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The Clinical Relevance of EEG Interpretation

E. Niedermeyer

ABSTRACT
There is need nowadays to re-emphasize the capabilities of electroencephalography: a method representing the extremely important function/dysfunction-orientation in neurological thinking and practice. Valuable and relevant messages to the clinician naturally require solid EEG training and the resulting expertise.
The idea that valuable EEG information is limited to the field of epileptology is erroneous. A plethora of clinically relevant messages can be derived from the EEG in nonepileptic conditions and, above all, in metabolic (and so called "mixed") encephalopathies where neuroimaging has almost nothing to offer.
The discussion of EEG and epileptology only skirts pediatric conditions (and most of the epileptic syndromes). It is shown that EEG reading in epileptology is a lot more than simply "hunting spikes." A strong plea is being made against the presently fashionable overuse of the term "nonconvulsive status epilepticus."
Continuing neglect of functional/dysfunctional orientation can seriously endanger the entire field of Neurology.

Event-Related Correlations in Learning

Impaired Children During A Hybrid Go/No-Go Choice Reaction Visual-Motor Task

Jurriaan M. Peters, Deborah P. Waber, Gloria B. McAnulty and Frank H. Duffy

ABSTRACT
One hundred sixty-nine learning impaired (LI) and 71 non-learning impaired (NLI) children underwent a hybrid go/no-go choice reaction time visual-motor task to study the behavioral and physiological fundamentals of learning disorders. A left button was pressed for Left Arrow (LA) stimuli, a right for Right Arrow (RA) stimuli, none (no-go) for a non-directional arrow. Stimulus specific visual evoked potentials were formed and, with PZ as index electrode, were lag-correlated to frontal electrodes to form Event-Related Correlations (ERC). Exploratory t-statistic significance probability maps (t-SPM) were used to define regions of interest (ROI).
Behaviorally, there was a right-hand advantage over the left in the NLI group, but less in the LI group. Electrophysiologically, RA and LA conditions increased correlation between visual areas (PZ) and contralateral frontal areas (F3 and F4). A unilateral ROI, at electrode FC1, also preceded both left- and right-handed responses. Neurobehaviorally, increased visual-motor correlation was associated with better performance, especially for the left hemisphere, at F3 and FC1. Surprisingly, visual-motor correlations were not associated with performance for the NLI group in the RA and no-go condition. Our data support previously reported difficulties of learning impaired children in low-level information processing. Furthermore, we hypothesize that LI, in contrast to NLI children, demonstrate difficulty in automatizing routine tasks.

Quantitative Electroencephalographic Studies of Cue-Induced Cocaine Craving

Malcolm S. Reid, Leslie S. Prichep, Debra Ciplet, Siobhan O'Leary, MeeLee Tom, Bryant Howard, John Rotrosen and E. Roy John

ABSTRACT
Quantitative electroencephalographic (qEEG) profiles were studied in cocaine dependent patients in response to cocaine cue exposure. Using neurometric analytical methods, the spectral power of each primary bandwidth was computed and topographically mapped. Additional measures of cue-reactivity included cocaine craving, anxiety and related subjective ratings, and physiological measures of skin conductance, skin temperature, heart rate, and plasma cortisol and HVA levels. Twenty-four crack cocaine-dependent subjects were tested for their response to tactile, visual and audio cues related to crack cocaine or neutral items. All measures were analyzed for significant difference by comparing cocaine versus neutral cue conditions. An increase in cocaine craving, anxiety and related subjective ratings, elevated plasma cortisol levels, and a decrease in skin temperature, were induced by cocaine cue exposure. Distinct qEEG profiles were found during the paraphernalia handling and video viewing (eyes-open), and guided imagery (eyes-closed), phases of cocaine cue exposure. During paraphernalia handling and video viewing, there was an increase in beta activity accompanied by a drop in delta power in the frontal cortex, and an increase in beta mean frequency in the occipital cortex. In contrast, during guided imagery there was an increase in theta and delta power in the frontal cortex, and an increase in beta power in the occipital cortex. Correlation analyses revealed that cue-induced anxiety during paraphernalia handling and video viewing was associated with reduced high frequency and enhanced low frequency EEG activity. These findings demonstrated that EEG activation during cue-induced cocaine craving may be topographically mapped and subsequently analyzed for functional relevance.

P300 (Latency) Event-Related Potential: An Accurate Predictor of Memory Impairment

Eric R. Braverman and Kenneth Blum

ABSTRACT
To determine if P300 latency changes precede and correlate with memory and mental status, patients (N=1506 aged 20-100 years) who received medical and psychiatric diagnoses (from 1997 to 2002), were assessed for P300 (N=1496), WMS-III (N=694), and MMSE (N=456). Patient and control groups included, a) normal WMS-III on all 4 subscales (N=36), b) normal WMS-III and MMSE (N=189) with subjective memory/mental status complaints, and c) medical patients with normal WMS-III and no memory complaints (N=205), and d) P300 control group without medical, psychiatric or memory problems for ROC.
Patients with impaired/borderline memory had a prolonged P300 latency (P<0.02) compared to age matched non-impaired controls; in patients with normal WMS-III/MMSE, with subjective mild memory/mental status impairment, P300 latency was prolonged compared to controls (P=0.0004). The P300 latency increased by 0.72ms per year (P=7.9x10-65) and voltage decreased by 0.03dV per year (P=6.7x10-10), and both parameters were linearly correlated with the age of the subjects.
Male subjects had an average voltage of 6.1dV and female 6.8dV(P=0.00009). Statistically, prolonged latency began at age range 41-50 (P=0.0002); reduced P300 voltage began at age range 51-60 (P=0.003). WMS-III memory decline for all measures began in females at age range 61-70 (P value at least=0.02) and for males at age range 61-80 (P=0.02). Prolonged P300 latency (P<0.0001) and memory impairment (at least <0.02) were greater for females than males. MMSE memory decline, male and female, began at age range 81-90 (P value of at least 0.00007).
In our logistic regression model P300 latency was more predictive of WMS-III impairment than MMSE >24. In patients whose WMS-III score is impaired ≤ 69, or borderline ≤ 79 (P at least =0.004), a P300 latency more prolonged than the norm ($\geq 300 + 30 +$ Age) identifies these patients, whereas a MMSE >24 failed. With the ROC curve, we confirmed that P300 latency could accurately identify borderline/impaired memory.

Value of the Early Electroencephalogram After a First Unprovoked Seizure

A. Schreiner and B. Pohlmann-Eden

ABSTRACT
Studies on the predictive value of the electroencephalogram (EEG) concerning the risk of seizure recurrence have shown contradictory results. We prospectively studied the predictive value of the standard EEG and EEG with sleep deprivation for seizure relapse in adult patients presenting with a first unprovoked seizure.
EEGs were performed on 157 adult patients within the first 48 hours of the first seizure. Additional EEGs with sleep deprivation were obtained in 60 cases. The standard EEG was abnormal in 70.7% and significantly associated with an increased risk of seizure recurrence [risk ratio 4.5, 95% confidence interval (CI) 1.8; 11.3, p=0.001]. Subgroup analysis revealed the highest recurrence rates for patients with focal epileptiform activity (risk ratio 2.2, CI 1.2; 4.2, p=0.01). EEGs with sleep deprivation were abnormal in 48.3% of all cases and revealed epileptiform discharges in 13.3% of the patients who had no epileptiform activity in the standard EEG.
Routine EEG revealed abnormalities in 60 of 94 patients who presented with normal neurologic status on admission. Further neuroradiological examinations detected previously unknown brain lesions in 19 of these cases, particularly cerebrovascular disease (CVD, n=7), brain tumors (n=6), and posttraumatic scars (n=4).
In conclusion, the EEG is important for the early detection of focal nonepileptic and epileptic abnormalities after a first unprovoked seizure in adult patients and may provide valuable information on previously unknown disorders, particularly CVD and cerebral tumors. The abnormal EEG is a highly significant predictor for seizure recurrence. An additional EEG with sleep deprivation is helpful in cases when standard EEG does not reveal epileptiform discharges.

EEG and Behavioral Changes Following Neurofeedback Treatment in Learning Disabled Children

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ABSTRACT
Neurofeedback (NFB) is an operant conditioning procedure, by which the subject learns to control his/her EEG activity. On one hand, Learning Disabled (LD) children have higher values of theta EEG absolute and relative power than normal children, and on the other hand, it has been shown that minimum alpha absolute power is necessary for adequate performance. Ten LD children were selected with higher than normal ratios of theta to alpha absolute power (theta/alpha). The Test Of Variables of Attention (TOVA) was applied. Children were divided into two groups in order to maintain similar IQ values, TOVA values, socioeconomical status, and gender for each group. In the experimental group, NFB was applied in the region with highest ratio, triggering a sound each time the ratio fell below a threshold value. Noncontingent reinforcement was given to the other group. Twenty half-hour sessions were applied, at a rate of 2 per week. At the end of the 20 sessions, TOVA, WISC and EEG were obtained. There was significant improvement in WISC performance in the experimental group that was not observed in the control group. EEG absolute power decreased in delta, theta, alpha and beta bands in the experimental group. Control children only showed a decrease in relative power in the delta band. All changes observed in the experimental group and not observed in the control group indicate better cognitive performance and the presence of greater EEG maturation in the experimental group, which suggests that changes were due not only to development but also to NFB treatment.

Patterns of Interictal Spike Propagation Across the Central Sulcus in Benign Rolandic Epilepsy

Ki-Young Jung, Jae-Moon Kim and Dong Wook Kim

ABSTRACT
It has been reported that the rolandic area generating spikes is hyperexcitable, and that rolandic spikes propagate across the central area. However, the pattern of rolandic spike propagation and how the dipolar distribution of the spikes is related to the propagation pattern have not yet been studied.
Thirty-nine EEGs from 27 patients with benign rolandic epilepsy (BRE) were examined. Sequential topographic mapping in 4-ms steps was used to analyze the pattern of spike propagation. The locations of maximum negative foci, the presence and distribution of the dipolar field, and the propagation pattern were examined.
Dipoles were present in 23 (85.2%) out of 27 patients and in 43 (72.9%) out of 59 foci. Thirty-two foci (54.2%) in 20 patients demonstrated a propagation pattern. The typical pattern consisted of propagation from central to mid-temporal locations across the central sulcus. Most spike foci exhibiting a propagation pattern had a dipolar distribution (87.5%; p=0.008).
These results suggest that rolandic spikes originate from sulcal or gyral cortices on either side of the central sulcus, and that spike propagation can ensue by intracortical spreading across the central sulcus.

Abstracts:

Abstracts of presentations at the 5th Annual Meeting of the EEG and Clinical Neuroscience Society (ECNS) September 17-21, 2003, at Houston, Texas, USA.

Topographic Quantitative EEG and Cognitive Evoked Potentials Before and After Liver Transplant

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Alterations of the standard analog EEG associated with severe liver disease are well known. However, topographic quantitative EEG methods have seldom been used to assess the neurophysiological sequelae of liver disease and its treatment. Eight patients undergoing liver transplantation received quantitative Neurometric EEG study and both auditory and visual P300 evoked potential studies before and subsequent to liver transplantation. Quantitative EEG measures were averaged over eight anterior leads (Fp1, Fp2, F7, F8, F3, F4, Fpz, Fz) , three central

leads (C3, C4, Cz), and eight posterior leads (T5, T6, P3, P4, O1, O2, Pz, Oz). Both the quantitative EEG and P300 data were analyzed using all eight subjects and also by eliminating two subjects who experienced multiple post-transplant rejection problems. Liver transplantation resulted in numerous statistically significant improvements in the quantitative EEG profile, the most important of which included significant reductions in theta absolute power over central leads and significant reductions of theta relative power over anterior, central, and posterior leads. In addition, beta absolute power was significantly increased over posterior leads, and beta relative power was significantly increased over central and posterior electrode sites. All of these changes were apparent with analyses that included as well as excluded the two subjects with rejection problems. However, when the two cases with potential transplant rejection were removed from analyses, alpha relative power was found to be significantly elevated over anterior, central, and posterior cortex, and the auditory P300 latency showed a significant movement toward normalization (pre-transplant mean = 392 msec; post transplant mean = 333 msec., p = .024). Analyses of delta activity and inter-hemispheric coherence values were unrewarding. Evoked potential amplitudes did not change with transplantation, and visual P300 latencies did not change as well. It is suggested that topographic quantitative electrophysiology, perhaps combined with objective neurocognitive measures, may permit more refined assessment of the clinical course following liver transplant.

EEG Highlights

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Career highlights from 1960 to the present will be described. Early work with psychiatric and EEG evaluations of epilepsy was followed by numerous studies of electroconvulsive treatment. A double-blind EEG and clinical study of flurothyl induced seizures compared with ECT revealed similar efficacy with ictal differences and less confusion and memory loss with flurothyl. Other studies compared right, left and bilateral ECT and examined effects of ACTH 4-10 and pemoline on ECT induced memory changes. A 1964 study of EEG emotional activation bore striking resemblance to mood provocation tasks used in fMRI today. Strict diagnostic criteria and structured interview approaches were applied before the advent of standard interview schedules. Applications of these methods combined with EEG studies led to better separation between affective disorders and schizophrenia with important prognostic implications. Clinical EEG studies were conducted in selected populations including autistic children, child and adult inpatients, referrals from law enforcement agencies, and follow ups of stereotaxic amygdalotomy for seizure and behavior disorders.

Numerous controlled studies of specific EEG waveforms in psychiatric populations were reported. Sleep deprivation and multiple agents for EEG laboratory sedation were examined. Evoked potentials and CNV were investigated before and during unilateral ECT, and in autistics, hospitalized adults, and normal volunteers and patients taking lithium. QEEG was utilized to compare diagnostic groups and controls with a variety of psychotropic agents. Double-blind comparative studies of ECT, lithium and drug combinations in the treatment of mania were reported with clinical and quantitative EEGs demonstrating associations with therapeutic modality and patient response. The clinical utility of EEG monitoring during drug and somatic therapies was emphasized.

Posters:

Clinical Implications of Excess Parasympathetic Responses to Sympathetic Challenges

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Autonomic nervous system (ANS) monitoring based on real-time heart rate variability and wavelet spectral analysis provides an independent, objective means of monitoring both ANS branches at the same time. Recent findings from concurrent parasympathetic and sympathetic measurements in response to sympathetic stimuli have uncovered an unexpected, clinically relevant condition, which has been labeled the Paradoxic-Parasympathetic Syndrome (PPS). PPS is a dynamic ANS imbalance that seems to accompany many diffuse and ill defined symptoms mostly occurring together, including sleep difficulties, night edema (with jittery legs), mild cognitive difficulties, and low grade morning headaches. PPS has also been found to manifest as different disorders in different patients.

PPS seems to destabilize the disease response or the therapy response or both. Whether PPS is the cause of the disorder or is caused by the disease or a little of both is not known, and probably an individual by individual issue, however, physicians have observed that correcting for this dynamic autonomic imbalance can reduce the severity of the disease or disorder, and in some cases eliminate the symptoms all together. The current working hypothesis is that PPS is independent of the clinical state of the patient and can be treated independently.

Current therapy for PPS targets systemic parasympathetic outflow from the ANS centers in the Medullary Brainstem. To date, patients with healthier ANSs have had this imbalance corrected in 9 to 12 months and have been weaned, thus, utilizing the plasticity of the patient's nervous system to re-establish and maintain a new more appropriate operating balance for the patient.

Sample longitudinal studies from ADD patients are included to illustrate the syndrome and demonstrate the possible therapy plans. The patients are diagnosed with ADD or ADHD and some included depression. The patients (as previously diagnosed) were on Aderol or Ritalin. After beginning the ANS therapy (25 mg Elavil QHS with 100 mg Norpace BID) the patients were weaned from the Aderol or Ritalin with no change in their ability to concentrate and focus. As and if needed, patients can be titrated up to 50 mg Elavil and 200 mg Norpace). In some cases, orthostasis can exist or can be unmasked as the PPS is reduced. In these cases, 2.5 mg ProAmatine BID for four to six months, or until the orthostasis is resolved. The patients depicted here all reported feeling "more alive" and still able to concentrate and focus, even after being weaned from therapy and are now drug free.

Effects of Industrial Solvents on Human Autonomic Nervous System

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Introduction: It has been shown in anesthetized animals that heavy metals and industrial solvents affect blood pressure (BP), heart rate (HR), and HR variability (HRV). It has also been shown that these agents affect the functioning of sympathetic nerves (Kobayashi, et al., 1983; Kobayashi, et al., 1987; Laine, et al., 1996; Xu, et al., 2002). Recently we studied workers in heavy industry and compared their autonomic test results with patients with known damage to medullary autonomic centers.

Methods: Seven workers (ages 36 to 57), three age matched normals, an elderly normal, and two patients were studied. The two patients include, one (age 54) with known medullary autonomic injury due to auto accident, and the other with late stage diabetes and cancer (age 79) with proven severe autonomic neuropathy. A non-invasive, autonomic monitor was used to measure the subjects' and patients' autonomic responses at rest and to challenges: a five minute period of rest, a one minute parasympathetic challenge of deep breathing, a 1:35 minute sympathetic challenge of a series of short Valsalva maneuvers (10-15 seconds), and a quick postural change from sitting to standing and remain standing for five minutes. Autonomic nervous system (ANS) responses were computed using continuous wavelet transform analysis of published HRV practices using respiration (Akselrod, et al., 1981, 1985, 1987, 1988).

Results: All seven workers showed altered resting and dynamic autonomic functioning as compared with their age matched normals and published HRV normal ranges. Baseline measures of workers' ANS activity declined with time of exposure, with the parasympathetic measure declining faster. All workers, except those with the shortest exposures, showed little if any parasympathetic response to deep breathing and highly altered ANS responses to sympathetic challenge, including an excess parasympathetic response (paradoxic parasympathetic syndrome, PPS: an unexpected increase in parasympathetic activity in response to a sympathetic challenge). The workers' autonomic responses to postural change were not correlated; however, it has been reported that orthostasis can be masked by PPS (Stoupakis, et al., 2002). Workers with the longest exposures matched or nearly matched both the resting and dynamic responses of the two patients, and were significantly lower than the elderly normals' autonomic responses.

Conclusions: The results of autonomic testing seem to indicate a significant correlation between severity of autonomic dysfunction and time of exposure to industrial solvents. The test results from those with long term exposures indicate autonomic dysfunction characteristic of patients with known autonomic damage. Thus, it seems as if long-term exposure to industrial solvents can accelerate autonomic demise, similar to severe injury or chronic disease and hasten "autonomic aging."

QEEG and SPECT Measures in Acute Tryptophan Depletion Trial

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Introduction: This study explores the effects of tryptophan depletion on the simultaneously acquired brain electrical activity (quantitative EEG) and blood flow (HMPAO based SPECT). It is hypothesized that tryptophan depletion, compared to placebo, will produce significant physiological changes in the brain.

Methods: Five volunteers, 60% male, with a mean age of 34.4(21.5) years, underwent double-blind acute tryptophan depletion and placebo trials administered on two different days in counterbalanced order. At 5 hours post-depletion, a personalized negative mood-inducing script was played while ligand was administered and qEEG and SPECT studies were conducted. QEEG data were analyzed by choosing artifact free epochs, transforming the data to absolute power measures, and paired t-statistics were applied to evaluate the effects of tryptophan depletion versus placebo. The SPECT analysis was conducted by means of automated analysis via SPM99 and also analyzed via paired t-test.

Results: Compared to placebo, tryptophan depletion resulted in significant changes in both qEEG and SPECT. In qEEG, tryptophan depletion produced an overall decrease in the delta, theta and beta frequencies, but a selective increase in the alpha power with dominant frontal distribution. As reported previously (Pergadia et. al, in press), SPECT analysis showed that tryptophan depletion produced significant bilateral hypoperfusion to the frontal lobes.

Conclusions: In accordance with our hypothesis, tryptophan depletion produces significant physiological changes in the brain. Both the qEEG and SPECT measures detect a significant change in activity with a reasonable co-localization to the frontal lobes.

Cortical Excitability in Cocaine-Dependent Subjects

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Introduction: Cortical excitability, as measured by transcranial magnetic stimulation (TMS), has been shown to be abnormal in a number of psychiatric populations. We have previously shown that motor threshold (MT) was elevated, indicating decreased excitability, in at least three-week abstinent cocaine-dependent subjects. In the current study we aimed at replicating our initial finding, exploring other TMS-based measures of excitability, and examining correlation with psychosis proneness.

Methods: Nineteen cocaine-dependent and 11 healthy control subjects (matched for overall age and gender distribution) were examined. Both resting motor threshold (RMT) and activated motor threshold (AMT), as well as the duration of the silent period (SP) obtained via 120% MT stimulation were examined. The cocaine experience questionnaire (CEQ) was administered to determine whether a subject developed psychotic symptoms during cocaine use.

Results: Both RMT and AMT were significantly elevated on left-side stimulation ($p<0.04$ and $p<0.03$, respectively) in cocaine-dependent subjects as compared to healthy controls. Right hemisphere stimulation resulted in strong trends in the same direction. No SP changes were noted. Patients with no paranoid experiences tended to have higher MT as compared to subjects reporting paranoid experiences.

Conclusions: These data support our initial finding of decreased cortical excitability in abstinent cocaine-dependent subjects. We interpret this finding as a compensatory mechanism against the stimulating and epileptogenic effects of cocaine. Further exploration of these abnormalities remains necessary.

Relationship Between Pre-stimulus EEG and Evoked Potential Morphology

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Objectives: Our laboratory has shown recently that phase synchronization in the 2-12 Hz frequency range is the primary mechanism for the generation of auditory EP components with 50-200 ms latency. However, there exists a sizeable inter- and intra-individual variability in the degree of phase synchronization. We hypothesize that some of this variability is due to fluctuations in level of alertness. Therefore, we examined the relationship between pre-stimulus EEG characteristics (the amount of alpha/theta power), and degree of phase synchronization and evoked potential morphology.

Methods: Auditory evoked potentials were obtained from 20 normal subjects and 19 schizophrenia patients. A double-tone burst paradigm was followed, where each subject listened to 60 to 100 pairs of identical tones of 1000 Hz. Pairs of stimuli were presented continuously with an inter-stimulus interval of 8 s, and the two tones in a pair were separated by 0.5 s. EEGs were recorded from channel Cz, and sampled at 1000 Hz. Trials with more than 75mv deflection in either positive or negative direction were rejected from further analysis. Power spectra were computed from 0.5s pre-stimulus interval for all the trials, and the relative powers in the alpha (8-13 Hz) and theta (4-7 Hz) bands were computed. The single trials were grouped into 6 classes on the basis of the pre-stimulus alpha and theta power. These classes are supposed to index the level of alertness.

Results: Grand ensemble averages of the artifact free trials in each group were computed. There was no significant difference in the peak-to-peak amplitude of N100-P200 in different classes. Also, it was found that the trials in the different alertness classes had the same degree of phase synchronization.

Conclusions: Fluctuations in level of alertness, as indexed by the amount of pre-stimulus alpha or theta activity, do not explain the intra- and inter-individual phase synchronization differences.

Impulsivity and the Error-Related Negativity

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Introduction: The error related negativity (ERN) is an event-related potential (ERP) component associated with "execution errors" (fast guesses) and thus, may be related to impulsive responding. This study explored the ERN and its relation to the personality factor of impulsivity in a task involving rewards and punishments.

Methods: ERPs were collected from 20 Rice University undergraduates (9 females, 5 left-handed) while performing a modified Eriksen Flanker Task (Eriksen and Eriksen, 1979). Participants were instructed to respond to the central target letter, flanked by congruent, neutral or incongruent distracter letters. The targets had associated monetary reward (correct responses to targets) or punishment (incorrect responses to nontargets). Subjects completed the Barratt Impulsivity Scale (Barratt, 1993) and were divided into low and high impulsive groups by median split.

Results: Behaviorally, the reaction times (RTs) were faster for the high-impulsives ($p = 0.08$), although the low-impulsives did have faster RTs for errors to congruous, punishing stimuli (stimulus x flanker x response x impulsivity $p =. 003$). In the ERP data, there was a trend for a stimulus x response x impulsivity interaction ($p = 0.08$) indicating a greater ERN to punishing stimuli among low-impulsives.

Conclusions: Low-impulsives showed greater sensitivity to errors associated with punishment than with rewards, as indexed by the ERN, unlike the high-impulsives, who were equally sensitive to errors associated with reward and punishment. Behavioral data suggests that the errors made by the high-impulsives may be caused by "fast guesses," as indexed by faster RTs.

Analysis of Auditory Evoked Potentials Elicited by Repetitive Stimuli

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Objective: To investigate the role of phase synchronization of the spontaneous electroencephalogram in the generation of auditory evoked potential in response to repetitive stimuli.

Method: Trains of six brief auditory tones were presented to 12 healthy subjects, and the responses were obtained. Each tone was 4 msec in duration with a 1 msec rise/fall time, and 0.5 sec separation between successive tones. The first five tones were of 1000 Hz with the sixth tone of 1500 Hz. Trains of tones were presented with an inter-stimulus interval of 8 sec. Single-trial auditory evoked potentials were decomposed into sinusoidal, exponentially decaying/increasing components using the piecewise Prony method. Pre- and post- stimulus phase histograms were compared to determine the degree of phase synchronization produced by auditory stimulations.

Results: It was observed from the analysis of the single trials that the phase synchronization in the 4-12 Hz band decreased from the first to the second tone. This is similar to what we have seen in a double stimuli paradigm. The degree of phase synchronization stayed low through the fifth response. The response to the sixth stimulus differed from the previous five responses, and appears primarily due to an increase in the 0-4 Hz activity, not unlike what we have observed in an oddball paradigm.

Conclusions: No consistent phase synchronization takes place with repetition of identical stimuli. Presentation of a deviant stimulus following a train of identical stimuli results in an increase in neuronal activity.

Electric Brain Responses Indicate Preattentive Processing of Abstract Acoustic Regularities in Children

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Introduction: Successful adaptation to rapidly changing acoustic environments requires fast detection of potentially important events, which must be then followed by further processing of the unexpected sounds to evaluate their importance. The human brain can preattentively detect deviations from the regular characteristics of the recent acoustic input by a neuronal mechanism that is reflected by the mismatch negativity (MMN) event-related brain potential (ERP) component. The MMN is most commonly elicited by infrequent deviant sounds differing in some acoustic parameter, such as frequency, intensity, or duration, from a repeating (standard) sound.

Methods: This study investigated the preattentive processing of abstract acoustic regularities in children aged 8–14 years. Event-related brain potentials (ERPs) were elicited by frequent ("standard") pairs ascending in pitch (the second tone having a higher frequency than the first tone) and by infrequent ("deviant") pairs descending in pitch. In Easy condition, the second tone of the pair was always one step higher (standard) or lower (deviant) than the first tone, while in Hard condition, the second tone was randomly 1–10 steps higher or lower than the first tone.

Results: In Easy condition was found: (1) the mismatch negativity (MMN), and (2) subsequent positive P3a-like deflection. In Hard condition, the amplitude of MMN was lower over frontal sites than in Easy condition, while the temporal component of MMN was not impaired by complexity of abstract regularities.

Conclusions: These results suggest that the complexity of the auditory stimulation affects preattentive auditory change detection in children.

New Approach in Estimation of EEG Complexity

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Introduction: Our approach is motivated by the need to generate a rigorous measure of the degree of complexity of the EEG for possible diagnosis of functional brain disorders. Complexity used in the investigations of EEG usually relies on the entropy (or close "nonlinear characteristics") of dynamic systems, or on Shannon entropy, which we feel is inconsistent a priori. This is because the basic assumption of nonlinear dynamics is a stationarity of the system under consideration. But non-stationarity is one of the main features of the EEG. On the other hand, using the classical Shannon entropy for the characterization of the EEG signal is not adequate, because the Shannon entropy specifies the complexity of the probability distribution or the "abundance of typical trajectories" of the (stationary!) sequence of random variables.

Methods: A new approach to the estimation of EEG complexity is proposed. The approach is based on the idea that complexity can be measured by the fraction of the data which one needs to recover the EEG signal by given collection methods with given accuracy.

Results: Statistical differences between the values of complexity for healthy and schizophrenic subjects were determined.

Conclusions: This new approach to the estimation of EEG complexity may offer better understanding of brain function in normal and schizophrenic subjects.

Brain Computer Interface (BCI) on the Basis of Frontal EEG Asymmetry

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Introduction: The BCI system makes it possible for people to interact with computer-based systems through conscious concentration on their thoughts (J.R.Wolpaw, et al., 2002). A few scalp electrode brain signals are processed, including EEG feature extraction and neural network classification to recognize what mental task the user is concentrating on. Each mental task is associated with a simple command, such as "Move the cursor to the right." One of the main problems of contemporary BCI systems is very poor resolution of mental task classification (usually no more than 3-4), based on one-channel EEG patterns (J. del R. Millan, et al., 2002). Progress is likely by using amplitude distinctions between two channels of EEG as a signal for BCI.

Methods: Six healthy male subjects participated. The EEG signals were recorded from electrodes F3, F4, C3, C4, P3, P4, O1 and O2. These signals were used for calculation of the asymmetry of spectral power [ASM=Log (Ch4-Ch3/Ch4+Ch3)]. Feedback with ASM was provided at each second.

Results: It was shown for the users that it is possible, especially for ASM of frontal alpha, to classify about 6-8 quasi-stable mental states as commands for the BCI system. Usually relatively greater alpha activity at the left frontal is involved in acquiring a more positive state of mood.

Conclusions: These data suggest that the left-right balance of frontal alpha activity can be used for multi-dimensional BCI control.

Effects of Repetitive Transcranial Magnetic Stimulation on Forced Swim Test and Long Term Potentiation in Rat Hippocampus

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Introduction: Repetitive transcranial magnetic stimulation(rTMS) is a promising treatment of major depression in humans, yet its neuronal mechanism is still unknown. In this study, the effects of rTMS on immobility in Forced Swim Test(FST) model of depression and on long-term potentiation(LTP) in the perforant path projections to the dentate gyrus were examined.

Methods: After young male Sprague-Dawley rats were treated with single rTMS(1000 stimuli at 10Hz), the Porsolt Swim test(5-min test) was performed. Then, the treatment of rTMS was repeated for one week, followed by additional 5-min Porsolt Swim tests. LTP in the perforant pathway was measured on the following day.

Results: After a single treatment session, rTMS rats were not different from sham control in immobility times. But after seven sessions, rTMS reduced immobility times in additional 5-min tests. The population EPSP slope of rTMS rats was enhanced compared with that of sham control.

Conclusions: These results suggest that rTMS has an antidepressant-like effect, and it enhances the synaptic efficacy in hippocampus, which may be relevant to its antidepressant effect.

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QEEG and Brain SPECT Measures in Adult Psychiatric Patients Acutely Challenged with Methylphenidate

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Introduction: Complex clinical neurobehavioral presentations with co-morbid diagnoses present challenges in developing therapeutic strategies. QEEG methods can be useful in evaluating efficacy of pharmacological treatments. In this study we questioned whether clinical conceptualization of the patient leading to treatment with dopamine-augmentation is supported by the results of acute challenge with oral methylphenidate on qEEG measures.

Methods: We evaluated 1 female and 10 male patients' qEEG response to 10-20mg oral-dose of methylphenidate by comparing baseline-qEEG activity to activity 60-90min. post-drug administration. In addition, we evaluated brain perfusion with HMPAO brain-SPECT in parallel with qEEG. QEEG data were analyzed in NeuroGuide and paired t-tests were used comparing baseline and post-drug qEEGs. SPECT brain-activity was analyzed using SPM99.

Results: Our data indicated that only 3 of 11 patients studied responded in a predictable way to acute methylphenidate-challenge. The remaining patients did not show predicted response patterns. The expected response to methylphenidate was characterized by elimination of excessive frontal delta and theta. Baseline SPECT results of the 3 responders were characterized by relatively mild deficits.

Conclusions: Predication of response to methylphenidate based on clinical presentation was shown to be only minimally efficacious. Both milder SPECT deficits and frontal slowing on qEEG are predictive of response to methylphenidate treatment. QEEG in parallel with challenge studies may be a useful predictor of successful treatment with methylphenidate. Our results show promising implications for predictive use of neuroimaging techniques and drug-challenge studies. One limitation of this study includes our single-dose evaluation. Future studies may consider a dose-response paradigm.

Do State Scale of Dissociation (SSD) Scores Predict the EEG Parameters that Accompany Dissociative States? A Pilot Study In 16 Psychiatric Patients

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Introduction: Previous studies of an association between dissociative experiences and EEG activity relied on measurements of a dissociative trait, or tendency to dissociate. This study measured spontaneous state symptoms of dissociation and concurrent EEG parameters.

Methods: Sixteen psychiatric patients [mean age 32 (19-53) years; M:F = 3:13] with a high tendency to dissociate [mean Dissociative Experiences Scale / DES score = 51 (18 – 81)%] underwent an EEG recording. They completed the psychometrically validated, 56-item, self-report State Scale of Dissociation (SSD) immediately before and after a 15 minute EEG recording. The first 4 minutes of the EEG recording (artifact-free) were digitalised, Fast Fourier transformed, and spectrally analysed. The entire EEG recording was visually analysed.

Results: Visual analysis of the EEGs showed 8 normal and 8 abnormal EEGs. The abnormalities varied between grades 1 and 3, and were located in the right temporal area in 5 of the 8 patients. Several SSD variables correlated directly with relative beta power, and indirectly with relative alpha, theta, and delta power, at central, temporal, and frontal electrodes. Regression analyses demonstrated that the depersonalisation and hypermnesia subscales of the SSD were the best predictors of the digital EEG variables. The administration of the SSD immediately after the EEG recording yielded the best predictions.

Conclusions: The sample was small and medication exerted a confounding effect. Preliminary analyses suggest that SSD scores might predict the concurrent EEG parameters of dissociative states. The study population should be enlarged to include patients with a variety of psychiatric disorders.

Impulsivity and ERPs in a Computerized Gambling Task

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Introduction: In gambling tasks, ventromedial prefrontal lesion patients and drug addicts show impulsive decision-making in which immediate rewards are chosen over long-term gains. The current study examines ERP differences between high and low impulsive normal subjects during a computerized gambling task.

Methods: Eighteen participants, separated into high and low impulsive groups by median split on Barratt Impulsivity Scale score, viewed and accepted or declined individual cards from an advantageous deck containing small rewards and punishments (net gain), or disadvantageous deck containing large rewards and punishments (net loss), in a modified version of the Iowa Gambling Task. Which decks were advantageous and disadvantageous was not known to the subjects prior to participation.

Results: High impulsive subjects had lower central parietal P3 amplitude than low impulsive subjects ($p < .05$). A trend for deck by group by laterality interaction ($p = .053$) was found for the frontal P2a index of reward processing, which was larger over left prefrontal electrodes to disadvantageous deck choices made by high impulsive individuals, whereas low impulsive individuals showed a reduction in left P2a amplitude to disadvantageous deck choices.

Conclusions: The P3 results suggest less efficient cognitive processing in a complex decision making task in high-impulsive individuals. The reward value of the disadvantageous deck appeared greater to high impulsive individuals than for low-impulsive individuals, as indexed by the P2a, showing that high impulsivity influences decision-making by enhancing the appeal of immediate large rewards in the disadvantageous deck over the long-term accumulation of small rewards in the advantageous deck.

Assessing Brain Function with Combined qEEG, SPECT, and Neuropsychological Measures in Clinical Populations

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Introduction: A focus of current scientific research has been to investigate the relationship between multiple neuroimaging modalities with neurocognitive functioning. Brain imaging techniques such as qEEG and SPECT make it possible to first specifically probe and co-register functional and structural abnormalities in the brain and then correlate focal brain abnormalities with neuropsychological measures. This brain-to-behavior approach may lead to more accurate evaluation and diagnosis of neurobehavioral and neurocognitive disorders to improve treatment efficacy in clinical populations.

Methods: Four right-handed and one left-handed male psychiatric patients, (mean age 65±12), with questionable neurocognitive deficits underwent evaluation including qEEG and HMPAO based SPECT, acquired simultaneously, and neuropsychological testing. A toxicological urine screen was conducted on day of testing. Data from qEEG studies were analyzed using both linked ears reference and Laplacian reference in Neuroguide. SPECT scans of each individual patient were compared to normal controls through SPM 99 analysis. Neuropsychological results were scored and normed according to age and education.

Results: In all cases, correlations between EEG frequencies and brain perfusion were found. Areas with decreased orbito-frontal perfusion showed frontal slowing (delta/theta frequencies). Hyperperfusion was associated with activity in the beta spectrum. These deficits generally correlated with neuropsychological deficits characterized by slowed psychomotor performances as well as a variety of attentional deficits.

Conclusions: Findings of functional brain abnormalities from co-registration of qEEG and SPECT identified deficits within specific anatomical substrates that correlated with diminished performance on associated neuropsychological measures. This brain-to-behavior approach will have useful application in assisting to better characterize clinical populations.

Assessing Local Brain Function with Quantitative EEG and Conventional EEG in Patients with Cerebral Infarction in Correlation with SPECT Scans

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Introduction: Stroke is one of the main causes of neurological disabilities. Therefore, it is very important to evaluate patients with techniques that could reliably assess brain function. It has been reported that brain electrical activity is related to cerebral perfusion. We performed this study to determine and compare the accuracy of conventional EEG and qEEG

based upon a comparison against a normal database, and brain SPECT.

Methods: Six patients (age 65 ± 12) with diagnosis of cerebral infarction were studied with conventional EEG, qEEG, and HMPAO based SPECT. The HMPAO was administered while the EEG activity was being recorded. A toxicological

urine screen was conducted on the day of testing. SPECT analysis was conducted by means of SPM 99. QEEG data was analyzed by standardized protocol involving Neuroguide database. Correlations between SPECT findings and qEEG absolute and relative powers were evaluated.

Results: Conventional EEG was non-localizing upon visual inspection. Considerable correlations between brain activity and brain perfusion were found with qEEG and SPECT. Brain areas on SPECT scan with significantly decreased perfusion showed increased activity in delta and theta frequencies and simultaneously showed decreased activity in alpha and beta frequencies. Increase in beta activity was associated with areas of increased perfusion on SPECT scan.

Conclusions: These findings indicate that qEEG results based upon a comparison against a normal database can more accurately reflect local brain function that parallels SPECT findings. In comparison with conventional EEG, quantitative EEG can be a more powerful tool in clinical evaluation of stroke patients.

Quantitative EEG in Late-Onset Schizophrenia

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Background and Objectives: A variety of EEG abnormalities may occur in schizophrenics who had a typical onset of the disorder in early adulthood. The purpose of this study was to investigate EEG findings in patients with late-onset schizophrenia (onset of illness between ages 40 and 60).

Methods: Ten patients (one male, nine females, average age 52.8 years old) with late-onset schizophrenia underwent MRI of the brain and recording of quantitative EEG.

Results: MRI results for seven of the subjects were within normal limits and the other three showed nonspecific changes. Quantitative analysis of EEG variables revealed that for eight of the subjects, absolute power and relative power for the four EEG frequency bands, overall mean frequency, mean frequency for each of the EEG frequency bands, and inter- hemispheric coherence values did not vary significantly from a normative base of age matched normal subjects.

Conclusions: Results obtained to some degree replicate the single previous EEG study of late-onset schizophrenia (Sachdev et al., Internat. Psychogeriatrics, 11: 421-429, 1999). These findings suggest that the neurophysiological etiology and mechanism of late-onset schizophrenia may differ from that of schizophrenia with a typical age of onset, and that brain abnormalities are not an inevitable accompaniment to late-onset schizophrenia.

P300 Based Brain Machine Interface

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Objective: To develop and test advanced signal processing technology to detect the P300 component on a single trial basis. This would make it possible to develop an effective brain-machine interface (BMI), which could be used to (partially) restore communication capabilities in paralyzed subjects and/or offer them some form of control over their environment.

Methods: A double-stimulus paradigm was used, in which two different visual stimuli were presented. One of the stimuli was presented more frequently (the standard stimulus, 55-85% occurrence) than the other (the rare or target stimulus, 45-15% occurrence). Two types of experiments were conducted: In the first experiment the subject had to respond to the presentation of the rare stimuli by pressing the right button on a mouse. In the second type of experiment the subject had to count the number of occurrences of the target stimuli. Each symbol was presented for 60 ms with a varying inter-symbol duration (2 s, 1 s and 0.5 s). EEG was obtained from 16-channels using the 10-20 system, band pass filtered between 0.3 and 50Hz, and sampled at 250Hz. The EEGs were decomposed into various frequency bands (Delta, Theta, Alpha and Beta) using the piecewise Prony method, and an amplitude threshold detection algorithm was applied to the 0-4 Hz activity of the Pz channel. The threshold was determined on the basis of the 95% percentile of the pre-stimulus amplitude of the first twenty trials. A P300 is detected if the 0-4 Hz activities exceed the threshold within the 300-450 ms post stimulus interval. A second type of detector uses principles derived from pattern recognition, and uses the power and amplitude in various frequency bands.

Results: Correct detection rates of 85% with less than 30% false alarms have been obtained. The second detector gave correct detection rates of 95% with less than 5% false alarms.

Conclusion: Effective single trial detection of P300 activity appears possible. Work is currently in progress to determine which combination of channels, features and stimulus characteristic provides optimal performance.

Improving Separation of EEG Components by Combining Bandpass Filtering and Independent Component Analysis (ICA)

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Introduction: Renewed hopes in EEG analysis are associated with application of Independent Component Analysis (ICA), a powerful tool for separating signal components. However, when it is applied to raw EEG, the basic ICA assumptions of independence of sources may not hold. Bandpass filtering can dramatically relax conditions of independence and, therefore, improve the performance of ICA (Cichocki, Georgiev, 2003). It also can improve

separation of weak components. Here we propose to use for filtering the classical EEG bands, which approximately reflect the functional structure of EEG frequency spectrum.

Methods: This approach was tested on 14-channel EEG recorded in a memory experiment (2 sets of 160 trials for each of 7 subjects). The EEG was cleaned from artifacts, filtered in 5 bands (4-7 Hz, 7-10 Hz, 10-13, 14-17 Hz, 18-21 Hz) and further decomposed with Pearson ICA (Karvanen, Koivunen, 2002). Mean power of filtered EEG channels and of independent components was compared between waiting, memorizing and retaining conditions separately for each set of trials.

Results: Number of trial sets with significant effects of conditions was higher for independent components than for channels. Amongst components demonstrating such effects were components consistently found in most of the subjects.

Conclusions: Filtering in classical EEG bands followed by ICA enables extraction of EEG components sensitive to brain loading. Since each component has its own scalp distribution, more reach information, comparing to usual mapping, can be obtained. Results produced with the proposed approach can be easily analyzed in the framework of traditional EEG frequency components.

Elevated Psychophysiological Response to Induced Stress Associated with the Presence of Controversial Paroxysmal EEG Waveforms

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Several controversial paroxysmal EEG waveforms occur more often among patients with psychiatric symptoms than among controls. However, these findings are often dismissed as normal EEG variants. In this study 49 non-psychiatric Behavioral Medicine Clinic patients received a wake and sleep EEG study, which was either normal (n = 28) or contained a paroxysmal waveform such as 14 & 6/sec. Positive Spikes, Paroxysmal Slow, Small Sharp Spikes, Mitten patterns, Rare Fast, 6/sec Spike-Wave, (n = 21). In a laboratory stress assessment, heart rate, systolic BP, peripheral skin temperature, and frontalis EMG were recorded during resting baseline and after induction of cognitive stress. EEGs were read blind to the clinical complaint or results of stress testing. Following stress, 82.4% of paroxysmal EEG subjects but only 30.4% of normal EEG subjects had skin temperature changes greater than 10 F., and paroxysmal EEGs were strongly associated with absoulte skin temperature changes above the median ($X2 = 8.29$, $p < .005$). Mean absolute skin temperature change was higher for positive EEG patients ($t = 4.04$, $df = 37$, $p < .005$). The point-biserial correlation between positive EEG and skin temperature change was robust ($r = .52$, $p < .001$). Absolute heart rate change was trichotomized and a significant relationship between increased heart rate stress response and paroxysmal EEG was seen ($X2 = 7.66$, $df = 2$, $p < .05$). The point-biserial correlation between heart rate change and EEG was substantial ($r = .45$, $p < .01$). Systolic BP changes were similar to those for heart rate. Nearly 71% of paroxysmal EEG subjects but only 33.3% of normal EEG subjects responded to stress with a paradoxical reduction of EMG ($X2 = 5.22$, $p < .025$), and the mean EMG change was significantly lower for positive EEG subjects ($t = 2.16$, $df = 36$, $p < .05$.). The results demonstrate an altered psychophysiological stress response in patients with controversial paroxysmal EEG waveforms, suggesting that these EEG patterns have biological relevance.

Disruption of Executive Attention in Schizophrenia

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Introduction: Disruption of attention is a hallmark symptom of schizophrenia. Neuroimaging techniques have been successfully used to study executive attention, and event-related potentials have been used to show reductions of components associated with impairments of attention evident in schizophrenia. Prior studies have shown a consistent reduction of the auditory P300 in schizophrenia, while the visual attention findings have been mixed. Both the auditory and visual N2b components (an earlier, modality specific attention index) have been shown to be reduced in schizophrenia, sometimes despite a sparing of the visual P300. Thus, there may be a dissociation between the N2b and P300 attention effects in the auditory and visual modalities in schizophrenia.

Methods: This study used a mixed design including a visual oddball, an auditory oddball and a simultaneous presentation of both auditory and visual stimuli. Subjects were tested on a target detection task with stimuli being either an “X” or a “T” in the visual condition and either a high or low tone in the auditory condition. Ten patients

with schizophrenia and ten healthy controls were tested while recording their EEG data using a 128-channel Geodesic net. Analyses were made on the target minus standard waveforms.

Results: Preliminary results show a reduction of the N2b component in the patient group in both the auditory (p=.0044) and visual (p=.0081) conditions. The P300 showed no significant difference between the groups.

Conclusions: These preliminary results suggest that the modality-specific N2b component is more vulnerable in patients with schizophrenia than the P300 index of general attention.

Symposia

Symposium 1: Comparative Methodology for Spectral Analysis of Cognitive Potentials: From FFT to High-Resolution Time-Frequency Domain Analysis

From Frequency Domain Fourier Components to High Resolution Time-Frequency Components

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In the presence of an external stimulus, the functioning brain emits electrical signals, which can be recorded as event-related potentials (ERP). Analysis of the ERP signals has been the subject matter of many applications in the field of cognitive psychophysiology. The analysis of the event-related oscillations (EROs) in the ERP waveform has been performed through the Fourier Transform. This transform assumes linearity of the system, and it does not provide information on the time-frequency domain localization of the oscillatory components. Of the techniques that provide temporal information, digital filtering suffers because it assumes that a component is an oscillation of a certain frequency range that extends over the recording time. The wavelet analysis also represents oscillatory time signals. If a distinct wavelet basis component does not exist for the ERP signal, components cannot be validly separated in the time-frequency plane by the rectangular tiling patterns of the wavelet transforms. Contemporary research showed that ERP components represent the superposition of nonstationary oscillations of various frequencies over the time axis. Time-frequency signal processing is a natural tool for the analysis of this type of non-stationary signals. The newly developed Short-time Cohen's Class of Distributions (STC) used a sliding window filtered Wigner distribution, and the energy of the ERP was divided into six energy levels, whereafter the time-frequency representation of each level was obtained using STC. The sub-band decomposition not only represented the components of the low amplitudes but also demonstrated the spectro-temporal relations of ERP components. Finally, the obtained time-frequency distributions corresponding to each of the six sub-band signals were fused by using a frequency weighting to provide the overall time-frequency representation.

The newly developed Time-Frequency Component Analyzer (TFCA) utilized a novel fractional domain warping concept to provide very high resolution time-frequency representation for mono- or multicomponent signals with both linear or curved time supports. By conducting Wigner analysis on adaptively chosen warped fractional Fourier domains, the TFCA provided the time-domain representation of the constituent components of the composite signal with unprecedented accuracy. The TFCA thus provided an overall time-frequency representation of the ERP signals, which constituted the time-frequency representations corresponding to the individual signal components that could be subject to detailed post-processing. Using TFCA, the signal components could be extracted from the recorded ERP signal very accurately. The newly developed time-frequency domain high resolution techniques (namely, STC and TFCA) lead to another understanding for the term "component." Components are not the peaks on the time axis (ERP), not oscillations of a given frequency (EROs), not related to the offshoots of adaptive frequency templates over time (WT), but are time-varying energy distiributions (STC) or islets of frequency integrations over the time axis (TFCA).

Electrical Activity of the Brain is Represented by Oscillatory Activity of Various Frequency Ranges

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Time-domain electrical activity of the brain is represented by event-related potentials (ERPs). Research on the transient time-domain activity and the discovery of time-domain components has contributed much to the enlightenment of the intricate machinery of the brain. However, the pioneering work at the turn of the century on gamma and on alpha activity inspired the study of oscillatory activity of the brain. This new window, evaluated as a "paradigm change," led to a set of Fourier components that ranged in frequency from the delta to the gamma range. Research findings and the theory of oscillatory neural assemblies demonstrated that the oscillatory activity of the brain was the valid index of brain's cognitive processing. The oscillatory activity proved fruitful in explaining higher information processing operations, such as pattern recognition and memory. Research has reached a level where it is not any more a global type of memory that is studied with a specific oscillatory component but subtypes of memory with interacting components. As the basic unit of analysis, oscillatory responses proved fruitful in demonstrating the impact of such subtle factors as individual differences. In line with the principle of superposition, research has shown that the morphology of the ERP components for different experimental paradigms, and thus cognitive functions, represented a specific pattern of superposition of various frequency ranges that represented multiple functions.The temporal superposition of such oscillatory components, and the spatial coherences between them, formed the basis for the super-synergy in the brain that derived from the selectively distributed parallel processing in the brain with bottom-up and top-down operations. With such an architecture and functioning, the brain should be dynamic in nature and also nonstationary over time. Thus, refined studies on oscillatory dynamics should use high resolution techniques for extracting the uncontaminated time-frequency oscillatory components that become integrated for performing the intricate information processing operations, of especially humans.

Wavelets in the Analysis of Event-Related Signals of the Brain

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Event-Related Potentials (ERPs) are regarded as the superposition of oscillatory components occupying distinct frequency bands related to functional and behavioral processes of the brain. Digital filtering techniques along with Amplitude Frequency Characteristics (AFC) are widely used in order to extract the oscillatory components of ERP. However, ERP signals are nonstationary in nature. Their frequency content changes with time, thus digital filtering is not suited to analysing them. To capture the nonstationary content of ERPs to some extent, Short-Time Fourier Transform (STFT), in which the signal is divided into fixed size windows and then Fourier transformed, can be used. The use of a fixed window size (or equivalently scale) restricts the resolution in STFT, thus wavelet decomposition with varying window size (scale) is better suited to ERP signal analysis. In this paper, ERP signals under different cognitive paradigms are analyzed in a wavelet-based framework. Results for different wavelet bases, including the well-known quadratic B-spline, are presented. In order to obtain the oscillatory ERP components with known frequency bands, nonlinear subband decomposition structures are used. The obtained results of wavelet based analysis are compared with those of the STFT based analysis, and it is found that wavelet based analysis provides improved results. However, the data dependent nature of the subband decomposition parameters creates significant difficulties in practical applications of wavelet based analysis. More importantly, ERP signal components cannot be separated in the time-scale plane by the rectangular tiling patterns of the wavelet transforms, hence more powerful joint time-frequency analysis techniques are required.

Joint Time-Frequency Analysis of Event-Related Energy Distribution of the Brain: Short Time Cohen's Class of Distributions (STC)

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The fundamental problem in sciences that study the brain is to understand the mechanisms by which an immense number of neurons in the human brain interact to produce higher cognitive functions (Freeman, 1975). Event-related potentials (ERPs) are neuroelectrical brain waveforms that are obtained in response to external or

internal stimuli, and are signals used in the investigation of dynamic mechanisms of the brain in biological entities, humans or animals. High frequency components of event-related potential (ERP) to easy oddball paradigm (standard and deviant) recorded at the Fz recording site of the 10-20 system are analyzed in time-frequency domain by means of Short Time Cohen's Class of Distributions (STC). The present study specifically emphasizes the energy of a signal that is time-varying and is not uniform. The spectro-temporal characteristic of the high frequency components of the ERP waveforms, including beta and gamma waves, were represented. This representation was achieved through the STC, a newly developed technique involving a running window over the data stream. STC allowed a natural way of representing the signal and provided more detailed information on the time-varying energy generated by the brain activity undergoing information processing. STC also allowed the demonstration of the spectro-temporal relations of components including the low level ones. Particularly, the energy distribution of the gamma and beta components of the ERP manifested a structure that may lead to a deeper understanding of brain dynamics.

A New Technique for Joint Time-Frequency Analysis of Event-Related Signals of the Brain: Time-Frequency Component Analyzer (TFCA)

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In the presence of an external stimulus, the functioning brain emits electrical signals that can be recorded as the Event-Related Potential (ERP) signals. The analysis of the ERP signals by conventional methods, such as digital filtering and wavelet decomposition, reveals that they can be modeled as superposition of some oscillatory and non–stationary signal components, which are localized in time and frequency. Time-frequency representations provide the distribution of the signal energy as a joint function of both time and frequency, thus they present a more complete picture of the ERP signals than other conventional approaches. However, digital filtering and wavelet decomposition fail to realistically capture the time–frequency domain localized nature of the ERP signal components. A new algorithm, time–frequency component analyzer (TFCA), is proposed for analysing multicomponent signals with localized time-frequency supports. Recently, the TFCA had been adapted to the analysis of ERP signals. The TFCA provides high resolution description of the time–frequency domain distribution of the individual signal components. TFCA accomplishes these functions by making use of a novel fractional Fourier domain warping concept; the time–frequency analysis of the signal components was made by using the recently developed directionally smoothed Wigner distribution algorithm. While providing time–frequency distributions that are as sharp as the Wigner distribution, the TFCA suppresses the undesirable cross–cross and auto–cross terms in the Wigner distribution. TFCA also extracts the components from the composite signal with unprecedented accuracy. The analyzed signal components are extracted sequentially in component-specific warped fractional domains. With the aforementioned attributes, TFCA is an ideal technique for studying the multicomponent, nonstationary ERP signals.

Symposium 2: Electrophysiological Substrates of Impulsivity and Impulse Control Disorders

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***Stanford MS*, Baylor University, Waco, Texas, USA**
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Impulsivity is a diagnostic feature of a wide range of psychopathologies. It is especially pervasive in the diagnostic criteria for impulse control disorders (e.g., substance abuse, ADHD, impulsive aggression). It is also implicated in selected personality disorders, especially Cluster B (e.g., Antisocial and Borderline P.D.s) and in other selected AXIS I disorders (e.g., mania and bulimia). Although impulsivity is a broadly used construct in psychopathology, its definition and measurement are controversial. Moeller et al. (2001 Am J. Psychiatry) defined impulsivity as "a predisposition toward rapid, unplanned reactions to internal or external stimuli without regard to the negative consequences of actions, either for themselves or others." This is an adequate description clinical definition, but it is clear from the use of the term impulsivity in DSM-IV-TR, and from research, that impulsivity is multidimensional. This symposium will address the use of EEG and selected ERPs in both construct and predictive

validity studies of impulsivity to help clarify its dimensionality. Basic questions involving "brain triggers" for impulsive acts, conscious awareness of impulsive or "automatic" reactions, what happens in the brain when a person makes an error of commission, and how do the electrophysiological measures relate to both impulsive behaviors and neural transmitter substrates, will be broached. An overview of this area of research will be followed by presentations of specific research results.

Impulsivity and Consciousness

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Impulsivity is a diagnostic construct that is pervasive in a wide range of impulsive control and behavioral disorders. It is multidisciplinary and controversial with no universal agreement on its definition. This paper will address the role of consciousness in impulsive acts (e.g., impulsive aggression) and discuss potential "triggers" in the brain related to "automatic" behaviors in general and impulsive acts more specifically. Measurements of impulsivity from different disciplines will be compared using a general systems theory model of personality. Within this model impulsiveness is proposed to be related to the processing of sequential information that underlies performance on tasks (laboratory and everyday behavioral) which have specific timing and rhythm requirements. It is proposed that working memory and neural gating play key roles in this information processing.

Increased Impulsivity is Related to Auditory Event-Related Potentials in Cocaine Dependent Subjects

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Previous studies report reduced amplitude of the P300 event-related potential in cocaine-dependent individuals. Cocaine dependence is also associated with increased impulsivity, possibly due to deficits in cognitive function that are associated with reduced P300 amplitude. In the current study, we examined the relationship between cocaine dependence, impulsivity, and P300 amplitude. We hypothesized that cocaine-dependent individuals would exhibit increased impulsivity and reduced P300 amplitude relative to controls, and that P300 amplitude would be inversely related to impulsivity. An auditory-oddball event related potential task, along with a self-report (Barratt Impulsiveness Scale-11) and a behavioral laboratory measure of impulsivity (Immediate and Delayed Memory Task), were assessed in healthy controls (n = 13) and subjects who met DSM-IV criteria for current cocaine dependence (n=15). P300 amplitude was reduced for the cocaine group relative to controls. Self-reported and behavioral impulsivity scores were elevated among the cocaine dependent group, with a significant inverse correlation between self-reported impulsivity scores and P300 amplitude. This correlation remained after taking into account the number of antisocial personality disorder symptoms. This study supports the hypothesis that the basic neurophysiology responsible for the P300 amplitude in cocaine dependent individuals may also be responsible for processes leading to increased impulsivity.

Evoked and Event-Related Potential Differences Related to Impulsive Aggressive Behavior

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Impulsive aggression is an emotionally charged, uncontrolled type of aggressive display. This loss of behavioral control is spontaneous and out of proportion to the eliciting stimuli. Previous research has shown a number of evoked (EP) and event-related potential (ERP) differences in impulsive aggressive individuals compared to non-aggressive controls and other aggressive subtypes (e.g., premeditated). These differences suggest that impulsive aggressive individuals have irregularities in both early sensory/attentional processing (P1-N1-P2) and later cognitive (P3) and emotional (LPP) processing. Few studies, however, have attempted to develop an overall model of

impulsive aggression from these results. This presentation will present a profile of EP/ERP differences that appear to underlie impulsive aggressive behavior. The usefulness of electroencephalographic techniques in assessing treatment outcome in impulsive aggressive individuals will also be discussed.

Symposium 3: P300 and Its Relationship to Medical, Neuropsychiatric and Developmental Problems

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The P300 test (considered akin to an EKG) is documented to be a nonspecific, but sensitive marker of brain (mind-body) dysfunction for neurological, psychiatric, medical, and developmental problems. The most prominent finding is a delay of the P300 latency, which has been found to be associated with memory loss and Alzheimer's disease.

The number of people worldwide aged 60 years or older will increase from 1 in 10 currently to 1 in 5 by 2050. The need to identify objective data of early memory impairment is great because after age 60, the incidence of dementia doubles every 5 years, and prevalence rises from 1 percent at age 60 to 39 to 47 percent in persons 85-95 years old.

Our objective is to determine if P300 latency changes precede and correlate to memory, psychiatric and mental status changes in a population from 20 to 100 years old.

Patients (N=1506) received medical and psychiatric diagnoses (from 1997 to 2002), and were assessed for P300 (N=1496), WMS-III (N=694), and MMSE (N=456). Patient control groups included, a) normal WMS-III on all 4 subscales (N=36), b) normal WMS-III and MMSE (N=189) with subjective memory/mental status complaints and c) medical patients with normal WMS-III and no memory complaints (N=205), and d) P300 control group without medical, psychiatric or memory problems for ROC.

Setting: Patient data was recorded in a Post-Hoc primary care setting.

Results and Conclusion: Patients with impaired/borderline memory have a prolonged P300 latency ($P<0.02$) compared to age matched non-impaired controls; in patients with normal WMS-III/MMSE, with subjective mild memory/mental status impairment, P300 latency was prolonged compared to controls ($P=0.0004$). The P300 latency increased by 0.72ms per year ($P=7.9x10\text{-}65$) and voltage decreased by 0.03dV per year ($P=6.7x10\text{-}10$), and both parameters are linearly correlated with the age of the subjects. Gender differences were as follows: Male subjects had an average voltage of 6.1dV and female 6.8dV($P=0.00009$). Statistically, prolonged latency began at age range 41-50 ($P=0.0002$); reduced P300 voltage began at age range 51-60 ($P=0.003$); WMS-III memory decline for all measures began in females at age range 61-70 (P value at least=0.02) and for males at age range 61-80 ($P=0.02$); prolonged P300 latency ($P<0.0001$) and memory impairment (at least <0.02) was greater for females than males, MMSE memory decline, male and female, began at age range 81-90 (P value of at least 0.00007). In our logistic regression model P300 latency was more predictive of WMS-III impairment than MMSE >24. In patients whose WMS-III score is impaired ≤ 69, or borderline ≤ 79 (P at least =0.004), a P300 latency more prolonged than the norm ($\geq 300 + 30 + \text{Age}$) identifies these patients, whereas a MMSE >24 failed. With the ROC curve, we confirmed that P300 latency could accurately identify borderline/impaired memory.

Neurophysiological Analysis of Processing Speed Reductions in Aging and Mild Cognitive Impairment

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Processing speed in simple behavioral tasks predicts age-related changes in more complex, fluid intelligence tasks. The purpose of this study was to examine what processing speed indicates in terms of brain and cognitive function in aging and mild cognitive impairment. Mild cognitive impairment (MCI) is an episodic memory deficit that is often a transition state between normal aging and Alzheimer's disease. Slower processing speed may result from quantitative changes in similar processes across the lifespan, and/or may be the net result of qualitatively different processes. Effects of parametric manipulations of independent variables on ERPs and reaction time in each group were assessed to define quantitative or qualitative differences in IV-DV associations between groups. Independent variables were chosen to influence response preparation or stimulus evaluation in separate

experiments. Scalp ERPs before and after stimulus presentation were recorded from young, elderly, and MCI subjects performing visual choice reaction time tasks. Results indicated quantitative group differences between young and elderly subjects (prestimulus slow waves, P300 latency) and elderly vs. MCI (P300 latency). Qualitative group differences were also observed. Only young subjects exhibited significant correlations between slow wave amplitude and reaction time, and P300 latency increased as a function of stimulus evaluation demands. In elderly, but not young, subjects P300 latency varied with response preparation. Results suggest that processing speed reductions in aging may be associated with both quantitative and qualitative differences in the association between brain activity and cognitive function. When differences were observed between elderly controls and MCI they were quantitative in nature. Findings will be discussed with respect to theories of cognitive aging and the distinction between normal aging and preclinical Alzheimer's disease.

P300 Normative Comparisons

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A meta-analysis of the last 30 years of P300 research was conducted. Tabulation of means and standard deviations of the latencies and amplitudes of the P300 acquired using the "Odd-Ball" paradigm are presented. Expected latency and amplitude values as a function of age and gender are also presented in graphic and tabular form. The reliability and validity of P300 normative values will be discussed in the context of different experimental designs and with respect to comparative analyses of different studies. Clinical correlation and predictive validity of deviation from expected normative values, including "confidence" intervals and Gaussian distributions, will be presented.

Symposium 4: Special Emphasis Panels That Review Grant Applications for the Small Business Innovation Research (SBIR) and Small Business Technology Transfer (STTR) Programs at the National Institutes of Health

***Etcheberrigaray R*, Center for Scientific Review, National Institutes of Health, Bethesda, Maryland, USA**

The U.S. Department of Health and Human Services uses scientific review groups or study sections called special emphasis panels (SEPs) Scientific Review Groups (also termed Study Sections) that are established to conduct the initial peer review of certain grant applications for scientific/technical merit. SEPs are often used to review the peer review of research proposals on specific topics and proposals submitted in response to special program announcements when a particular set of expertise is required. SEPs may also be used in other special circumstances. SBIR and STTR grant applications are among those proposals normally reviewed by SEPs under the SBIR and STTR programs.

A SEP is developed and coordinated by a Scientific Review Administrator (SRA), who invites recognized experts from the business community (typically from the biotechnology, medical instrumentation, and small pharmaceutical sectors) and from academic institutions. Because a significant number of the projects are expected to result in clinical applications (e.g., new treatments, instruments, or diagnostic aids), clinical expertise is normally included in the panels. One of the panelists is designated as Chair and helps the SRA direct the meeting.

The SBIR program is a government set-aside program (2.5% of an agency's extramural budget) for domestic small businesses concerns to engage in Research and Development (R/R&D) that has the potential for commercialization. The STTR program seeks to foster collaborations between academic and for-profit organizations. Congress established the SBIR in 1982 and the STTR in 1992. The SBIR program was established under the Small Business Innovation Development Act of 1982 (P.L. 97-219), reauthorized until September 30, 2000, by the Small Business Research and Development Enhancement Act (P.L. 102-564), and reauthorized again until September 30, 2008, by the Small Business Reauthorization Act of 2000 (P.L. 106-554).

The STTR program was established by the Small Business Technology Transfer Act of 1992 (Public Law 102-564, Title II), reauthorized until the year 2001 by the Small Business Reauthorization Act of 1997 (P.L. 105-135), and reauthorized again until September 30, 2009, by the Small Business Technology Transfer Program Reauthorization

Act of 2001 (P.L. 107-50). This program requires that collaborations between academic and for-profit organizations be established.

At the National Institutes of Health, there is a SBIR/STTR, one of the SEP in the Brain Disorders and Clinical Neuroscience Integrated Review Group that is particularly relevant for this symposium. This SEP focuses on novel medical devices and monitoring systems. A significant proportion of these projects is related to clinical neurophysiology applications, such as those related to seizure prediction, sleep monitoring, source localization, evoked potentials in cognitive assessments, new electrodes, and other topics.

Symposium 5: Noninvasive Functional Brain Mapping

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Functional Brain Mapping based on intracranial source imaging can visualize the relationship between brain structures and their function. Recent advances in recording technology allow for high temporal and spatial resolution of the externally-recorded neurophysiological signals, while new mathematical models provide accurate descriptors of the underlying intracranial generators. The procedure combines recordings of ongoing or evoked activity with MRI scans, and allows to identify the brain areas involved in several sensory and behavioral functions, such as attention, memory, and language. Contributions to this symposium should deal with innovations in hardware, software, or experimental tasks, and present results obtained in normal controls or patients.