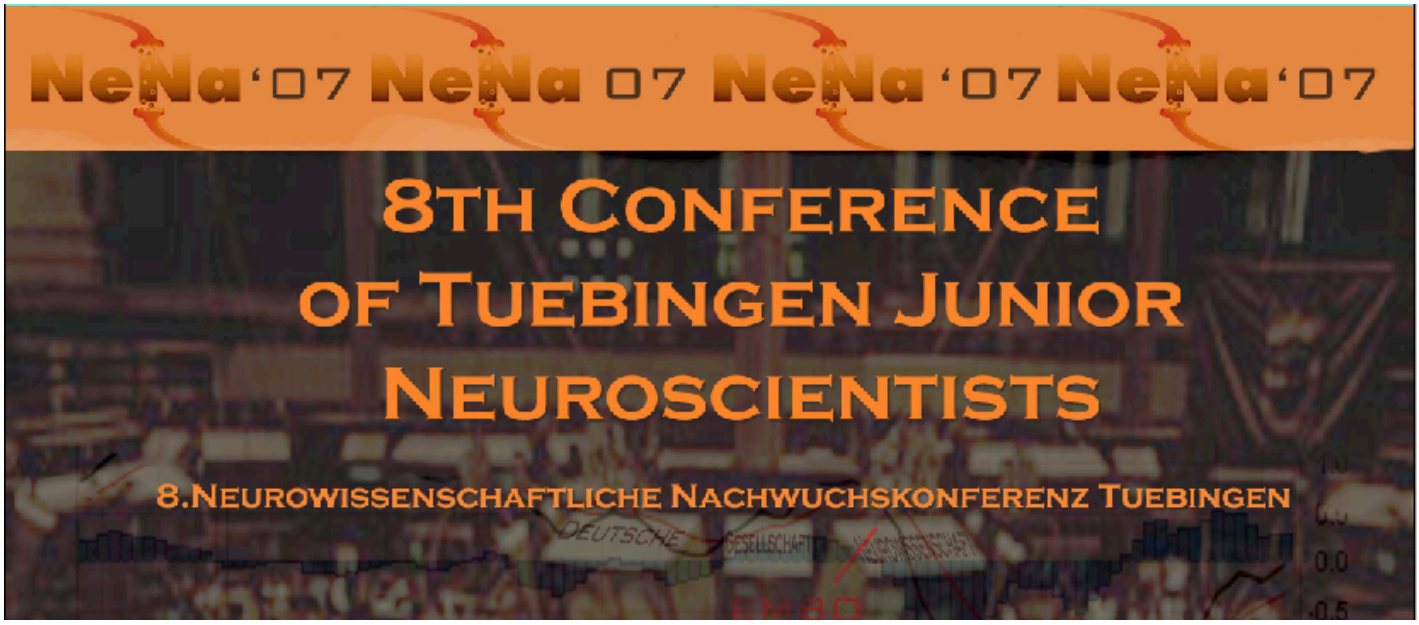


## Preface

The NeNa ("Neurowissenschaftliche Nachwuchskonferenz" - "Conference of Junior Neuroscientists") is intended to serve as a platform where young neuroscientists can meet and network. Organized by PhD students from neuroscience research groups in Tübingen, the NeNa attracts participants not only from Tübingen but also nationally as well as internationally.

This year the conference title is **"Survival Skills for Scientists - about grant applications and networking".** We understand that it is not an easy task to understand the functioning of the scientific establishment. Most scientists (students included) are brimming with new ideas and strategies that have to be usually validated experimentally. However, any scientific enquiry seldom commences with bench work and loads of data. The true start is actually in understanding the scientific system - from tackling the paperwork, obtaining licenses, and importantly, getting appropriate funding for the project. This will be the focus of this year's special lecture by Prof. Dr. Klaus-Peter Hoffmann, who is currently Professor and Chair for Zoology and Neurobiology at the Ruhr-University Bochum, Germany. He has also been the President of the German Neuroscience Society from 2005 to 2007, as well as the Chairman of a number of national and international Committees and Societies. Talking about the Scientific establishment from the point of view of a senior scientist, we hope to benefit from Prof. Hoffmann's experience and expertise, learn more about existing networks and how they can be put to use, and furthermore, about the do's and don'ts concerning grant applications.

The conference is the ideal forum for junior scientists to network; to share experiences, problems and ideas (via poster or talk) in an interdisciplinary and intercultural setting, allowing for the debate of key issues, and the identification of emerging obstacles and challenges for us rising scientists.

We would nevertheless like to thank all the participants in helping establish the NeNa as not only a conference series but also as an academic tradition.

The NeNa Team
Tübingen, November 2007

# PROGRAM

## Monday, Nov 26, 2007

| | |
|---|---|
| **11:00** | **Arrival in Freudenstadt** |
| ***12:00*** | ***Lunch*** |
| *13:00 – 13:15* | *put up posters* |
| **13:15 – 15:15** | **Session I** |
| 13:15 | Ilka Diester:<br>Correlated discharges of different celtypes in the monkey prefrontal and posterior parietal cortex during a numerosity discrimination task |
| 13:45 | Konstantin Tziridis:<br>Reaching related neurons in the dorsal pons of rhesus monkeys |
| 14:15 | Artin Atabaki:<br>Retinotopic modulation of the dorsal fronto-parietal network during covert search |
| 14:45 | Vishal Kapoor:<br>Does covert inhibition facilitate the dynamic control of decision making? |
| *15:15* | *Coffee break* |
| **15:45 – 18:00** | **Poster Session I (odd numbers)** |
| ***18:00*** | ***Dinner*** |
| **19:30** | **Evening lecture:<br>Prof. Klaus-Peter Hoffman** |

## Tuesday, Nov 27, 2006

| | |
|---|---|
| ***8:30*** | ***Breakfast*** |

| | |
|---|---|
| **9:30 – 12:00** | **Session II** |
| 9:30 | Mariana Melcon:<br>How echolocating bats solve range ambiguity problems |
| 10:00 | Sonja Seeger-Armbruster:<br>Role of serotonin transporters in animal models of Parkinson's Disease: Electrophysiological and behavioural studies |
| 11:00 | Ruediger Sadler:<br>Reconsolidation-blockade of amphetamine-induced conditioned place-preference |
| 11:30 | Michael T. Lippert:<br>Voltage Sensitive Dye Imaging of Crossmodal Interaction in Rat Neocortex |
| ***12:15*** | ***Lunch*** |
| **13:30 – 15:30** | **Break/Hike** |
| *15:30h* | *Coffee break* |
| **15:45 – 18:00** | **Poster Session II (even numbers)** |
| ***18:00*** | ***Dinner*** |
| **19:00 – 20:00** | **Session III** |
| 19:00 | Merim Bilalic:<br>Why good thoughts block better ones:<br>The pernicious Einstellung (mental set) effect |
| 19:30 | Lisa Dopjans:<br>Cross-modal transfer in face-recognition |

## Wednesday, Nov 28, 2006

| | |
|---|---|
| ***8:30*** | ***Breakfast*** |

| | |
|---|---|
| **9:30 - 12:00** | **Session IV** |
| 9:30 | Mustafa Cavusoglu:<br>Cerebral blood flow measurements using arterial spin labeling |
| 10:00 | Kirti Dhingra:<br>Smart Contrast Agents in Magnetic Resonance Imaging |
| 10:30 | Hendrik Jünger:<br>Congenital hemiparesis with different types of cortico-spinal (re-)organization: neuromodulative effects of constraint-induced therapy |
| 11:00 | Alper AÇIK:<br>Simultaneous EEG recording and Eye-tracking during Active Viewing |
| *11:30* | *Feed-back* |
| *12:00* | *Coffee break or to-go sandwich lunch* |

| | |
|---|---|
| **12:30** | **Departure, bus to Tuebingen** |

# Talks

**T1**

## Correlated discharges of different celltypes in the monkey prefrontal and posterior parietal cortex during a numerosity discrimination task

Ilka Diester

Hertie-Institute for Clinical Brain Research, Tübingen, Germany

The neuronal diversity of the cerebral cortex raises the question of how different classes of neurons, most importantly pyramidal cells and interneurons, contribute to neuronal processes and how they communicate. The presence of correlated discharges can offer insights into the patterns of connectivity. Here, we investigate which neuronal classes participate in a numerosity discrimination task and how cells interact.

We trained two monkeys in a delayed match-to-sample task to discriminate numerosities. While the monkeys performed the task, we recorded 694 and 435 single-units in the prefrontal and posterior partieal cortex, respectively. Putative interneurons and pyramidal cells were distinguished based on their spike width. We tested cells for numerosity selectivity by 2-way-ANOVAs ($p < 0.05$) and calculated crosscorrelograms for simultaneously recorded neurons.

Numerosity selectivity differed in interneurons and pyramidal cells but there was no celltype-related bias in the distribution of preferred numerical values. By testing each pair of simultaneously recorded neurons for presence of significant cross-correlation peaks, we found that about 5 % of prefrontal neurons and 25 % of posterior parietal neurons were significantly correlated. Due to the strong involvement of interneurons in the task and the functional relevance of correlated discharges between cells, these preliminary results suggest that intracortical mechanisms process numerosity within local circuits.

**T2**

## Reaching related neurons in the dorsal pons of rhesus monkeys

Konstantin Tziridis

Hertie-Institute of Clinical Brain Research, Department of Cognitive Neurology, Tübingen, Germany

Visual guided hand movements rely on the complex interaction of different visual and motor areas of the cerebral and cerebellar cortex. In both cortices areas can be found that are interested in eye or hand movements or in both motor modalities together. These areas work on different reference systems for the different effectors. The focus of our investigation lies on the major connecting anatomical interface between the two cortices: the pontine nuclei (PN). We concentrated our recordings in two male rhesus monkeys on the dorsal and dorsolateral PN because it is well known, that neurons there are active before different kinds of eye movements and projecting to the cerebellum. We asked if we can find neurons that are active before or during arm reaching movements and if they are modulated by eye movements during coordinated eye and hand movements. Additionally we investigated the reference system these neurons are coding for by letting the monkeys perform saccades or reaching movements from different starting positions respectively.
Our results show that hand movement related neurons (HMRN) in the dorsal and dorsolateral PN are as frequent as eye movement related neurons (EMRN) while they are anatomically positioned more medial than the EMRN. The activity of the HMRN changes earlier than the activity of the EMRN while we could not find strong interaction of both types of neurons with the other motor modality during coordinated movements.
Preliminary data for the reference system shows that the neurons in the dorsal and dorsolateral PN receive input from different frontal and parietal areas of the cortex coding for eye centred or non-eye centred reference frames.
In summary we find “private channels” of cortico-ponto-cerebellar communication for eye and hand movements respectively, coming from different parts of the cortex that are not interacting with each other on the level of the pons.

Supported by DFG SFB550/A7

**T3**

# Retinotopic modulation of the dorsal fronto-parietal network during covert search

Artin Atabaki

Hertie-Institute of Clinical Brain Research, Department of Cognitive Neurology, Tübingen, Germany

## Abstract

**T4**

## Does covert inhibition facilitate the dynamic control of decision making?

Vishal Kapoor[1], Aditya Murthy[2]

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[2]National Brain Research Centre, Nainwal More, Manesar Haryana, India

A planned action awaiting execution requires withholding a prepared response. We asked whether such a form of inhibition would interact with online decision processes that require changes in planned responses when new goals are unexpectedly specified. To investigate this issue with respect to oculomotor control, subjects performed, in separate sessions, standard visually-guided (SV) saccades, or memory-guided (MG) and delayed visually-guided (DV) saccades, both of which required withholding a planned saccade. To probe control, a second target (target-step) was presented in some trials after a variable delay, which instructed subjects to redirect their gaze to the newly specified target. The time taken to cancel or inhibit the saccade directed at the initial target, the target step reaction time, was calculated using a race model that hypothesis a covert inhibitory process, and was found to be significantly smaller for Memory Guided Redirect task (MGR; 94 ms) and Delayed Visually-guided Redirect task (DVR; 96 ms) compared to Standard Visually-guided Redirect task (SVR; 117 ms), suggesting facilitation of online inhibition in MGR and DVR. These results suggest that a tonic level of inhibition interacts with online decision processes to potentiate inhibitory control during double-step tasks.

**T5**

## How echolocating bats solve range ambiguity problems

M. L. Melcón, Y. Yovel, A. Denzinger, H.-U. Schnitzler

Animal Physiology, Zoological Institute, University of Tübingen, Germany

Echolocating bats need to correctly assign returning echoes to the emitted calls. When doing so, two possible sources of uncertainty might confuse them: they could assign an echo returning from the last call to the previous call (ambiguity type I) or an echo from the former call to the last one (ambiguity type II). In both cases a virtual pulse-echo pair corresponding to a virtual object is created. In the first case it is further away than the real object, while in the second it is closer.
This confusion increases while bats are approaching targets, since they tend to emit groups of calls with short and rather constant pulse intervals (PIs). In the present work we studied how echolocating bats deal with such confusion by enforcing ambiguity and testing their reaction. We compared the echolocation behaviour of bats that landed on a grid with the echolocation behaviour when a second object was positioned at different distances behind the grid, thus causing both types of ambiguity.
The bats exhibited two different patterns. Some bats changed their echolocation behaviour in the ambiguous situation by decreasing the number of calls per group towards the end of the approach phase, leading to an increased rate of changing the PI. We hypothesize that this change of the temporal pattern of calls enabled bats to identify virtual objects in highly ambiguous scenarios and could be interpreted as a change from an ambiguity non-resistant to an ambiguity resistant pattern. Other bats did not change their echolocation behaviour but already used the pattern with a high rate of changing PIs. We therefore suggest that the temporal pattern of calls might play an important role in dealing with ambiguity.

**T6**

## Role of serotonin transporters in animal models of Parkinson's disease: electrophysiological and behavioural studies

S. Seeger-Armbruster and A. von Ameln-Mayerhofer

Dept. Neuropharmacology, University of Tübingen, Germany

One of the most common animal models of Parkinson's disease (PD) is the toxin-induced hemiparkinsonism in rats (unilateral 6-OHDA lesion in the medial forebrain bundle). Such a lesion mimics the dopaminergic denervation of the striatum in PD patients. As consequences of the lesion behavioural and electrophysiological differences occur in comparison to control animals.
The present study was carried out with hemiparkinsonian and sham-lesioned male Sprague-Dawley rats. Four weeks after the lesion the behavioural deficits were measured in different established tests. The rats were first observed in a drug free state in the stepping and the whisker test to examine possible forelimb akinesia. Additionally, rotational behaviour after s.c. administration of apomorphine (0.25 mg/kg) was tested in rotometer bowls.
Extracellular single cell recordings were carried out (with platinum/tungsten electrodes) bilaterally in anaesthetised hemiparkinsonian and sham-lesioned rats. With this setup, an irregular (55 % of recorded neurons) and bursting firing pattern (33 %) in the SNr ipsilaterally to the 6-OHDA lesion and a regular firing pattern in the contralateral SNr could be reproduced. The recorded neurons in the sham-lesioned rats predominantly showed regular firing pattern (66% ipsilateral SNr; 60% contralateral SNr) and no bursting firing pattern.

The aim of the present study was to examine the antiparkinsonian effect of S-MDMA which binds to SERT (serotonin transporters) and leads to strong serotonin release.
For this purpose, S-MDMA was administered systemically (i.v.) in a cumulative dosage regimen (0.375 and 0.75 mg/kg). S-MDMA showed different dose dependent effects on the spontaneous activity of the lesioned and the control SNr. The regular and irregular firing patterns (contralateral SNr in 6-OHDA-lesioned and bilaterally in sham-lesioned rats) were not affected by S-MDMA. On the other hand, the bursting firing pattern in the 6-OHDA-lesioned SNr could at least be partly normalised by the S-MDMA application.

**T7**

## Reconsolidation-blockade of an amphetamine-induced conditioned place-preference (CPP)

Prof. Dr. Werner J. Schmidt, Dr. Volker Herzig, Rüdiger Sadler

Dept. Neuropharmacology, University of Tübingen, Germany

Male Sprague-Dawley rats were conditioned by repeated administration of d-amphetamine in a CPP-apparatus. To receive severe baseline-values a three-day pretest was conducted. Test-animals hereafter were assigned to the CPP compartments following a biased design.
The conditioning-phase consisted of 6 pairings of d-amphetamine (2 mg/kg) and saline on 12 consecutive days (day 5-16); test-animals were divided into 4 groups after a posttest (day 17), in a way to obtain comparable CPP-values and SEMs. All groups received MK-801 (NMDA-Antagonist; 0.1 mg/kg) and/or Saline immediately after and with one hour delay after each of ten reactivation sessions (days 19-28). The place conditioning behaviour was blocked in both groups receiving MK-801 at the early point in time (Posttest-II, days 29-31). The effect was reliable in the first of nine Delay-tests (days 41-121, latency between tests was 10 days) after a period of ten days, but varied strongly in the following 8 Delay-tests. A final reinstatement-trial (day 196) in a drugged state (1 mg/kg of d-amphetamine) delivered inconsistent results.
Taken together, the reconsolidation-blockade was successful, and is a very promising strategy to block drug-associated memories. In contrast the actual therapy of extinction is much less effective.

This study was funded by the BMBF; 01EB0110 Baden-Württemberg consortium for addiction research.

**T8**

## Voltage Sensitive Dye Imaging of Crossmodal Interactions in Rat Neocortex

Michael T. Lippert

MPI for Biological Cybernetics, Tübingen, Germany

Responses to crossmodal stimuli have been observed in a wide range of brain regions, where they have been studied in great detail. Although many crossmodal areas have been characterized, the spatiotemporal characteristics of such activity are still largely unknown. We used voltage-sensitive dye imaging (VSDI) to address this question. For the presented study, three cortical regions in rat were imaged: primary visual cortex (V1), barrel field of primary somatosensory cortex (S1bf) and parietal association area (PA, flanked by V1 and S1bf). We find that sensory-evoked population activity can propagate in the form of a distinct wave, robustly in either crossmodal direction, i.e. from S1bf to V1, or from V1 to S1bf. In single trials, the waveforms changed continuously during propagation, with dynamic variability from trial to trial, which we interpret as evidence for cortical involvement in the spreading process. We further investigated the propagation of spontaneous sleep-like waves in this area using a novel flow-detection algorithm. Results of these experiments show that spontaneous activity also tends to propagate parallel to the crossmodal axis, rather than orthogonal to it. Taken together, these findings demonstrate that cortical networks can show pre-attentive crossmodal propagation of activity, and suggest a potential mechanism for the establishment of crossmodal integration.

**T9**

## Why good thoughts block better ones: The pernicious Einstellung (mental set) effect

Merim Bilalic

Experimental MRI Section, Dep. of Neuroradiology, Tübingen, Germany

The Einstellung (mental set) effect occurs when the first idea that comes to mind, triggered by familiar features of a problem, prevents a better solution being found.

Here we show that the effect can be quantified and the mechanism that produces it demonstrated. The presence of a familiar solution to a problem reduced the ability of expert chess players to find a better one to that of players about three standard deviations below them in skill. Players reported that they were looking for a better solution but analysis of their eye movements showed that they continued to look at features of the problem related to the solution they had thought of first. The mechanism which allows the first schema activated by familiar aspects of a problem to control the subsequent direction of attention may explain why scientists undervalue or ignore results that do not fit their favoured theories and why people show biases in hypothesis testing.

**T10**

## Cross modal transfer in face recognition

Lisa Dopjans, Christian Wallraven, Heinrich H. Bülthoff

Max Planck Institute for Biological Cybernetics, Dept. Cognitive & Computational Psychophysics, Tübingen, Germany

Prior studies have shown that humans can recognize faces by touch alone (Kilgour and Lederman, 2002). Here we want to shed further light on haptic face recognition with five experiments using a well-defined stimulus face space based on the morphable MPI-Face-Database.
Experiment 1 used a same/different task with sequentially presented faces which established that subjects were able to discriminate faces haptically, using short term memory. In Experiment 2 we used an old/new recognition task to assess whether participants were able to learn and recognize faces haptically. Moreover, we addressed the question whether participants were able to generalize information from haptically learned faces to the visual domain - a question directed at probing the representation underlying multi-sensory face recognition. In Experiment 3, we changed the design such that haptic memory was refreshed before each test-block by repeated exposure to the three learned faces. In Experiment 4, we interchanged learning and recognition modality with respect to Experiments 2 and 3, testing within-modality recognition in the visual domain and cross-modal transfer by haptic recognition of the face masks. We found that participants were indeed able to learn and recognize small faces haptically, with haptic memory being a crucial factor for recognition performance. Moreover, we found participants to be able to generalize information from haptically learned faces to the visual domain and vice versa, however, with a clear advantage for vision as the learning modality. In Experiment 5, we used a haptic version of the inversion paradigm to study how orientation sensitive haptic face recognition is and to shed further light on the nature of information underlying haptic face processing. As we failed to find a haptic face inversion effect, we suggest that participants rely more on featural than configural information processing in haptic face recognition.
Finally, we will briefly discuss current experiments that look at size-dependent effects of haptic face recognition.

**T11**

## Cerebral blood flow measurements using arterial spin labeling

Mustafa Cavuşoğlu, Kâmil Uludağ

High-Field MR Center, Max-Planck Institute for Biological Cybernetics, Tübingen, Germany

Arterial Spin Labeling (ASL) is a magnetic resonance imaging (MRI) method to map the cerebral blood flow (CBF). ASL present a non-invasive alternative to the contrast agent techniques used typically to study vascular and neuronal diseases such as stroke, arteriostenosis, schizophrenia, alzheimer, epilepsy …. ASL techniques are capable of providing quantitative information about local tissue blood flow by tracking the inflow of magnetically labeled arterial blood into an imaging slice. The delivery of the tagged water to each image voxel is measured. Because ASL is completely noninvasive, the tagging can be repeated many times to obtain a high signal-to-noise ratio (SNR). ASL produces perfusion maps of human brain with higher spatial and temporal resolution than any other existing technique. Furthermore, ASL has extensively been used to study brain function mostly simultaneously with the blood oxygenated level dependent (BOLD) signal. BOLD signal provide a high functional contrast to noise ratio, but the analysis and interpretation of BOLD contrast functional data is complicated by the fact that the MRI signal change is related to the underlying neuronal activation through CBF, CBV and oxidative metabolism (CMRO2). In contrast to baseline BOLD signal, baseline CBF measured using ASL provides valuable information of the brain's respective state. In addition, ASL techniques are an important tool to study the physiological basis of functional neuroimaging techniques such as BOLD signal. In the study presented at the conference, we evaluated critically three different ASL sequences and compared established methods to determine absolute values of CBF from ASL data.

**T12**

# Smart Contrast Agents in Magnetic Resonance Imaging

Kirti Dhingra[1], M.E. Maier[2], N.K. Logothetis[1]

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Magnetic Resonance Imaging (MRI) is one of the most versatile techniques in clinical and experimental *in vivo* imaging. It has excellent spatial resolution but the sensitivity however is much lower than the other nuclear imaging techniques which ould be overcome by using contrast agent (CA). By accelerating the longitudinal or transverse relaxation of water protons, CA increases the signal to noise ratio, which, in turn, positively influences the image contrast. Nowadays, more than 30% of MRI examinations benefit from the use of paramagnetic contrast agents. Further improvement came with the development of 'smart contrast agents (SCA)' which are capable of reflecting a change in biological activity in their local environment compared to classic contrast agent hich are mostly nonspecific and provide only anatomical information. Many SCA have been developed showing sensitivity to pH, partial oxygen pressure (pO2), ion and metabolite concentration, or enzyme activity. SCA showing sensitivity to Ca2+ concentration changes are of extreme importance. Ca2+ is one of the most important secondary messengers in the brain. Fluorescent imaging has greatly explored the critical role played by this ion. However the role played by Ca2+ is yet to be explored noninvasively using MRI which doesn't suffers from depth penetration limits like in fluorescent imaging. Our lab in MPI for biological cybernetics is dedicated in developing such probes for MRI which could reveal the dynamics of C2+ concentration changes. In my talk I'll give a brief overview of designing strategies to develop such probes and also the recent development made in that direction.

**T13**

# Congenital hemiparesis with different types of cortico-spinal (re-)organization: neuromodulative effects of constraint-induced therapy

H. Jünger[1,2] M.D., N. Kuhnke[3] M.D., M. Wilke[1] M.D., M. Walther[3] M.D., S. Berweck[4] M.D., V. Mall[3] M.D., M. Staudt[1,2] M.D

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[4] Pediatric Neurology und Developmental Medicine, Dr. v. Haunersches Kinderspital München, Germany

## Objectives

Constraint-Induced Movement Therapy (CIMT) is an effective functional approach focussing on hand motor improvement in hemiparetic patients. Here, we asked whether, in congenital hemiparesis, 1) CIMT induces neuroplastic effects and if 2) neuroplastic and behavioural effects differ with regard to different patterns of cortico-spinal (re-)organization.

## Methods

Two patient groups with different patterns of cortico-spinal (re-)organisation were recruited: Group 1 consisted of seven patients with unilateral cortico-subcortical stroke and preserved crossed cortico-spinal projections from the lesioned hemisphere to the paretic hand (group 1, mean age 16.9 years). In Group 2, eight patients with unilateral periventricular lesions and (re-)organized ipsilateral cortico-spinal projections from the contra-lesional hemisphere (group 2, mean age 16.6 years) were included. Before and after CIMT (12 days, constraint 12h / day, individual “shaping” lessons 2h / day), all patients were studied by Wolf Motor Function Test (WMFT), Transcranial Magnetic Stimulation (TMS) and fMRI.

## Results

Motor function of the paretic hand improved in all patients after CIMT. However, WMFT-Results revealed that the behavioural benefit was less in Group 2 compared to Group 1. Both groups showed significant neuroplastic changes after CIMT. Interestingly, the direction of the observed changes differed between the two groups: When the primary motor representation (M1) was still located in the lesioned hemisphere (Group 1), MEP amplitudes and fMRI activation increased after therapy, whereas when M1 had been reorganized into the contra-lesional hemisphere, MEP amplitudes and fMRI activation decreased.

## Conclusion

We could show that CIMT induces neuroplastic changes in congenital hemiparesis and that these changes differ with regard to corticospinal reorganisation.

Supported by the German Research Council DFG (STA 859/1-1, BE 3235/1-1, MA 3306/1-1)

**T14**

## Simultaneous EEG recording and Eye-tracking during Active Viewing

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[2]University Medical Center Eppendorf, Department of Neurophysiology and Pathophysiology, Hamburg, Germany

Due to methodological constraints, electrophysiological studies of human vision under natural viewing conditions are scarce, with the vast majority of EEG studies explicitly requiring subjects not to move their eyes. These constraints include eye-movement related artifacts in EEG recordings and difficulty obtaining accurate eye-position data under such experimental settings. Here we use a high-speed (1250 Hz) eye-tracker synchronized with a 128-channel EEG system. Employing a regression-based EOG artifact reduction method, we remove eye-movement related artifacts from the recorded data. The change in power topographies and the drop in the variance of the EEG signals around the saccades but not around the fixations show that most artifacts have been removed. The eye tracking accuracy remains between 0.2-0.4 degrees during the experiment. Applying this method to simple active vision tasks, we first demonstrate differences between saccade triggered and event (stimulus onset) triggered averages of the same data. Furthermore we compare foveation related signals between saccade and stimulus flashing conditions, and find differences in terms of both curve shape and brain activity topographies. This shows that processing of visual stimuli after self-induced (eye movements) and spontaneous changes in the visual environment are qualitatively and remarkably distinct. Overall, this combined EEG and Eye-tracking methodology provides an extremely promising means of addressing fundamental unanswered questions in natural, active vision.

# Posters

**P1**

## Oscillatory correlates of visuo-motor integration: Investigation of healthy controls and schizophrenic patients

Carola Arfeller[1,2], Christoph Braun[2], Albrecht Rilk[1], Surjo Soekadar[1], Christian Plewnia[1]

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To master various complex cognitive tasks, specialized groups of neurons in distinct brain regions must effectively interact. Yet, it is unclear how this fine-tuned coordination is achieved. To date, the most common theory is that groups of neurons are temporarily bound to functional networks by coupling their oscillations. It is suggested that coherence, a measure for the similarity of two or more distinct oscillatory signals independent of their amplitudes, serves as indicator for functional integration. Depending on the level of the recorded signal global coherence and coherence of task specific regions can be distinguished. Whereas short distance synchronization tends to occur at higher frequencies (γ-band), long-distance synchronization at lower frequencies [θ (3-8 Hz), $\alpha$ (8-13 Hz) and β (13-30)]. The best method to quantify coherence of task specific regions is MEG. It combines high temporal with good spatial resolution. Visuomotor integration is a suitable model to investigate mechanisms of multimodal integration, since the relevant regions of the involved modalities are spatially distinct and located on the brain's surface. Although several studies on healthy people address this issue, data on patients are still rare. For instance, schizophrenia is considered as a disorder of neural connectivity. Earlier studies on coherence in patients with schizophrenia have found increased global coherence compared to control subjects, especially in the lower frequency bands. However, little is known about the oscillatory interactions of task specific areas and their correlation with performance as well as disorder-specific parameters in these patients. More findings about the fundamentals of oscillatory dynamics underlying visuomotor integration not only in healthy people, but also in schizophrenic patients might yield new insights into pathophysiological processes of disorders of neural connectivity and may provide new treatment perspectives.

**P2**

## Mapping Of Transcription Start Sites Of Human Retina Expressed Genes, A First Insight In The Control Of Its Gene Regulation.

R.E. Carpio, V.Roni, B.Wissinger

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Proper assembly of the machinery carrying out transcription initiation is a key regulatory step in the execution of the correct program of mRNA synthesis and use of alternative transcription start sites (TSSs) is a mechanism for cell and tissue specific gene regulation. Our knowledge of transcriptional initiation sequences in the human genome is limited despite the availability of the complete genome sequence. Genome wide experimental and bioinformatics approaches are improving on the knowledge of TSSs, but they lack in information concerning genes expressed in a restricted manner or at very low levels, as tissue specific genes.
In this study we describe the mapping of TSSs of genes expressed in human retina. Genes have been selected on the basis of their physiological or developmental role in this tissue. Our work combines in silico analysis of ESTs and known algorithm predictions, together with their experimental validation via Cap-finder RACE and Luciferase Reporter gene Assay.

We report here the TSSs mapping of 54 retina expressed genes: we retrieved new sequences for 41 genes, some of which contain not yet annotated exons. Results can be grouped in five categories as compared to the RefSeq: (i) TSS located in new first exons, (ii) splicing variation of the second exon, (iii) extension of the annotated first exon, (iv) shortening of the annotated first exon, (v) confirmation of previously annotated TSS. In silico and experimental analysis of the transcripts proved to be essential for the ultimate mapping of TSSs. The new TSSs and transcribed sequences are essential for further exploration of the promoter and other cis-regulatory sequences at the 5´end of the genes.

**P3**

## Neural model for the visual recognition of goal-directed movements

Falk Fleischer[1], Antonino Casile[1], Martin Giese[1,2]

[1]Dept. of Cognitive Neurology, Hertie Institute for Clinical Brain Res., Germany
[2]School of Psychology, University of Wales Bangor, UK

The visual recognition of goal-directed movements is crucial for the learning of actions, and possibly for the understanding of the intentions and goals of others. The discovery of mirror neurons has stimulated a vast amount of research investigating possible links between action perception and action execution. However, it remains largely unknown what the precise nature this visuo-motor interaction is, and which relevant computational functions can be accomplished by purely visual processing.
We present a neurophysiologically inspired model for the recognition of hand movements demonstrating that a substantial degree of action understanding can be accomplished by appropriate analysis of spatio-temporal visual features. The model is based on a hierarchical feed-forward architecture for invariant object and motion recognition employing principles that are similar to the ones that have been established for stationary object recognition. The model addresses in particular how invariance against position variations of object and effector can be accomplished, while preserving the relative spatial information that is required for an accurate recognition of the hand-object interaction. It is demonstrated that the model is able to correctly classify different grasp types determining whether the action matches correctly the object affordance.
The model demonstrates that well-established simple physiologically plausible neural mechanisms account for important aspects of visual action recognition without the need of a detailed 3D representation of object and action. It complements existing models and provides a basis for a further quantitative analysis of visual influences on action recognition.

Supported by the DFG, EU, Volkswagenstiftung and the Hermann and Lilly Schilling Foundation.

# P4

## Analyzing perceptual representations of complex, parametrically-defined shapes using MDS

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Prior studies have shown that humans can create a perceptual space of 3D objects that is highly congruent to the physical stimulus space when the underlying stimulus space varies in two different dimensions like global shape and local texture (Cooke et al., 2006). But what happens if the stimulus space varies in more than two dimensions? And what happens if those dimensions are not as intuitive as "shape" and "texture"? As a first step to answer these questions, a stimulus space of complex, shell-shaped objects was generated using the mathematical model of Fowler, Meinhardt and Prusinkiewicz (1992) that describes growth parameters of shells. The objects varied in three dimensions each of which controlled a different aspect of its shape. In psychophysical experiments participants viewed pairs of objects and rated the similarity between them. Multidimensional scaling (MDS) was used to calculate the perceptual space. Contrary to previous experiments, this space showed only little congruency to the physical stimulus space. Additional free categorization and sorting tasks revealed that humans found it difficult to reconstruct the dimensions of the physical stimulus space. In future experiments, we plan to compare these visual similarity ratings to haptic similarity ratings to study cross modal interaction when a complex three-dimensional stimulus space is explored.

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## Role of acetylation in axon outgrowth and regeneration

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Spontaneous axon regeneration following injury in the central nervous system is extremely limited due to the presence of an inhibitory environment, mediated by disrupted myelin and extracellular matrix, and to a deficiency of the intrinsic pro-axon outgrowth gene expression program in neurons.
Molecular interventions, which target the extrinsic inhibitory environment, are only partially able to promote axon outgrowth and regeneration.
We have employed a novel strategy to switch the intrinsic neuronal genetic program from a “non permissive” to a “permissive” pattern for neurite/axon outgrowth by increasing acetylation. Previously, increased neuronal acetylation has been shown to protect form apoptosis and to promote differentiation, whose molecular mechanisms are partially shared during neurite outgrowth.
Here, we enhanced endogenous histones and transcription factors acetylation in neurons by using the deacetylase inhibitors Trichostatin A and Butyric acid. This leads to increase transcription and to a switch in the transcription pattern.
We demonstrate that increasing acetylation leads to enhanced axon outgrowth and reduced growth cone collapse in embryonic and post-natal neurons on both permissive and non-permissive (myelin) substrates. In addition, we show that the acetyltransferases CBP/p300 and P/CAF and specific transcription factors such as p53 may be involved in such effects. Studies to further clarifying the molecular mechanisms are under way and *in vivo* experiments in models of axon injury will address the relevance of acetylation on axon regeneration.
These findings may contribute to developing new strategy for axonal outgrowth and regeneration after injury.

**P6**

## In vivo ablation of microglia in a transgenic mouse model of Alzheimer`s disease

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The pathological hallmarks of Alzheimer's disease (AD) include the presence of β-amyloid plaques, neurofibrillary tangles and neuron loss. These pathological changes are invariably accompanied by an inflammatory reaction involving resident microglia cells and peripheral macrophages. It is known that peripheral macrophages and resident microglia cells are attracted to and surround amyloid depositis in transgenic mouse models of cerebral Alzheimer´s disease (AD). The role of these microglia cells remains unclear although they have been suggested to remove amyloid fibrils in response to immunisation against the β-amyloid (Aβ) protein.

We aimed at further characterizing the reaction of microglia and macrophages in AD using the HSVTK mouse model where microglia can selectively be ablated. Therefore APPPS1 transgenic mice, showing rapid and early onset of AD pathology, were crossed with HSVTK mice expressing a mutant thymidine kinase (TK) under the CD11b promotor, which allow the induction of microglia cell death, by converting antiviral nucleotide analog prodrugs such as ganciclovir (GCV) into a toxic triphosphate. Systemic administration of GCV to APPPS1/TK mice via ALZET osmotic pumps, leads to a massive microglia ablation within 7 – 12 days. We investigated the effect of microglia ablation on cerebral amyloidosis using sterological analysis of plaque load. We found no changes on plaque load after ganciclovir treatment for up to 4 weeks.

Furthermore, we inverstigated microglia dynamics in vivo. Therefore APPPS1/TK mice were crossed to transgenic mice expressing eGFP under the microglia specific Iba1-promoter resulting in eGFP positive microglia cells. Under the conditions of GCV application, microglia ablation could be observed in vivo, using multiphoton microscopy. Visualizing the kinetics of microglia ablation in the living mouse, we observed no difference in plaque formation or homeostasis. Thus we conclude that resident microglia might not be able to limit or influence plaque formation in APPPS1 mice.

**P7**

## Colour and spatial cue for action: Subliminal colour cue effects motor behaviour

Iliya Ivanov

We addressed two important implications from Millner and Goodel`s theory on dissociation of vision for perception and for action. i)Colour processing in the Ventral stream is not integrated in the visual guidance of body movements; ii) The access of colour information to motor systems is obligatory based on visual awareness. To address the first notion we employed a Redundant-target paradigm in which subjects reacted to spatial, colour or combination of both (redundant) targets. Further, our subjects reacted to isoluminant coloured targets preceded by subliminal incongruent ones. A second condition without subliminal priming target was compared against the first one. The observed Reaction time gain is interpreted as resulting from combined sensory information in reaching some decision criterion. We also show that stimuli blocked from awareness (subliminal cues) are able to delay the fast motor responses. Overall, the results are inconsistent with the theory of independent action and perception pathways and provide behavioural evidence for interactions between ventral and dorsal streams.

**P8**

## Behavioural, metabolic and morphological effects of chronic THC and Cannabidiol administration in adult Lister hooded rats (*Rattus norvegicus*)

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So far, more than 480 substances have been isolated from the hemp plant *Cannabis sativa* L. with delta-9-tetrahydrocannabinol ($\Delta^9$-THC) and cannabidiol (CBD) as two of the most important compounds. The wild cannabis plant exhibits 5 to 10 % $\Delta^9$-THC and up to 5 % CBD whereas cultivated plants used for drug production contain up to 25 % $\Delta^9$-THC and less than 0.5 % CBD. $\Delta^9$-THC has been identified as the major psychoactive compound and is held responsible for the twofold increase in the relative risk for schizophrenia in adolescent vulnerable cannabis users. In contrast, CBD appears to act non-psychoactively and might be used as a potential antipsychotic substance in schizophrenia treatment. In a first double-blind controlled clinical trial with 42 patients fulfilling DSM-IV criteria of acute paranoid schizophrenia or schizophreniform disorder, we already showed that CBD decreased psychotic symptoms and that it induced fewer side effects compared to the antipsychotic drug amisulpride.

To investigate the mode of action of CBD as an antipsychotic, we are currently conducting behavioural as well as metabolic and morphological animal experiments targeting the endocannabinoid system. The first study of this series is done with adult Lister hooded rats which are chronically treated with either THC, CBD, amisulpride, vehicle or saline.

The behavioural tests are analogous to those used to characterise schizophrenic patients. The metabolic investigations include µPET analysis of glucose metabolism as well as the analysis of eicosanoid concentrations in the rat brain by LC-MS/MS. Furthermore, we are investigating cannabinoid receptor-1 (CB1) density and distribution with autoradiography, and the CB1 mRNA expression using in-situ hybridization.

In the next study, we will investigate the behavioural, metabolic and morphological effects of chronic THC and CBD administration in pubertal Lister hooded rats and the effects of CBD treatment after chronic pubertal THC administration.

**P9**

## The Angioarchitecture of the Macaque Monkey Visual Cortex

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While neurons communicate, they consume energy and oxygen, which is supplied by the blood stream. Changes in local cerebral blood flow and in oxygen consumption can be measured using functional magnetic resonance imaging (fMRI). This technique is one of the most frequently used tools to non-invasively monitor neuronal activity in the human. However, the mechanisms that are coupling the neuronal activity with the vascular response are not well understood so far. Additionally, there is only insufficient quantitative anatomical data on the microvascular system. For example, the regional distribution of the smallest vessels (capillaries) that are crucial for the exchange of gases and metabolites is still unclear.
Quantitative data about the brain's microvasculature could provide new insight into the regulatory properties and dynamics of the neurovascular system and may lead to a better interpretation of the non-invasive functional imaging signals. The goal of my PhD project is a complete quantitative and qualitative description of the angioarchitecture of the macaques visual cortex. As part of the thesis project I have quantified the vascular density in the visual cortex of the macaque monkey in an immunohistochemical and histological approach. So far, we were able to show the characteristic vessel distribution across the different cortical layers and to detect significant differences between the primary and the higher order visual cortices. Therefore, caution is advised when in a vision-based task the functional signals from different regions of the visual cortex are compared.

**P10**

## Characterizing Leucine-rich repeat kinase 2 (LRRK2) dimerization

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Parkinson disease (PD) is the second most common neurodegenerative disease and the most common cause of parkinsonism, a disease syndrome defined by characteristic clinical symptoms (resting tremor, rigidity, bradykinesia, and postural instabilitiy), resulting from a selective degeneration of dopaminergic neurons in the substantia nigra.

*Leucine-rich repeat kinase 2 (LRRK2)* is the latest gene revealed to cause monogenetic parkinsonism, with mutations exceedingly abundant compared to other known gene mutations in parkinsonism. What is more, patients harbouring *LRRK2* mutations show astonishingly diverse neuropathologic features ranging from α-synucleinopathies (Lewy bodies) and tauopathies (neurofibrillary tangles) to pure nigral degeneration without accompanying protein abnormalities. Thus, LRRK2 is supposed to act as a pivotal player in the genesis of neurodegeneration.

The gene product of *LRRK2* is a huge multi-domain protein (2527 amino acids, ~286 kDa) residing in the cytoplasm, probably associated with membranous structures.

Besides various predicted protein-binding domains, LRRK2 contains a GTPase and a kinase domain – both shown to be catalytically active – and has been allocated to the tyrosine kinase like (TKL) branch of the human kinome. Like many other kinases, two close TKL relatives (RAF1 and MLK3) have been shown to form dimers, suggesting LRRK2 to dimerize also.

To investigate LRRK2 dimerization potential, a Y2H interaction study with the predicted LRRK2 domains was conducted, proposing the central RocCor (Roc, Ras of complex proteins; Cor, C-terminal of Roc) domain as core interaction region. These results were confirmed by successful co-immunoprecipitation of differentially tagged RocCor proteins from HEK T 293 cells. Interestingly, the RocCor domain also interacts with full-length LRRK2, and RocCor domains containing familial *LRRK2* mutations are still able to bind to the wild-type domain. The interaction between RocCor domains is independent of GTP, even though the domain is able to bind GTP. Future approaches will analyze the orientation of the RocCor interaction as well as the functional relationship between LRRK2 dimerization and kinase activity.

**P11**

## How Does My Finger Jointly Act With Yours?

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Joint action refers to the actions which two or more people coordinate in space and time to produce a change in the environment. (Sebanz, N. et al., 2006). By using functional magnetic resonance imaging (fMRI) we investigated the neural correlates of joint action. We scanned 18 subjects while they cooperate with the experimenter in the scanner room. The task involved creating a particular shape (straight line or v shape) by moving two individual arms of a stick by using the index finger. In the joint action condition each player had to move his half of the stick as quick as possible in order to jointly create the desired shape. Most importantly, to jointly achieve the team's goal, the scanned player had to perform his actions by combining the desired target shape with the observed finger movements of the other player (experimenter). Additionally, we had control conditions in order to locate the motor and visual brain regions that are active during mere execution and observation of the same actions. In the execution condition the subject moved his stick singly whereas he observed the same action done by the experimenter in the observation condition. Conjunction of these two conditions revealed activations in the fronto-parietal mirror areas. Later to identify the brain regions selectively active in performing joint actions we contrasted the joint action condition with the sum of the control conditions. Our results revealed that performing joint actions activates the opercular part of the left Inferior Frontal Gyrus and left Inferior Parietal Lobule (IPL) more than the control conditions. Both regions were not within the mirror areas identified by the conjunction between viewing actions and executing individual actions but were adjacent to them. Moreover the posterior part of the bilateral Superior Temporal Sulcus (STS) and Lingual Gyrus of the bilateral Occipital Lobe were found to be more active for joint actions. These findings suggest that engaging in joint actions requires brain regions that are outside but neighboring to the mirroring areas.

**P12**

## "What's on my mind" areas and stress: comparing neurotic brains

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Neuroticism is a personality trait characterised by an increased sensitivity to external stressors. In this fMRI study, we compare 3 groups of students: students who are sensitive to negative social evaluation and students whose scores are high on irritation/frustration sensitivity questionnaire with the low scoring students whose questionnaire scores are the lowest 20% of the total of 400 students.

Our fMRI scanning procedure is as follows: Subjects undergo a 90-minute scanning procedure. The first task is to compare the facial expressions versus shapes (Hariri et al., 2002). The second task is the Ultimatum Game where the subjects have to accept or reject an offer from different proposers. The proposer splits 10 euros either fairly of unfairly. After the subjects finished these tasks, they are asked to perform the first task again. This time they are told that the experimenters are observing them through the camera and are evaluating their performance. The last task is 2 runs of a mental arithmetical task (Siegrist et al., 2005) in which subjects can make real money (between 20 – 30 euros). During the second run of this task, fake technical difficulties creating wrong feedbacks; make the subjects loose 80% of their gains.
If subjects complain about the wrong feedback, they are told that they are doing mistakes. After these tasks, we test the effect of verbal remarks from the experimenter with a 6-minute single trial fMRI run. Before this run the experimenter tells the subjects to lie still in the scanner and stop moving three times with insistence. Additionally, during this trial we will measure the heart rate. Finally, the experiment ends with an 8 minute of resting-state.
For the facial expressions task, we expect highest Amygdala activity in high scoring neurotic students and visa versa. For the ultimatum game, we expect differences in insular cortex activity (Sanfey et al., 2003) during the presentation of unfair offers to be correlated with personality differences. Stronger activation of the Anterior Cingulate Cortex is expected for high neurotic individuals. Additionally default mode or 'What's on my mind' areas will be compared between groups.
This PhD project started in January 2007. Here I present the first part of the experiment where we are testing students. In the future we will use female monozygotic twins, discordant for neuroticism.

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**P13**

## Coregistration of Ultrasound and fMEG data

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In fetal magnetoencephalography (fMEG) the availability of the anatomical information is a critical and important issue.
On one hand high resolution imaging techniques (for instance MRI or TAC) are barely applicable because of their invasivity, on the other the localization of fetus's organs under study (head, heart) is not direct as for adult MEG studies.
Moreover, to minimise fetus movements between the functional and the anatomical session, and to allow the superimposition of the two modalities to take place, the proximity of the functional and anatomical equipments is important.
In order to overcome these difficulties a 3D Ultrasound (US) system is used. It has the minimal invasivity required to obtain clear images from the fetus, it is equipped with tracking sensors and a reconstruction software, which allow the localization of points in a volume and it is portable.
In the present study the US examination has been performed to get the necessary anatomy of the interesting volume of activity (the head of the fetus) to be coregistered and fitted for a conductive model estimation.

With the help of US and functional fMEG information a beamformer algorithm has been applied with the aim of estimating the sources of fetal brain activity.
Preliminary results of coregistration of one phantom and one subject are shown, and related to the last one a source time course is presented in the case of an evoked potentials experiment.

**P14**

# A new hardware-software coil positioning system for interleaved TMS/fMRI: A motor cortex stimulation study

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An important practical challenge in interleaved TMS/fMRI is the accurate positioning of the coil inside the scanner. We describe a novel method which allows accurate coil placement inside the MR scanner using pre-planned coil positions previously determined with a neuronavigation system. The method was successfully used in a pilot study on the motorcortex which served to demonstrate the viability of our overall TMS/fMRI setup.

Coil positions-of-interest are initially determined using a neuronavigation system (BrainView, Fraunhofer IPA, Stuttgart, Germany) and saved in respect to the coordinate system defined by a high-resolution T1 image. Inside the scanner, the position of the subject‘s head is determined using a fast FLASH image, which is automatically coregistred to the high resolution image. Based on the coregistered images, the software automatically determines the parameters for a coil holding device for targeting the pre-planned position. The accuracy of the method was tested in phantom measurements. Mean deviation between pre-planned coil positions marked on a spherical phantom and the position given by the setup was 3.895 mm. This demonstrates a good spatial accuracy in the range previously reported for offline neuronavigation systems[1].

In the pilot study, paired pulse TMS on the motor cortex was investigated in 6 subjects. Whole-brain echo planar images were acquired at 3T. The coil was positioned above the hot spot of the motor cortex (M1) which had previously been determined using the neuronavigation system. Subjects participated in four runs of supra motor threshold stimulation (120% MT), three runs at 80% MT stimulation and one run with volitional movement (acoustically triggered by pulses at 50% MT). A run took 8 minutes in which 27 paired pulses were applied. The group activation maps are in good concordance with previous findings[2,3]. In particular, for 120% MT stimulation, significant responses were observed in the primary auditory cortex, M1/S1, the supplementary & cingulate motor areas and the thalamus. The observed activation pattern showed robust overlap with the results of the volitional finger movements.

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**P15**

## Dendritic spine turnover: a neuronal correlate of learning? - Behavioural experiments and *in vivo* imaging in pyramidal neurones of the adult mouse barrel cortex

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This project investigated changes in the physical shape of neurones as a result of a behaviourally-relevant learning experience. Dendritic spines are the site of a majority of excitatory connections in the neocortex. They can turn over or change shape on timescales ranging from minutes to days. Previous studies have demonstrated that spine dynamics can be influenced by experimental modifications. However, these studies either solely assessed baseline structural plasticity, or they caused extensive modifications of neuronal input, thus creating 'exceptional' situations for the organism; neither of these approaches reflect the challenges posed by a truly behaviourally-relevant learning experience. This project addresses this issue specifically. The area of the mouse primary somatosensory cortex representing whisker tactile stimuli (the barrel cortex) is the model system of choice. This cortical region is known to exhibit both physiological and structural plasticity as a result of experience. A transgenic mouse expressing yellow fluorescent protein in cortical pyramidal neurones was bilaterally implanted with cranial windows over the barrel cortices. This enabled the long-term monitoring of dendritic spine dynamics *in vivo*. The mouse was trained on an operant conditioning task using electrical microstimulation of the barrel cortex as a conditioned stimulus (CS). The animal successfully learned to discriminate and appropriately respond to two CSs with different behavioural significance. Before and during the learning period, spine dynamics were monitored daily in two-photon imaging sessions for selected dendrites of barrel cortex layer V neurones. A decrease in the average spine turnover (the rate of spine appearances and disappearances) was observed during the behavioural training period, as opposed to the pre-training baseline period. The research project I present here sets a framework for future studies seeking to elucidate the nature and extent of plastic changes in the neurones of a primary sensory cortical area in the context of a learning task.

**P16**

## Head positioning sensitivity study in magnetoencephalography using a spherical head model

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Magnetoencephalography (MEG) is a technique for evaluating brain function by the measurement of the magnetic fields generated by the brain, being the magnetic counterpart of electroencephalography.
These extremely feeble magnetic fields can be detected by low-temperature superconducting sensors (SQUIDs), immersed in liquid helium at 4.2K. Earlier MEG systems had one or few sensors and were unable to localize the source of the generating currents in the brain, while present-day systems have hundreds of sensors in a helmet-shaped dewar. A snapshot of the magnetic field distribution enables the investigation of the underlying current dipoles. The helmet is designed for an "average" adult head, but is suboptimal for children and newborns. Due to the smaller head size of a newborn, complications on head positioning arise, and these difficulties may render the detection of small responses in the subject's brain more difficult than in an adult or even unfeasible. This study investigates the dependency of the sensitivity of the system with the head position by means of a spherical head model, aiming to optimize the positioning according to the region of the brain that is expected to be activated during the experiments.

**P17**

## Evaluation of motor and cognitive effects of systemic MnCl2 injection: Implication for longitudinal MRI studies

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Manganese-enhanced MRI (MEMRI) is a new tool for in vivo brain imaging. The technique is based on the fact that Mn2+ ions reduce the longitudinal (i.e. spin-lattice) relaxation times, T1, of water protons. Consequently T1-weighted MR images show enhanced signal intensity at the locations where Mn2+ ions accumulate. When administered systemically, Mn2+ reaches the brain and enters the cells via voltage-gated calcium channels. Therefore, Mn2+ accumulation in the brain is proportional to the neural activity, allowing in vivo visualization of functional maps. However, the technique presents several drawbacks that can challenge its applicability, the most important being the potential toxicity of the ion in the tissue, leading to neuronal death when applied in high doses or motor disorders after chronic exposure.
The toxic effects of MnCl2 on motor activity and learning were evaluated in Sprague-Dawley rats. Two ways of MnCl2 administration were compared. In Exp.1, naïve rats were given access to a running wheel (3h/day; 6 days). On day 7, MnCl2 (0.1, 0.2, and 0.5 mmol/kg) was injected (s.c.) 3h prior the running test. Control rats received saline injection. A significant dose-dependent decrease of motor activity was observed for all doses. In Exp.2, rats were first implanted (i.p.) with osmotic pumps loaded with MnCl2 (0.5 mmol/kg; 1.0 \u03bcl per hour; 7 days) or saline and then given access to the running wheels. The motor activity did not differ between the two groups. In Exp.3, rats were trained to perform a T-maze alternation task and after reaching an asymptote performance the effect of acute s.c. injections of MnCl2 (0.1 and 0.5 mmol/kg) was tested. Manganese did not affect the choice accuracy, however, the highest dose resulted in increased response latency, as expected from Ex! p.1 results. In Exp.4 rats with implanted Mn- or saline-loaded pumps were trained on the same T-maze alternation task. We found no differences in any of the learning parameters studied, between the two groups. We conclude that most common protocols of functional MEMRI produce undesirable behavioral effects that can be avoided by the gradual release of MnCl2 via osmotic pump delivery. The reported protocol represents an appropriate alternative for longitudinal studies using this very important technique.

**P18**

## Face categories in the interior-temporal cortex of the macaque monkey

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Ambiguous stimuli constitute a powerful method to dissociate between the physical properties of the stimuli and their representation in the brain. Following this idea, we applied a new computer-vision algorithm based on Support-Vector-Machines (SVMs) to create three-dimensional morphed faces (linear interpolated) between humans and monkeys in order to investigate how species-dependent face information is encoded in the inferior-temporal (IT) cortex of the macaque brain. Previous psychophysical experiments using these stimuli have shown that human subjects tend to classify ambiguous morphs as discrete instances of the human/monkey categories ('categorical perception'). Moreover, subjects draw the category boundary closer to their own species (at approximately 60%human/40% monkey).

We recorded the single-unit-activity (SUA) of 118 neurons and the local field potential (LFP) at 58 sites of the IT cortex of one macaque monkey during fixation of these morphed stimuli. Out of a total of 118 single units, 85% were visually responsive, 23% were selective to faces, 12% selective to monkeys and 14% to humans, according to standard criteria. To analyze the population activity, we trained different classifiers (k-Nearest Neighbor, Support vector Machines, K-Means) to learn the representation (SUA and LFPs) of human and monkey faces and tested them with the ambiguous stimuli. We found that, symmetric to the findings in humans, ambiguous faces are categorized by the pattern classifiers in a manner implying a categorical representation of the faces. Furthermore, the classifiers drew the category boundary closer to the monkey category (at approximately 40%human/60% monkey) for both kinds of neural signals.
In contrast to the linear change of the morphed faces, our preliminary results showed that the neural representation of the species information is nonlinear. This nonlinearity suggests an 'own-species' advantage in the encoding of face stimuli. Consistent with learning theories, this advantage seems to be better reflected in our data by a sharper tuning of the monkey-selective cells compared to the human-selective, and not by a difference in the number of cells.

**P19**

## The growth associated protein 43 is transcriptionally regulated by acetylated p53 via CBP/p300 signaling during neurite outgrowth and axon regeneration

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The growth associated protein 43 (GAP-43) is a key factor for axon growth and regeneration. However, its gene regulation is poorly understood, and no transcription factors have been proven to bind to any specific GAP-43 gene regulatory elements in a chromatin environment.
Clarification of GAP-43 transcriptional regulation would allow better understanding of how axon growth and regeneration are controlled.

Here, we report that the tumor suppressor p53 is a transcription factor for neuronal GAP-43. p53 acetylated at K373 preferentially binds specific elements on the GAP 43 promoter in a chromatin environment. In addition, it drives GAP-43 expression and neurite outgrowth in cultured neurons preferentially via a CBP/p300 acetylation dependent signaling pathway. Moreover, we demonstrate that acetylated p53 K373 and CBP are induced following nerve transection, and that p53 is required for GAP 43 induction during axon regeneration *in vivo*.
This data contributes to the understanding of gene regulation in axon outgrowth and may open new avenues for targeting molecular pathways to promote axon regeneration.

Keywords: gene regulation, GAP-43, neurite outgrowth, p53, axon regeneration.

**P20**

## Visual motion processing: illusions of speed

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Our perception of speed is not exclusively determined by the velocity of the stimulus. The waterfall illusion is a prominent example of motion perception without a moving stimulus. Here, we focus on the effect of stimulus size on speed perception. Initially, we tried to document that monkeys share the size-speed illusion with humans.
We used a sequential two-alternative forced choice task in which the monkeys had to compare the speed of two sequentially displayed motion stimuli. Two saccade targets were shown after the presentation of both stimuli; selection of the left target signalled that first stimulus appeared faster, selection of the right target signalled that second stimulus appeared faster. We used velocities in the range between 10 and 20 deg/s. The radius of the first stimulus was 10 deg, the radius of the second stimulus could be either identical or 5 or 20 deg, respectively. We fitted the psychophysical data with a logistic function. The point of subjective equality of speed (PSE) as a measure of the illusion changes according to the size of the second stimulus: if the first stimulus was smaller, the second stimulus has to be faster (approx. 2 deg/s). If the second stimulus was smaller, the first stimulus has to be faster.
We recorded single-unit activity from area MT while the monkey fixated a stationary target. Firstly, we determined the receptive field and the preferred direction of an isolated neuron. We fitted the directional sensitivity of each neuron by von Mises distributions. Local-field detectors were separated from wide field detectors by their responses to increasing stimulus size. We measured the individual speed transfer function with stimulus sizes varying from 5 to 40 deg of each neuron. The neuronal response to a given velocity did not reveal a systematic influence of stimulus size. Of course, the response strength of local motion detectors declines with increasing stimulus size. We fitted speed tuning transfer functions to our data and determined the optimal velocity of each neuron for each stimulus size. This optimal velocity increased with increasing stimulus size. This clearly indicates that the activity of MT neurons display the speed illusion, or, in other words, the cause of the illusion is rather early in motion processing.

Supported by EU (MEST-CT-2004-504321) and DFG IL 34/6-1

**P21**

## Understanding of proportionality in primates

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Many behavioural studies have demonstrated that non-human primates can assess quantitative information. For example, monkeys are able to judge absolute discrete quantities (such as numerosity) as well as continuous magnitude (e.g., length). Many vital decisions require not only absolute discriminations of quantity, but also an understanding of the relations between quantities. In conflicts, the ratio of adversaries vs. allies is the decisive variable as opposed to the absolute set sizes. Whether monkeys understand abstract relationships between quantities, however, remains unknown.

To investigate this question, we trained monkeys in a delayed match-to-sample task to match proportions in visual displays. The monkeys had to judge the length of a test line relative to the length of a reference line. Ratios of ¼, ½, ¾ and 4/4 were shown. Control stimuli were applied to ensure that the monkey could not use the absolute lengths of the test or reference lines to solve the task.

Overall, the monkeys' performance was 85.4% accurate. Analoguous to numerosity discrimination in primates, we found that performance improved the more remote the non-match proportions from the sample proportion were (distance effect). This resulted in Gaussian discrimination curves centered around the sample proportions. To test whether the animals could also discriminate proportions they had not been trained on, we applied transfer tests showing novel proportions (3/8 and 5/8). The animals also reliably discriminated transfer tests, thus, demonstrating that it had generalized the concept of proportionality. In addition, we tested human subjects with the identical protocol. Interestingly, their behavioural performance resembled that observed in monkeys.

In summary, we could show that non-human primates are able to reason quantitatively and grasp the concept of proportionality. Moreover, the monkeys' performance was comparable to human's ability to discriminate fractions.