

Abstracts of presentations at the 6th Annual Meeting of the EEG and Clinical Neuroscience Society (ECNS) and the 1st Joint Meeting of the International Society for Neuroimaging in Psychiatry (ISNIP) in Irvine, California, September 28 – October 2, 2004.

Abstracts

Invited Presentations

EEG Coherence Development in Normal and AD/HD Children

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McCarthy R, Selikowitz M, Sydney Developmental Clinic, Sydney, Australia

Our initial coherence study investigated differences in intrahemispheric and interhemispheric EEG coherences between AD/HD and control children, and between children with the Combined (AD/HDcom) and Inattentive (AD/HDin) types of AD/HD. At shorter inter-electrode distances, AD/HD children had elevated intrahemispheric coherences in the theta band and reduced lateral differences in the theta and alpha bands. At longer inter-electrode distances, AD/HD children had lower intrahemispheric alpha coherences than controls. Frontally, AD/HD children had interhemispheric coherences elevated in the delta and theta bands, and reduced in the alpha band. An alpha coherence reduction in temporal regions, and a theta coherence enhancement in central/parietal/occipital regions, were also apparent. Generally, AD/HDcom children displayed greater anomalies than AD/HDin children. However, we found it difficult to interpret these results because of the relative paucity of developmental data on EEG coherence. This paper presents the results of subsequent developmental studies of normal control children and the two subtypes of AD/HD (both males and females) for 1 year bands from age 8 to 13 years. We found that EEG coherences in normal children of this age range develop systematically with age. These developmental effects vary substantially with gender, brain region and frequency bands, and provide a useful developmental context for interpreting the coherence anomalies found in AD/HD children.

EEG Oscillations, Drive Reduction, and Synaptic Reorganization

Barry SM
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Introduction: The integration of a body of both animal and human EEG findings in my laboratory and recent neurobiological concepts has led to a new theoretical model linking the mammalian EEG to the emergence of higher learning and memory capabilities. Studies examining the EEG correlates of learning and memory tasks documented unique components associated with response-reward contingencies. These components reflected the effects of motivational changes related to these contingencies. Animal studies in this series provided a basis for analysis of underlying neural mechanisms mediating these changes and their implications for learning.

Method: Surgically prepared cats were trained in several studies using operant conditioning with food reward to achieve either bar press or specific EEG responses. Identical response-reward EEG contingencies were documented. Subcortical EEG and unit correlates of these cortical EEG responses were tracked to identify relevant pathways. EEG data from humans studies involving related tasks were examined to see if similar response-reward contingencies existed.

Results: A post-reward synchronous EEG pattern in the dominant frequency range was observed in all of these studies. Dubbed as "PRS", this response was positively correlated with the desirability of reward, rate of response acquisition, and stability of learning. Associated electrophysiological changes in animals confirmed mediation by thalamo-cortical oscillatory mechanisms, and contingent activation of gabaergic neurons in a distinct basal forebrain region known to inhibit arousal pathways.

Conclusions: It is proposed that rewards which produce drive reduction create reward-response activation of neural circuits which inhibit arousal pathways to the forebrain. This results in hyperpolarization of related thalamic relay neurons, intrathalamic oscillations, and propagation of burst discharges within circuits related to target cortical neurons. Recent cellular findings indicate that the combined affect of these events would be to transiently reduce input to these cortical circuits and simultaneously produce long-term potentiation of their post-synaptic elements, often lasting more than 24 hours. With repeated, tran-

sient exposure to these effects relevant neuronal organization is both stabilized and consolidated. Emergent EEG characteristics resulting from structural and functional evolution of the forebrain may have thus become the engine for higher learning.

REFERENCES

1. Serman MB, Wyrwicka W, Roth SR. Electrophysiological correlates and neural substrates of alimentary behavior in the cat. *Ann NY Acad Sci* 1969; 157: 723-739.
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ECNS-2004 Presidential Address Neurobehavioral Electrophysiology: A New Discipline.

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Electrophysiological diagnostic or therapeutic techniques are largely non-invasive and relatively inexpensive. The application of these technologies to the differential diagnostic, prognostic, and the therapeutic needs of neuropsychiatric conditions could have a significant impact on the practice of neuropsychiatry as well as psychiatry in general. The presentation will cover the scope of this new field, the essential differences between NeuroBehavioral Electrophysiology (NBE) as a psychiatry-based discipline and the well-established discipline of Clinical Neurophysiology (CN). Finally, two possible models of development will be discussed: separate or joint NBE/CN laboratories.

ISNIP Early Career Contribution Award: Why data-driven fMRI Approaches are Useful in Hypothesis-Based Studies: Introduction and Examples

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Functional MRI provides a powerful tool for noninvasively investigating the living brain. However the complexity of both the noise and the signals in fMRI data is becoming increasingly apparent. Over the years, data driven approaches for analyzing fMRI data have provided a useful tool for improving our understanding of the properties of the fMRI data. In this talk, I will discuss one approach in particular which has been used in a number of recent studies, independent component analysis. The method will be introduced and applied in two examples: a study of simulated driving while intoxicated, and a study of synchronous temporal lobe activity in schizophrenia. I will close with a few thoughts on where these methods may be headed in the future.

Event-Related Potentials and Mild Cognitive Impairment

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Mild cognitive impairment (MCI) describes non-demented older individuals with an isolated episodic memory deficit that is often a transition state between normal aging and Alzheimer's disease. Previous event-related potential studies in MCI report larger amplitudes for an early auditory cortical potential (P50) and longer P300 latencies. Here, auditory cortical potentials (P50,N100,P200) and middle latency responses (MLR) occurring at the time of the P50 (Pa,Nb,P1) were examined in MCI and age-matched controls. Stimulus presentation rate, which modulates component amplitudes, was varied (2/sec, 1/1.5 sec, 1/3 sec) during passive listening. P50 amplitudes were larger in MCI at all rates, while N100 and P200 had larger amplitudes in MCI at rates < 2/sec. There were no significant group differences in MLR amplitudes, however, a slow potential during the MLR time period was larger in MCI. In a separate study the association between P50, P300, and later conversion to Alzheimer's disease was assessed prospectively in MCI subjects. At baseline event-related potentials were measured while subjects performed an auditory target detection task. After 1-4 years of follow-up subjects were classified as having either a stable diagnosis of MCI (n=30), or a diagnosis of Alzheimer's disease (n=8). Results indicate that

subjects who subsequently converted to Alzheimer's disease had significantly larger P50 amplitudes and longer P300 latencies relative to stable MCI's. Findings will be discussed with respect to clinical and neuropathological aspects of Alzheimer's disease and possible applications to early detection. Supported by NIH grant AG-019681.

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Barry SM

University of California

Los Angeles, California, USA

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Symposia

Symposium #1

Symposium #2

Symposium #3

Cerebral Connectivities After Physical and Emotional Trauma Connection-Disconnection Mapping

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Cerebral connectivities are inferred from EEG coherence and correlation indices that are scaled between 0 to 100%. This paper uses conjoint mappings of Connection ($C = 0 - 100\%$) and Disconnection ($D = 100 - C$) indices as co-requisite scores that allow clinicians to: a.) infer the dominant CD state among all recording locations and frequency bands; b.) Ascertain the agreement between raw CD indices and normative database statistics and c.) Minimize false positive and false negative decisions.

CD mapping indices (e.g., coherence and cross-correlation) are obtained from all pair-wise combinations ($N=171$) of the 19-channel International 10/20 electrode system. The mappings are improved by computing the average CD index for each electrode location, in addition to standard between-electrode CD indices. Normative statistical comparisons are based on bootstrapped distributions that provide z-score and percentile results as distribution-free, exact probabilities.

The current report demonstrates how CD mappings are used to: a.) Make single-blind predictions about the presence and direction of coup-contrecoup injuries in cases of TBI; b.) Characterize cerebral connectivities in cases of childhood sexual abuse and c.) Scale real-time EEG operant conditioning treatment effects.

qEEG and Behavioral Indices for Neurofeedback Effectiveness

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Brain Injury (TBI) symptoms provide a complex challenge for neurotherapists when designing efficient therapeutic protocols. Since TBI almost always involves cerebral connectivities, CD mapping methods have been used to study brain function throughout the neurofeedback (NF) process (i.e., before, during & after). In addition, a variety of other cerebral indices have been used to monitor NF (i.e., magnitude, synchrony, coherence, correlation). Not surprisingly, recordings obtained during NF tend to be more stable, so that statistical deviations can be defined more readily. This is called the NF Diagnostic (NFD) effect. A substantial reduction in CD statistical deviations during NF supports the notion that a particular NF treatment protocol has been effective.

In addition to within-session NFD results, a number of other measurements are used to evaluate NF effectiveness over several sessions. These include: a) a medical and psychological multidimensional survey of complaints (SCL 90R), and b) the Integrated Visual-Auditory continuous performance test (IVA). Since these studies are among the first to evaluate brain function during NF sessions, the techniques and protocols seem most likely to lead to an increase in understanding and gains in effectiveness. Depending on available time, up to 5 TBI case studies, using qEEG-guided NF will be discussed.

Symposium #4

Thirty Years of Hypofrontality Research in Schizophrenia

Buchsbaum MS and Schröder J

Thirty years ago, in 1974 Ingvar and Franzen published their seminal paper entitled "abnormalities of cerebral blood flow distribution in patients with chronic schizophrenia" and formulated the concept of "hypofrontality" in schizophrenia. Up to now, Ingvar's and Franzen's original work stimulated numerous researcher who confirmed and extended the original observation of a decreased frontal to occipital cerebral blood flow in chronic schizophrenia. The concept of "hypofrontality" can not only be regarded as one of the major contribution for our understanding of this devastating disease, but also established neuroimaging as a reliable tool in neuroscience. In the present symposium, both, the development and future directions of the concept of "hypofrontality" will be discussed.

Regulation of the Limbic Brain by Frontal Cortical Mechanisms

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We have used pain experience and pain expectation as a model to study the effects of the cognitive mind-set in the regulation of subcortical structures. Systematic manipulation of the context surrounding standardized exposure to nociception has proven very fruitful. As predicted from animal studies, phylogenetically older structures like the amygdala are activated in situations of distress, i.e. both in pain and in the context of a pain threat. Explicit manipulations of expectancy have been used as to investigate the role of the frontal lobes. The orbitofrontal cortex has been demonstrated to be a regulator of amygdala activity. When, the contextual mechanisms are used as to reduce the pain expectancy or the pain experience the activity in the orbitofrontal cortex increases and reciprocally the amygdala activity decreases. This changing pattern corresponds to decreased ratings on the subjective level both for experience and expectancy. Finally we have successfully extended this regulating mechanism outside the field of pain by performing analogous studies in presentation of anxiety provoking pictures. The ability to suppress phylogenetically old mechanisms from the frontal cortex represents an important development that underlies social cooperation. Such cooperation involves suppressing phylogenetically older reflex-type responses.

Symposium #5

Proton Magnetic Resonance Spectroscopy of Neuronal Circuits Implicated in Tourette Syndrome

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OBJECTIVE: Abnormalities of circuits involving the cortex, striatum, and thalamus are thought to underlie Tourette Syndrome (TS). The purpose of this study was to examine neuronal abnormalities in TS using proton magnetic resonance spectroscopy (MRS).

METHODS: Nineteen males with TS (age:10.5±2.0 years) and 28 controls (age 11.0±2.9 years) participated. Seven patients were medication-free at the time of the study, while the others were taking stimulants (n=4), dopamine antagonists (n=4), and alpha agonists (n=5). Fourteen patients had attention-deficit/hyperactivity disorder. Spectra were acquired using a 3.0 T head only scanner with a multi-slice spin-echo MRSI sequence. Spectra from left and right frontal cortex, caudate nuclei, putamen, and thalamus were fit, and N-acetylaspartate (NAA), creatine, choline, and glutamate were quantified.

RESULTS: Patients had a significant increase in glutamate in the right putamen and significant reductions in NAA in the right and left frontal cortices and the left putamen. Patients also had significant reductions in choline in the right and left putamen.

CONCLUSIONS: These results suggest abnormalities of glutamatergic activity, neuronal density, and membrane metabolism in components of the neural circuits implicated in TS. While the results of this study are intriguing, they must be interpreted cautiously due to its limitations (small sample, possible confounding effects of medication and comorbid diagnoses).

O'Neill J, Chair
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1H MRS in Children with Obsessive Compulsive Disorder, Major Depression and ADHD

Rosenberg DR
Wayne State University
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Magnetic Resonance Spectroscopy in Childhood Autism: Longitudinal Findings

Friedman SD
University of Washington School of Medicine

Magnetic Resonance Spectroscopy of Pediatric Bipolar Mania

Davanzo PA
UCLA Neuropsychiatric Institute
Los Angeles, California

Magnetic Resonance Spectroscopy in Children and Adolescents with Tourette Syndrome

Nicolson R
University of Ontario
London, ON, Canada

Symposium #6

Neurophysiological Studies of Psychosis: QEEG, Event-Related Potentials, P300 and Current Source Density

Flor-Henry P, Alberta Hospital Edmonton, Edmonton, Canada
Gordon E, Brown K, Harris A, Williams L, Westmead Hospital and The University of Sydney, Australia
Kayser J, Tenke CE, Gil R, Bruder GE, New York State Psychiatric Institute, New York, USA
Koles ZJ, University of Alberta, Edmonton, Alberta, Canada

The proposed symposium illustrates the increasingly varied and sophisticated techniques of neurophysiological research applied to psychopathology which progressively lead to a clearer understanding of the complex cerebral changes which are associated with the schizophrenic syndrome. The symposium demonstrates how electrophysiologic recordings can provide fundamentally new insights into basic and clinical research questions when combined with innovative methodological approaches. By addressing the topic of neurophysiologic abnormalities in psychosis, the symposium will showcase source analysis of EEG spectra, principal component analysis of current source density, transformations of ERP waveforms, and concurrent registrations of various electrophysiologic (e.g., ERPs, gamma activity) and autonomous measures (e.g., skin conductance), all unique, state-of-the-art extensions of existing methodologies. By reaching beyond the scope and the limitations of traditional EEG recordings, these approaches allow more powerful inferences about brain function than previously possible.

Hemispheric Differences Between Male and Female Patients Suffering from Depression: EEG Source Localization Evidence (LORETA)

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Twenty-six male depressives and 38 female depressives, unmedicated and dextral, were studied and compared to 65 healthy male controls and 80 healthy female controls, again all dextrals. The EEG was recorded with a 48-channel system. 20 1-second artefact 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 four conditions: resting (Eyes Open, Eyes Closed) during cognitive activation of the dominant hemisphere (Word Finding) and of the non-dominant hemisphere (Dot Localization). 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) and beta 2 (21-

50Hz). When compared to controls male depressives showed increased sources in the right hemisphere. In female depressives however, the sources were more frequently bilateral and lateralized to the left hemisphere. When male depressives are compared to female depressives the sources, in general, are right hemispheric in males and left hemispheric in females. On the basis of these findings one might speculate that, at the subjective level, pathological depression in men is more purely affective whereas in women a verbal cognitive component would be more prominent.

Central and Autonomic Disconnections in Schizophrenia

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We propose that the breakdown in schizophrenia reflects across scale (from neuronal to whole-brain) disturbances, multiple, concurrent disconnections (supraregional), and both deficits and abnormal excesses of function. These complex functional disconnections may be manifested as a range of neurocognitive and behavioural disturbances. Some may be common to the diagnosis of schizophrenia. Others may be specific to distinct syndromes, reflecting the balance between disturbance and attempted compensatory processes.

We used a multi-modal database to test specific complementary hypotheses of brain and autonomic disconnections (with respect to a normative database of 100 subjects). Both first episode (n=80) and chronic (n=40) patients were examined.

Results showed convergent evidence for disturbances across early to later stages of information processing, in the integration of brain networks, and in the interaction between autonomic and central systems. Specifically, patients with schizophrenia (compared with controls) showed: increased slow-wave qEEG theta and delta (beyond the effects of medication); with decreased alpha and beta; but absence of delayed alpha frequency with increased cognitive load; general inhibition of target auditory oddball ERPs (N1, P2, N2, P3) to task-relevant stimuli; additional ERP disturbances for task-irrelevant background stimuli (decreased N1, earlier P2); decrease in early and late Gamma (40 Hz) phase synchronisation from 0 to 300ms post-stimulus particularly frontally and in the left hemisphere; excessive SCRs most apparent in paranoid schizophrenia –but simultaneous fMRI and SCR recording showed specific reductions also apparent in amygdala and medial prefrontal regions for threat-related face stimuli. Consistent biological associations with “the three syndromes” were also found with most of the above measures.

ERP Generators of Visual and Auditory Word Recognition Memory in Schizophrenia: Principal Components Analysis of Laplacian Waveforms

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By recording 30-channel, nose-referenced EEGs during a visual continuous word recognition memory paradigm, we have previously reported a preserved ERP ‘old-new effect’ (enhanced positivity at medial-posterior sites between 300 and 800 ms to correctly recognized repeated items) in schizophrenia. However, patients showed reduced early negative potentials (N1, N2) and poorer recognition accuracy. To investigate the impact of modality and EEG reference, the present study recorded 30-channel ERPs from 16 schizophrenic patients and 26 healthy adults in visual and auditory task versions of the same paradigm, and included reference-free Laplacian (current source density, CSD)

transformations to the analysis of the original and rereferenced (linked mastoids) ERP waveforms. Although only subjects performing above chance were included, patients performed more poorly than controls in both modalities.

Spatially and temporally overlapping ERP and CSD components were measured by unrestricted, Varimax-rotated, covariance-based principal components analysis. Replicating and extending our prior findings, patients showed reduced N1 and particularly reduced N2 to both visual and auditory stimuli. The topography of N2 reduction in patients was modality-specific, most marked at medial-central (auditory) and posterior sites (visual), suggesting that the functional classification process underlying N2 amplitude is impaired in schizophrenia. Both patients and controls showed a robust auditory ‘old-new effect’, superimposed on the N2/P3 transition. In the visual modality, Laplacian transformations and rereferenced ERPs revealed an ‘old-new effect’ for patients and controls in both modalities, but this effect was not present in patients for the original, nose-referenced ERPs. Data-driven analysis of reference-free CSD waveforms can better differentiate task-related contributions of ERP generators in schizophrenic and healthy adults during recognition memory, which may be masked by volume-conducted activity inherent to reference-dependent surface potentials.

The Detection of Abnormalities in the Source-Current Density in the Brain Associated with Schizophrenia

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A factorization method that is effective for detecting the differences in the spatial patterning of the two EEG populations is discussed. The method is a simple form of independent component analysis where the separation criterion is based on the proportion of the combined variances that each component can account for in the two EEG populations. Those components that account for maximal variance in one population and minimal variance in the other are used to estimate the differences in the cortical source-current densities underlying the EEGs from the two populations. We have tested this method on a group of 57 male subjects with schizophrenia and a group of 65 matched controls. To elicit differences, comparisons were made during resting conditions and during verbal and spatial cognitive challenges to the subjects. Estimates of the source current density were derived from 43-electrode recordings of the EEG reduced to the delta, alpha and beta frequency bands. The patients were unmedicated and were selected according to the DSM-IV criteria. As a group, they were severe, chronic states with both deficit negative and superimposed florid psychotic symptomatology. The results confirmed that schizophrenia is a disorder centered in the left temporal and bilateral frontal lobes. They also showed that, in schizophrenia, functions normally performed by these regions in controls are assumed by homologous regions in the opposite hemispheres.

Symposium # 7

Symposium # 8

“Combining Electrophysiology and Functional Neuroimaging: Methodological Aspects and Future Applications”

Maurer K, Dierks T

Integration of Neurophysiology and Neuroimaging Using ERP, Event Related fMRI, and SPECT

Pogarell O, Mulert C, Karch S, Jäger L, Tatsch K, Möller H-J, Hegerl U

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Complementary methods for the analysis of brain function are required for a broad understanding of brain structural and functional integration. The combination of neurophysiological (EEG, event related potentials) and neuroimaging techniques

(fMRI, SPECT) provides both high temporal and spatial resolution of brain activity and allows for the assessment of different aspects of brain neurochemical function. We have studied healthy subjects and psychiatric patients using neurophysiological techniques (EEG, event related potentials), fMRI, and SPECT to gain insight into the multiple neurophysiological and neuroimaging interactions. For a more comprehensive understanding of the brain activity underlying the P300 paradigm we have established a combined EEG/fMRI set-up for simultaneous measurements during an auditory oddball paradigm to achieve both a precise localization and a high time resolution of target detection. Neurochemical brain activity has been studied by combining SPECT with the monoamine transporter ligand β -CIT and the assessment of the loudness dependence of auditory evoked potentials as a neurophysiological serotonergic marker.

Investigating Working Memory Retrieval With ERP and fMRI: Timing and Localization of Load Effects on the Visual P300

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Goebel R, Universiteit Maastricht, Netherlands
Linden DEJ, University of Frankfurt, Germany, and University of Wales, Bangor, United Kingdom

Introduction: The identification and correct recognition of objects is crucial for the retrieval of information from working memory (WM). We explored the spatio-temporal characteristics of cortical activity in the retrieval phase of a visual delayed discrimination task. Our particular focus was on the P300 component of the ERP, which has long been associated with retrieval processes.

Methods: Eighteen healthy subjects underwent sequential ERP (63 channels) and fMRI measurements during the WM task. ERPs were calculated separately for the two load conditions (load1 and load3). fMRI-guided source modelling was performed using BrainVoyager/BESA. Foci of fMRI activity during retrieval were identified with a regression analysis and used for seeding of regional sources (RS). Electrical brain activity was modelled by discrete multiple sources. A 4-shell spherical head model was applied to compute the source activities.

Results: The ERP analysis showed a centro-parietal late positive complex (P300) which was split into two peaks at about 350 and 580 ms. fMRI identified both load-sensitive (in the insula and cingulate gyrus) and load-insensitive retrieval foci (inferior temporal cortex, intraparietal sulcus). The fMRI-guided seeding procedure resulted in ten RS explaining 99% of scalp ERP variance. It revealed that the parietal activation was sustained and contributed both to the P350 and the P580, while temporal sources contributed mainly to the P350, and insula mainly to the P580.

Conclusion: The combination of fMRI and ERP is capable of revealing the sequential contribution of brain areas to a complex cognitive task like WM retrieval and their modulation by cognitive load.

Combining Electrophysiology and fMRI in the Study of Brain Function

Maurer K, Chair (Frankfurt, Germany)
Dierks T, Co-chair (Bern, Switzerland)

Papers:

Methodological Issues Regarding Simultaneous EEG and fMRI Acquisition

Cohen MS, Los Angeles, USA
 (Not confirmed)

Combined EEG and fMRI in the Study of Visual Oddball Paradigms

Bledowski C, Prvulovic D, Wibrals M, Hochstetter K, Scherg M, Goebel R, Maurer K, Linden DEJ
Frankfurt, Germany
 (Confirmed)

Simultaneous ERP and Event-Related fMRI: Focus on the Time Course of Brain Activity in Target Detection

Pogarell O, et al., Munich, Germany
 (Not confirmed)

Functional Correlations Between Resting EEG and Metabolic Changes Measured by fMRI

Dierks T, König T, Hubl D, Melie L, Strik W, Bern, Switzerland
(Confirmed)

Probing Cognitive Dysfunction in Schizophrenia With Combined EEG and fMRI

Maurer K, Haenschel C, Bittner RA, Härtling F, Rotarska-Jagiela A, Oertel V, Singer W, Linden DEJ
(Confirmed)

Cerebral Connectivities in Childhood Sexual Abuse

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Childhood sexual abuse (CSA) has been the subject of much recent controversy as a result of Rind, Tromovitch and Bauserman's (1998) meta-analytic examination of CSA, which found a weak relationship between childhood sexual abuse (CSA) and self-reported psychopathology in college samples. There have been few studies of CSA, which look beyond self-report. The present study is an exploration of the relationships between CSA, qEEG, neuropsychological, and psychological measurements in 20 high-functioning, non-medicated adults without PTSD and in 5 like adults with PTSD.

The objectives of this study were to: a) examine electroencephalographic (EEG) abnormalities associated with CSA, b) investigate cortical coherence in the groups using CD mapping methods (Hudspeth, 2004) to describe and infer underlying functional disconnections, and c) integrate personality differences associated with CSA with EEG differences. CD mapping methods indicated an overall pattern of disconnection, most evident in right fronto-temporal regions. Personality testing using the Minnesota Multiphasic Personality Inventory - Revised Version (MMPI-2) indicated the CSA groups exhibited poorer adjustment than normals, despite high average IQ for the groups. EEG abnormalities were not useful in differentiating the group from normals. Walker's (2003) theoretical modular coherence model was utilized to integrate coherence and personality variables and provide treatment options.

Plasticity of Frontal Cortex Activation During Training

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It is generally accepted that increased task load corresponds to an increased cerebral activation of the cerebral sites involved in the respective task. While this relation applies for cross-sectional studies, little is known about potential longitudinal changes of cerebral activation during training. In a first study, we examined the activation of frontal and parietal cortices during a visual spatial working task before, during, and after 4 weeks of daily training using functional magnetic resonance imaging (fMRI). Results indicated an U-shaped course of cerebral activation during training: While cerebral activation increased with initial performance gains, activation returned to baseline with consolidation of performance gains at the end of the study.¹ These findings can be extended to declarative memory functioning as indicated by the results of an ongoing trial. In contrast, single case studies suggest that training of working memory tasks may increase frontal activation in patients with schizophrenia.^{2,3} These findings have potential implications for neuroimaging studies in general since training effects occur regularly whenever similar tasks are repeatedly given. Moreover, the studies emphasize the prospect of investigating cerebral mechanisms underlying training and optimizing the respective programs.

REFERENCES

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2. Wexler et al. Am J Psych 2000; 157: 1694-1697
3. Wykes et al., Br J Psych 2002;181: 144-152

Courses

Transcranial Magnetic Stimulation In Psychiatry

Avery D

In this course, repetitive transcranial magnetic stimulation (TMS) in psychiatry will be reviewed. The topics covered will include: the basic physics of TMS, efficacy studies of TMS in psychiatric disorders, especially major depression, safety and side effects of TMS, magnetic seizure therapy, basic animal studies, human neurophysiology studies and functional neuroimaging studies.

TMS is a technique that allows stimulation of the cortex using an electromagnetic coil. A powerful electromagnetic coil induces a rapidly changing magnetic field which in turn induces an electrical current. Unlike electricity, magnetic field does not meet resistance from the skin and bone of the scalp, and the changing magnetic field creates a relatively focal electrical current in the cortex. Four meta-analyses of the studies of the efficacy of TMS indicate superiority over sham stimulation in the treatment of depression. Thus far, no memory deficits have been shown in the studies of depression. In addition, TMS has been studied in other disorders such as bipolar disorder and schizophrenia. Some seizures have occurred with TMS. However, since the safety guidelines from the NIH were published in 1998, there have been no seizures when those guidelines have been followed. Recently, higher dose TMS has been used to intentionally induce seizure activity (magnetic seizure therapy) to determine whether the therapeutic effects of ECT can be achieved with less memory disturbance. Basic animal studies of non-convulsive TMS and magnetic seizure therapy will be reviewed. Human neurophysiology and functional imaging studies may shed light on the mechanism of action of TMS.

fMRI: An Introduction

Keihl K

The course will cover basic though advanced techniques for the analyses of functional magnetic resonance imaging (fMRI) data. Special emphasis will be paid on fMRI analyses using Statistical Parametric Mapping (SPM). The course will cover basic experimental design, issues with movement artifacts in fMRI, spatial normalization, spatial and temporal filtering (ie smoothing) and basic random and fixed effect statistical models. Some advanced techniques, such as independent components analyses will also be offered.

The course is designed for social scientists and emphasis will be placed on understanding the principles of brain imaging analyses and will not rely heavily on the mathematical implementation of image analyses.

General Posters

QEEG as a Evaluation Tool of Bipolar Disorder Patients

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Introduction: Bipolar disorder is one of the most difficult conditions to diagnose, in part because there are no reliable diagnostic laboratory tests characterizing this condition. A small number of reports have attempted to correlate brain activity with clinical presentation of manic and depressive episodes. Thus, in this study, we investigated patients with bipolar disorder and the relationship between Eyes Closed background activity qEEG and their clinical presentation.

Methods: Ten patients between 35-65 years of age who meet DSM-IV criteria for Bipolar Disorder were selected. All patients were receiving standard treatment for bipolar disorder including mood stabilizers and antidepressant agents. One-minute of artifact-free epochs were selected and compared to normal controls using Neuroguide software. Based on the results of the topographic mapping, two groups emerged; Group "A" (GA) presented with a spectrum of excessive slow wave activity, Group "B" (GB) did not present with the slow wave patterns. The two groups were compared utilizing independent t-tests. In addition, mood state was compared between the groups by using Beck Depression Inventory (BDI).

Results: Significant differences between two groups were found in qEEG and on the measure of depression (BDI). Excessive frontal theta activity was found in the GB as compared to GA. In addition, post hoc analysis showed statistically significant higher BDI scores in GB 34.75+10.34 as compared to GA 14+4.32.

Conclusion: Clinically stable Bipolar disorder patients, treated with similar medications, exhibited distinct patterns of electrophysiological activity. This activity correlated well with the depressive symptoms. The GB showed more frontal theta activity and severity of depression.

Functional MRI Imaging of Primary Taste Perception in Healthy and Bulimic Female Subjects

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Introduction: Bulimia Nervosa is characterized by very distinct, potentially harmful eating behaviors. These include binge eating, often focused on sugar-rich food and altered psychophysical responses to sweet taste. This study attempted to test whether bulimic patients have altered taste perception mechanism.

Methods: we examined the differences in sweet taste perception between 4 bulimics and 6 non-bulimic, physically healthy, right-handed female volunteers, testing responses to gustatory stimuli at the psychophysiological level and the CNS processing level. A psychophysical test was conducted, in which subjects were asked to grade their hedonic experience and sweetness level in response to sugar solutions of various concentrations on a visual analogue scale. In another experiment the subjects were given repeated tiny boluses of solutions alternating between plain water and 10gr% sucrose, using the same paradigm, which was to be conducted during the fMRI scan. Subjects were asked to grade the level of sweetness every 3 seconds, a rate identical to the volume sampling rate (TR). The time pattern of subjective taste level evaluation varied dramatically between bulimics and non-bulimics.

Results: The hedonic experience, the level of sweetness and the observed response curves were similar between the two groups. However, fMRI analysis, aimed at tracking primary cortical processing revealed consistent, highly significant regions of activation in peri-sylvian regions bilaterally, with stronger signal on the right, with specific right middle temporal activation in the bulimic subjects.

Conclusions: These results may indicate that the psychophysiological differences originate at a higher level of processing than the primary gustatory cortex.

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Keywords: functional-MRI; taste; Bulimia-Nervosa

Preferred Mode of presentation: Oral Presentation

Evidence for Somatosensory Cortical Disorganization in Psychosis

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Introduction: Two previous publications have suggested anomalous (decreased or reversed) asymmetry of the MEG M20 somatosensory evoked fields (SEF) in psychosis. Patients with schizoaffective disorder demonstrated a decrease in or reversal of normal asymmetry (Reite et al, *Biol. Psychiat.* 46:133-6, 1999). Similarly, bipolar patients who had a history of psychosis, but not those without a history of psychosis, demonstrated a decrease in or reversal of asymmetry (Reite et al, *Am. J. Psychiat.* 156(8):1159-63, 1999). Information on neuroanatomical structures associated with those source locations was not available at that time. This study examines neuroanatomical correlates of source generators in a subset of those subjects for whom MRIs were available.

Methods: MRI data obtained at 1.5T was available from 48 subjects (8 controls, 20 schizoaffective, 8 psychotic bipolar, and 12 non-psychotic bipolar). Central sulci were identified from sagittal series and previously determined M20 source locations superimposed. Both hemispheres of each brain were examined and M20 sources scored as (1) in or posterior to central sulcus, or (2) anterior to central sulcus. Fischer exact tests were used to determine the significance of location variability.

Results: Control subjects and non-psychotic bipolar subjects did not differ in source location ($p=0.693$ for left hemisphere and $p=0.535$ for right hemisphere), with the majority of sources (15 of 20) in the left hemisphere located in or posterior to central sulcus and an approximately equal distribution on the right side (11 anterior and 9 in or posterior). Psychotic bipolar subjects exhibited no significant difference possibly due to the small subject group encompassed. Schizoaffective subjects exhibited an altered asymmetry in the left hemisphere compared to the control group ($p=0.001$) with a majority of source locations anterior to central sulcus.

Conclusions: These findings suggest that M20 source location difference in subjects with psychosis may reflect different regions of sensory cortex generating the response, possibly reflecting cortical disorganization associated with psychosis. Supported by USPHS MH47476 and MH64502.

Decrease in Left Ventral Anterior Cingulate Perfusion Correlates with Antidepressant Response to Partial Sleep Deprivation (PSD)

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Introduction: This study used functional MRI (fMRI) to investigate mechanisms of antidepressant effect of 1 night's PSD in current major depression.

Methods: 17 unmedicated unipolar outpatients (HDRS17 > 16, M/F 5/12, 42.8 + 9.7 years) & 8 controls (M/F 4/4, 35.0+9.5 years) received 3 nights (adaptation, baseline, & PSD—during which they were kept awake after 3 am) polysomnography. Subjects received anatomical & functional MRI using pulsed arterial spin labeling, with baseline & PSD blocks in randomized counterbalanced order. Data were analyzed using AFNI 2.56b. Stripped brains were segmented by fitting a 3-compartment Gaussian mixture model to the intensity histogram. Resulting gray matter masks were transformed into Talairach space and merged with Talairach daemon-based region of interest (ROI) templates to create standardized yet individualized ROI templates, which were used to mask perfusion data.

Results: As hypothesized, decrease in left ventral anterior cingulate perfusion from baseline to PSD scans correlated directly with the decrease in the modified HDRS17 (omitting sleep & weight loss items) between baseline & PSD conditions (1-tailed Pearson correlation coefficient .457, $p < .033$). No other ROIs showed correlations between change in modified HDRS17 & change in perfusion.

Conclusion: These preliminary data—the first using fMRI—are consistent with previous PET & SPECT findings of sleep deprivation and depression in linking decreased brain activity in this area with clinical improvement.

MEG Tactile M50 Source Movement In Bipolar Patients

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Introduction: Sensory evoked fields are not necessarily produced by stationary sources. MEG recordings have demonstrated movement of auditory and somatosensory source generators over short time periods (msec), possibly reflecting spreading cortical activation. The present study examined source movement of the tactile M50 response in both control and bipolar subjects.

Methods: We recorded the contralateral M50 component of the somatosensory evoked field (SEF) produced by tactile stimulation of the thumb and little finger in 10 controls and 10 subjects with bipolar disorder, using a 37-channel Magnes I instrument. Movement of the source location estimates over a 15 msec time period surrounding the max RMS of the M50 component was estimated in both hemispheres.

Results: Primary findings were related to group differences in right hemisphere source movement. Sources moved lateral to medial in control subjects for both digits, whereas in bipolar subjects source movement was reversed. In the left hemisphere, source movement did not differ between groups.

Conclusions: These findings support the concept of movement of SEF source estimates over very short time periods, and such movement may differ in the right hemisphere of bipolar subjects. These findings might best be used to design more targeted hypotheses that can be tested in both hemispheres simultaneously with whole head MEG instruments. Supported by MH64502.

Clinical Correlates of Quantitative EEG Alterations in Alcoholic Patients

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Introduction and Methods: Quantitative EEG (frequency analysis, absolute and relative powers of the four classical bands) was assessed in 174 alcoholic patients admitted in our facility for deintoxication process. All underwent psychiatric, medical and neurological examination prior the EEG recording.

Results: Only 10 patients had normal QEEG, and the alteration most frequently found (53 cases) was a decrease of power in slow (delta and theta) bands with a concurrent increase in beta band, followed by 41 with decreased power only in slow bands, and 23 with only increase in beta band. Seventeen had decrease in both slow and alpha bands without beta alterations. Alterations in slow and beta bands were uncorrelated. However, a significant ($p < .05$) correlation was found between decreased power in slow bands and cortical atrophy as revealed by MRI, concurrent abuse of other drugs, arterial hypertension and time elapsed from the beginning of alcoholic habits, but not with age, nor any other psychiatric feature. On the other hand, increased power in beta band correlated with the use of psychoactive medication (benzodiazepines and neuroleptics), sensoriperceptual alteration (hallucinations, illusions), and family history of alcoholism, but not family history of mental disease.

Conclusions: It is concluded that decreased power in slow bands in alcoholic patients may be an indicator of chronic brain damage at the cellular level, while increase in beta band is mainly related to medication use, but also to neuronal hyperexcitability, even linked to a genetic trait.

Abnormal Brain Maturational Trajectory in Pediatric Obsessive-Compulsive Disorder (OCD): A Pilot Voxel-Based Morphometry (VBM) Study

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Introduction: Prefrontal abnormalities have been reported in pediatric patients with obsessive-compulsive disorder (OCD) [1]. Voxel-based morphometry (VBM) assesses differences in gray matter concentration at a microstructural level [2]. This is the first study, to our knowledge, using VBM to examine regional gray matter concentrations in pediatric OCD patients.

Methods: Subjects were 21 treatment-naïve patients (mean age 13; 7 males) diagnosed with first-episode OCD and 15 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 ($p=0.0001$, uncorrected) was employed to identify suprathreshold voxels.

Results: VBM analysis revealed significant negative correlations between age and gray matter concentrations in controls and patients. The negative correlations were more prominent in the dorsolateral prefrontal cortex (DLPFC) in controls compared to patients.

Conclusions: These results may suggest that pediatric OCD patients have abnormal age-related changes in gray matter concentrations in the DLPFC. These observations are consistent with previous reports of increased N-acetyl aspartate (NAA) in the DLPFC in pediatric OCD subjects[1]. These potential brain maturational deviations in OCD may reflect a failure in synaptic proliferation or a defect in peri-adolescent pruning processes.

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Menstrual Cycle Does Not Alter Anterior-Posterior Location Estimates for MEG Auditory Source Generators

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Introduction: Previous studies have suggested that (1) the MEG auditory M100 evoked field component, generated in secondary auditory cortex, exhibits greater asymmetry (further forward in right hemisphere) in individuals with higher scores on the block design test suggesting improved spatial performance (Reite et al *Br Res Bull* 32:325, 1993), (2) women generally exhibit less M100 asymmetry than men (Scheuneman et al., *Brain Research Bulletin* 26:747, 1991) and score lower on block design, and (3) hormonal variations across the menstrual cycle may influence spatial performance in women (Hausmann et al., *Neuropsychologia* 40:808, 2002). The present study was designed to examine how a primary auditory cortex source, the 40Hz steady state response (SSR) source location, noted to exhibit M100 like asymmetry, might vary across the menstrual cycle, as a possible explanation for some of these observations.

Methods: Auditory 40-hz steady state responses (SSR) were recorded in eight healthy adult women, who were not taking hormonal contraceptives, using a Magnes I 37-channel gradiometer at both onset and mid-points in their menstrual cycles. Stimuli consisted of 2-msec, 65-dB SPL biphasic pulses delivered every 25 msec for a total of 500msec, with an ISI of 1.5 sec. M100 sources could also be estimated from this data.

Results: SSR source localizations at the two time periods did not show a difference in hemispheric lateralization. Using a t-test for independent samples, mean anterior-posterior coordinates for the sources were compared at onset and the mid-point of the cycle and were not statistically different ($p = .8$).

Conclusions: Menstrual phase does not appear to alter SSR source locations. Secondary auditory cortex sources (M100 components) are in the process of being examined, but preliminary analysis fails to support significant associations between menstrual cycle and source location alterations. Supported by USPHS MH64502.

Passive ERP Measures of Automatic Information Processing in Dementia, Delirium and Normal Aging

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Introduction: Little research has been done to date into information processing in delirium, and knowledge in this area mainly stems from clinical observations. Research paradigms suited to patients with marked cognitive impairment are very limited. Mismatch negativity (MMN) and P3 event related potential (ERP) paradigms have been administered successfully in cognitively impaired patients, testing sensory memory and automatic attention without subjects having to comprehend and remember specific instructions.

Methods: Automatic information processing was compared in delirium, dementia and normal aging by studying MMN and P3 ERP components. ERPs were recorded from 40 cognitively normal older people, 15 dementia patients and 5

patients with delirium. Subjects were presented with a passive auditory oddball paradigm while reading a self-selected magazine. A total of 525 tone trials were administered in random order, including 105 rare stimuli ($p=0.2$). Stimuli were administered binaurally via headphones for 80 ms with an fixed inter-stimulus interval of 1 second.

Results: MMN and P3 responses from delirious patients did not differ significantly from responses of demented patients or cognitively normal subjects.

Conclusions: Automatic processing as indexed by passive MMN appears to be relatively intact in delirium. It is possible to study information processing in delirious and demented patients.

Improvement in Alpha EEG Selectivity and Negative Symptoms in Schizophrenia following rTMS Treatment

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Introduction: rTMS has demonstrated value in altering symptoms of neuropsychiatric illness. Negative symptoms of schizophrenia are among the most difficult to treat with pharmacological intervention. We report that rTMS can tune the alpha EEG and improve negative symptoms of schizophrenia. The purity (bandwidth) and the persistence (ring-down time) of a resonant system can be described by quality factor, Q , defined as $Q = (\text{Stored Energy} / \text{Energy Lost Per Cycle})$. The greater the Q , the higher the selectivity (i.e., purer oscillation and longer ring-down). For small damping it can be identified with $Q = f_p / (f_1 - f_2)$, where f_p is the resonant frequency, and $f_1 - f_2$ is a half-power bandwidth (HPB) around the resonance. Human EEG has been demonstrated to have strong resonant features, especially in the alpha frequency band.

Methods: In this sham-controlled and crossover study, we used rTMS to challenge the alpha activity to identify the quality of EEG resonance in schizophrenic patients ($N = 16$) with predominantly negative symptoms. rTMS rate was set at subject's peak frequency. Magnetic pulses at 80% motor threshold intensity were delivered through a 9-cm circular coil at bilaterally prefrontal area. Treatment was consisted of 10 daily sessions for each condition followed by a 2-week washout between treatments. During each session, rTMS was given 2 seconds per minute for a total of 20 minutes. Sham stimulation was conducted in the similar manner except that the coil was not plugged into the electricity. A separate coil placed 2 ft away was charged to simulate the acoustic effect of the active stimulation. Clinical symptoms and EEG were evaluated at baseline and after 10 treatment at each condition.

Results: Analysis of single channel EEG at Fz showed a significant increase in patients' alpha EEG selectivity ($Q = 2.60 \pm 0.61$; $t_{14} = 19$, $p = 0.001$) after rTMS as compared with baseline ($Q = 2.17 \pm 0.42$). Power density at peak frequency was also increased but did not reach statistical significance ($p = 0.07$). No significant changes in EEG selectivity or power were observed with sham. Using 11 cases who had completed both EEG and clinical evaluations, Clinical improvement in negative symptoms was predicted by the degree of increase in Q factor ($R = 0.61$, $p = 0.04$; $n=11$).

Conclusions: These data provide evidence that human alpha EEG can be tuned by direct electromagnetic stimulation. The association between changes in the alpha selectivity and clinical symptoms suggests that the timing (purity and persistence) of rhythmic brain activity may play a critical role in cognitive process. The potential role of EEG tuning in symptom improvement will be discussed in light of other supportive materials.

Effects of Vagus Nerve Stimulation on the Hypothalamic-Pituitary-Adrenal-System in Treatment-Resistant Depression

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Introduction: Vagus nerve stimulation (VNS) is suggested to have an antidepressant effect in patients with treatment-resistant depression (TRD). A hypothesis of the VNS mechanism is the influence on the Limbic System and consequently on the Hypothalamic-Pituitary-Adrenal (HPA)-System. The purpose of our study was to investigate whether there are correlations between the alteration of plasma cortisol levels (PCL) after dexamethasone/corticotropin-releasing hormone (DEX/CRH) test and regional cerebral blood flow (rCBF) after VNS treatment in patients with TRD.

Methods: Before and after 4 weeks of VNS treatment, 99mTc-HMPAO SPECT brain scans and measurements of PCL after DEX/CRH test were performed in 12 patients with TRD. SPM99 analysis was performed to investigate correlations

between the alteration of rCBF and PCL ($p < 0.001$; voxel threshold 50). Patients were rated by Hamilton Rating Scale for Depression (HRSD) to assess clinical response.

Results: All patients showed a decrease in HRSD scores; 5 of 12 patients showed significant reduction of symptoms measured by HRSD (> 50% reduction). The SPM99 analysis found significant positive correlations between the changes of rCBF and changes of PCL in the subgenual cingulate (BA 25), the brainstem, and the left temporal cortex (BA 22). Negative correlations were found in medial prefrontal cortex (BA10).

Conclusions: Limbic and prefrontal cortical functions involving the subgenual cingulate and prefrontal cortex are strongly associated with negative mood. The correlation between alterations of rCBF in these depression-relevant structures and expected corresponding changes of PCL after DEX/CRH test supports the hypothesized effect of VNS on the HPA-System.

Anomalous Laterality of MEG Secondary Auditory Cortical Source Locations is Not Found in Bipolar Disorder

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Introduction: A number of studies have found evidence of disturbed asymmetry in location estimates of the 100 msec latency auditory evoked field component (M100 generated in secondary auditory cortex) in schizophrenia. This is usually in the direction of a decrease in normally expected (right anterior to left) asymmetry in the schizophrenic groups. A fundamental question is whether these findings might be indicative of psychosis more generally, or were specific to schizophrenia.

Methods: The present study examined M100 source locations over L and R hemispheres in 59 individuals (37 controls, 22 currently euthymic bipolar patients, 14 with a history of psychosis and 8 without a history of psychosis). M100 components in response to 30 msec 80dB SPL 1kHz tone bursts ($N=200$, ISI = 4 sec) delivered to the contralateral ear were recorded with a 37 channel 4-D Magnes I gradiometer system, with sources estimated using a single moving dipole model. The M100 was estimated as having been produced by two temporally consecutive generators in each hemisphere providing estimates for an early and late source (Teale et al, Neuroreport 9:2647, 1998).

Results: Both early and late sources demonstrated the expected anterior-posterior asymmetry in all three groups, and groups were not separable by source locations. Mean anterior-posterior coordinates for the early source were compared across all three groups using ANOVA and were not different ($F(2,56) = 0.14$, $p = .9$). Similar analyses were used with the late source ($F(2,57) = .21$, $p = .8$). Source latencies did not significantly differ between groups.

Conclusions: These findings suggest individuals with bipolar disorder, either psychotic or non-psychotic do not evidence functional auditory asymmetry of the type found in individuals with schizophrenia. Thus, asymmetry may track schizophrenia rather than a history of having been psychotic. Supported by USPHS MH64502.

Does Long-Term Meditation Affect Visual Stimuli Appraisal?

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Introduction: The aim of this study was to reveal EEG correlates of the affective and non-affective pictures appraisal in healthy adults practicing Sahaja yoga meditation.

Methods: The neutral, pleasant and unpleasant stimuli from International Affective Picture System were presented to Sahaja yoga meditators ($n=21$) and non-meditators ($n=20$). Subjects were asked to evaluate emotional category of every picture instantly. The 62-channel EEG was recorded continuously and then subjected for off-line event-related synchronization and desynchronization analysis.

Results: Irrespectively of picture emotional category meditators demonstrated overall lower synchronization in delta (2-4 Hz), theta-1 (4-6 Hz), theta-2 (6-8 Hz) and gamma (30-45 Hz) frequency range at 100-600 ms after stimulus onset. Namely, in response to the emotional (both pleasant and unpleasant) pictures meditators show lower delta synchronization in the 400-600 ms time window in parieto-temporal cortical regions. Distinct dominance of the right hemispheric delta synchronization to unpleasant stimuli seen in non-meditators was not observed in meditators. Although both groups successfully performed appointed task of stimulus emotional categorization, meditators reported lower level of subjective affective arousal after completion of the task.

Conclusions: Generally the process of picture appraisal goes in meditators with lower (thriftier) cortical resources recruitment. Almost double lower reactivity of delta oscillators during categorization of emotional pictures proofs performance of such tasks to be easier for meditators who are more experienced with their own feelings evaluation. Additionally, appraisal of unpleasant stimuli seems to make a lower affective impact on meditators.

Age and Diffusion Tensor Anisotropy in Adolescent and Adult Patients With Schizophrenia

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Introduction: White matter organization can be assessed with diffusion tensor MRI imaging.

Methods: We imaged 37 schizophrenic adults (27m, 10f, age mean=43, range=20-66) and 29 adolescents (15m, 14f, mean age=16.07, range=13-21) experiencing their first psychotic episode. Controls comprised of 37 normal adult volunteers (23m, 14f, age mean = 44.1, range=22-85) and 17 normal adolescents (9m, 8f, mean age=16.88, age range= 13-21). T1-weighted MRI scans were acquired with a slice thickness of 1.2 mm. The diffusion tensor sequence acquired 14 slices. We used multiway repeated measures MANOVA with age (adult, adolescent) and diagnostic group (normal, schizophrenic) as independent groups and hemisphere, dorsoventral position, and anteroposterior position as repeated measures to assess ROI in major white matter tracts.

Results: Adolescent schizophrenics showed significantly higher anisotropy in the ventral portions of the internal capsule compared with normal adolescents, but this difference was not present in adults. In the more posterior frontal white area we confirmed our earlier results of diminished anisotropy in adult patients compared with adult controls, but found that adolescents had higher anisotropy in this region. In both the frontal cingulum bundle and the entire arch we similarly found significant decreased anisotropy in adult patients but increases in adolescent patients compared with controls.

Conclusion: These results suggest that aberrant white matter myelination or pruning may be altering white matter organization in schizophrenia.

Structural Synchronization of the Multichannel EEG in Adolescents with Schizophrenic Spectrum Disorders

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Introduction: There are some abnormalities of spatial connectivity in schizophrenic patients both adults and children. Correlation and coherency functions of multichannel EEG signals usually are calculated to study the EEG wave synchrony between cortex areas. We applied our new technology (JUMPSYN 01[®]) to find out the structural EEG synchrony in schizophrenics, which evaluates coincidence between structural events in EEG.

Methods: The EEGs of 45 adolescents with schizophrenic spectrum disorders and 39 sex- and age-matched healthy subjects were analyzed (rest condition with eyes closed, 16 electrodes of 10/20 system). Our new technology for EEG adaptive segmentation (SECTION 01[®]) was applied and the index of structural synchrony (IS) in all pairs of channels was calculated as degree of coincidence between the quasi-stationary segments boundaries in EEGs.

Results: In the most of pairs of channels with statistical significant differences between the groups IS was higher in healthy group mainly in "right-centro-posterior" zones, including channels O2, P4, Pz, T6, ?4, Cz, and in "left-centro-anterior" zones, including T5, ?3 and F3.

Conclusions: The application of JUMPSYN 01[®] to studies in schizophrenia has yielded new findings that are consistent with the known hypothesis that an altered sequential or temporal structure of EEG in the spatial domain is a key feature of this disorder.

Distinguishing Normal Aging From Early Stage Alzheimer's Disease and Related Disorders: EEG Variance Techniques

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Objective: We hypothesized that a quantitative EEG (qEEG) method for measuring EEG variability may quantify information which could improve the classification accuracy of subjects with normal aging vs. mild cognitive impairment (MCI) or mild dementia due to Alzheimer's Disease and Related Disorders (ADRD). In this context, EEG variability corresponds directly to the Fisher information statistic (1959), which showed that the variability of a data set is related to the information it contains.

Sample: The cross-sectional sample consisted of 48 subjects (32 normal aging and 16 ADRD: n=3 mild dementia, n=13 MCI FAST stage 3).

Methods: During EEG recording, subjects performed two visual delayed recognition tasks. These EEG data were used to compute qEEG measures of the variance of posterior cortical activity during the first 150 milliseconds (ms) after stimulus onset, and the variance of anterior cortical activity during the second 150 ms epoch. The ratio, anterior/posterior cerebral qEEG value, was then computed for each subject, and the optimal cutoff value identified to discriminate normal from impaired subjects.

Results: A qEEG cutoff ratio of 1.00 correctly discriminated 30 of the 32 normal aging subjects (94% specificity) and 14 of 16 MCI-to-mild ADRD subjects (88% sensitivity). Both false negatives had recently begun cholinesterase inhibitor treatment, which normalized their memory test scores. Both false positives were volunteers for the normal aging group but found to have non-progressive cognitive impairment.

Conclusion: These initial results are comparable to the accuracies reported by PET scan studies of normal aging vs. AD with mild cognitive impairment and warrant further evaluation.

Somatotopic Organization May Be Different in Patients With Bipolar Disorder

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Introduction: MEG based evidence of altered tonotopy has been described in schizophrenia (Rojas et al, Biol. Psych. 52:32, 2002). This study examined somatotopy in subjects with bipolar disorder, again using MEG based metrics.

Methods: We recorded sensory evoked fields (SEF) over the contralateral hemisphere in response to tactile stimulation to the lip, thumb, and little finger in 38 individuals (16 controls and 22 bipolar patients, including 12 with a history of psychosis), using a Magnes I 37 channel gradiometer. The 50 msec latency component (30 msec for the lip) was modeled using a single moving equivalent current dipole. Taking the thumb generator location as a reference point we computed difference vectors to the other two locations, and used the magnitudes and direction cosines of these vectors to quantify somatotopic organization in the two groups in each hemisphere.

Results: Mean vector difference magnitudes (the Euclidean distances) for the lip-thumb and little finger-thumb generators were compared across the groups using ANOVA and were not significantly different. Similar analyses using MANOVA were used to evaluate the respective direction cosines with following results: the relative inferior-superior distance between the thumb and little finger was significantly larger in the left hemisphere for controls ($C_{\text{mean}} = .57$, $B_{\text{mean}} = .10$), and relative location and distance between the lip and thumb was significantly different in both hemispheres across the groups ($C_{\text{mean}} = .03$, $B_{\text{mean}} = -.33$). There were no other group differences.

Discussion: These findings suggest individuals with bipolar disorder may have differently organized somatosensory cortex. Limitations include small sample size and lack of simultaneous recordings from both hemispheres. These observations might inform replication studies. Supported by USPHS MH64502.

Neurobiological Correlates of Delta Sleep Reduction in First Episode Schizophrenia

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Introduction: Delta-sleep reduction has been demonstrated in acute, chronic, remitted, never-medicated and treated schizophrenia patients.¹ Prefrontal cortex has been implicated in the generation of delta-sleep and prefrontal abnormalities have been demonstrated in schizophrenia. We examined the neurobiologic correlates of delta-sleep (Stages 3/4 NREM sleep) reduction in first-episode treatment-naïve schizophrenia patients.

Methods: We obtained whole-night polysomnographic recordings and structural MRI scans on a 1.5T GE whole-body scanner on a series of patients (n=31). We performed whole-brain voxel-wise simple regression of delta-sleep duration to the gray matter concentration using statistical parametric mapping v2 (SPM2). As an internal replication of the findings, we compared the patients using a median split of the delta duration using ANCOVA controlling for age and gender. All p values were false discovery rate (FDR)-corrected for multiple comparisons.

Results: Both analyses yielded similar results. Reduced delta-sleep duration was associated with reductions in gray matter concentration in bilateral prefrontal cortex ($p=0.057$), posterior hippocampus ($p=0.018$), orbitofrontal cortex ($p=0.05$) and left superior temporal gyrus/insula ($p=0.007$). Volume-of-interest plotting of the gray matter concentrations against the delta-sleep duration further confirmed these correlations.

Conclusion: Altered delta-sleep in schizophrenia may be associated with specific neuroanatomic deficits in the frontotemporal region. This observation is consistent with previous observations of relationships between delta deficits, negative symptoms, prefrontal hypometabolism and prefrontally mediated cognitive dysfunction in this illness. Further studies to validate these findings using region-of-interest analysis are in progress.

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QEEG Profile Can Differentiate Between High and Low Beck Depression Inventory Among Group of Cocaine Abusing Patients

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Introduction: Previous studies have linked qEEG to patient outcome in cocaine abusers. In this study, we are investigating utility of qEEG profile in identifying depression status of cocaine abusers.

Methods: Twenty six cocaine abusing patients between 30 –69 years of age were selected. QEEG were obtained by Neuroscan software and linked ears montage was used. One minute artifact free epoch were selected and compared to normative database using Neuroguide software. Each patient was matched for gender, age and handedness. Based on qEEG profile alone, two groups of patients emerged. Group 1 showed excessive deficiency in Delta frequencies where as Group 2 did not. The independent t-test was used to compare the means Beck Depression Inventory between the two groups.

Results: QEEG profiles were significantly different and were classified in two groups. Group 1 showed excessive relative power deficit in Delta (1.0 3.5 Hz) frequencies. Where as Group 2 did not show deficit in Delta frequencies. Mean Beck Depression Inventory score of group 1 was 30.18 with standard deviation of 8.5. Group 2's mean Beck Depression Inventory score was 19.8 with standard deviation of 11.06. The difference in mean of the two Beck Depression Inventory group was statistically significant with $p = 0.011$.

Conclusion: Electrophysiology of cocaine abusers shows notably different qEEG profiles. These profiles correlated well with Beck Depression Inventory scores. Group with deficiency in delta frequencies showed significantly higher BDI scores. Utility of qEEG as adjunct to clinical presentation

EEG of MDMA Abusers during Abstinence

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Increases in MDMA abuse have been reported among young individuals. Grand Mal seizures have been observed after large doses (10-12 pills) of MDMA.^{2,5} Smaller acute doses of MDMA given to MDMA-naive subjects cause decreases in delta, theta and alpha EEG power but increases in beta power.³ In addition, MDMA use has been reported to positively correlate with EEG alpha and beta power.¹ Moreover, abstinent MDMA abusers were reported to show increases in theta, alpha1 and beta power when examined under an eyes-open condition.⁴ Thus, the present study was carried out in order to further investigate the effects of chronic MDMA abuse on EEG activity. Sixteen MDMA abusers were tested during abstinence. Seventeen control subjects were tested as a comparison group. Three minutes resting eyes closed EEG were recorded from 16 electrodes (F_{p1}, F₇, F₃, C₃, T₃, T₅, P₃, O₁, F_{p2}, F₈, F₄, C₄, T₄, T₆, P₄, and O₂). The EEG was converted to six frequency bands (delta, theta, alpha1, alpha2, beta1 and beta2) using a fast Fourier transform. Absolute log theta and alpha1 power was significantly higher at posterior sites for the MDMA abusers than the control subjects (group x electrode interaction: $p < 0.05$ with Greenhouse-Geisser adjustment). The increase in theta power in MDMA abusers that we observed is consistent with increases theta power observed by Gamma and associates.⁴ Because increases in theta are associated with disease states such as dementia, the EEG findings in these ecstasy abusers suggest that MDMA use may be associated with a drug-induced neuropathological state. More research is necessary to test these ideas.

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Age-Related Alterations of Visuospatial Processing Measured with fMRI

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Introduction: Functional Magnetic Resonance Imaging (fMRI) has emerged as a powerful tool to gain insight into age-related changes of brain function. These changes are interesting in that they can provide a better understanding of physiological and pathophysiological mechanisms behind age-related general cognitive decline.

Methods: In this study, 32 elderly (mean age 65.6 years) and 14 young subjects (mean age 26.1 years) performed an angle discrimination task with increasing task demand using event-related fMRI. Modulation of task demand was performed by presenting clocks with different angular disparity and length of the hands and measured by behavioral performance.

Results: An overall slower processing time was found for the elderly subjects. In both age-groups, brain activation was found in the cortical network subserving visuospatial processing in Brodmann area (BA) 7 within right and left superior parietal lobules (SPL). By using a quantitative approach to test for group-by-task condition interactions, and at the same time taking the individual responses into account, age-related slowing of processing speed could be related to a corresponding decrease in BOLD signal amplitude. The increase of BOLD signal amplitude with increasing task demand was more pronounced in the young group. Moreover, a constant relationship was found between processing time and BOLD signal change (i.e. the product) across age for each clock category, indicating that the total brain activity for visuospatial processing of one specific clock stimulus remains approximately constant during aging.

Conclusions: Taken together, the results suggest that the neuronal network for visuospatial processing becomes less efficient and "slower" with aging.

Intracranial Distribution of Diffusely Decreased Slow EEG Activity Differs in Depressed and Non-Depressed Alcoholic Patients

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Introduction: Previous results of our group and other authors have suggested that decrease in slow (delta and theta bands) of the EEG may be related to chronic neuronal damage or atrophy. However, a diffuse decrease of slow band activity can be found in many different disorders, and some researchers have regarded this feature as possibly artifactual in nature.

Methods: To further clarify this controversy, we compared the intracranial current source density of EEG crossspectral data corresponding to the delta (0.5-3 Hz) band using Low Resolution Electric Tomography (LORETA) from 27 male alcoholic patients whose QEEGs showed diffusely decreased delta activity, 15 of them with clinical depression and 13 without depression. Patient data was compared to 20 healthy male control subjects.

Results: Statistical non-parametric mapping showed highly significant differences of both groups of alcoholic patient respect to controls. However, although surface recording in all patients showed decreased delta power across all 10-20 electrode sites, significant differences between LORETA from depressed alcoholic and controls were found only in both temporobasal and temporomedial (parahippocampal gyrus) areas, while the nondepressed alcoholic patients differed from controls in bilateral posterior cingulum and left temporobasal and medial areas, while no significant differences between controls and nondepressed patients were found at right temporobasal or right parahippocampal areas.

Conclusions: We regarded these findings as additional evidence supporting the specificity of decreased delta power in QEEG as a sign of neuronal impairment from different causes, and the role of impairment at right temporobasal and temporomedial areas in the pathogenesis of depression.

Aberrant Target Detection Processing in Healthy Subjects at Risk for Depression: an Event-Related Brain Potential Study

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Introduction: Depression is associated with well-documented deficits in high-order cognitive processes¹ such as memory, attention, target detection, and executive functions which are assumed to be connected with altered cortical-limbic circuits as shown by neuroimaging studies.² There is no consensus whether the cognitive dysfunctions in depressed patients represent a state-related or a trait-related change. This study was to explore the effect of familial risk for mood disorders on cognitive functions in unaffected offspring of depressed patients.

Methods: A Go/No-go event-related brain potential (ERP) experiment was employed to elicit ERP components N2b and P3b as indicators of response inhibition/target selection in two groups of healthy age-, gender- and education-matched subjects with (high-risk, HR) and without a family history of depression (each group, n=14). The paradigm involved the presentation of large letters "H" or "O" (targets) and small letters "h" or "o" (non-targets). The subjects had to respond to the target presentation by pressing a button (with the right hand for larger "H" and with the left hand for larger "O").

Results: The HR group showed reduced amplitudes of the N2b-P3b complex at T3 and T4 in contrast to the control group. Statistically significant difference between both groups for the source estimation of the P3b peak was found at the left middle temporal gyrus (Brodmann area 21/22), which was analyzed by low-resolution electromagnetic tomography (LORETA).

Conclusions: The data suggested that the familial risk could significantly influence the P3b amplitude. The P3b amplitude decrement might be a biological marker for vulnerability for depression.

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An Evaluation of the Usefulness of the N100 and P200 Component as Measures of Sensory Gating

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Background: It has been shown that the evoked potential abnormalities in association with schizophrenia include decreased amplitude of the evoked response (EP) components with latency between 50 and 250 ms, and the decreased ability to attenuate the amplitude of the responses with stimulus repetition (sensory gating). In the present study, we investigate the hypothesis that no such gating occurs when pairs of non-identical stimuli are presented, and whether population differences exist.

Methods: EPs were obtained using three double stimuli (S1 and S2) paradigms (A, B and C), with 0.5s between stimuli, and 8s between pairs. Protocol A used pairs of two identical stimuli, whereas protocol B and C used a higher-frequency tone and lower-frequency tone for the second stimulus, respectively. Data were collected on four different occasions from 10 schizophrenia patients and 9 healthy age and gender-matched control subjects. The EP components P50, N100 and P200 were identified for the S1 and S2 stimuli and their amplitudes measured for each subject.

Results: The P50 amplitude for S1 was significantly larger than for S2 in the A protocol ($p < 0.05$) for the normal controls, but no significant S1 versus S2 differences were found for the B and C protocol. The normal controls produced S1 N100 and P200 components that were significantly larger than the S2 amplitudes for all three protocols ($p < 0.002$). The results were mixed in case of the schizophrenia subjects: significantly smaller S2 responses were found for P200 in all three protocols ($p < 0.002$), and N100 for the A and B protocol ($p < 0.04$), and P50 for the B protocol only ($p < 0.004$). The schizophrenia population generally had smaller S1 EP amplitudes than the control group, however, this reached statistical significance only for P50, C protocol; N100, B and C protocol; and P200, A, B, and C protocol ($p < 0.05$). Smaller S2 amplitudes were seen for the P200 component only in protocol A and C ($p < 0.05$).

Conclusions: As expected, the normal subjects showed sensory gating for the P50, N100 and P200 component when pairs of identical stimuli were presented. In case of P50, no such gating was seen when non-identical stimuli were presented, however the N100 and P200 showed similar gating as observed for the identical stimuli paradigm. This suggests that P50 represents a different aspect of the gating process than the later components, replicating an earlier report (Boutros et al., Psych Res 8; 88(2):119-30, 1999). Schizophrenia subjects showed a gating deficit for the P50 component (identical stimuli), but not for the other components. This suggests that P50, N100 and P200 are not redundant, but measure different aspects of the gating function. Interestingly, the B protocol elicited significant P50 gating for the schizophrenia group, but not for the normal controls.

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Keywords: Auditory evoked potential; Sensory gating; Schizophrenia

Use of Serial Urine Drug Screens in Detecting Covert Drug Abuse Exclusions in Electrophysiological Research

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Background: Abuse drugs are an important class of variables that can alter a variety of electrophysiological measures. For this reason current use of such drugs often constitute important exclusion criteria in research studies that use electrophysiological measures as dependent variables. Unfortunately the common reliance on single urine drug screens may not be adequate to identify covert drug use.

Method: Normal subjects for a quantitative EEG and neurocognitive study of marijuana use received urine drug screens twice per week for eight weeks (16 screens) before being accepted into the study. All subjects denied abuse drug use (except THC for marijuana users) on (1) telephone prescreening, (2) formal in person screening, (3) drug history interviews and (4) during psychiatric screening by a board certified psychiatrist. Marijuana users were excluded if any urine was positive for cocaine, amphetamines, opiates, barbiturates, benzodiazepines or alcohol. Controls positive for any abuse drug including THC were also excluded.

Results: For marijuana users the first urine screen accounted for 53% of all exclusionary positive urines that were detected. However, first detection of abuse drugs continued throughout the 16 urine screens. The cumulative percentage of first drug use detections as a function of number of urine screens is: urine test 1 (53%), 2 (62.1%), 3 (65.2%), 4 (75.8%),

5 (81.8%), 6 (84.8%), 7 (89.4%), 8 (93.9%), 10 (95.5%), 11 (97%), 13 (98.5%), and 15 (100%). Similar findings characterize controls. Serial urine screen data is also subdivided by abuse drug category.

Discussion: Single drug screens detect only about half the subjects with covert drug use and studies that rely on a single screen may be seriously compromised. While 16 screens may be prohibitively costly, 4 screens will detect about 75% and 7 screens about 90% of covert drug users.

Association Between Smoking Tendency and Dopamine Transporter Binding – a Dual Isotope SPECT Study

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Introduction: The mesolimbic dopaminergic system has been shown to play a role in reinforcing of the effects of smoking. To delineate the relationship between the pre- and post-synaptic dopamine neurons and the degree of addiction in smokers, we examined central D₂-family receptors and dopamine transporters (DAT) of smokers with various degrees of addiction using the dual-isotope SPECT imaging technique.

Methods: 10 smokers and 12 healthy non-smokers were recruited. Striatal dopamine D₂/D₃ receptor densities were approximated using SPECT and [¹²³I] IBZM, while DAT densities were approximated using SPECT and [^{99m}Tc] TRODAT-1. The smokers completed the Fagerström Test for Nicotine Dependence (FTND).

Results: After factoring out age, a decrease in DAT in the striatum of smokers is noted (p<.05). However, D₂/D₃ receptor bindings in smokers do not differ from those of non-smokers. Their DAT bindings correlate positively with FTND scores (p<.01).

Conclusions: These findings suggest that central dopamine functions, particularly in the presynaptic sites, may be related to the degree of dependence on smoking.

Reduction of Left Caudate Volume in Offspring of Patients with Schizophrenia

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Objective: The basal ganglia represent target fields for dopaminergic tracts that are believed to be involved the pathogenesis of schizophrenia. Basal ganglia play a critical role in higher cognitive functions such as attention, working memory, and goal-directed behavior. Previous studies have reported caudate nucleus to be larger in chronic schizophrenia patients treated by (conventional) antipsychotics and smaller in drug naïve patients supporting a significant influence of dopamine tone in caudate nucleus volume. Studying at-risk relatives would be valuable as the risk of schizophrenia increases by the proximity of genetic relationship and help understand biological markers. In this study we measured the caudate volume in adolescents with at least one parent with schizophrenia.

Method: Right and left Caudate nucleus were measured using MRI (1.5 mm T1 coronal images resampled in AC PC Talairach space) in 29 young non-psychotic offspring (15 males and 14 females, mean age 14.9 years, Std 3.4) of patients with schizophrenia and 31 comparison subjects similar in age and sex with no family psychiatric history.

Results: Left caudate was significantly smaller in offspring, controlling for age and intracranial volume (Table).

Conclusion: These findings provide new evidence that caudate volume reduction may be a trait related neuroanatomical abnormality in the genetically vulnerable individuals. Further studies and follow up will help understand the role of caudate in the premorbid vulnerability and progression in to later schizophrenia.

Region of interest	Normal controls mean (standard deviation) N=29	High risk offspring mean (standard deviation) N=31	Multivariate analysis with age and intracranial volume as covariates
Right caudate volume in CC	5.141 (0.625)	4.787 (0.593)	F=2.62 P=0.111 (df=59)
Left caudate volume in CC	5.324 (0.595)	4.899 (0.596)	F=4.901 P=0.031* (df=59)

Brain SPECT Usefulness for Optimizing Treatment of Children with Multiple Comorbidities and Serious Learning Difficulties, as Screened by Educational Psychological Testing

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Introduction : Within the spectrum of learning difficulties in children there is a subset of subjects with multiple comorbidity. This requires careful evaluation and complex neuropsychiatric treatment in order to improve functional status. This work is based on 24 consecutive children referred for brain SPECT, to assist in the final decision about treatment.

Methods : Longitudinal follow up with Educational Psychological testing as well as input from parents and teachers, identified subjects in need of help because of major and/or persistent, failure to progress. High Resolution Brain SPECT: 99mTc-HMPAO; triple head camera and multiple variants of slices and functional 3D displays in native space and in Talairach space (via Neurostat automatic program). A complete neuropsychiatric evaluation was correlated with the results and resulted in a tailored medication (Rx) protocol.

Results : Brain SPECT identified a variety of features based on relative perfusion changes of various types and combinations: diffuse +/- localized increases +/- decreases. In 11/24 the abnormal features were predominantly extreme localized increases with or without diffuse increase. In 13/24 there were areas of cortical underperfusion combined with marked subcortical localized increases. The optimized Rx regimen varied from single to multiple medications and to brain stimulation (VNS). It resulted in: a) improvement {marked: 8 ; moderate:7; partial:1}; b) failure:1 ; c) family/ patient non compliance: 5.

Conclusion : Brain SPECT is a clinically relevant procedure for the evaluation of comorbidity and thus for optimization of Rx in complex comorbidity cases with LD.

Magnetoencephalography (MEG) Reveals Epileptiform Activity in Adults with Autism Spectrum Disorders

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Introduction: There is increasing awareness that many children with autism spectrum disorders (ASDs) demonstrate epileptiform activity on EEG, even in the absence of a clinical seizure disorder. Since ASD are also associated with morbidity in adults, this study sought to extend those observations to an adult population.

Methods: Seven high functioning adults (5 male, 2 female, age range 22 to 51) with autism spectrum disorders (ASD) were studied with whole head MEG. One had a history of seizures years ago as a child but none were currently having clinical seizures.

Results: Four of the seven subjects showed epileptiform activity, usually spikes. In two cases spikes were seen independently in the left and right peri-sylvian areas, with the other two subjects showing only left sided spikes. One of the patients also showed independent left and right frontal spikes.

Conclusions: These data indicate that epileptiform activity similar to that seen in children with ASD can be seen in adults with ASD and no clinical seizures. The possibility that pharmacologic treatment directed toward reducing this activity may result in a reduction of autistic features in some patients may be worthy of further investigation.

Correlation Between Performance on Rey Complex Figure (RCF) Test and Functional Brain Imaging Studies- QEEG and SPECT Scan.

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Introduction: The Rey Complex Figure (RCF) is commonly used neuropsychological measure of visuoconstructive skills. This study was design to identify areas of the brain, measured by blood perfusion and brain electrical activity in which abnormalities had the most significant impact on RCF test performance.

Methods: 17 patients (age 56 ± 22) with varying diagnoses were studied with RCF, SPECT and QEEG. RCF data showed bimodal distribution and was split at the 5th percentile creating two groups with significantly impaired performance (group A) and less impaired performance (group B). SPECT analysis was conducted with SPM99. QEEG data was analyzed with Neuroguide. Correlation between SPECT and QEEG were evaluated.

Results: Comparison of SPECT scans between the normal control group and the experimental group showed statistically significant decrease in blood flow in the frontal and parietal lobes (group A) and in the parietal lobe (group B) with greater involvement of the right hemisphere in both groups. The majority of focal findings in QEEG involved amplitude asymmetry and coherence. Amplitude asymmetry was observed in the frontal lobes in both groups but group A showed changes in theta and alpha frequency. Group B showed changes only in alpha activity. Coherence findings in group A (alpha and theta frequency) and in group B (alpha frequency) were confined to the right hemisphere.

Conclusion: Degree of abnormalities found in SPECT and QEEG correlated with performance on RCF. Intact function of the right hemisphere and particularly frontal lobes seems to play the key role in performing RCF without errors.

Neural Correlates of Cognition Deficits in Alzheimer's Disease – A PET Study of Resting Cerebral Glucose Metabolism

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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: 47 subjects with AD and eleven controls were analysed. Subjects underwent extensive medical and neuropsychological (CERAD) assessment, and were investigated by FDG PET. Correlations between cognitive function according to the CERAD and cerebral glucose metabolism were generated.

Results: Firstly, immediate recall was significantly correlated with temporo-parietal glucose metabolism whereas delayed recall also showed frontal activation ($p < 0.05$). Secondly, semantic fluency was significantly associated with left side temporo-parietal and bilateral frontal glucose metabolism ($p < 0.05$). Thirdly, 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 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.

Functional NIRS Imaging a Aid for Child With Cerebral Palsy

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Objective: QEEG and bold fNIRS are known as noninvasive method of functional brain mapping. Our objective is to determine the distribution of cerebral oxygenation, blood flow and metabolic status in four cortical areas (fronto-parieto-temporo-occipital) in the normal and pathological brain.

Methods: We monitored CBV and COV in real time with a 32-channel fNIRS imaging during we used simultaneous sEMG and EEG. Twenty patients participated in this study : spastic diplegia ($n = 6$, two males, four females ; mean age 11.3 years), stroke ($n = 2$), brain injury ($n = 2$), depression ($n = 6$), schizophrenia ($n = 4$). Eight healthy volunteers were tested. Fourier's transformation was employed to obtain cross spectrum matrices, which were then used to calculate the intra-hemispheric and interhemispheric coherences expressed by the Z transformation.

Results: The results show that : in depression and schizophrenia alterations of [oxy-Hb] and [deoxy-Hb] in the left frontal lobe were examined ; in spastic patients fNIRS demonstrated an increase of CBV in the right frontal region. With treatment most children can significantly improve their abilities. Muscle relaxation was confirmed and cocontraction's relation to strength and motor function was determined. The EEG-NIRS measurements shown the changes in the prefrontal cortex and a positive cross-correlation in occipital cortex between alpha activity and [deoxy-Hb] changes.

Conclusions: Functional NIRS can detect changes in the concentration of [oxy-Hb] and [deoxy-Hb] in tissue. This technology could allow us to determine electrophysiologic abnormalities of psychiatric disorders and can be used to indicate cerebral edema and improve clinical care, especially in children with spastic hemiplegia of various etiologies.

Voxel-Based Relaxometry in Autism

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Introduction: While neuroimaging studies have suggested neurobiological abnormalities in autism, the neuronal abnormalities underlying these findings remain unclear. Transverse relaxation time (T2) imaging provides the opportunity to examine tissue abnormalities in vivo, with increased T2 reflecting increased tissue water and therefore reduced density. In this study, we used whole-brain voxel-based relaxometry to examine T2 abnormalities in patients with autism.

Methods: Eighteen males with autism (age: 9.3 ± 3.1 years) and 20 male controls (age: 10.7 ± 2.8 years) participated in this study. The diagnosis of autism was made using DSM IV criteria, and all patients had a non-verbal intelligence greater than 70. All controls were screened using the K-SADS to exclude psychiatric disorders. The groups did not differ significantly in age, sex, race, or non-verbal intelligence, although more patients than controls were not right-handed (5/18 vs. 0/20). All subjects completed a magnetic resonance scan using a 3T MRI scanner. T2 images were acquired using a GES-FIDE sequence. T2 maps created from this data were warped to stereotactic space, smoothed, and statistically compared.

Results: Patients with autism had widespread increases in T2 in gray and white matter, particularly in the frontal lobe and corpus callosum, when compared to controls.

Conclusions: To our knowledge, this is the first study to specifically examine T2 relaxation time in autism. The increased T2 in the corpus callosum and other white matter regions suggests reductions in tissue density and is consistent with the theory that autism is associated with cortical underconnectivity.

Morphological Abnormalities of the Mid-Latency Auditory Evoked Responses in Schizophrenia

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Introduction: Morphological abnormalities of the mid-latency auditory evoked responses (MLAERs, P50, N100, P200) have not been thoroughly examined as compared to latency and amplitude changes.

Methods: An a priori defined set of morphological criteria was used to classify the morphology and latency of the MLAERs of a group of stable outpatients with schizophrenia (N=27) and age and gender matched healthy control subjects (N=22). The morphology of the MLAERs was considered abnormal if one or more of the components fell outside the expected latency range, if one or more of the components were missing, or if a later occurring component was smaller in amplitude than an earlier occurring one.

Results: Of the 27 schizophrenia subjects 20 had waveforms that were deemed atypical, while only 8 from the control group were classified as atypical ($X^2=5.52, p<0.02$). The most common morphological deviations were severe latency shift, absence of one or more of the components, a smaller later as compared to an earlier component. The latencies of the P50 and N100 components, identified based on morphology, were significantly prolonged in schizophrenia patients.

Conclusions: These pilot data suggest that morphological abnormalities of the MLAERs in schizophrenia patients are significant and should be taken into consideration when examining the MLAERs of this patient population. Identifying the components based on morphological criteria could lead to the discovery of latency abnormalities that could otherwise be missed.

Schizophrenics Exhibit Abnormal P200 Amplitude to an Auditory Train Paradigm as Compared to Healthy Controls

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Introduction: A great majority of previous literature has focused predominantly on sensory gating measures derived from P50 auditory Event Related Potentials (ERP). However, research suggests that the P200 response emanates from a different location in the brain and is also associated with different stages of auditory sensory processing mechanisms making it worthy of additional exploration.

Methods: 8 subjects with a current diagnosis of schizophrenia and healthy controls (8) were age and gender matched (+5yrs) and subjected to a non attentive auditory train paradigm of 60 trains per session for 2 days. Each train consisted of 5 – 1000Hz clicks that were delivered with stimulus onset asynchrony of 500 ms and a 6th click of 500Hz.

Results: The schizophrenic patients exhibited an abnormal attenuation of P200 amplitude which subsequently decreases following the first click in the train as compared to healthy controls.

Conclusion: The difference in attenuation of the P200 response was evident between schizophrenics and healthy controls to a non attentive auditory train paradigm. This represents an aberrant processing of auditory information processing in schizophrenics at the stages that are specific to the P200 time range.

Combined Use of Auditory Evoked Response (AER) and SPECT in Differentiation of Patients With PTSD

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Introduction: Post Traumatic Stress Disorder (PTSD) has been characterized by abnormal neurophysiological responses to neutral stimuli (Paige, Reid, Allen, & Newton, 1990; Lewine, Thomas, Provencal, Edgar, Miller, & Canive, 2002; Metzger, Carson, & Paulus, in press) and by differences in regional cerebral blood flow (rCBF) patterns relative to normal controls (Bonne, et al., 2003; Lucey, et al., 1997; Mirzaei, et al., 2001; Sachinvala, Kling, Suffin, Lake, & Cohen, 2000). However, the aforementioned studies have yielded mixed results. Based on these findings, we hypothesized that intensity related auditory evoked responses (AER) and rCBF would differentiate two types of PTSD patients from one another.

Methods: 12 male Vietnam veterans diagnosed with PTSD were assessed using a neutral auditory intensity paradigm (60 db, 70 db, 80 db, etc.) and Brain SPECT. N1 and P2 components for each intensity were measured at the CZ. The N1/P2 amplitude difference was used to characterize patients as augmenters (Group 1) and reducers (Group 2) placed. Group 1, had a positive correlation between the intensity of the stimulus and the amplitude of the response. In contrast Group 2 demonstrated a negative correlation between stimulus intensity and response. Statistical Parametric Mapping (SPM 99) was used to characterize differences in SPECT between the two groups.

Results: Group 1 exhibited a significant excess ($p < .05$) in rCBF in the left limbic region and a significant bilateral deficit ($p < .05$) in rCBF in the prefrontal cortex when compared to Group 2.

Conclusions: In agreement with our hypothesis, data demonstrated that PTSD patients have different patterns of response to auditory stimuli that are associated with significant differences in rCBF.

Inter-Rater Agreement and Test-Retest Reliability of Atypical Versus Typical Auditory P50 - N100 - P200 Morphology Using Schizophrenics And Normal Controls

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Background: The morphology of the mid-latency auditory evoked response includes three peaks of increasing amplitude (P50-N100-P200) beginning with a P50 peak between 30 and 80 msec post stimulus. In research this complex is often

discarded if the P50 latency is delayed or the overall morphology distorted. However, atypical morphologies may constitute statistically reproducible phenomenon of potential research relevance.

Method: Auditory evoked potentials were retrieved from 13 schizophrenics and 9 controls. Subjects received tests on two days with 9 subjects tested a third day. P50, N100, and P200 latencies were measured by consensus agreement (two authors) and consensus ratings were made of atypical versus typical complex morphology. Complexes were rated atypical if any peak departed from the traditional latency range (P50, 30-80 msec; N100, 75-150 msec; P200, 150-250 msec), later peaks were lower amplitude than earlier peaks, or peaks were missing or bi-fed.

Results: For all subjects (n=22) there was 81.8% agreement on atypical-typical classification ($C^2 = 6.858$, $df=1$, $p=.009$; $f = 0.558$, $p=.004$). With third day tests included (40 pairs of tests) there was 75% agreement ($C^2 = 10.421$, $df=1$, $p=.001$; $f=0.51$, $p=.001$). Using all 40 pairs of tests, controls showed high test-retest correlations for P50 ($r=0.72$, $n=13$, $p=.005$) and N100 latencies ($r=0.73$, $n=13$, $p=.004$). In contrast, test-retest correlations were not found with schizophrenics (P50, $r=0.03$, $p=ns$; N100, $p=0.34$, $p=ns$).

Discussion: Atypical mid-latency auditory evoked potential morphology is a reproducible phenomenon with high test-retest reliability. As such it may prove to be a useful electrophysiological research measure in studies of psychopathology.

Concurrent Verbal Stimuli Induces Less Activation of Left Primary Auditory Cortices During N1 Component Generation

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Introduction and Methods: Source-current density estimates during the N1 component of auditory ERP to a frequent tone in an auditory oddball paradigm applied to 10 normal subjects were estimated via low resolution electric tomography (LORETA) in three conditions: Standard (1, detecting and counting the infrequent tones), distractor (2, listening to irrelevant relaxing sounds) and verbal (3, the memorization of a list of high-frequency-low imagery nouns).

Results: Bilateral selective activation of primary auditory cortices during N1 peak was observed in the three conditions. However, the source-current density was significantly attenuated in condition 2 and 3 compared to condition 1, but the degree of attenuation was much higher at the left auditory cortex during condition 3, while in condition 2 the attenuation was symmetrical.

Conclusions: These data supports previous findings about the limited neural resource model of sensory processing and the reassigning of resources for processing verbal stimuli occurs mainly at left primary auditory cortex.

Neuroimaging of Nicotinic Acetylcholine Alpha4beta2 Receptor Distribution in Early Alzheimer's Disease With the Novel PET-Tracer 2-18F-A-85380

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Objectives: Nicotinic cholinceptive dysfunction is a leading neurochemical feature of neurodegenerative diseases especially in Alzheimer's disease (AD). Nicotinic acetylcholine receptors have attracted interest as potential therapeutic targets. Aim of our study was to investigate the acetylcholine alpha4beta2 receptor distribution in early AD with the novel PET-tracer 2-18F-A-85380.

Methods: PET/CT scans were performed in 3 patients with early AD and 3 healthy controls after i.v. injection of 2-18F-A-85380. ROI analysis and voxel-by-voxel analysis using SPM99 were performed to investigate hemispheric and group differences.

Results: ROI-analysis showed no left/right hemispheric differences within the control group. Left/right difference with a significantly lower tracer accumulation in the left temporal cortex was identified within the group of AD patients. While the ROI analysis revealed no further significant differences in any other of the examined regions or the comparison of both groups, the SPM analysis showed areas of decreased tracer uptake in the left temporal cortex, midbrain, and the lower brainstem in AD patients compared to controls.

Conclusions: The preliminary results of nicotinic acetylcholine alpha4beta2 receptor distribution in early Alzheimer's disease reveal specific cerebral regions in the left temporal cortex, the midbrain, and the lower brainstem that might be relevant in early diagnosis and/or therapeutical management of early AD. Investigations of larger study populations are needed to confirm the consistency of our results.

Acetazolamide Enhanced SPECT Scan Revealing Functional Impairment Not Otherwise Discernible in a Patient With Minimal Traumatic Brain Injury (mTBI)

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Introduction: Minimal traumatic brain injury (mTBI) is a head injury characterized by lack of either localizing neurological findings or clear anatomical brain imaging findings. Imaging studies have shown that functional imaging modalities are more sensitive for detection of brain damage in mTBI than CT or MRI, yet a subgroup of mTBI patients who have a clear clinical syndrome, in the absence of findings on any imaging modality still remains. Injection of acetazolamide, a vasodilator agent which interferes with regional cerebral blood flow (rCBF) control, is known to enhance perfusion differences in SPECT scans of cerebrovascular disease, has been utilized in this case to demonstrate rCBF differences in the brain of a patient with mTBI.

Methods: A patient suffering from aggressive personality changes and cognitive impairment following a motor vehicle accident was admitted for psychiatric evaluation. The patient suffered from mild, non-localizing neurological signs, impaired abstraction, severe headache and severe, aggressive outbursts. Repeated MRI and CT scans were clear. Treatment with valproate was initiated. The patient underwent SPECT scans with and without acetazolamide injection, both before treatment and after 2 weeks of treatment.

Results: Baseline SPECT did not reveal specific perfusion changes, but following acetazolamide injection an increase in prefrontal and anteromedial temporal perfusion was evident. Following treatment with valproate, SPECT without acetazolamide challenge, showed similar increase relative to the baseline pretreatment scan. Concomitant clinical improvement was noted.

Conclusions: Acetazolamide challenge SPECT can demonstrate functional alteration in brain tissue, undetectable in either anatomical imaging studies, or functional imaging without challenge.

Keywords: SPECT; acetazolamide; minimal-traumatic-brain-injury (mTBI)

Preferred Mode of presentation: Poster Presentation

MEG Auditory SSR Source Locations Do Not Appear to Differ in Bipolar Disorder

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Introduction: We recently found the auditory MEG 40Hz steady state response (SSR), generated in primary auditory cortex, exhibited less than normal right anterior to left asymmetry in schizophrenia, and sources were significantly further anterior in the left hemisphere. (Teale et al, Biol. Psych. 54:1149, 2003). This study examines SSR source locations in bipolar disorder, to address the question of specificity of abnormal source locations to schizophrenia. We also examined SSR source location estimates with respect to Heschl's gyri, presumed location of primary auditory cortex.

Methods: Auditory 40Hz SSR were recorded from 20 control and 20 subjects with bipolar disorder (15 with a history of psychosis) using a 37 channel Magnes I instrument. Stimuli consisted of 2-msec, 65-dB SPL biphasic pulses delivered every 25 msec for a total of 500msec, with an ISI of 1.5 sec. Source estimates were based on a single dipole model, providing a single 3-D location for the SSR. MRIs were obtained at 1.5T and Heschl's gyri centroids obtained as previously described (Rojas et al Am. J. Psychiat. 154:1655, 1997).

Results: Groups did not differ with respect to asymmetry, with sources being significantly further anterior in the right hemisphere compared to left ($F(1,38)=.00, p=.97$). In both groups SSR sources were within 5mm of Heschl's centroids in both hemispheres with similar directional relationships.

Discussion: These findings suggest the anomalous asymmetry previously noted for auditory 40Hz SSR location in schizophrenia is not observed in bipolar patients, and may be specific to schizophrenia. In both controls and bipolars, source locations are consistent with Heschl's gyri generators. Supported by USPHS MH64502 and MH47476.

Volume Reduction in the Superior Temporal Gyrus is Specific to Schizophrenia

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Introduction: A number of studies have demonstrated reduced superior temporal gyrus (STG) volumes in schizophrenia, although there have been negative findings as well. It is unclear whether reduced STG volumes are specific to schizophrenia or whether they may be generally associated with psychotic disorders.

Methods: We have examined STG volumes obtained from 158 subjects, including 46 with schizophrenia, 24 with schizoaffective disorder, 43 with bipolar disorder (16 without history of psychosis and 27 with psychosis) and 45 never mentally-ill controls. T1-weighted MRI images of the head were acquired at 1.5 T using either a GE or Phillips imager. The STG was manually traced from the MRI data and total brain volumes were also measured for the purpose of correcting the STG volumes for inter-group differences in brain size.

Results: There was a trend towards significance for all individuals with psychosis (schizophrenia, bipolar disorder with psychotic features, schizoaffective disorder) to have smaller STG volumes than those without psychosis (controls and bipolar disorder without psychotic features), $p = .07$. This finding, however, appeared to be driven primarily by the schizophrenia group, whose STG volumes were significantly lower than every other individual group (all $p < .05$). There were no other group differences approaching significance.

Conclusion: Psychiatric illness per se or even psychotic illnesses specifically, are probably not related to smaller STG volumes. Our findings support the conclusions of McCarley et al. (Arch Gen Psych 59:321, 2002) that STG volume reduction is specific to schizophrenia. Supported by USPHS Grants MH47476 and MH64502.

Event-Related Potentials Indicate Deficient Working Memory in Post-Traumatic Stress Disorder

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Introduction: Neuropsychology studies of post-traumatic stress disorder (PTSD) demonstrate abnormal executive functions, including working memory, for neutral stimulus information. This study employs event-related potentials (ERP) to examine working memory in PTSD.

Methods: ERPs were recorded at 124 scalp sites from 10 patients and 10 controls. They performed two visual target detection tasks with identical neutral stimulus sequences, where targets were a fixed word or repeated words. In the latter case, target features are frequently updated in working memory. The effects of working memory updating were evaluated with mixed factorial ANOVA of ERP peak amplitude and latency.

Results: PTSD patients were slower and less accurate than controls in target detection. Updating representations in working memory involved enhanced activity in ERP components between 100-600 ms, especially large fronto-parietal positive peaks at 400-600 ms in controls. This fronto-parietal ERP activity was diminished in PTSD and an associated PET study shows similar deficits in fronto-parietal activity.¹

Conclusions: The prefrontal and parietal cortex are important components of executive systems, which interact with medial temporal areas to facilitate episodic memory. The abnormal function of these regions during neutral information processing could contribute to difficulties with concentration and episodic memory in PTSD.

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Disorder or Deceit? The Quantitative EEG and Brain SPECT Data of Three Women Diagnosed with Multiple Personality Disorder

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Introduction: Although brain imaging studies can help settle the dispute as to whether or not Dissociative Identity Disorder (DID), formerly called Multiple Personality Disorder (MPD), is a bona fide mental illness, the results from past studies are inconsistent and potentially misleading^{1,2}. Based on previous research, it was hypothesized that the within-subject variability of electrical brain activity (EEG) and relative cerebral blood flow (rCBF) would be no greater in patients with MPD than in normal controls. It was also hypothesized that MPD patients would have significant abnormalities in EEG and rCBF related to mental illness.

Methods: Quantitative EEG and SPECT were used to assess brain function in three women who met the DSM-III criteria for MPD, and six women who did not. QEEG records were viewed and analyzed with NeuroGuide, NeuroStat and LORETA. SPM99 and the MedX Visualization and Analysis Software were used to assess SPECT scans.

Results: The within-subject variability of qEEG and rCBF was greater in the MPD subjects than in the controls, particularly with regards to high frequency EEG activity. This variability, however, was not large enough to propose that MPD subjects became different people when they switched personalities. In addition, all three MPD subjects had fairly global abnormalities in brain function that often involved the temporal lobes.

Discussion: The majority of patients who are diagnosed with DID are suffering from a severe psychiatric disorder. Additional studies are needed to know the extent to which psychiatric patients and normal controls can alter brain activity.

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Agentic Extraversion, Executive Control and Dopamine: Is it All in the Resting EEG?!

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Introduction: Based on recent cognitive neuroscience findings concerning the role of the dopaminergic system in certain aspects of executive control we developed a novel EEG index in order to capture individual differences in the underlying neural mechanisms. In this study, with reference to recent work linking the agency facet of extraversion to both the dopaminergic system and executive control, we tested whether the new EEG index (which can be easily obtained from the resting EEG) and a behavioral indicator of executive control processes (performance in the n-back task) are modulated by personality and pharmacological manipulations of the mesocorticolimbic dopamine system.

Method: 40 healthy male volunteers either high or low in agentic extraversion received either placebo or a selective D2 antagonist (sulpiride 200 mg) before resting EEG was recorded and four versions of an n-back-task (0-back to 3-back) were administered.

Results: Replicating prior results, under placebo introverts had higher reaction times than extraverts, specifically in the more difficult tasks. Under sulpiride these differences were reversed. While no reliable effects were observed for measures of frontal EEG alpha asymmetry, the new EEG index was modulated by sulpiride in parallel to reaction times: Under placebo it was larger for introverts relative to extraverts, under sulpiride, it was larger for extraverts relative to introverts.

Conclusions: The results are discussed with an emphasis on the potential use of the novel index in research on the neurobiology of both normal personality (i.e. extraversion) and mental disorders hypothesized to involve the dopamine system (e.g., ADHD and disinhibition).

P50 Sensory Gating: Impact of High vs Low Schizotypy Personality and Smoking Status

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Introduction: Smoking tobacco can facilitate early sensory gating in schizophrenics and enhance prepulse inhibition hemispheric asymmetry in individuals with schizotypy personalities. We assessed the effect of smoking on sensory gating in low and high schizotypy groups.

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 using Raines' (1991) Schizotypal Personality Questionnaire; half of each smoked tobacco cigarettes. Using a paired-tone paradigm (40 pairs; 70 dB, 1000 Hz), smokers were tested while abstaining and after smoking. Non-smokers were tested similarly without smoking.

Results: N40-P50 sensory gating and P50 amplitude was greater at midline than left/right hemispheric sites. At central region, high schizotypys showed less sensory gating than low schizotypys in the non-smoker group. Among low schizotypys, smokers showed less sensory gating than non-smokers at fronto-central and central regions. Low schizotypys showed significantly greater P50 amplitude in left than right frontocentral hemispheres. High schizotypys showed more P50 amplitude in right fronto-central/central regions than did low schizotypys. In central to parietal regions, smokers showed a greater left than right hemisphere P50 amplitude in central to parietal regions, whereas the non-smokers showed the opposite asymmetry with a greater right than left hemisphere P50 amplitude.

Conclusion: Chronic rather than acute smoking effects occurred. Like schizophrenics, high schizotypy individuals exhibited poorer sensory gating in the central region. Understudied hemispheric differences emerged for schizotypy groups in the fronto-central and central regions and for smoking groups in the central to parietal regions.

Investigating Working Memory Retrieval With ERP and fMRI: Timing and Localization of Load Effects on the Visual P300

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Introduction: The identification and correct recognition of objects is crucial for the retrieval of information from working memory (WM). We explored the spatio-temporal characteristics of cortical activity in the retrieval phase of a visual delayed discrimination task. Our particular focus was on the P300 component of the ERP, which has long been associated with retrieval processes.

Methods: Eighteen healthy subjects underwent sequential ERP (63 channels) and fMRI measurements during the WM task. ERPs were calculated separately for the two load conditions (load1 and load3). fMRI-guided source modelling was performed using BrainVoyager/BESA. Foci of fMRI activity during retrieval were identified with a regression analysis and used for seeding of regional sources (RS). Electrical brain activity was modelled by discrete multiple sources. A 4-shell spherical head model was applied to compute the source activities.

Results: The ERP analysis showed a centro-parietal late positive complex (P300) which was split into two peaks at about 350 and 580 ms. fMRI identified both load-sensitive (in the insula and cingulate gyrus) and load-insensitive retrieval foci (inferior temporal cortex, intraparietal sulcus). The fMRI-guided seeding procedure resulted in ten RS explaining 99% of scalp ERP variance. It revealed that the parietal activation was sustained and contributed both to the P350 and the P580, while temporal sources contributed mainly to the P350, and insula mainly to the P580.

Conclusion: The combination of fMRI and ERP is capable of revealing the sequential contribution of brain areas to a complex cognitive task like WM retrieval and their modulation by cognitive load.

Single-Trial EP Analysis Improves Separation of Normal and Schizophrenia Subjects

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Introduction: The inhibitory gating mechanisms assessed by various parameters of the P50 and N100 auditory response have been consistently reported abnormal in schizophrenia patients. Most of the published studies have used ensemble averaging to improve the signal-to-noise ratio of individual components. This approach, however, does not provide information on the dynamics of the brain process underlying the gating mechanism. To address this issue, we have recently developed an iterative procedure that relies on independent component analysis (ICA) and can separate the activity specific to the experimental stimuli from unrelated ongoing processes. In addition to improving the signal-to-noise ratio of average components this procedure allows for clear responses to be seen on single trials. In this study, we compared the ability of the new procedure to separate normal controls from schizophrenia patients against plain ensemble averaging. In particular, we analyzed the auditory N100 responses obtained in a paired-stimulus paradigm to identify those response parameters that provide maximum separation of the groups.

Methods: Data from 23 normal and 15 schizophrenia subjects were analyzed. Responses were obtained in a paired-stimulus paradigm, in which an S1 stimulus is followed by an S2, approx. 500 msec later. The intertrial interval was equal to 8 sec. For each response, we measured component amplitude and latency. A logistic model tree (LMT) scheme was then used to classify the responses of the two groups, separately on each method, while the performance of the classification procedure was quantified using 5-fold cross-validation approach.

Results: We found that normal controls tended to respond earlier and individual responses had significantly increased amplitudes ($p < 0.01$) compared to the schizophrenia patients. Also, the normal response latencies were considerably less variable, compared to schizophrenia subjects, who exhibit widely dispersed latencies. Overall, the S1 latency was the most significant discriminatory feature ($p < 0.01$) in separating the two groups and it was followed by the S2 latency ($p < 0.01$). The S2 amplitude, though relatively larger in normals ($p < 0.05$), was the least discriminatory feature. The single trial-based method yielded 93% classification accuracy, with a sensitivity and specificity of 93% and 92%, respectively. Overall, the new method gave approximately 20% better classification performance compared to plain averaging.

Conclusions: The above results support our hypothesis that single-trial analysis can drastically improve the separation of the two groups and suggest that temporal variability plays a significant and complex role in the previously reported sensory gating deficits in schizophrenia patients.

Acknowledgement: The data used in this study were provided by Dr. Nash Boutros of Yale University. This work has been supported in part by a training fellowship from the W.M. Keck Foundation to the Gulf Coast Consortia through the Keck Center for Computational and Structural Biology, and by a grant from the Texas Learning and Computation Center (TLC2).

Neural Responses to Acoustic Startle Modification

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Introduction: Motor responses to startling stimuli are robustly blunted when immediately preceded by nonstartling stimuli (i.e. prepulse inhibition or PPI). We have systematically developed the methods to examine the neural correlates of acoustic PPI in hippocampal formation (HF) and other brain structures implicated in cognition using an event-related design while continuously measuring EPI BOLD contrast in a 3T scanner.

Methods: Nine right-handed subjects (Mean age 23y: 5m, 4 f), who previously demonstrated $>40\%$ PPI in a mock scanner setting heard 200 pseudorandomized trials of Pulse alone (40 ms of 107dB) and Pulse preceded 120 ms earlier by Prepulse (88dB). 25 coronal slices were obtained covering the corpus callosum, and EMG of eyeblink was recorded.

Results: Individual subjects showed activation in the auditory cortex and cingulate, which was highly significant ($P < 10^{-7}$) but similar across trial types when subject data were combined. The only brain region to differ significantly between trial types was a 5 voxel cluster in the left HF. Comparison of the Impulse Response Function (IRF) in the HF ROI demonstrated an initial significant reduction of the BOLD response that was not seen with pulse alone. In contrast, IRFs in cingulate and auditory cortex ROIs were classic appearing and similar.

Discussion: The significance of this novel finding is unclear, but could reflect the normal protective mechanism induced by the prepulse to instinctively limit cognitive overload. These results may provide insight into the significance of HF pathology in severe mental illness.

Subdural Recordings of Cortical Activity Elicited in a 6 Tone Paradigm

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Introduction: Effects of stimulus repetition are investigated in auditory sensory gating experiments. In those experiments two clicks separated by 500 ms and longer intervals of silence between the pairs are applied as stimuli and the decrease of the event-related potential (ERP) component P50 serves as critical variable. The functional foundation of sensory gating is yet not fully understood. The current study investigated the decrease of the ERP components P50 and N100 in 6 tone paradigm.

Methods: Data were obtained from 29 patients with epilepsy undergoing a presurgical evaluation by subdural and depth electrodes. Subjects were stimulated with trains of six clicks. Clicks were separated by 500 ms and trains by 5000 ms. The 6th stimulus in the train deviated in frequency and duration. ERPs were averaged for each stimulus position.

Results: Both the P50 and N100 were significantly reduced from the 1st to 2nd stimulus. After the 2nd stimulus no further decrease of the P50/ N100 occurred, while the deviation of the 6th stimulus resulted in a response recovery of both ERP components. However, the P50 of the 6th stimulus was still significantly smaller than the P50 of the 1st stimulus. The tone deviation also elicited a mismatch negativity (MMN). The MMN was observed at temporal electrodes, but in two patients also over the inferior lateral frontal gyrus and in one patient at an interhemispheric lead close to the cingulum.

Conclusion: The P50 suppression by a repeated stimulation as investigated in sensory gating experiments seems to be completed after the 2nd stimulus.

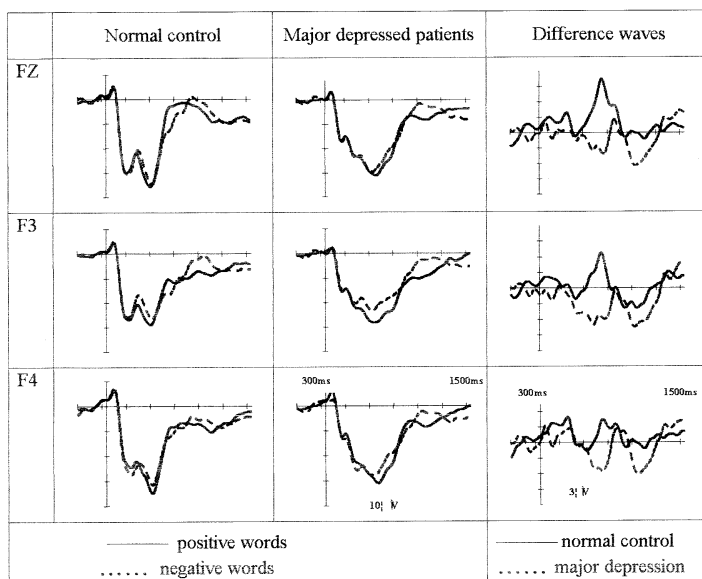
Opposite ERPs Effects of Recognition of Chinese Emotional Content Words Between Major Depressed Patients and Healthy Subjects

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Objective: To investigate Event-related Potentials (ERPs) effects of recognition of chinese emotional content words between major depression and healthy subjects.

Methods: Record the effects of ERPs in 16 major depressed patients and 16 healthy subjects while they performed a visual Chinese emotional content words recognition task. The study used a word identification task that participants responded faster to concrete (negative 20%, positive 20%) than to abstract words (neutral 60%), press right buttons finding positive and left buttons of negative.

Results: (1) The ERPs shows similar wave (N1,P2,N2,P3 slow positive wave) but its components were difference between depressed patients and normal group. Depressed patients showed a smaller amplitude of P300 in response to negative content words than to positive words; normal controls showed the opposite pattern. (2) Subtract methods showed a significant negative difference component for pos-



itive/negative words in normal controls, related to emotional experience of an individual, appeared in the period of 400 to 800 ms post stimulation which was predominant at the left frontal area (Fz\F3\FC3\FCz), and Depressed patients showed positive difference waves which was predominant at the right frontal area (F4\FC4). (3) t-test Significance Probability Mapping (t-SPM) for difference component between normal controls and depressed patients shows significance difference which was predominant at the left central-prefrontal cortex.

Conclusions: ERPs opposite effects was also elicited by recognition of Chinese emotional content words discrimination. We assume that opposite effects might reflect the lack of positive (no negative) emotional experience at the left frontal brain in major depressed patient. (This work was supported in part by Projects for Young Scientists' Fund of National Natural Science foundation of China (30100054).

The Contribution of Contextual Processing Problems to Reduced Mismatch Negativity (MMN) in Schizophrenia

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A reduction in the auditory event-related potential (ERP) component known as mismatch negativity (MMN) in schizophrenia is a highly replicable result. Multiple factors arising from the possible nature of auditory system deficits in this disorder have been proposed to explain this reduction. Elicitation of MMN requires an effective detection of a mismatch between current stimulus and the representation of regularity or 'context' stored in memory. The present study extends earlier work from this research group by testing the hypothesis that individuals with schizophrenia have problems utilizing context in processing stimulus relevance. MMN produced by individuals with schizophrenia is compared to that of age-matched healthy controls recorded during both a standard duration deviant condition and temporal context condition. The temporal context condition features a 50 ms tone presented at a standard stimulus onset asynchrony (SOA) of 400 ms and rare deviants presented at earlier SOAs. Tones were presented binaurally over headphones whilst nose-referenced ERPs were recorded from 64 electrode sites with attention directed towards a silent movie with subtitles. The amplitude of the MMN elicited by the contextual deviant was significantly reduced in the schizophrenia group compared with controls, suggesting these individuals have difficulty encoding temporal context. Interestingly, this reduction was even more significantly reduced than in the standard duration condition. This report represents preliminary analysis of data from a larger project testing individuals with schizophrenia, unaffected first-degree relatives and controls. The project incorporates behavioral performance measures of context processing, further manipulation of context in EEG paradigms and source localisation investigations.

Electrophysiological Evidence of Distractibility in ADHD Children

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Introduction: Abnormal distractibility may account for different patterns of academic and behavioral problems in children with attention deficit hyperactivity disorder (ADHD). The aim of the present study was to compare distractibility in ADHD and control children as indicated by distraction of visual-task performance caused by task-irrelevant novel sounds and by event-related brain potentials (ERPs) associated with involuntary orienting of attention to these sounds.

Methods: ERPs were recorded from 10 children fulfilling the DSM-IV criteria for ADHD and from 10 age-matched controls (8-10 years old). The P3a and frontally distributed late negativity (LN) ERP components elicited by novel sounds and the distracting effects of these task-irrelevant sounds on the performance in a forced-choice visual discrimination task were compared between the two groups.

Results: The performance of visual task in ADHD children was less accurate than in the control children. Moreover, in both groups, the reaction times to visual targets were longer after an occurrence of a novel sound than after an occurrence of a repeating tone indicating that the novel sounds distracted the children's task performance. In both groups, the distracting novel sounds elicited a biphasic P3a and frontal late negativity (LN) ERP components. However, the early phase of P3a had significantly smaller amplitude over the left hemisphere and the late phase of the P3a was significantly larger over posterior brain areas in the ADHD children than in the control group. Moreover, the LN was smaller in amplitude in the ADHD group than in the controls.

Conclusion: The ERPs to novel sounds reveal deviant covert processing of distracting auditory events in ADHD children that may underlie their attentional problems.

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Methylphenidate Response in the Treatment of Vascular Depression as Measured by Quantitative Electroencephalography

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Introduction: Vascular depression is a clinically defined syndrome often characterized by resistance to treatment, and no current evidence exists to guide practitioners regarding treatment options. Vascular depression and associated cognitive deficits have been reported to respond to methylphenidate, however, the electrophysiological reasons surrounding such response are unclear.

Methods: Patients meeting clinical criteria for a diagnosis of vascular depression underwent quantitative electroencephalography with methylphenidate challenge. POMS scores were used to detect acute mood changes after methylphenidate dosing as compared to baseline. Limited neuropsychological testing focusing upon executive function was also performed prior to and after methylphenidate dosing.

Results: Five of eleven patients demonstrated robust mood improvement as defined by a significant reduction in the POMS-depression subscale. Patients demonstrating improvement in mood showed statistically significant increases ($p < 0.05$) in the absolute and relative power of both delta and theta activity in the prefrontal regions with a trend toward neurophysiological normalization. Increases in delta and theta activity in responders were accompanied by associated decreases in relative alpha and beta powers, and resultant increases in the delta:alpha and theta:beta ratios.

Conclusions: Methylphenidate may be a useful augmentation strategy in patients suffering from vascular depression and associated cognitive deficits. Quantitative electroencephalography may be used to better understand electrophysiological responses to methylphenidate in this condition as well as possibly serve as a predictor of patient response. Further studies are needed to better delineate the role of quantitative EEG in the diagnosis and treatment of vascular depression and associated cognitive deficits.

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Disorder-Specific Neuroanatomical Differentiation of Emotional Stroop Interference Effects in Obsessive-Compulsive Disorder, Panic Disorder and Hypochondriasis

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Introduction: Attentional bias to disease-relevant emotional cues is considered to be of importance in the causation and maintenance of affective symptoms in various anxiety disorders. Neuropsychological studies using the emotional Stroop task, have reported conflicting results concerning the disease-specificity of the attentional bias. Moreover, although frontal-striatal and limbic circuits have been suggested to be involved in attentional bias and fear, respectively, the neuroanatomical correlates underlying the emotional interference effects across different anxiety disorders have not been investigated so far.

Methods: A functional MRI version of an emotional Stroop task was used in 16 patients with obsessive-compulsive disorder (OCD), 15 patients with panic disorder (PD), 13 patients with hypochondriasis and 19 healthy control subjects. The paradigm consisted of congruent color words, incongruent color words, OCD-related negative words, panic-related negative words and neutral words.

Results: In OCD patients, notwithstanding unaffected performance, color-naming OCD-related words was correlated with increased activation of right ventrolateral prefrontal cortex, bilateral anterior cingulate cortex, left striatum and hypothalamus and bilateral amygdala and temporal cortex. Compared to control subjects, no regions of increased activation were found in OCD patients during color-naming panic-related words. In PD patients, in contrast, frontal-striatal involvement was found during color-naming both OCD-related and panic-related words. However, color-naming panic-related words was significantly slowed and was correlated with additional activation of right amygdala and hippocampal gyrus.

Conclusions: The present results support the hypothesis of disease-specific attentional bias correlating with frontal-striatal and limbic activation. In addition, a disease-specific neuroanatomical differentiation of the emotional interference effects across different anxiety disorders is found. While OCD patients show attentional bias to their disease-specific words only, correlating with the activation of those regions associated with unconscious emotional stimulus processing and fear response, PD patients show more general attentional bias to emotional cues and activation of brain regions considered to be involved in automatic emotional processes as well as modulatory cognitive processes in response to the emotional state.

Imaging the Genetic Influences on Brain Morphometry in Schizophrenia

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Introduction: Genetic and environmental factors contribute to small defects in the development of brains in schizophrenics. To investigate the genetic contribution to this, we selected 17 polymorphisms located in candidate genes related to neurogenesis and mapped to genomic loci associated with schizophrenia. These polymorphisms were genotyped in 25 schizophrenic patients from a Brazilian cohort, for which brain morphometry data was collected. The polymorphisms selected include 10 coding SNPs (Single Nucleotide Polymorphisms); 3 non-coding SNP (one intronic and two located in promoter regions); one trinucleotide insertion; one deletion of 16,7kb; and two CAG polymorphic repeats.

Methods: Total brain scanning was performed in 25 schizophrenic patients with a General Electric 1.5T magnetic resonance device. Regions of interest were manually delimited at every 1mm coronal slices and their volume obtained by multiplying area values on serial slices. Genotyping was performed using a series of molecular biology protocols including sequencing single-nucleotides, standard PCR products using fluorescent dyes, PCR-RFLP and other approaches.

Results: Crossing genotype and MRI data revealed significant statistical associations: Left Frontal Gyrification Index (GI) reduction in heterozygous individuals (G/A) for the JAG2 gene ($p=0,03$); alterations in ventricular volumes in heterozygous (C/G) and homozygous (G/G) individuals for REELIN gene ($P=0,01$) and rightward GI asymmetry for heterozygous (G/A) individuals for the PCDH12 gene ($P=0,008$).

Conclusion: The association of genetics and MRI data is a powerful tool to study the genetic influence on brain development. However, an increment in the number of patients studied is still needed for confirming these preliminary findings.

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Demonstrating Prepulse Inhibition of Acoustic Startle in Normals During fMRI

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Introduction: Clarifying the neuroarchitecture of prepulse inhibition of acoustic startle with event related FMRI is appealing, but several barriers exist.

Methods: Six healthy controls with > 50% PPI in a mock scanner underwent four 10 minute runs during which they each heard a total of 100 pulse alone (40 ms white noise @ 107 db) and 100 prepulse plus pulse (20 ms @ 88 dB, followed 120 ms later by pulse) trials. Continuous assessment of the BOLD response was obtained in a 3T scanner using an EPI. MRI-compatible carbon electrodes (Magnilink, Neuroscan) were attached to each subject: two sub-clavicular, and two above and below each eye. Principle components analysis removed the influence of ballistocardiogram waveform (Neuroscan, 4.3), and the effects of pulse and gradient artifacts were minimized with low pass filters. On epoched waveforms, we then determined the direction, timing and extent of the first peak. This information was used to determine whether a response had occurred (if not scored intensity = 0) or if the trial was to be rejected. Intensity on other non-rejected trials was defined on rectified traces as the area under the curve between 20 and 320 ms post-pulse.

Results: One subject had < 25% measurable responses on pulse trials on each of the four runs, and one other had > 50% trial rejections on two of four runs. Over the remaining 22 runs (total 1100 trials), PPI was a 42 + 24% (range: 17 to 62%) in the five subjects. PPI on Run 1 = 35 + 33%, Run 2 = 39 + 20, Run 3 = 40 + 15 and Run 4 = 56 + 26%.

Conclusions: These preliminary data indicate that PPI of acoustic startle can be obtained during continuous fMRI scanning, and is stable across runs.

Reduced Cortical Folding in Individuals at High Risk for Schizophrenia

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Introduction: The gyrification index (GI), the total cortical contour divided by the outer contour, is a measure of cerebral cortical folding. Studies have documented its reduction in individuals with schizophrenia, and this investigation attempts to examine the gyrification pattern in individuals at high risk (HR) for developing schizophrenia.

Methods: Using MRI scans and the Brains2 software, GIs were calculated for nine HR male adolescents (at least one first-degree relative with schizophrenia) and 12 male controls (no family history of schizophrenia). Using the coronal slice just anterior to the corpus callosum, the total and outer contours were manually traced to allow calculation of the GI.

Results: The mean age did not differ between HR and control groups (HR=15.5±2.9 years, range=10.3-18.5; control=14.5±5.3 y, range=8.6-25.5; df=17.7, t=-0.575, p=0.573). The mean intracranial volume did not differ significantly between the groups (HR=1484±150 cc, range=1334-1749; control=1605±115 cc, range=1387-1855; df=19, t=2.09, p=0.051). In the measured slice, the left GI was lower in the HR group when compared to controls (HR=2.93±0.26, range=2.57-3.34; control=3.28±0.28, range=2.93-3.80; t=2.92, df=19, p=0.009). However, no significant difference in the right GI was observed between the groups (HR=3.02±0.28, range=2.56-3.45; control=3.11±0.16, range=2.87-3.43; t=0.945, df=19, p=0.356).

Conclusions: These results suggest reduced cortical gyrification in the left frontal lobes of persons at high risk for schizophrenia. This finding is consistent with studies of schizophrenic patients and supports genetic and neurodevelopmental models of the disorder.

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Methylphenidate Changes Auditory Information Processing, Combined Meg/EEG Study

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Introduction: Auditory event-related potentials and event-related fields have been shown to be altered in Attention Deficit and Hyperactivity Disorder (ADHD), thus indicating deficits in auditory information processing. Methylphenidate (MP) is a psychostimulant drug, which improves attention and memory in patients with ADHD. However, neural mechanisms of MP action are not properly understood.

Present study investigates whether a single dose of MP affects neurophysiological measures of information processing in healthy adults studied with simultaneous whole-head magnetoencephalography (MEG) and electroencephalography (EEG).

Methods: Monaural left ear auditory stimuli were presented in oddball paradigm with infrequent deviant tones differing in frequency and duration. Neuronal activity was recorded with simultaneous whole-head MEG and EEG in 13 healthy subjects (5 females; aged 27±5 years) after oral administration of 40 mg MP or placebo in a randomised, double-blind, cross-over design. Both electric and magnetic P1, N1, P2 and MMN components were analysed. Magnetic counterparts were analysed using single equivalent dipoles. Visual Analogue Scales (VAS) was used to detect subjective effects of the drug.

Results: MP increased arousal level in VAS. According to our preliminary analysis, MP changed dipole strength and locations of MMN to frequency deviations in MEG responses. MP also reduced P200 amplitude in EEG.

Conclusions: Our findings suggest that MP may change neural bases of auditory information processing. Dopamine and norepinephrine neurotransmitter systems could be responsible for modulation of this processing.

EEG and Multimodality Evoked Potentials in Neonatal Hypoxic - Ischemic Encephalopathy A Developmental and Prognostic Study

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Introduction: Prediction of handicap and developmental delay following hypoxic-ischemic encephalopathy depending on clinical criteria is difficult. This work aims at: (1) studying the predictive role EEG and EP compared to the developmental outcome in neonatal HIE, (2) identifying the severity of the future handicap in relation to the degree of test abnormality.

Methods: 31 full-term neonates with HIE and 15 age matched controls had EEG, median (MNSEP) and posterior tibial nerves (PTNSEP) somatosensory evoked potentials, and visual evoked potentials (fVEP) during the first 28 days, and a follow up testing at the age of 6 months. The three-point EP score (Scalais et al, 1998) and the four-point score for EEG (Pressler et al, 2001) were used to grade the different tests. Neurologic examination and Developmental evaluation using Denver Developmental Screening test (DDST) were carried-out at the age of 6 months then the degree of handicap was classified as: mild, moderate and severe.

Results: There was statistically significant relation between the EEG, MNSEP, fVEP results and DDST results ($p=0.001$, < 0.00001 , < 0.00001 for EEG, MNSEP, fVEP respectively). The sensitivity was 90.5%, 86.4%, and 81.8% for each test respectively, the positive predictive power was 90.9%, 95.0%, 78.3% and the negative predictive power was 77.8%, 95.0% and 50% respectively. The grade of the test abnormality was found to be significantly related to the degree of handicap. Test grades II, III are associated with severe sequelae however grades 0/I are associated with normal outcome or a mild developmental delay.

Conclusion: This study confirms that the reliability of EEG and EP complementary diagnostic and prognostic tests reflecting the status of the CNS in neonates with HIE.

Schizophrenia: The Relationship Between Frontotemporal EEG Coherence and Regional Brain Metabolism Measured by ^{18}F FDG PET

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Introduction: Studies of patients with schizophrenia provide extensive evidence of disturbed function of both local and distributed prefrontal neuronal circuits.^{3,4} The level of connectivity and disconnectivity provides a compelling framework to explain the above results. The disconnection theory of schizophrenia refers to the failure of proper integration or collaboration between two or more cortical areas, or subpopulations of neurons. These functionally specialized systems are required for the sensorimotor integration and cognitive mapping of reality. The connection between two or more areas is developed through the ontogeny and also by experience-based postnatal plasticity.¹ Previous studies have revealed disturbances in the electroencephalographic coherence in schizophrenia, mainly in the left fronto-temporal cortex, as an objective neuro-physiological marker of abnormal neuronal connectivity and impaired information processing.

Methods: In the prerequisite analysis we confirmed the reduction of fronto-temporal EEG coherences in our cohort of schizophrenic patients in comparison with matched healthy volunteers (N=32). In each EEG recording, 12 artifact-free segments of a 5 s length were subjected to coherence analysis after digital filtering of 0.5 to 45 Hz and converting to source derivation, which is mathematically closely related to the Laplace difference equation and can eliminate all reference and most volume conduction effects. As our a priori hypothesis was to identify the relationship between fronto-temporal EEG coherences and regional brain metabolism, we calculated the intrahemispheric coherence function between frontal and temporal electrodes on both hemispheres (F7-T3, F3-T3, F3-T5, F8-T4, F4-T4 and F4-T6) in the broad frequency range from 0.5 to 25 Hz. EEG coherence values of patients and healthy controls were compared by means of two-way analysis of variance (ANOVA) with group and gender being the independent variables. To avoid a type I error, all results were subjected to Bonferroni correction method. To reveal a possible influence of antipsychotic medication, an additional ANOVA was performed within the patient group with medication dose as a covariate. Besides that, Pearson correlation coefficients were computed to investigate if the antipsychotic medication (in chlorpromazine equivalents) influenced the EEG coherence values. By the use of Statistical Parametric Mapping (SPM99) we then analyzed the relationship between the fronto-temporal EEG coherence and regional brain metabolism measured by the uptake of ^{18}F fluoro-deoxyglucose (^{18}F FDG) in the group of schizophrenic patients.

Results: Comparison of EEG coherences by means of two-way analysis of variance (ANOVA) revealed that schizophrenic patients had significantly lower EEG coherences in derivations from the left hemisphere (F7-T3, F3-T3 and F3-T5) as well as from the right hemisphere for F8-T4 and F4-T6 coherence (all ≤ 0.001). In the group of schizophrenic patients we found a (1) significant negative correlation between fronto-temporal EEG coherence and FDG uptake in the temporal cortex (Brodmann area 24, 28, 38, hippocampus), rectal and medial frontal gyrus (BA 11 and 25), (2) significant positive correlations between fronto-temporal EEG coherence and FDG uptake in neocortical regions (BA 19, 4, 6, 8, BA 7, 46).

Conclusions: In our study we evaluated both the EEG coherence and ^{18}F FDG PET with the aim to clarify the relationship between fronto-temporal connectivity and regional metabolism, in other words between disconnection and regional dysfunction. We found that the level of fronto-temporal EEG coherence correlates negatively with ^{18}F FDG uptake in the temporal lobe, limbic lobe, rectal and medial frontal gyrus. In accordance with this observation, the lower the connectivity, the higher the metabolism is in mediofronto-temporal (limbic) regions. This finding supports the hypothesis, that decreased inhibition from the prefrontal cortex (fronto-temporal disconnection) leads to higher activity of the medio-temporal cortex and medio-frontal cortex. This finding is consistent with the notion that schizophrenia involves pathology and dysfunction within a widely distributed neocortical-limbic neural network.² The results provide evidence for a relationship between reduced connectivity of the fronto-temporal cortex assessed by means of EEG coherence and FDG uptake changes primarily in the limbic system.

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Thalamic Abnormalities and Cognitive Impairment in Schizophrenia

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Background: Structural neuroimaging studies of schizophrenia have found abnormalities in the thalamus involving the mediodorsal nucleus, the pulvinar and centromedian nucleus. There is increasing evidence implicating abnormalities in the mediodorsal nucleus (MDN) and its projections to the dorsolateral prefrontal cortex in mediating cognitive impairment in schizophrenia. This study will investigate the relationship between MDN size and cognitive performance in patients with schizophrenia.

Methods: A sample of 20 patients with schizophrenia, 20 first degree relatives, and 20 controls will undergo cognitive tests of working memory (N-back) and receive high-resolution MRI scan of the brain. Voxel-based morphometry will be used for image analysis.

Results: We expect to find a positive relationship between MDN size and working memory performance. Specifically, we predict that patients will perform worse on the working memory task, and will have smaller MDN than controls. Moreover, first-degree relatives of patients with schizophrenia who also have deficits on the n-back task will also have this structural finding.

Conclusions: The study is expected to add to the growing evidence of thalamic abnormalities in schizophrenia and highlight the probable role of MDN in mediating cognitive impairment.

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P300, Dopamine Transporters and D₂/D₃ Receptors in Smokers – a Combination of Dual Isotope SPECT and ERP Studies

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Introduction: Chronic nicotine exposure leads to changes in the dopaminergic reward circuits. P300, a commonly used positive event-related potential (ERP), has been shown to be influenced by smoking and dopaminergic activities. The objective is to explore the impact of smoking in vivo both from neuro-imaging and neurophysiology perspectives. The relationships between both pre-and post-synaptic dopamine systems and P300 were assessed.

Methods: Ten healthy male smokers were included. Data related to smoking were collected. All of the subjects were assessed by dual isotope SPECT using both [¹²³I] IBZM and [^{99m}Tc] TRODAT-1 ligands (for measuring D₂/D₃ and dopamine transporter (DAT) binding activities, respectively). In addition, the classical odd-ball paradigm was used to measure their auditory ERP (amplitude and latency of P300 over Pz, were obtained).

Results: DAT density correlates significantly with the latency of P300 in Fz, Cz and Pz ($p < .05$), but not with the amplitude. There is no significant correlation between D₂/D₃ receptor density and ERP variables.

Conclusions: DAT density is correlated with the latency of P300. The findings indicate that dopamine functions, especially at the presynaptic level, may affect P300 performance in smokers.

Comparison of Detectable Duration of Auditory Stimuli in Sensory Gating

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Introduction: Sensory gating is considered a sensitive measure of neural auditory processes in the brain. Not all previous work on this phenomenon has used the same stimulus type, raising the question as to whether different stimuli will produce different and therefore incomparable results.

Methods: We test here for differences in response due to different stimulus characteristics, by presenting a stimulus set twice, with two different stimulus characteristics, clicks versus beeps, to the same subjects. The subjects are all smokers, tested while abstaining and after smoking either a nicotine or denicotinized cigarette. Gating of auditory evoked potentials P50, N100 and P200 are examined as group(2; nicotine vs. denicotinized) by stimulus(2; beep vs. click) by time(2; before/after smoking) for differences in gating at electrode sites FCZ and T8. Gating was taken as ratio of response to second stimulus of a pair to the response to the first stimulus of a pair.

Results: No differences were found with respect to stimulus changes. A positive result was a pre-/post-smoking difference in the P200 gating at T8.

Conclusions: Sensory gating as measured by suppression of auditory evoked potential in a paired stimuli paradigm is insensitive to differences in stimulus characteristics in terms of a detectable tonal quality vs. a transient click of too short a duration to detect as tonal. An unexpected non-stimulus related result suggests that further investigation of normal responses to the paired-stimuli paradigm may produce interesting and potentially useful data.

Affective Chronometry of Emotional Perception in High Anxiety Individuals: EEG Investigation

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Introduction. The main objective of the present study was to examine whether high trait anxiety influences the dynamics of brain activity within the early stage of emotional responding.

Methods. The 62-channel EEG was recorded while control (n=18) and high anxiety (HA, n=18) subjects viewed sequentially presented neutral, threatening and pleasant pictures (exposition time = 6000 ms). Event-related synchronization and desynchronization of EEG was used as an adequate method for studying time course of emotional cortical activation.

Results. Between-group differences, associated with stimulus emotionality, were linked to the test period of 0-1000 ms after stimulus onset and theta frequency bands. HA vs. controls exhibited deficient theta-1(4-6 Hz) synchronization in the

right prefrontal cortex along with a tendency to relatively larger synchronization in the left prefrontal cortex in response to both threatening and pleasant stimuli. In the posterior cortical regions of both hemispheres HA revealed the largest theta-2 (6-8 Hz) synchronization to threatening and the lowest synchronization to pleasant stimuli.

Conclusions. It is concluded that pronounced theta-2 synchronization in the posterior cortex (extensive working memory processing) along with relatively larger theta-1 synchronization in the left prefrontal cortex (analytical cognitive strategy) observed in HA in response to threatening stimuli may reflect neurophysiological basis of uptake of threatening information in HA. Overall the findings suggest that EEG oscillations in the theta band reflect personality differences within the early stage of emotional responding.

The Influence of Gender and Age on Sleep Macroarchitecture in Healthy and Depressed Children and Adolescents

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Introduction: Sleep macroarchitecture in adults with depression is heavily influenced by gender. It is not known whether these gender-dependent sleep macroarchitectural disturbances in MDD appear early in development. The primary aim was to evaluate the influence of gender and age on differences in sleep macroarchitecture in healthy and depressed children and adolescents.

Methods: 128 children and adolescents, ages 8-18 years of age, participated in the study. Seventy-five (39 F, 36 M) symptomatic depressed outpatients were compared to 53 normal controls (28 F, 25 M) matched for age. All of the outpatients met DSM-IV criteria for nonpsychotic depression and were unmedicated at the time of study. Night 1 served as lab adaptation and sleep EEG analyses were based on night 2 data. Visual stage scoring was conducted according to standard criteria. MANOVA evaluated the group by gender by age interactions first, followed by simpler effects as warranted. Least-squares multiple comparisons evaluated differences between individual means.

Results: There were significant three-way (group, gender, age) interactions for total sleep period, percent spent in stage 1, stage 2, and slow-wave sleep and REM latency. The age effects were evident in most sleep measures, especially total sleep period. The adolescent depressed males showed the greatest age-related changes in sleep with increased stage 1, decreased stage 2 and slow-wave sleep, and shortened REM latency.

Conclusions: These findings suggest a differential developmental influence on sleep in early onset depression that is heavily dependent on gender. The age-related changes in sleep architecture appear to be gender and disease-dependent.

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Repetitive Transcranial Magnetic Stimulation in Bipolar Depression

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Objective: Repetitive transcranial magnetic stimulation (rTMS) has been demonstrated to be effective in depressive disorders in many studies. But this promising method has not been specifically studied in bipolar depression in which antidepressive medications can precipitate manic episode and lead to rapid-cycling disorder.

Methods: Five patients having bipolar depression were applied rTMS in an open and uncontrolled study. Hamilton Depression Rating Scale were given the patients before the treatment after ten sessions of rTMS. Fifty percent decrease in the scale was evaluated as 'response'. The patients also used antidepressive, antipsychotic or mood stabilizing drugs.

Results: All of five patients responded to the rTMS therapy.

Conclusion: rTMS may be an effective and safe measure in the treatment of bipolar depression.

Transcranial Magnetic Stimulation Therapy in Refractory Depression

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Neuroscientists has become increasingly concerned with brain stimulation techniques. Electroconvulsive treatment (ECT) is a traditional therapeutic method that stimulates brain electrically. In recent years transcranial magnetic stimulation (TMS) treatment has emerged as a promising research and clinical tool. In TMS short though power magnetic currents are directed into the brain by means of coils located on the skull. Improvement in depression, loss of energy and cognitive decline has been observed by safe and painless magnetic stimulation activating the neural circuit. In repetitive TMS (rTMS) the current is sent in a 'pulsed' fashion.

In our clinic 40 outpatient cases diagnosed as having depression according to the DSM-IV were applied rTMS with total 2000-5000 pulses. The patients had treatment-resistant depression and were continuing to take medicine. Before and after the rTMS treatment the patients were given HAM-17 and taken quantitative EEG (QEEG).

After 10 sessions of rTMS HAM scores were decreased 30-50 percent. This was evaluated as a rapid improvement. Cognitive decline and loss of energy were the most rapidly improving symptoms. In QEEG a general increase in delta and theta power was observed, an effect that are seen following antipsychotic administration.

These results suggest that rTMS enhances recovery from depression in patients that continue to use antidepressive drugs. rTMS lead to neuroleptic-type changes in neuronal activity.