examine information specific working memory processes, electrophysiological measures like ERPs offer a high temporal resolution to examine working memory processes which operate on a sub-second time scale. The major goal of this project is to combine the SPECT and the ERP technique to examine the spatio-temporal dynamics of working memory processes when object, spatial or temporal information (i.e. duration of presentation) has to be retained in working memory.

Three memory task and corresponding perceptual “baseline” tasks were designed. In the *object memory task* four abstract geometrical objects (S1) had to be retained in working memory for a period of 5 seconds for comparison with a subsequent S2. In the *spatial memory task* the two dimensional layout of four small squares had to be retained for the same time period whereas in the temporal task, the duration of a dot, presented in the center of the computer screen had to be retained. In all three memory tasks the retention interval had a duration of 5 s and an “old/new” decision was required upon presentation of S2. A pilot experiment was performed to adjust the task difficulty across the three memory tasks. In the three corresponding perceptual tasks the same physical stimuli were employed as in the memory tasks, however the S1-S2 intervals were reduced to 250 ms. The duration of all six tasks was restricted to 8 minutes.

In this year (1996) the SPECT data were collected from 30 subjects. 10 subjects performed one of the three memory and perceptual task combinations, with each subject participating in three experimental sessions: After a training session, regional cerebral blood flow (rCBF) was measured in two different sessions while the subjects performed either the memory or the perceptual task. The radionuclide imaging procedure included injection of 350 MBq Tc-99m-ECD (Neurolite) into an antecutibal vein ca. 1 minute after the onset of the memory/perception task. 15 minutes after the end of the tasks rCBF activity was registered by means of a rotating gamma camera system (CERA-SPECT) with a spatial resolution of 6-8 mm.

Collection of the SPECT data is finished and analyses of the performance and rCBF data is in progress. As expected, task performance was highly similar for the three memory tasks (ca. 80% correct responses) and the three perceptual tasks (ca. 95% correct responses). For the analysis of the rCBF data subtraction images (i.e., memory - perceptual task) will be calculated to obtain an estimate of the cortical and subcortical systems engaged in the rehearsal of object, spatial and temporal information. The ERP data will be collected from the same subjects in 1997.

3.2.7 Exploring sequential processing in visuospatial working memory

Bublak, P.

Verbal working memory is assumed to comprise a modality specific (phonological) store and an active rehearsal loop (Baddeley, 1986). A similar model was proposed for visuospatial working memory (e.g. Logie, 1995), but was not supported by the same bulk of evidence as is the case in the verbal domain. A recently published paper (Jones et al., 1995) proposed a functional equivalence of verbal and visuospatial *sequential* working memory, based on similar serial position curves and interference effects for both types of information. The hypothesis of a functional equivalence between verbal and visuospatial memory, together with the assumption of a similar organisation of these two representational systems, predicts the existence of three effects in testing sequential visuospatial working memory, which were explored in three experiments.

Experiment 1 investigated a visuospatial similarity effect in sequential visuospatial memory by comparing a sequential with a simultaneous presentation of visuospatial items (dot locations), using a 2AFC-item recognition paradigm. Subjects were presented with six items either simultaneously or sequentially (1 sec per item). After a brief delay (5 sec), they had to decide, which of two simultaneously presented items was part of the memory set of six items seen previously. By varying the distance between the two comparison items (near versus far), two conditions of difficulty were realized. The results show a comparable effect of distance for both conditions of presentation. This is compatible with a visuospatial similarity effect supporting the store component of the working memory model even in the case of sequentially presented items. There was, however, an overall better performance in the simultaneous condition, probably arising from more efficient encoding of simultaneously presented dot locations. Further investigations are required to test the factors influencing encoding efficiency.

Experiment 2 investigated the interaction between the temporal and spatial distance of visuospatial items (dot locations). Six items were presented sequentially (1 item per second), followed by a short delay (5 sec). After the delay, subjects had to make a recency judgement for two simultaneously presented studied items. There were two conditions of spatial distance ("near" versus "far") and five conditions of temporal distance. The results indicate an interaction between temporal and spatial distance: subjects performed equally well in both spatial conditions when there was a close temporal relation between the items, but better in the "far" condition, when items were temporally further separated. These results are compatible with the functional relation between a store and a rehearsal component of working memory. The results are valid, however, only for those subjects reporting visual strategies. Further investigations, using a task interference paradigm, will be necessary to prevent subjects from using a verbal strategy.

Experiment 3 was concerned with the question, if chunking of visuospatial items was possible. Two conditions were realised. The first one was a sequential presentation of six items (500 ms per item), the second one a presentation of twelve items. The temporal presentation rate of the second condition was designed to induce a pairwise encoding of six item pairs. A recency judgement concerning two temporally adjacent studied items had to be made after a brief delay (5 sec). The results show qualitative similarities between condition 1 and condition 2. For example, in both conditions there is a recency effect and performance is worse for horizontally located items. In condition two, there is no performance difference between the two items within one item pair. Overall performance is better in condition 1, however. These results indicate, that chunking of visuospatial items is possible, but not very effective.

3.2.8 Processing novel and deviant auditory stimuli: An event-related potential and dipole-model analysis

Opitz, B. & Mecklinger, A.

Recent research indicates that the mismatch negativity (MMN), a fronto-centrally negative ERP component peaking around 200 ms is associated with auditory memory processes. This MMN is evoked by deviant stimuli in a repetitive auditory environment. In contrast, uninstructed novel auditory events generate a fronto-centrally distributed positivity, the novel-P3, peaking around 300 ms. While the MMN has been associated with automatic change detection processes, the novel P3 is assumed to be related to the momentary shift of attention towards unexpected environmental changes. According to Näätänen (1992) the detection of a 'mismatch' between a novel stimulus and a representation of the environment in auditory sensory memory is necessary to elicit the novel P3 component. However, it is unknown so far to what extent the early proportions of the novel P3 and the MMN arise from similar neuronal networks. Thus, the major goal of the present study was to examine the neuronal networks underlying deviancy and novelty processing in auditory memory.

This study used high-density (128 channel) event-related potentials to examine the neuronal correlates of processing novel and deviant auditory stimuli in more detail. Blocks of stimuli were presented containing either 20% novels or 20% frequency deviants (two tone conditions) or 10% novels and 10% deviants (three tone condition). Novel stimuli were selected from 165 unique sounds. In a pilot study these sounds were classified according to their meaning and subsequentely divided into two subgroups: meaningful and nonmeaningful novels. Subjects either performed a tracking task (unattend condition) or silently counted the deviants (attend condition).

In the unattend condition, deviant tones generated a frontally distributed negativity between 170 and 250 ms with polarity reversal at the mastoids. This negativity was defined as the MMN. It was highly similar in timing and scalp topography in the two tone and the three tone conditions. Both types of novel stimuli generated a large anteriorly distributed novel-P3, peaking around 270ms in the two tone as well as in the three tone conditions.

In the attend condition the MMN was increased in amplitude and followed by a topographically different N2b and a parietally maximal P3b. Although the amplitude of the P3 for both novel types was increased in the attend condition, this effect was larger for the nonmeaningful novels. The difference between the P3 amplitudes to meaningful and non-meaningful novels was largest at parietal electrode sites. This result might indicate a higher degree of “targetness” for nonmeaningful novels as compared to meaningfull novels in the attend condition. Furthermore, we obtained a parietal more-negative waveform with right hemisphere dominance subsequent to the P3 for the meaningful novels, as compared to the nonmeaningful ones. This negativity could be interpreted as a N400 component, possibly reflecting the conversion of meaningful sounds into a verbal category and the access to semantic memory.

The scalp potential distribution for the early (170-250ms) proportions of the deviant and novel waveforms in both, the attend and unattend conditions is highly similar, despite the reversed polarity of the MMN and novel-P3. Equivalent current dipole (ECD) analyses suggest that similar neuronal networks including the auditory cortices (same dipole orientation for novels and deviants) and more superior and medial cortical regions (opposite dipole orientation for novels and deviants) are involved in generating this scalp potential pattern. Preliminary ECD analyses suggest that for later, in contrast to earlier, proportions of the deviant and novel waveforms different cortical regions are activated. These results might indicate that early processing (i.e., change detection) is highly similiar for both stimulus types, whereas differential processeing for novels and deviants does not occur before 250 ms.

The ambiguity related to the precise location of activated brain structures which is inherent in the dipole modeling approach will be resolved by using whole-head MEG recordings and by combining the spatio-temporal modelling approach with structural and functional imaging techniques providing neuroanatomical constraints for the inverse solution. The development of MEG and fMRI experiments is in progress and further analyses of the ERP data will be provided to obtain additional evidence for the present dipole modelling results.

3.2.9 Subprocesses underlying predictable switches between cognitive tasks

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

Cognitive processes require control processes to organize them. These executive mechanisms are assumed to be part of the working memory system and also functionally distinct from the processes they organize. The architecture of these executive mechanisms, however, is poorly understood so far. In this project we examined the executive mechanisms required to voluntarily shift between two simple intentions. More specifically, we investigated task-set reconfiguration while subjects switched between two simple cognitive tasks. Previous studies have shown that multiple processes like residual activation of the task-set of the previous trial, or response tendencies triggered by the presence of task-irrelevant stimulus features can contribute to the costs of switching between two tasks (Rogers & Monsell, 1995). Therefore the analyses focused on a decomposition of the subprocesses underlying task switch costs.

Twenty subjects performed two tasks in each of which three objects were presented at different locations on a computer screen. They were either required to classify the objects as rounded or edged or to classify the location of the upper and lower objects relative to the objects presented in the middle of the screen. A task-cue (i.e., background screen color) was provided on each trial and subjects switched between the tasks on every second trial. Two experimental conditions were examined: In the neutral condition the irrelevant attributes (those to which the subjects had to respond when performing the other task) were not presented to the subject whereas in the crosstalk condition, the irrelevant attribute could either be mapped to the same response (congruent) or the other response (incongruent) as the relevant attribute. These two conditions allow to examine the contribution of task-cuing and cross-talk effects to the switch costs.

When subjects had to switch between two tasks, large switch costs (slower reaction times and increased error rates) emerged as compared to the conditions when the same task was performed repeatedly. Further analyses showed that these switch costs were larger in the crosstalk than in the neutral condition. Within the crosstalk condition they were larger for incongruent than for congruent trials. These results indicate that the activation of primed (previously performed) task set interferes with the execution of an actual task set. These task-cuing effects seem to outweigh the benefits on congruent trials in the crosstalk condition in which the irrelevant attributes were mapped on the same response as the relevant one.

Currently a modified task version is developed in which subjects have to switch on every fourth trial. Both task versions will be employed to examine executive mechanisms in frontal and temporal lobe patients in near future.

CLINICAL NEUROPSYCHOLOGY 3.3

DAY-CARE CLINIC 3.3.1

Since many fundamental questions in cognitive neuroscience ask for complementary investigations with both healthy volunteers and brain-injured patients, a day-care clinic for 25 neurological patients with mainly cognitive or language deficits was founded at the University of Leipzig (Director: Prof. Dr. D.Y. von Cramon).

The clinic was opened on February 5th 1996. During the first year 108 patients took part in the program, some of them several times. Patients with brain injuries due to different etiologies are treated, the main etiological groups being

- cerebrovascular diseases (infarction of the brain, intracerebral haemorrhage)
- neurosurgical diseases (aneurysms, AV malformations, brain tumors)
- cerebral hyopxia
- traumatic brain injuries

The clinical staff consists of 29 members coming from 10 different vocational domains, among them physicians, neuropsychologists, speechtherapists and a computer engineer. Building up the clinic, basically meant development in four different domains:

1. Recruiting patients and establishing a stable clinical supply, including cooperation with other units of the Leipzig University Medical School.
2. Advanced training for therapists in order to teach them for the special field of neurospychological rehabilitation with brain-injured patients.
3. Organization of logistics and administration in the day-care clinic.
4. Getting research projects with the MPI and other external cooperators started.

In the clinic the two main neuropsychological topics of the MPI “working memory” (3.3.1.1 - 3.3.1.3) and “language and text processing” (3.3.1.4 - 3.3.1.6) are examined in brain injured patients. From April to December 1996 38% of all patients treated in the clinic were examined in the MPI.

Theoretical models of cognition and hypotheses concerning functional representation of cognition in the brain are evaluated by testing patients with focal lesions. Factors such as lesion site, etiology, biochemical and pharmacological changes as well as psychological factors such as depression or anxiety may critically influence brain-behavior relationships and have to be taken into account for theoretical models. On the other hand, findings in basic research can open new perspectives for understanding clinical patterns of disturbances and to develop therapeutical strategies.

In order to affiliate basic research in the MPI with clinical work, interface positions have been established. They are partly engaged in clinical assessment and therapy in order to get in contact with therapists and patients. Their main responsibility, however, is to design clinical experiments. A neurologist is running and supervising clinical studies in the MR tomograph. In addition there are interface positions in order to develop paradigms for the examination of working memory and language processes in neurological patients. Methodologically research with patients is based on behavioral observations, as well as on measures of brain activity during cognitive processing (ERP, MEG, fMRI).

3.3.1.1 A clinical test of executive function

Bublak, P., Matthes-von Cramon, G. & Schubert, T.

The action of working memory comprises storing and actively using a limited amount of information for guiding upcoming action (cf. Fuster, 1985; Baddeley, 1986; Goldman-Rakic, 1987). It is assumed to be the elementary function supporting executive processes like planning actions or making decisions (cf. Tranel et al., 1994). Empirical evidence from various sources strongly suggests that the prefrontal cortex plays a central role in mediating this important function (e.g. Cohen et al., 1994; Owen et al., 1990; Petrides, 1994). Patients suffering from prefrontal lesions are known to have major deficits in solving complex tasks assessing executive functions, like the Wisconsin Card Sorting Test or the Tower of London Test, although they perform normally on a series of intelligence or memory measures (Damasio & Anderson, 1993). For example, they usually show a normal digit or block span, which are widely used tasks that assess short term storage capacity (Lezak, 1995). A possible reason for this may be that the span measures do not call for a substantial involvement of executive control processes. That is, a subjects' "work space" for actively using stored items may lie well beyond his/her digit or block span. Our intention is to test executive functions, which are necessary for such active use of stored items, by means of a task that demands coordinating information held in working memory. According to Yee et al. (1991), coordination is the establishment of a goal-directed correspondence between two types of information.

Based on the work of Carlson et al. (1993) we designed a new working memory paradigm, which comprises a verbal as well as a visuospatial task. In the verbal task, the subject has 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. A coloured cue is shown during task progression, determining the mental operation to be executed by the subject. A black cue (short term memory condition) indicates, that recall is demanded in the same order as the digits are presented (e.g. the digits 3 6 7 5 have to be recalled in that order). A green cue (working memory condition I) indicates, that the subject has to reorganize the digits prior to recall, so that the first green digit is followed by the first red digit, then the second green digit and the second red digit (e.g. the list 3 6 7 5 has to be recalled as 3 7 6 5). Finally a red cue (working memory condition II) indicates, that recall is demanded in the order “first red digit, first green digit, second red digit, second green digit” (e.g. 3 6 7 5 has to be recalled as 7 3 5 6). After the presentation phase, a delay of four seconds follows, in which the subject has to rehearse/reorganise the digits. Immediately following is a random time interval (maximum of 2 seconds), so that subjects are prevented from anticipating the recall period. During recall, four pairs of digits are successively presented, one digit to the left, the other to the right of center. Each digit was part of the list, but only one digit per pair is appropriate for the response. The subject has to press the left/right response button, if the left/right digit is the correct answer. Which digit is the correct answer, depends on the current experimental condition, as determined by the cue. The same task structure holds for the visuospatial task, in which four out of eight fixed positions are presented successively.

Currently experiments are being performed using normal subjects. The effects of cue position are investigated to better understand the cognitive mechanisms at different task stages. The results acquired to date show a significant effect of the working memory conditions compared to the short term memory condition. This effect is strongest when the cue is presented after the delay, indicating a substantial coordination cost in this condition. Interestingly, coordination costs, though weaker, still persist even if the cue is presented before the delay period. Further analysis of these results will help to better understand the task characteristics, and to choose the most appropriate task type for the assessment of brain damaged patients. Patients of interest are those suffering from cerebral hypoxia and those with prefrontal dysfunction. A comparison of these groups may permit the dissociation of storage deficits (presumably present in hypoxic patients) from “pure” executive deficits (presumably evident in frontal patients). Another group of interest are patients suffering from Parkinson’s disease, because they are known to show modality specific deficits in visuospatial tasks.

3.3.1.2 Visual recognition memory performance in patients with cerebral hypoxia: A combined behavioral and event-related potential (ERP) analysis.

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

In parallel to the project outlined in (Project 3.3.1.1), this study examines cognitive dysfunctions and behavioral alterations in patients suffering from ischemic/oligemic cerebral hypoxia due to cardiac arrest. More specifically, this study investigates the subprocesses underlying visual recognition memory in this group of patients by means of a combined analysis of ERPs and performance measures. Prior neuroanatomical work suggests that medio-basal temporal lobe structures (i.e. the CA1 region of the hippocampus) whose integrity is critical for recogntion memory functions is priorly affected by cerebral hypoxia.

Patients with cerebral hypoxia, as well as a group of age matched-controls, performed two versions of a recognition memory task, requiring either old/new judgments for object forms or spatial locations. A visual discrimination task with negligible memory requirements served as a control condition. The EEG is recorded from 19 electrodes and ERPs are calculated for each task. This experimental design allows us to examine ERP components related to visual discrimination performance (i.e., P300) as well as ERP indices of active retrieval of object forms and spatial locations, so-called old/new effects. These effects result from the fact that previously studied items evoke more positive ERP components starting around 300 ms after stimulus onset than previously unstudied items. The combined analyses of ERP old/new effects, and behavioral indices of recognition memory, focuses on dissociations in the nature of the recognition judgments (familiarity-based judgments vs. judgments based on active retrieval of working memory information), as well as on the neuronal structures involved in the generation of recognition-related ERP components.

So far, six patients have been investigated. Preliminary analyses show that the P300 component in the visual discrimination task is highly similiar in timing, amplitude and scalp topography for all patients and the age-matched controls, indicating that the patients generate reliable ERP components in tasks imposing negligible memory demands. For the control group subjects a high level of recognition memory performance was obtained (around 95% correct judgements) and in both tasks reliable old/new effects were found. These effects started around 300 ms and were more anteriorly distributed in the object task than in the spatial task. In contrast, these old/new effects were absent or even inverted in polarity in both tasks for all patients investigated so far. Despite this sparing of the ERP old/new effects, the patients' recognition memory performance was well above chance (i.e., % correct judgements above 70%). We take these preliminary results to suggest that visual recognition memory in patients with cerebral hypoxia relies to a large extent on the activation of an item's familiarity rather than on the active retrieval (i.e. concious recollection) of the study episode. Further experimention will be required to examine the extent to which integrity of the medial-temporal lobe is reqired for the active retrieval of working memory information.

3.3.1.3 Working memory in patients with Parkinson's disease

Müller, U., Bublak, P. & Schubert, T.

Cooperation: Prof. A. Wagner / M. Reuter; University of Leipzig, Neurology

Patients in the early stages of idiopathic Parkinson's disease provide an interesting clinical model to investigate the role of dopaminergic and basal ganglia mechanisms in working memory. Several studies report on problems with dual-task performance and deficits in internal attentional control as well as sequencing and temporal organization of information.

In cooperation with the Department of Neurology at the University of Leipzig we have started a project on cognitive dysfunctions in Parkinson's disease. All patient are submitted to extensive diagnostical procedures including neurological scoring (UPDRS), neuroimaging (CT, MRI, IBZM-SPECT, ß-CIT-SPECT), computerized movement analysis, neuropsychiatric ratings and neuropsychological screening with a clinical test battery to exclude non-ideopathic etiologies as well as major depression and dementia.

With elaborated paradigms from experimental psychology we want to differentiate the "memory" and "working" subcomponents of working memory dysfunction. Related studies examine the interdependence of subtle working memory deficits with problems in speech comprehension and shift of intention neuropsychological testing of patients with Parkinson's disease *off* and *on* dopaminergic medication, together with findings from functional neuroimaging studies in normal volunteers and patients, relate disturbed cognitive processes to distinct neuronal structures and neurotransmitter function.

3.3.1.4 Syntax processing: The involvement of mediobasal temporal structures as indicated by focal brain lesions

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

The issue of which brain structures are involved in the processing of semantic and syntactic information is central to recent cognitive neuroscience. For semantic processes PET and fMRI studies have identified a network of brain areas that are active whenever semantic information is being processed. For syntactic processes a similar description is still lacking. While a PET study that varied the complexity of syntactic processes found a selective activation of Broca's area (Stromswold et al., 1996), another PET study reported the frontal poles to be specifically activated during syntactic processing (Mazoyer et al., 1993). Electrophysiological and magnetophysiological correlates of normal subjects brain activity suggest that at least during first-pass parsing, cortical as well as subcortical areas are activated.

Another way of approaching this issue is to investigate the event-related brain activity in subjects suffering from particular brain lesions. Earlier studies had shown that the processing of syntactic phrase structure violation was correlated with an early left anterior negativity followed by a late centro-parietal positivity. A case study with a patient suffering from a large left anterior lesion revealed that this patient did not show a left anterior negativity in response to a phrase structural violation, although he showed a late positivity (Friederici, Hahne & von Cramon, under review).

In the present study we investigated a total of 10 aphasic subjects, 3 with subcortical lesions and 7 with cortical lesions at various sites.

The stimulus material used in this experiment consisted of sentences that were either correct, contained a semantic selectional restriction violation or a syntactic phrase structural violation.

Sentences were presented auditorily to the subject and they were required to judge after each sentence whether it was grammatically correct or not.

ERP averaged per subject over correctly answered trials, revealed that patients with lesions in the anterior temporal white matter isolating mediobasal temporal structure such as, for instance, the amygdaloid complex, the (head of the) hippocampus proper, or parts of the ento- or perirhinal cortex, do not show an early negativity (syntactic first-pass), but possibly a late positivity (thematic role assignment and reanalysis) and a N400 (lexical-semantic integration). In contrast, patients with circumscribed temporo-parietal lesions display the early syntactic component but no N400 nor a late positivity. The role of Broca's area in this context remains questionable. Control participants present all three components.

These data seem to indicate that the intactness of mediobasal temporal structures appears a necessary condition for the early left anterior negativity to appear in the ERP. This in turn suggests that these structures are important for first-pass parsing processes. Second-pass parsing processes reflected in the late positivity seem to be unaffected by these lesions. We may speculate that the early left anterior negativity reflects a fast checking mechanism for the correctness of local phrase structure that supports normal on-line syntactic processing, whereas the late positivity reflects the evaluation of structural dependencies at a secondary level. If this is true than the present data certainly suggest that the fast checking mechanism is not a necessary condition for off-line grammatical judgment, as these patients not only displayed a late positivity but also performed significantly above the level of chance when judging the sentence's grammaticality.

3.3.1.5 Multilevel representation of text information in brain-injured patients

Guthke, T. & Ferstl, E.

The investigation of text comprehension in brain damaged patients is important for theoretical and clinical reasons. From a cognitive neuroscience viewpoint it is interesting to investigate whether cognitive deficits resulting from brain damage influence the construction of a multilevel representation of text information. 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 the proposed empirical study we will investigate the multilevel representation using a word recognition task. The subjects have to read texts about 100 words long and afterwards to decide whether or not a test sentence is part of the text. Test sentences include old verbatim test sentences, paraphrase (single word change: synonym), two types of inferences (instrument, purpose), and two types of other novel sentences (contextually appropriate but very unspecific, unrelated to the content of the text). We will register reaction times and the acceptance rate. In our study with normal subjects (Guthke & Beyer, 1995) we found the proportion of "Yes" answers dependent on the type of test sentences. This effect is in good agreement with the theoretical assumptions of van Dijk & Kintsch (1983). For example, the rank position of the acceptance rate of inference statements among the various test sentence types is predicted correctly by the hypothesis that inference statements differ from the text at the surface and the propositional level but that they are part of the same situation model.

We are interested in the question if brain damaged patients with various etiologies (cerebral hypoxia, frontal lobe dysfunction, infarction of medial cerebral artery) and neuropsychological syndroms (amnestic, executive dysfunction, aphasic) are also able to build such a multilevel representation of the text.

Specifically, we will look for relations between the type of brain damage and processing deficit. In this regard the investigation of inference processes is very important because they are essential in building the situational model. Inferences establish connections between text and prior knowledge structures of the reader, and therefore activate information about events, facts, and topics that are not mentioned in the text.
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.

Evidence from the literature on cognition and discourse processing in brain-injured patients suggests differences between these types of patients. For example the work by Ulatowska & Chapman (1994) about the relative preservance of macrostructure in aphasic patients 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. Whereas patients with executive dysfunction should have more problems to build the situation model of a text (see for example the description of nonaphasic communication disorder in Glindemann & von Cramon, 1995). Previous research suggests that prefrontal damage leads to an impairment in executive functions. Thus, for this patient group, controlled, strategic inferences are expected to be difficult. Moreover, right-hemispheric damage might lead to impaired attentional focussing, so that coherence breaks might go unnoticed, and the necessary inferencing processes are not initiated. Automatic inferences, however, depend heavily on the appropriate activation of relevant semantic knowledge. For Broca aphasics, this process seems to be relatively intact, whereas for Wernicke aphasics, deficits have been observed (Milberg & Blumstein, 1981). To be able to control for this factor, the project will be conducted in close collaboration with the project on *Lexical access in brain-injured patients: behavioral and event-related potiential evidence* (Kotz et al., in preparation).
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) about 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.

Change of perspective as a retrieval aid for brain-injured patients

3.3.1.6

Ferstl, E. & Guthke, T.

Text comprehension requires the interplay of language specific and general cognitive processes. To derive the surface structure of a text (which encodes the linguistic information), syntactic and semantic knowledge is needed. Deriving the macrostructure of a text (which corresponds to a representation of the main ideas; vanDijk & Kintsch, 1983), requires organization of explicit information and the use of appropriate general world knowledge during encoding. Finally, goal oriented strategies and knowledge dependent processes come into play during retrieval and application of the resulting representations.

In an empirical approach to text comprehension, it is therefore 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. Although the perspective influenced the first recall, the irrelevant items had been encoded nevertheless. Subsequently, it has been argued that the perspective effect is due to omission of irrelevant items rather than to the addition of previously unrecalled information (Baillet & Keenan, 1986), and that only low-span readers are sensitive to perspective or reading goal (Lee-Sammons & Whitney, 1991).

In the present study, we adopt this paradigm to study text comprehension in brain-injured adults. The small, but growing literature in this area holds that, despite impaired sentence level comprehension, aphasic patients are able to use general world knowledge and thus succeed in deriving a good macrostructure (Chapman & Ulatowska, 1994). In contrast, non-aphasic patients, such as patients with closed-head injury, right-hemispheric lesions or pre-frontal lesions, might not apply appropriate strategies to structure their comprehension processes or to activate relevant background knowledge (e.g., MacDonald, 1993; Glindemann & von Cramon, 1995). This results in a blurred distinction between the levels of representation, in incoherent representations, or in an understanding which is not integrated with the background knowledge.

Following these observations, we can derive the following hypotheses: Aphasic subjects are expected to be able to take advantage of the perspective during encoding. In addition, they are expected to benefit from the change of perspective, despite their lower level of performance. In contrast, subjects with non-aphasic deficits might not be able to make strategic use of the perspective, both during encoding and retrieval. In particular, patients with pre-frontal lesions are expected to show intrusions, recall irrelevant details and/or persevere without being able to utilize the new perspective.

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 is about two children walking through a city, and can be read either from a tourist's point of view, or from an inhabitant's. The stories are about 400 words long.

To confirm the intuitive relevance of the story statements, we conducted a rating task with 18 students. The stories were divided into small idea units. The subjects rated each unit according to how important it was for the alternative perspectives. Based on the results of this task, the stories were slightly modified, so that the number and average ratings of the relevant items are now comparable across perspectives. For the auditory presentation the resulting texts were tape recorded at a slow, but normal, reading rate.

The procedure was slightly modified, to take into account the special needs of brain-injured patients. We use two texts in separate sessions, approximately one week apart, in order to evaluate the consistency of the results. To facilitate comprehension, the texts are first presented auditorily. Afterwards subjects have the opportunity to read the stories themselves. Instead of written recall, subjects are asked to retell the story, and their recall is tape recorded. Because there is little agreement about appropriate criteria for defining subject groups, the patients in our study are not assigned to experimental groups a-priori. Rather, we propose to test patients with different etiologies, identify patterns of text comprehension deficits, and correlate these patterns with a variety of neuropsychological and medical assessments.

Data collection is in progress. Preliminary analyses of five participants' recall protocols provide some support for our hypotheses. Overall, 35% of the perspective relevant items were recalled, and all five subjects recalled the main ideas of the texts. This shows that the difficulty level of the stories is appropriate for our subject group. Perspective had differential effects. One patient with mild, amnestic aphasia was not able to utilize the encoding perspective during the first attempt, but the change of perspective enabled him to additionally retrieve relevant items during the second. Two non-aphasic patients with diffuse brain damage showed a perspective effect during the first recall. Similar to low-span readers (Lee-Sammons & Whitney, 1991), these subjects were also sensitive to the change of perspective. They omitted encoding relevant items during the second attempt, but could not recall additional items relevant to the new perspective. Finally, two non-aphasic patients with lesions to the left frontal lobe showed no evidence for the use of perspective during the second recall.

3.3.2 EXTERNAL COOPERATION

In cooperation with Prof. Eran Zaidel, UCLA, mechanisms underlying spatial orienting in the split brain were investigated. Experiments with a commissurotomy subject were carried out in Los Angeles. Experiments with normal observers, in continuation of previous work at the Free University of Berlin, were run in Leipzig.

3.3.2.1 Redundant targets effects in a commissurotomy subject

Pollmann, S. & Zaidel, E.

In target detection experiments, responses are speeded by the simultaneous presentation of a second, redundant, target. This redundant targets effect (RTE) was recently investigated in a callosotomy subject (Reuter-Lorenz et al., 1995). In this study, patient J.W., compared to normal observers, displayed an enhancement of the RTE for bilateral redundant targets, i.e. one target in each visual hemifield. This enhancement was not visible for redundant targets presented within the right visual hemifield (RVF).

In J.W., again contrary to the normal control observers, the bilateral redundancy gain exceeded a limit set by mere probability summation for independent, race-like processing of two simultaneous events (Miller, 1982). This limit is given by the ‚race inequality‘ (Miller, 1982):

$$P(RT < t | s1 and s2) \leq P(RT < t | s1) + P(RT < t | s2) \quad \text{(Eq. 1)}$$

A redundancy gain exceeding this limit suggests some form of “coactivation” (Miller, 1982). The importance of the race inequality is that it gives an upper limit for the redundancy gain that can be explained by any race model. The reasoning is that response latencies in race models are determined by the distributions of two random variables x_1 and x_2, where x_i is the time needed to respond to a signal on channel i. I.e. x_1 gives the distribution of response times to a target appearing at Location 1, and x_2 gives the response time distribution for target appearance at location 2. On redundant targets trials, when a target appears at Location 1 and another target at Location 2, response time is the minimum of x_1 and x_2 (Miller, 1982). Therefore, the cumulated probability for a response to the redundant targets at a given time t post stimulus onset cannot be higher than the sum of the cumulated probabilities for responses to single targets in either channel. If it exceeds this limit, the gain cannot be explained by the race model.

For the explanation of redundancy gains that exceed the boundary of the race inequality, a coactivation process is the primary alternative. Whereas in race models, as the name implies, the faster channel elicits the response, leaving the second channel irrelevant for the response, coactivation models allow for a combined effect of both channels to elicit a response. A neural mechanism realising race-like processing would be lateral inhibition, allowing the first incoming signal to be passed on to the next neuron, blocking later inputs from competing channels from being processed further. A neural realisation of a coactivation process is spatial summation, where the transmitter release of numerous synapses from multiple axons converging on a target neuron act together to reach threshold level excitation. Another well known process that may be combined with spatial summation is temporal summation, where excitation threshold is reached only after repetitive firing over a certain time period.

In the callosotomy study of Reuter-Lorenz et al. (1995) luminance onsets had to be detected. The enhanced, coactivation-like redundancy gain observed in J.W. when redundant targets were presented bilaterally, contrasted with an RTE within the RVF that was much less pronounced and did not violate the race inequality. This dominance of the bilateral redundancy gain, of course, was astonishing because commissurotomy clearly reduces the potential for interhemispheric integration.

To test the generality of the pattern of between and within-field redundancy gains in the split brain, we tested a commissurotomy subject on two different versions of a tachistoscopic visual search task. In separate experiments, we used both pop-out targets, differing from the distractor stimuli in a basic visual feature and less salient targets differing only in the conjunction of their components. Moreover, we compared bilateral redundant target presentation with redundant target presentation within both LVF and RVF so that within- and between hemispheric contributions could be assessed separately.

We tested L.B., at the time of testing a 45 year-old commissurotomy patient who underwent complete section of the corpus callosum, hippocampal and anterior commissures for relief of intractable epilepsy in 1963 when he was 12 years, 11 months of age. Details of his neurological history and status are available elsewhere (Bogen & Vogel, 1975). Magnetic resonance imaging confirmed that his forebrain commissures were completely sectioned (Bogen, Schultz & Vogel 1988).

L.B. previously demonstrated an inability to match complex shapes presented bilaterally (Zaidel, 1995). He was also unable to match shape or name between the visual fields in the Posner / Mitchell letter matching task (e.g. AA: same form, Aa: same name; Eviatar & Zaidel, 1994).

Three neurologically normal subjects, all students of the University of Leipzig, were tested as controls. Their age range was 22 - 28 years, two were female, one male. All were right-handed, assessed with the Edinburgh-Handedness-Inventory (Oldfield, 1971). The experiments were tachistoscopic visual search tasks where a target stimulus had to be selected among distractor items in a display containing five stimuli arranged like the 5 on a die. In Experiment 1, an inverted T had to be detected among upright T. In Experiment 2, the target was a 45° tilted T. The difference between these targets, determined in previous experiments, was a “pop-out” characteristic of the tilted T that was absent for the inverted T.

Results and Discussion: L.B. showed a strong redundancy gain when two targets were presented bilaterally. In the within-hemifield conditions he showed no redundancy gain. The redundancy gain was observed in left and right hand responses for low salience targets and in the right hand for pop-out targets.

Normal controls showed redundancy gains within LVF, within RVF and for bilateral targets. Individual subjects showed redundancy gains in some conditions, the frequency of significant redundancy gains was about equal for these three conditions. There was no indication of a stronger gain in the bilateral condition in the normal control subjects.

These results parallel the data from callosotomy subject J.W. (Reuter-Lorenz et al., 1995). Remember that J.W. showed a redundancy gain exceeding probability summation only in the bilateral condition, like L.B. In contrast to L.B., J.W. displayed a redundancy gain for redundant targets presented in the RVF, however, the within-field redundancy gain remained within the limits of the race model. Thus for both the bilateral redundancy gain was the dominant effect.

The enhanced bilateral redundancy gain, previously described for detection tasks, was also present in visual search. Furthermore, the pattern was similar for high and low-salience targets. Taken together, the independence of the enhanced bilateral target RTE in splits from changes of the visual processing demands suggests that this effect is elicited at a later processing stage.

A new finding is the difference of the RTE for left and right hand responses (Fig. 1). While previous studies reported analyses averaged over response hand and for right hand responses alone (Reuter-Lorenz et al., 1995), we analyzed effects separately for both hands. Surprisingly, there seemed to be a qualitative difference in the RTE for the left and the right hand. While the data for the left hand were compatible with a race explanation of the redundancy gain, right hand responses violated the race inequality (Miller, 1982), suggesting coactivation. This pattern of results was found consistently in the experiments with low and high-salience targets.

Reuter-Lorenz et al. (1995) proposed a model for the unusually strong bilateral redundancy gain that is basically composed of two assumptions. They posit that there is tonic inhibition of hemispheric motor commands. Responses can be facilitated by disinhibition of this tonic inhibition. This disinhibition occurs whenever both hemispheres elicit response preparation signals for the same motor response in parallel. This model is able to explain the pronounced bilateral redundancy gain in our data, but it is hard to see how it could account for the coactivation versus race data for the response hands.

Instead, we would like to propose an alternative model of bihemispheric coactivation in the motor pathway that accounts for the data of normals and commissurotomy subjects in luminance detection (Reuter-Lorenz et al., 1995) as well as visual search tasks and is able to explain the differences due to response hand in the current experiments.

As discussed in the introduction, RTE which violate the race inequality are not compatible with a probabilistic race explanation. However, it should be kept in mind that the reverse is not true, non-violations of the race inequality are no proof against coactivation. Consider spatial summation as an example. A number of axons each may convey input signals from two "channels". However, one channel may be represented by a large number of axons, whereas the other channel may be represented by just a few axons. Input from the weak channel will reduce the number of neurons (or the amount of transmitter release per synapse) in the strong channel that are needed to reach threshold at the neuron of convergence. This is a coactivation process. However, for the contribution from the weak channel the effect of coactivation will be rather small and may or may not, dependent on the strength of coactivation, exceed the boundary of a race explanation. Thus there is no need to posit two hemispheric race- versus coactivation processing modes in order to account for the present data. Instead, we propose that bihemispheric target processing of bilateral redundant targets leads to coactivation in the motor pathway, and that the coactivation is stronger in commissurotomy subjects.

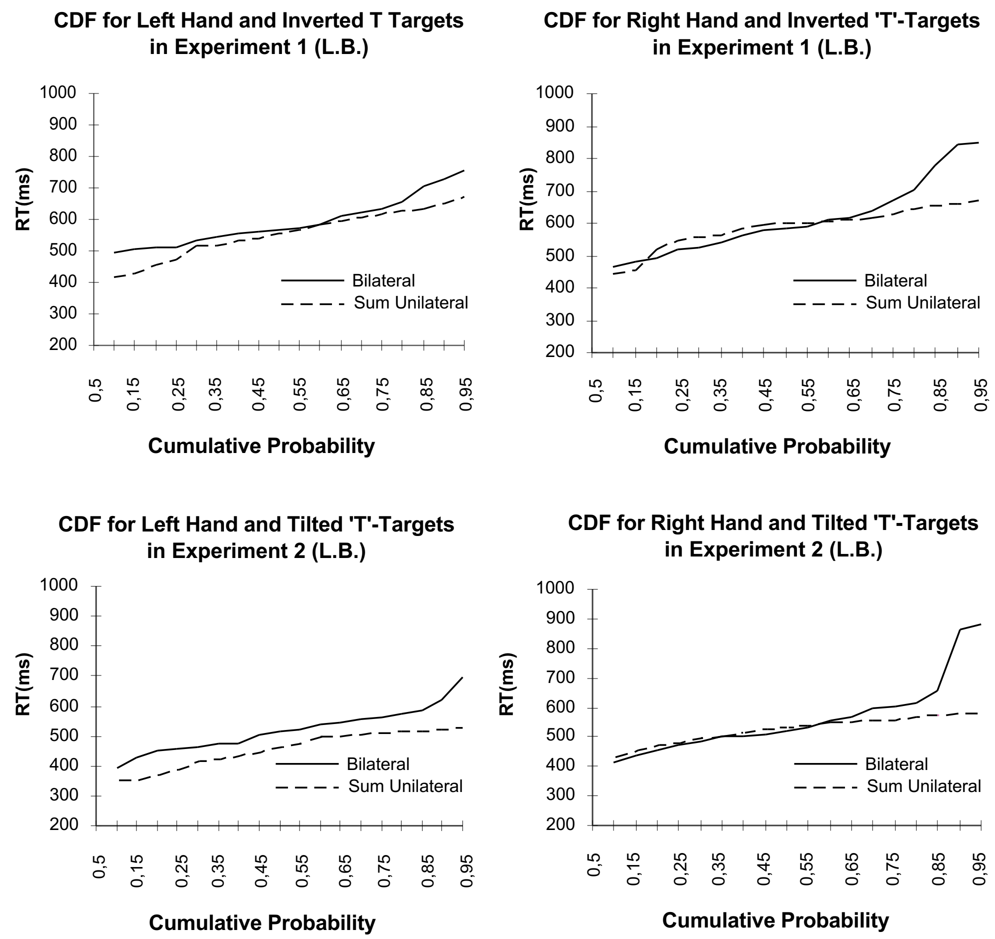


Figure 1.

The data can be accounted for by a model of coactivation via temporal summation in the motor pathway

- Both disconnected hemispheres are capable of eliciting motor responses in each hand, the contralateral motor pathway being dominant.
- Both motor pathways converge on a common structure. Their inputs lead to spatial summation at this structure. Over time, activation builds up via temporal summation.

- The enhanced bilateral redundancy gain observed in commissurotomy subjects is due to a lack of interhemispheric coordination of processing steps, which results in an enlarged average time lag between left and right hemispheric signal arrival times at the coactivation stage. Longer time lags entail stronger activation via temporal summation.
- Hemispheric response preparation signals are always integrated by a coactivation process. The strength of coactivation determines whether the RTE exceeds the race boundary.
- A hemispheric processing advantage leads, by coactivation of the contralateral motor pathway, to a stronger RTE in the ipsilateral hand.

3.3.2.2 A receptive-field based gradient for spatial orienting: Evidence from commissurotomy

Pollmann, S. & Zaidel, E.

One of the most striking findings in commissurotomy subjects is the absence of effects in everyday situations. Consider orienting in space: Split brain subjects show an apparent perceptual unity of the visual field. While extinction-like phenomena have occasionally been reported in laboratory experiments, clear signs of neglect and extinction have hardly been observed.

We investigated covert orienting within search displays in commissurotomy subject L.B. (see project 3.3.2.1). The task used was a tachistoscopic visual search task that had yielded an extinction-like effect of pop-out distractors on contralateral targets defined by feature conjunctions. We investigated whether there was a distractor effect between the visual fields after commissurotomy and whether a lateral asymmetry would occur like that observed in normals, with distractors in the right visual hemifield being more disturbing for contralateral target search than distractors in the left visual hemifield (LVF).

L.B. was tested on two separate occasions. in both testing sessions he was asked to respond to a lateralized Target, an inverted *T* in a display consisting of upright *Ts*, by pressing a button with the ipsilateral hand. Like normals, he showed a substantial slowing of response speed in the distractor condition. Compared to normals, however, he showed a reversal of the distractor asymmetry, LVF-distractors being more effective than RVF-distractors.

In an additional experiment target and distractor stimuli were reversed, so that he had to respond to pop-out targets in the presence of conjunction distractors. His responses mirrored that of normals in that a contralateral distractor effect was present, but did not interact with the hemifield of target presentation.

L.B.s data can be summarized in the following way: Like normals he showed a laterally asymmetric distracting effect for stimuli presented in the hemifield contralateral to target appearance. The asymmetry of the distractor effect depended, as in the normal controls, on high distractor salience. The data can be explained by the same processing assumptions as in normals: Automatic, stimulus driven, orienting within the visual field does not lead to lateral asymmetries. An asymmetry is observed when automatic orienting is misleading and controlled reorienting is invoked.

Within this model the reversed contralateral distractor asymmetry found in L.B. has to be explained.

We have localized the source of the contralateral distractor asymmetry to attentive processing. Based on numerous studies of neglect patients and normals, and electrophysiological studies of spatial orientation in animals, Bisiach & Vallar (1988) have proposed a model of spatial orienting that is based on electrophysiological data of receptive field properties of high level visual neurons in the monkey. These neurons commonly have large receptive fields with a characteristic distribution: Most receptive fields cover areas in the contralateral visual hemifield, a still sizeable number of neurons has bilateral receptive fields, and a minority of receptive fields is ipsilateral. To account for the laterality of neglect symptoms, Bisiach & Vallar proposed that the contralateral- ipsilateral receptive field ‚gradient' is steeper in the left hemisphere, leading to the strong orienting tendency towards the right observed after right hemispheric damage. In addition, Heilman & van den Abell (1979, 1980) had reported behavioral and electrophysiological evidence for a stronger right-hemispheric activation in tasks demanding spatial processing.

Taken together, the asymmetric receptive field gradient model of Bisiach & Vallar (1988) and the RH activation dominance assumption may explain the reversal of the contralateral distractor effect observed in a commissurotomy subject.

The difference between spatial processing in splits and normals is the absence of ipsilateral stimulus processing in both hemispheres. In a normal subject, both LVF and RVF stimuli will lead to strong activation in the right hemisphere. The overall dominance of RH-activation level, together with the weak contra- / ipsilateral gradient will largely override the asymmetric effects of the steeper left-hemispheric gradient. The result is a weak tendency to orient to the right. The steep left-hemispheric gradient leads to strong rightward orientation tendency if the RH-orienting system is ineffective due to a lesion.

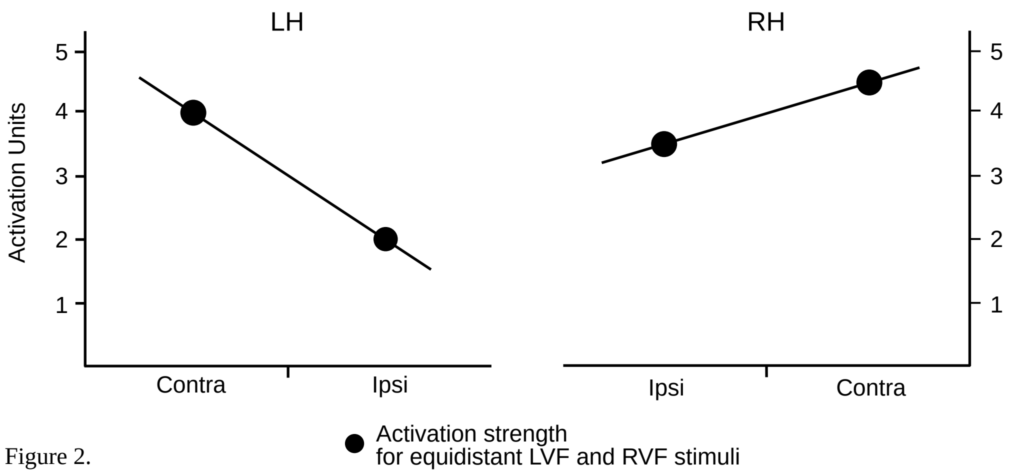


Figure 2.

In the split brain, a completely different pattern emerges. Since there is no ipsilateral callosal relay of visual information, an RVF-stimulus will induce strong activation in the LH and no activation in the RH. Conversely, an LVF stimulus will activate only the RH. Under the assumption, that RH-activation is generally dominant, The LVF stimulus will induce a higher activation than the RVF-stimulus, although the RVF stimulus activates the "high end" of the LH-gradient (see Fig. 2).

3.3.2.3 Evaluation of brain diseases by quantitative magnetic resonance metabolic, perfusion, and diffusion imaging

Norris, D.

The institute is part of a European-wide collaboration organised by European-Union within the BIOMED-II programme. The aims are the methodological refinement and clinical testing of NMR methods for detecting perfusion and diffusion, as well as proton spectroscopic imaging methods.
Funds for this project have now been released by the EU, and it will be started in 1997.

in cooperation with:
Institut für Medizinische Physik der Universität Wien, Austria,
Klinikum der Albert-Ludwigs-Universität Freiburg, Germany,
Fachbereich Biologie/Chemie der Universität Bremen, Germany,
Dansk Videncenter for Magnetisk Resonans, Copenhagen, Danmark,
Institut National de la Santé et de la Recherche Médicale, Grenoble, France,
Universita' degli Studi di Bologna, Bologna, Italy,
Delft University of Technology, Delft, The Netherlands,
University College and United Medical and Dental Schools of Guy's and St. Thomas' Hospitals, London, The United Kingdom

Functional Magnetic Resonance Imaging (fMRI) is a relatively new tool for the investigation of brain-behavior relationships. While considerable effort has gone into improving physical parameters of the fMRI-experiment, less effort has so far been devoted to the optimization of the psychological experiments used in fMRI. Consequently, a broad range of methodical questions remains to be addressed. Among them are some that seem of central importance for the usefulness of fMRI as a tool in cognitive neuroscience:

Interdependence of cognitive processes

Following the PET-tradition, cognitive fMRI-experiments have often relied on “subtraction-logic”, i.e. the assumption that tasks can be designed in a way that allows to assess the brain activation related to a single processing step by subtracting the activity associated with processing task conditions that differ only in the demand for a critical cognitive process. This approach, advocated by Donders, relies on the assumption of pure insertion, that is the addition of a process does not influence the remaining processes engaged by a task. Given the high interconnectivity of the brain this may often be no realistic assumption. An alternative approach, proposed by Sternberg, is the additive factors logic. Applied to fMRI this implies to look at changes in the activation pattern that are induced by changes in the degree one cognitive process is utilized to solve a task under different experimental conditions. Comparing results obtained with the subtraction and additive factors setup should allow an improved evaluation of the independence or interdependence of cognitive processes needed for a task.

Retest-reliability of fMRI-data

The retest-reliability of fMRI-data is frequently used in an implicit sense to evaluate data quality. However, explicit tests have been scarce. In the published data, retest reliability for cognitive tasks within the same subject was rather high. We aim to investigate to what degree non-correspondence of activation patterns between test and retest depends on changes in cognitive processing.

Within-trial activational time course

The standard fMRI-experiment today is characterised by blocked presentation of experimental conditions. This paradigm has several drawbacks. Not all cognitive experiments can be run in blocked fashion, subjects may learn to circumvent the processing that the experimenter intends them to perform when they discover a regularity within a block. Another important drawback is that the timecourse of activation within a trial cannot be measured.

The limiting factor for the measurement of activational timecourses for randomly presented trials is the need to wait between trials for the rise and decay of the fMRI-signal. The long intertrial-intervals needed limit the number of trials that can be measured within a reasonable time. Thus minimization of the intertrial interval's duration is a major methodological goal.

Temporal and spatial resolution of fMRI activation sequences

While fMRI allows a very precise spatial localization of function, its temporal resolution is rather poor. However, an fMRI-experiment can be optimized to gain either a relatively good spatial or temporal resolution. By combining experiments optimized in the spatial or temporal domain, the temporal limit for the sequencing of activation onsets in spatially distinct areas of the brain will be investigated.

Cognitive fMRI studies on our system will begin after completion of functional imaging studies with sensory and motor paradigms that are currently carried out as a quality control (see 4.7). During the last year, behavioral experiments were carried out in preparation of the planned cognitive fMRI-studies. This preparatory work is subsequently reported for two projects. In one project (3.4.1) a dual task paradigm will be used to investigate subtraction versus additive factors methods. In the second (3.4.2) temporal differentiation of memory activation and verification processes was achieved in preparation of the measurement of within-trial activational time courses.

Involvement of prefrontal cortex in dual task processing

3.4.1

Schubert, T.

Recently D´Esposito et al. (1995) presented empirical evidence for the involvement of the prefrontal cortex (PFC) in the co-ordination of dual-task performance in a study using functional Magnetic Resonance Imaging (fMRI). The aim of our study is to investigate in detail which functional role the PFC plays in dual task processing. We assume, that the PFC is involved in solving possible conflicts between potentially interfering actions by sequencing their execution temporally. A second goal of this investigation is to prove whether localization and amount of fMRI activation depend on the difficulty of certain cognitive processes. This second goal is a rather methodical goal directed towards the interpretation of fMRI data.

For a detailed investigation of these questions it is necessary to use a dual-task paradigm which allows precise assumptions about the nature of interference between two tasks and allows a stepwise increase in difficulty of the two tasks. In our behavioral study we used a dual task paradigm which meets these requirements, the paradigm of the Psychological Refractory Period. Subjects had to carry out two choice reaction tasks together with a variable interval between them (SOA). In the first step it was asked which processing stages in both tasks interfere each with other. Is there a central interference at the stage of response selection or a peripheral interference at the stage of motor responses? The Critical-Path technique (Schweickert, 1983) was used to decide between these possibilities. This technique predicts different effects of difficulty of response selection stage in task 2 and SOA on reaction time for centrally or peripherally localized interference. In the case of a centrally localized interference, difficulty of response selection stage in task 2 and SOA should interact additively with the reaction time in task 2 (Rt2). In the case of a peripherally localized interference these factors should interact underadditively with Rt2.

In the first experiment we varied the difficulty of the response selection stage by increasing the number of response alternatives from one to two. The results yielded an under-additive interaction of SOA and response selection difficulty on Rt2. Nevertheless, this result is confounded by a methodical problem. Conditional stimulus presentation probability in the situation with one stimulus increases with increasing SOA. Therefore the underadditive interaction could be a result of changed expectational state and motor preparation in the condition with one alternative assumed to depend on SOA. This would mean that underadditive interactions between SOA and response selection difficulty should not be interpreted as evidence for a peripheral interference when conditions with one and two alternatives are compared.

To prove whether the underadditive interaction depends on expectational state and motor preparation in the condition with one alternative we varied the stimulus presentation probability in this condition (50% versus 100%) in a second experiment.

The results of the experiment showed that the underadditive interaction disappeared with 50% stimulus presentation probability. In contrast the underadditive interaction emerged under the condition of 100% stimulus presentation probability. Thus, the results of this experiment indicate that the occurrence of an underadditive interaction depended on stimulus presentation probability. Therefore, the results object to the interpretation of underadditive interactions between SOA and response selection difficulty by a peripheral interference in the stage of motor execution when conditions with one and two alternatives are compared.

In the third experiment difficulty of response selection in task 2 was varied by increasing the number of response alternatives from two to three. Difficulty of response selection stage in task 1 was held constant. The results yielded a clear additive effect of SOA and difficulty of response selection on reaction time in task 2. This is strong evidence for a central interference in the stage of response selection.

To summarize, the experimental data support the assumption of a central interference in dual task performance which is localized at the stage of response selection. From a methodical point of view the data confirm the possibility to increase difficulty of certain processing stages in a dual task and to determine the localization of interference between both tasks. In future research this experimental procedure will be adopted for planned fMRI experiments to analyze the dependence of localisation and amount of fMRI activation on difficulty of certain cognitive processes such as response selection and stimulus perception.

3.4.2 Working memory and long term memory

Zysset, S. & Pollmann, S.

This research investigates the role of prefrontal "working memory"-areas in the utilization of stored information. Previous work has shown that retrieval from long term memory and from primary (working) memory can be dissociated by behavioral measures. The project aims to overlapping as well as distinctive areas of activation in a delayed matching to sample and a matching to "memory set" experiment (Conway & Engle, 1994). It is postulated that the same prefrontal areas are active in both tasks, i.e. that the same "working memory" structures are involved in the processing of perceptual as well as stored information. Furthermore, it is assumed that posterior areas involved in the processing of sensory information will also be active in the memory set task. We specifically hypothesize that prefrontal cortex is involved only in retrieval from working memory, not from long-term memory. This hypothesis is derived from the finding of Conway & Engle (1994) of an interaction between working memory span and search in active memory but not between working memory span and retrieval from long-term memory.

In the "memory set" experiment, different sets of stimuli are learned before testing. In the experiment, individual sets have to be retrieved when an associated symbol is presented. Then, a stimulus is presented and the subject has to indicate whether the stimulus is a member of this set or not. Retrieval from long-term memory and from primary memory both contribute to reaction time when the set indicator and the probe stimulus are presented simultaneously. When there is a sufficiently long SOA between set indicator and probe stimulus, retrieval from long-term memory can be assumed to be completed, resulting in a measurement of retrieval from primary memory. The difference in reaction time between these two conditions can be viewed as the time it takes to activate the sets from secondary memory to primary memory.

The experimental control of the temporal separation of activation and verification onsets may allow the discrimination of signal changes associated with activation and verification processes.

In a first experiment, we investigated whether the set-size independence of retrieval from long-term memory found by Conway & Engle could be demonstrated with a different learning strategy and with shorter SOA.

According to Conway and Engle (1994), the process to activate a set from secondary to primary memory is independent of set size. This process should be terminated after 600-800 ms. But what really does happen during this 600 ms? Is this process of activation really as fast for all different set sizes? To further test this conclusion of Conway and Engle, we used shorter SOAs (0, 200, 400, 600 and 800 ms) in our first experiment. We used letter sets of the size 2, 4, 6 and 8. A letter appeared in two different sets, which means that there was an overlap between the different sets.

To learn the different letter sets, the sets were not presented as a whole, but the subjects had to learn with a trial and error procedure. The idea behind this learning procedure was to prevent the subjects from chunking the sets. This procedure leads to a much higher number of trials (>1200) than the paired presentation.

There were main effects for set size and SOA, but the interaction of SOA by set size was not significant. This supports the finding that retrieval from secondary memory is independent of set size. The reaction times of the SOAs of 200-800 ms did not differ from one another (see Fig. 1), leading to the conclusion, that the process of activation is faster then 200 ms. In comparison to Conway and Engle, the process of activation, defined by the difference in reaction time between the SOA and the No-SOA condition, was much shorter (130 vs. 400 ms). As in the experiments from Conway and Engle, items from set 2 were processed much faster then items from the other sets.

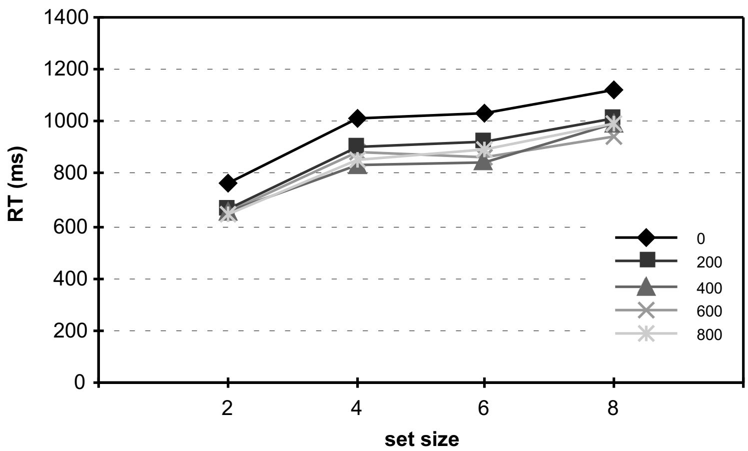


Figure 1. Mean reaction time for Experiment 1 as a function of set size and delay.

In a further experiment we tested different forms of presentation and longer SOA. Set size 2 was dropped, as such small sets seem to be processed differently. SOAs of 0, 1 and 2 seconds were used and there was no overlap between the different sets. Individual trials were either presented in random order, or were presented in blocks of the same delay or set size.

Reaction time with SOAs of 1 or 2 seconds do not differ from another and are the same for all forms of presentation. This is an important finding for further fMRI studies, as it shows that longer SOAs can be used without effecting the pattern of results. Thus the experiment with 2 s SOA between cue and probe presentation can be used to investigate temporal asynchronies of fMRI signal changes associated with memory activation and verification processes. Methodologically, this implies that averaged activational timecourses over individual trials can be analyzed within the fMRI-experiment.
The reaction time for SOA > 0 s remained the same over all forms of presentation. However, reaction times for SOA = 0 s differed between experiments. In random presentation, the difference in reaction time was around 300-400 ms, equivalent to the findings of Conway & Engle (1994). If the presentation was blocked by delay, the reaction time for no SOA was slightly reduced and the activation from secondary memory depended on set size. Blocking by set size, allowing for continouos activation of the memory set, reduced the delay-dependent difference in reaction time to about 100 ms, not as expected to nearly zero. This suggests, that not only activational processes were included in the reaction time differences.

Cognitive processes in man are usually studied by stimulation experiments. Responses are recorded by methods like functional MRI, EEG, MEG, SPECT and PET, which map different aspects of the underlying cognitive process. Because these different methods yield complimentary information about the anatomical, metabolical and neuro-physiological state of the brain, integrated data evaluation is highly desirable and will lead to results not achievable with one modality.

The Workgroup on Signal and Image Processing (SIP) focuses on the development and installation of new algorithms to improve the information yield from these experiments. The line between technical development and research is hard to draw during the startup-phase. To promote a solid ground for future research, we found it necessary to give this year's work a rather broad range of topics. While building and reviewing the tools necessary for our work we have found that a number of basic image and signal processing tasks required a closer look. Often a task needed a more complex implementation for stable performance in a routine environment. Two core projects, the implementation of an integrated signal and image processing environment, and the development of new visualization methods, are reported under "Technical Development" (4.1; 4.2).

During the next year we will focus on two important topics: (i) the description of individual neuroanatomy (3.5.1) and (ii) the segmentation of structural and functional fMRI data (3.5.2; 3.5.3).

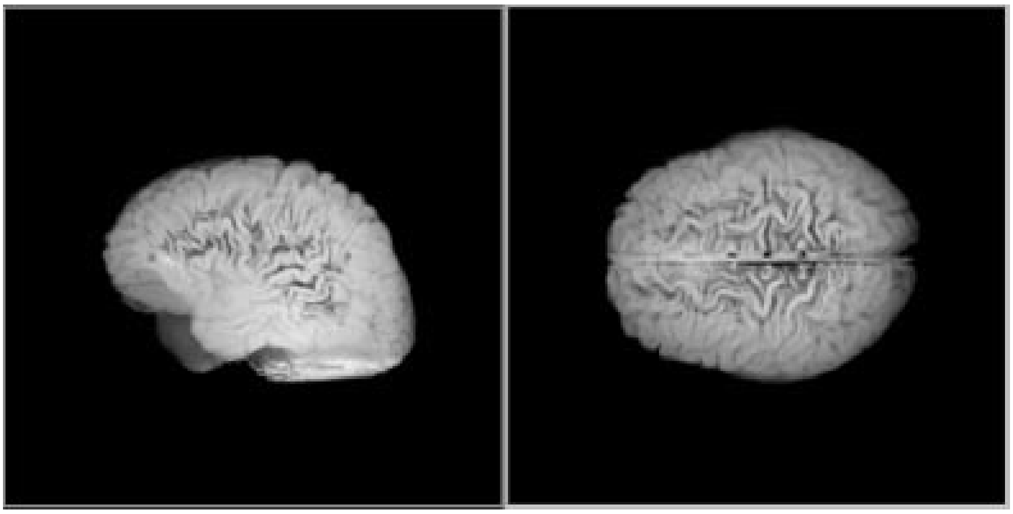


Figure 1. 3D reconstruction of a MR brain dataset

3.5.1 Analysis of individual neuroanatomy from MR tomograms

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

The exact identification of loci in MR tomograms as anatomical locations is a prerequisite for a neuroanatomical discussion of fMRI experiments. Furthermore, the analysis of neuroanatomical features as revealed by MRI allows the in-vivo study of the variability of brain structures. This offers the opportunity to obtain further insight into structure-functional relationships in the brain.
A first step considers the automatic extraction of sulcal bottom lines from MR images of the human brain. Sulcal bottom lines are of interest because they allow us to represent an entire sulcus by a tree like structure of curves rather than of surfaces, and thus present a highly condensed representation of prominent landmarks. Their automatic detection will serve as a useful tool in human brain mapping as it will help to perform comparative studies across subjects. Previous investigations of sulcal structure and variability were based on manual segmentations and were therefore restricted to very few data sets. Automatic procedures for extracting prominent features as landmarks in MRI data have either concentrated on lines of maximal curvature or on the detection of sulcal skeletons and sulcal surfaces. The idea of extracting sulcal bottom lines has not been reported in the literature so far. Its prime advantage is that it allows the incorporation of depth information in the structural analysis.

The method consists of four major steps:

1. Detection of sulci
We begin by classifying the image into three classes such that each voxel is labelled as either “white matter”, “gray matter” or “exterior/CSF”. We then employ a so-called “morphological closing” procedure which fills up the sulci thus producing an idealized smoothed surface of the brain. Subtracting white matter from the closed image yields the sulci.

2. Depth measurements
Each voxel in the sulcus interior receives a “depth” label corresponding to its depth as measured from the surface of the “closed” image. The technique used here is the so-called “constrained distance transform”. This technique allows us to measure distances within 3D objects where distances are measured along paths that can be forced to avoid obstacles of arbitrary shape. In the present application, the paths whose lengths we want to measure lead from any point in the sulcus interior towards the idealized smoothed surface of the brain while the white matter is considered an “obstacle” to be avoided. Each sulcal point receives a label indicating the length of the shortest such path leading from this point towards the surface.

3. Extraction of the sulcal medial surface
Each sulcus is thinned in a parallel 3D topological thinning scheme to obtain a medial surface. Thinning (sometimes also called “skeletonization”) reduces the object to a one-voxel thick surface that captures its most salient geometric features so that the resulting object is reminiscient of a “skeleton” (Fig. 2). The thinning procedure used here is a

variation of Tsao's method, where in addition to the standard method we use a distance transform to ensure that the skeleton resides in the object's center. Thinning procedures are notoriously susceptible to noise. In particular, small protrusions in the object's boundary may lead to spurious branches in the skeleton. To overcome this problem we use both pre- and postprocessing. In the preprocessing step, the object's boundaries are smoothed prior to the thinning using an iterated Gaussian filter. The postprocessing is performed after the following step described below.

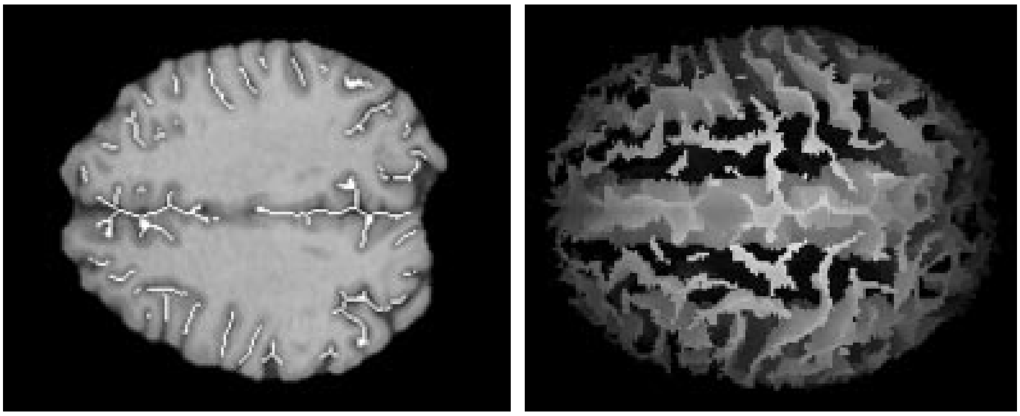


Figure 2. Sulcal skeletons shown in a MR slice (left) and as a 3D reconstruction (right)

4. Extraction of sulcal bottom lines

Sulcal bottom lines are obtained by progressively eroding deeper levels of the medial surface until the bottom line is reached so that the surface skeleton is now further reduced to a structure of curves. The procedure used here is a variation of a topological sequential thinning where in contrast to the usual topological thinning the order of erosion is governed by depth. The erosion process leaves the topology of the medial surface intact, i.e. the number of connected components as well as the number of branches remain unchanged.

Small branches resulting from an incomplete skeletonization are now pruned in a final postprocessing step. The pruning of curve structures is much more robust than the pruning of entire surface structures, which is why this step is best performed at this point rather than at an earlier stage.

This method was applied to seven T1 weighted MRI data sets from three different MR scanners. The results were checked manually by two human experts (neurologists) doing random checks. The results were found to be correct in almost every case. The only errors that were found are related to the following systematic problems.

Firstly, the cerebellum blocks part of the occipital lobe so that these areas cannot be reached by the "sulcus filling" procedure and are thus not accessible to the algorithm unless the cerebellum is removed prior to the execution of the procedure. Secondly, the algorithm blindly interprets every cavity or indentation within the white matter as a sulcus. Therefore, structures such as the basal ganglia and the ventricles are filled with a "sulcus" line unless those structures have been masked out beforehand. For the same reason, the Cisterna pontis and Cisterna vallecula cerebri are also wrongly interpreted as "sulci" causing a conglomeration of lines around the brain stem connecting the two hemispheres.

In our experiments, we used a visual editor to manually break and remove such obviously incorrect lines. With the exception of those systematic errors, the results were found to be correct. Figure 3 shows the bottom lines resulting from one such experiment. The depth at each node is color coded. Figure 3 also indicates how the verification was done: the mouse cursor is linked to the sagittal, coronal and axial slices of the data set so that a mouse click onto a node in the graph automatically positions the cursor to the corresponding location in the MR data set. In this way, the expert can assess the correctness of the location of a node.

The method presented above will serve both as a tool for landmark extraction as well as a tool for investigating the morphometry of sulci. Future work will focus on a classification of sulcus types and on studying interpersonal variability of sulcal structures. The depth information made available by this tool will hopefully help to address these issues from a new viewpoint.

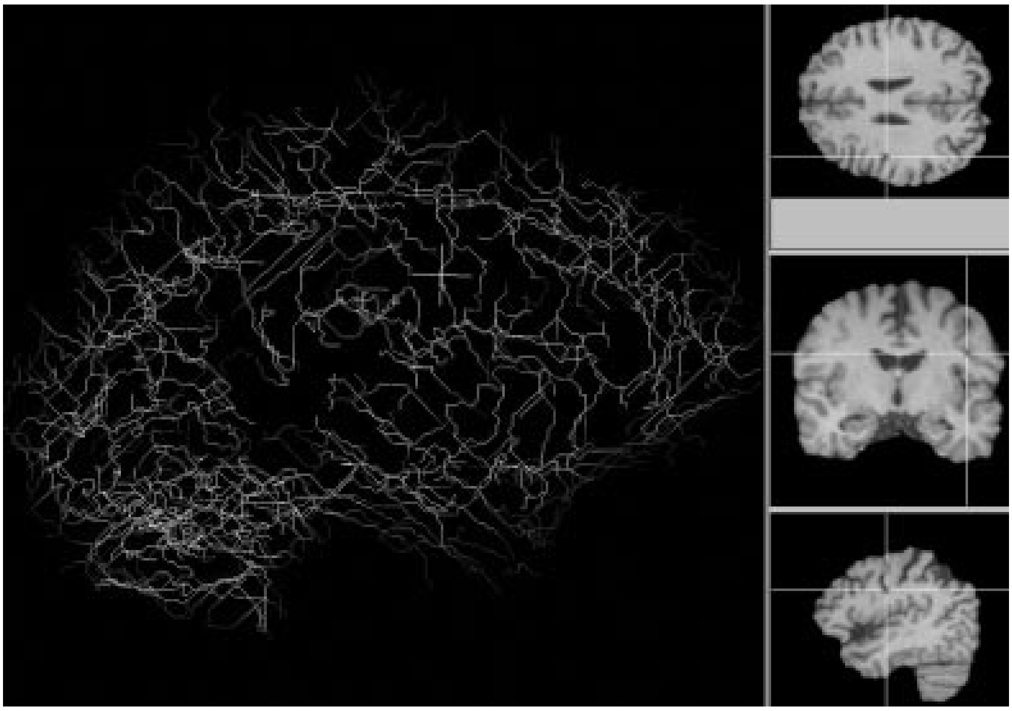


Figure 3. Sulcus bottom lines derived from a high-resolution MR tomogram

Removal of non-brain parts in MR tomograms of the head

3.5.2

Palubinskas, G.

The segmentation of the outer layers of the head (skin, bone, meninges) from the brain in MR tomograms is necessary for further anatomical analysis. We have developed an automatic procedure for the removal of non-brain parts in multi-slice MR images. An adaptive filtering step and the detection of the commissura anterior and posterior are included, which leads to an automatic adaption of the stereotactical coordinate system. However, the performance of this segmentation step is affected by noise, intensity variations due to inhomogeneities, and the partial volume effect. Thus, filtering and segmentation are essential pre-processing steps which determine the quality of any subsequent analysis. We describe the development and implementation of new filters and segmentation algorithms with an increased accuracy, efficiency and level of automation.

Noise removal with adaptive edge preserving filters
Conventional smoothing filters (like mean or median filters) remove noise quite effectively, but blur the edges of objects in an image. Advanced edge preserving filters such as the sigma (Lee) or the anisotropic diffusion filter preserve edges much better, but are charaterized by a number of parameters and require much more computation time.

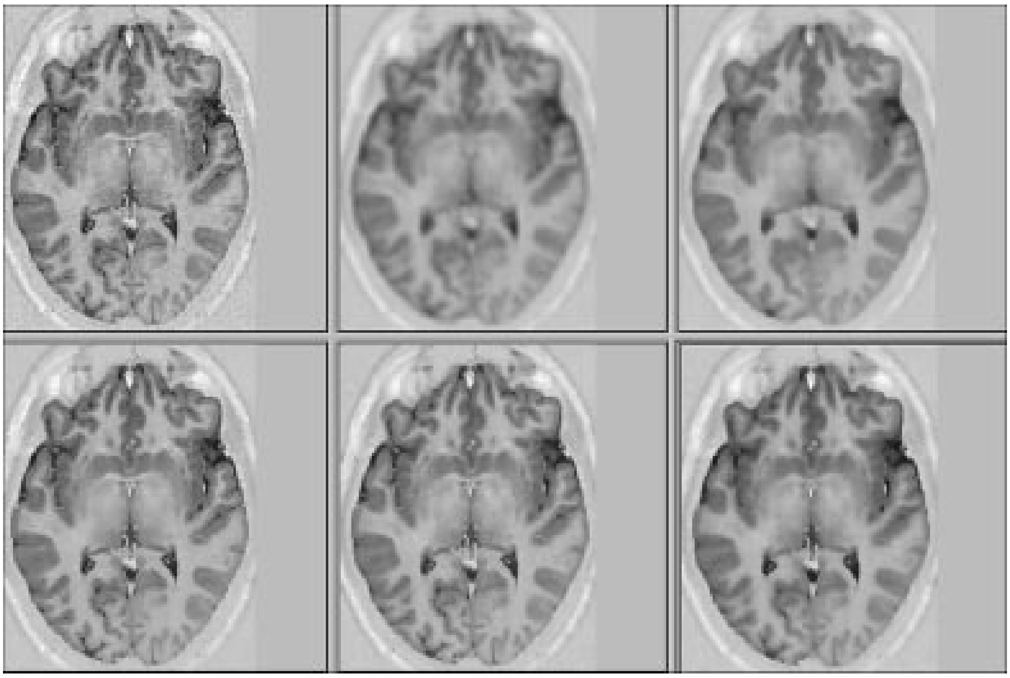


Figure 4. Top row: comparison of conventional filters (original image, mean, median). Bottom row: comparison of adaptive filters (extended sigma filter, anisotropic diffusion filter, cracking plate approximation filter).

We propose an extension of the sigma filter, in which the value of the sigma parameter is derived from a noise profile and is thus adapted to the entire volume. This noise profile is estimated from the most homogeneous regions in the volume. The number of regions is controlled by noise thresholds which are computed from the noise profile. This extension allows the main parameter of a sigma filter to be chosen automatically for different regions of the dataset. The second parameter of a sigma filter, the window size, is also dynamically controlled using the standard deviation of the intensity and the noise profile in a certain region. We thus obtain a parameter-free sigma filter.

We introduce a new quality criterion - the difference of two noise profiles (one for the original image and the second after filtering) - as a quantitative measure for the smoothing and edge preserving properties of a filter. A comparative study of various filters (mean, median, sigma, anisotropic diffusion, cracking plate approximation) based on the new filter quality criterion and visual analysis was performed on magnetic resonance images of human head (see Fig. 4). The extended sigma filter proved to be superior in its edge preserving properties, smoothing strength and speed.

Brain peeling

Existing brain peeling procedures for single-echo MRI data are semi-automatic, inaccurate, and time consuming. We have developed an automatic procedure for the removal of the outer layers of the brain ("peeling") which is accurate and fast.
This procedure consists of the following steps:

- pre-processing of MRI (noise removal, intensity correction),
- construction of an initial binary mask (k-means segmentation with binarization),
- post-processing of this mask (filling of holes, noise removal),
- selection of the brain in this mask (finding the largest connected component)
- refinement of the brain mask (closing, filling of holes),
- extraction of the brain from the input image by using the refined mask.

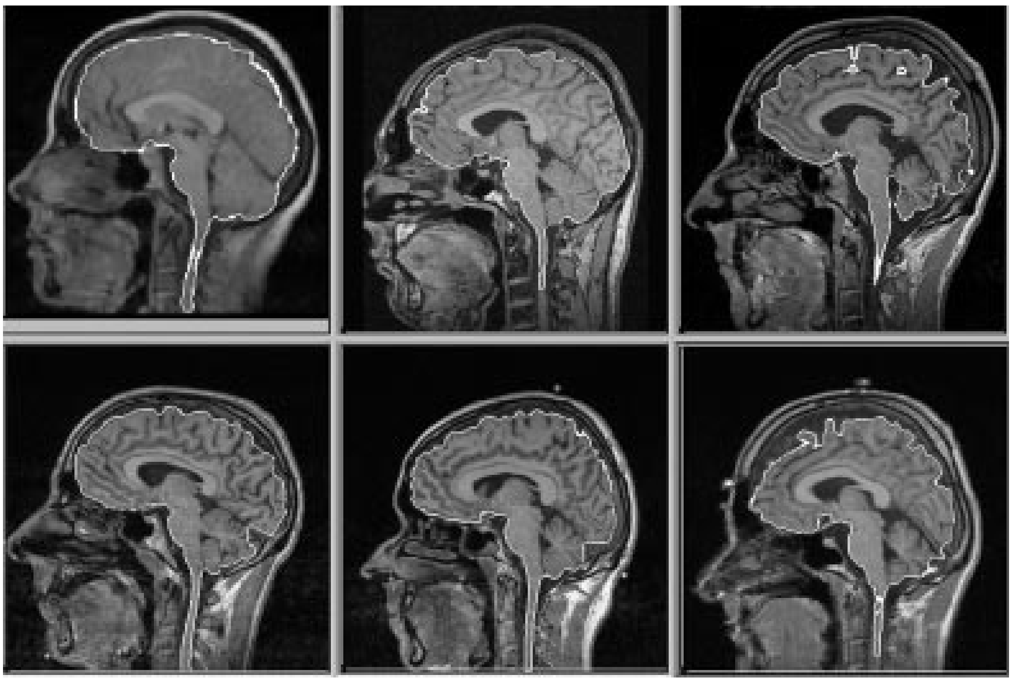


Figure 5. Brain peeling of 6 MR datasets.

The standard approach to separate the brain from its connected tissues uses morphological operations and offers a limited variety of sizes of structuring element. This is the main reason why this procedure is inaccurate and time-consuming. Replacing these morphological operations by computing the distance transform and subsequent binarization removes these obstacles. The size of structuring element is now defined automatically using a priori anatomical information. The results of our procedure in 6 MR datasets is presented in Figure 5. It is useful to pre-process the MRI datasets by the adaptive filter described above. While this leads to a larger structuring element (due to the loss of detail), it gives a better visual appearance in the final brain mask.

3.5.3 Segmentation of structural MR images

Descombes, X., Palubinskas, G., Rajapakse, J., Kruggel, F. & von Cramon, D.Y.

Image segmentation is a basic problem in "low level" image processing. A low level task consists of 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. A segmentation algorithm assigns a label referring to a specific class or area to each voxel. So the problem can be divided into three parts: information extraction, classification and regularization.

Before classifying data, we first have to define the relevant feature to be classified and extracted. Considering a "classical" segmentation problem, the intensity level of a voxel is a classified feature and thus the first problem can be overcome. However, for some applications we have to extract textural features or to combine different sources of information. The next step is classification of the data. Given the set of relevant features we have to divide it into different clusters. To find 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 of adding some *a priori* knowledge to the classification. When classifying voxels, some errors arise depending on noise, inhomogeneities, partial volume effects, etc. Regularization and statistical methods (MRF, Maximum Entropy, etc.) are thus used to inject constraints on the solution such as spatial homogeneity.

The segmentation goal with structural MRI is to differentiate between brain tissues and/or anatomical objects. The applications include brain morphology, tissue measurements, sulcal and gyral pattern detection and brain peeling. Some algorithms are already available but improvements which account for inhomogeneities are needed. We have focused our work on two main points concerning segmentation of structural MR images. Firstly, we have implemented the CVC algorithm (Contextual Variance Clustering) algorithm. This clustering algorithm is an improvement with respect to k-means or fuzzy c-means in case of strongly mixed distributions. However, inhomogeneities are not tackled in this method and they actually are the major limitation to current segmentation algorithms. The second point thus concerns the correction of inhomogeneities. In a given volume, intensity variations can be due either to inhomogeneities or to different kinds of tissue. To estimate the amount of inhomogeneity we need to distinguish between these two sources of variation. However, if we perform a classification without inhomogeneity correction, we obtain a poor result and then the correction will be biased. Estimating inhomogeneities without taking into account the different tissues will also lead to poor results. Ways to handle this problem are described in greater detail in the following chapter.

3.5.4 Inhomogeneity correction of MR data sets

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

Segmentation is the process of separating image elements with similar characteristics into the same class. Segmentation of MR head scans separates various tissues and anatomical structures in the brain. A major obstacle to any automated method of segmentation of MR images is the presence of intensity inhomogeneities which are spatial intensity variations over the same class of tissues or structures not caused by random noise. Although the inhomogeneities are due to many unfavorable characteristics of the scanners and imaging objects, the majority of the inhomogeneities are caused by the irregularities of the radio-frequency field (B1). The inhomogeneities caused by irregularities in B1 field appear as low frequency variations in the intensities of images across the field of view and from slice to slice.

Most classical image processing techniques such as thresholding, and edge and region detection schemes fail to segment MR images satisfactorily because of their inability to counter the presence of inhomogeneities. Although statistical techniques have attempted to overcome errors due to inhomogeneities, in our experience, these methods do not seem to give correct classification results over a wide range of imaging conditions, and none of the methods uses the information from the connectivities seen amongst the image elements.

A statistical approach for the segmentation of MR images in the presense of noise and intensity inhomogeneities is presented. Noise and inhomogeneities are incorporated explicitly into a *measurement model*, and the connectivity and neighborhood correlations in a segmentation are incorporated into a *prior model*.

The measurement model of the image is given as:

$$\text{(1)} \qquad y_i = (1+\beta_i) * \mu (x_i) + \eta_i$$

where $\mu(\bullet)$ denotes the mean intensity of the given tissue class, η_i denotes the random noise signal at the *i th* voxel site, and η_i represents the variation of the gain of the signal due to the intensity inhomogeneities. The field β is referred to as the bias field and represents the inhomogeneity profile over the image. The noise distribution is assumed to be random, white and Gaussian and the class conditional probability at the *i th* voxel site can be written as :

$$\text{(2)} \qquad p(y_i \mid x_i) = \frac{1}{\sqrt{2\pi\sigma^2(x_i)}} \exp\left(-\frac{1}{2} \left(\frac{y_i - (1+\beta_i)\mu(x_i)}{\sigma(x_i)} \right)^2 \right)$$

where $\sigma(\bullet)$ is the noise variance of the given tissue class.
The prior model of the segmentation is considered to be a 3-dimensional MRF which is capable of taking into account the piecewise contiguous nature of the image segments. From the Hammersly-Clifford Theorem, the prior probability of the segmentation is given by a Gibbs distribution and the prior model can be characterized as :

(3) $$p(x) = \frac{1}{Z}\exp\left(-\sum_{c\in C} V_c(x)\right)$$

where *Z* is the normalizing constant. We use a class of Gibbs distributions known as multilevel logistic (MLL) model to represent the energy potentials of the cliques. The two parts of the proposed model are characterized by the corresponding probability density functions (eq. (2) and (3)). We attempt to find estimations that give the *maximum a posterior probabilities* (MAP) of the segmentation and the model, given the image data. Therefore, the optimal estimations of the segmentation and the model are given by:

(4) $$\hat{x} = \arg\max_x\ p(x, \hat{m} \mid y)$$

(5) $$\hat{m} = \arg\max_m\ p(\hat{x}, m \mid y)$$

Since the simultaneous estimation of x and m is not possible, the two estimations are evaluated separately. A first step finds the segmentation and second step finds the model. Using a known segmentation, the model parameters can be evaluated and with known model parameters, a segmentation can be found. The segmentation process starts with an initial classification obtained from an isodata algorithm.The optimal segmentation is derived as an approximation to MAP estimation using a greedy algorithm based on an iterative conditional modes (ICM) algorithm. The segmentation and model are alternatively and iteratively evaluated until a convergence of the segmentation is achieved. A four-class synthetic MR image and an inhomogeneity bias field were simulated using a rational Gaussian (RAG) function (Fig. 6). The segmentation results from the present method were compared with other statistical methods such as isodata, maximum likelihood criteria (MLC) and unbiased MAP criteria. The results with the proposed method showed superior performance over the other methods. With the outer layers of the brain (skull, muscles, and meninges) removed (or peeled or shelled) from the MR head scans, the brain scans can be classified into three classes, namely, white matter, gray matter, and cerebrospinal fluid (CSF).

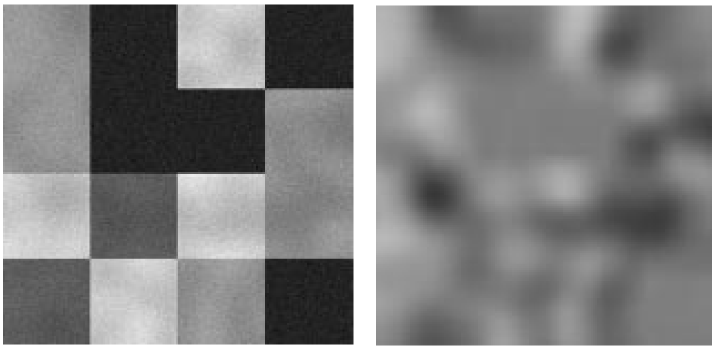


Figure 6. Application of the algorithm to a synthetic image (left) and the estimated inhomogeneity profile (right).

Ten peeled brain scans from Mass. General Hospital were segmented using the proposed algorithm. Twenty three brain scans were obtained from KFA Juelich, Germany and the unpeeled scans were segmented for five classes; background, fat, white matter, gray matter, and CSF. The results with the clinical brain images showed promise and sufficient accuracy so that our method can be successfully applied to clinical and research applications (Fig. 7).

The accuracy of the segmentation depends on the validity of the model of the segmenting image. Since there is no way of measuring the amount of inhomogeneities, it is not possible to assure the accuracy of our segmentation. Therefore, we compared performance of our algorithm against other statistical techniques with simulated MR images. Although the multiplicative assumption for the inhomogeneities results in a mathematically tractable model, the reaction between the inhomogeneities and the image may be more complex. Our method has two major drawbacks. Firstly, it depends on an initialization. If the initialization is far from the final segmentation, the algorithm may end up in a local minimum of the energy function. The second drawback is the use of a low pass filter in computing the bias field in the measurement model. No previous method has incorporated both inhomogeneities and a prior model for the segmentation of MR images. Since we have introduced a method to successfully estimate the inhomogeneities, an extension of our approach to include tissue dependencies and localizations may be useful.

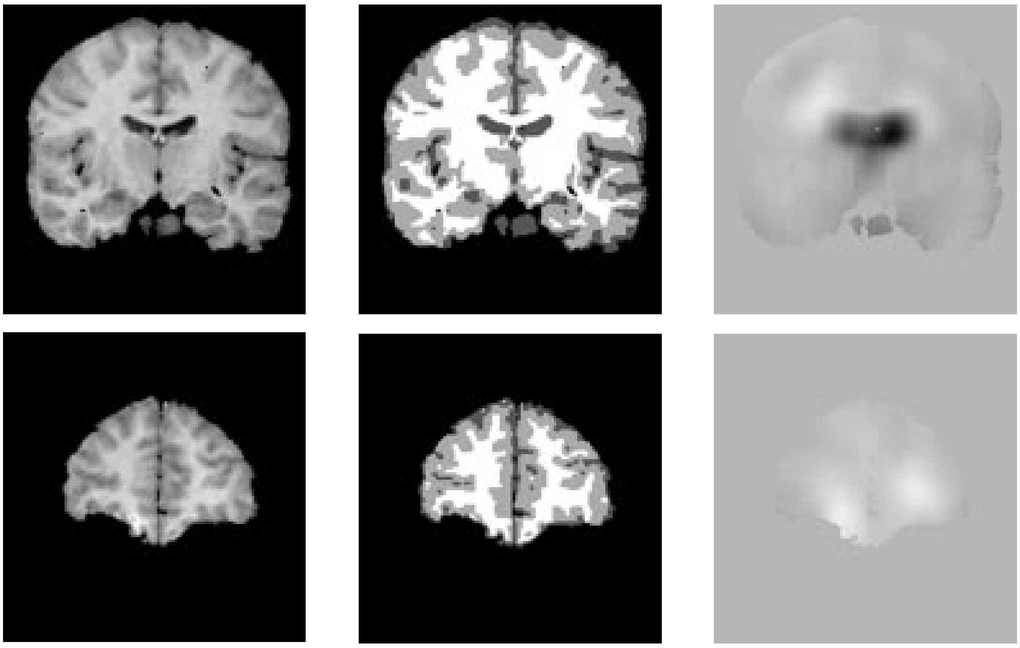


Figure 7. Application of the algorithm to a 3D MR dataset. Shown are the original dataset (left column), the resulting segmentation (center), and the estimated inhomogeneity profile (right).

An alternative algorithm that we consider now is based on Markov fields. A first Markov field which leads to stepwise constant realizations, models the tissue map, whereas the bias field is modelled with a Markov field leading to smooth varying realizations. These two coupled Markov fields are optimized using a MCMC (Markov Chain Monte Carlo) method. This methodology is currently being tested for different optimization schemes and initializations.

Statistical analysis of fMRI data

3.5.5

Descombes, X. & Rajapakse, J.

Segmentation can also improve fMRI analysis. Spatial interactions can improve statistics used in detecting significant activation areas and suppress noise. The extraction of relevant information is a crucial point for these applications. Considering the time series of a given voxel as a noisy blurred signal should allow us to use signal processing techniques as a pre-processing step before applying statistical analysis. The segmentation of fMRI can be achieved using statistical maps or temporal classification schemes.

Statistical analysis: detection of an activated area

The detection of activated areas can be roughly divided in two problems: (i) extract the information from the data by a statistical test leading to a z-score map, (ii) analyse this map to extract activated areas.

From PET studies, numerous statistical techniques have been proposed to analyse fMRI data (t-test, ks-test, correlation...). A well known package called SPM (Statistical Parametric Map) can be used as a reference. So a first step in this work was an evaluation of these techniques. However, all these tests are local tests in the sense that they do not take into account any spatial information. A first improvement consists in considering spatial interactions between voxels. Although these interactions should not be as strong as in the classical segmentation problem, we can consider that activated areas cover several connected voxels. Contextual methods based on a Bayesian framework define a first step.

We have extended the t-test into a ct-test (contextual t-test) to use spatial information. We denote the different samples involved in the t-test by a coefficient depending on the similarity between the sample and the average of its neighbors. In this way, noisy pixels are excluded of the statistical test. Statistical maps that we obtain are thus much less noisy. Further, we propose to use contextual information to analyse the statistical map. Activated areas are roughly characterized by a high response on the statistical map. However, a simple threshold leads to a noisy result. The solution should thus be regularized to lead to a realistic result. We have modelled the activation map as the realization of an Ising model using the statistical map as an external field. A simulated annealing optimizing the MAP (Maximum A Posteriori) criteria has been implementing. We thus obtain a non-noisy activation map. Further work is required to compare these results with other methods consisting of analizing the connected componants obtained with a given threshold.

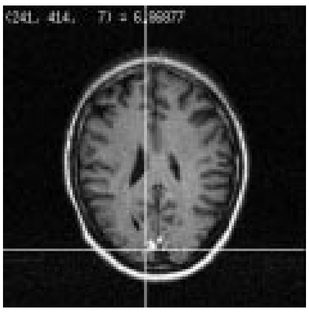


Figure 8. Functional activation in the visual cortex as detected in a fMRI experiment

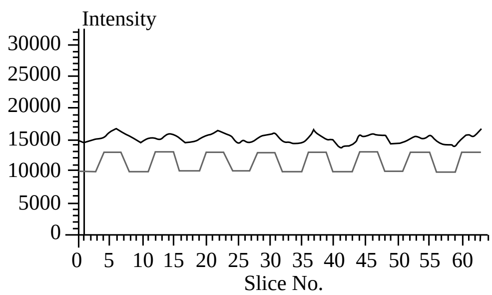


Figure 9. Time course of the signal in a apecific voxel site

Reconstructing time evolution of an activated voxel

As we have a time series of slices, we find the activation of a given voxel as a time dependent signal to which a series of predefined experimental states are assigned (0 and 1 in the simplest case). The signal is known and defined by the experiment. We can consider that this signal is filtered by a black box (brain + MR + ...). The filter can be modelled by a convolution, a time shift and additive noise. We restore the resulting signal using energy minimization techniques or entropy maximization techniques. First, this restoration can improve the statistics used to detect activated areas. In a second step, we can estimate quantities such as the time shift or the convolution kernel.

3.5.6 Spatio-temporal analysis of EEG - data

Uhl, C.

The goal of the analysis of spatio-temporal signals q(x,t) obtained from EEG / MEG / fMRI - measurements during cognitive experiments is to answer two questions: Where are the active regions in the brain ? How do these regions interact ? Thus, one is interested both in a decomposition of the signal, $q(\mathbf{x},t) = \sum_i \xi_i(t)\, v_i(\mathbf{x},t)$ and in the dynamics of the systems in terms of differential equations, $\dot{\xi}_i = f[\{\xi_j\}]$. The spatial modes, v_i (x), can thereby represent interacting dipoles or current distributions. Conventional methods are data driven and focus either on spatial localisation or on temporal aspects of the signal.

Spatial analysis

A decomposition of the signal is obtained by minimizing a cost function, $f_s = \| q(\mathbf{x},t) - \sum_i \xi_i(t) v_i(\mathbf{x}) \|$ with respect to the "modes", under a certain norm and considering anatomical constraints. The amplitudes are obtained by projecting the signal onto the modes, $\xi_i(t) = P_q[v_i(\mathbf{x})]$. However the underlying dynamics of the system are completely neglected in the cost function f_s and no information about the interaction is gained: the minimum of the cost function optimum represents the best convergent decomposition, but is not optimal with respect to an understanding of the underlying dynamics.

Temporal analysis

Temporal analysis focuses on time series of single electrodes and yields a differential equation by minimizing a cost function, $f_t = \| \dot{\xi}(t) - \sum_i a_i \xi^i(t) \|$ with respect to the coefficients a_i. Other examples of temporal analysis are given by characterization of the time series by its power spectra, Lyapunov exponents and fractal dimensions. However these methods neglect the spatial dimension of the problem.

Spatio-temporal analysis

To fill the gap between these two approaches a new model-based algorithm for spatio-temporal signal analysis has been developed. It aims at *simultaneously* optimizing coefficients describing *spatial* distributions and the *dynamics* of the system .This is accomplished by minimizing a cost function, which is a combined version of cost functions f_s and f_t: $f_{st} = \| \xi_i[v_i] - \sum_j a_j \xi_j[v_j] - \sum_{jk} a_{jk} \xi_j[v_j] \xi_k[v_k] - \ldots \|$. The minimum of this cost function (with respect to spatial modes $v_i(x)$ and with respect to the coefficients a_j, a_{jk},...) represents the best choice of both spatial modes and coefficients describing the dynamics. To reduce the dimensionality of finding the best solution of all possible interactions and all possible spatial distributions, one should restrict oneself on a certain class of dynamics: i.e. a model in which one assumes a certain type of differential equation and searches spatial modes and temporal coefficients for that model.

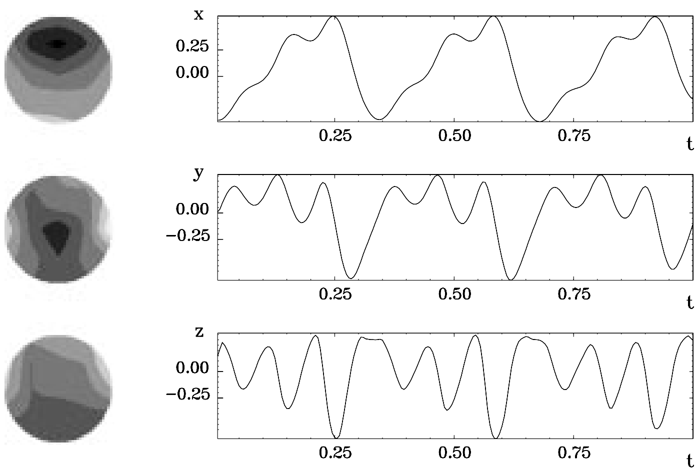


Figure 10. Spatial modes and corresponding amplitudes which model EEG-data of petit-mal epilepsy.

EEG - Analysis of epileptic seizures

Previous results of this method applied to EEG - data of petit-mal epileptic seizures are presented and discussed. There, the underlying model was assumed to be a differential equation of the form, $\dot{\xi}_1 = \xi_2$, $\dot{\xi}_2 = \xi_3$, $\dot{\xi}_3 = f[\xi_1, \xi_2, \xi_3]$. Figure 10 shows the spatial modes and corresponding dynamics obtained by minimizing the cost function belonging to the differential equation. Figure 11 shows the phase portrait of the amplitudes, which demonstrates some characteristic features of so called Shilnikov dynamics, which could be inherent in petit-mal epilepsies, i.e. for petit-mal epilepsies the observed dynamics seem to be characteristic.

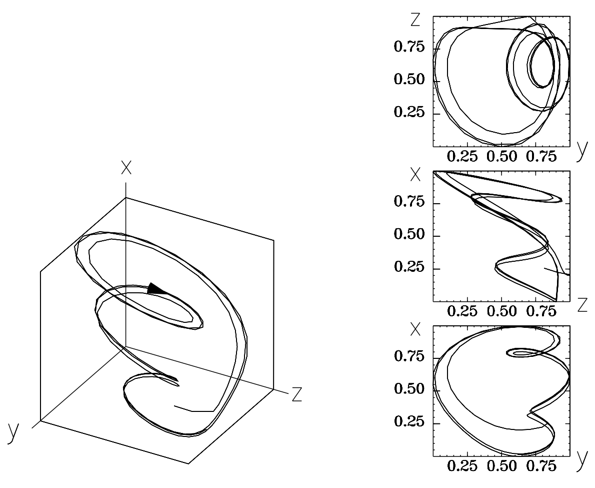


Figure 11. Phase portrait of the amplitudes: Shilnikov dynamics

Experiment of the phi - phenomenon

The motivation of this experiment was to investigate whether spatial and temporal analysis yields a model which is an appropriate basis for the presented spatio-temporal analysis. Two alternating blinking points are presented. The inter-stimulus interval (ISI) is continuously reduced. At the beginning of a trial the subject observes an apparent motion. This perception breaks down at a certain critical value of ISI and the subject observes two blinking points. Figure 15 shows the relative frequency of movement perception of a subject as a function of ISI. For spatial analysis principle component analysis (PCA) of averaged EEG - data was chosen, i.e. the cost function, $f_s = \left\langle (q^{(\alpha)}(\mathbf{x},t) - \sum_i \xi_i(t) v_i^{(\alpha)}(\mathbf{x}))^2 \right\rangle_t$ was minimized for different time segments α. The spatial modes obtained corresponding to the "movement perception phase" and to the no movement perception phase did not differ significantly from each other. Therefore from this spatial analysis perspective no spatial difference can be found in the EEG - data of the experiment. The reason for this is either that there is no spatial difference in the potential on the surface of the head or that the experiment is not well suited to the observation of differences between the two phases. The breakdown of the "movement perception phase" is spontaneous and not directly triggered by the stimuli presented. By averaging the data the differences between the two phases may cancel out.

In a temporal analysis, channel-averaged power spectra of trial-averaged EEG - data were investigated. An interesting feature was observed in the comparison of two frequency contributions in the EEG - signal (the frequency c1 corresponding to the occurrence of "left point - ISI - right point" and the frequency c2 corresponding to the presentation of only one point). Figure 12 shows the relation of c1/c2 of a subject as a function of ISI. A correspondence of this relation to the relative frequency of movement perception (Figure 13) can be observed. The increase of the relation c1/c2 at small values of ISI is due to a second phase transition, where the subject focuses on one blinking point.

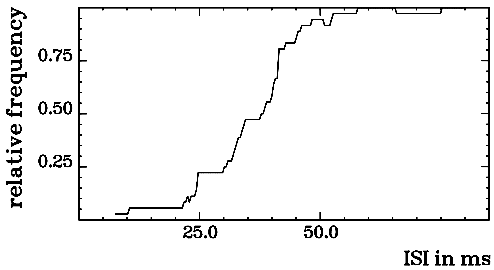


Figure 12. Relation c1/c2 in dependence of ISI

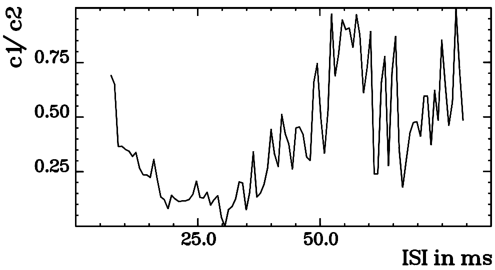


Figure 13. Relative frequency of movement perception

The spatio-temporal approach to EEG signal analysis consists of two basic steps: (i) the development of a model and (ii) minimizing the corresponding cost function. When applying this method to EEG data, an important result of this analysis is the observation of characteristic dynamics which seem to be inherent in the EEG of petit-mal epilepsies. The temporal analysis of the EEG data of the phi - experiment yielded encouraging results and provided starting points for developing a model of the underlying mechanisms of the phenomenon. However, there are problems related with this experiment because the spontaneous breakdown of the "movement-perception-phase'' is not directly triggered by a presented stimulus. Further work will involve spatio-temporal analysis of different ERP-experiments.

A finite element model of the human brain

3.5.7

Hartmann, U. & Kruggel, F.

Finite element methods are common in the engineering sciences to analyze mechanical, electrical or structural properties of systems. Transferring this method to MR tomograms permits the analysis of the reaction of the brain to mechanical stress (hemorrhage), injuries (trauma), deformations (tumors, edema), and to build electro-magnetical models for the analysis of dipole sources.
The first application of FEM in the medical field was the design of prostheses but currently research is also being undertaken on different types of human soft tissue organs. Some of the principle questions that cannot be studied in vivo but may be clarified by the model are:

- How do external forces (i.e. a hit on the forehead) deform the brain and its structures? Given the location of the blow, is it possible to estimate the resulting brain damage?
- We would like to explain structural changes in the brain caused by space-consuming processes (i.e. growth of metastases or intracranial hemorrhages). Thus, we want to model the statics of the brain.
- The model should examine whether the deformation of brain structures leads to disturbances of cognitive functions.

Due to the complexity of human brain structures a lot of problems arise when building FE models of the brain. First, we need a segmentation of the objects in the head into “materials” of homogenous properties. The next step consists of the formation of finite elements by the introduction of a 3D mesh. Finally, we need to set up and solve the differential equation system.
The basis of our model is a 3D MR-dataset of the brain. Methods for segmentation of MR-images provide a classification of “materials” (e.g white matter, CSF) in the brain. After the raw data have been processed with our segmentation tools structures of interest are labeled so that the structures can be separately addressed.
Starting from our pre-processed MR-dataset we generate a 3D-mesh consisting of a finite number of elements (that is where the name originates), which in our case are tetrahedral or hexahedral elements. Although the research on 3D-meshing is very active and a number of algorithms are available we found that none of the solutions satisfied our needs.
For this reason we built our own voxel-based mesh generator. Whereas the geometry for most mesh generators is given by a triangulated surface or by a mathematical function, our mesh generator uses the fact that the space in which our objects are embedded is pre-structured. In other words, all of our objects are described as a composition of discrete elements (voxels). We could directly interprete the voxels as finite elements, but with regard to numerical stability we decided to transform the isotropic voxel space. This transformation is governed by two parameters which denote the minimum and maximum size of cubes which result from the collection of voxels with the same label. From the anisotropic cube mesh which is the result of the collection phase we can switch to a tetrahedra mesh by subdividing the cubes into tetrahedra. This mesh generator has the following advantages:

- It is very fast. Producing a mesh consisting of 10 000 tetrahedra is a matter of seconds.
- It uses a very stable algorithm. For example there are no delicate procedures to determine the geometry of a structure.
- The tetrahedra produced by the mesh generator are regular and thus suitable with regard to the numerical stability of FEM.

For our future FEM simulations we can choose between three different discretisations of the space in which the brain is described. We can use an isotropic hexahedral or tetrahedral mesh either evolving from an anisotropic or an isotropic cubical mesh. This decision is also being reflected in the shape of the FE-stiffness matrix.
After the assignment of material properties to the brain structures, the building of the FEM equation system is done by a 3D integration over each element and the condensation of these element stiffness matrices to a global stiffness matrix. For this purpose we used a software package which has been adapted to our problem. We optimized the program by implementing different parallel sparse matrix solvers (the iterative conjugate gradient method and a direct matrix factorisation method).

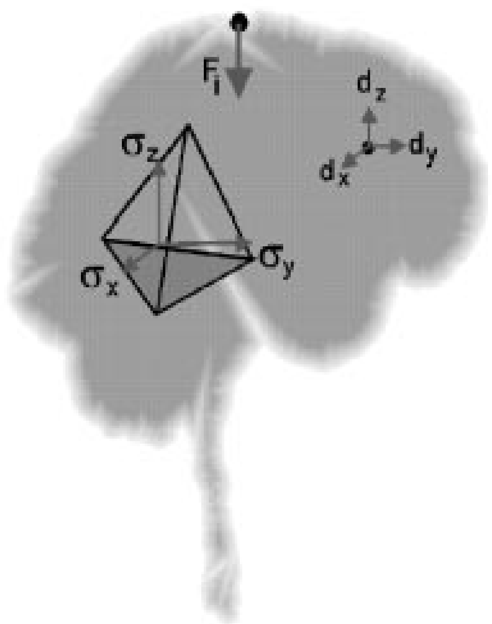
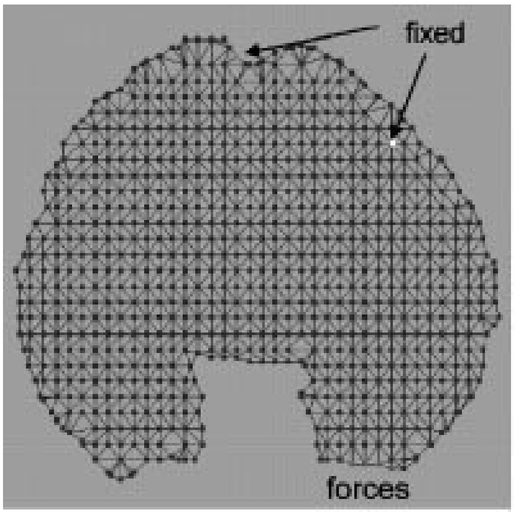
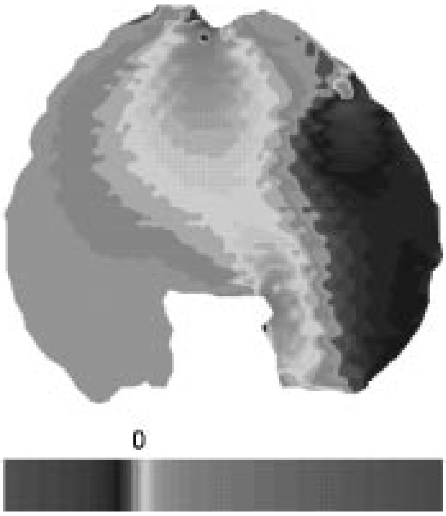


Figure 14. The brain shown as a continuous elastomechanical body which is fixed at one point. The figure demonstrates symbolically that the brain is approximated by tetrahedra. At one node a force is applied and as a consequence all the other nodes are shifted more or less until the total potential energy of the body reaches a minimum (extremal principle). d_i denote the nodal displacements in their respective directions, σ_i represent the stress component within a tetrahedron.

The study of the elastomechanical response of a brain due to forces yields several results. First the spatial displacements of the nodes (the corner points of the tetrahedra) are calculated. The new locations of the nodes are visualized as the displacement plot, which shows the body under consideration in his new equilibrum state. From the displacements a stress and strain analysis can be carried out.
We triangulated a pre-processed MR tomogram (Fig. 15) and applied a force to the frontal region. Figure 16 visualizes the stress component σ_y in a contour plot.
Now we are making our first steps towards the calculation of more realistic cases. The coup - contrecoup phenomenon could quite easily be simulated for models consisting of up to 500.000 tetrahedra. On our parallel computer solution of the equation system takes less than ten minutes. With little expense internal brain structures (i.e. the

ventricles) can be extracted and be evaluated separately. 3D displacement plots of these structures are available.





Figures 15 and 16. Stress and strain analyses carried out in two and three dimensions.

The finite element method is a fruitful approach to answer the questions listed above. Now that two of the main steps, the generation of 3D meshes and the parallelization of the FElt-package, have been accomplished, the modeling phase of this project is almost finished. Further features of interest are the time-dependent analysis and the nonlinear theory of elasticity. By implementing these additional capabilities into the package we would gain a very powerful tool for the simulation of the clinical cases described above.

3.6 NUCLEAR MAGNETIC RESONANCE

The last year has seen significant changes in the position of the NMR-group. During the first part of the year (Jan-March) some experiments were performed using a Medspec 3T/60 system in Ettlingen. These served primarily to acquaint the group with the software environment and pulse programming language of the Bruker system. The Institute's Medspec 3T/100 system was delivered to Leipzig on the 17th April. The official opening of the new building and system took place on the 4th of June with the system being available to the Institute from July onwards.

The sophistication of, and large amount of infrastructure required for, modern fMR investigations has required that most of the group's energies have been expended either on overcoming problems associated with the installation or on technical developments. Those projects that have borne results that can be classified as research have largely been based on computer simulations which could be pursued independently of the installation of the system.

A considerable amount of effort has been applied to embedding the group in the local and international environment. These collaborative projects are expected to yield results in the medium term. The group is part of a Biomed-2 project supported by the European Union. Good contacts have been established within Leipzig to the neurological department of the University with which projects examining both chronic and acute stroke will be started in 1997.

The group benefited significantly from the visits of two scientists: Dr. T. Redpath of Aberdeen University (2 months) and Prof. Dr. H. Merkle (University of Minnesota). The former worked on a number of projects including navigator echoes for diffusion imaging, calculation and measurement of obtainable signal to noise ratios and T1 contrast development. Prof. Merkle was largely involved with the development of a high sensitivity resonator for examining the upper head.

Fast functional imaging: GRASE

3.6.1

Jovicich, J. & Norris, D.

Echo planar imaging (EPI) is the standard method for measuring brain activation in fMRI. The main advantage of the method is that it is very fast: one image can be acquired in less than 0.1s. This is of particular advantage when images from extensive spatial regions are required. The method is essentially a gradient echo (GRE) sequence and this means that it is sensitive to T2*. In other words, the NMR signal is related to both spin dephasing induced by static magnetic field inhomogeneities, produced mainly around larger venules/veins, and dephasing of spins diffusing in the vicinity of small vessels (less than 30 μm diameter). This makes the method very sensitive to functional activation changes (T2* changes), but also to blood flow changes in large vessels, therefore affecting the accuracy of fMRI identifications of activated cortex. The main disadvantage of EPI is that data acquisition time is limited by T2*, so the spatial resolution is low: the pixel size is usually larger than 2 mm.

Spin echo (SE) sequences are also used for fMRI. They use strong radio frequency (RF) pulses to refocus the spin dephasing from static magnetic field inhomogeneities. SE sequences are therefore sensitive mainly to spin diffusion taking place during the time prior to the echo, i.e., to T2. Simulation results indicate that vessels of less than 30 μm diameter will dominate the contrast changes in SE images, resulting in a more accurate determination of the cortical activation areas. However, because of the need of refocusing pulses and long echo times to allow for enough spin dephasing accumulation (enough functional contrast), SE sequences are much slower than EPI (about 20s per image). In addition, the use of 180° refocusing pulses brings the problem of high RF power deposition, particularly at high magnetic fields.

GRASE (GRadient And Spin Echo) is a relatively new fast sequence (one image can be acquired in less than 0.3s) that combines advantages of EPI and SE sequences. As EPI, GRASE is a one-shot method but it alternates between gradient and RF refocusing within the echo train and consequently forms the images faster and with less heat deposition than SE methods. The effect of the RF refocusing pulses is that signal decay is effectively limited by T2, allowing a longer acquisition time and therefore a spatial resolution (under 1 mm) that is better than that given by EPI. Contrast in GRASE images results from a combination of T2 (mainly) and T2* effects.

To our knowledge there are no published results describing the implementation of GRASE at 3.0 T or the use of GRASE for fMRI (at high or low fields). Our interests are therefore to implement the GRASE pulse sequence on our 3T system and then to investigate the limits of its spatial and temporal resolution as well as the sensitivity of the method to detect functional related NMR signal changes.

It is of interest to estimate the functional contrast that a GRASE fMRI study would give and to compare these results with those given in the literature for SE (dependent on T2 changes) and GRE fMRI studies (dependent on T2* changes). We performed a computer simulation to calculate this and our results suggest that the functional contrast given by GRASE would be basically that given by a SE sequence (Jovicich & Norris, 1996).

A program was written to calculate the point spread function (PSF) of the GRASE sequence. The PSF of a sequence is a mathematical function that predicts what would the image of a point source be like when imaged with the corresponding sequence. A point source is an ideal concept that means that the source is concentrated at an infinitely small point in space. Due to the imperfections of any real imaging method, the PSF will usually consist of a peak centred at the position of the source. The height of the peak is related to the sensitivity of the imaging method (the signal intensity). The overall shape of the PSF, particularly the broadness of the central peak, determines the spatial resolution. The PSF is strongly dependent on the phase encoding order used during the data acquisition. By comparing the PSF of different pulse sequences one can make predictions about the relative sensitivity, spatial resolution and artefacts given by different methods.

The point spread function (PSF) of GRASE was calculated to compare the effects on the PSF of using standard and new phase encoding order methods. We have found a phase encoding order scheme that has not been proposed before for GRASE and that, according to the computer simulations, seems to provide better sensitivity and better spatial resolution than the methods proposed so far. It is, however, difficult to make an accurate quantitative statement about how good the method will be in a real situation. Once GRASE is installed, phantom tests will be performed to evaluate and compare this new method with the currently existing ones.

In conclusion, the computer simulations have given us a better understanding of how the functional contrast given by GRASE would compare to that given by the conventional GRE and SE sequences. Several phase encoding order schemes have been considered to try to optimize the PSF of GRASE for fMRI. Our simulations suggest that one of these methods, never proposed before for GRASE, might improve the sensitivity and the spatial resolution of GRASE fMRI maps. We are currently implementing and testing the sequence on our 3 Tesla system. Phantom tests will be done to study and optimize time and spatial resolution as well as contrast for different phase encoding orders.

3.6.2 Mechanism of the fast response

Dymond, R. & Norris, D.

The Fast Response (FR) is a small negative dip in the MR signal from the visual cortex arising 400ms after the onset of visual stimulation (Ernst & Hennig, 1994). If this effect results from the early local increase in paramagnetic deoxyhaemoglobin concentration measured in optical imaging experiments (Turner & Grinwald, 1994), then there are two important implications for functional investigations: first the FR offers a superior temporal resolution to that attainable using standard BOLD techniques and second, since the FR appears prior to the haemodynamic response, the signal change will be localised to the activated cortical columns and will not originate from neighbouring superperfused parenchyma. However, fMRS PRESS experiments have shown the amplitude of the negative dip to decrease with increasing echo time, a finding which appears to contradict the assumption that the underlying mechanism is T_2* dephasing due to elevated deoxyhaemoglobin levels. The aim of this study was to develop a model for the mechanism of the FR based on the early increase in deoxyhaemoglobin which would account for this echo time trend.

The proposed model is based on the competitive interaction of static spin dephasing and molecular diffusion attenuation within the voxel of interest. For an isolated vessel, the intrinsic field gradients produced by the early rise in deoxyhaemoglobin, and consequently the static dephasing effects, are greatest immediately adjacent to the vessel surface. Since the diffusion effect is proportional to the square of the field gradient, it too is greatest close to the vessel surface. Diffusion attenuation increases with the cube of echo time. This means that, at longer echo times, the diffusion will dominate, reducing the contribution to overall signal from regions of maximum dephasing.

Two computer simulations were used to test the model. These were numerical solutions of the Bloch equation for the development of transverse magnetisation in the region of a cylindrical paramagnetic vessel:

$$\frac{\partial m}{\partial t} = -i\gamma \left(\frac{K\cos 2\theta}{r^2}\right) m + D\nabla^2 m$$

Constant K takes into account the main field strength, the concentration of deoxyhaemoglobin in the blood, and the vessel radius. The aim of the first simulation was to investigate the interaction of dephasing and diffusion. Intrinsic field gradients were linearised by dividing a basic vascular unit containing a single vessel into incremental cubes whose side corresponded to the expected diffusion length for a given experimental duration. The gradient magnitude was then assumed to be constant within each of these increments. The product of dephasing and diffusion attenuation was summed over all increments of the vascular unit. To obtain a value for the total signal change arising from the VOI, an orientational average was performed over all possible vessel orientations and the result corrected on the basis of the estimated percentage of the VOI occupied by activated visual cortex. The second computer model was a Monte Carlo simulation of intra-voxel dephasing, based on that developed by Ogawa et al. for investigation of the BOLD effect (Ogawa et al., 1993). The aim here was to assess the validity of the assumptions made in the initial simulation, and to study the FR signal arising from smaller vessels .

The findings of these simulations can be summarised as follows:

- Simulation of a PRESS experiment confirmed the predictions of the model and yielded an echo time trend similar to that reported by Hennig (Hennig et al.,1995).
- Simulation of a gradient echo experiment gave a percentage signal change which increased steadily throughout the normal range of echo times.

- Capillaries were found to produce a similar Fast Response amplitude to that obtained from larger vessels, but the capillary contribution was not orientation dependent and showed a more marked variation with echo time.
- Computation of values for absolute gradient echo signal change indicated that it may be possible to select an optimum echo time for detection of the Fast Response.

Our results suggest that the Fast Response is indeed a form of negative BOLD effect which, owing to its early appearance and good spatial localisation, offers considerable promise for future fMR applications. Computer simulations have validated our theoretical model and have indicated optimal experimental parameters for FR detection. By incorporating these findings into the design of a suitable experiment, it should be possible to obtain FR amplitudes well in excess of the 1-2% signal change detected in prior studies.

3.6.3 Perfusion imaging

Schwarzbauer, C.

Regional blood flow is closely related to local neuronal activity in the brain. Recently, a non-invasive method for magnetic resonance imaging of the regional blood flow has been presented (Schwarzbauer et al., 1996). It is based on magnetic labelling of tissue water proton spins employing a slice-selective and a nonselective inversion recovery experiment. The feasibility of this approach has been demonstrated in an *in vivo* experiment on rats. In comparison to a similar technique presented by Kwong et al. (1995), this technique compensates for systematic errors due to the different longitudinal relaxation times of tissue and blood and therefore yields more accurate results. The aim of the present project is to implement this imaging technique on the whole body MR scanner in Leipzig.

Currently, mainly the BOLD (*blood oxygen level dependent*) contrast (Ogawa et al., 1990) is used to localize regions of altered neuronal activity in the brain. The mechanism of the BOLD contrast has not yet been completely understood. There is evidence that changes in both blood oxygenation and regional blood flow contribute to the measurable signal change. Quantitative perfusion imaging offers an interesting alternative approach for functional neuroimaging. On one hand, a well defined physiological quantity, namely the regional blood flow, is used to characterize functional activation. On the other hand, simultaneous measurement of perfusion and BOLD contrast will lead to a better understanding of the underlying mechanism of the BOLD contrast.

A single-shot inversion recovery MRI technique for high-speed mapping of the longitudinal relaxation time (T_1) was implemented on the MR scanner in Karlsruhe. The accuracy of this technique was tested in a phantom experiment using a set of sixteen agarose gel samples with different T_1 values. A T_1 map was calculated from the inversion recovery images of the phantom using a previously developed IDL routine. The measured T_1 values were in excellent agreement with the T_1 values obtained from a spectroscopic control experiment ($r = 0.9998$).

Based on the high-speed T_1 mapping experiment described above, the quantitative perfusion imaging technique consisting of a slice-selective and a nonselective measurement of T_1 was implemented in Karlsruhe. Due to lack of time no further testing or optimization of this sequence was possible in Karlsruhe.

A previously written computer program designed to calculate perfusion maps from the slice-selective and nonselective inversion recovery images was implemented and optimized on the INDY workstation in Leipzig.

After the installation and quality control of the MR system in Leipzig, the perfusion imaging technique was tested and implemented. So far only perfusion changes are measurable, which is sufficient to locate functional activation. In order to attain absolute values of the regional blood flow, several technical issues must be resolved. The main problem is that a nonselective inversion of all water proton spins within the upper part of the body including the heart is required. A straightforward solution would be to use the whole body coil for both signal transmission and detection. However, using the whole-body coil for signal detection results in an extremely poor signal-to-noise-ratio (SNR) as a result of the low filling factor (volume of interest = brain, sensitive volume of the coil = almost whole body). This difficulty can be solved by using the whole-body coil only for RF transmission and a separate receiver coil whose sensitive volume is optimally adapted to the volume of interest, namely the brain. A suitable receiver coil has been built by Dr. Merkle (University of Minneapolis) during his visit as a visiting scientist at our institute. The remaining problem to be solved is that the transmitter and receiver coil must be actively decoupled. A theoretical concept for active decoupling has been developed in co-operation with Dr. Merkle (University of Minneapolis) and Herrn Ihrig (Bruker, Karlsruhe) and is currently being tested experimentally.

In order to evaluate the sensitivity of the perfusion imaging method *in vivo*, it is planned to measure the change of the regional cerebral blood flow following hemodynamic stimulation with carbogen on healthy volunteers. This experiment has been approved by the local ethical committee. In co-operation with the Institut für Anesthesiologie (Universität Leipzig) a suitable respiration circuit has been developed to supply the volunteers with either Carbogen or fresh air.
As mentioned above, there is evidence that the BOLD contrast depends on both the regional blood oxygenation level and the regional blood flow. In a further study it is planned to investigate this dependency on 20 healthy volunteers. The experiment consists of alternating visual stimulation and carbon dioxide induced hypercapnia. During visual stimulation both the regional oxygen consumtion and the regional blood flow is altered, whereas under hypercapnia only the regional blood flow is increased. Simultaneous measurement of the BOLD contrast and the regional blood flow will therefore reveal to what extent the BOLD contrast is dependent on the regional blood flow. If both parameters are separable it will be possible to obtain information on the change of the regional oxygen consumption during functional activation. This study has already been approved by the local ethical committee. It will be performed in co-operation with the Institut für Anesthesiologie (Universität Leipzig).

4.1 Image and signal processing environment

Kruggel, F. & Lohmann, G.

An analysis of currently available signal and image processing environment shows that no package is suitable to fulfill the data processing needs of our institute. To facilitate the combined analysis of MRI, EEG and MEG experiments we have developed an integrated processing environment called BRIAN (Brain Image Analysis).

The analysis of cognitive processes in man usually involves multiple examination modalities which map different aspects of the brain. Among these procedures, at least one modality yielding anatomical information (i.e. MRI) besides one or more functional modalities (fMRI, PET, SPECT, EEG, MEG) are involved. Because these different examination methods yield complimentary information about the anatomical, metabolical and neurophysiological state of the brain, a combined data evaluation is highly desirable and will lead to results not achievable within one examination domain. We have developed a program package for the handling of image datasets (MRI, PET, SPECT, CCT) and signal datasets (EEG, MEG) which allows a combined analysis of these data sources in a 5-dimensional coordinate space (x, y, z, time and modality).

Design Outline

We want to address the needs of two different groups of people working with our package. The first group consists of the medical and technical personnel involved with the generation and routine analysis of the datasets. The second group consists of the scientists who perform data exploration as well as researcher who develop and integrate new image processing algorithms. While the first group expects a highly interactive and easy-to-use environment with well laid-out work paths, the second group requires an open environment which allows the rapid prototyping of new functions or image processing chains.

Thus, the design outline of our package consists of two layers. A highly interactive first layer features easy-to-use viewers for visualization, editors for interactive measurements or marking and dialog boxes for the execution of pre-defined high-level processing chains. Physicians and trained personnel use this layer for day-to-day tasks like aligning a PET scan to a MRI dataset, performing a volumetric analysis based on a segmentation or evaluating an ERP experiment by combining MRI and EEG data. The second layer allows an experienced user to extend the functionality of this package by integrating new modules, defining image processing chains or by modifying parameter sets.

This two-layer structure is reflected in two components of the package (i) an interactive kernel for viewing and editing datasets and (ii) a visual editor for the design and execution of image processing chains. Both parts are described below in more detail.

Viewers and Editors

The first layer of functionality is provided by a kernel containing the interactive display and editing capabilities of the package. Datasets in our problem domain fall into three categories:

- *Volumes:* 3D volume datasets from MRI and PET examinations to be displayed as images (slices or projections),
- *Signals:* 2D (position vs. time) datasets from EEG and MEG measurements usually displayed as curves, and
- *Geometrical Objects:* Surfaces defined in 3D which stem either from measurements with a tracking device or are computed from volumetric datasets. Space-filling geometric meshes for finite element analysis and CSG models of anatomical objects also belong to this category.

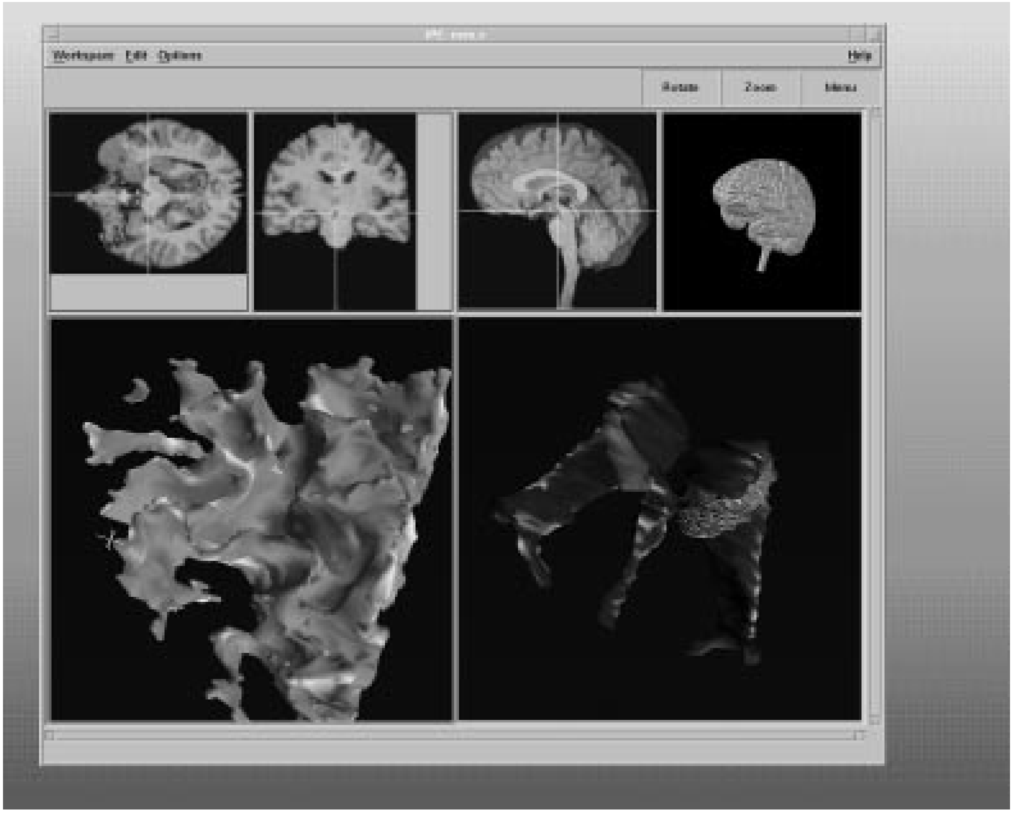


Figure 1. Example BRIAN workspace showing two geometrical viewer windows (bottom row), a volume renderer (top right) and three orthogonal viewers (top left). All viewers are connected via links, so that cursor movements are coordinated.

For these three data categories we provide separate viewers (for the display) and editors (for the modification of a dataset). Wherever appropriate, these viewers allow a *combined display* of datasets from two categories: a geometrical object (i.e. the surface of a tumor) is rendered inside a volumetric dataset of the brain; the electric potential recorded on the scalp is mapped as a color-coded texture onto the geometrically defined surface of the head. Furthermore, viewers may be *linked*: cursor movements or contrast adjustments in an orthogonal viewer are propagated to the other projections (or the 3D viewer); selection of a time point in a signal viewer maps the activity onto the head's surface display; selecting a position on this surface highlights the nearest electrode trace in the signal viewer.
Interactive editors provide functions for which currently no automatic procedures exist,

for example: the definition of the stereotactical coordinate system in a volume dataset by marking reference structures; the collecting of segments which form an anatomical object ("intelligent paintbrush"); the hand-segmentation of anatomical objects in a volume dataset. To avoid a cluttered screen, a single display pane provides 4x3 windows for viewers. Windows may be enlarged or linked to exchange information. Care has been taken to allow near-real-time interaction on standard workstations without specialized hardware. Drag-and-drop functionality is implemented for frequent operations like displaying the contents of a file by dropping it on a window, moving a window on the display pane, or saving the contents of a viewer into a file. The state of the kernel including all viewers may be saved into a file as a "workspace". Figure 1 presents an example.

Processing Modules

The second layer of functionality is provided by external processing modules. Analysis algorithms under development, complex or time-intensive non-interactive applications (i.e. registration of datasets), or infrequent operations (i.e. data conversion) are placed into self-contained modules.

Currently, our package contains about 90 modules falling roughly into the following categories:

- access to a distributed network-wide database,
- import/export facilities to standard formats and devices,
- 3D operators for images (filters, segmentation procedures, morphology and arithmetic operators),
- 2D operators for signals (filters, time-correlation, principal component analysis),
- operators for geometrical objects (extraction and concatenation of boundaries, surface fitting, fitting of deformable models),
- correlation modules (intramodal (MRI-fMRI), crossmodal (MRI-PET, MRI-EEG, MRI-MEG)),
- 3D and signal editors for the interactive manipulation of these datasets,
- a series of "standalone" viewers (signal, 2D images, 3D surfaces, 3D volumes).

Much of our previous work has gone into the development of these modules and has been cited here for reference. These modules extend the basic functionality of the interactive programs by adding the image and signal processing part.

A visual programming tool for the rapid development of processing chains is integrated within the viewing environment. Processing modules are represented visually as small buttons in an process editor. Applying the dataflow approach of well-known image processing packages like Khoros or AVS, the functional dependency between modules is represented by unidirectional links between these buttons. Clicking on a module button opens a dialog window in which parameters of a module may be supplied. During the execution of such a chain, the processing status of a module is indicated by changes of the button's color. Input to and output from a processing chain are linked either to external files or run directly into windows of the viewing environment.

The native modules allow pipe- and file-based connections. In the context of the visual editor we favor file-based data connections, because a processing chain is easier to restart and intermediate results are available. Given the processing time of single modules ranging from seconds to hours the additional time for file i/o is considered insignificant.

This environment was conceived as our design tool for new algorithms as well as a test bed for the development and stability of processing chains. Figure 2 shows such a processing chain involved in the removal of non-brain parts in a MR tomogram of the head. Once the functionality of a specific chain has settled it is repackaged into a single module.

Figure 2. Example view of a processing chain in the visual editor. Individual modules are represented a small buttons whose status is color-coded. The result of a chain is either displayed in a stand-alone viewer or fed back into a workspace window.

Implementation Framework

Our BRIAN package has been implemented in the C/C++ programming language using X-Windows 11R6 and Motif 1.2.4 as a graphical user interface. For the display of object surfaces, OpenGL (or its public domain clone Mesa) is employed. Some of the time-consuming modules have been parallelized using the Message Passing Interface (MPI) on a workstation net. File I/O is based on the Vista toolkit which is machine-independent and allows a very flexible and extensible handling of various data representations. The package has been ported to standard Unix workstations from different vendors and works in a heterogeneous environment.

4.2 Design and implementation of a multimodal viewer for biomedical datasets

Dörr, M. & Kruggel, F.

Visualization is usually the last step in a data processing chain. It defines the interface to researchers interpreting the data. Neuroimaging experiments yield a large amount of data. Often two or more modalities have to be shown together, especially a mapping of functional data onto an anatomical dataset. We are dealing with the following data classes:

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

It is worthwile to implement a versatile and intuitive environment to visualize these highly complex combinations of datasets.

Visualization methods

A high resolution MR dataset of the head forms the basis of all visualization methods. Reconstructions of this dataset are computed by volume rendering techniques like gray level gradient shading or the vbuffer technique. While these methods feature a realistic and detail-preserving rendering, they have to be enhanced to allow a mapping of the functional modalities onto this realistic head model.

Time depending modalities are usually recorded at scattered data points (the electrodes or magnetical sensors), which placed on or near a subject’s head. To reconstruct the activity between the recording sites interpolation methods like the nearest-neighbor technique or the computionally more intensive spherical spline interpolation are employed. This interpolation technique is integrated within the volume renderer to allow data mapping onto a surface (skin or brain) given by the MR data.

Functional datasets with spatially varying quantities may also be mapped onto a surface of the head model, or merged with the MR data to be shown at the real location where the activation was encountered. For 3D mapping a transparent volume rendering will be involved, whereas for the 2.5D data mapping a trajectory through the volumes collects the activity information to display on the surface. This mapping can be extended in time to display functional activity in time and space. Special emphasis is placed on a realistic, “meaningful” presentation of the data, which are often incomplete and noisy. We use techniques like adaptive and color dependent filtering to improve the image quality.

Interaction

Using 2D input devices (i.e. a mouse) to navigate within 3D datasets causes problems. Thus, we integrated 3D devices developed for CAD environments which provide a more intuitive interaction with the model. The projection of 3D data onto a 2D image for display on a computer screen introduces ambiguities in overlapping objects. For some applications it is advantageous to use a stereoscopic rendering which is available through LCD shutter glasses.

Instruments like cutting planes and probe cursors provide another level of interaction and thus support a further analysis of the experimental data. To allow an efficient use of these interaction modes, high rendering rates are a necessity. The parallel computer, which was installed at our institute recently, provides enough computing power to fulfill this task.

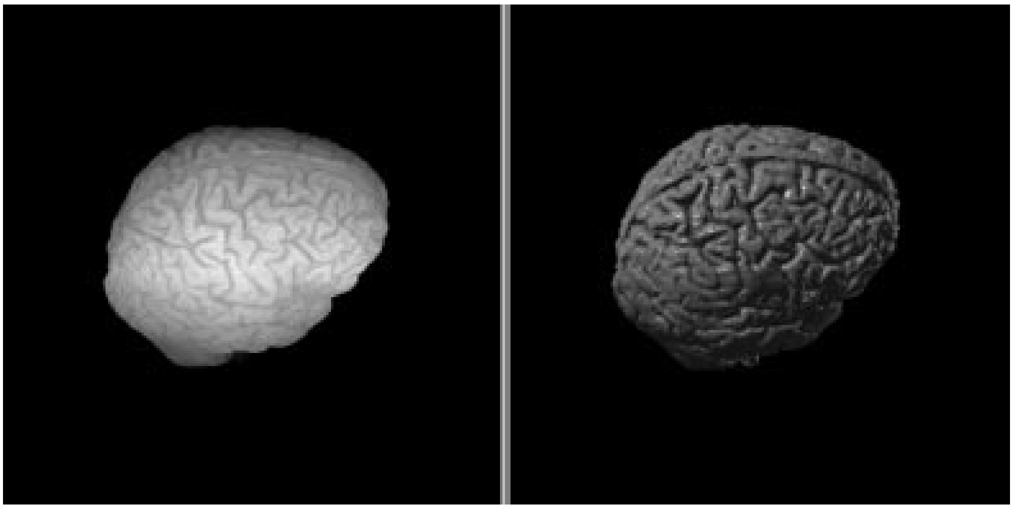


Figure 3. Comparison of two rendering techniques: vbuffer rendering (left) and gray level gradient shading (right)

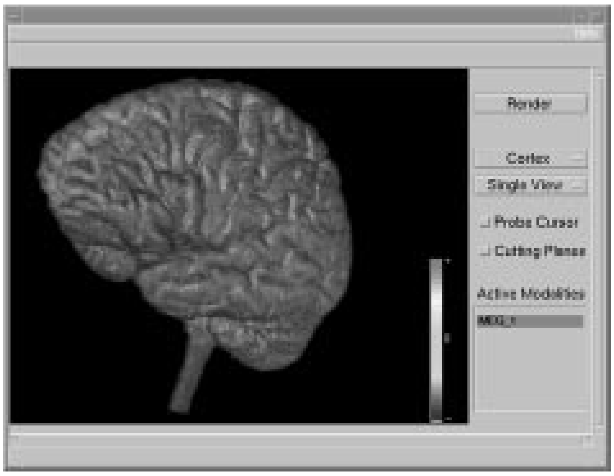


Figure 4. Mapping of a MEG dataset onto a brain surface extracted from MRI data

Whole head MEG system

4.3

Maeß, B., Oertel, U. & Knösche, T.

Since December 1996, the magnetoencephalography device (Magnes WH 2500 by BTi, Inc.) is operational. It is a whole head sensor array consisting of 148 magnetometer channels and 11 reference channels used for noise compensation. There are 64 EEG channels available giving us the opportunity to measure both modalities simultaneously.

Because of the rather high environmental noise level the magnetically shielding chamber is supported by an active shielding. The use of the active shielding and at least three magnetometer reference channels seems to be required for measurements at normal day time.

In December a couple of piloting experiments were conducted. First, the so-called phantom was measured to learn more about the way of doing experiments and data analysis. The accuracy of the fitted dipole positions was better then 3 mm for signal strengths of about 10 pT. The accuracy was better then 5 mm for signals of about 1 pT.

Secondly, MEG data of two subjects was collected. Subjects were required to simply lay on the back and not to move. Eyes were open and a cross at chamber ceiling was fixated. Subjects had to listen to a series of 100 sinusoidal tones of 2000 Hz. Epochs starting 200 ms before the onset of a tone and lasting 800 ms were collected. All epochs were simply averaged and baseline corrected using the pretrigger interval. The spatial magnetic field distributions at 100 ms after tone onset are shown in Figure 5. The result displays nicely dipolar responses at 100 ms above the temporal regions of both hemispheres as expected for the activation of the primary auditory cortex.

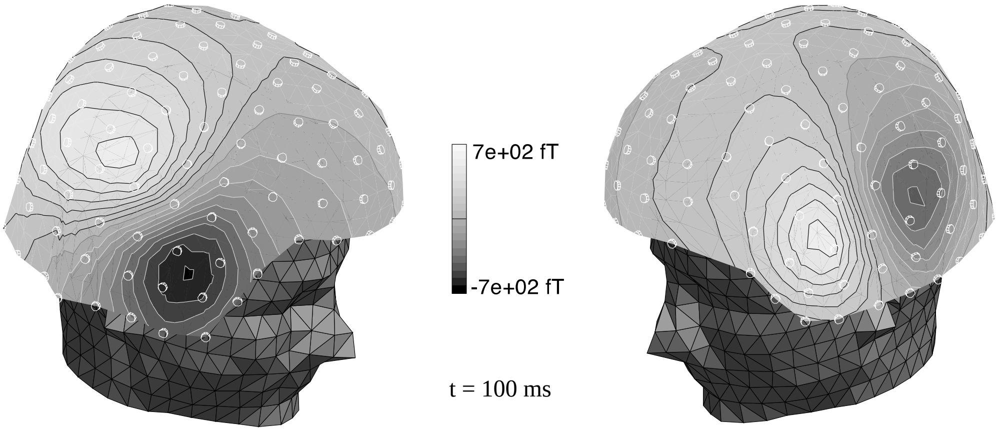


Figure 5: Event-related magnetic fields, 100 ms after onset of a auditory stimulus (2000 Hz sine), measured with the new 148 channel MAGNES WH2500 system, together with realistically shaped model of the subject's head.

4.4 Unix implementation of the ERP evaluation package (EEP 3.0)

Nowagk, R. & Pfeifer, E.

In October 1995 a project has been started to migrate our DOS-based EEG processing tools (Pfeifer, 1992) to Unix platforms. Since EEP is a toolkit, not a monolithic application, we proceed step by step in completing this task. Currently, the Unix EEP package is a collection of new, improved and replaced modules with some evaluation tools still being incomplete or not yet available at all.

Specifically, all standard evaluations requiring EEG/MEG raw data access can be performed using the new software. The tools needed to process the resulting ERPs are still under development.

We took this project as an opportunity to introduce some changes in the basic design, mainly with respect to the increasing amount of data acquired. Some of the new concepts and functions are described below.

Signal Archives

In the DOS package the raw data records are used as “work files” which means that the evaluation partly depends on modifying the original record. This is an easy and robust technique but with our huge records it leads to some performance deficits and prevents efficient backup strategies. Furthermore it makes on-line compression/decompression (see below) hard to implement.

In the new version we use the same raw data files as “signal archives”. There are no longer any write accesses to existing archives. All frequently changed evaluation data are stored separately. Any modification of signal values (e.g. filtering) results in a new signal archive.

Using this concept we can protect the valuable original measurements against accidental overwriting, reduce the backup expense and use the data directly from read-only archive media like CD-ROM.

Raw Data Compression

As a result of the intensive use of our 128-channel EEG equipment we already ran out of mass storage capacity several times - not to mention the additional bulk of data soon coming from the 150-channel MEG system which is just about to pass its initial test phase. Thus, the compression project rapidly proceeded from a vague idea to a high priority task.

To fit our needs a compression algorithm is not allowed to perform data reduction by throwing away specific aspects of the data. Moreover, it should be working as an invisible process behind all read/write accesses (on-line) rather than requiring explicit compressor / decompressor calls (off-line). In addition we require a reasonably fast access to any portion of the compressed data. Naturally, with these constraints we could not expect to achieve extreme compression ratios of up to 1/100 as one does with “lossy” compression algorithms common in the field of multimedia.

The realized algorithm works in two steps. First we predict signal values and store the differences between the predicted and the real values (residuals). To predict a signal we adaptively choose the best of three methods: assuming a constant signal, assuming a constant slope or assuming equal signal tracks of neighbouring channels. This choice is made for each signal section (usually 1 sec) and each channel. In a second step, using a simplified Huffman-coding technique, we can then store most of the residuals in 4..9 bit instead of the original size of 16 bit.

With this technique we typically yield file sizes ranging from less than 30% (128 channel EEG) to about 40% (64 channel EEG) of the uncompressed size. Since the algorithm isn't very complex its computation consumes just about the time which is gained from the reduced data traffic, so the overall run-time performance is not impaired.

Eye Artifact Compensation

Our new package offers tools to compensate for artifact components in the EEG as caused by eye blinks or eye movements.

Basically we record the electrooculogram (EOG), apply a principal components analysis (PCA) yielding two statistically independent EOG components and determine their “propagation” into the individual EEG channels via linear regression. To correct an EEG channel the corresponding PCA-transformed EOG components are weighted with the propagation factors for this channel and are finally substracted from the EEG.

Earlier studies have shown that one has to distinguish between blinks and eye movements for the assumption of linear EOG propagation to hold. According to our experience it is rather difficult to automatically classify blinks/movements with robust and reliable results. Thus, instead of improving automatic signal classifiers we rather tried to implement a comfortable interactive tool which minimizes the user interaction required for manual classification.

In a first step one has to pick out some prototypic eye blinks and eye movements. Appropriate EOG sections to look for such artifacts are located automatically using a signal variance criterium. The estimation of propagation factors is based on the selected set of artifact instances. This step usually doesn’t take more than a few minutes.

For the artifact removal further interaction is needed to specify the factor sets to be applied to the EEG epochs of interest (trials). All the trials that were rejected according to some conventional criterium (variance, threshold) are offered for classification. One has to decide for each trial, whether it should be corrected at all and, if yes, which factor set to apply. Assuming a proper rejection input this step can also be completed within a reasonable amount of time.

Practice and further validation will have to show whether the advantage of having more trials to average justifies the time expense and really leads to more accurate results.

4.5 Medspec 3T/100 system: Quality control

NMR-group

The initial 6 weeks of operation were largely occupied by training our three radiographers, and by an intensive quality control procedure. In this the NMR-group split into three subgroups which examined: radio-frequency electronics and coils; gradients and power supplies; magnet, shims and software. This process made it possible to eliminate a number of minor faults and produced a baseline documentation for the system. It also had the advantage that at least one group member became closely acquainted with each element of hardware. The resulting documentary report extends to 80 printed pages. It would be inappropriate to report the experimental details here, but the general conclusion reached was that despite a number of minor problems the hardware is essentially sound. It was however established that considerable effort needed to be expended in order to develop a stable software platform for the implementation and routine use of experiments developed within the group. This development has been undertaken by the staff scientists and is expected to reach fruition by the end of 1996.

Development of a visual projection system for fMRI experiments

4.6

Pollmann, S.

A visual projection system was developed for visual stimulus presentation in the magnet. The system consists of a LCD-projector (Polaroid Co.) with a specially adapted lens that is positioned outside of the magnet chamber, a projection opening in the shielding equipped with a waveguide tube, a rear-projection screen positioned inside the magnet and a mirror that allows the subject to view the stimuli presented on the screen.
The distance between projector and projection screen is 570 cm at a distance of 50 cm between rear-projection screen and reflecting mirror. The distance between projector and screen can be varied. At a distance of 570 cm the projection covers an area of 34 x 25,5 cm, equivalent to a visual field of 35° x 27°. The mirror, mounted on glasses with optical correction, fits into a headcoil of 27 cm inner diameter.
The projector has a resolution of 640 x 480 pixels and a presentation rate of 30 Hz. It was equipped with a lens according to the above specifications by Fa. Wenzel, Jena. The projector is positioned behind the magnet room and projects onto the the rear-projection screen which is mounted behind the subject's head. The projector is driven by a PC in the control room, connected via a 30m cable.
For the purpose of high frequency shielding the projection opening was equipped with a waveguide of 10 cm diameter and 100 cm length. The projection opening itself can be variably positioned within an area of 80 x 40 cm to accommodate a wide range of potential projection methods. Currently the optical axis runs 10 cm above and parallel to the magnet axis. The projection screen is positioned behind the head of the subject.

First fMRI results

4.7

*Wiggins, C.J.,
Niendorf, T.,
Pollmann, S. &
Hund, M.*

Work began in mid-September on developing fMRI protocols. For this initial stage two simple tasks were used, one consisting of a visual stimulus and the other a motor task, in order to judge the performance of the protocols without reference to more complicated, cognitive paradigms. Initially the visual stimulus and the visual cues for the motor task were delivered using the visual presentation system obtained from Resonance Technology Inc. (Van Nuys, CA, USA), and later experiments were conducted with the LCD projection system (Polaroid Co.) when this became available. The stimuli were controlled by ERTS software (BeriSoft, Frankfurt am Main, Germany), which itself was triggered from the MRI computer. For the majority of studies a FLASH sequence was used, using TE=40ms and TR=80ms with a 128x64 matrix, allowing acquisition of an image in less than 6 seconds. 64 consecutive images were acquired per scan, alternating between four images without task and four images with task. Three slices were examined in each subject, acquired in consecutive scans. Slice thickness was 5mm with 2mm interslice gap.

For the visual task, an 8Hz alternating checkerboard pattern was used, with a central fixation point. Subjects were asked to simply fixate on the point during the experiment. Slices were chosen so that the central slice coincided with the cingulate gyrus, with the other two slices positioned As can be seen from the example image below, clear activation of the visual cortex could easily be detected (Fig. 6).

For the motor task, subjects were asked to rapidly perform a simple finger tapping task consisting of a repetitive opposition movement of the first two digits. Three slices were chosen parallel to the AC-PC line in a distance of about 1 cm, 1.7 and 2.4 cm from the vertex. To inform the subjects when to perform the task and when to remain still visual cues were used, consisting of a red screen for no task and a green screen for when the task should be performed. As expected, these results were more prone to movement artefacts than the visual studies. An improved head restraint has therefore been developed. An example image is displayed in Fig. 6.

Further experiments have also been performed using the MUSIC imaging sequence. MUSIC is a variant of the FLASH technique which allows simultaneous acquisition of multiple image slices.

In the coming year more complex studies including cognitive fMRI projects are planned. In addition, other imaging techniques, such as EPI and GRASE, will be brought into use.

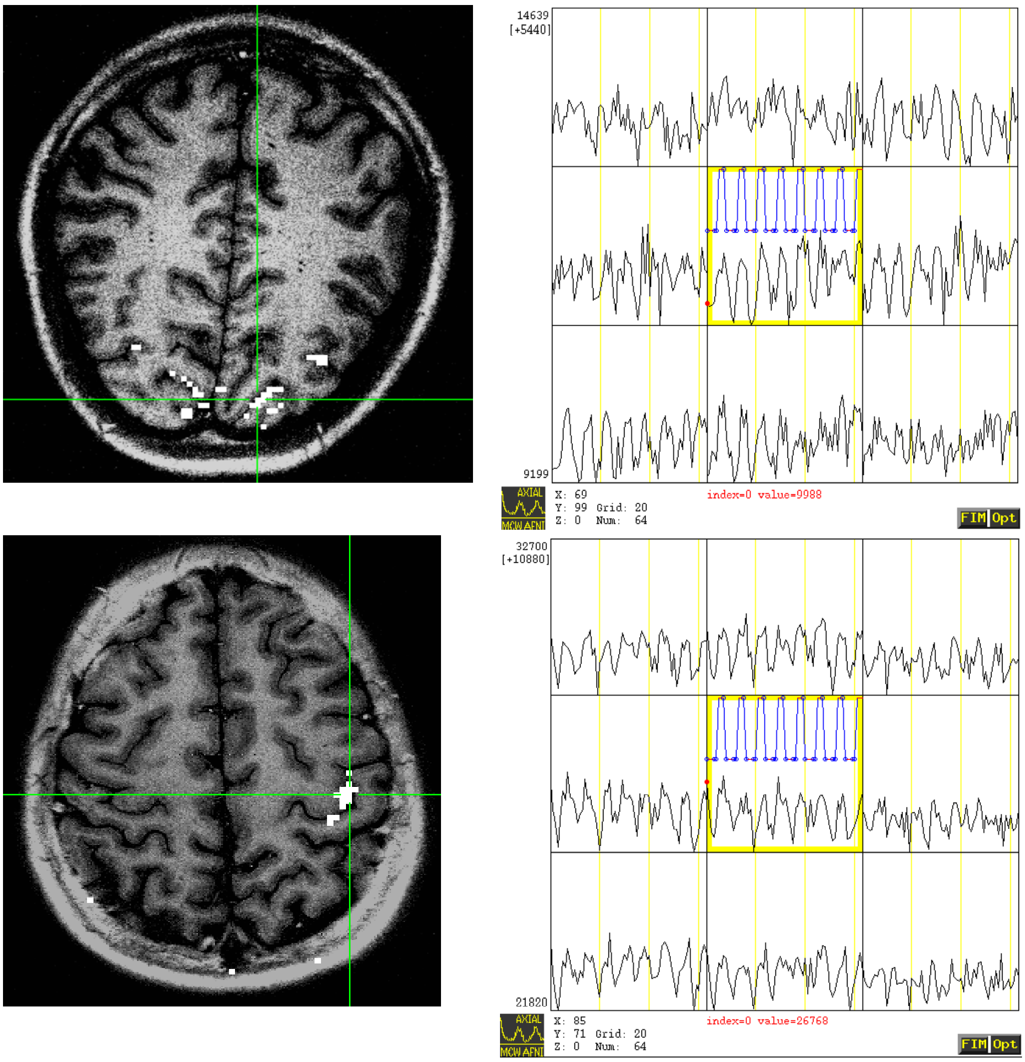


Figure 6. Visual and motor cortex stimulation using the FLASH technique

Functional MRI images of activation in the visual cortex (upper) and the motor cortex (lower). On the left is the image with activated regions overlaid in white. On the right is the timecourse plot of image intensity for the pixel indicated by the crosshairs on the image, as well as the timecourses for the surrounding eight pixels. The upper trace in the central graph indicates the off and on stimulation pattern.

Implementation of a multislice FLASH technique (MUSIC)

4.8

Niendorf, T.

This project pursues the implementation of the MUSIC technique, which is a version of the FLASH (Fast Low Angle SHot Imaging) experiment in order to achieve a robust imaging sequence providing both a reasonable spatial resolution and an enhancement in the temporal resolution compared to FLASH, which is of high relevance for reproducible functional imaging studies.

The most widely used fast imaging methods for mapping brain activity are EPI (Echo Planar Imaging) and FLASH. EPI in its single excitation version offers an excellent temporal resolution but a limited inplane resolution of usually not better than a 128*128 data matrix elements due to its sensitivity to B_0 inhomogeneities . This effect is especially pronounced at high magnetic field strengths including our 3 T system. An improved inplane spatial resolution can be achieved employing the FLASH technique. However the strong T_2^*-weighting, required to make the sequence sensitive for changes in the blood oxygenation level necessitates a long evolution time between the RF excitation and the data acquisition This manifests itself in data registration from generally only single slice.

One way of making the FLASH technique faster and thus facilitating the acquisition of multi slice data without a significant worsening in the time resolution is taken by the echo-shifted gradient recalled FLASH method (ES-FLASH) (Lui et al., 1993). During the long echo time TE the same slice is excited again, whereby the desired gradient recalled echo is shifted into a subsequent repetition time period. This means that the echo time is longer than the repetition time TR, and thus results in a drastic TR reduction. The main disadvantages are:

- Due to the quick repetition of consecutive excitations a smaller flip angle is used than in the FLASH experiment at the expense of a signal to noise loss. Even when employing the same flip angle as applied in the FLASH experiment this technique gives a lower signal to noise ratio, because the direct signal of the primary gradient echo is not used.
- The incomplete dephasing of unwanted echo signals due to limitations in the maximum gradient strength may induce image artefacts.

Another possibility to circumvent the limited temporal resolution related drawbacks of the basic FLASH technique has been proposed by Loenecker et al. (1996). In contrast to conventional gradient echo techniques, where the detection of multi slices is performed sequentially MUSIC uses interleaved slice excitation and echo acquisition to achieve equal T_2^* sensitisation for each slice. The delays between consecutive slice excitations are identical to consecutive acquisition periods. In consequence it is possible to acquire a multi slice data set using the MUSIC technique within the same time as for a single slice data acquisition with FLASH, whereby the T_2^* sensitivity and the signal to noise ratio are identical to those of the basic FLASH experiment. Despite the fact that the corresponding time resolution is still lower than that of multi slice EPI experiments MUSIC is an alternative tool where there is an interest in a higher inplane spatial resolution.

In a second stage the MUSIC technique was modified by the introduction of multiple gradient recalled echoes for two reasons:

- The acquisition time is much shorter than the duration of the slice selection. Therefore additional compensation delays are introduced in the acquisition period in order to achieve an equivalent T_2^* weighting for all slices. This time is now used for the acquisition of multiple echoes giving additional information.
- Changes in the local concentration of oxy/desoxyhaemoglobin induce changes in T_2^*. Therefore it is desirable not only to acquire images with different T_2^*-weighting but also to generate T_2^* maps, which provide a more quantitative basis for the interpretation of functional data sets.

The MUSIC technique has been implemented on the 3 T system in Karlsruhe. This work focused on both the solution of problems related to the Bruker ParaVision software and the examination of the Bruker hardware capabilities, and concentrated on the preparation of an user interface providing an comfortable tool for routine users. The sequence was applied successfully in phantom experiments and *in vivo* experiments. The application was therefore extended to functional studies in order to ascertain neuronal active brain areas during visual stimulation. Hardware problems due to instabilities in the gradient amplifiers prevented the acquisition of reliable data sets in Karlsruhe. The signal intensity scatter varied between 20-25 % in conjunction with a systematic signal decrease of about 15 % attributed to imperfections in the head coil design. In comparison a signal intensity change of approximately 5 % was expected during the stimulation periods. The Leipzig system is significantly more stable.

The main problems with the multi echo experiments are:

- A frequency shift between images, which were reconstructed from only odd or even echoes. This frequency shift manifests itself in an alternating shift in the position of the images along the read out direction.
- The present approach involves only a very small range of T_2^*-weighting, which is insufficient for accurate data evaluation.

Further work needs to focus on the following:

- The MUSIC sequence is now being introduced stepwise into functional human studies. For this purpose the sequence is used in visual and motor cortex stimulation experiments using defined experimental conditions in order to examine its application for the reproducible identification of activated areas.

- The MUSIC technique will be used for the simultaneous localisation and differentiation of spatially remote activated brain areas .MUSIC will be employed in a reliable experimental animal model at the MPI for neurological research in Cologne (Bruker, 4.7 T system) in order to examine its application for the precise identification and differentiation of spatially remote activation areas. For this purpose the directly adjacent somatosensory cortical areas of the forelimb and the hindlimb of α-Chloralose anaesthetised rats will be activated by electrical stimulation of the fore- and hindpaw. The acquired knowledge will then be transferred to Leipzig and the investigations will be extended to human studies. In human studies visual-auditory stimulation paradigms could be used to study modality-specific suppression effects. Being able to detect spatially remote active brain areas including the measurement of thalamic activation changes is relevant for a number of existing projects.

4.9 EEG recording during MRI scanning

Wiggins, C.J. &
Kruggel, F.

The techniques of MEG, EEG and functional MRI (fMRI) are of great value to neuropsychological research. However, the techniques have differing properties. MEG and EEG detect the very early, neurological response of the brain, but suffer from a limited spatial resolution. fMRI, however, detects the rather slower haemodynamic response of the brain, but with much superior resolution. It is attractive to combine MEG or EEG with fMRI. Such a combination is presently impossible for MEG and fMRI, due to the sensitivity of the MEG detectors to the main magnetic field of the fMRI, as well as to the time varying fields that are used in the MR imaging process. Conversely, combining EEG with fMRI, while presenting a range of technical challenges, is worthy of consideration.

The problems with combining the two techniques fall into two obvious categories: the effects of the EEG equipment on the MRI measurement, and the effects of the MRI equipment and imaging process on the EEG measurement.

The EEG equipment can effect MR imaging in two basic ways: One is that the introduction of any additional cabling into the MR room can introduce noise sources which can affect image quality. This is also true of the dozens of cables that are already present in an MRI system, and the technology for filtering such cables is well established. More problematic is the interaction of the EEG electrodes and leads with the radiofrequency (RF) pulses that are used in MRI. The positioning of wires around tissue can act as a shield to the RF pulses, reducing the MR excitation and attenuating the signal on reception. This is also a safety issue as the presence of conductors in the RF field can act to concentrate the field and cause tissue burning. Limiting the number of electrodes, combined with appropriate materials and positioning for the electrodes and leads, should minimise both the shielding and RF pickup effects.

The effect of the MR experiment is rather more serious. For EEG measurements, signals of the order of 10mV are being measured. However, a length of wire moving in a static magnetic field such as are used in MRI can easily evoke potentials that exceed this by one or two orders of magnitude. The voltage evoked is directly proportional to field strength, so this is a particular concern due to the high field system that is installed in Leipzig. Additional artefacts can be generated due to the time varying gradients used in the MR imaging process, although their magnitude is much smaller. Another source of interference is the RF pulses used in MRI, which, although of a frequency (125MHz for the Leipzig system) which is orders of magnitude higher than that of the EEG signal, are of quite high power (2 to 15kW). There is an additional interference source, which arises directly from the subject: the pulsatile nature of blood flow can, due to the conductive properties of blood, act to produce a cardiac related potential, the cardio-ballistic effect.

A study was conducted during 1996 to establish the feasibility and requirements of a combined EEG and fMRI system. Initially this work was hampered by the lack of suitable EEG recording equipment for recording within the MR environment and the fact that the MR system had not yet been installed. The initial work was undertaken with the assistance of colleagues at the Physikalisch-Technische Bundesanstalt in Berlin. With a simple arrangement of a preamplifier and an oscilloscope, the detection of a-waves was achieved. However no MR measurements were made.

After the MR system was installed and tested in Leipzig, experiments were undertaken to determine which sources of interference were most significant, and attempts made to combat them. The most significant source of interference, unsurprisingly, was found to be the high power RF pulses, which easily saturate the preamplifier. This can result in long dead-times during which the preamplifier recovers. Provision of an input filter to protect the preamplifier input has had a dramatic effect, reducing the dead time to the order of tens of milliseconds, and even this may be further improved. The effects of wire vibration were controlled by suitable fixation. Gradient induced signals were also detected, but the severity of these were found to be variable, depending on imaging parameters such as the imaging sequence used, slice orientation, etc. However the signals induced in this way were of quite a low amplitude and should be extremely reproducible, as the timing of the MR sequence is precisely controlled (see Fig. 7).

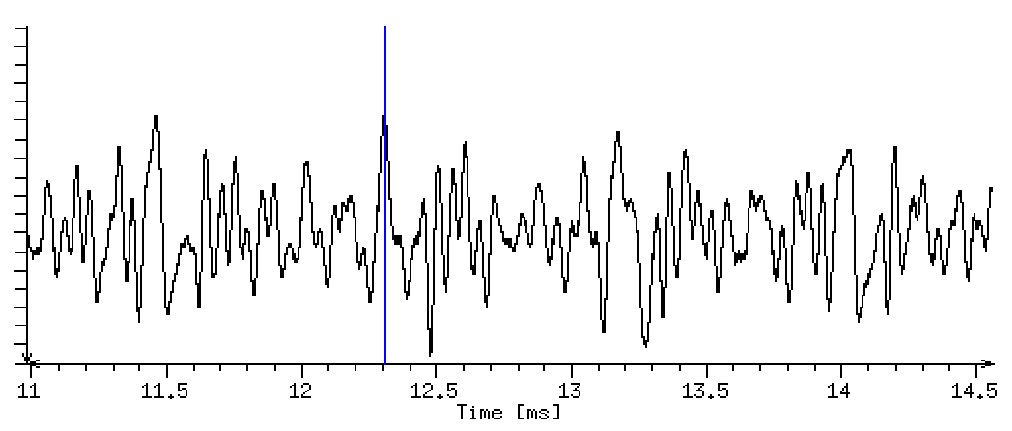


Figure 7. EEG trace as detected in 3T magnetic field.

To complete the system, a PC-based A/D acquisition board has been purchased. A software module has been written for EEG recording of 50-500 samples per second on 8 bipolar channels with adjustable gain. The program stores the data in Vista format to allow inspection and processing by the BRIAN package.

The completion of an initial system with four channel recording will take place in December 1996. The next stage of research will involve determining under what conditions the measurements can take place (e.g. whether the measurements are truly simultaneous or take place in adjacent blocks of time, which MR imaging sequences are most suitable, etc.) and to what extent the MR induced artefacts can be removed through post-processing.

Navigator echoes: Correction of motion artefacts in diffusion weighted MR images **4.10**

Koch, M., Redpath, T.W. & Norris, D.

Introduction — Applications of diffusion weighted imaging:

- Diffusion weighted imaging (DWI) has proven helpful for the early detection of cerebral infarction. Diffusion weighted images show ischemic regions several hours before they appear abnormal in T_2 weighted images.
- Using diffusion weighting in different directions, anisotropy of water diffusion can be measured. 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 using diffusion tensor imaging (DTI)[1]. In contrast to DWI, DTI is a relatively new method.
- The electrical conductivity tensor is believed to be co-axial with the diffusion tensor. Information from DTI could thus be used for improved EEG/MEG source reconstruction.

Method (I) — Principle of diffusion weighted imaging[2]:
A typical diffusion weighted imaging sequence is shown in Fig. 8. The first gradient pulse, which may be applied in *y* direction, causes the nuclei to precess with a frequency that is proportional to their *y* coordinate. At the end of the gradient pulse the nuclei have accumulated a phase shift, $\Delta\varphi$, proportional to their precession frequency. $\Delta\varphi$ varies linearly with the *y* coordinate. On switching off the first diffusion gradient, all nuclei return to the same original Larmor frequency. After a delay t_D = 10 to 100 ms, the spins are rephased by a second diffusion gradient of same amplitude and duration but of opposite sign. In total, no phase change results. If, however, a nucleus has experienced Brownian motion during t_D, the phase shifts imposed by the first and second gradient are not equal since the rephasing depends on the *new* location of the nucleus. A net phase shift, $\Delta\varphi \neq 0$, results. Because of the random nature of diffusional motion the phase shifts of all nuclei in the sample are randomly distributed. As the detected MR signal emerges from the *vector* sum of all magnetic moments, the contributions of the individual spins cancel out. This results in a lower signal than without diffusion. The ratio of the signals with and without diffusion weighting,

$$\frac{S}{S_0} \sim e^{-bD},$$

depends on duration, δ, and amplitude, G_D, of the diffusion gradient pulses, and on the time Δ between the onset of the two gradient pulses. These influences are brought together into the *b* factor. Neglecting gradient pulses other than the diffusion pulses, $b = \gamma^2 \mathbf{G}_D^2 \, \delta^2 (\Delta - \delta / 3)$. *D* is the apparent diffusion coefficient.

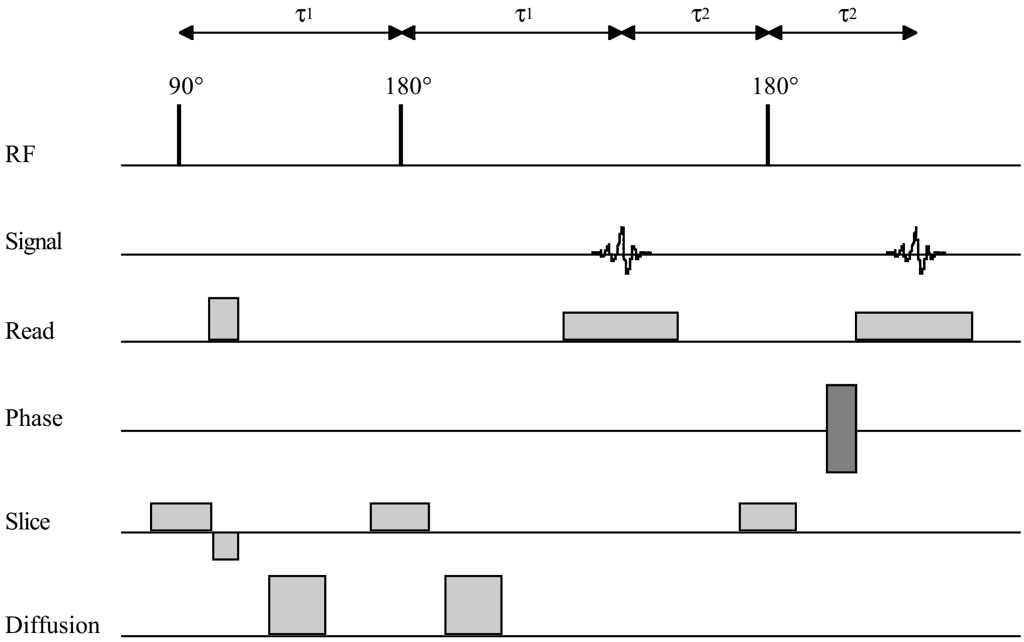


Figure 8. Diffusion weighted spin echo sequence with navigator echo.

Problem — Coherent motion causes artefacts:
Unfortunately, a DWI experiment that is sensitive to incoherent motion in the 10 μm range is also sensitive to coherent subject motion. Those phase shifts Δφ which are due to *coherent* motion are *not* randomly distributed. Hence the magnetic moments do not cancel out.

Usually, one spatial dimension, the *x* direction, say, is encoded with the precession frequency of the nuclei. To acquire information on the *y* positions, a series of echoes is recorded. The phases of the spins contributing to an echo are determined by a preceding phase encoding gradient that is varied from echo to echo. If between the two diffusion gradient pulses coherent motion in the diffusion gradient direction occurs, the resulting phase shift Δφ adds to the phase which is imposed on a spin by the phase encoding gradient. Given that the Δφ values differ between echoes, distortions in the phase encode direction are induced. Subject motion and pulsatile brain motion can therefore drastically degrade the quality of diffusion weighted MR images. This problem does not occur in single shot techniques such as EPI. With EPI, the effect of motion is the same on all acquired echoes. However, if a segmented version of EPI is used to enhance image resolution, sensitivity to bulk motion is reintroduced by including more than one diffusion-sensitive period.

Method (II) — Correction of motion artefacts[3]:

One approach to overcome this problem is the recording of navigator echoes. These additional echoes are acquired without any phase encoding. The information on spin phases which is included in a navigator echo can be used to correct for the effect of motion on the subsequent imaging echo. For each phase encoding step, both navigator and image echoes are Fourier transformed in the readout direction. The first navigator echo is chosen as the reference echo, and the phase of each complex value of the navigator echo profiles is normalized by subtraction of the reference profile phases. The image profile data are then corrected by the normalized phases of the corresponding navigator profile. The navigator phases have to be added rather than subtracted because of the 180° pulse in between image and navigator echo.

The navigator echo approach can correct for linear and rotational rigid body motion. Linear rigid body motion along the diffusion gradient (G_D) direction produces a spatially uniform phase shift. Rotations about axes orthogonal to G_D introduce a linear phase variation along the direction perpendicular to G_D and the rotational axis. A linear phase variation in the phase encode direction cannot be properly corrected for by using a navigator echo[3]. Therefore, the phase encode direction should always be in the G_D direction. This requirement cannot be satisfied in DTI because diffusion tensor experiments rely on the application of different diffusion gradient directions. Recent publications suggest the use of two orthogonal navigator echoes to account for rotations about all directions, irrespective of the choice of the phase encode direction[4].

Results — Completed work and future projects:

The Bruker MSME (multi slice multi echo) sequence was modified in order to include diffusion weighting. One navigator echo was incorporated before each imaging echo. The correction algorithm was implemented using IDL® (Interactive Data Language). Studies on a water phantom were performed where motion was induced by shaking the phantom before the measurement. The correction algorithm failed to correct the severe distortions present in the images just after shaking. This was probably due to the water not moving as a rigid body. Subsequently, brain images were acquired on three volunteers. The implemented navigator technique proved capable of removing even severe ghost artefacts in these brain images. ($b \approx 150$ s mm^{-2}, $G_D = 15$ mTm^{-1} , $TE_{eff} = 106$ ms, TR = 1.6 s. Matrix size 256x256, field of view 25 cm, slice thickness 5 mm.) An experimental test of the sensitivity to the ‚correct‘ choice of the phase encode direction is in progress. The combination of the navigator echo technique with cardiac and respiratory gating has yet to be evaluated.

4.11 High *T*1 contrast 3D MRI of the brain

Norris, D.

Aim

This project aims to produce highly resolved images of the brain with a good T_1 contrast. A particular goal is to produce images on a 256x256x128 matrix with an in-plane resolution of better than 1 mm, and a slice thickness of 1.5 mm for use in the *Neuro-informatik* group.

Experimental Constraints

As the main magnetic field strength increases the T_1 relaxation times both lengthen and converge. This makes it difficult to use protocols developed for use at 1.5 T as the grey/white matter T_1 values change from 990 ms/570 ms at 1.5 T to 1350 ms/940 ms at 4 T. Furthermore the maximum duration of the investigation should not exceed about 40 minutes as this is difficult for patients and volunteers to tolerate, and increases the chance that the data is corrupted by motion artifacts.

Candidate Sequences

The requirement to acquire 256x128 phase-encoding steps within about 40 minutes means that roughly 14 data lines per second have to be recorded. This acquisition rate can easily be achieved with a spoiled FLASH sequence, but it is questionable as to whether an adequate T_1 contrast can be generated using this sequence at high field strengths. A T_1 contrast can only be generated with this sequence if all transverse magnetization is spoiled between excitations, a feature which has not yet been successfully demonstrated on our system; an investigation of this sequence was hence deferred. All the other candidate sequences require a preparation period of the magnetization prior to imaging. The most effective means of preparing T_1 contrast is by means of an inversion-recovery (IR) sequence, in which the equilibrium magnetization is inverted, and allowed to recover prior to being converted to transverse magnetization and imaged. In order to develop a reasonable contrast the inversion delay has to be of the order of 1 s, and during this period no data can be acquired. It is thus necessary to acquire about 30 lines of data per inversion if the maximum experimental duration is not to be exceeded. This initself is sufficient to exclude the IR-RARE sequence: first because RARE has a high intrinsic T_2 contrast, which in this situation will act to diminish the T_1 contrast, and second because the 30 or so 180° refocusing pulses required would probably cause an unacceptable level of power deposition in the subject. IR-FLASH , and variants thereof, thus appear to represent the only chance of obtaining suitable data sets within the required time. The group at Birmingham, Alabama, has published high quality IR gradient-echo images at 4 T, but the TR required was 2.5 s, which would again lead to long experimental durations (1). In contrast the IR variant MDEFT has produced high quality images at 4 T with a TR of 1.2 s (2), and hence this sequence was examined more closely.

The MDEFT sequence

In its simplest form the MDEFT sequence consists of a train of RF pulses:

90°-τ-180°-τ-90°-τ-180°-.....

where the 90° pulse can be the excitation pulse for a spin- or gradient echo imaging sequence. In the 3D variant (3) a string of a pulses is applied after the preparation sequence: $90°\text{-}\tau\text{-}180°\text{-}\tau\text{-}n\alpha$

In the current implementation τ is 550 ms, and n is 32. Each α pulse is the excitation pulse for a FLASH imaging sequence, with α being 30°. The time between α pulses is 14 ms leading to a total experimental duration of just over 30 mins. Data are acquired on a 240x240x192mm field of view. One advantage of MDEFT is that the 90° pulse acts like a "reset" for the magnetization: irrespective of the state of the longitudinal magnetization prior to the 90° pulse it is subsequently zero. This makes it possible to apply the 90° pulse immediately after the last α pulse without a delay for magnetization recovery which is necessary in classical IR sequences. The magnetization after the second τ period is given by

$$M_z(2\tau) = M_0\left[1 - \exp\left(\tau/T_1\right)\right]^2$$

i.e. the magnetization shows a quadratic dependence on T_1, which to some extent ameliorates the loss of contrast caused by moving to high field.

Future work

The current implementation can be improved with respect to the basic pulse sequence, mainly by improving the efficiency of the FLASH sequence. This should reduce the total experimental duration, without a reduction in signal to noise ratio. The possibility of collecting more than the current 64 data lines per preparation experiment could also be examined. An RF resonator which was designed for brain rather than head imaging would increase sensitivity. It would be advantageous if flow artifacts could be reduced, but ECG triggering would lead to a significant increase in experimental duration. The most promising approach is to saturate blood outside the slice.
There is some scope for examining 2D, multi-slice applications of this sequence. For example a sequence

$$180°\text{-}\tau\text{-}N\theta_n\text{-}\tau\text{-}180°\text{-}\tau\text{-}....$$

where $\cos(\theta_n) = \tan(\theta_{n-1})$, θ_N=90° and N=4 would make it possible to acquire a 2D image on a 512x512 matrix in just over 2 minutes. It could also be of interest to compare a short *TE* spin-echo readout with gradient-echo readout, as spin-echo sequences suppress susceptibility effects whereas gradient-echo can be used to enhance these. The contrast from blood vessels can thus be enhanced in gradient-echo, which may be useful if the images are being used as templates for functional activation, but may not be so advantageous for image segmentation.

Conclusion

Although 3T is probably not the optimum field strength for producing high contrast T_1 images it should prove possible to overcome these difficulties using methods developed in 4 T imaging laboratories.

5 OTHER ACTIVITIES

5.1 Teaching

SOMMERSEMESTER 1996

Gedächtnisstörungen in der klinischen Praxis
Universität Leipzig
von Cramon, D.Y., Guthke, T., Matthes-von Cramon, G., Müller, U., Thöne, A.

Methoden der biomedizinischen Kernspinresonanz-Bildgebung und -Spektroskopie
Universität Leipzig
Norris, D.

Grundkurs Neuroanatomie II
MPI für neuropsychologische Forschung
Müller, U., Kruggel, F.

Experimentalpsychologisches Praktikum
Freie Universität Berlin
Hahne, A.

Einführung in die Psycholinguistik
Freie Universität Berlin
van Kampen, A.

WINTERSEMESTER 1996 / 97

Neuropsychologische Falldemonstrationen
Universität Leipzig
von Cramon, D.Y., Hund, M., Müller, U., Pollmann, S. und Mitarbeiter der Tagesklinik für kognitive Neurologie der Universität Leipzig

Kognitive Prozesse und ereigniskorrelierte Hirnpotentiale
Universität Leipzig
Friederici, A.D., Mecklinger, A., Gunter, T.

Methoden der biomedizinischen Kernspinresonanz-Bildgebung und -Spektroskopie
Universität Leipzig
Norris, D.

Membership in Scientific Institutions and Boards:

Senat der *Deutschen Forschungsgemeinschaft*
Vorstand der *Berlin-Brandenburgischen Akademie der Wissenschaften*
Kuratorium der *Wernher von Braun-Stiftung*
Editor-in Chief of the *Zeitschrift für Experimentelle Psychologie*
Member of the Editorial Board of *Cognition*
Member of the Editorial Board of the *Journal of Psycholinguistic Research*
Member of the Advisory Board of the *Neurolinguistik*
Head of the Working Group "*Regelwissen und Regellernen in biologischen Systemen*" at the *Berlin-Brandenburgischen Akademie der Wissenschaften*

Prof. Dr. D.Y. von Cramon

Nomination Committees (*University of Leipzig*):

Neurosurgery
Neurology
Biological Psychology
Medical Computer Science
Computer Network and Distributed Systems
Signal and Image Processing
IDZL: Research Group for Neuroscience
ZHS: Committee for Cognitive Sciences

Membership in Scientific Academies and Societies:

Deutsche Akademie der Naturforscher LEOPOLDINA
International Neuropsychological Symposium
European Neurological Society
Memory Disorders Research Society
Deutsche Gesellschaft für Neurologie
Deutsche Gesellschaft für Neuroradiologie
Deutsche EEG-Gesellschaft
Deutsche Gesellschaft für Neurotraumatologie und klinische Neuropsychologie

Membership in Scientific Institutions and Boards:

Member of the Scientific Advisory Board of the *Forschungszentrum Jülich*
Member of the *Gemeinsame Kommission Klinische Neuropsychologie (GKKN)*
Chairman of the *Committee 1.08 (Behavioural Neurology) of the Deutsche Gesellschaft für Neurologie*

5.4 Guest Lectures

PD Dr. Arno Villringer, Humboldt-Universität Berlin
Physiologische Grundlagen der neuronal-vaskulären Koppelung
10.01.1996

Prof. Dr. Rudolf Rübsamen, Universität Leipzig
Inhibition formt die Antwort-Areale zentraler auditorischer Neurone
17.01.1996

PD Dr. Rudolf Friedrich, Universität Stuttgart
Zur Analyse raumzeitlicher Strukturen von Magnetenzephalogrammen
24.01.1996

Dr. Henk Haarmann, Carnegie Mellon University, Pittsburgh, USA
Working memory, working brain: converging evidence from normal and aphasic sentence comprehension
31.01.1996

Prof. Dr. Kamil Ugurbil, University of Minnesota
Studies of brain function using high field magnetic resonance imaging
06.02.1996

Dr. Dick Smid, Universität Magdeburg
Temporal organization of selective attention to color and shape
14.02.1996

Dr. Peter Börnert, Philips Forschungs-Laboratorium Hamburg
High Field Imaging
19.02.1996

Dr. A. Kleinschmidt, Universität Düsseldorf
Funktionelle Magnetresonanz-Tomographie des Gehirns:
Strategien und Befunde
21.02.1996

Dr. Erich Schröger, Universität München
Mismatch Negativierung: Ein Indikator obligatorischer Aspekte auditiver Reizverarbeitung
28.02.1996

Prof. Dr. Peter Frensch, MPI für Bildungsforschung Berlin
Implizites Sequenzlernen
27.03.1996

Prof. Dr. David Swinney, University of California
Lexical and structural processes during language comprehension
08.07.1996

Dr. Peter Hagoort, MPI Nijmegen
The electrophysiology of parsing
10.07.1996

Prof. Dr. Pienie Zwitserlood, Universität Münster
Die Rolle der Morphologie beim Sprachverstehen
17.07.1996

Dr. Gregoire Malandain, INRIA Sophia, France
Digital topology: application to 3D images
25.07.1996

Prof. Dr. Armin Fuchs, Florida Atlantic University
Phasenübergänge im menschlichen Gehirn
07.08.1996

Dr. Mark Symms, National Epilepsy Centre, Chalfont St. Peter, UK
Diffusion Imaging with EPI
17.09.1996

Prof. Dr. Adalbert Meyer-Heinricy, Universität Bremen
NMR measurements of cell cultures
18.09.1996

Prof. Dr. Josef P. Rauschecker, Georgetown Institute for Cognitive and Computational Science, Washington, USA
Processing of complex sounds in higher auditory areas of nonhuman primates and man
23.09.1996

Prof. Dr. Hellmut Merkle, University of Minnesota; USA
Radio frequency coil design
30.09.1996

Dr. Thomas W. Redpath, University of Aberdeen, UK
Signal to noise ratio (snr) measurement
30.09.1996

Dr. Ken Kwong, Massachusetts General Hospital, Boston
Functional and perfusion imaging
02.10.1996

Prof. Dr. Rudolf Rübsamen, Universität Leipzig
Ist der Einsatz artspezifischer akustischer Signale notwendig zur Charakterisierung von Neuronen im auditorischen Vorderhirn?
11.12.1996

Dr. Giordana Grossi, University of Oregon
Name task: not all the letters are the same
17.12.1996

Dr. J. Haueisen, Universität Jena, Biomagnetisches Zentrum
Finite Elemente Modellierung zur Untersuchung des Einflusses von Leitfähigkeitsänderungen und ausgedehnten Quellen auf neuromagnetische Felder
18.12.1996

5.5 Congresses, Workshops and Colloquia

Workshop

Visuospatial attention in the normal and split brain - ERP and behavioural data
07.05.1996

> Mechanisms of visual spatial selective attention as indexed by electrophysiological measures
> *Zani, A. (CNR Roma)*
>
> Electrophysiological and behavioural measures of spatial attention and visuo-motor integration in a callosotomy patient and normal controls
> *Proverbio, A.M. (Università di Trieste)*
>
> Visual search in the split brain: interhemispheric effects
> *Pollmann, S. (MPI of Cognitive Neuroscience Leipzig)*

Opening Ceremony of the Magnetic Resonance Tomograph Bruker MEDSPEC 30/100
04.06.1996, first part of the new institute building

Scientific Colloquia

Forschungsziele der MR-Gruppe des MPI für neuropsychologische Forschung Leipzig.
PD Dr. David Norris, MPI für neuropsychologische Forschung Leipzig, Leiter der MR-Gruppe

Ausgewählte Aspekte zur ultraschnellen MR-Bildgebung.
Dr. Peter Börnert, Philips Forschungslaboratorium, Hamburg

6 DEGREES, HONORS AND AWARDS

6.1 Degrees

Jens Bölte	Doktor der Philosophie, Dr. phil., Free University of Berlin
Notger Müller	Doktor der Medizin, Dr. med., Free University of Berlin
Rosemary Dymond	Master of Engineering Science, Oxford University
	Master of Science in Medical Physics, Aberdeen University
Monika Hofmann	Master of Science in Linguistics, Free University of Berlin
Martin Meyer	Diplom in Psychology, Free University of Berlin

6.2 Honors and Awards

Prof. Dr. D. Y. von Cramon	Director of the Day-Care Clinic of Cognitive Neurology, University of Leipzig
	Deutsche Akademie der Naturforscher LEOPOLDINA
Prof. Dr. A. D. Friederici	Director of the Interdisciplinary Center for Cognitive Science, University of Leipzig
	Leibniz-Preis der Deutschen Forschungsgemeinschaft (DFG)

Our library has now been opened for the public readership, especially for the members of the University of Leipzig. Local branch libraries and the library of the Max Planck Institute cooperate closely on several fields. This cooperation has affected both libraries positively - especially by helping to avoid double acquisition of books in psychology and neurology.
The contruction period has not been finished yet. Goals for the next year are a catalogue of journals of the MPG which will be located in the World Wide Web and the access to Psychlit via the OVID-client of the MPG on the basis of our proposal.

Descombes, X. (1996).
Application of stochastic techniques in image processing for automatic tissue classification in MRI and blood vessel restoration in MRA.
Technical Report KUL/ESAT/MI2/9603, *Laboratory for Medical Imaging Research (ESAT-Radiology)*. K.Univ. Leuven, Leuven.

Descombes, X., Mangin, J.F., Pechersky, E., & Sigelle, M. (1996).
Fine structure preserving Markov model for image processing.
In *9th Scandinavian Conference on Image Analysis SCIA'95*, Uppsala, Sweden, June 6-9, 1995, (pp.349-356). Uppsala, SCIA.

Dijkhuizen, R., van Lookeren Campagne, M., Niendorf, T., Dreher, W., van der Toorn, A., Hoehn-Berlage, M., Verheul, H.B., Tulleken, C.F.F., Leibfritz, D., Hossmann, K.A., & Nicolay, K. (1996).
Status of the neonatal rat brain after NMDA-induced excitotoxic injury as measured by MRI, MRS and metabolic imaging.
NMR Biomedicine, 9, 84-92.

Dymond, R.C., Redpath T.W., & McKiddie, F.I. (1996).
Application of the principle of optical phase-contrast microscopy to velocity phase-encoded MRI of blood flow in the aorta.
British Journal of Radiology, 69, 410-414.

Eulitz, C., Maeß, B., Pantev, C., Friederici, A.D., Feige, B., & Elbert, Th. (1996).
Oscillatory neuromagnetic activity induced by language and non-language stimuli.
Cognitive Brain Research, 4, 121-132.

Flögel, U., Willker, W., Engelmann, J., Niendorf, T., & Leibfritz, D. (1996).
Adaption of cellular metabolism to anisosmotic conditions in a glial cell line, as assessed by 13C-NMR spectroscopy.
Developmental Neuroscience, 18, 449-459.

Foody, G.M., Palubinskas, G., Lucas, R.M., Curran, P.J., & Honzak, M. (1996).
Identifying terrestrial carbon sinks: Classification of successional phases in regenerating tropical forest from Landsat TM data. *Remote Sensing of Environment*, 55, 205-216.

Friederici, A.D. (1996).
Auf der Suche nach den neuronalen Grundlagen der Sprache.
In *Jahrbuch 1995 der Berlin Brandenburgischen Akademie der Wissenschaften* (pp. 151-168). Berlin, Akademieverlag.

Friederici, A.D. (1996).
Auf der Suche nach den neuronalen Grundlagen der Sprache.
Universitas, 51, 583-596.

Friedrich, R., & Uhl, C. (1996).
Spatio-temporal analysis of human electroencephalograms: Petit-mal epilepsy.
Physica D, 98, 171-182.

Friedrich, R., Jirsa, V.K., Haken, H., & Uhl, C. (in press).
Analyzing spatio-temporal patterns of complex systems.
In H. Kantz, J. Kurths, & G. Mayer-Kress (eds.), *Nonlinear techniques in physiological time-series analysis.* Berlin, Springer.

Gorrell,P. (1996).
Parsing theory and phrase-order variation in german V2 clauses.
Journal of Psycholinguistic Research, 25, 135-156.

Gorrell, P. (in press).
The subject-before-object preference in german clauses.
In B. Hemforth, & L. Konieczny, (eds.), *Cognitive parsing in german.* Dordrecht, Kluwer.

Gorrell, P. (in press).
Review of construal by L. Frazier & Clifton.
Journal of Linguistics.

Gorrell, P. (in press).
Sentence processing.
In R. Wilson, & F. Keil (eds.), *The MIT encyclopedia of the cognitive sciences.* Cambridge, MIT Press.

Gunter, Th.C., Jackson, J.L., & Mulder, G. (1996).
Focussing on aging: An electrophysiological exploration of MMN - Selective attention on the vertical meridian and attentional processes during reading.
Biological Psychology, 43, 103-145.

Gunter, Th.C., Stowe, L.A., & Mulder, G. (in press).
When syntax meets semantics.
Psychophysiology.

Hund, M., Rezai, A., Kronberg, E., Cappell, J., Zonenshayn, M., Ribary, U., Kelly, P.J., & Llinas, R. (in press).
MEG-mapping: Basis of a new functional risk-profile (FRP) in the selection of patients with cortical brain lesions.
Neurosurgery.

Knösche, T.R., Praamstra, P., Stegeman, D., & Peters, M.J. (1996).
Linear estimation fiscriminates midline sources and a motor cortex contribution to the readniness potential.
Electroencephalography & Clinical Neurophysiology, 99, 183-190.

Mittelhäußer, G., & Kruggel, F. (1996).
Fast segmentation of brain magnetic resonance tomograms.
In N. Ayache (ed.), *Computer Vision, Virtual Reality and Robotics in Medicine, Lecture Notes in Computer Science,* Vol. 905, (pp. 237-241). Springer, Berlin.

Müller, N., Mecklinger, A., & Friederici, A.D. (in press).
Memory for object identity and spatial location: An ERP analysis of encoding and retention of information in working memory.
In T.F. Münte, & H.J. Heinze (eds.), *Mapping cognition in time and space: Combining EEG, MEG with functional imaging.* Boston, Birkhäuser.

Müller, U., Frieboes, R., & Cramon, D.Y. von (1996).
Diagnose und Therapie emotionaler Instabilität nach Hirninfarkt.
In H.-J. Möller, F. Müller-Spahn, & G. Kurtz (Hrsg.), *Aktuelle Perspektiven der Biologischen Psychiatrie* (pp. 112-116). Wien, Springer.

Müller, U. (in press).
Pharmakologie.
In P. Frommelt, & H. Grötzbach (Hrsg.), *Neurorehabilitation.* Berlin, Blackwell.

Niendorf, T., Dijkhuizen, R.M., Norris, D.G., van Lookeren Campagne, M. , & Nicolay, K. (1996).
Biexponential diffusion attenuation in various states of brain tissue: Implications for diffusion-weighted imaging.
Magnetic Resonance in Medicine, 36, 847-857.

Opitz, B., Mecklinger, A., Maeß, B., & Pfeifer, E. (in press).
The P300 evoked by visual object and spatial target stimuli: A whole head MEG analysis.
Proceedings of the Third International Hans Berger Congress. Jena, Univ. Jena.

Palubinskas, G. (1996).
A comparative study of smoothing filters in magnetic resonance images.
In *Proceedings of IASTED International Conference on Signal and Image Processing 1996 (SIP'96)* (pp. 155-159). Anaheim, IASTED/ACTA Press.

Palubinskas, G. (1996).
Adaptive filtering in magnetic resonance images.
In *Proceedings of the 13th International Conference on Pattern Recognition, Vol.3, 1996 (ICPR'96)* (pp. 523-527). Los Alamitos, IEEE Computer Society Press.

Palubinskas, G. (1996).
Classification of agricultural crop types using SPOT HRV and ERS-1 SAR in test site Ostalb .
Zeitschrift für Photogrammetrie und Fernerkundung, 5, 155-162.

Schwarzbauer, C., Morrissey, S.P., Deichmann, R., Hillenbrand, C., Syha, J., Adolf, H., Nöth, U., & Haase, A. (in press).
Quantitative magnetic resonance imaging of capillary water permeability and regional blood volume with an intravascular MR contrast agent.
Magnetic Resonance in Medicine.

Supprian, T., Müller, U., Hofmann, E., & Becker, T. (1996).
Psychiatrische Folgeerkrankungen nach Schädel-Hirn-Trauma - eine Literaturübersicht.
Psychiatrische Praxis, 23, 161-167.

Ullsperger, P., & Mecklinger, A. (1996).
P300 as an index of cognitive adaptation.
In C. Ogura, Y. Koga, & M. Shimokochi (eds.). *Recent advances in event-related potentials: Proceedings of the 11th International Conference on Event-related Potentials (EPCI)* (pp. 47-51). Amsterdam, Elsevier.

Vandermeulen, D., Descombes, X., Suetens, P., & Marchal, G. (1996).
Unsupervised regularized classification of multi-spectral MRI.
In K.H. Höhne, R. Kikinis (eds.).*Proceedings on Visualization in Biomedical Computing VBC'96,* Hamburg, 1996 (pp. 229-234). Berlin, Springer.

Wallesch, C.W., Müller, U., & Herrmann, M. (in press).
Aphasia: Pharmacological treatment options.
CNS Drugs.

Wijers, A.A., Mulder, G., Gunter, Th.C., & Smid, H.G.O.M. (1996).
Brain potential analysis of selective attention.
In O. Neumann, & A.F. Sanders (eds.), *Handbook of perception and action,* vol.3: Attention (pp.333-386). London, Academic Press.

Wijers, A.A., Mulder, G., Gunter, Th.C., & Smid, H.G.O.M. (1996).
Die hirnelektrische Analyse der selektiven Aufmerksamkeit.
In O. Neumann, & A.F. Sanders (eds.), *Enzyklopädie der Psychologie: Themenbereich C, Theorie und Forschung*: Serie 2, Kognition; Band 2. Aufmerksamkeit (pp. 479-558). Göttingen, Hogrefe.

Hund, M., Rezai, A., Kronberg, E., Ribary, U., Kelly, P.J., & Llinas, R. (1996).
MEG-mapping: Basis of a new functional risk-profile in the management of cortical brain lesions.
Aktuelle Neurologie, 69, Suppl. Deutscher Neurologen-Kongreß, Göttingen, 46.

Jovicich, J., & Norris, D.G. (1996).
Functional neuroimaging with GRASE: A comparison with GRE and SE sequences.
Proceedings of ESMRMB, Prague, 135.

Mecklinger, A. (1996).
Working memory for object forms and object locations.
In H.-G. Geissler & Th. Lachmann (eds.). *Short-term Storage and Processing in Human Cognition: Dynamic characteristics and neuronal mechanisms.* Leipzig, proArt, 17.

Morrissey, S.P., Deichmann, R., Adolf, H., Schwarzbauer, C., Nöth, U., Simonis, C., Jung, S., Hartung, H.-P., Toyka, K.V., & Haase, A. (1996).
Gd-enhanced T1 mapping in experimental allergic encephalomyelitis after anti-ICAM-1 treatment: dissociation of clinical and MRI findings.
Proceedings of ISMRM, 508.

Müller, U., Pollmann, S., & Cramon, D.Y. von (1996).
Dopaminerge Modulation des visuell-räumlichen Arbeitsgedächtnisses durch Bromocriptin.
Fortschritte der Neurologie Psychiatrie, 64, Suppl. 2, 46.

Müller, U., Pollmann, S., & Cramon, D.Y. von (in press).
Effects of bromocriptine and pergolide on visuo-spatial working memory in man.
Movement Disorders.

Müller, U., Wenzel, R., Arnold, U., Villringer, K., Ziegler, S., Minoshima, S., Bartenstein, B., Schwaiger, M., & Villringer, A. (1996).
Functional plasticity after subcortical stroke studied with stroop-like cognitive activation and PET.
NeuroImage, 3, Suppl., 500.

Palubinskas, G. (1996).
Filtering in MR images: noise estimation and comparison of filters.
Proceedings of 2nd Workshop on Automatic Analysis of Tomographical Data (AATD'96).

Palubinskas, G. (1996).
Thresholding sigma filter for magnetic resonance images of human brain.
Proceedings of 20th Annual Conference of the German Classification Society (GfKl'96), 110.

Uhl, C., & Friedrich, R. (1996).
Spatiotemporal signal analaysis: Recognition of interacting modes.
Proceedings of ICPR'96, II, Track B, 55.

Uhl, C., & Friedrich, R. (1996).
Spatiotemporal signal analysis with applications to EEG-analysis.
NeuroImage, 3, Suppl., 260.

Vos, S., Kolk, H., Gunter, Th.C., & Mulder, G. (1996).
Is there a capacity, specific for syntactic processing?
Brain and Language, 55, 92-95.

Friederici, A.D., & Hahne, A.
Developmental patterns of brain activity for semantic and syntactic processes.
Workshop "How to get into language? Approaches to bootstrapping in early language development", Berlin, Germany, September 1996.

Friederici, A.D., Mecklinger, A., Steinhauer, K., & Meyer, M.
Solving syntactic ambiguity on-line: The use of case marking information in processing non-preferred structures.
The Ninth Annual CUNY Conference on Human Sentence Processing, City University of New York, New York, USA, March 1996.

Gorrell, P.
Diagnosis and Determinism.
Ninth Annual CUNY Conference on Human Sentence Processing, New York, March 1996.

Gunter, Th.C., Friederici, A.D., & Mecklinger, A.
On the automaticity of syntactic processing.
Cognitive Neuroscience Society, Third Annual Meeting, San Francisco, California, USA, April 1996.

Hahne, A., & Friederici, A.D.
Zur Automatisierung sprachlichen Regelwissens im Erst- und Zweitspracherwerb.
Arbeitstreffen der Arbeitsgruppe RULE der Berlin-Brandenburgischen Akademie der Wissenschaften, Groß-Dölln, Germany, October 1996.

Hahne, A., & Friederici, A.D.
Arbeitet der achtjährige Parser bereits automatisch?
38. Tagung experimentell arbeitender Psychologen, Katholische Universität Eichstätt, Eichstätt, Germany, April 1996.

Hahne, A., & Friederici, A.D.
Differential brain activities for syntactic processing in children and adults.
XXVI International Congress of Psychology, Montréal, Canada, August 1996.

Hahne, A., & Friederici, A.D.
Automatisierung von Sprachverarbeitungsprozessen: Differentielle Hirnaktivitätsmuster bei Kindern und Erwachsenen.
40. Kongreß der Deutschen Gesellschaft für Psychologie, München, Germany, September 1996.

Hund, M.
MSI of visually triggered finger movements. Magnetic Source Imaging (MSI): Clinical Applications,
MEG-Workshop, Opening of the Neuromag-122 TM, University of Heidelberg, Germany, October 1996.

Lohmann, G., & Kruggel, F.
Extracting lines of maximal depth from MR images of the human brain.
13th International Conference on Pattern Recognition 1996, Vienna, Austria, August 1996.

Maeß, B., Groß, J., Dammers, J., Barnes, G., Joannides, A.A., Müller-Gärtner, H.-W., & Friederici, A.D.
Neuromagnetic recordings during auditory sentence perception.
10th International Conference on Biomagnetism, Santa Fe, USA, February 1996.

Mecklinger, A.
Gedächtnis für Objekte und räumliche Relationen bei visueller und sprachlicher Kodierung.
Arbeitstreffen der Arbeitsgruppe RULE der Berlin-Brandenburgischen Akademie der Wissenschaften, Groß Dölln, Germany, October 1996.

Mecklinger, A.
Working memory for object forms and object locations.
Conference on short-term storage and processing in human cognition. Leipzig, Germany, November 1996.

Mecklinger, A., Friederici, A.D., Naumann, P., & Gunter, Th.C.
Monitoring memory performance for abstract and concrete nouns with high density ERP recordings.
Cognitive Neuroscience Society, Third Annual Meeting, San Francisco, USA, April 1996.

Mecklinger, A. Meinshausen, R.M., Friederici, A.D.
Visual-spatial memory in humans: Evidence for dissociable systems for spatial and object information.
Symposium on Rules of Spatial Memory Organization. Akademie der Wissenschaften, Berlin, Germany, February 1996.

Müller, U., Pollmann, S., & Cramon, D.Y. von
Dopaminerge Modulation des visuell-räumlichen Arbeitsgedächtnisses.
4. Drei-Länder-Symposium für Biologische Psychiatrie. Würzburg, Germany, October 1996.

Palubinskas, G.
Filtering in MR images: Noise estimation and comparison of filters.
2nd Workshop on Automatic Analysis of Tomographical Data (AATD'96), München, Germany, April 1996.

Uhl, C. , & Friedrich, R.
Spatiotemporal signal analaysis: Recognition of interacting modes.
13th International Conference on Pattern Recognition, Vienna, Austria, August 1996.

Ullsperger, P., Mecklinger, A., & Güssow, T.
Dipole source activity of the novel P3 during performance of an oddball task, mental rotation, and text processing.
8th International Congress of IOP, Tampere, Finland, June 1996.

Vos, S.H., Kolk, H.H., Gunter, Th.C., & Mulder, G.
Is there a capacity specific for syntactic processing?
An ERP study. Annual meeting of the Academy of Aphasia, London, UK, November 1996.

Gorrell, P.

Sentence processing and reanalysis: An examination of the diagnosis model.
Universität Jena, Jena, December 1996.

Gorrell, P.

German Clause Structure and Parsing Theory.
Universität Potsdam, Potsdam, April 1996.

Hahne, A.

The temporal structure of syntactic parsing in language comprehension: Evidence from event-related brain potentials.
University of Wisconsin, Madison, USA, August 1996.

Kotz, S.A.

Semantic representations in the bilingual memory system.
Eunice Kennedy Shriver Rehabilitation Center, Waltham, USA, January, 1996.

Mecklinger, A.

Raum-zeitliche Aktivierungsmuster im Elektroenzephalogramm als Indikatoren kognitiver Prozesse.
Quantitativ Ökonomisches Kolloquium des Fachbereichs Wirtschaftwissenschaften der FU Berlin, Berlin, Germany, February 1996.

Mecklinger, A.

"I remember where I saw it but I don't remember what it was" On the modularity of visual working memory.
Colloquium des Max-Planck-Instituts für biologische Kybernetik, Tübingen, Germany, July 1996.

Mecklinger, A.

"Ich weiß noch wo es war, nur nicht mehr was es war": Dissoziierbare Systeme beim Abruf von Raum- und Objektinformation aus dem Arbeitsgedächtnis.
Kolloquium des Instituts für Psychologie der Universität des Saarlandes, Saarbrücken, Germany, December 1996.

Müller, U.

Stellenwert von Psychopharmaka in der neuropsychologischen Rehabilitation.
Neuropsychologisches Kolloquium, Städtisches Krankenhaus München-Bogenhausen, Abteilung für Neuropsychologie, München, Germany, March 1996.

Schubert, T.

Die Lokalisation des Flaschenhalses bei Doppelaufgaben.
Kolloquium des Lehrstuhles für Kognitive Psychologie der Humboldt-Universität zu Berlin, February 1996.

Schubert, T.

Die Lokalisation von Interferenzeffekten bei der gleichzeitigen Bearbeitung zweier Aufgaben,
Kolloquium des Lehrstuhls Biologische Psychologie der Humboldt-Universität Berlin, December 1996.

Uhl, C.

Signal and image processing at the Max-Planck-Institute of Cognitive Neuroscience.
Center of Complex Systems, Florida Atlantic University, Boca Raton, USA, June 1996.