Research Results of the BCF presented at the SfN conference 2013

Location: Halls B-H

Time: Sunday, November 10, 2013, 1:00 PM - 5:00 PM

Program#/Poster#: 257.04/KK3

Topic: C.18. Drugs of Abuse and Addiction

Support: NIH-NIAAA#16658

Title: Mapping the brain functional and structural connectivity of mu-opioid receptor knock-out mice

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Abstract: A non-invasive insight into the brain's intrinsic connectional architecture of functional networks (FN) has only become possible since the development of resting-state functional magnetic resonance imaging (rsfMRI). In humans, the default mode functional networks and their alterations in pathologies are intensively studied. Moreover, when combined with diffusion tensor magnetic resonance imaging (DT-MRI) and fiber tracking investigations [1], recent studies demonstrate the structural connectivity features underlying the FN and their remodeling mapped by rsfMRI [2]. However, the intrinsic connectional architecture of functional and structural networks in the mouse brain remains a significantly underexplored research area. The goal of the present study was to bridge this gap by unifying and adapting the rsfMRI/DT-MRI techniques for studying the functional and structural connectivity pattern in mouse models of brain disorders. We focused our investigation on mapping the brain connectional networks of mu-opioid receptor (MOR) knock-out mice (Oprm1-/-), an extensively used model of drug addiction and reward [3].
Mouse brain MRI was performed with a 7T small bore animal scanner and a mouse head adapted cryogenic surface coil (Bruker Germany) both allowing for high signal-to-noise ratio and short acquisition times at high resolution. rsfMRI and DT-MRI data was acquired from 8 weeks old wild type (n=14) and Oprm1-/- (n=14) male mice using single shot Gradient Echo Echo Planar Imaging (GE-EPI) and 4 shot DT-EPI sequences. Group Independent Component Analysis (ICA) of rsfMRI data allowed the identification of elementary functional clusters of the Oprm1-/- mouse brain. Their connectional relationship was tested with partial correlation and graph theory providing a comprehensive picture of Oprm1-/- brain functional connectivity. As a step forward, the identified functional clusters were subsequently used as regions of interest in a fiber tracking algorithm, for mapping structural connectivity. We focused our analysis on brain

networks involving areas known for their clustered expression of MOR such as striatum, amygdala and thalamus. Our experiment broadens the knowledge about functional and anatomical connectivity in mouse models of brain disorders uncovering also the involvement of the mu opioid receptor in brain networks remodeling. This non-invasive study design forms also the basis for longitudinal investigations, opening a perspective towards testing therapeutic compounds and their influence on the progress of disease patterns.
[1] Harsan et al, PNAS 2013; [2] van den Heuvel et al, HBM 30, 2009; [3] Kieffer et al, ProgNeurobiol 66, 2002

Disclosures: A. Mechling: None. **T. Arefin:** None. **H. Lee:** None. **M. Reisert:** None. **S. Ben Hamida:** None. **J. Hennig:** None. **D. von Elverfeldt:** None. **B. Kieffer:** None. **L. Harsan:** None.

Poster

257. **Opioids: Neural Mechanisms of Addiction**

Location: Halls B-H

Time: Sunday, November 10, 2013, 1:00 PM - 5:00 PM

Program#/Poster#: 257.05/KK4

Topic: C.18. Drugs of Abuse and Addiction

Support: 1R21DA030225

Title: Novel mechanism for opioid drug action: Implications of Redox/Methylation signaling

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Abstract: Drugs of abuse, including opioids, act upon molecular mechanisms which support attention, awareness and consciousness. Attention is closely linked to learning and memory, & frequent drug use results in persistent behavioral changes, including withdrawal syndromes, indicating that neuronal systems have adapted to repeated drug use. Mounting evidence indicates that epigenetic changes, specifically alterations in patterns of DNA and histone methylation, can produce long lasting alterations in gene expression, affecting learning, memory and behavior. Thus, the activities of methylation-related metabolic pathways in neuronal cells could help explain at least some molecular aspects of the acute and longer-term effects of opioid class of drugs of abuse. We investigated acute and long-term effects of selected opioid drugs and their mechanism of influence on pathways of sulfur metabolism, redox and DNA methylation status in cultured neuronal cells. We found that morphine dose dependently inhibited EAAT3, which transports cysteine, a precursor for glutathione (GSH) synthesis. Subsequent decreases in

Parkinson's disease can be attributed to deterioration of these neurons. Advanced age is the leading risk factor for Parkinson's, which suggests that changes that occur in dopamine neurons during normal aging may contribute to disease development. In the absence of synaptic input, intrinsic ion channel conductances drive dopamine neurons to spontaneously fire action potentials in a rhythmic pacemaker-like pattern. Previous studies suggest that the unique set of ion conductances used for pacemaking could be responsible for the age-related changes in substantia nigra dopamine neurons. Traditional tissue isolation methods are not conducive for patch clamp electrophysiological recordings in brain slices from old mice. We have observed that transcardial perfusion of ice-cold aCSF before slicing helps preserve the integrity of dopamine neurons and allows for physiological studies in aged mice. Here we show that substantia nigra dopamine neurons from mice aged 25-32 months (old) have comparable membrane capacitance and input resistance to neurons from mice aged 2-7 months (young). However, neurons from old mice have slower firing rates, narrower spike widths and more variable inter-spike intervals when compared to neurons from young mice. I_h and SK channel-mediated afterhyperpolarization currents are similar in neurons from old and young mice, but dopamine neurons from old mice have significantly smaller L-type calcium currents. This evidence provides a plausible mechanism to explain the decrease in firing rate and fidelity observed in slices from older mice. As pharmacological antagonism of L-type calcium channels has been proposed as a potential treatment for the early stages of Parkinson's disease, our results could point to a limited temporal window of opportunity for this therapeutic intervention.

Disclosures: S. Branch: None. **A.L. Sharpe:** None. **M.J. Beckstead:** None.

Poster

327. **Modulation of Neuronal Firing I**

Location: Halls B-H

Time: Monday, November 11, 2013, 8:00 AM - 12:00 PM

Program#/Poster#: 327.04/G51

Topic: B.10. Intrinsic Membrane Properties

Support: BMBF 01GQ0830 BFNT Freiburg

Title: A sub-threshold bifurcation as the determinant for spiking precision in neocortical pyramidal cells

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Abstract: Pyramidal cells lock their firing with millisecond precision to strong stimuli, but can show long and variable spike delays under conditions resembling sparser input regimes. This behavior has been observed in experiments, and is in line with established dynamical models of spike generation for integrator neurons, commonly referred to as type-I cells. Recent in vivo recordings in different animals and cortical layers revealed that sparse activity regimes are more prevalent than previously thought. However, eliciting spikes at all with sparse input requires a certain degree of synchronization, which is, in turn, difficult to achieve with cells firing with variable spike delays. It is, thus, unclear in how far networks consisting of pyramidal cells could sustain activity modes with sparse firing.
To resolve this ambiguity, we iterated experiments for the characterization of spiking precision in neocortical pyramidal neurons with refinements of generic models for spike generation. Our experiments revealed that, even though pyramids in the neocortex are classical type-I cells, they show precise PSP-spike coupling under most conditions mimicking sparse network activity, except for a small window that allows for the occurrence of the variable spike delays typical for type-I cells. This window was opened if cells could retain a high input resistance at membrane potentials close to spiking threshold. However, increases in leak conductance diminished this window of imprecise spiking and turned pyramids into cells that couple their spikes precisely to even small stimuli, a behavior typical for type-II (or resonator) neurons. In contrast to previous studies in cells within other brain regions, we could show that this change in precision of PSP-spike coupling is not associated with a switch from type-I to type-II dynamics, but depends on the presence of a second qualitative change, or bifurcation, in the dynamics of the spike generating mechanism, that occurs below threshold. Applying phase plane analysis of two-dimensional generic models of spike generation, we formulate a mechanistic description of the underlying dynamics, and use it as a new approach to understand PSP-spike coupling.
Our results imply that spiking precision in pyramidal cells during sparse activity can be controlled by various mechanisms that influence input resistance, including both, intrinsic as well as network mechanisms. The theoretical framework we propose is not limited specifically to neocortical pyramids, but is generally applicable to any neuron with type-I spike dynamics and, thus, can be utilized to understand PSP-spike coupling in a wide variety of neurons throughout the brain.

Disclosures: C. Boucsein: None. **J. Ammer:** None. **J. Benda:** None.

Poster

327. **Modulation of Neuronal Firing I**

Location: Halls B-H

Time: Monday, November 11, 2013, 8:00 AM - 12:00 PM

Program#/Poster#: 327.05/G52

Time: Monday, November 11, 2013, 8:00 AM - 12:00 PM

Program#/Poster#: 336.17/S14

Topic: C.08. Epilepsy

Support: German Federal Ministry of Education and Research FKZ 01GQ0420

German Federal Ministry of Education and Research FZK 01GQ0830

DFG within the Cluster of Excellence BrainLinks-BrainTools.

Title: Local interplay between hippocampal single cell firing and network oscillations is preserved under epileptic conditions

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Abstract: Epileptic seizures in mesio-temporal lobe epilepsy (MTLE) are transient events although the associated histological changes in the hippocampal network are persistent. How these changes contribute to the generation of epileptiform activity (EA) might not be trackable during excessive epileptic discharges. In contrast, EA-free activity might allow to identify modified properties of the hippocampal network rendering it seizure-prone.
We take advantage of the intrahippocampal kainate mouse model of MTLE, in which a unilateral injection of kainate into the dentate gyrus (DG) induces histopathological changes resembling human MTLE. In these animals, EA-free activity comprises network oscillations comparable to those found in healthy animals, such as theta and gamma rhythms.
Recently, we showed that the coupling in theta rhythm between the histologically normal medial entorhinal cortex (MEC) and the sclerotic DG was phase-shifted in epileptic animals (Froriep et al. 2012, Epilepsia). Whether the phase-modulation of neuronal firing by this rhythm present under healthy conditions is preserved under epileptic conditions and whether phase-shifted network oscillations are accompanied by shifted single neuron activity remains unclear.
Hence, we investigated the phase relationship of multi-unit activity (MUA) and local filed potential (LFP) rhythms by implanting custom-made multi-site silicon probes to simultaneously record both, LFP and MUA in several substructures of the entorhinal-hippocampal (EC-HC) loop of freely behaving mice.
We found that neurons in the non-sclerotic but strongly epileptic zone of all investigated substructures of the EC-HC loop fired phase-coupled with respect to theta and gamma LFP oscillations. Theta phases at which cells fired in epileptic animals were comparable to those in

healthy mice. Furthermore, the preferred coupling phases of neurons in the DG were independent of the distance to the most prominent histological changes. Therefore, shifted LFP theta rhythms between MEC and DG in MTLE imply a shift in single cell firing and thereby tune the hippocampal network towards seizure susceptibility via pathological plasticity.

Disclosures: A. Kilias: None. **U.P. Froriep:** None. **U. Häussler:** None. **A. Kumar:** None. **C.A. Haas:** None. **U. Egert:** None.

Poster

336. **Epilepsy: Network Activity and Oscillations**

Location: Halls B-H

Time: Monday, November 11, 2013, 8:00 AM - 12:00 PM

Program#/Poster#: 336.18/S15

Topic: C.08. Epilepsy

Support: NIH Grant 1K08NS069783

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Citizens United for Research in Epilepsy

Dr. Michel and Mrs. Anna Mirowski Discovery Fund for Epilepsy Research

Rachleff Scholars Program, University of Pennsylvania

Title: Temporal dynamics of neocortical high frequency oscillations in human epilepsy

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Abstract: High frequency (100-500 Hz) oscillations (HFOs) recorded from intracranial electrodes are a potential biomarker for epileptogenic brain. HFOs are commonly categorized as ripples (100-250 Hz) or fast ripples (250-500 Hz), and a third class of mixed frequency events has also been identified. We hypothesize that temporal changes in HFOs may identify periods of increased likelihood of seizure onset. 86,151 HFOs from five patients with neocortical epilepsy implanted with hybrid (micro + macro) intracranial electrodes were detected using a previously

validated automated algorithm run over all channels of each patient's entire recording. HFOs were characterized by extracting quantitative morphologic features and divided into four time epochs (interictal, preictal, ictal, and postictal) and three HFO clusters (ripples, fast ripples, and mixed events). We used supervised classification and nonparametric statistical tests to explore quantitative changes in HFO features before, during, and after seizures. We also analyzed temporal changes in the rates and proportions of events from each HFO cluster during these periods. We observed patient-specific changes in HFO morphology linked to fluctuation in the relative rates of ripples, fast ripples, and mixed frequency events. These changes in relative rate occurred in pre- and postictal periods up to thirty minutes before and after seizures. We also found evidence that the distribution of HFOs during these different time periods varied greatly between individual patients. These results suggest that temporal analysis of HFO features has potential for designing custom seizure prediction algorithms and for exploring the relationship between HFOs and seizure generation.

Disclosures: W.C. Stacey: None. **A. Pearce:** None. **D. Wulsin:** None. **B. Litt:** E. Ownership Interest (stock, stock options, royalty, receipt of intellectual property rights/patent holder, excluding diversified mutual funds); Neuropace. F. Consulting Fees (e.g., advisory boards); NeuroVista. **A. Krieger:** None. **J.A. Blanco:** None.

Poster

336. **Epilepsy: Network Activity and Oscillations**

Location: Halls B-H

Time: Monday, November 11, 2013, 8:00 AM - 12:00 PM

Program#/Poster#: 336.19/S16

Topic: C.08. Epilepsy

Support: DFG SFB 780

DFG SFB TR3

DFG Cluster of Excellence BrainLinks-BrainTools

Title: The neurogenic niche is irreversibly changed in experimental epilepsy

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Abstract: Temporal lobe epilepsy (TLE) is characterized by increased structural plasticity in the dentate gyrus, including granule cell dispersion (GCD) and altered neurogenesis in the subgranular zone (SGZ). Using the intrahippocampal kainate model for TLE we have shown that neurogenesis was completely lost in the septal hippocampus, spatially overlapping with the septotemporal extent of GCD (Häussler et al., 2012, Cerebral Cortex). In contrast starting from a transition zone in the intermediate hippocampus, neurogenesis was strongly increased in the SGZ of the intermediate and temporal ipsilateral and in the entire contralateral hippocampus. Intrahippocampal recordings revealed that this region-dependent modulation of neurogenesis was related to differential strength of status epilepticus at respective sites.
Here, we investigated (a) whether a strong pro-proliferative stimulus can reactivate neurogenesis and (b) whether a physiological stimulus can rescue neurogenesis when applied during the whole period of epileptogenesis.
To this end, we performed an unilateral intrahippocampal kainate injection (KAIhipp) in adult mice followed by (a) systemic kainate injection (KAIsys) 21 days later, or by (b) voluntary wheel running for 14 days after KAIhipp. To monitor cell proliferation, mice were injected with bromodeoxyuridine (BrdU) 6 days after KAIsys or for 10 days during the running period. We performed double-immunostainings for BrdU and nestin, glial fibrillary acidic protein (GFAP) or doublecortin (DCX) and quantified proliferating cells and young granule cells.
We show that one day after KAIhipp neuronal stem cells in the SGZ survive, whereas principal cells in the CA region and interneurons in the dentate gyrus die. Yet, when adding the KAIsys at day 21, cell proliferation and neurogenesis could not be reactivated in epileptic mice, in contrast to naïve controls that showed strongly increased neurogenesis. We thus tested, whether voluntary wheel running, which strongly stimulated neurogenesis in naïve mice, might rescue neurogenesis in epileptic mice when applied for two weeks starting immediately after injection. Our data reveal that the loss of neurogenesis in KAIhipp mice was persistent at two weeks after the injection, in spite of physical activity. We thus conclude that the neurogenic niche is irreversibly changed in the intrahippocampal kainate mouse model for TLE.

Disclosures: U. Haussler: None. **T. Gremmelspacher:** None. **A. Hubbe:** None. **C.A. Haas:** None.

Poster

336. **Epilepsy: Network Activity and Oscillations**

Location: Halls B-H

Time: Monday, November 11, 2013, 8:00 AM - 12:00 PM

Program#/Poster#: 336.20/S17

Topic: C.08. Epilepsy

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Abstract: Motor skill is usually understood as a capability to perform faster and at the same time more accurate movements than other, unskilled, individuals. In this study we investigated motor skill learning using a path tracking task, where subjects had to track various curved paths as fast as possible, in the absence of any external perturbations. Importantly, we used different paths for every trial. We found that subjects become better with practice: only 30 minutes of practice brings substantial improvement and after 4-5 days of training performance approaches its asymptote. We next asked what changes in the motor system lead to this speed increase. To probe subjects' feedback corrections, we used a cursor jump paradigm and found no difference in the magnitude of visuomotor reflex reaction between naive, trained and expert groups. To probe subjects' feedforward planning, we used a "searchlight" paradigm, where only a short segment of the path ahead of the cursor was left to be seen. We found that subjects with a higher tracking skill demonstrated higher searchlight sensitivity: they were more strongly handicapped by very short searchlights than the subjects with poor tracking skills. It means that as the training proceeds, subjects increasingly rely on planning the movement ahead of time. We interpret this finding as an indication that motor skill is associated with increased confidence in the reliability of the movement controller.

Disclosures: L. Bashford: None. **C. Mehring:** None. **D. Kobak:** None.

Poster

471. **Voluntary Motor Control: Motor Learning II**

Location: Halls B-H

Time: Monday, November 11, 2013, 1:00 PM - 5:00 PM

Program#/Poster#: 471.16/GGG32

Topic: D.17. Voluntary Movements

Support: NWO Veni grant 451-10-017

ERC starting grant 283567

NWO Vici grant 453-11-001

Title: Generalization of context-dependent internal models

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Abstract: Intracellular recordings of neurons in *vivo* are becoming routine, yielding rich insights in neural dynamics and the integration of information by neurons under realistic situations. In particular, these methods have been used to estimate the mean excitatory and mean inhibitory conductances experienced by the soma. We first present a novel method to estimate the effective somatic excitatory and inhibitory conductance as well as their rate and event size from the intracellular *in vivo* recordings. We apply this technique to the intracellular recordings from the primary motor cortex of awake behaving mice.
Next, we study how dendritic filtering affects these estimates. While the effects of the inputs on the conductance change are mostly local, the effects on the membrane voltage extend further, resulting in the misestimation of the compound excitatory and inhibitory conductances. Using analytical treatment of a simplified model and simulations in a detailed model, we show how much both the mean as well as the variation of the dendritic synaptic conductances are underestimated by the methods based on conductance measurements at the soma. We discuss the influence of the synaptic distance from the soma on the underestimation for both excitatory as well as inhibitory inputs for different realistic neuronal morphologies.

Disclosures: **M. Pelko:** None. **P. Puggioni:** None. **I. Dugiud:** None. **M. van Rossum:** None.

Poster

708. **Dendritic Excitability and Synaptic Integration**

Location: Halls B-H

Time: Wednesday, November 13, 2013, 8:00 AM - 12:00 PM

Program#/Poster#: 708.09/F1

Topic: B.10. Intrinsic Membrane Properties

Title: The cellular mechanism of dendritic calcium spikes in the apical dendrite of L5 pyramidal neurons

Authors: *A. KORNGREEN[1], M. ALMOG[2]
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Abstract: Hodgkin and Huxley characterized two voltage-gated channels in the giant squid axon. It took them two years of hard work to arrive at their famous model. They enticed an entire generation of biophysicists to do voltage-clamp experiments and build more and more complex models of many types of neurons. Today, sixty years later, we should have had already good

and oriented Gabor patches. In the third frame (1500 ms) some of the Gabor patches were arranged to form a figure together with two RF Gabor patches and the others were part of the background. The figure was either an open or a closed contour. The monkeys were trained to report whether the contour was open or closed when cued by the contrast change of the fixation dot (1000 ms after onset of the third frame).
In our analysis we focused on the 1500ms time segment which contained the figure. During this phase of the trial we observed slight rate increase in multi-unit activities within the first 100 ms of the segment when the RFs were part of the figure. On the contrary when the RFs were not part of the figure there was a significant decrease in spike rate. In addition there was a smooth increase in firing rates towards the time point where the monkey was allowed to respond. The cross-correlation analysis showed these spiking activities are rhythmic: gamma band in earlier time period and beta band in the later time period.

Disclosures: **S. Van Stijn:** None. **H.S. Lee:** None. **W. Singer:** None.

Poster

825. **"Vision: Processing of Contrast, Orientation, and Color"**

Location: Halls B-H

Time: Wednesday, November 13, 2013, 1:00 PM - 5:00 PM

Program#/Poster#: 825.09/BB12

Topic: D.04. Vision

Support: Eurospin PhD Programme

Neuroinformatics Doctoral Training Centre

Title: Iso-orientation tuning of surround modulation in V1 allows for unbiased orientation coding

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Abstract: Surround modulation in V1 is a well studied phenomenon, whereby the response of a neuron to a center stimulus is modulated by the presence of a surround stimulus. It is thought to be relevant for saliency and contour detection (see e.g. Li, 1999, Proc. Natl. Acad. Sci. USA) . In most cases the effect is suppressive, and most models assume that it is strongest when the surround stimulus is aligned with the neuron's preferred orientation. However, a recent study showed that for the majority of V1 neurons, the suppression effect depends on the relation between center and surround orientation, being strongest when they are co-aligned, regardless of the preferred orientation (Shushruth et al., 2012). We investigated the impact of this finding on

population encoding of the stimulus.
First, we compared two firing rate based models from Shushruth et al.'s work. In the first (classical) model the surround modulation depended on on a neuron's preferred orientation. In the second model the modulation depended more strongly on the center orientation due to strong recurrent connections between neurons. We then tested the encoding of a center orientation in the presence of a surround. We show that the classical model had a strong surround dependent bias, while the second model had a comparatively small bias. However, besides the surround modulation tuning difference, the models also had differently shaped tuning curves. Furthermore, in the second model the surround modulation still depended slightly on a neuron's preferred orientation. These problems made it hard to attribute the bias differences solely to the surround modulation tuning.
To control for these problems we developed two phenomenological models for which the surround modulation either depended solely on the preferred orientation or on the center orientation, but were otherwise identical. In this case the bias remained for a preferred orientation dependent model, but completely disappeared for a center orientation dependent model, which we could prove mathematically.
Our results suggest that iso-orientation tuned surround modulation allows for unbiased coding of the center orientation, despite changed neuronal activity in the presence of a surround.

Disclosures: S.W. Keemink: None. **C. Boucsein:** None. **M.C. Van Rossum:** None.

Poster

825. "Vision: Processing of Contrast, Orientation, and Color"

Location: Halls B-H

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Program#/Poster#: 825.10/CC1

Topic: D.04. Vision

Support: German Federal Ministry of Education and Research (BMBF) grant 01GQ0420 to BCCN Freiburg

German Federal Ministry of Education and Research (BMBF) grant 01GQ0830 to BFNT Freiburg*Tübingen

Title: Physiological correlates of fast stimulus processing in the rat visual cortex

Authors: A. I. JASPER[1,2], S. ROUX[1,3], D. SUCHANEK[1], *A. AERTSEN[1,2], C. BOUCSEIN[1,2]
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Abstract: Psychophysical experiments with humans and monkeys have shown that reaction times in visual categorization tasks can be as short as 250-290 ms. In addition, these short reaction times seem to be robust to different kind of object categories and therefore could serve as a lower limit for information processing. Interestingly, stimulus characterization by neurons in the visual system is usually studied by averaging the response of a neuron over several trials and seconds. In view of the short behavioral reaction times, this approach is clearly not adequate to explain the neuronal contribution to fast signal processing. In particular, it ignores the potential information that might be present in the early transient neuronal response.
To assess the extent to which tuning properties of neurons in primary visual cortex (V1) are present in the early transient response, and to test if these are comparable to the characteristics of the sustained response, we performed in-vivo extracellular recordings in primary visual cortex (V1) of anaesthetized rats upon presentation of drifting square wave gratings in eight different directions. Since the transient response might depend of the starting phase of the grating, we presented each direction with four different starting phases. We then compared the preferred orientation derived from the transient response to that from the sustained response. Our data shows that orientation selectivity can, indeed, be found in the transient response. Moreover, the tuning properties of the transient responses were largely in line with those obtained from the sustained responses. Our data, therefore, suggests that rats can rely on clear tuning in the early transient response of V1 neurons, reducing the need for averaging over time or large cell populations.
References
Freedman, DJ, Riesenhuber, M, Poggio, T, Miller, EK (2001). Categorical representation of visual stimuli in the primate prefrontal cortex, Science 291, 312-316
Thorpe, SJ and Fabre-Thorpe, M (2001). Seeking categories in the brain, Science 291, 260-262
Fabre-Thorpe, M (2011). The characteristics and limits of rapid visual categorization, Frontiers in Psychology 2: 243

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Poster

825. **"Vision: Processing of Contrast, Orientation, and Color"**

Location: Halls B-H

Time: Wednesday, November 13, 2013, 1:00 PM - 5:00 PM

Program#/Poster#: 825.11/CC2

Topic: D.04. Vision

Poster

833. Brain-Machine Interface V

Location: Halls B-H

Time: Wednesday, November 13, 2013, 1:00 PM - 5:00 PM

Program#/Poster#: 833.07/NN10

Topic: D.18. Brain-Machine Interface

Support: BMBF Grant #0316064

DFG ExC 1086

Title: Acute and chronic µECoG-based brain mapping using a wireless implant system in a large animal model

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Abstract: Recently, there is a growing interest in developing micro-scale electrocorticography (µECoG) electrode arrays to record brain activity for applications in brain-machine interfaces, for which (i) biological stability and compatibility, and (ii) reproducibility of the recorded neural activity are important. A major aim of the present project was to evaluate the implantable system "BrainCon", which consists of a µECoG array produced with novel laser-based manufacturing methods, a subcutaneous transmitter unit, and an extra-corporeal unit connected via an infrared optical link and induction coupling, according to the two main criteria mentioned above, and to test whether the "BrainCon" system is suitable for chronic application.
We mapped the somatosensory cortex in acute experiments as a basis for chronic studies. Acute tests in minipigs with 4x12 contact arrays (3.5-mm or 1.68-mm inter-electrode distance), as well as acute and chronic tests in sheep (ovis orientalis aries) with 4x8 contact arrays (1.5-mm inter-electrode distance) were carried out. For all tests, the array was placed over the left somatosensory cortex. For the acute and chronic tests under anaesthesia, different combinations of stimulation sites and electrical stimulation intensities were tested. In addition, contra- and ipsilateral somatosensory stimulation was performed, both in the anaesthetized and awake

animals in order to evoke somatosensory responses in the chronic experiments.
Acute results showed that significant changes in stimulation-related potentials and spectral power were reproducibly detectable. Moreover, amplitude and location of these changes were modulated by stimulation intensity and site in a somatotopic manner. Power increases upon stimulation of a particular site were often restricted to one or a few adjacent electrodes, especially in the high-gamma frequency range. First chronic results also showed that somatosensory responses could reliably be measured over several months, both in the anaesthetized and awake animals.
The reproducible, highly focal potential and power changes confirmed that the employed µECoG array is capable of detecting differential signals down to a mm scale. Therefore, µECoG recordings from small cortical regions may provide non-redundant, highly informational signals. Thus, the present findings thus demonstrate the feasibility of both acute and chronic µECoG recordings using the wireless "BrainCon" implant.

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Poster

833. **Brain-Machine Interface V**

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DFG ExC 1086

Title: The Braincon platform software architecture for invasive closed-loop Brain-Machine Interfaces and electrical stimulation

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Abstract: Closed-loop brain-machine interfaces (BMIs) promise to restore movement to people with paralysis, enable communication with locked-in patients and facilitate stroke rehabilitation. Typical BMI software systems repeatedly execute four steps: data acquisition, feature extraction, decoding, and feedback presentation to the user. Depending on the use, data acquisition encompasses reading different types of data from different types of devices, e. g. electrocorticography (ECoG) data from amplifiers or movement data from joysticks. Different feature extraction and decoding algorithms, e. g. Fourier transform, support vector regression or Kalman filters can be used. Feedback to the user can be auditory, visual or directly applied to the brain by electrical stimulation.
Here, we introduce the Braincon platform software and present its architecture. All functionality (e.g. data acquisition and decoding) is organized in modules interacting through well-defined interfaces. Modules can be exchanged and connected to each other by configuration, i.e. no re-compilation is required. This allows re-use of frequently used modules and simplifies testing, since modules can be tested separately. In addition, modifications and extensions of the software design can be implemented faster and easier. We can use demanding feature extraction and decoding algorithms, as the Braincon Software Platform executes them in a multi-threaded manner, making efficient use of multi-core processors. Modules for visual feedback allow different views and the possibility of interaction for the user and the technical assistant. The assistant's view can provide additional information (e.g. online decoding accuracy) and allow online modification of parameters depending on subject performance. Special modules were designed for data acquisition from the Braincon implant (CorTec GmbH, Freiburg, Germany) to enable ECoG recordings from and electrical stimulation of specific brain areas. Electrical

stimulation can be elicited through a script for brain mapping or online for closed-loop stimulation feedback.
The Braincon platform software targets research studies and clinical applications. It was already successfully applied in a research study for online classification of actual and imagined wrist movements. Currently, we are using the software in a research study investigating continuous 1D arm movements in a game-like paradigm. Furthermore, as an example of a clinical application, we implemented online decoding of hierarchical discrete decision processes in an ongoing study to control spelling software and assistive devices for severely paralyzed patients.

Disclosures: **J. Fischer:** A. Employment/Salary (full or part-time):; CorTec GmbH, Freiburg, Germany. E. Ownership Interest (stock, stock options, royalty, receipt of intellectual property rights/patent holder, excluding diversified mutual funds); CorTec GmbH, Freiburg, Germany. **T. Milekovic:** None. **C. Mehring:** None. **J. Hammer:** None. **J. Rickert:** A. Employment/Salary (full or part-time):; CorTec GmbH, Freiburg, Germany. B. Contracted Research/Research Grant (principal investigator for a drug study, collaborator or consultant and pending and current grants). If you are a PI for a drug study, report that research relationship even if those funds come to an institution.; BMBF grants 0313891, 01GQ0420 and KMU-Innovativ. E. Ownership Interest (stock, stock options, royalty, receipt of intellectual property rights/patent holder, excluding diversified mutual funds); CorTec GmbH, Freiburg, Germany. **A. Aertsen:** None. **T. Ball:** B. Contracted Research/Research Grant (principal investigator for a drug study, collaborator or consultant and pending and current grants). If you are a PI for a drug study, report that research relationship even if those funds come to an institution.; BMBF grant 0313891.

Poster

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Title: Clustered relevance vector machines for transfer learning to accelerate p300 speller training

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Abstract: The P300 Speller is a system that allows users to control a computer using only P300 event-related potentials (ERP) detected via electroencephalogram. Thus, it can function as a

or silently (covert). We tested the predictive power of a high gamma (HG; 70-150 Hz) based neural decoding model to reconstruct continuous spectrotemporal auditory features of self-generated, overt speech. Data were split into separate sets for model training and for model validation. Two models were built from the training data: a linear model based on the spectrotemporal envelope of the subject's own voice and a nonlinear model based on the modulation content. Reconstruction accuracy was evaluated on the validation data as the correlation between actual and predicted speech features. For both models, reconstruction accuracy was significant in each subject (randomization test, $p < .001$ for each). We then used the overt-trained models to decode spectrotemporal features from brain activity in the covert speech condition. We used a speech recognition algorithm based on dynamic time warping to realign the imagined speech reconstruction with the spoken audio signal - allowing a direct estimation of the reconstruction accuracy. HG activity in the STG during speech imagery encoded both linear and nonlinear spectrotemporal features of speech (randomization test, $p< .005$ for each subject). These results indicate that a spectrotemporal representation of imagined speech can be reconstructed from models that are built from an overt speech data set, supporting a shared neural substrate for covert and overt speech. The findings also suggest that the spectrotemporal features of imagined speech can be extracted from ECoG signals, providing a basis for development of a brain-based communication method for patients with disabling neurological conditions.

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Poster

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Topic: D.18. Brain-Machine Interface

Support: BMBF GoBio

BMBF KMU-innovativ

Title: Invasive BMI - one way forward to a desirable treatment option? A survey on paralyzed patients' attitudes, state of knowledge and ways of information retrieval

Authors: C. SCHWARTZ[1,4], J. LAHR[5,6], *S. CARDOSO DE OLIVEIRA[8,2], B. HEIMBACH[7], A. AERTSEN[1,2,3], C. WEILLER[7,2], T. BALL[5,1,2], J. RICKERT[1,4]

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Abstract: Brain-machine interfaces (BMI) are an emerging therapeutic option for paralyzed patients to gain control over assistive technology devices (ATD). BMI approaches can be broadly classified into two classes: Invasive BMIs, using intracranially implanted electrodes, and non-invasive BMIs, based on surface electrodes or extra-corporeal sensors.
Invasive BMIs have a favorable signal-to-noise ratio and thus allow the extraction of more information than non-invasive ones, but are associated with the risks related to the neurosurgical implantation. Current non-invasive BMI approaches typically struggle, among other problems, with long setup-times and intensive training.
Recent studies have started to investigate the attitudes of paralyzed patients eligible for BMIs towards this emerging technology, particularly in patients suffering from amyotrophic lateral sclerosis (ALS). The results indicated that paralyzed patients are indeed interested in BMI technology. Little is known, however, on the degree of knowledge that paralyzed patients have on BMI approaches on the one hand and on how patients retrieve information on ATDs on the other. Further, it is not yet clear, if paralyzed patients would accept intracranial implantation of BMI electrodes (given satisfactory and reliable decoding) and if a broader range of patients with diseases such as stroke or spinal cord injury would also be open to this new kind of treatment.
Using a questionnaire, we interviewed 131 paralyzed patients on their opinion about invasive BMIs and on their attitude towards invasive BMI treatment options. The majority of the patients knew about and had a positive attitude towards invasive BMI approaches. Especially the group of ALS patients was open to invasive BMIs. Further, the survey revealed that, for paralyzed patients, the internet is an important source of information about ATDs. Consequently, websites tailored to prospective BMI users may help to put this targeted audience in touch with researchers and developers of BMI technology and further to facilitate the recruitment of motivated patients for upcoming BMI studies.

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Poster

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Support: German Federal Ministry for Education and Research, Grant 0316064- Braincon

Title: An implantable brain-computer interface for chronic cortical recording and stimulation using a micro-ECoG electrode array

Authors: *J. RICKERT[1], F. KOHLER[2], J. FISCHER[3], T. FEHRENBACHER[3], A. GKOGKIDIS[4], R. MOHRLOK[5], J. PAETZOLD[5], K.-H. BOVEN[5], C. HENLE[3], W. MEIER[3], M. RAAB[3], J. S. ORDONEZ[2], X. WANG[4], M. GIERTHMUEHLEN[4], T. BALL[4], K. FOERSTER[4], J. HABERSTROH[4], T. M. FREIMAN[4], T. STIEGLITZ[2], M. SCHUETTLER[2]
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Abstract: Introduction
Bi-Directional brain-computer-interfaces (BCI) have the potential of treating a variety of conditions such as movement and mood disorders. Furthermore, they can allow heavily impaired patients to communicate with their environment. In our work, we describe the technological platform of an implant with the potential of being used for both applications and the outcomes of pilot chronic animal studies.
Materials and Methods
The device interfaces with the cortex by a grid-type electrode array, suitable for high-resolution electrocorticography (Micro-ECoG) as well as for electrical stimulation. The grid electrode consist of a 4 x 8 array Pt/Ir electrodes, having a diameter of 1.1 mm and a centre-to-centre distance of 4 mm. It is fabricated from multiple layers of silicone rubber, Parlyene-C polymer, and Pt/Ir foil, which were cut to shape layer-by-layer using an automated laser. The result is a flexible printed circuit board with integrated stretchable tracks which run to an edge of the grid, forming weld-pads for the electrode cable to be spot-welded to. The cable has a length of 50 cm and is made from individual MP35N wires of 0.07 mm diameter bundled in silicone rubber tubing of 1.8 mm diameter. The electrode cable is soldered to the electrical feed-through contacts of the ceramic package which hermetically encloses the implant electronics. The ceramic package is casted in silicone rubber, lectrically insulating the cable contacts. The electronics amplify (200x) and digitize (1kS/s, 16bit) the ECoG signals from 16 electrodes and permit voltage-controlled electrical stimulation of max. 17 V via 8 electrodes. The implant

communicates at 1Mbit/s with a body-external transceiver unit (BETU) through an infrared optical link. Power is inductively supplied to the implant by a 16 MHz alternating magnetic field generated by the BETU. The BETU is powered by and communicates with a laptop computer using a USB link.
Prototypes were implanted in three sheep and periodically tested for functionality by recording of Micro-ECoG, evoked either by electrically stimulation of lips and tongue, by direct brain stimulation using the implant's pulse generator, or by gently stroking the animal's cheeks.
Results
The total size of the implant electronic housing is 5 x 34 x 78 mm^3. It was implanted in the sheep's back and the cable was subcutaneously routed to the head. A stable wireless link to the BETU through tissue of up to 2 cm thickness was obtained. All described methods of evoking cortical responses resulted in successful Micro ECoG recordings. Up to date, all three implants remained fully functional and are well tolerated by the animals. The longest implantation time was 10 month.

Disclosures: **J. Rickert:** A. Employment/Salary (full or part-time):; CorTec GmbH. B. Contracted Research/Research Grant (principal investigator for a drug study, collaborator or consultant and pending and current grants). If you are a PI for a drug study, report that research relationship even if those funds come to an institution.; German Federal Ministry for Education and Research. **F. Kohler:** F. Consulting Fees (e.g., advisory boards); Cortec GmbH. **J. Fischer:** A. Employment/Salary (full or part-time):; CorTec GmbH. **T. Fehrenbacher:** A. Employment/Salary (full or part-time):; CorTec GmbH. **A. Gkogkidis:** None. **R. Mohrlok:** A. Employment/Salary (full or part-time):; Multi Channel Systems GmbH. **J. Paetzold:** A. Employment/Salary (full or part-time):; Multi Channel Systems GmbH. **K. Boven:** A. Employment/Salary (full or part-time):; Multi Channel Systems GmbH. **C. Henle:** A. Employment/Salary (full or part-time):; CorTec GmbH. **W. Meier:** A. Employment/Salary (full or part-time):; CorTec GmbG. **M. Raab:** A. Employment/Salary (full or part-time):; CorTec GmbH. **J.S. Ordonez:** F. Consulting Fees (e.g., advisory boards); CorTec GmbH. **X. Wang:** None. **M. Gierthmuehlen:** None. **T. Ball:** None. **K. Foerster:** None. **J. Haberstroh:** None. **T.M. Freiman:** None. **T. Stieglitz:** F. Consulting Fees (e.g., advisory boards); CorTec GmbH. **M. Schuettler:** B. Contracted Research/Research Grant (principal investigator for a drug study, collaborator or consultant and pending and current grants). If you are a PI for a drug study, report that research relationship even if those funds come to an institution.; German Federal Ministry for Education and Research. F. Consulting Fees (e.g., advisory boards); Cortec GmbH.

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