Abstracts

Abstracts of presentations at the 7th Annual Meeting of the EEG and Clinical Neuroscience Society (ECNS) and the 2nd Joint Meeting of the International Society for NeuroImaging in Psychiatry (ISNIP), in Munich, Germany, September 6-10, 2005.

ECNS Presidential Address

A Four-step Approach for Developing Diagnostic Tests in Psychiatry

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A four-step approach for developing diagnostic tests in psychiatry is proposed. **Step1:** a biological variable is observed to be deviant from healthy controls in a particular patient population. The demonstration of test retest reliability of the finding using blinding procedures is an essential component of this early step. Confirmation by independent groups is essential for this particular test to move into the next step of development. **Step 2:** is the demonstration of potential clinical usefulness of the specific finding. The two most important objectives at this step are demonstration of difference between the target patient population and appropriate control groups (these should be groups of patients with diagnoses that commonly appear on the differential diagnostic lists of the target disorder. This is an important point as a biological abnormality may be common to two disorders that hardly ever appear on the same differential diagnostic list (e.g., schizophrenia and dementia in a young adult). While such finding would be of considerable scientific interest, it would not particularly decrease the diagnostic potential of the finding. On the other hand, an abnormality that is equally common to disorders that frequently need to be differentiated from one another (e.g., Bipolar Disorder and Schizophrenia) is not likely to be useful clinically. Estimation of the effect size of the finding could be a reasonable guide to which findings should be considered good candidates for Step 3 studies. During **Step 3:** the performance characteristics of the test should be established. Specifically, the sensitivity, specificity, positive and negative predictive values of the biological marker should be examined. These data should allow the estimation of the added diagnostic value resulting from incorporating the test into the work-up of a particular patient. The choice of the "gold standard" or reference test is an essential component of this step. At this step, the clinical characteristics of the patient group identified by the test are usually further delineated. Factors such as effects of illness duration and severity and the effects of medications should also be defined during step three. At this step, the test would be considered "promising" for development as a diagnostic test. **Step 4:** defines the clinical application of the test and helps standardize the technique used in large and multicenter clinical trials. Multicenter trials should pave the road towards standardization of laboratory procedures used to conduct the test as well as providing data regarding cost effectiveness and impact on both short-term and long-term clinical outcomes.

Symposia

Symposium: Psychosis and Neuronal Synchronization

Summary Abstract

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An increasing body of evidence supports the hypothesis that synchronous oscillations may reflect the mechanism by which the brain integrates the activity of spatially distributed neural populations related to the same object.

Abnormalities in synchronization could underlie a variety of perceptual and cognitive abnormalities observed in patients with schizophrenia, such as hallucinations, aberrant semantic associations and loss of conscious experience unity and continuity.

In the proposed symposium, different methods and experimental paradigms used to investigate abnormalities of synchronization in schizophrenia will be presented .

Dean Salisbury will present data from an experiment investigating gamma power in the EEG to words and to non-words in schizophrenia and well controls. Elliot Hong will discuss whether the gamma-to-beta shift in response to the first stimulus (S1) in the P50 paired click paradigm may contain critical electrophysiological signals which modulate the S2 suppres-

sion. Silvana Galderisi will illustrate the results of an auditory P300 experiment in which amplitude, topographic descriptors, current source density, coherence and induced gamma band have been investigated in a group of patients with schizophrenia. Thomas Koenig will cover synchronization in schizophrenia using time- and frequency-domain approaches.

Induced 40-Hz Gamma Activity, Event-Related Coherence and P300 in Schizophrenia

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Introduction: Recent pathophysiological models of schizophrenia involve disturbances of the functional connectivity within distributed neural networks. P300 abnormalities in schizophrenia might reflect a failure to integrate different components of a complex process (i.e., perceptual categorization and working memory). In the present study, P300 abnormalities and disturbances of functional connectivity, as reflected by induced 40-Hz gamma activity and event-related coherence, were investigated in patients with schizophrenia.

Methods: In clinically stable patients with deficit (DS) or nondeficit schizophrenia (NDS) and matched healthy controls (HCS), event-related potentials (ERPs) were recorded during a three-tone oddball task. Amplitude, topography and cortical sources, as assessed by LORETA, were measured for each ERP component. Fronto-temporal event-related coherence (ERCoh) was assessed and induced 40-Hz gamma power was calculated for 6 partially overlapping segments of 300 msec, from -300 to 750 msec of the ERP epoch.

Results: With respect to HCS, NDS showed reduced P300 amplitude over the left posterior regions, a rightward shift of the positive centroid and reduced current density in left associative cortical areas, reduced gamma power (in segments 4 and 6), as well as decreased alpha2 and beta3 ERCoh. The rightward shift of the positive centroid and the early gamma power (in segment 2) were positively associated with psychotic symptoms.

Discussion: Our findings suggest disturbed cortical integrative functions, involving the left hemisphere, for P300-related processes in nondeficit schizophrenia. In the time window preceding the P300, hyperactive sensory integration is associated with psychotic symptoms.

Gamma / Beta Oscillation and Sensory Gating Deficit in Schizophrenia

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Introduction: Sensory gating can be measured by the suppression of auditory evoked potentials in a paired-click paradigm. The normal gating of the P50 response to the second stimulus (S2) is impaired in many schizophrenic patients. Various in vitro and in vivo evoked potential paradigms have shown that stimulus evokes early gamma frequency oscillation, which is followed by beta frequency oscillation. The gamma-to-beta shift in response to the first stimulus (S1) in the paired-click paradigm may contain critical electrophysiological signals that modulate the S2 suppression.

Methods: Evoked potential at the gamma (30 - 50 Hz) and beta (14 - 26 Hz) frequencies after S1 stimulus was evaluated. A multiple regression was used to determine whether gamma and/or beta oscillations after S1 contribute to the S2 amplitude.

Results: An analog of gamma-to-beta oscillation can be observed in human scalp evoked potentials in response to single click auditory stimulus in schizophrenic patients and in normal controls. Post-S1 beta frequency response was inversely correlated to the S2 P50 response in patients with schizophrenia, but not in normal controls.

Discussion: The findings are consistent with the a priori hypothesis of the study: post-S1 beta oscillation negatively contributes to S2 amplitude in schizophrenia. In other words, less P50 gating may be associated with less post-S1 beta amplitude or vice versa. Because the gamma and beta components appeared coupled, it remains to be determined whether a coupling mechanism of gamma/beta oscillation or individual frequencies is related to the S2 amplitude in patients with schizophrenia.

Exogenous and Endogenous Gamma Activity in Chronic and First Episode Schizophrenia

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Introduction: Gamma EEG activity (40 Hz) is likely related to the synchronous coordination of multiple distributed neural circuits. Endogenous gamma activity may reflect synchrony of distributed processing cortical modules involved in cognitive processing. To assess the integrity of semantic memory distributed stores in chronic schizophrenia, endogenous gamma was examined to words and non-words. Exogenous gamma activity is driven by an external 40 Hz stimulus. Driven gamma, reduced in chronic schizophrenia, may probe local circuit integrity. Endogenous gamma was examined in first hospitalized schizophrenia to assess local circuit integrity.

Methods: Endogenous gamma activity was examined in 5 chronic schizophrenia patients and 6 controls on a lexical decision task wherein cue words were followed by related or unrelated words, or by pronounceable non-words. Gamma activity was measured by FFT of the averaged responses to word targets and non-word targets. Exogenous gamma was examined in response to 40 Hz click trains in 10 first hospitalized schizophrenia patients and 10 controls, quantified by FFT.

Results: Chronic patients showed significantly less endogenous gamma to real words than to non-words, in contrast with the normal pattern of increased gamma to real words. First episode schizophrenia patients showed significantly reduced endogenous gamma.

Discussion: Chronic schizophrenia is characterized by abnormal activation of distributed semantic memory stores, which may relate to some aspects of thought disorder. First hospitalized patients, though generally less impaired than chronic patients, show severely abnormal exogenous gamma activity. Thus, abnormalities of local circuit integrity and efficiency may play a central role in initial disease manifestation.

Synchronized Brain Activity During Schizophrenia

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Introduction: Many parts of human cognition are covered, i.e., they are not driven by direct external input and do not produce immediate overt responses. The covert cognitive state is, however, relevant for the appropriate evaluation of the environment and the selection of behavioral responses. Abnormal internal states may therefore be prior to abnormal perceptions and behavior observed in schizophrenics.

Methods: Spontaneous brain activity can be measured and quantified by EEG. Physically, changes of EEG topography indicate changes of active brain regions and therefore, assumingly, a change of momentary cognitive state. When studying changes of EEG topography, one finds that these changes are discontinuous and separated by periods of quasi-stable topography of about 100 msec durations. These periods (microstates) assumingly represent basic steps of information processing and correspond to transient, highly synchronized global brain events.

Results: In schizophrenic patients, the duration of EEG microstates is reduced; this predominantly affects microstates with certain topographies. When using measures of synchronization between different brain regions, schizophrenics show less synchronized activity. This reduction is most prominent in the theta band that has been associated with working memory functions in awake subjects.

Discussion: We conclude that we observe a reduced and abnormal synchronization between brain regions in patients with schizophrenia.

Symposium: Combining Electrophysiology and Functional Neuroimaging

Summary Abstract

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In the last years increasing effort has been spent in combining fMRI and EEG. This is mainly due to the fact that a combination offers both high spatial and high temporal resolution. Several groups have focussed their activities in this new area in the investigation of target detection: the event related P300 potential has been widely used in neurophysiological research. One reason for its broad application in neurophysiological research is the fact that in mental diseases like schizophrenia attenuations of the P300 amplitude and latency have been described. For a comprehensive understanding of the brain activity underlying the P300 paradigm / target detection a combination of EEG and fMRI is most appropriate to get a precise localization and a high time resolution of the underlying brain activity. In this symposium principal aspects of the combination of fMRI and EEG will be addressed as well as results of an investigation of patients with schizophrenia in comparison to healthy controls using simulataneous EEG and fMRI.

Simultaneous Functional Magnetic Resonance Imaging (fMRI) and Event-Related Potential (ERP) Analysis of Neurobiological Correlates of Disturbed Cognitive Functions in Patients with Schizophrenia

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Information processing deficits such as memory abnormalities and attentional disturbances are central features of schizophrenia. Event-related potentials (ERPs) have been used to investigate the biological nature of these deficits. The event-related P300, for example, is a cognitive ERP that is thought to reflect the mental processes underlying the allocation of attentional resources to an incoming stimulus, the evaluation of and the subsequent memory mechanisms engaged for that stimulus. It has several components that seem to be independently generated in different brain structures. Imaging studies, for example, revealed that P300 experiments elicit activations in a widespread cortical network, including the supramarginal gyrus, supplementary motor cortex, insula, middle frontal gyrus, and superior temporal gyrus. Reduction of the auditory P300 amplitude is one of the most robust biological findings in schizophrenia. Besides, it is assumed that P300 associated cognitive and thought disorders in schizophrenia patients depend on dysfunctions in dorsolateral prefrontal cortex, and the anterior cingulate cortex.

The aim of the study was to examine differences in locations and extent (fMRI) as well as time courses (EEG) of the various neural generators of the event-related P300 potential between schizophrenic patients and controls, while holding vigilance and habituation constant due to simultaneous acquisition. The study comprised 10 patients with schizophrenia (according to DSM IV; PANSS) and 10 controls with no history of neurological and psychiatric injury. The P300 was recorded using auditory stimuli by employing the so-called oddball paradigm, in which subjects were required to respond by button press to infrequent tones presented in a series of frequent tones of a different pitch. The discrimination between the two stimulus categories produced the positive-going P300 component. FMRI-data (1.5T Sonata scanner (Siemens); gradient echo EPI sequence; 12 slices; matrix: 128x128; slice thickness: 8mm; interslice-gap: 0.4 mm; interleaved acquisition) were acquired in temporal synchrony to the task. BrainVoyager was used to compare differences in task specific BOLD responses as well as the differences between schizophrenic patients and healthy controls. EEG signals were recorded simultaneously (64 channels; Cz reference; 1000 Hz sampling) and grand mean waveform was obtained and sampled according to the task (rare vs. frequent tone). Our preliminary data indicate that we could replicate findings of previous P300 studies for healthy participants revealing BOLD activations mainly in frontal, especially SMA/cingulate cortex, insula and middle prefrontal gyrus, temporal and parietal brain structures just as a positive deflection mainly in midline fronto-parietal regions after about 400 ms following rare stimuli in the ERP recordings. In patients with schizophrenia, we found reduced P300 amplitudes and reduced BOLD activity in several regions including the cingulate and parietal cortex.

Mental Chronometry of Working Memory Retrieval: a Combined fMRI and ERP Approach

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We integrated event-related potential (ERP) and functional magnetic resonance (fMRI) data in the framework of fMRI-constrained source analysis to decompose the processing stages of brain activation during working memory (WM) retrieval ("mental chronometry"). The ERP and event-related fMRI responses of 18 participants were computed to the test object in the retrieval phase of a visual WM task. We used the fMRI activity to define a model for discrete multiple regional sources of the ERP activity.

The test objects elicited a sequence of ERP deflections labelled N174 (at PO8), P308 (at FCz), P366 and P585 (at Pz). Guided by the principal clusters of fMRI activity our source model resulted in 14 regional sources. Analysis of the source time courses revealed an early transient activation of inferotemporal cortex, which was accompanied by the onset of a sustained activation of posterior parietal cortex. We furthermore observed late transient responses in ventrolateral prefrontal cortex and late sustained activity in medial frontal and premotor areas. We propose that these neural signatures reflect the cognitive stages of task processing, perceptual evaluation (inferotemporal cortex), storage buffer operations (posterior parietal cortex), active retrieval (ventrolateral prefrontal cortex) and response organization (medial frontal and premotor cortex).

Symposium: New Physiological Approaches to Study and Treatment of Mood and Sleep Disorders

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In healthy subjects sleepiness impairs the ability to perform attention-based activities and reduces reaction time, vigilance, alertness, concentration, etc. It also accompanies the majority of mood disorders. Recently, the development of fundamental and applied research in the fields of physiological biofeedback and physiological regulation led to discovery of new approaches to detecting sleepiness in healthy individuals and to treatment of mood disorders. The application of these approaches became of both practical and theoretical importance in the studies and treatment of mood and sleep disorders. The symposium is aimed on highlighting the perspectives of application of several new methods of objective measurements of sleepiness and antidepressant treatment, such as sleepiness detection and testing of driving performance with biofeedback computer game-like systems, waking EEG recording, treatment of depression with combination of sleep deprivation and melatonin, etc.

Psychic Correlates of the Ability to Acquire Control Over Emotional Stress Response With the Help of Biofeedback Relaxation Training

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The ability to control emotional response to stress might be acquired by means of biofeedback training. The training becomes fun when procedure of treatment mimics a computer game. Our Institute invented several biofeedback systems for enjoyable relaxation training that combine the biofeedback device, computer game, alertness test and non-invasive detector of imbalance in autonomic tone. To validate one of these systems (RALLY), we tested psychological states of 25 subjects aged between 18 and 26 years before and after biofeedback relaxation training. They completed 10 30-min relaxation sessions divided by 1-3-day intersession intervals. To learn the art of relaxation, the subject must succeed in the on-screen competition between two drivers. The main (relaxation) task is to increase speed of the on-screen car by slowing

down heart rate. The additional (performance) task is to react as quickly as possible on the randomly appeared obstacles (rocks on the on-screen road). The results of psychological testing indicate the significant reduction of the levels of neuropsychic tension ($p<0.001$), frustration ($p<0.05$), depression ($p<0.01$), and anxiety ($p<0.001$). The success in relaxation training negatively correlated with pre-training levels of anxiety ($r=-0.42$, $p<0.05$), depression ($r=-0.56$, $p<0.01$), novelty seeking (-0.53, $p<0.01$), hysteria (-0.42, $p<0.05$), and psychopathia (-0.52, $p<0.05$). The improvement in performance negatively correlated with pre-training levels of anxiety ($r=-0.43$, $p<0.05$), extraversion ($r=-0.44$, $p<0.05$) and psychopathia ($r=-0.43$, $p<0.05$), and positively correlated with novelty seeking ($r=+0.43$, $p<0.01$). Overall, the training with RALLY provides considerable benefits for psychic and physiological functioning

Length of Sleep in Winter Depression: Comparison of Electroencephalographically Measured and Retrospectively Reported Seasonal Variations

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Symptom as hypersomnia is common for seasonal depression of the winter type. It is not known, however, whether this symptom relates to seasonal variations in objective sleep measures. This report is aimed at comparison of objectively and retrospectively reported sleep lengths in winter depression. In the survey of 2200 adults from Turkmenia, Siberia and Alaska, 80 female respondents retrospectively reported winter type of seasonal variations of mood, while 651 female respondents denied seasonal mood variations. Additionally, 56 female winter depressives and 46 female healthy non-seasonals were selected for clinical study, and some of them participated in night sleep recording in winter ($n=21$ and 10, respectively) and in summer ($n=13$ and 7, respectively). Electroencephalographically documented sleep length (in hours) in winter depression was found to be longer than in healthy non-seasonals both in winter (7.3 vs. 6.4, $p<0.05$) and in summer (7.1 vs. 5.9, $p<0.05$). However, no significant difference between sleep length in winter and summer was found (0.2 vs. 0.7). By contrast, retrospective reports indicate seasonal variations in sleep length in winter depressives (clinical study: 10.1 vs. 6.9, $p<0.0001$, and survey: 8.2 vs. 6.4, $p<0.001$), and bigger amplitudes of these variations in winter depressives than in non-seasonals (clinical study: 3.1 vs. 0.8, $p<0.001$, and survey: 1.9 vs. 1.0, $p<0.001$). In sum, the comparison of the objective measurements of the amplitudes of seasonal deviations in sleep length with those retrospectively reported suggests that winter depressives tend to overestimate the danger of annual changes of their sleep for normal physiological functioning.

Symposium: Epilepsy and the Interictal Dysphoric Dysorder (IDD) - a Key to Understanding Mood Control the Hippocampus and Its Relationship to Cognition and Mood in Epilepsy

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It is well known that not only seizures but also memory deficits can reduce the quality of life of patients with temporal lobe epilepsy (TLE). Meanwhile, neurologists are also beginning to realize that depressive mood disorders may be an equally - or even more - important determinant for the quality of life in TLE. Several studies have shown that both structural lesions like hippocampal sclerosis and epileptic activity may be predisposing factors for the development of depressive disorders. However, it is still an open question how exactly temporal lobe seizures, their lateralization, neuropsychological deficits and depression are linked.

Using invasive recordings of limbic event-related potentials we have identified specific cognitive (sub)processes that the human hippocampal formation subserves: It contributes to the detection of (verbal) novelty, the detection of meaning in visual stimuli, and the detection of known among unknown faces. Moreover, the human hippocampus participates in sensory gating and is sensitive to syntactic errors in spoken language. In sum, the human hippocampus may participate in “relevance detection,” thus mediating encoding for declarative memory. While verbal novelty detection may be lateralized to the dominant hemisphere, non-verbal “relevance detection” may not.

Future studies are necessary to address the question whether impairments of specific neuropsychological (sub)processes may contribute to the development of mood disorders in TLE rather than the epileptogenic process as such.

Symposium: Cerebral Correlates of Neuropsychological Deficits in Mild Cognitive Impairment and Early AD

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Purpose: In patients with Alzheimer's disease (AD), volumetric studies revealed a specific atrophy of brain areas such as the temporal lobe, which could not be attributed to whole brain atrophy and occurred in the very early stages of the disease. According to the hypothesis of a stepwise neural degeneration in AD, functional diversity of cerebral dysfunction prior to neural cell loss was hypothesised. In order to investigate a broad range of cognitive dysfunction and its neural substrates, we applied the CERAD (Consortium to Establish a Registry for Alzheimer's Disease) battery and a Positron Emission Tomography (PET) of resting glucose metabolism.

Methods: Up to now, 47 subjects with mild cognitive impairment (MCI) and AD and 11 controls were analysed. Subjects underwent extensive medical and neurospychological (CERAD) assessment, and were investigated by FDG PET. Correlations between cognitive function according to the CERAD and cerebral glucose metabolism were generated.

Results: First results demonstrate that first, immediate recall was significantly correlated with temporo-parietal glucose metabolism, whereas delayed recall also showed frontal activation ($p<0.05$). Second, semantic fluency was significantly associated with left side temporo-parietal and bilateral frontal glucose metabolism ($p<0.05$). Third, constructional praxis showed a significant correlation with bilateral parietal and frontal glucose metabolism ($p<0.05$).

Conclusions: This is the first study investigating an association between cerebral glucose metabolism and cognitive function as measured by the CERAD in patients with AD. The finding of a distinct pattern of neural activity during cognition processes in AD may both facilitate early diagnosis of the disease and differentiation from other forms of cognitive impairment.

Structural MRI-findings in Mild Cognitive Impairment and Alzheimer´s Disease

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Introduction: This study investigates morphological brain changes in subjects with mild cognitive impairment (MCI) and Alzheimer´s disease (AD) using both, manual tracing and voxel-based morphometry (VBM).

Methods: Twenty-one subjects with MCI, 21 healthy controls and 10 patients with AD were examined with magnetic resonance imaging (MRI). For the analysis of the MRI data two different methods -region of interest (ROI)- guided manual tracing of predefined neuroanatomical substructures as well as rater-independent VBM - were applied.

Results: Manual tracing demonstrated a significantly reduced volume of the right parahippocampal gyrus in MCI subjects compared with controls. VBM did not reveal any significant structural differences between those two groups. In AD, both methods revealed significant atrophy of medial temporal lobe substructures (hippocampus, parahippocampal gyrus), the temporal lobe in general and parts of the frontal lobe.

Discussion: Structural brain alterations are already verifiable in the assumed preclinical stage of AD. In the detection of these discrete atrophic changes, ROI-based measurement seems to be more sensitive than VBM.

Executive Dysfunction in Mild Cognitive Impairment and Early Alzheimer´s Disease

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Introduction: Executive dysfunction in Alzheimer's disease (AD) is associated with delusions, agitation and disinhibition, rapid progression and care dependency. We correlated resting cerebral glucose metabolism in Alzheimer's disease (AD) and mild cognitive impairment (MCI) with scores on the Trail Making Test (TMT) as a measure of executive function.

Methods: Ten patients with AD, 10 patients with mild cognitive impairment (MCI) and 14 controls were included. We compared resting cerebral glucose metabolism in patients with that in controls and correlated TMT scores with cerebral glucose metabolism. Neuropsychological correlates of the TMT were also investigated.

Results: Patients had reduced frontotemporoparietal and posterior cingulate metabolism compared to controls. TMT-A correlated with left middle frontal, TMT-B and TMT-Q with right middle frontal and TMT-B with right precentral glucose metabolism. TMT-A and TMT-B scores correlated ($p<0.05$) with word fluency and recall subtests of the CERAD (Consortium for the Establishment of a Registry for Alzheimer's Disease) neuropsychological test battery, TMT-Q with delayed constructional praxis scores ($p<0.05$).

Discussions: PET and neuropsychological correlates indicate that executive function measured by TMT is frontal lobe mediated and demands working memory. The neuropsychological correlates of the tasks confirm the complexity of the task.

Deficits of Autobiographical Memory in Early Alzheimer´s Disease: Evidence from Clinical and Neuroimaging Studies

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Deficits of autobiographical memory (AM) appear early in the course of dementia, particularly in Alzheimer's disease (AD). However, methodological difficulties have so far prevented a systematic investigation of AM. We therefore developed the Bielefeld Autobiographical Memory Inventory (BAGI) as a standardized instrument to reliably assess AM in five periods over the life span. Moreover semantic, i.e., general facts and episodic, i.e., vivid, emotionally colorized components of AM are differentiated. Our study also aims to investigate clinical cerebral changes in patients with mild AD and mild cognitive impairment and to address potential compensatory effects.

Using the Bielefeld Autobiographical Memory Inventory (BAGI), we investigated autobiographical memory decline in patients with mild cognitive impairment and mild Alzheimer´s disease (n=49). Results were correlated with data from neuroimaging studies.

While semantic autobiographical memory performance showed only minor, nonsignificant differences between groups, the episodic component (free recall) is already significantly impaired in early Alzheimer's disease. In contrast, only minor nonsignificant changes are found in mild cognitive impairment. Analyses of the number of details reported revealed consistent findings with even more pronounced deficits in the Alzheimer's disease group.

The results demonstrate that autobiographical memory is already impaired in the early stages of Alzheimer´s disease whereas in mild cognitive impairment only non-significant changes arise. Episodic autobiographical memory deficits in Alzheimer´s disease may correspond to a diminished activation of medial temporal substructures, while patients with mild cognitive impairment are at this stage sufficient to compensate for slight atrophic changes. This hypothesis will be discussed on the basis of current PET-studies.

Symposium: Neuroimaging in OCD

Summary Abstract

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Functional abnormalities of the frontal-striatal and limbic circuits have been implicated in the pathogenesis and maintenance of obsessive compulsive disorder (OCD). Resting state in OCD is associated with increased activity of the ventral parts of the frontal-striatal circuitry. After symptom provocation, activation of limbic structures (mainly the amygdala) is increased, possibly due to decreased top-down control by the dorsal frontal-striatal circuit. Decreased responsiveness of the dorsal frontal-striatal regions seems to explain the decreased executive performance in OCD patients as well. Additional recruitment of posterior brain regions, brainstem and anterior cingulate cortex seems to reflect compensatory and stress-related processes and increased error detection. Dysfunctional neurotransmitter interactions, i.e., serotonergic-dopaminergic and glutamatergic-serotonergic, also seem to be involved in the pathogenesis of the disorder. In addition, studies in obsessive-compulsive children have shown early changes (both structural and neurochemical), suggesting developmental abnormalities.

MRI Findings in Pediatric Obsessive-Compulsive Disorder (OCD) Patients

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Introduction: Structural neuroimaging studies, using Region of Interest (ROI) methods, have consistently identified alterations in fronto-striatal-thalamic circuitry in adult and pediatric OCD patients. Voxel-based morphometry (VBM) is a neuroimaging approach that assesses differences in gray matter concentration at a microstructural level across the whole brain. Although VBM has been used to study adult OCD patients, to our knowledge, there are no VBM studies of pediatric OCD patients.

Methods: Subjects were 18 first-episode, treatment-naïve OCD patients (mean age 13; 6 males) and 18 healthy controls (mean age 13; 6 males). T1-weighted SPGR images (124 1.5mm thick coronal slices) were acquired on a 1.5T G.E.system. VBM analysis was conducted using SPM 2b. The images were spatially normalized and then segmented into gray, white and CSF compartments using probabilistic classification. Gray matter images were smoothed with a Gaussian smoothing kernel (12 fwhm). A preset threshold (p=0.005, uncorrected) was employed to identify suprathreshold voxels.

Results: VBM analysis revealed structural alterations in superior frontal, middle frontal, orbitofrontal, inferior frontal (BAs 6, 9, 11, 44) and caudate gray matter regions in patients compared to healthy controls. VBM analysis also revealed significant age-related gray matter changes in patients that were qualitatively different from healthy controls.

Discussion: These specific patterns of structural alterations in pediatric OCD patients both support and complement prior neuroimaging studies using an ROI approach. Age-related gray matter differences between patients and controls may reflect abnormal brain maturational trajectories in pediatric OCD patients. These preliminary findings, as well as a review of structural neuroimaging findings in pediatric OCD, will be discussed.

Functional and Structural Imaging in Obsessive-Compulsive Disorder

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Obsessive-compulsive disorder (OCD) is a neuropsychiatric disorder characterized by intrusive thoughts (obsessions) and repetitive, ritualised behavior (compulsions). Common themes for these obsessions are contamination, aggression, and sexuality; compulsive behaviors are typically checking, washing/cleaning, symmetry behavior, and hoarding. Although OCD has been classified as an anxiety disorder, patients with OCD often have comorbid Tourette's syndrome, and may present with soft neurological signs; moreover, obsessive-compulsive symptoms have been observed as part of basal ganglia disorders as well as in patients with lesions of the prefrontal cortex. These clinical findings point to the involvement of prefrontal-striatal circuits in the etiology of OCD, which has been further underlined by neurosurgical results in intractable OCD, since all proposed methods directly or indirectly disconnect these loops. Since the 1980s, neuroimaging tools have been employed to investigate the pathogenesis and etiology of OCD; these include volumetric, resting state, and activation studies, whereas biochemical studies have been rare. In the present paper, we will discuss both volumetric and functional imaging studies in OCD. Most morphometric studies have used region of interest techniques, although a few voxel-based studies have recently been published. Functional studies have included resting-state as well as activation (task vs. baseline) designs. With regard to the latter, both symptom provocation and cognitive paradigms have been employed. It is concluded that whereas structural imaging studies have yielded mixed results, functional imaging studies have generally supported neurophysiological models of OCD positing abnormal prefrontal-striatal function, in particular increased activity of (para)limbic ventral regions as well as altered responsiveness of dorsal prefrontal areas.

At the Cross-Roads of Corticostriatal and Limbic Circuits

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Obsessive and compulsive disorders have long been associated with disturbances in prefrontal cortical, striatal and limbic structures. The results of neuroimaging studies have strengthened this association in recent years. Changes in activity patterns in particular structures, however, most probably indicate disturbances in the functioning of cortical subcortical-circuits in which the prefrontal cortex, basal ganglia and limbic structures form the nodal points. The prefrontal cortex consists of a number of cytoarchitectonically and functionally distinct cortical areas that project in a topographical way to the stria-

tum. This highly ordered corticostriatal system forms the basis for a number of parallel cortical-basal ganglia circuits that ultimately lead back to the prefrontal cortex. In this view, sensorimotor, cognitive and emotional-motivational behavioral processes are supported by parallel, functionally segregated circuits. An important question in the context of OCD concerns the interactions between emotional and cognitive processes. Both at the level of the prefrontal cortex and the striatum intersections exist with limbic circuits that originate in the medial temporal lobe, i.e., the amygdala and hippocampus. At these cross-roads integration of limbic, emotional information and prefrontal corticostriatal, cognitive processes takes place. In addition, the prefrontal cortex has direct projections to the medial temporal lobe as well to the monoaminergic, gain-setting systems in the brain stem. Finally, the above-mentioned parallel cortical-basal ganglia circuits appear to be interconnected via several specific pathways providing the possibility for the integration of emotional and cognitive processes.

Nuclear Medicine Methods in Obsessive Compulsive Disorder - Evidence of Monoaminergic Dysfunction

Pogarell O, **Ludwig-Maximilians-University, Munich, Germany**

The development of structural and functional neuroimaging techniques has substantially contributed to the current understanding of the pathophysiology of neuropsychiatric disorders.

Obsessive compulsive disorder (OCD) is a clinically defined condition, characterized by the occurrence of intrusive and inappropriate repetitive thoughts and/or behaviors. Neuropsychiatric research of the past two decades with advanced neuroimaging techniques, neurophysiological and pharmacological studies has provided growing evidence for a neurobiological basis of this disorder. The selective efficacy of serotonergic agents suggests that central serotonergic neurotransmission is involved in the pathophysiology of OCD. Accordingly, data on PET and SPECT studies with respective radioligands as well as neurophysiology techniques are indicative of a central monoaminergic dysfunction.

In conclusion, current neurobiological models of OCD point at both functional neuroanatomical and neurochemical (monoaminergic) alterations of central nervous system function.

Symposium: Electrophysiological Tools for Understanding the Brains Chemistry

Summary Abstract

Juckel G, Pogarell O, Norra C, Hegerl U

Monoaminergic systems play key roles in various psychiatric and partly neurological diseases. Progress in further understanding of their pathophysiology and psychopharmacological treatment is hampered by the lack of valid indicators of such neurotransmitter systems.

Concerning the serotonergic system, several basic and clinical studies suggest that the loudness dependence of auditory evoked potentials is such a valid indicator. In the proposed symposium, the relevant findings for this assumption will be presented (Juckel, Norra) and clinical applications to, e.g., prediction of pharmacotherapy will be discussed (Pogarell, Hegerl).

Preclinical Studies on the Relationship Between Loudness Dependence of Auditory Evoked Potentials and the Central Serotonergic Neurotransmission

Juckel G, Wutzler A, **Charité University of Medicine, Berlin, Germany**

A valid indicator of central serotonergic neurotransmission would be useful for various diagnostic and psychopharmacological purposes in psychiatry. However, known peripheral serotonergic measures only partially reflect serotonergic function in the brain. Previous findings suggest that the loudness dependence of auditory evoked potentials (LDAEP) is closely related to central serotonergic activity. A study in cats examines the effects of microinjection of a 5-HT1A agonist (8-OH-DPAT) and a 5-HT 1A antagonist (spiperone) into the dorsal raphe nucleus (DRN) on AEP recorded epidurally from the primary and secondary auditory cortex in behaving cats. We found a stronger LDAEP only from the primary auditory cortex

after 8-OH-DPAT, which inhibits the firing rate of serotonergic DRN neurons, and a weaker intensity dependence after spiperone, which increases serotonergic cell firing, as compared to baseline measurements. In a recent study in rats, we found a close negative correlation between extracellular serotonin levels in the auditory cortex, as measured by invivo microdialysis, and the LDAEP recorded epidurally from the same area of the auditory cortex. These results demonstrate that the LDAEP is inversely related to serotonergic neuronal activity and that it may be a promising tool for assessing central serotonergic function in humans (e.g., identifying patients with low serotonergic neurotransmission).

Electrophysiological Effects of Acute Tryptophan Depletion on Human Serotonergic Functions

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Introduction: The tryptophan depletion test (TDT) represents an established human challenge for temporary reduction of tryptophan levels and studies of central nervous serotonin functioning. Based on animal studies, the TDT suggests an inverse influence of the serotonergic neurotransmission as represented by auditory evoked potentials to stimulus intensity or startle but similar effects in humans remain unclear. On the other hand, neuro-psychiatric disorder with assumed serotonergic dysfunction, e.g., mood disorder, schizophrenia, personality disorder or substance abuse have shown to be correlated to these non-invasive electrophysiological measures.

Methods and Results: Applying a double-blind cross-over TDT-protocol in female volunteers, augmentation of stimulus intensity responses with significant individual change rates was partly more pronounced in the depletion condition, but there was only a slight increase of the overall resulting loudness dependence of auditory evoked potentials (LD) as opposed to the controls. When regarding auditory sensory gating and processing, TDT led to significant reduction of mean amplitudes and a tendency towards suppression of the prepulse inhibition in the depletion condition.

Discussion: Despite a strong depletion situation the results of a homogenous study population provide some minor arguments for the hypothesis of serotonergic modulation on auditory evoked measures, i.e., LD or startle. The small size of the study group as well as interactions with other transmitter systems may have to be taken into account. Thus, animal studies will have to be discussed in respect to the complex neuroanatomy and pharmacology of 5-HT receptors and in contrast to a more general manipulation of the human serotonergic system by TDT.

Serotonin and Dopamine Transporter Availabilities Correlate with the Loudness Dependence of Auditory Evoked Potentials

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Michael Zaudig M, **Psychosomatic Hospital, Windach, Germany**

Dysfunction of brain serotonergic activity is involved in the pathophysiology of various psychiatric disorders. The central serotonergic system can be assessed in vivo using a neurophysiological paradigm, the loudness dependence of the N1/P2 component of auditory evoked potentials (LD), and with single photon emission computed tomography (SPECT) and [123I]ß-CIT, a ligand for serotonin (SERT) and dopamine transporters (DAT). Aim of the study was to correlate different serotonergic measures in psychiatric patients. Ten subjects received both neurophysiological and imaging investigations. Evoked potentials were recorded following the application of acoustic stimuli with increasing intensities. The LD of the relevant subcomponents was investigated using dipole source analysis. SPECT was performed 18 to 24 hours after injection of a mean 140 MBq [123I]ß-CIT. As a measure of brain SERT and DAT availabilities a ratio of specific to nonspecific [123I]ß-CIT binding for the midbrain and pons (SERT) and striatum (DAT) was used. The LD of the right tangential dipole correlated significantly with both SERT and DAT availability (Pearson´s correlations: rho = 0.69, $p < 0.05$, and rho = 0.80, $p < 0.01$, respectively).

Associations between LD and both SERT and DAT availabilities validate the use of neurophysiological approaches as noninvasive indirect measures of neurochemical brain function and point at a hypothesized interconnection of different monoaminergic systems.

Symposium: New Evidence for Glutamatergic Dysfunctions in Neuropsychiatric Disorders

Impact of In Vivo Measured Cerebral Glutamate on Human Behavior: the Sensation Seeking Personality Trait

Götz T, Bajbouj M, Gallinat J, **Charité University Medicine, Campus Mitte and Moabit, Berlin, Germany**
Seifert F, Schubert F, **Physikalisch-Technische Bundesanstalt, Berlin, Germany**

Introduction: Human personality traits are based on individual differences in brain functions. Most major current models of personality include the dimension of introversion/extraversion, or novelty seeking at a fundamental level. Animal investigations indicate that glutamatergic neurotransmission plays a role in novelty induced exploratory behavior. In humans, brain imaging studies reported evidence for the involvement of the anterior cingulate cortex (ACC) in personality traits like novelty seeking. It is hypothesized that the glutamate concentration in the ACC of healthy subjects is related to this behavioral trait.

Subjects and Methods: The Sensation Seeking Scale (SSS), reflecting a tendency toward exploratory excitability in response to novelty has been applied to 39 healthy subjects. PRESS-based measurement of glutamate was performed with single voxel technique (ACC and left hippocampus) in a 3 tesla MR scanner. Absolute glutamate concentrations were determined and corrected by individual cerebrospinal fluid fractions.

Results: Significant negative correlations (controlled for age) between glutamate levels in the ACC and the Sensation Seeking Sum score (SSS: r=-0.405, p=0.012), as well as two subscales were observed. A significant negative correlation was observed also for the hippocampal glutamate concentration and the SSS (r=-0.330, p=0.046).

Discussion: For the first time, significant correlations between absolute cerebral glutamate concentrations and behavioral traits in humans have been reported. These observations are in line with the function of the ACC in mediation of motivated behavior, executive processes, and social interaction. Studies on behavioral effects of cerebral glutamate are important in psychiatric research and may help to develop new agents for psychiatric pharmacotherapy.

Impact of In Vivo Measured Hippocampal Glutamate Concentration on Cerebral Theta Oscillations

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Seifert F, Schubert F, **Physikalisch-Technische Bundesanstalt, Berlin, Germany**

Introduction: Theta rhythm appears to be an invaluable key to the understanding of associative processing capacities of the human central nervous system. Theta activity has been related to mental tasks in humans and animal investigations deal with theta oscillations occurring in the hippocampus during mnemonic tasks. Evidence is growing that theta rhythm has an important role in facilitating temporal cooperation related to information flow through the hippocampus. Since the major hippocampal neurotransmitter in the hippocampus is glutamate, its role in hippocampal-cortical interaction was investigated using theta oscillations as a surrogate parameter.

Methods: Theta power (FFT) was computed in the time range of 0-1500 ms after presenting target tones within an auditory oddball paradigm. Frequency band partition was: delta=0.5-4.0Hz, theta=4.5-8.0Hz, alpha=8.5-12.5Hz, beta=18.5-30.0Hz. PRESS-based measurement of glutamate was performed with single-voxel technique (anterior cingulate (ACC), left hippocampus) in a 3 tesla MR scanner. Absolute glutamate concentrations were determined and corrected by individual cerebrospinal fluid fractions.

Results: The most pronounced theta activity after target tones occurred at midline electrodes. Significant positive correlations between hippocampal glutamate levels and theta power at frontal-central electrodes were observed. No significant correlations between ACC or hippocampal glutamate concentrations and other frequency bands were observed.

Discussion: For the first time, a relationship between hippocampal glutamate concentration and functional cortical activity has been observed in humans. The result is in line with the pivotal role of the hippocampus in tasks involving working memory and target detection as well as the pivotal role of glutamate as neurotransmitter in the limbic system.

Genetic Variations of the NR3 Subunit of the NMDA Receptor Modulate Prefrontal Cerebral Activity in Humans

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Sander T, **Max-Delbrück-Centrum, Berlin, Germany**

Introduction: Glutamatergic activity and N-methyl-D-aspartate (NMDA) receptor variations has been implicated in the pathophysiology of schizophrenia as well as dysfunctional prefrontal cortex activity. Recently, a novel NMDA receptor subunit, NR3A, has been discovered in the brain and shown to decrease NMDA receptor activity by modulating the calcium permeability. Moreover, a single nucleotide polymorphism (SNP) of the NR3A subunit has been described. In this study, the effect of the genetic variation (SNP) of the NR3A subunit was investigated for the first time in humans using the auditory evoked P300 component, which is known to have prefrontal generators.

Methods: The P300 component was measured in 281 healthy subjects and the NR3A genotype was determined. The sample was divided into three groups according to the genotypes A/A (n=41), G/A (n=118), G/G (n=122) and between group comparisons were calculated (1) P300 amplitudes and (2) current source density analysis (LORETA)).

Results: ANOVA showed a significant effect of the genotype on the P300 amplitudes at electrodes Fz and Cz. Contrast analysis showed higher amplitudes in A/A subjects compared to G-carriers at Fz electrode and higher amplitudes of A/A vs. G/G subjects at the Cz electrode. Performance of source analysis (t-map comparison for P300 time frame) revealed that this difference was mainly due to a higher activation in the lateral prefrontal cortex in A/A compared to G/G individuals.

Discussion: The data indicate that genetic variations of the NR3A subunit of the NMDA receptor are relevant for prefrontal stimulus processing in humans. This result is compatible with the role of glutamate in prefrontal activation and may facilitate the research in glutamate models of schizophrenia.

Metabolic Changes Within the Left Dorsolateral Prefrontal Cortex After Repetitive Transcranial Magnetic Stimulation in Patients with Major Depression

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Introduction: The dorsolateral prefrontal cortex (DLPFC) is involved in the pathophysiology of major depression. Repetitive transcranial magnetic stimulation of the left DLPFC is one stimulation technique that has shown some antidepressant properties in a number of studies. In this study, we monitored the effects of rTMS on nuclear resonance magnetic detectable metabolites like n-acetyl-aspartate (NAA), choline (CHO), creatine (CRE) and glutamate (GLU).

Methods: Eighteen patients with a diagnosis of major depressive episode (DSM-IV) were treated with ten sessions of repetitive transcranial magnetic stimulation of the left DLPFC. Magnetic resonance spectroscopy was carried out at baseline and after rTMS-treatment with a 3-Tesla-scanner (MEDSPEC 30/100, Bruker Medical). Compounds were fitted with prior knowledge for frequency, linewidth and phase.

Results: Seven out of 18 patients were treatment responders, defined as a 50% reduction of the Hamilton Depression Rating scale. No changes in the cingulum signals were detected after rTMS. As compared to the non-responder, responders had a lower glutamate concentration in the left dorsolateral, prefrontal cortex. A significant correlation between HAMD-changes and an increase in glutamate in the left DLPFC was observed. Moreover, there was a trend of glutamate elevation with increasing stimulation intensity.

Discussion: Our results indicate that major depressive disorder may be accompanied by state-dependent metabolic alterations, especially in glutamate metabolism, which can be reversed dose-dependently by rTMS.

Symposium: Characterizing Cortical Function and Dysfunction in Epilepsy

Summary Abstract

Knake S, Hamer HM, **University of Marburg, Gemany**
Krakow K, **University of Frankfurt, Germany**
Werhahn K, **University of Mainz, Germany**

Recent functional neuroimaging methods have been used to delineate cortical function and dysfunction in patients with epilepsies: The first two talks will concentrate on the use of modern non-invasive imaging techniques to characterize the irritative zone generating interictal epileptiform discharges and to delineate structural and functional cortical pathologies. Data show that enhanced MRI technology has the capability to improve significantly the epilepsy syndrome diagnosis on one hand and it will focus on technology, which has already reached a stage where it can be used in clinical practice. The third talk will investigate the pathophysiology of focal motor seizures by invasive and non-invasive multimodal recordings and correlates stimulation studies with epileptic signs and symtpoms. A fourth talk will comprise TMS in epileptic patients and will update on the potential of this method in the diagnostics and therapy of epilepsy.

New Imaging Techniques in Epilepsy

Knake S, **Philipps-University, Marburg, Germany**

MRI has become an extremely valuable tool for presurgical evaluation of epilepsy patients by enabling detection of anatomical lesions that are candidates for the epileptogenic zone. The importance of detecting a concordant lesion on MRI is reinforced by the impact this has on predicting surgical outcomes. We used multimodal imaging, including different new structural and functional imaging techniques to improve the detection of subtle structural lesions and to help to define the seizure onset/irritative zone in 70 patients (pts) with medically intractable focal epilepsies. All have had phase 1 video-EEG monitoring. Patients were evaluated within their presurgical diagnostic workup using a standardized protocol including high-resolution 8-channel array surface coil MRI (3T) (SC-MRI), whole head 306-channel MEG/64-channel EEG, high resolution Diffusion Tensor Imaging (DTI) at 3T. Later, cortical thickness and subcortical volumety and segmentation were performed using semi-automated image analysis tools:

All imaging techniques provided valuable information towards presurgical evaluation:

SC-MRI improved the detection of focal lesions and improved the specificity of the diagnosis in 18/50 pts (36%). In some cases SC-MRI improved the confidence in the MEG/EEG evaluation. Simultaneous MEG/EEG-evaluation detected MEG-only spikes in 16% (8/50 pts). dSPM improved the prediction of the size and location of the irritative zone by showing propagation with high spatiotemporal resolution. TI detected more diffuse microstructural changes in the wm than suspected on either visual interpretation or by MEG/EEG. Automated analysis for cortical thickness analysis detected more widespread cortical thickness changes than suspected on either visual interpretation or on MEG/EEG.

Combined multimodal imaging provides more information than any modality alone. This may improve selection of surgical candidates and improve predictions of postsurgical outcome. Further correlation with post-surgical outcomes is required.

Characterizing the Cortex in Epilepsy Using TMS

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Transcranial magnetic stimulation (TMS) was first introduced by Baker et al. in 1985 to study the corticospinal motor conduction. However, from early on it became apparent that TMS can also be used as a non-invasive tool to evaluate distinct excitatory and inhibitory functions of the human cerebral sensorimotor cortex. Epileptic conditions are characterized by heterogeneous and dynamic pathophysiological processes leading to an altered balance between excitatory and inhibitory influences at the cortical level. Therefore, TMS has been regarded as a promising tool to assess noninvasively pathophysiological mechanisms and effects of antiepileptic drugs in patients with epilepsy. Moreover, it is well known that the excitability of cortical networks can be modulated by trains of regularly repeated magnetic stimuli. Hence, repetitive TMS (rTMS) has been tried as a therapeutic intervention in patients with epilepsy. The studies using TMS in epilepsy showed that changes of motorcortical excitability can be detected both in generalized and focal epilepsies. In the latter group there can

even be remote changes of motorcortical excitability, which seem to be more prominent with extratemporal or neocortical temporal lobe than with mesial temporal lobe epilepsies. In focal epilepsies, these changes seem to correlate with the occurrence of interictal epileptiform EEG abnormalities, and preliminary data suggest that excitability changes might be detectable minutes prior to seizure onset using TMS. Whether changes of cortical excitability as measured by TMS can be used as a prognostic tool is unclear. Attempts to use rTMS as a treatment have had little success so far, although this might be too early to say. It seems, however, to be accepted, that TMS cannot yet reliably be used for seizure induction in patients with epilepsy; safety limits in using rTMS must strictly be adhered to in order not to evoke epileptic seizures in healthy or non-epileptic subjects.

Imaging Epileptic Activity and Eloquent Cortex Using fMRI

Krakow K, **University of Frankfurt, Mainz, Germany**

Since the demonstration a decade ago that functional magnetic resonance imaging (fMRI) is able to provide high spatial resolution maps of brain function, considerable effort has been directed at applying this technique to study patients with epilepsy, in particular patients with intractable epilepsy considered for epilepsy surgery. Successful epilepsy surgery is vitally dependent on the accurate determination of the epileptic focus and of the risks of postoperative neurological deficits. First, through determination of eloquent cortical areas, fMRI may predict a deficit in cognitive (e.g., language and memory) or sensorimotor functions that might arise from surgical intervention. Second, asymmetries in the activation pattern may facilitate the lateralization and localization of a functional-deficit zone. For example, identification of functionally hypoactive temporal lobe structures in memory paradigms, which are normally known to be associated with symmetrical temporal lobe activation, may have predictive value for lateralization of seizure foci in temporal lobe epilepsy. Finally, fMRI can provide more direct evidence for the localization of epileptic foci through ictal or interictal blood oxygenation level dependent (BOLD) activation studies. It could be demonstrated that ictal fMRI is capable of imaging reversible BOLD signal changes associated with epileptic seizures, with the abnormality localized closely to the site of maximum electric abnormality. However, ictal fMRI is not routinely practicable for several reasons: Most ictal events are associated with head and body movement and impairment of consciousness, usually to a degree that the required level of cooperation for an MRI scan cannot be achieved. Furthermore, seizures occur usually unpredictably and are short lasting. It is therefore impracticable for a patient to lie in a MR scanner awaiting the onset of a seizure. For these practical issues, the investigation of ictal activity will be limited to highly selected patients who have very frequent seizures without gross head movement, or have epilepsy syndromes with seizures occurring predictably, e.g., reflex epilepsies.

Compared with ictal fMRI, mapping of interictal epileptiform discharges (IED) has several advantages: (1) IED are a common phenomenon in patients with epilepsy; (2) IED are not associated with stimulus-correlated motion; and (3) fMRI activation associated with single discharges is less likely to be confounded with propagation effects compared with ongoing ictal activity. As IED are by definition a sub-clinical phenomenon, a second modality is necessary to identify these events. Hence, this approach was only made possible by recording EEG during fMRI (EEG-correlated fMRI). However, the clinical interpretation of the fMRI maps is difficult; mainly because results of EEG-correlated fMRI have not been systematically validated with a gold standard, which are intracranial recordings and outcome after epilepsy surgery. Before EEG-correlated fMRI might be used as a decisive method in the presurgical assessment of epilepsy patients, the relation between fMRI results, invasive EEG recordings and surgical outcome in relation to resection of the activated area has to be established. Currently, EEG-correlated fMRI has to be considered a research tool providing insights to the pathophysiological processes underlying epileptic disorders. It remains unclear if the method will also be used for the routine clinical work-up of epilepsy patients in the future.

Pathophysiology of Focal Motor Seizures

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Introduction: Focal motor seizures are a frequent epileptic phenomenon. However, there are little data about their pathomechanism.

Methods: Nine patients were analysed who experienced focal clonic seizures during prolonged video-EEG monitoring with subdural electrodes on the precentral gyrus .One patient had additional bilateral subthalamic nucleus (STN) depth electrodes. In 5 patients, the EEG was co-registered with the EMG of muscles that were involved in the clonic seizures. The frequency, pattern and evolution of the ictal EEG was analyzed, and its relationship to STN and EMG activity was studied. In

4 additional patients with subdural electrodes, focal clonus was elicited by electrical stimulation of the motor cortex, and 3 patients underwent intraoperative stimulation of the spinal cord.

Results: Focal clonic seizures were always associated with a polyspike-wave pattern in the EEG of the primary motor area (frequency range: 1.6 - 3.4 Hz). At seizure onset, the ictal EEG derived from the precentral gyrus consisted of repetitive spiking (median: 19.5 sec), accompanied by a continuous increase in muscle tone. This evolved to a pattern of polyspike-wave complexes that was associated with clinical clonus. The clonic muscle contractions consisted of bursts of compound muscle action potentials (CMAP), which occurred synchronously in agonistic and antagonistic muscles and were separated by periods of complete muscle relaxation. Each series of CMAP followed the polyspikes in the EEG with a latency of 17 - 50 ms. Only some of the cortical spikes were followed by ipsilateral STN spikes. Rhythmic clonic muscle responses, which resembled closely clonic seizures, could be elicited by cortical stimulation with 20 Hz-50 Hz. The stimulation-clonus also consisted of simultaneous activation of agonistic and antagonistic muscles alternating with periods of muscular silence despite continuous stimulation. Clonus frequency decreased from 4.0-8.0 Hz at 50 Hz stimulation to 3.0-3.5 Hz at 20 Hz paralleled by a prolongation of the trains of CMAP. The relaxation periods remained stable. The number of stimuli which formed a train of CMAP and which were blocked during relaxation increased towards the end of the stimulation periods. Increasing intensity of stimulation at the same frequency converted a clonic to a tonic response. There was always a 1:1 relationship between stimulus and CMAP during spinal cord stimulation at all stimulation frequencies applied.

Discussion: The study suggests that focal clonic seizures are focal tonic-clonic seizures. The stimulation-clonus resembled closely the epilepstic clonus that was generated by localized polyspike-wave activity in cortical primary motor areas. Both clonic patterns consisted of simultaneous contractions of agonistic and antagonistic muscles at regular intervals separated by muscle relaxation. Activation of the STN did not appear to be an essential component of clonic seizures. We hypothesize that during cortical stimulation, clonus is elicited by synchronous activation of pyramidal tract (PT) neurons, which results in excitation of intracortical GABAergic interneurons by recurrent axon-collaterals. This leads to stepwise hyperpolarization of PT neurons intermittently suppressing the output of PT neurons despite continuous stimulation.

Symposium: EEG (Current Source Density) and Evoked Potential Studies in Schizophrenia and Depression

Flor-Henry P, **Edmonton, Alberta, Canada**
Kayser J, Bruder GE, **New York, USA**

Advanced analytic techniques of multi-channel EEG recordings are increasingly employed in the study of psychiatric populations. This symposium illustrates how Current Source Density (CSD) and Principal Components Analysis (PCA) of event-related brain potentials (ERP) can advance our understanding of memory deficits in depression and schizophrenia, or the effects of pharmacological treatment in psychiatric patients. In the first presentation entitled “Probing the Event-Related Potential (ERP) Old/New Effect During Continuous Recognition Memory Tasks in Affective Disorders,” Dr. Kayser will report results using PCA of CSD-transformed ERPs that were obtained in depressed patients and healthy adults during recognition memory tasks. In one study, participants were tested for auditory and visual word recognition memory using 31-channel ERP recordings. In a second study, high-density (72-channel) ERP recordings were obtained during recognition memory tasks using non-words and unfamiliar faces. Dr. Bruder will then present on “Electrophysiologic Correlates of Cognitive Subprocesses Contributing to Verbal Working Memory Deficits in Schizophrenia,” reporting CSD-PCA analyses of ERPs from 13 schizophrenia patients and 17 healthy controls during the Word Serial Position Test, a working memory task. Finally, Dr. Flor-Henry will report “Risperidone Induced Changes in Lateral EEG Organization in Schizophrenia”: changes in EEG topography, measured by 48-channel Current Source Densities. The EEG changes are all in the low frequency bands - in the beta frequencies there are no significant differences before and after treatment. Before treatment the sources are increased in the right hemisphere whereas after risperidone they are increased in the left hemisphere in the frontotemporal regions.

Identifying Generators of Visual Recognition Memory (Old/New) Effects in Affective Disorders: A Principal Components Analysis (PCA) of Laplacian Waveforms

Kayser J, Tenke CE, Gates NA, Kroppmann CJ, Sedoruk JP, Griggs CB, Stewart JW, Quitkin FM, Bruder GE, **New York State Psychiatric Institute, New York, NY, USA**

Event-related potential (ERP) correlates of mnemonic processes have rarely been assessed in mood disorders, despite considerable behavioral evidence of impairment. The typical ERP finding for healthy adults during explicit memory tasks is the so-called "old/new effect," an enhanced posterior positivity between 300 and 800 ms for repeated items, which is assumed to index conscious recollection. This study compared 67-channel, reference-free current source densities (CSD; Laplacian) derived from surface potential ERPs recorded during visual recognition memory tasks using unknown faces (college yearbook) and pronouncable pseudo-words (e.g., "cernor") from 30 unmedicated outpatients (major depressive disorder or dysthymia, DSM-IV) and 30 healthy adults, all right-handed. Patients performed more poorly than controls, with both groups having better memory for faces than pseudo-words. Unrestricted principal components (Varimax) were derived from CSD waveforms to identify and measure neuronal generator patterns. Two prominent CSD factors, related to current sources at parietal and temporal sites, revealed old/new effects at mid-frontal (422 ms peak latency) and inferior-parietal sites (809 ms). These sources and their old/new effects were reduced in patients at parietal and mid-central sites, especially for faces. Task-specific CSD topographies (< 300 ms) were comparable across groups, dissociating neuronal generators of early word and face processing. The combination of PCA and CSD methodologies can help to identify neuronal generators underlying memory impairments in depression.

Electrophysiological Correlates of Cognitive Subprocesses Contributing to Verbal Working Memory Deficits in Schizophrenia

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New York State Psychiatric Institute, New York, NY, USA

Reduced working memory (WM) is a primary cognitive deficit in patients with schizophrenia and yet the extent to which cognitive subprocesses contribute to their verbal WM impairments is unknown. The fine temporal resolution of multi-channel event-related brain potential (ERP) topographies was used to provide a window into the different stages of processing (sensory processing, encoding into a WM representation, maintenance of this information) that may contribute to abnormalities of verbal WM in schizophrenia. Long EEG epochs (>10 s; 0.01 Hz high pass) were recorded from 13 patients having schizophrenia spectrum disorders and 17 healthy controls during a visual Word Serial Position Test (WSPT). Each trial consisted of a 4-word encoding sequence (500 ms exposure, 1,000 ms ISI), a 4.5 s retention interval, a probe word, and a delayed response to indicate its position. Reference-free current source density (CSD) transformations were used to simplify and sharpen ERP topographies derived from 31-EEG channels, followed by principal components analysis (PCA) to summarize the underlying neuronal generator patterns. Patients had poorer performance than controls (72.9% vs. 88.2% correct), and also reduced P3 source activity during word encoding and retrieval, particularly at left inferior parietotemporal sites. Healthy controls showed a build-up of mid-frontal negative slow wave (SW) activity during encoding of words, which was absent in patients. In contrast, stimulus-related N1 activity over left inferior-parietal sites and sustained mid-frontal SW negativity during the retention interval were comparable across groups. However, the sustained mid-frontal SW negativity was significantly related to working memory performance in controls, but not in patients. Advanced electrophysiologic techniques provide new evidence that verbal WM deficits in schizophrenia involve a disturbance of a network of frontal and parietotemporal processes, primarily affecting the encoding and early storage of WM representations.

Risperidone Induced Changes in Lateral EEG Organization in Male Schizophrenics: Source Localization (LORETA)

Flor-Henry P, Lind JC, Koles ZJ, **Alberta Hospital Edmonton, Edmonton, Alberta, Canada**

Nine unmedicated, dextral male schizophrenics were tested before treatment with risperidone average dose 4 mg (range 3-6) and again 3 months later (range 63 - 164 days). The EEG was recorded with a 48-channel system. Twenty 1-second artifact free segments were analyzed at sampling rate of 256/sec and Fast Fourier Transformed leading to 46 x 46 complex-valued cross-spectral matrices, at a frequency resolution of 1 Hz. There were two conditions: resting (Eyes Open, Eyes Closed). Current source density was calculated according to the LORETA algorithm, which describes the cortical current source with a 7mm spatial resolution in the delta (2-3Hz), theta (4-7Hz), beta 1 (14-20Hz), beta 2 (21-50Hz) and gamma (38-42Hz). The EEG changes in the Eyes Closed condition are all in the low frequency bands, delta, theta and alpha - in the beta and gamma frequencies there are no significant differences before and after treatment. Before treatment the sources are increased in the right hemisphere whereas after risperidone they are increased in the left hemisphere in the frontotemporal regions. In the Eyes Open condition the sources are increased bilaterally (L > R) in the delta and theta and in the right hemisphere (alpha) before treatment relative to the medicated state. Considering the 2-6Hz band (Eyes Closed) risperidone leads to increased sources in the left temporoparietal region, as was found by Yamada et al., (2004) in 14 male volunteers 4 hours after olanzapine (1.25 mg). The implications of these findings will be discussed.

Symposium: Insights from ERPs into Emotional Disorders by Means of Oddball Designs

Fast K, **Ludwig-Maximilians University, Munich, Germany**

The ability to regulate emotion is one of the most pervasive challenges by which human beings are confronted. All emotional regulation processes may be considered as adaptive, in the sense that emotions need to be regulated for individuals to function within their environments. Therefore, if these processes malfunction, this would result in maladaptive behaviors. Accordingly, many psychopathological states, such as depression, anxiety, psychopathy, alexithymia or schizophrenia, present different patterns of emotional disturbances. Indeed, many studies have been performed with such patients, showing specific disorders in the recognition of emotional facial expressions. However, at the present state of knowledge, no evidence has been collected in order to determine at which level of the information processing (attentional, perceptive, executive) these deficits are situated (as compared with control normal subjects). The principal scopes of our studies are (1) to define whether the deficits in the recognition of emotional facial expressions are situated at the attentional, perceptive or executive levels; and (2) to index these deficits at the neurophysiological level.

For this purpose, ERPs will be used in order to be able to temporally constrain the different stages implied in emotional processes. With a temporal resolution up to 1ms, ERPs tap characteristic task-related changes in the electrical activity of the cortex by averaging across EEG segments that are synchronized to a repeated stimulus. A classical design used in ERP studies is the “oddball” paradigm, in which subjects are asked to detect, amongst a series of standard stimuli, an infrequent deviant one. The detection of stimulus change may play a role in directing attention to events of biological importance. This is indexed by three main ERP components. First, when subjects are placed in attentive conditions, deviant stimuli evoke a N2b component, peaking at occipital electrodes around 250 ms, which indicates a switch of attention to biologically significant events in order to cope with them. Second, a P3a component is maximally recorded at frontal sites around 300 ms, which is functionally related to the detection of stimulus novelty. Third, a P3b component is maximally recorded at parietal sites around 450 ms, and this component is generally referred to later conscious, decisional and premotor response-related stages. In this way, by using oddball designs, it is possible to generate different waveforms indexing different steps in the information processing system. Indeed, an effect circumscribed to response-related stages (decision-making, response premotor preparation) implies a modulation of the P3b component (but not of the attentional N2b). However, a behavioral effect originating at the attentional level and extending to behavioral responses will affect both components (N2b and P3b modulations).

The present symposium will show four different ERP studies, which intendend by means of emotional oddball designs, to define where originates the deficit of emotional disturbances in psychopathy or anxious and depressive states (M. Rossignol), alexithymia (N. Vermeulen) and alcoholism or schizophrenia (P. Maurage. S. Campanella). Our main scope will be to understand the functional origin of these deficits and their neural correlates in order to have a better understanding of the clinical symptomatology of these patients, the final goal being to optimize the therapeutical approach.

Emotional Oddball Designs and Psychopathological Populations: Insights From ERPs A General Introduction

Campanella S, **Catholic University of Louvain-La-Neuve, Belgium**

The ability to regulate emotion is one of the most pervasive challenges by which human beings are confronted. All emotional regulation processes may be considered as adaptive, in the sense that emotions need to be regulated for individuals to function within their environments. Therefore, if these processes malfunction, this would result in maladaptive behaviors.

Categorical discrimination of human facial emotional expressions has been shown in normal subjects to have an early perceptual origin, around 150 ms, in the occipitotemporal regions. Extensions of these results to different psychiatric disorders (such as depression, generalized anxiety disorder, alexithymia or alcoholism) will be discussed, as deficits in emotional decoding were often described in these clinical populations, but were not yet circumscribed at an attentional, perceptual or post-perceptual level.

Is the Abnormal P300 in Psychopathology Just a Consequence of a Dysfunction in Earlier Components? P100 and N170 Components Are Disrupted in Alcoholism and Schizophrenia

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A deficit in the P300 component is very frequently observed among patients with psychopathology, but the earlier components of the ERP are seldom examined. Fourteen schizophrenic patients and 10 alcoholic patients were confronted with pictures from the Ekman and Friesen series in an event-related potentials study, and compared to 15 normal controls. Participants were confronted with a visual face-detection task, in which they had to detect, as quickly as possible, deviant faces amongst a train of standard stimuli (neutral faces). Deviant faces changed either on identity (different identity, neutral expression), or on emotion (same identity, happy, fearful or sad expression). ERP results suggest that schizophrenic and alcoholic patients have a disruption of the P100 and N170 components, for the amplitude as well as for the latency. This reduction of the visual P100 and the face N170, recorded at occipitotemporal sites, is observable for emotional and for identity faces, being therefore general to facial information. We suggest that this general visual processing deficit may be the cause, at least partly, of the P300 disruption.

The N300 Component Is Modulated by Anxiety and Psychopathic Tendencies ERP Correlates of Emotional Facial Discrimination in Subjects With Mood Disorders

Rossignol M, Campanella S, **Catholic University of Louvain-La-Neuve, Belgium**

The N300 component is a negative deflection appearing 250-350 ms after stimulus onset. Studies have shown that this component is particularly sensitive to emotional stimulation, and reacts more to affective features of stimuli than to physical characteristics. Consequently, if the N300 component reflects an affective processing, we can postulate modulations of its features in psychopathological states.

We will present two studies that provide evidence of a modulation of the N300 component by two different psychopathological states, namely anxiety and psychopathic tendencies.

In both studies, subjects were confronted to an emotional oddball paradigm analyzed in 32-channels averaged ERPs, where frequent stimuli were neutral faces. In the first study, subjects with high or low psychopathic tendencies (determined by the Minnesota Multiphasic Personality Inventory, MMPI-2) had to detect rare stimuli with happy, sad or fearful expressions. In the second one, low and high anxious subjects (defined by the Spielberger State and Trait Anxiety Inventory, STAI) had to detect rare fear or happy faces.

The first study suggests that subjects with low psychopathic tendencies are more efficient in the detection of emotional deviant faces. The emotional deficit of subjects with high tendencies was indexed by a decreased N300 component.

The second study mainly shows that high anxiety does not modify early perceptual or attentional processing, whereas later components are modified. Indeed, highly anxious subjects are faster to detect deviant faces as suggested by earlier reaction times and P3b component. However, they show a reduced ability to process the emotional content of faces, this deficit being indexed by a decreased N300 component. Consequently, we interpret the earlier P3b observed in highly anxious subjects as a way to overcome the deficient emotional appraisal by a more salient conscious processing.

We suggest that this kind of emotional oddball designs would allow us to better define the origin of functional bias described in different psychopathological populations.

Impaired Categorization of Emotional Faces in Alexithymia : Evidence From Event-Related Potentials (ERPs)

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Luminet O, **Belgian National Fund for Scientific Research**

In this study, we examined the moderating impact of alexithymia (i.e., a difficulty identifying and describing feelings to other people and an externally-oriented cognitive style) on the automatic categorization of affective information displayed on faces. Literature evidences that alexithymia is associated with a higher prevalence of emotional disorders and physical illnesses and is an important risk factor that leads to a reduction of life expectancy. Previous studies clearly identify an impaired recognition of emotional expression in high alexithymia scorers at a controlled level. However, up to now, no study directly assessed earlier stages of categorization of facial expression. We used Event-Related Potentials (ERPs) to temporally locate the deficit of emotional processing in alexithymia in a modified visual oddball task using morphed emotional faces. In this task, participants had to quickly detect a deviant (rare) morphed face that shared (Within) or not (Between) the same emotional expression than the frequent one. Results showed an overall delayed ERPs' responses related to the attentional processing of emotional faces in high alexithymia scorers. These results also indicate an impaired categorization of facial expression, particularly for anger.

Symposium: Affective Modulation of Memory and Cognition

Summary Abstract

Fast K, **Ludwig-Maximilians University, Munich, Germany**

The interdisciplinary field of cognitive neuroscience in psychiatric disorders has provided ample evidence for the benefits of examining psychological constructs across multifunctional levels of analysis. Such an eclectic approach on affectvie modulation of memory and cognition will only make sense if research considers on the one hand how basic affective processes influence cognition and on the other hand how cognitive processes modulate affect. Recent research results in a remarkable convergence of evidence in highlighting the importance of the role of crucial limbic structures, especially of the amygdala and the hippocampus, in emotional processes. New understanding of the impact of stress on different brain stuctures and cognitive processes has been developed. The existence of an integrated system consisting of many brain regions, e.g., the mesolimbic dopamin pathways underlying processes of reward and aversive input, is supported by recent neuropsychological, neurophysiological and neurofunctional studies. An integration of these findings might have important implications for understanding and classifying various psychiatric disorders based on changes in the affective modulation of memory and cognition as well as in the cognitive regulation of emotional processes. Contributions from research in amnesia, PTBS, BPS, schizophrenia, depression and healthy people should reflect the new integrative approaches and rapid progress in cognitive and emotional neuroscience in psychiatric disorders.

Neural Correlates of Attachment Narratives in Borderline Personality Disorder: A Study Using the Adult Attachment Projective in an fMRI Environment

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Introduction: Attachment representation has emerged as an important construct in understanding the development of psychopathology and in targeting areas for intervention. Several studies indicate that individuals diagnosed as borderline might be distinguished from other clinical groups by their propensity to be insecure preoccupied attachment and unresolved with respect to attachment-related traumas. This study examines representational and neural patterns in borderline patients in relation to concurrent activation of attachment.

Methods: The participants in this research are 12 female borderline patients and 19 non-patient controls who were administered the Adult Attachment Projective (AAP)[1] in a functional neuroimaging environment. The AAP, a new projective measure of adult attachment, is comprised of seven attachment scenes to which individuals are asked to tell a brief story. We used an fMRI-adapted AAP methodology[2,3] to assess attachment status, and to obtain a preliminary picture of the underlying neural processes associated attachment activation, while subjects were speaking overtly about attachment stories in a standardized setting. Functional imaging data were acquired on a 1.5 Tesla Siemens Magnetom Symphony.

Results: FMRI acquisition using the fMRI-adapted AAP methodology revealed the results, that Borderline patients, as compared to non-patient controls, showed significant higher activation in the right frontotemporal cortex - brain region associated with autobiographical memory retrieval, right ventral prefrontal cortex and right frontopolar cortex[4]. In the AAP narratives Borderline patients were more likely to be judged unresolved with respect to abusive attachment experiences than non-patient controls. Irrespective of classification group status, traumatic dysregulation on a representational linguistic level[5] was significantly greater in borderline patients than non-patient controls, especially in response to pictures that portrayed characters facing attachment stressors alone.

Discussion: Faced with appraisals of attachment pictures, borderline patients showed higher activations in brain regions related to autobiographic memory retrieval[6] compared to non-patient controls. Autobiographic memories constitute the portion of the episodic memory system that is composed of significant life episodes. The combined results of our work on a neurobiological and linguistic level highlight the hypersensitivity of borderline individuals to the state of being alone without attachment figures, that is "representational attachment isolation" triggered by individual autobiographic traumatic memories of abuse and emotional neglect.

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Neuropsychological and Neurobiological Correlates of Affective Dysregulation in Patients With Stress-Related Disorders

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Introduction: Stress-related disorders are closely associated with changes in memory and inhibition concerning affective stimuli. Chronic stress or single traumatic events can be regarded as evoking either affective bias or suppression in

emotional information processing. The aim of our research approach is to show distinctions in group performance related to different levels of emotion-dependent information processing leading to a general model of affective dysregulation.

Methods: Several experimental behavioral tasks as well as functional neuroimaging focussing on aspects of deliberate and automatic control of neutral and affective information processing were applied in patients with experienced traumatic incidents, PTBS, BPS, depression and in different healthy control groups.

Results: Our data give evidence for changes in interaction between emotional and cognitive processes as well as in the underlying neurofunctional networks in stress-related disorders compared to other clinical groups and healthy controls.

Discussion: Although the process of regulation is based on similar neuronal systems in all assessed groups, distinct functional brain activation supports discriminative explanations for cognitive regulation. It is indicated that especially the variable envolvement of the frontotemporal conjunctions might be critical for the distinct clinical and neuropsychological symptoms in cognitive modulation of emotional processes and affective influence on cognitive processes.

Brain Imaging Correlates of Patients with Emotion-Related Memory Disorders

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Introduction: Emotion-related memory impairments are usually confined to the autobiographical domain and are found in patients with dissociative amnesias. Major stress or psychic/psychosomatic trauma events are regarded as provoking such amnesias.

Methods: Static and functional neuroimaging as well as detailed and comprehensive neuropsychological testing were applied.

Results: The patients included all suffered from retrograde autobiographical amnesia while their other memory domains (semantic memory, procedural memory, priming) were either largely unimpaired or could be regained within a short period. Autobiographical amnesia either affected their whole past life or significant portions of it (e.g., 6 or 13 or 14 years). After syndrome onset patients frequently appeared emotionally flattened and, though they were able, to reacquire knowledge about their past, they did so in a more neutral, unaffected way, which, however, might be interpreted as a mechanism of self-protection. Brain imaging with FDG-positron-emission-tomography revealed a reduced glucose level in frontal and temporal (or temporoparietal) regions, affecting the right hemisphere more than the left one. Functional imaging with fMRI or 15O-PET showed a differential activation for remembered (or reacquired) as opposed to forgotten material.

Discussion: Consequently, our data show that environmentally induced stress situations may change brain activity and cerebral metabolism persistently. The data also indicate that the brain's circuitry in getting access to previously stored information is altered. Especially frontotemporal regions of the right hemisphere may be sensitive to autobiographical old memory processing.

Neural Correlates of Affective Hyperarousal in Borderline Personality Disorder - General fMRI Findings and Preliminary Data About the Effects of Psychotherapy

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Introduction: Using functional neuroimaging affective hyperarousal in BPD can be linked to dysfunctional activation of both, limbic and neocortical areas. A pilot study examined whether increased regulation of arousal in borderline personality disorder (BPD) following dialectical-behavior-therapy translates into changes in the neural systems involved in affect regulation.

Methods: In contrast to pre-post designs frequently used in fMRI-designs for psychotherapy research, five sequent fMRI scans were performed before, during and after a 14-week in-patient treatment program of Dialectical-Behavior-Therapy (DBT). Six female BPD patients and 6 female healthy controls were included in an event-related fMRI design that induced emotional arousal by showing standardized images.

Results: In contrast to controls BPD data revealed decreased correlation between individual appraisal of arousal intensity and activation in cingulate areas, in prefrontal and temporal gyri, in the posterior cingulate cortex and in the left insula. Only DBT responders displayed additional decreases in medial and ventrolateral frontal areas, in the left amygdala and the hippocampus bilaterally.

Discussion: Identified changes resemble the results of functional neuroimaging studies on psychotherapy effects in other mental disorders.

Theory of Mind, Perspective Taking and Schizophrenia

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The reconstruction of psychopathological symptoms as neuropsychological core disturbances is a prominent research strategy in schizophrenia research. It allows the characterization of candidate brain regions that are pathophysiologically relevant. In this respect, the following two cognitive mechanisms appear to be crucial for the development of schizophrenia: first, disturbances of the so-called theory of mind (TOM) ability that allows us to predict and explain other peoples behavior and, second, disturbances of self-consciousness that allows representation of one's own mental or bodily states as one's own mental or bodily states and comprises essential constituents such as the experiences of ownership, body-centered spatial perspectivity, and long term unity of beliefs and attitudes. We present a taxonomy that differentiates different levels of self-conscious states. This taxonomy will be enriched by different experimental approaches that operationalize the specific difference of first-person- (1PP) centered upon one's own body as opposed to the third-person-perspective (3PP). These capacities can be mapped to the brain employing functional imaging methods. It can be shown that the medial anterior prefrontal cortex in addition to medial parietal and posterior temporal regions are candidate brain regions in which this differential capacity appears to be implemented. The relevance for different psychopathological phenomena and its potential for the pathophysiological explanation of schizophrenia will be discussed. This research strategy allows the study of the pathophysiology of schizophrenia that is motivated by its psychopathology and which is based on a cognitive model of the disease.

Symposium: Voluntary Eye Movements and Motor-Sensory Interaction

Summary Abstract

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This symposium is devoted to processes and sequences when humans execute voluntary saccades, with particular attention to the time period to action. One of the classical concepts of sensory-motor interactions is unidirectional causality: a certain sensory input causes a directed motor action. Many actions are however self initiated. These are less commonly studied, lacking a proper timing signal for external analysis, however the last decades witnessed an increasing awareness that visual and cognitive processes involved in "planning" and "action" may be experimentally separable (Glover 2004). Current studies using functional MRI (fMRI), wavelet transformed EEG (wEEG) and single pulse TMS (sTMS) provide complementary spatial and temporal precision to study voluntary saccadic eye movements in humans.

Neuroscientists have developed detailed understanding of the elements of the complex system of the self and voluntary action. Current studies begin to address the importance of brain circuits necessary for voluntary, willful action. The saccadic eye movement system is eminently suitable for such studies. Clinical studies of voluntary saccades in Parkinson's disease and Alzheimer's disease, addressing the role of dopamine, are of particular neurphysiopathological importance, and conversely the physiological studies will contribute to the understanding of these disorders.

1. Scientific aims: to present a critical summary of state of the art experimental evidence of neuronal mechanisms of voluntary saccades in humans; focused presentation of current methodology which allows experimental approaches to voluntary action. There is a need to appreciate the power and the limitations of the available techniques.

2. Educational Aims: support and broaden graduate education in clinical "system" neuroscience.

3. Perspectives: build bridges between experimental researchers and clinical neuroscience.

Saccadic Eye Movements and Schizophrenia

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Lack of initiative like deficit symptoms of schizophrenia are among the most detrimental aspects of the disease process and are also most resistant to the current pharmacological interventions. Severity of this symptom in schizophrenia has been found to be related to the severity of cognitive impairment.[1]

By use of a number of experimental paradigms, saccadic eye movements have consistently been shown to be impaired in individuals with schizophrenia and their relatives.[2] More recently, existence of a separate brain circuitry for the self-initiated, purposeful action that might account for the saccadic errors observed in this patient group is argued. Similar visuocognitive changes have been noted in patients with Parkinson's disease, who also display a type of dysexecutive syndrome.[3] It is discussed that the study of the saccadic eye movements might help understanding of the neuronal correlates of the willful, goal-directed action of human beings.[4,5]

In conclusion, the concept of saccadic eye movements is one of the proposed "endophenotypes" of neuropsychiatry, which might provide insight into the pathophysiology and genetics of schizophrenia. Further research on this subject might help us to develop better treatment options for schizophrenia, to identify individuals at risk of developing the disease and even perhaps to cure them readily before the disease prevails.[6]

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Intrasaccadic Modulation of Gamma Power Is Not Due To Attention Shift

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Introduction: Our purpose was to investigate the presence of intrasaccadic gamma power modulation for covert and overt attention shift, evoked by auditory stimuli. Previously, we gave evidence that gamma power of the human EEG is modulated by voluntary saccades peaking just before new fixation. Gamma modulation was evident in the light and in the blindfolded subjects. Since saccades are accompanied by attention shift, we wondered if intrasccadic gamma power increase is due to a shift of attention and not due to the saccadic eye movement per se. In Parkinson's disease patients we find that gamma power modulation is absent intrasaccadically in a about half of the patients tested, whether or not they execute normal voluntary saccades. Could this deficit be due to a known visuo-spatial impairment in these patients?

Methods: EEG with 26 electrodes was recorded using 19 subjects. Saccades were recorded with EOG and infrared signals (ISCAN). Subjects executed saccades between 2 markers subtending in 40° to a lower (left saccade) and a higher (right saccade) tone when the tone was different from the previous one (odd-ball paradigm). 100 tones were presented in four conditions: saccades in the light, saccades being blindfolded, tones without eye movements, covert attention shift. For every subject, average latency and saccadic length time was calculated using the light saccade condition. These values were used to analyze EEG segments in the no eye movement and attention shift conditions. To quantify gamma power Continuous Wavelet Transform was used followed by Hilbert transform. Statistics were General Linear Model.

Results: Gamma power increased intrasaccadically in the light and in the blindfolded condition. No such modulation was present in the covert attention shift condition.

Discussion: Gamma power modulation is present during saccades either triggered by voluntary decisions, visual or auditory cues. It is not present for covert attention. These results are in agreement with our hypothesis that intrasaccadic

gamma modulation may represent updating processes during saccades. Therefore, in Parkinson's disease the deficit in intrasaccadic gamma is not simply due to impaired shift in visuo-spatial attention.

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Slow Ballistic Eye Movements and Gamma-Modulation in Persistent Vegetative State

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Introduction: Power in the gamma band EEG is modulated during saccades in normal subjects. The function describing gamma power in the perisaccadic time window shows an inverted "U" shape: it peaks just prior to new fixation. The function is most evident over posterior recording sites. This perisaccadic gamma power function is preserved even when the observer is blindfolded.

Objective: To evaluate whether persistent vegetative state (PVS) severity correlates with the presence and power modulation of EEG with conjugate eye movements in PVS patients. We looked for PVS staging correlation with spontaneous Slow Ballistic Eye Movements (SBEM) in individual patients.

Methods: Glasgow-Coma-Scale and Coma-Remission-Scale were carried out in 14 PVS patients. Two groups were determined: chronic patients and those in recovery. EEG and simultaneous electro-oculogramm were recorded in all patients. To quantify the power of the gamma frequency band EEG in connection with the conjugated spontaneous Slow Ballistic Eye Movements, we applied Wavelet Transform, followed by Hilbert transform. We quantified gamma power distribution relative to the timing of the eye movements, and correlated the clinical and the neurophysiological measures.

Results: All patients in persistent vegetative state (PVS) showed gamma activity.

Gamma activity was modulated in association with SBEM in all patients. Similarly to the results in normals (Bodis-Wollner et. al 2002), gamma power minimum occurred prior to the eye movements and gamma power maximum during the eye movements in less severely affected patients. In severely affected patients there was no evidence of a temporal relationship between gamma power and the phase of the eye movement.

Discussion: SBEM-dependent gamma modulation is connected with improvement in PVS.

Saccades in Darkness Evoke Retinotopic BOLD-Activation in Early Visual Areas

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The role of V1 in self generated saccades is an open question. We investigated with fMRI whether early visual areas located at the vicinity of the occipital pole are differentially activated when subjects perform self generated saccades in the left and right visual hemifields.

Prior to every scan the subjects saw a fixation cross jumping in an outline face from the root of the nose to the left or right eye and back. The root of the nose was horizontally centered in the visual field. The subjects were instructed to imagine that face and to perform self initiated saccades to the imagined structures of the face during the fMRI measurement. The eye movements were performed in total darkness to avoid confounds with external visual stimulation. The horizontal and the vertical electrooculogram (EOG) were recorded to assess the eye position during MR-scanning. The latency and the direction of the saccades were extracted from the EOG recordings and used to define the model for the event related fMRI-analysis.

Saccades in the subjective left visual field were accompanied by a stronger BOLD response at the right occipital pole than saccades in the subjective right visual field. Conversely, saccades in the right visual field were associated by a stronger activation at the left occipital pole.

We found that early visual areas, presumably V1, are activated when subjects perform self generated saccades even in total darkness. The spatial specifity of the BOLD-response for saccades in the visual field indicates that this activation is retinotopically organized.

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Symposium: QEEG Analyses of Audio-Visual Entrainment Therapy for Medication Resistant Depression

QEEG Evidence for the Efficacy of Auditory-Visual Entrainment Treatment of Refractory Depression

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It is well established that the number of people diagnosed and suffering from depression is on the increase. Many of these people have had minimal or no response to first line pharmacological interventions, or due to other medical reasons they are not an option. This set of patients represents an ongoing challenge within the psychiatric arena. As a result, there has been a growing need for non-medication approaches to treatment. Current research and evolving treatment options challenge the old bias that medications are the only way to produce measurable brain changes. One area of treatment focus that is evolving new strategies includes the areas of brain stimulation methods, which include vagal stimulators, transcranial magnetic stimulation, cranial electric stimulation and audiovisual stimulation.

The purpose of this study was to examine the use of auditory visual EEG entrainment (AVE) at a 14Hz beta frequency to decrease symptoms of depression with corresponding changes in underlying abnormal neurophysiology. The subjects (N=16) ranged in age from 21-54 and were screened utilizing BDI-II and broken into 2 groups (N-8): simulated and AVE treatment with a cross-over design. Both groups were given the BDI-II and QEEG testing at baseline, 4 weeks following either AVE or simulated treatment, and then again after an additional 4 weeks after a switch in treatment in the crossover design. Results revealed significant changes in reduction of symptoms of depression only after 4 weeks of AVE therapy ($p>.01$) using an independent group T-test of the BDI-II scores. Multiple univariate and multivariate QEEG scores adjusted for normal age deviations demonstrate significant change in scores over time, principally in anterior cortical regions noted for mood regulation. The findings from this study indicate that AVE therapy may be a viable non-medication therapeutic intervention.

Neurometric QEEG and VARETA Correlates of PMS Subtypes

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The purposes of this research were to: (a) describe, compare, and contrast patterns of brain function through the use of neurometric QEEG analyses in women with perimenstrual (PMS) symptoms and in women with no or mild perimenstrual symptoms, and; (b) determine the association of patterns of brain function with perimenstrual symptoms, anxiety, depression, and cortisol levels during postmenstrual and perimenstrual phases among the symptomatic and asymptomatic women. Criteria for differentiating PMS symptoms and groups without PMS symptoms were developed based on an adaptation and further delineation of the symptom list identified by Woods and associates (1987). Groups of women with perimenstrual magnification (PMM) of existing symptoms were also identified. In order to minimize group differences in brain functional measures in this study, all QEEG variables were log and Z-transformed relative to age (John et al., 1977; 1988), and neurometric clinical discriminant scores were computed to estimate the statistical probability of the presence of the QEEG pattern associated with major affective disorder for each subject. Key QEEG variables were determined by using analysis of variance to identify those that were significantly different between symptom groups for each menstrual cycle phase. Categorization of PMS types was the dependent variable for analyses.

During the follicular phase of the menstrual cycle, the stepwise multiple regression resulted in a multiple R of 0.56 and a R^2 of 0.31. Contributing variables in the order of their significance were: Hamilton Depression Score (p = .0000); Negative Life Events (p=.0000); bipolar alpha relative power in the anterior regions of the brain (p = 003); state anxiety (p = .04); theta coherence in the right temporal regions (p = .04); theta coherence between the left and right parietal regions (p = .12); and beta asymmetry within the left temporal regions of the brain (p = .16). During the luteal phase of the cycle, a multiple R of 0.72 resulted with a R^2 of 0.52. Predictor variables in the order of their contributions were: state anxiety (p = .0000); daily hassles (p = .0000); combined asymmetry in the anterior regions of the brain (p = .004); Hamilton Depression Score (p = .004); salivary cortisol level (p = .007); negative life events (p = .03); theta asymmetry in the central regions (p = .02); bipolar alpha coherence within the left frontal brain regions (p = .04); and, positive life events (p = .29).

Therefore, there is a relationship between brain function, and several of the identified emotional and social variables in each menstrual cycle phase for predicting symptom group categories. The prominence of these variables varies across stages in their contributions to the R^2. Stress-related variables provided a higher degree of prediction in the luteal or perimenstrual phase when PMS symptoms are most likely to occur. Measures of brain function contributing to the R^2 are anatomically consistent with brain regions noted for mood regulation. While the total number of univariate measures that differentiated the groups in each of the phases was not notably different (39 versus 29 for the postmenstrual and perimenstrual phases, respectively), nearly all of the variables were different in the profile patterns in each phase. Since previous research has shown that neurometric QEEG measures on test-retest over time are very stable in normal populations, the nearly complete difference in brain function patterns that differentiated these groups in the different phases over time reflects changes attributable to influencing factors likely associated with menstrual cycle changes.

The results also demonstrated that the difference between these groups depends principally on a gradient of changes in brain intrahemispheric coherence measures affecting principally the left frontal and left frontal-temporal regions. In addition, differences include to some extent changes in the coherence pattern between left and right frontal regions, as well as changes in coherence measures between left and right parietal regions.

These results indicate there are different patterns of brain function in the luteal phase of the menstrual cycle phases that differentiate women with and without PMS symptoms that may correspond to differences in mood lability, stress tolerance, and other factors of psychological functioning. VARETA (Variable Resolution Electromagentic Tomography) source localization algorithms were applied to each group's maximal deviation in the .39 Hz EEG spectra across phases and were examined in order to provide a descriptor of neuroanatomical contributors to the group differences.

Electrophysiological Correlates of Error Processing in Psychiatric Diseases

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Error processing has been investigated in a variety of psychiatric illnesses like obsessive-compulsive disorder (OCD), major depressive disorder (MDD), schizophrenia, and borderline personality disorder (BPD). Three ERP components have been intensively discussed in this context: the error negativity (Ne) / error-related negativity (ERN) and the "early" error positivity (EPe), which are thought to reflect automatic error processing, and the "late" error positivity (LPe), which is supposed to mirror the awareness of erroneous responses. It has been shown that patients with OCD have enlarged (more negative) ERN/Ne amplitudes compared to matched control subjects, whereas patients with BPD or schizophrenia have smaller (less negative) ERN/Ne amplitudes, possibly reflecting deficits in cognitive control mediated by frontal-striatal-thalamic circuits. In addition, patients with MDD show a smaller feedback-related ERN/Ne following an erroneous trial than healthy controls, indicating a catastrophic response to perceived failure. For patients with schizophrenia it has been demonstrated that improvement of clinical symptoms is related to increase of ERN/Ne amplitudes.

In conclusion, it seems a reasonable target for further studies whether error-related ERP components correlate with clinical outcome and can predict therapeutic response.

General Posters and Oral Presentations

Can Routine EEG Findings Replace Eye Blink Reflex in Diagnosis of Startle Reaction?

Mert Savrun B, Savrun F, Poyraz BC, Bozhuyuk E, Uysal O, Arikan MK, **University of Istanbul, Turkey**

Startle reaction is viewed as one of the critical symptoms in acute stress reaction and posttraumatic stress disorder.[1-3] This symptom might provide insight into the physiological basis of these phenomena. It is difficult to objectively identify and evaluate startle reaction in these disorders both at presentation and subsequently under drug treatment; as the only widely-accepted electrophysiological measure to assess startle reaction is the eye blink reflex that is not carried out routinely in everyday practice. In one study, Arikan et. al. reported that EEG measures of the reactivity to eyelid opening could effectively predict startle reaction in patients of acute stress reaction; thus routine EEG could be utilized in the diagnosis of startle reaction.[4]

In this study, the relationship between EEG measures of the reactivity to eyelid opening and eye blink reflex is investigated, and the findings are discussed with regard to their potential contributions to clinical and preclinical psychiatry.

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Startle Reaction In Depression: EEG Measures of the Reactivity to Eyelid Opening

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It is reported that startle reactions can be observed in depressed patients.[1] Depressed patients might also have alterations in their eye blink reflexes when compared with healthy controls.[2] In one study, Arikan et al. reported that EEG measures of the reactivity to eyelid opening could effectively predict startle reaction in patients of acute stress reaction; thus routine EEG could be utilized in the diagnosis of startle reaction.[3] In this study, the relationship between self-reported startle reaction and suicidal ideation in depressed patients is assessed, and EEG measures of the reactivity to eyelid opening are used to predict this association.

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Panic Disorder and Startle Reaction

Poyraz BC, Bozhuyuk E, Bayar MR, Uysal O, Arikan MK, **University of Istanbul, Turkey**

There are reports of association between panic disorder and startle reaction.[1] Patients with panic disorder might also have alterations in their eye blink reflexes when compared with healthy controls.[2] In one study, Arikan et al. reported that

EEG measures of the reactivity to eyelid opening could effectively predict startle reaction in patients of acute stress reaction; thus routine EEG could be utilized in the diagnosis of startle reaction.[3] In this study, the relationship between self-reported startle reaction and the symptom of "fear of dying" in patients with panic disorder has been assessed, and EEG measures of the reactivity to eyelid opening are used to predict this association.

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Startle Reaction in Schizophrenia

Bozhuyuk E, Poyraz BC, Duran A, Uysal O, Arikan MK, **University of Istanbul, Turkey**

There are reports of altered startle reaction in schizophrenic patients.[1-3] In one study, Arikan et al reported that EEG measures of the reactivity to eyelid opening could effectively predict startle reaction in patients of acute stress reaction; thus routine EEG could be utilized in the diagnosis of startle reaction.[4] In this study, the relationship between self-reported startle reaction and delusions of persecution in patients with schizophrenia is assessed, and EEG measures of the reactivity to eyelid opening are used to predict this association.

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The Effect of Amitriptyline on Startle Reaction In Patients with Depression

Poyraz BC, Bozhuyuk E, Savrun BM , Uysal O, Arikan MK, **University of Istanbul, Turkey**

It is reported that startle reactions can be observed in depressed patients.[1] Depressed patients might also have alterations in their eye blink reflexes when compared with healthy controls.[2] In one study, Arikan et. al. reported that EEG measures of the reactivity to eyelid opening could effectively predict startle reaction in patients of acute stress reaction; thus routine EEG could be utilized in the diagnosis of startle reaction.[3] In this study, depressed patients with suicidal ideation are assessed by use of EEG measures of the reactivity to eyelid opening both at baseline and 6 weeks after the beginning of amitryptyline treatment; and the findings are correlated with the antidepressant response.

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The Effect of Imipramin on Startle Reaction in Patients with Panic Disorder

Bozhuyuk E, Poyraz BC, Bayar MR, Uysal O, Arikan MK, **University of Istanbul, Turkey**

There are reports of association between panic disorder and startle reaction.[1] Patients with panic disorder might also have alterations in their eye blink reflexes when compared with healthy controls.[2] In one study, Arikan et. al. reported that

EEG measures of the reactivity to eyelid opening could effectively predict startle reaction in patients of acute stress reaction; thus routine EEG could be utilized in the diagnosis of startle reaction.[3] In this study, patients with panic disorder having the complaint of "fear of dying" are assessed by use of EEG measures of the reactivity to eyelid opening both at baseline and 6 weeks after the beginning of imipramin treatment, and the findings are correlated with the treatment response.

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The Effect of Haloperidol on Startle Reaction in Patients with Schizophrenia

Bozhuyuk E, Poyraz BC, Savrun BM, Uysal O, Arikan MK, **University of Istanbul, Turkey**

There are reports of altered startle reaction in schizophrenic patients.[1-3] In one study, Arikan et. al. reported that EEG measures of the reactivity to eyelid opening could effectively predict startle reaction in patients of acute stress reaction; thus routine EEG could be utilized in the diagnosis of startle reaction.[4] In this study, patients with schizophrenia currently having delusions of persecution are assessed by use of EEG measures of the reactivity to eyelid opening both at baseline and 6 weeks after the beginning of haloperidol treatment, and the findings are correlated with the antipsychotic response.

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Prediction of Sertraline Response in Posttraumatic Stress Disorder Patients by the Use of EEG Measures of the Reactivity to Eyelid Opening

Bozhuyuk E, Poyraz BC, Yavuz R, Uysal O, Arikan MK, **University of Istanbul, Turkey**

Startle reaction is part of the diagnostic criteria for posttraumatic stress disorder (PTSD).[1-3] In one study, Arikan et. al. reported that EEG measures of the reactivity to eyelid opening could effectively predict startle reaction in patients of acute stress reaction; thus routine EEG could be utilized in the diagnosis of startle reaction.[4] They also argued that it might be possible to predict the effectiveness of drug treatment by measuring the drug's acute effects on startle reaction. In this study, we investigate whether acute effects of sertraline on measured startle reaction could predict anti-PTSD response to treatment with sertraline.

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Startle Reaction in Alzheimer's Disease

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Altered startle reaction has been reported for Huntington's dementia.[1] In one study, Arikan et al reported that EEG measures of the reactivity to eyelid opening could effectively predict startle reaction in patients of acute stress reaction; thus routine EEG could be utilized in the diagnosis of startle reaction.[2] In this study, the relationship between reported startle reaction and the stage of dementia in patients with Alzheimer's disease is assessed and EEG measures of the reactivity to eyelid opening are used to predict this association.

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The Effect of Cognitive Activators on Startle Reaction in Alzheimer's Disease

Poyraz BC, Bozhuyuk E, Bayar MR, Uysal O, Arikan MK, **University of Istanbul, Turkey**

Altered startle reaction has been reported for Huntington's dementia.[1] In one study, Arikan et al reported that EEG measures of the reactivity to eyelid opening could effectively predict startle reaction in patients of acute stress reaction; thus routine EEG could be utilized in the diagnosis of startle reaction.[2] In this study, patients with Alzheimer's disease are assessed by use of EEG measures of the reactivity to eyelid opening both at baseline and 6 weeks after the beginning of Gingko biloba extract treatment, and the findings are discussed.

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Generalized Anxiety Disorder and Startle Reaction

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There are reports of association between anxiety disorders and startle reaction.[1] In one study, Arikan et al reported that EEG measures of the reactivity to eyelid opening could effectively predict startle reaction in patients of acute stress reaction; thus routine EEG could be utilized in the diagnosis of startle reaction.[2] In this study, the relationship between self-reported startle reaction and the symptoms of generalized anxiety disorder (GAD) as defined by DSM-IV TR in patients with GAD is assessed and EEG measures of the reactivity to eyelid opening are used to predict this association.

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The Effect of Venlafaxine on Startle Reaction in Patients with Generalized Anxiety Disorder

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There are reports of association between anxiety disorders and startle reaction.[1] In one study, Arikan et al reported that EEG measures of the reactivity to eyelid opening could effectively predict startle reaction in patients of acute stress reaction; thus routine EEG could be utilized in the diagnosis of startle reaction.[2] In this study, patients with Generalized Anxiety

Disorder (GAD) are assessed by use of EEG measures of the reactivity to eyelid opening both at baseline and 6 weeks after the beginning of venlafaxine treatment, and the findings are correlated with the treatment response.

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Effects of Acute Tryptophan Depletion on the Loudness Dependence in Healthy Female Volunteers

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Introduction: Several studies suggested that the loudness dependence of the N1/P2 - component of auditory evoked potentials is a specific marker for the activity of the serotonergic system. Findings in patients with psychiatric diseases (depression, borderline personality disorder) supported this hypothesis. Studies using the method of acute tryptophan depletion in healthy volunteers failed to prove a significant effect of lowered tryptophan levels on the loudness dependence of the N1/P2 - component.

Methods: Fourteen healthy female volunteers ingested twice a highly concentrated amino acid mixture with (+)TRP or without (-)TRP in a double-blind cross-over study design: In the (-)TRP condition mean plasma levels of tryptophan decreased to 22.3% in relation to the individual basic value. Sinus tones of 1000 Hz of different intensity levels (60-90 dB) were presented binaurally. A 32-multichannel EEG was recorded continuously. Following the averaging procedures we performed dipole source analysis [BESA] applying a model of a tangential and radial dipole per hemisphere.

Results: In the (-)TRP condition subjects showed increasing N1/P2 - amplitude diferences according to increasing stimulus intensity with significant differences within the (-)TRP group. This effect was not found in the (+)TRP condition. The loudness dependency, measured as median slope, was not significantly altered in the (-)TRP condition as compared to the (+)TRP condition. But there was a trend towards a higher intensity dependency in the (-)TRP condition. There were no significant differences for latencies between both study conditions.

Discussion: In line with results of other studies no significant effect of acute tryptophan depletion on the intensity dependence of the N1/P2 - component of auditory evoked potentials could be found. Probably a lowered plasma level of tryptophan does not affect the function of the serotonergic system in the same way as it is assumed to be affected in mentally ill patients. In further studies the influences of other neurotransmitters on the loudness dependence will have to be considered.

P300 Topography and Cortical Source Imaging in Subjects with Bulimia Nervosa

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Introduction: In patients with bulimia nervosa (BN) several neuropsychological dysfunctions have been reported, mainly involving visuospatial abilities, attention, non-effortful learning and executive control. In the same patients, a few studies investigating event-related potentials (ERPs) showed, with respect to controls, a larger amplitude and a prolonged latency of the P300 component elicited by target stimuli, an index of effortful processing. In the present study we evaluated topographic and tomographic characteristics of the auditory P300 in a group of drug-free bulimic patients and one of sex- age- and education-matched healthy controls (HC).

Methods: ERPs were recorded during a three-tone oddball paradigm, in which rare targets were randomly intermixed with rare non-target and frequent standard tones. Topography of P300 was investigated by means of the brain electrical microstate (BEM) technique, while brain sources of the same component were explored by the low-resolution brain electromagnetic tomography (LORETA).

Results: Topographic characteristics of P300 did not show any difference between patients and healthy controls. LORETA showed that, in patients with BN vs. HC, P300 current source density was increased in the left fronto-temporo-parietal regions and in the cyngulate gyrus, while processing rare non-target stimuli. No group differences were observed for target and frequent standard stimuli.

Discussion: In line with previous findings, our results demonstrate preserved effortful processing and impaired automatic allocation of attention in BN patients.

Response Inhibition in Alcoholism: a Simultaneous EEG and Functional MRI Study

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Introduction: Frontal lobe pathology in alcoholism has been well documented. Morphological abnormalities were found as well as electrophysiological and neuropsychological variations and alterations in the cerebral blood flow, especially during tasks sensitive for frontal lobe functions including cognitive inhibitory processes. It is assumed that control processes are impaired in alcohol addicts and may be assessed by a so-called Go/NoGo paradigm. The aim of the present study is to examine which brain regions correlate with deficient control processes in alcohol-dependent patients.

Methods: The study comprises 12 detoxified alcohol subjects. The results are going to be compared to those of age and gender matched healthy controls. Neuronal activity changes are measured during an auditory Go/NoGo paradigm requiring a button-press response in the Go condition and the withholding of the response during the NoGo task.

Results: Preliminary results showed that primarily the inferior prefrontal area, the middle and inferior frontal gyri and the anterior cingulate cortex seemed to be involved in response inhibition. Frontal responses were reduced in alcohol subjects. Besides we found that healthy controls showed additional temporo-parietal activation during the NoGo condition. Concerning evoked potentials, we saw a positive-going P300 over frontocentral sites for the NoGo condition, which was reduced in alcoholics compared with healthy controls.

Discussion: We found reduced cerebral blood flow and evoked potentials in frontal as well as parietal brain regions in alcohol subjects. We assume that frontal dysfunction might be more distinct in patients with abnormalities in affect and emotion, poor motivation or a tendency to impulsivity.

Can Structural MRI Findings be of Diagnostic Value for Schizophrenia?

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Introduction: A classification of mental disorders using biological indices rather than clinical description would be desirable. In order to specify structural characteristics of the brain MRI, we introduced discriminant function analysis and the voxel-based morphometry of SPM99.

Methods: The first analysis was conducted to elucidate a statistical model to classify male healthy subjects (n=30) and schizophrenia patients (n=30) according to the current diagnostic system of ICD-10. The second analysis was performed to be prospectively validated a statistical model by successfully classifying a new cohort that consists of 16 healthy male subjects, 16 schizophrenia patients, and 25 patients with schizotypal disorder.

Results: More than 85 % of the subjects were correctly classified by the eigenimage of the discriminant analysis. The pattern of eigenimage was characterized by negative loadings in the medial and lateral prefrontal regions and the positive loadings in the basal ganglia and cerebellum. As further validation, the eigenimage correctly assigned more than 80% of a new group of healthy subjects and schizophrenia patients. Schizotypal disorder patients occupied an intermediate position.

Discussion: These findings indicate that certain characteristic distribution of structural gray matter change is pathognomonic and have diagnostic value of schizophrenia. In order to improve diagnostic specificity further analysis is essential within cohorts of schizophrenia spectrum disorders.

The Effects of Exercise on Brain Electrical Activity and its Relationship to Mood

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Introduction: Exercise is often used to treat anxiety and depression. Limited research suggests that exercise can also influence QEEG. As a result, we hypothesized that 30 minutes of aerobic exercise would contribute to regional increases in brain electrical activity that were associated with an improvement in mood.

Methods: Seven healthy males between the ages of 24 and 69 who exercised regularly (3 - 5x a week) were included in this study. Eyes closed QEEG were recorded before and after participants rode a TechnoGym upright stationary bicycle at 75-80% of their anaerobic threshold for 30 minutes. QEEG were recorded from 19 electrodes and referenced to linked ears. QEEG files were edited and analyzed with NeuroGuide and NeuroStat. Edited QEEG files were between 30 and 97 seconds long with individual electrode split-half and test-retest reliabilities no less than .90. The POMS, BDI, and STAI were used to assess pre- and post-exercise mood states.

Results: Following exercise the participants demonstrated a bilateral statistically significant increase ($p < .001$) in alpha absolute power in the frontal lobes and a decrease in negative mood states, particularly anger.

Discussion: Exercise may help ameliorate affective symptoms by having a soothing effect on the brain. Additional research is necessary to establish the duration of this change. Patients with affective disorders may benefit from having an exercise regimen included in their treatment plan.

Frontal Alpha Activity in Aggressive Children and Adolescents With Mood and Disruptive Behavior Disorders

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Introduction: EEG studies with nonclinical samples have demonstrated that elevated relative left frontal activity is associated with anger, aggression, approach tendencies, and increased behavioral activation. The main objective of this study was to determine whether these findings are generalizable to psychiatric pediatric patients with affective and disruptive behavior disorders coupled with impulsive aggressive behavior. Building on prior research, the study tested the hypothesis that proneness to impulsive aggression would be related to greater relative left frontal activation. It was also predicted that there will be a positive correlation between the magnitude of increased left frontal activation and the severity of psychiatric dysfunction.

Methods: The sample consisted of 65 male pediatric psychiatric patients with mood and disruptive behavior disorders coupled with aggressive and antisocial conduct. Subjects ranged in age from 5 to 17 years, with a mean age of 11 (SD = 2.8). At the time of qEEG examination, 47 subjects were medicated and 18 subjects were medication-free.

Eyes closed one-hertz alpha absolute power was computed in Neuroguide 1.7.4.

Results: Forty-one subjects (63%) had significant greater relative left frontal activation, 15 subjects had greater relative right frontal activation, and 9 subjects showed no significant frontal alpha power asymmetry. Relatively greater left frontal activity correlated positively with the severity of psychiatric disturbance.

Discussion: The findings suggest that elevated left frontal activity may be one locus of neurophysiological disruption in pediatric psychiatric patients with aggressive and impulsive behavioral tendencies.

Kinematical Analysis of Handwriting Movements in Patients Suffering from Depression

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Background: Motor retardation is a relevant aspect of depression. Kinematical analysis of movements can be applied to explore which type of motor dysfunction is associated with this disorder. Using this tool, we aimed to investigate fine motor performance in patients suffering from depression. In this context, we hypothesized that depressed patients draw and write significantly slower than controls and that motor disturbances become more pronounced under bi-manual demands.

Methods: We examined 37 depressed patients and 37 healthy subjects using a digitizing graphic tablet and subsequent kinematical analysis of handwriting and rapid drawing movements. Both groups were comparable regarding mean age, gender distribution, handedness (preponderance of right-handers) as well as educational level.

Results: Depressed patients performed drawing with significantly less regular velocity than controls ($p < 0.001$), but normal velocity. Motor differences between depressed patients and controls did not increase under bi-manual demands. Handwriting of depressed patients was abnormally slow ($p = 0.04$).

Discussion: Irregular patterns of velocity peaks in depressed patients point to basal ganglia dysfunction and/or deficient activity of the sensorimotor cortex and the supplementary motor area as a possible substrate of hand-motor disturbances in depression.

Effects of Reboxetine and Citalopram on Hand Motor Function in Depressed Patients

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Background: Many antidepressants have motor side effects. Computerized methods allow the objective registration of drug-induced movement disorders in depression. A selective noradrenaline re-uptake inhibitor (reboxetine) and a SSRI (citalopram) were compared regarding motor side effects after four weeks of treatment.

Methods: We examined different types of hand movements in 16 depressed patients receiving citalopram (flexible dosage) and 12 depressed patients treated with reboxetine (varying dosage) using a digitizing graphic tablet and software for the analysis of movement dynamics. Both groups were comparable regarding age, gender, handedness and the baseline Hamilton Depression Rating Scale total score.

Results: Reboxetine led to a significant improvement of repetitive drawing movements in depression. In contrast, citalopram revealed no pronounced effects on hand movements in depressed patients.

Discussion: Computer-aided analysis of hand movements is a valid and sensitive tool for the registration of differential pharmaceutical effects on motor function in depression.

Quantitative EEG and Neurofeedback in ADHD

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Introduction: Attention Deficit Hyperactivity Disorder (ADHD) is the most common mental dysfunction affecting about 3-5% of all children. A modem neurobiology oriented approach considers ADHD subtypes to be associated with the impairment of different neuronal circuits in the frontal lobe-basal ganglia-thalamic executive system (Castellanos, 1997; Kropotov, 1997). Neurofeedback is used in the treatment of ADHD. The nature of ADHD is complex, and requires a complicated neurofeedback protocol management.

Methods: Thirty-nine children with ADHD took part in the investigation. They were given relative beta training. A 19-channel EEG was recorded simultaneously for one training session, as well as before and after the course of neurofeedback.

Psychologiycal Test of Variables of Attention, or TOVA (Greenberg, 1987) was carried out before and after the course of neurofeedback.

Results: Widespread changes were observed in alpha, beta and theta range during one beta session. Twenty sessions of EEG relative beta training improved the quality of performance and led to a significant increase of beta rhythm in the frontal area and decrease of alpha rhythm in parietal and occipital areas.

Discussion: This study is the first to show that not only psychological indexes of behavior, but also quantitative EEG are “improved” after beta training, which in turn indicates that the neurofeedback training changes the executive system of the brain. Application of EEG spectrograms for constructing individual protocols of neurofeedback is discussed.

Electrophysiological Correlates of Error Processing in Patients with Borderline Personality Disorder

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Background: The electrophysiological correlates of impulsiveness were investigated in patients with borderline personality disorder (BPD) using event-related potentials (ERP).

Methods: Twelve patients with BPD and 12 healthy controls performed a Go/Nogo task while a 64 channel EEG was recorded. The focus was on three ERP components: the error negativity (Ne) / error-related negativity (ERN) and the "early" error positivity (EPe) reflecting automatic error processing and the "late" error positivity (LPe) which is thought to mirror the awareness of erroneous responses. All subjects were rated with the Barratt Impulsiveness Scale; Version 10 (BIS-10).

Individual mean reaction time residual scores (R-) were calculated for all participants. Less negative R- were regarded as indicating a more cautious (controlled) response strategy whereas more negative R- were interpreted to indicate a less controlled (i. e., more impulsive) response style.

Results: We found smaller amplitudes of the Ne/ERN in patients with BPD compared to controls. Moreover, significant correlations with the BIS-10 and R- could be demonstrated for the entire group. With regard to EPe and LPe, there were no differences between groups.

Discussion: ERP measures appear to be a valid tool to indicate levels of impulsiveness in BPD patients, opening a new approach to study clinical time courses of BPD.

Electrophysiological Correlates of Error Processing in Patients with Obsessive-Compulsive Disorder

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Introduction: Obsessive-compulsive disorder (OCD) has been related to deficits in action monitoring and error processing, and it has been hypothesized that hyperactive striatal-cortical circuits constitute the underlying pathophysiology.

Methods: Eleven patients with OCD and 11 matched healthy controls were rated with the Yale-Brown Obsessive Compulsive Scale (Y-BOCS) and performed a Go/Nogo task afterwards while a 64 channel EEG was recorded. Three ERP components were of special interest: the error negativity (Ne) / error-related negativity (ERN) and the "early" error positivity (EPe) reflecting automatic error processing and the "late" error positivity (LPe) which is thought to mirror the awareness of erroneous responses.

Results: Patients with OCD showed enlarged (more negative) Ne/ERN amplitudes compared to controls. Moreover, significant correlations with the Y-BOCS could be demonstrated for the entire group. There were no group differences with regard to EPe and LPe amplitudes.

Discussion: Our data corroborate previous studies on error processing in OCD. Whether the Ne/ERN amplitude is modulated by clinical course and treatment response appears to be a reasonable target for future ERP studies in OCD patients.

Electrophysiological Correlates of Error Processing in Patients with Major Depressive Disorder

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Introduction: Perceived failure is reported to have detrimental effects on subsequent performance in patients with major depressive disorder.

Methods: We investigated the error related negativity (ERN) / error negativity (Ne), an electrophysiological correlate of response monitoring, using a 64-channel EEG. Sixteen patients with DSM-IV major depressive disorder and 16 matched controls participated in an Eriksen flanker task with continuous performance feedback which signaled monetary reward.

Results: Compared to controls patients with major depressive disorder showed a less negative ERN/Ne in error trials (trial n) following error trials (trial n-1).

Discussion: This result might reflect impaired response monitoring processes in major depressive disorder resulting from an underactivity in a central reward pathway and / or a deficit in strategic reasoning.

Electrophysiological Correlates of Impulsiveness in Normals

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Methods: Electrophysiological correlates of impulsiveness were investigated in 32 healthy subjects using event-related potentials (ERP). Impulsiveness was determined by calculating individual reaction times (as function of general response speed) in order to split the entire group into two subgroups with a more controlled (n = 16) and less controlled (n = 16) response style. Participants performed a Go/Nogo task while a 64-channel EEG was recorded. Artifact-free EEG segments were used to compute ERPs on correct Go trials and incorrect Nogo trials, separately. Three ERP components were of special interest: the error-related negativity (ERN) / error negativity (Ne) and the "early" error positivity (Pe) reflecting automatic error processing and the "late" error positivity (Pe) which is thought to mirror the awareness of erroneous responses.

Results: Subjects with higher impulsiveness showed smaller amplitudes than subjects with lower impulsiveness for the ERN/Ne component and the "early" Pe component. With regard to the "late" Pe groups did not differ.

Discussion: Hence, ERP measures appear suitable for detailed analyses of impulsiveness in healthy participants. Moreover, present results argue for the necessity of careful control of impulsiveness when including normal comparison groups in the context of clinical studies.

Cognitive Functions and Brain Bioelectrical Activity of Hyperactive Children

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Introduction: The increase of nervous system disorders among children in the last years was observed. One of the most wide-spread groups of children with nervous system disorders is the group of hyperactive children.

Methods: The analysis of brain bioelectrical activity of 90, 4-7 years old, children with symptoms of hyperactivity was carried out. Behavior reactions (orientation in the closed labyrinth and latent period of simple and complex sensomotor reactions) of 90 children were observed. The cognitive functions of children were estimated. In the electroencephalograms (EEG) of hyperactive children separate diffuse slow rhythms and separate epi-complexes were registered.

Results and Discussion: In 45% of hyperactive children EEG disturbances in the frontal zones of brain hemispheres bioelectrical activity were observed. It showed that frontal regions control movement excitability processes from one side, and regulation of attention and emotional sphere from the other side and therefore regulate the behavior of children. The dysfunction of frontal zones is one of the main reasons for the complex of symptoms which are characteristic for hyperactive children. The correlation analysis of EEG and behavior reactions showed that those children in which EEG bursts of slow rhythms were registered and the quantity of slow rhythms increased after functional loads (sound, rhythmic light stimulus, hyperventilation) have decreased possibilities of orientation in the closed labyrinth and longer latent periods of simple and complex sensomotor reactions.

A Cross-Cultural Study of Facial Emotion Recognition Using an Event-related Functional MRI

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Introduction: Several psychological studies have shown that behavioral performance of face recognition task for the same-race face is superior to that for the other-race face. Recently, neuroimaging studies have investigated this phenomenon called "in-race advantage" and revealed differential activation in the face-related regions in the human brain. The present study aimed at elucidating how the brain activation differs when Japanese subjects judged the facial expression of the same- and other-race faces.

Methods: Twelve healthy Japanese volunteers participated in the study after giving informed consent. The subjects were scanned using 3T MRI scanner while they were judging expression (happy or neutral) of facial pictures of Japanese, Caucasian, and non-Japanese Asian. The imaging data were analyzed using SPM2 and a random-effects model.

Results and Discussion: The Japanese subjects' neural response to the Japanese faces was significantly ($p=0.001$, uncorrected) greater than that to the other-race faces. When the Japanese face was compared with the non-Japanese

Asian face, significant differences in activation were found in the right fusiform gyrus, right parahippocampal gyrus, and the left amygdala. The right parahippocampal gyrus and visual cortices showed greater activation for the Japanese faces than for the Caucasian faces. These differential neural responses in the limbic and other areas may be a neural basis of the in-race advantage.

Functional Connectivity Between the Auditory Cortex and the Anterior Cingulate Cortex (ACC) Using EEG and fMRI

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The ACC is seen in connection with various cognitive abilities, including attention control and conflict processing. In addition, several studies have shown that its function is disturbed in some psychiatric disorders, e.g., schizophrenia. Aim of this study is to show the functional connectivity between ACC and auditory cortex exemplarily. Doing this, special attention is paid to the gamma-frequency range (40 Hz) of the EEG, which plays an important role in the process of synchronizing cortical activation, as well as the amplitude of N1 and the fMRI BOLD signal in the examined cortical areas.

Healthy Subjects (n=20) have been examined via fMRI (1.5 T Siemens Sonata) and simultaneous EEG recording (64 channels, Brainproducts). Three different auditory choice reaction paradigms were used at different levels of difficulty / response conflict. During the measuring we turned the coolant pump of the MR off in order to avoid artifacts in the gamma frequency range. With rising difficulty of the paradigm the amplitude of the N1 and the activity in the gamma frequency range increases in the EEG (Fz). Similarly the number of activated voxels in the ACC region increases. Preliminary results suggest that the transient gamma peak after 50 ms post-stimulus is generated in both auditory and cingulate areas. This suggests a 40-Hz synchronization of both regions in cognitive information processing.

EEG Related Changes in Vigilance and Their Correlates in MRI Sequences

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Electroencephalogram (EEG) based measurement of different states of vigilance has become a well established tool in clinical diagnosis, whereas the anatomic and topographic correlates of this phenomenon still remain mainly unknown.

A solution to this problem could be achieved by measuring the association of EEG related changes in vigilance and simultaneous magnet resonance imaging (MRI) recordings. Therefore, 20 healthy volunteers aged between 19 and 34 years were tested for 35 minutes in resting conditions. As a method for reducing fMRI artifacts in EEG data an average subtraction method included in the Vision Analyser software was found to be superior to the independent component analysis (ICA) for its higher level of efficiency. According to indicators of the different states of vigilance like the anteriorization level of alpha waves, postulated by W. Ulrich, spectral bands are being determined with Fast Fourier Transformation (FFT) in 2-second epochs of the EEG recording. Afterwards the EEG epochs corresponding to four different levels of vigilance were related to the fMRI sequences. A fundamental issue now is to ascertain whether there is a connection between changes of vigilance in EEG and anatomic structures and their activation in the brain.

Positive findings within this study would push the frontiers of forecasting the global states of mind further on.

Measuring Reliability of Loudness-Dependent Auditory Evoked Potentials Connected to Central Serotonergic Neurotransmission in Functional MRI

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Central serotonergic neurotransmission has been subject of psychiatric research in order to identify its role in depression. Low serotonin levels are thought to be related to the depressive syndrome (e.g., therapeutic use of SSRI). Yet a practical and reasonable method to measure the quantity of central serotonergic neurotransmission still has to be developed. Preclinical and clinical evidence suggests a clear relationship between the firing rate of serotonergic neurons in the brain and the auditory N1/P2-component of loudness-dependent auditory evoked potentials. Recently a link between the N1/P2-component and functional MRI activity in the primary auditory cortex has been shown. The advantage of MRI in compari-

son to ERP analysis consists in the high-resolution spatial representation of brain activity, which is important since only the primary auditory but not the secondary auditory cortex shows a high serotonergic innervation. Earlier analyses have shown high test-retest reliability for the N1/P2 component. The present study is intended to analyze the retest reliability of the fMRI-sound level dependence measurements. In two runs healthy volunteers receive acoustic stimuli over MRI-capable headphones for 30 minutes. The first run consists of measuring a 64-channel electroencephalogram and stimulus-synchronized functional MRI. During the second run the N1/P2 component is measured outside the scanner. These runs are repeated one month later to evaluate retest reliability. Preliminary results indicate a close relationship between electroencephalography and functional MRI. The advantage of high-resolution, in-depth views of brain activity as provided by functional MRI yields a promising approach to an applicable determination of serotonin levels. The present study has to be completed to analyze the reliability of activity in the primary auditory cortex measured by functional MRI.

Altered Early Auditory Processing and Underlying Mechanisms in Major Depression Disorder Revealed by Combined MEG and EEG

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Introduction: We investigated whether major depression disorder (MDD) affects brain mechanisms of involuntary attention with combined MEG and EEG.

Methods: Twelve drug-free patients with unipolar MDD during acute episodes and 12 age- and sex-matched healthy subjects were presented with frequent standard, infrequent deviant tones (10 and 20% frequency change), and occasional complex novel sounds to the left ear.

Results: P50 and P50m latencies were decreased in patients with MDD as compared with those in healthy subjects. The amplitude of mismatch negativity (MMN), elicited to the 10% frequency changes, was in turn increased in patients with MDD. There were no differences in N1 and P3a responses in MEG and EEG.

Discussion: The pattern of MMN change observed in patients in MDD was similar to that obtained in healthy volunteers investigated for the effects of acute tryptophan depletion, a procedure known to decrease serotonin synthesis in the brain (Kähkönen et al. Psych Res Neuroimaging, 2005). Further, negatively charged visual stimuli decreased P50m suppression in healthy subjects (Yamashita et al. Eur Arch Psych Clin Neurosci, 2005), suggesting that depressed mood may affect early auditory processing. In conclusion, deficiency in serotonin metabolism may disrupt brain inhibitory mechanisms during acute episodes of MDD regulating early sensory and attentional processing. These effects are probably mediated through fronto-temporal neural circuit.

Award Posters

Volitional Action as Assessed by Magnetoencephalography

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Introduction: Volitional action has been studied using various paradigms. Free selection paradigms have shown intentional activity in the anterior cingulate (ACC). Go/nogo and free response paradigms have also shown the supplemental motor area to precede volitional movements. Our goal was to better define the spatiotemporal characteristics of volition using a novel magnetoencephalography (MEG) paradigm.

Methods: We used a modified go/nogo task in 5 healthy young adults. After a warning stimulus subjects were presented with either a green (go), red (nogo) or yellow stimulus (subject's choice to go/nogo). Data were collected with a whole scalp MEG system.

Results: There was a rapid rise of activity in the ACC region following S2 and preceding motor responses in all conditions. Primary motor activity was noted in both nogo conditions at similar latencies to go conditions. There was marked variability in patterns among subjects with regards to the yellow stimulus.

Discussion: The ACC appears to be important in both volitional movement and inhibition. Prior research using other tasks has shown the ACC with high stimulus-response conflict. The motor cortex was activated in nogo conditions, consistent with previous electrophysiological research. Variability in free selection conditions may reflect strategic and/or physiologic differences among subjects.

Chronic Mild Stress Induces Depressive Behaviors in Adult But Not Young Rats: Potential Role for AMPA Receptors

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Introduction: Chronic mild stress (CMS) in adult animals is known to induce depressive-like behaviors, but the effects of CMS on young animals has not been studied.

In this study we compared behavioral as well as neurochemical effects of CMS on young and adult male rats.

Methods: We have used a standard protocol of CMS (food and/or water deprivation, cage tilt, white noise and wet bedding). We performed measures of spontaneous locomotor activity in the home cage, explorative behavior in an open field, the forced swim test, preference for sweet solutions and sexual behavior tests. We have also compared expression of AMPA receptors within specific reward-related brain regions using immunohistochemistry.

Results: CMS in the adult group causes anhedonic effects such as decreases in male sexual behaviors and in sucrose preference, but no such difference was observed in the young group. The adult CMS rats visited the center of the open field less often than controls indicating some increased anxiety. Such effect was not observed in the young CMS rats. No significant effect of CMS was observed in the swim test or the spontaneous locomotion in either adult or young rats.

Discussion: The GluR1 subunit of the AMPA receptor in the prefrontal cortex was significantly decreased in both young and adult CMS groups, therefore this change cannot account for the anhedonic effects induced by CMS. In the nucleus accumbens, GluR1 receptor level was altered only in the adult CMS animals. This alteration possibly implicated the anhedonia observed in adult, but not in young rat.

EEG Effects of Gustatory, Olfactory and Visual Stimuli in Anorexia Nervosa

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Introduction: The effect of pleasant and unpleasant gustatory and olfactory stimuli, neutral and provocative visual stimuli was investigated in this study on the electroencephalogram (EEG) to obtain data corresponding to the possibly altered central processing mechanisms of these stimuli.

Methods: The pleasant and unpleasant gustatory and olfactory stimuli were exposed for 2 minutes. A neutral video film and one concerned with preparation of cake was shown, each for two minutes. Power spectrum analysis was performed on the EEG recorded according to the 10-20 system by Neuroscan. The EEG was recorded for 2 minutes during the smell exposure and visual stimuli, and right after the taste exposure.

Results: In AN patients lower dimensional complexity and higher theta power were observed than that seen in controls, independent of taste conditions. Higher Omega complexity was seen in control subjects on the left side irrespective of taste effects. No such hemispheric difference was observed in AN.

Discussion: The deviations from normal control state in AN patients (higher theta power and lower dimensional complexity) as revealed by linear and nonlinear EEG analysis, may correspond to long lasting effects of brain dysfunction. The lack of a significant Omega complexity change after the different taste exposures seen in AN patients may correspond to a decreased sensitivity to such stimuli in these subjects. Both in the control and in the AN group the odorant and the visual stimuli increased the beta1 and beta2 frequency bands, probably corresponding to increased level of vigilance.

Hemispheric Differences in N100 Auditory Sensory Gating in Schizophrenics

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Introduction: Auditory P50 sensory gating deficits are consistently documented in schizophrenics and may be related to impaired attention. Recent findings suggest selective left hemisphere deficits in schizophrenia, but hemispheric contributions to sensory gating are seldom explored. Furthermore, gating traditionally consists of P50 amplitude ratios between paired auditory stimuli. However, the N100 and P200 may provide additional indices reflecting different aspects of the gating process.

Methods: Auditory evoked responses to 60 binaural paired clicks (500 ms inter-click interval; 8 seconds between pairs) were obtained from 14 stable medicated (atypical anti-psychotics) outpatient schizophrenics and 14 individually age and gender matched healthy controls. Sensory gating was calculated as the ratio of P50, N100, and P200 amplitudes to the second and first stimuli measured at the left and right mid-temporal and frontal electrodes.

Results: A one-way ANOVA assessed gating differences between schizophrenics and controls. The mean left frontal N100 gating ratio was 90.3% (s=38.8%) for schizophrenics and 55.6% (s = 26.2%) for controls ($F = 7.597$, $p = .01$). No significant differences occurred at the right frontal site (71% vs. 59%). Mid-temporal gating approached a significant deficiency for schizophrenics on the left ($p=0.075$) but not the right ($p=0.189$).

Discussion: Preliminary data suggest that left hemisphere dysfunction may contribute to N100 sensory gating deficits in schizophrenics.

Semantic Integration in Deaf Signers and Hearing Nonsigners: an ERP Study

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Introduction: In order to investigate the modality specificity of the left hemisphere's dominance for language functions this study investigates semantic processes in German Sign Language (Deutsche Gebärdensprache = DGS), a language which uses visual-spatial Input- and Output-modalities. For sound language, the N400 component is a robust effect representing the semantic integration of a stimulus into a given context. The amplitude has its negative peak with a latency of 400ms after representing a semantically incongruent sentence-ending (e.g.: The coffee was too hot to cry). The effect even persists after presentation of word-pairs when the second word is semantically unrelated to the first word (e.g. coffee - tea; coffee - tape). ERPs are registered in deaf signers while they are watching video-taped semantically congruent and incongruent sign-pairs in DGS in search of the N400 in sign language.

Methods: Behavioral and ERP data are collected from 12 deaf signers and 12 hearing non-signers. They are matched for age, education and sex. All participants are right-handers. The stimuli are 80 pairs of semantically congruent and incongruent noun-adjective pairs in each groups' natural communication-modality (German for hearing paricipants and DGS for

the deaf). ERP signals are registered with a multichannel-electrode montage. Evaluation of N400 components will enclose a dipole source analysis.

Results and Discussion: Work is still in progress. In correspondence to lesion data and fMRI-studies on sign language processing that document overlapping perisylvian networks for sign and sound language, an N400 effect is expected for semantically incongruent sign-pairs in deaf signers. If so, this could be interpreted as evidence for the left hemisphere's language dominance being at least partly independent from Input- and Output-modalities.

Acknowledgement: The Research project is supported by a grant of the "Interdisciplinary Centre for Clinical Research" of the Medical Faculty of the RWTH Aachen University (BMBF grant No. 01KS9503/9).

Effects of Add-on Melatonin Administration on Sleep Behavior in Epileptic Children: a Randomized Double Blind Placebo Controlled Trial

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Introduction: Studies on sleep problems in children are promising, but limited. Children with epilepsy show higher rate of sleep problems and disturbed daytime behavior. Chronic sleep disorders can affect the child's development adversely, as sleep plays a major role in the early maturational processes in the brain

Methods: The study was a double-blind, randomized, placebo controlled trial in epileptic children. The effect of add-on melatonin on sleep behavior of children, aged 3-12 years, on valproate (VPA) monotherapy was evaluated using a parental sleep behavior questionnaire. The questionnaire is a validated instrument to facilitate investigation of sleep behavior in general pediatric population.

Results: Of the 31 patients who met the entry criteria, 16 randomly received add-on melatonin (MEL), whereas 15 received add-on placebo (P). The questionnaire showed good internal consistency in our patient population (Cronbach's alpha=0.83). The percentage decrease in the median total sleep score was 24.4 (range: 0.0-34.9) in the VPA+MEL group, as compared to 14.0 (range: -2.2-18.8) in the VPA+P group, the difference being statistically significant ($p<0.05$). The median percentage decrease in the parasomnias score was 60 (range: 0.0-70.8) in the VPA+MEL group as compared to 36.4 (range: 0.0-63.2) in the VPA+P group, the difference being statistically significant. ($p<0.05$). There was no significant difference between the percentage decrease in the daytime drowsiness scores, and sleep fragmentation scores. Parent-child interaction subscale scores were not significantly different between the age groups. The age of onset of seizures, and the type of seizures did not correlate significantly to the total sleep scores.

Discussion: The fact that sleep problems are known to complicate epilepsy, add-on melatonin, which has a wide safety window, can be of promise in pharmacotherapy of pediatric epilepsy.

Neuroleptics-Related Neuromuscular Dysfunction: Results of Large-Scale Prospective Comparative Study

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Introduction: The purpose of this study was to estimate prospectively the actual incidence and the severity of neuromuscular dysfunction in psychiatric patients treated with typical (TN) and atypical neuroleptic agents (ANA) and to evaluate them neurologically for possible muscular and peripheral nervous systems involvement.

Methods: We screened 590 adult patients who began their treatment with TN and ANA. Patients with idiopathic hyper-CKemia, suffering from any significant physical disorder, receiving parenteral medication/ECT were excluded. Blood samples for CK determinations were collected at baseline and at weeks: +1, +2, +3, +4, +8, +12 and every 3 months thereafter, up to one year. Patients with persistent hyper-CKemia were assessed neurologically for possible muscular and peripheral nervous systems involvement.

Results: We recruited 244 eligible patients receiving clozapine, olanzapine, risperidone, quetiapine, haloperidol and perphenazine. During the study, 1600 blood samples were collected and 11 evaluated patients were found having persistent hyper-CKemia - 545.5 ±230.7 IU/L, in range 250-950 IU/L. Five of these patients had complaints of some muscular weakness and in 2 of them clinical assessment revealed mild general muscular weakness, especially in the proximal parts of the limbs. Another 17 patients exhibited occasional hyper-CKemia, however, their neurophysiological examination did not revealed any kind of neuromuscular pathology.

Discussion: The incidence of the persistent hyper-CKemia in our sample (4.5%) is compatible with previous reports. However, the magnitude of hyper-CKemia is less than reported previously (1000-10000 IU/L). Majority of hyper-CKemic patients were treated with ANA (clozapine and olanzapine), however, only in a few of them (18%) some neuromuscular (mostly myopathic) dysfunction was found. Further investigation of neuromuscular dysfunction, its mechanisms and pathophysiological significance is warranted.

Cognitive Function in Schizophrenia Patients Evaluated by NexAde, Correlation to Disease Severity Parameters

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Introduction: Cognitive impairment among schizophrenia patients is well established, yet more data is needed regarding cognitive impairment in relation to disease severity parameters.

Methods: Fifty-two patients (25 females, 27 males, ages 30-55) participated in the study, all diagnosed with schizophrenia or schizoaffective disorder. The patients were compared to 50 age and sex matched controls.

NexAde is a computerized neuropsychological assessment software that was validated in a large group of memory impaired subjects and controls, including computer-naive patients (Comp Methods Prog Biomed 2004;73:43-53). The parameters measured by the software were: focused attention, sustained attention, memory recognition, memory recall, visuopatial learning, spatial short term memory, executive functions, and mental flexibility.

Demographic data, data about disease duration, PANSS, and Calgary depression scale (CDS), were also collected. All patients went through 1 (32 patients), 2 (12 patients) or 3 or more (8 patients) cognitive assessment sessions.

Multivariate analysis was performed as well as rule based prediction.

Results: The patients found the software friendly and easy to use, and all but 2 completed the test. Sustained attention, memory recall, executive functions, and mental flexibility, were inferior among patients as compared to controls ($p<.05$), and all were related to PANSS (positive, negative, and total), CDS and disease duration, with success prediction rate of 0.904, 0.808, 0.923, 0.846, respectively.

Discussion: Schizophrenia patients are impaired in some, but not all, cognitive functions assessed. Those functions are also related to disease severity. NexAde is suitable for use in patients with schizophrenia or schizoaffective disorder.

Brain Potential P3b Amplitude Correlates with Borna Disease Virus Infection in Obsessive-Compulsive Disorder

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Introduction: Borna disease virus (BDV) is found in obsessive-compulsive disorder (OCD) and is supposed to be a possible etiopathogenetic factor in this disorder. However, how BDV impacts behavioral and neurophysiological disturbances in OCD is still unknown. In the current study we are addressing the question, whether BDV infection in OCD patients leads to detectable changes in the neural correlates of cerebral information processing as quantified by event-related brain potentials (ERPs).

Methods: In a visual Go/Nogo experiment, attentional processes were investigated by ERP component P3b in OCD patients and healthy controls (n = 12, each). The patients were only differing by serum levels of BDV-specific circulating immune complexes (CICs) and formed into two subgroups by a median split: group H with high CIC levels and group L with low CIC levels.

Results: The OCD group H showed increased amplitudes of brain potentials (components N1 and P3b) compared to group L and controls. Statistically positive correlations were found between BDV-CICs and the mean amplitudes of target P3b over the parietal region. As based on LORETA analysis, OCD group H showed significantly higher localized brain activations for the target P3b at the left posterior cingulate (Brodmann area 29/31) compared to the controls.

Discussion: The present data show a significant correlation of BDV infection parameter (CICs) with neurophysiological abnormalities associated with a hyperactivity of striato-thalamo-cortical networks in OCD. It is suggested that such disturbance is influenced by BDV infection.

Gestalt Perception and Gamma-Band Oscillations in Schizophrenia

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Introduction: There is evidence to suggest that schizophrenia patients are characterized by deficits in the integration of stimulus-elements into coherent object representations as well as by abnormal gamma-band activity (Phillips, Silverstein, 2003). It is unclear, however, whether deficits in Gestalt perception are the result of abnormal gamma-band activity in schizophrenia patients or whether these two deficits are independent.

Methods: We studied perceptual integration with Mooney faces in schizophrenia patients (N=19) and normal controls (N=19). Mooney faces consist of degraded pictures of human faces where all shades of gray are removed, thereby leaving the shadows rendered in black and the highlights in white. Perception of Mooney faces involves the grouping of the fragmentary parts into coherent images and is related to synchronization of neural activity in the gamma-band in normal subjects (Rodriguez et al. 1999). We measured induced and evoked-gamma band power as well as phase-synchronization in response to Mooney faces in the scalp-recorded electroencephalogram (EEG) to examine the synchronization of neural circuits in schizophrenia.

Results: Compared to normal controls, schizophrenia patients: 1) were significantly impaired in the detection of faces; 2) showed both significantly reduced gamma-band power and phase synchronization; and 3) were characterized by reduced amplitudes of the P1 event related potential (ERP) component.

Discussion: The results provide evidence for the hypothesis that dysfunctional Gestalt perception is related to aberrant gamma-band activity in schizophrenia, suggesting that deficits in binding mechanisms may constitute a core impairment that underlies the fragmentation of mind and brain in the disorder.

White Matter Hyperconnectivity and Psychopathology of Schizophrenia - a Diffusion Tensor Imaging Study

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Diffusion Tensor Imaging (DTI) studies of fractional anisotropy (FA) values in schizophrenia patients suggest a widespread disturbance of white matter integrity. However, the relationship between these findings and psychopathology of schizophrenia is not well understood.

We examined a group of chronic schizophrenia patients, who underwent neuropsychological and clinical testing, including Positive and Negative Syndrome Scale (PANSS), followed by anatomical and spin-echo EPI DTI (TR/TE 5400/80ms, 40 slices, 1.8x1.8x2mm^3 voxel size) MRI scan. Diffusion weighted images were acquired in 6 directions with b value = 1000s/mm^2. The original voxel size was interpolated to 1x1x1mm^3. The data was aligned to high-resolution T1 weighted anatomical images and transformed into Talairach space. The resulting datasets were spatially smoothed with a 7mm Gaussian kernel. FA maps were calculated for all patients. Voxel-wise correlation coefficients between individual FA values and PANSS general score and positive and negative subscale scores were calculated.

FA values in corpus callosum and projection fibers to sensory cortex were positively correlated with general and negative subscale PANSS scores ($p<0.05$). FA values in left capsula interna and right inferior frontal gyrus were negatively correlated with positive subscale of PANSS while FA values in truncus of corpus callosum were positively correlated with that subscale.

Previous studies mainly focused on evidence for local hypoconnectivity. Our results suggest that widespread hyperconnectivity might also contribute to the psychopathology of schizophrenia. Such pattern of anatomical connectivity may result in dysfunctional coactivation of brain regions leading to difficulties in processing of relevant information.

Preattentive and Attentive Information Processing in Schizophrenia with Cannabis Abuse: an ERP Study

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Introduction: Cannabis abuse is discussed as an independent risk factor for schizophrenia. Little is known about the influence of cannabis use on the disrupted preattentive and attentive information processing in schizophrenia.

In a preliminary study we found a partial deficit in the late phase of the attentive sensory gating process in a group of healthy cannabis users. This deficit could not be demonstrated in schizophrenic patients with and without cannabis use.

In the present investigation we aimed to confirm those results in a much larger sample.

Methods: Clinically stable, medicated schizophrenic patients with and without former cannabis abuse (n=50), former cannabis users (n=25) and healthy controls (n=25) were examined in a passive auditory paired stimulus paradigm. The sensory gating index for the potentials P50, N100, P200 and N200 were measured.

Results: In contrast to our preliminary results we found no gating deficit in the late phase of the information processing in the larger sample of healthy cannabis users. Additionally, there was no marked gating deficit among the four groups with respect to the other evoked potentials. However, the schizophrenic cannabis users showed a significantly lower amplitude of P50 compared to the schizophrenic patients without cannabis use.

Discussion: Cannabis seems to impair auditory evoked potentials in schizophrenia even further which might correspond to its disease-deteriorating properties.

Sensory Gating of Intracranially Recorded Gamma Band Activity

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Introduction: Various cognitive processes are assumed to be reflected in gamma band activity (GBA) around 40 Hz. The functional relation between components of the auditory evoked potentials (AEPs) and GBA is still unresolved. We studied GBA in an auditory sensory gating experiment by intracranial recordings.

Methods: Cortical activity was recorded from lateral surface of the temporal lobe in 34 epileptic patients undergoing presurgical evaluation.

Results: In 18 patients, the AEP components P50 and N100 were observed at intracranial leads. At electrodes with maximal P50, evoked GBA occurred with a similar peak latency as the P50. However, the P50 amplitudes and power values of the evoked GBA (30-50 Hz) were only modestly correlated. Surprisingly, the peak frequency of the evoked GBA was on average relatively low (~25 Hz). Some of the subjects exhibited also an induced GBA, encompassing frequencies from 30 up to 200 Hz. The induced GBA was increased after stimulation for several hundred milliseconds. Single trial analysis revealed that this GBA consisted rather of small bursts than longer ongoing oscillations. Evoked and induced GBA, as well as P50 and N100, were strongly suppressed by stimulus repetition.

Discussion: Current data indicate that the intracranial P50 does not represent a subset of evoked GBA. However, the low frequency of the evoked intracranial GBA suggests that this activity is not equivalent to extracranially recorded GBA, which has normally a peak frequency of ~40 Hz. The functional significance of induced GBA is yet poorly understood.

The study was supported by the NIH (grant no. R01 MH063476).

Chronic Nicotine Effects on Cortical Current Density Patterns

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Introduction: Little is known about the neuropharmacology and sites of action of nicotine in the human brain. Extending our knowledge in this field might help in the development of new behavioral and pharmacological therapies to aid in treating nicotine dependence and to improve smoking cessation success rates. In this study, we addressed the question if a positive nicotine history may be related to permanently altered cognitive functions.

Methods: We investigated the cortical activation during a choice reaction paradigm (P300, auditory oddball) in a sample of 247 healthy subjects consisting of smokers, ex-smokers and never-smokers. Group differences of the cortical activation were investigated using Low Resolution Brain Electromagnetic Tomography (LORETA).

Results: Both current smokers and ex-smokers exhibited significantly diminished parietal (Pz) P300 amplitudes as compared to never-smokers ($p<.05$). Source localization revealed hypoactivation of posterior cingulate cortex in all subjects with a positive smoking history ($p<.01$). Additional deficits in current density were identified in medial orbitofrontal cortex for current smokers ($p<.05$) and in left dorsolateral prefrontal cortex for ex-smokers ($p<.05$).

Discussion: Positive smoking history seems to be related to altered information processing during target detection and is further discussed with respect to differential effects in current smokers and ex-smokers. It is speculated that deficits associated with a positive smoking history may be related to structural changes induced by chronic inhalative nicotine consumption.

Investigation of Corpus Callosum Microstructure in Bipolar Disorder With Diffusion Weighted Imaging

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Introduction: Structural and myelin abnormalities of corpus callosum (CC) have recently been shown in bipolar disorder (BD) with magnetic resonance imaging (MRI).[1,2] Diffusion weighted imaging (DWI) is a relatively new MR technique capable of examining molecular water mobility in brain tissue, detecting subtle abnormalities of anatomical structures that cannot be visualized by conventional MRI. The aim of our study is to investigate with DWI callosal microstructure organization in BD.

Methods: Fifteen patients with BD diagnosed with the IGC-SCAN interview (mean age = 49, SD = 12 years; 6 M, 9 F) and 19 normal controls were studied (mean age = 48, SD = 8 years; 9 M, 10 F). DWI images were acquired with a Siemens 1.5T scanner (TE=94ms, FOV=230x230, matrix-size=128x128; EPI factor=128). Regions of interests (ROIs) were placed in the left and right side of four callosal quartiles (i.e., rostrum+genu, anterior body, posterior body, splenium) on the non-diffusion weighted images (b=0) and were then automatically transferred to the corresponding maps to obtain the apparent diffusion coefficient (ADC) of water molecules.

Results: BD patients had greater ADCs for left anterior and posterior body and for right splenium compared to normal controls (Student t-test, $p<0.05$).

Discussion: These findings support the existence of microstructure disruption of CC in BD, which may ultimately lead to inter-hemispheric misconnection. Future longitudinal MRI studies in high risk and first-episode patients together with psychophysiological tests are indicated to further examine CC anatomical abnormalities and inter-hemispheric transmission in BD.

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Assessment of Mismatch Negativity and Sensory Gating in Schizophrenics and Healthy Controls

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Introduction: Two methods that have been widely utilized in assessing the degree of cognitive impairment in schizophrenic populations are Sensory Gating Indices and Mismatch Negativity based on amplitude and latency measures.

Methods: Ten Schizophrenics, (8 males, 2 females) were age and gender matched +/- 5 yrs to healthy controls, with each being subjected to two auditory paradigms. The paired click consisted of two stimuli at 1000Hz with an interstimulus interval of .5sec and 8 seconds between pairs. The MMN eliciting paradigm was composed of a 1000Hz frequent stimulus and a deviant 500Hz stimulus. Stimulus onset asynchrony was 1.25 seconds. The data used was collected the same day for both protocols.

Results: Neither schizophrenics nor healthy controls exhibited gating deficits to a paired click paradigm. Healthy controls showed a significant MMN response at central and frontal midline electrode locations while schizophrenic patients did not.

Discussion: A small but growing group supports the notion that in medicated schizophrenics gating deficits are not as severe as previous literature suggests. This effect could be due to various medications that could normalize gating in schizophrenics. In conclusion, MMN would be a more effective measure of cognitive deficits in medicated schizophrenics than sensory gating.

Increased Medial Thalamic Creatine/Phosphocreatine Found by Proton Magnetic Resonance Spectroscopy in Children with Obsessive-Compulsive Disorder Versus Major Depression and Healthy Controls

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Altered brain creatine-phosphocreatine (Cr) levels may reflect changes in brain energy utilization and have been implicated in the pathogenesis of obsessive-compulsive disorder and major depressive disorder. We used proton magnetic resonance spectroscopy to measure absolute concentrations of creatine-phosphocreatine in right and left medial thalamus in 18 pediatric patients with major depressive disorder, 9-17 years of age, 18 case-matched healthy controls, and 27 patients with obsessive-compulsive disorder, 7-16 years old. The two patient groups were psychotropic naïve and were not comorbid for the diagnosis of the comparison group. We found significantly increased left and right medial thalamic creatine-phosphocreatine concentrations in patients with obsessive-compulsive disorder compared with both healthy controls and patients with major depression. Creatine-phosphocreatine concentrations did not differ significantly between patients with major depression and healthy controls. Our data suggests that increased medial thalamic creatine-phosphocreatine concentrations in untreated obsessive-compulsive disorder patients reflects altered energy utilization in the medial thalamus and may differentiate patients with obsessive-compulsive disorder from healthy controls and patients with major depression. Although these results must be considered preliminary, further study of the diagnostic specificity of creatine-phosphocreatine in obsessive-compulsive disorder is indicated.

This work is supported in part by the State of Michigan Joe F. Young Sr. Psychiatric Research and Training Program, grants from the National Institute of Mental Health (MH65122, MH59299, MH02037, MH58681), NARSAD and the Miriam L. Hamburger Endowed Chair of Child Psychiatry at Children's Hospital of Michigan and Wayne State University and a pilot grant from the UCLA General Clinical Research Center.

Cortical Electrical Generators, Mental Chronometry and Psychotic Personality Traits

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Visual illusions represent a neurobiologically complex phenomenon, which have been claimed to be related to psychotic experiences. The aim of this study is to investigate the cortical source of electrical activity related to the processing of apparent motion illusions and to explore the relationship of such activity with psychotic personality traits, in healthy subjects.

The present study was carried out in 13 healthy, right-handed university students. An apparent motion illusion (a phi phenomenon, with two different alternation frequencies set at 4 and 30Hz) was used as experimental paradigm. The event-related potentials were assessed by the brain electrical microstates technique and the low resolution electromagnetic tomography (LORETA). Psychotic personality traits were assessed by means of MMPI-2.

Apparent motion perception was associated with the activation of brain areas close to MT/V5 region and of a wide neural network, including frontal, temporal, parietal and limbic regions. Subjects with psychotic traits, as compared to those without psychotic traits, showed greater activity of brain regions encompassing MT/V5, the lateral occipital cortex and temporoparietal, frontal and limbic areas in the left hemisphere, as well as a decreased activity of frontal and temporal areas in the right hemisphere.

In line with previous studies, our data confirm the involvement of MT/V5 in apparent motion illusions processing; "top-down" mechanisms, related to the activity of higher order cortices, seem to modulate the activity of this brain region. Our

findings seem also to suggest that hemispheric imbalance might play a crucial role in the development of psychotic symptoms in humans.

Auditory Sensory Gating and Visual Attention Performances: How They Correlated with Each Other?

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Introduction: Sensory gating is thought to prevent incoming irrelevant sensory information from entering into the higher cortex or modulate such incoming information, and thereby ensure normal information processing. It is thought to occur in the preattention stage of information processing. The contributions of attentional factors to sensory gating are not known. Functional attention was divided into three independent units: alerting, orienting, and conflict.

Methods: From 613 participants, 39 (18 men) right-handed undergraduates (Mean age = 18.87) were selected to represent four groups: High and Low Schizotypy groups; half of each group smoked tobacco cigarettes. P50-N40 sensory gating was measured with a paired-tone paradigm (40 pairs; 70 dB, 1000 Hz). Three attention components were tested by Attention Network Test (Fan et al, 2002).

Results: We found that alerting positively related to sensory gating; conflict negatively related to sensory gating; mean reaction time negatively related to sensory gating; and accuracy positively related to sensory gating. A greater number of correlations between sensory gating and attention were shown in the smoker group than in the non-smoker group. A greater number of correlations were shown in low schizotypy individuals than high schizotypy individuals.

Discussion: Attention components were related to different electrode sites; source localization was suggested to explore more neural mechanisms underlying these relationships. Different relationships between smokers and non-smokers, between low and high schizopal individuals were found in this study. Smoking and schizotypal personality were found to be the modulating factors on sensory gating; they may also influence the relationships between sensory gating and attention. The reasons need to be further explored.

Common Circuitry for Placebo Effect and Reward Anticipation

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Introduction: The Monetary Incentive Delay (MID) task has been used with fMRI to probe reward anticipation. Activated regions include several involved in the production of a placebo response by the endogenous opioid system. Neuroimaging was employed to determine how interindividual activation differences in reward anticipation might be associated with interindividual differences in anticipation of a placebo.

Methods: Eighteen healthy subjects underwent PET with [11C]carfentanil where pain was administered with and without expectation of analgesia. Whole-brain data was acquired, coregistered, and analyzed using SPM99. Subjects also completed the MID task during fMRI. Whole-brain data was acquired; first-level results were performed using SPM2, coregistered and used for group analyses.

Results: During anticipation of analgesia, significant increases in endogenous opioid activity were observed in the nucleus accumbens, thalamus, insula, and anterior cingulate. Significant correlations were observed between opioid release in the nucleus accumbens and fMRI activation during reward anticipation in the ventral pallidum ($p<0.001$, $z=4.95$) and anterior cingulate ($p<0.002$, $z=4.19$), and between opioid release in the thalamus and fMRI activation in insula ($p<0.000$, $z=5.12$) and prefrontal cortex ($p<0.001$, $z=4.63$); all results corrected for multiple comparisons.

Discussion: These associations suggest that common circuitry may underlie the anticipation of monetary rewards and the anticipation of placebo, and that this circuit can be effectively investigated using BOLD activation or endogenous opioid release. Furthermore, these findings reveal that individual variations in the response of neurotransmitter systems involved in the placebo effect are linearly correlated with those of brain regions responding to anticipation of a reward, even across modalities.

Supported by grants R01 AT001415 and R01 DA016423

Amplitude Abnormalities of Auditory Evoked Response Potentials in Schizophrenia

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Introduction: Morphological abnormalities in the mid-latency components (P50, N100 and P200) of the auditory event related potentials (ERP) is the focus of interest of this paper, as it might be used as a "Trait Marker" of schizophrenia.

Methods: Data were collected from 14 subjects (7 normal and 7 schizophrenic). ERPs were elicited using the double stimulus paradigm (S1, S2; ISI 500 ms). The multi-channel (7 channels) data was reduced using Principal Component Analysis (PCA). Both the Cz channel and the PCA component (accounting for maximum variance) were then scored at P50, N100 and P200 in the time domain. Power was extracted from the PCA component in the 0-20 Hz (LFR) and 20-50 Hz (gamma band) frequency band and compared between the two groups.

Results: The time domain analysis showed significant group differences in the P50, N100 and P200 amplitudes for the S1 stimulus in both the Cz channel and the PCA component ($p<0.05$). No differences were observed for the S2 stimulus. In the frequency domain analysis group differences were observed in the low frequency responses (0-20 Hz). No differences were observed in the gamma band responses (20-50 Hz).

Discussion: The present study is an extension of the work done by Clementz and Blumenfeld.[1] In addition to the P50 and N100 we find that there are significant differences between the normal and schizophrenic subjects for the P200 complex. Although PCA provides efficient representation of multi-channel data, it may work better with data that is correlated. A more effective analysis technique might be to use PCA only on those channels that are spatially close together, and then individually analyze the various components.

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Acknowledgments

The ECNS wishes to acknowledge the following for their support:

GE Healthcare
Lundbeck
Pfizer
Elsevier BV Amsterdam

This conference was supported by an R13 grant from the NIH.

This conference was also supported by an educational grant from Eli Lilly and Company.