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## PROCEEDINGS OF THE 2011 SAN MEETING

## SOCIETY OF APPLIED NEUROSCIENCE ABSTRACTS OF 3RD BIENNIAL MEETING, THESSALONIKI, GREECE

## Phantom Perceptions: The Analogy Between Pain and Tinnitus

Dirk De Ridder BRAI<sup>2</sup>N Belgium

Phantom perception refers to the conscious awareness of a percept in the absence of an external stimulus. Based on basic neuroscience on perception and clinical research in consciousness, phantom pain and phantom sound, a heuristic model for their origin can be developed. Phantom percepts result from sensory deafferentation and only reach awareness when increased gamma band neuronal activity in the primary sensory cortex is connected to a larger co-activated "self-awareness" or "global workspace" brain network, involving medial and lateral frontal and parietal areas. This could hypothetically be related to thetagamma coupled activity, with the theta carrier wave binding distributed gamma activity through phase synchronization or coherence. Activity in a salience network consisting of the dACC and anterior insula is required for the percept to reach consciousness. When associated with right-sided temporoparietal activity this could lead to priority in conscious perceptual processing. The salience network overlaps with a predominantly right-sided central autonomic control system and also influences limbic-auditory and -somatosensory interactions, which are essential for maintaining the percept into consciousness. This involves the subgenual anterior cingulate, nucleus accumbens and amygdala, modulating the reticular nucleus of the thalamus and thereby induces and/or maintains thalamocortical dysrhythmia. Memory mechanisms play a role in the persistence of the awareness of the salient phantom percept as well as in the reinforcement of the associated distress. Through the involvement of associative learning, the phantom percept becomes associated with distress, which in turn is reflected by a simultaneously co-activated nonspecific distress network consisting of the parahippocampal area, anterior cingulate cortex, anterior insula, and amygdala. Based on this pathophysiological analogy, it is not surprising that phantom sound and phantom pain share clinical and functional neuroradiological similarities as well as similar treatment approaches. Neuromodulatory treatments based on this pathophysiological knowledge should not be limited to auditory and sensorimotor cortex neuromodulation but should try to target hubs critically linking these different overlapping networks. This can be based on network science theories or a better understanding of the different networks involved in phantom percepts.

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## Applications of EEG-Based Brain Computer Interfaces for the Control of Electronic Devices

*Fabio Babiloni* University of Rome Sapienza

### Introduction

Brain Computer Interface (BCI) is a technology that allows users the capability to interact with devices by using the voluntary modulation of brain activity. The aim of this paper is to analyze whether the use of cortical activity estimated from noninvasive EEG recordings could be useful in detecting mental states and how this technology could be useful in clinical applications. It will review the 12 years of experience of the laboratory of Rome in the BCI field.

#### Methods

Estimation of cortical activity was performed on high-resolution EEG data related to the imagination of limb movements and detection of P300 gathered in a group of normal healthy subjects by using realistic head models. Cortical activity was estimated in Region of Interest associated with the subject's Brodmann areas by using depth-weighted minimum norm solutions. Comparisons between surface recorded EEG and the estimated cortical activity were performed. Subjects are asked to interact with different electronic devices of common use by using such a BCI system.

#### Results

With the proposed methodology healthy users are able to drive several mechanical and electronic devices by modulating their EEG activity related to motor imagery. BCI-based P300 was found a methodology easier to use for patients than motor imagery for driving devices. Rehabilitation tasks in patients involving motor imagery could be checked by using the BCI system.

#### Conclusions

EEG recordings can be used to drive electronic and mechanical devices in healthy subjects and in a group of patients. The presented approach could extend the possibility for a use of BCI system into the rehabilitation path for certain class of patients.

## Brain-Plasticity-Based Training Programs— Theory, Data, and Practice

Henry W. Mahncke Posit Science

Advances in the basic science of brain plasticity over the past 3 decades have revealed that the brain retains the fundamental ability to reorganize structurally, functionally, and chemically from childhood through adulthood and into old age. At the same time, advances in the study of perception and cognition in aging have demonstrated that the speed and accuracy of information processing is deeply related to cognitive function and that decline in such information-processing abilities are a significant contributor to age-related cognitive decline. These twin realizations, coupled with advances in computerized training technologies, have led to the development of "brain-plasticitybased" cognitive training programs that employ specific sets of stimuli and exercises designed to improve basic informationprocessing abilities and thus improve cognitive function and overall quality of life in normally aging individuals. Such programs offer a novel, safe, and effective way for older individuals to maintain or improve their cognitive function as they age. Here we will discuss the basic science of such approaches, recent clinical data from large-scale randomized controlled trials demonstrating the significant effects of such training programs on cognitive and quality of life measures, and issues arising in driving real-world use of such programs in various settings.

## Multimodal Virtual Reality and Enhancement of Human Performance

#### Miriam Reiner

Technion—Israel Institute of Technology

This talk will present findings on neural correlates and motor performance in virtual reality

and their implications to human enhancement. Three studies are presented: The first suggests enhancement in motor responses via two types of mechanisms-multisensory integration and their underpinning neural mechanisms. The second suggests enhancement of responses through the virtual hand illusion, a replica of the rubber-hand illusion. The third deals with neurofeedback and reports 2 studies recently completed: The first reports of a neurofeedback protocol that showed enhancement of motor performance, and the second suggests a neurofeedback protocol that showed increased levels of insights problem solving. The methodology for all these 3 studies is based on immersive presence of participants in a surrounding touch enabled virtual environment. While performing tasks in the virtual world, the participants are connected to an EEG system, SGR, heart rate variability, respiration, and eye-tracker for measures of pupil dilation/fluctuations. The virtual reality system enables "touch" of virtual objects. Touch is enabled by a robotic arm held by the participant. A major advantage of the virtual reality is full control of the stimuli in the virtual setting and fine-grained measures with a resolution hard to achieve otherwise. Results suggest that human response can be enhanced, that is, increased speed and accuracy of responses to multimodal stimuli, relative to unimodal. EEG analysis show as early as 30 ms interactions. The interaction becomes even more immersive when the well-known rubber-hand illusion is used to create projection of the body on a virtual hand, so that the participants act as if the virtual hand is their own hand. Functionality, performance, and learning have been found to be improved. The neurofeedback studies show improved speed and accuracy after neurofeedback, as compared to a control group. Implications for rehabilitation will be discussed.

## Current Interpretation of Electroencephalogram Alpha Activity

Olga Bazanova NIIMBB Russian Federation

No other EEG rhythm has such functional significance as the alpha-band range; this conclusion was made from numerous empirical data, theoretical computations and results of correlational investigation of fMRI, PET, and EEG. The recent identification of specific brain signatures involved in optimal cognitive and psychomotor functioning (peak performance) demonstrates an association with so-called alpha status. We review the emerging literature and take stock of several long-standing theories and widely held beliefs about alpha-activity indices of cognitive and psychomotor functioning. However, the great amount of information about alpha oscillations' role in processing mechanisms and neurophysiologic control creates terminological problems in establishing correspondence between described alpha mechanisms and the term alpha-rhythm EEG itself. Despite different aspects of alpha activity, which have been known since Berger's time, it is not clear which quantities characterize "alpha status": increasing or decreasing alpha amplitude and frequency, event-related synchronization, or desynchronization. Moreover, until recent times there have been deep gaps in our knowledge of experimental molecular-cellular mechanisms of alpha waves generators and alpha-activity appearance in the EEG. This attempt to elucidate alpha activity phenomena and current interpretations was made with reference to 94 literature reports. Taken together, alpha activity does not appear to critically depend on any single EEG range or brain region, and it is not especially associated with the occipital area as is sometimes hypothesized. At least 3 EEG features determine alpha activity: individual alpha frequency in the eyes-closed resting state, amplitude suppression in response to eyes open, and autorhythmicity appearing as alpha bursting segments in the EEG.

# Real-Time EEG-Based Personalized Digital Experience

Olga Sourina Nanyang Technological University EEG-based immersion is a new direction in research and development on humancomputer interfaces. It has attracted recently more attention from the research community and industry as wireless portable EEG devices became easily available on the market. EEG-based technology has been applied in anesthesiology, psychology, serious games, or even in marketing. As EEG signal is considered to have a fractal nature, we proposed and developed a novel spatiotemporal fractalbased approach to the brain state quantification. We discuss the real-time algorithms of emotion recognition and concentration level recognition and its integration in human-computer interfaces of EEG-enabled applications. The experiments on evoking emotions by music and sound stimuli are described. Models and algorithms of quantification of brain responses to external stimuli are discussed. The algorithms of the brain state quantification including emotion recognition would advance research on human-computer interaction, bringing the quantification methods and algorithms as new tools in medical, entertainment, and even digital art methodology applications and allowing us an integration of the brain state quantification algorithms in the human-computer interfaces. EEG-enabled applications such as serious games, emotional avatar, music therapy, music player, storytelling, and so on, are demonstrated.

#### Memory in the Lower Senses

### Per Møller University of Copenhagen, Denmark

Introspection suggests that we can remember stimuli and events in the lower "lower" senses (all but vision and audition). Whether these memories are genuinely "sensory" or whether they are rather of a verbal nature is not so obvious. In the presentation I will present recent data that show that genuine sensory olfactory memory systems do exist, and I will argue that olfactory (and taste and flavor) memories have different properties than visual and verbal memory. Incidental learning, as opposed to intentional learning, is rather the rule for lower sense memories, and the distinction turns out to be important for the properties of lower sense memory. I will review results which show that (nonsemantic) incidentally learned stimuli are remembered as well by elderly people as by young. This is in sharp contrast to most explicit visual and verbal memory results and resembles what is often found for implicit memory. These results might suggest why food preferences seem to be rather constant with age, despite dramatic changes in the perception of smell and flavor with age and, further, that memory might play a much more dynamic role for perception and appreciation in the lower senses than it does in vision and audition. Smelling is much less constrained than a spatiotemporally varying visual stimulus and memories and expectations might therefore play a relatively larger role for olfactory perception than for, say, visual perception. I will present a number of results which strongly suggest that vision and olfaction have different functional structures. We have demonstrated a double dissociation between memory and discrimination for vision and olfaction. Even though subjects discriminate better between a set of visual stimuli than between a set of olfactory stimuli, they remember them less well than they remember the olfactory stimuli. Furthermore, memories in the lower senses seem to rely much more on correct rejections than on hits: You remember what you have not encountered previously! "Novelty detection," thus, seems to be particularly important in the lower senses, which makes ecological sense, because the lower senses serve as protective systems with only a very limited behavioral repertoire: inhale or don't. Finally, I will present recent data which suggest that there is also a "working memory" system in human olfaction.

## Arousal Regulation as a PathogeneticFactor in Affective Disorders

Ulrich Hegerl, Peter Schönknecht, TilmanHensch, Sebastian Olbrich, Michael Kluge, Hubertus Himmerich, and Christoph Sander Universitätsmedizin Leipzig

A recently presented vigilance regulation concept suggests that the hyperactivity and sensation seeking observed during mania is an autoregulatory attempt to stabilize vigilance (central nervous arousal) by increasing external stimulation. Similar behavioral patterns are observed in overtired children and in patients with attention deficit hyperactivity disorder. Correspondingly the withdrawal and sensation avoidance in major depression is interpreted as a reaction to a state of tonically high vigilance (Hegerl, Himmerich, Engmann, & Hensch, 2010; Hegerl, Sander, Olbrich, & Schoenknecht, 2009). Indeed, under quiet resting conditions, both patients with attention deficit/hyperactivity disorder (ADHD) and mania show an unstable vigilance regulation with rapid drops to lower vigilance stages (e.g., assessed by an EEG-algorithm of vigilance), whereas hyperstable vigilance regulation is found in unmedicated patients with major depression (Hegerl et al., in press). In both ADHD and mania, sleep deficits aggravate the dysregulation of vigilance as well as the symptomatology. In depression, sleep deprivation reduces the hyperstability of vigilance, which explains its antidepressant effects. Among the far-reaching consequences of this concept is the question of whether psychostimulants have similar beneficial effects in mania as observed in ADHD. There is scattered but surprisingly strong evidence that psychostimulants are not detrimental in acute mania but might have similar rapid therapeutic

effects as observed in ADHD (Schoenknecht, Olbrich, Sander, Spindler, & Hegerl, 2011). The therapeutic role of methylphenidate in acute mania will be studied in an international controlled trial.

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## Learning Theory Principles in Neurofeedback

Leslie Sherlin International Society for Neurofeedback and Research

Neurofeedback is a process in which the electrical activity of the brain is recorded, quantified, and then presented back to the individual in the form of visual, auditory, or tactile stimuli. An a priori determination of the characteristics of the EEG is set as thresholds, and when the EEG activity falls within these thresholds, the feedback is presented to the individual as a reward signal. Details of how to apply rewards and the frequency to apply are not the only considerations involved in this complex learning process. The reward given when the EEG reaches threshold follows the principles of operant conditioning and was first demonstrated as early as 1941 (Jasper & Shagass, 1941). Since that time it has been established that many learning theory principles (classical conditioning, shaping, generalization, placebo, etc.) are involved in the application known as neurofeedback. This talk is aimed to elaborate on the learning theory principles involved in the effective application of neurofeedback.

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## Behavioral and Physiological Changes Following EEG Biofeedback

Andrew Hill, Whitney Eriksen, and Eran Zaidel Psychology and Brain Research Institute, UCLA

#### Introduction

We conducted a double-blind, placebocontrolled study of a short course of EEG biofeedback (EEGBF). We measured the changes in the behavioral and physiological correlates of hemispheric attention as well as changes in the ERP and in the spectral correlates of the biofeedback reward signal.

#### Methods

Participants received 1 of 4 biofeedback protocols (C3-A1 SMR, C4-A2 SMR, C3-A1 Beta, or Sham biofeedback) over 5 training sessions. Veridical feedback included a brief tone and visual reward of a progressing image display. Dense array (64-channel) EEG was recorded during biofeedback training and during a lateralized test of hemispheric attention (Lateralized Attention Network Test, or LANT) (Greene et al., 2008). The LANT was administered before biofeedback training and after 3 and 5 consecutive training sessions over 5 days. We predicted that lateralized training protocols would have asymmetric effects on the behavior and on the cortical neurophysiology of the two cerebral hemispheres.

#### Results

Behavioral: The biofeedback training protocols produced different behavioral effects on attention in the two hemispheres. Accuracy to targets proceeded by invalid cues yielded a significant interaction: Protocol (Sham, C3 SMR, C4 SMR, C3 Beta) × Session (1, 3, 5) × Visual Field (LVF, RVF); p < .025.

Physiological: Reward signals evoked by the training stimulus were characterized by a P50, an N100, and an early P300 ERP component. Training had a selective effect on the P300 component. Frequency reward bands also produced selective enhancements measured at the same scalp region.

#### Conclusion

We demonstrated for the first time that specific EEGBF protocols can affect cortical physiology in specific cortical regions and modulate information processing in specific functional modules. In particular, lateralized EEG biofeedback can have selective effects (a) on behavior (attention) in one cerebral hemisphere, (b) on the physiological signature of the reward signal at the training site, and (c) on the amplitude of the rewarded frequency band in electrodes around the training site.

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## Development of Neural Functional Connectivity Over the Lifespan

Winfried Schlee, Franka Glöckner, and Iris Kolassa Ulm University

Resting-state recordings are characterized by widely distributed networks of coherent brain activations. The development of these largescale functional networks of the human brain across the lifespan is not well understood. Using magnetoencephalography, we investigated how age-related functional resting-state brain connectivity links to cognitive performance in healthy aging of 53 participants ranging in age from 18 to 89 years. A beam-forming technique was used to reconstruct the brain activity in source space and the interregional coupling was investigated using partial directed coherence. Comparison of the network size revealed that slow frequencies engage larger networks than higher frequencies and show different development over the lifespan. Networks in the delta (2-4 Hz) frequency range decrease in size, whereas networks in the frequency range (>16 Hz) beta/gamma

increase with advancing age. Results show that the right frontal lobe and the medial temporal areas in both hemispheres are important relay stations in the expanding high-frequency networks. Furthermore, neuropsychological tests confirmed the tendency of cognitive decline with older age. The decrease in visual memory and visuoconstructive functions was strongly associated with the age-dependent enhancement of functional connectivity in both medial temporal lobes. Using functional network analysis this study elucidates important neuronal principles underlying age-related cognitive decline that are associated with mental deterioration in the senescence.

## Neurofeedback for Adult ADHD: Investigation of Theta/Beta Training

Sarah Wyckoff, Kerstin Mayer, and Ute Strehl Institute of Medical Psychology and Behavioral Neurobiology/Eberhard-Karls-University

Philipp Keune, Michael Schönenberg, and Martin Hautzinger Psychologisches Institut/Eberhard-Karls-University

## Introduction

Attention deficit/hyperactivity disorder (ADHD) is one of the most common disorders of childhood and persists into adulthood for approximately 5% of the population worldwide (Polanczyk, de Lima, Horta, Biederman, & Rohde, 2007). The primary symptoms of ADHD include inattentiveness, impulsivity, and hyperactivity. EEG analysis of adults with ADHD compared to healthy controls and/or normative database populations indicate significant differences in brain activity patterns (Clarke et al., 2008; Koehler et al., 2009; Loo et al., 2009; Thompson & Thompson, 2005). Some adults with ADHD show the typical increase in Theta/Beta ratios commonly reported in childhood populations (Bresnahan, Anderson, & Barry, 1999; Bresnahan & Barry, 2002). Neurofeedback training is a treatment method that utilizes operant conditioning to reinforce specific EEG activity. In a recent meta-analysis

of research focused on this treatment modality, a large effect size was found for neurofeedback on impulsivity and inattention in controlled studies and pre- and postdesigns (Arns, de Ridder, Strehl, Breteler, & Coenen, 2009). However, limited research has investigated the use of Theta/Beta neurofeedback as a treatment for adult ADHD.

#### Methods

Continuous 19-channel EEG was acquired from 15 adult participants who met Diagnostic and Statistical Manual of Mental Disorders (4th ed.) criteria for ADHD (combined, inattentive, or hyperactive type), without additional serious physical, neurological, or psychiatric disorders, and a full-scale IQ greater than 80. EEG recordings were collected pre/mid/ posttreatment and included EO, EC, P300, and CNV tasks, as well as ADHD behavioral questionnaires. Participants received 30 sessions of neurofeedback training in which Theta (4-7 Hz) activity was inhibited and Beta (13-21 Hz) activity was augmented at CZ (referenced to A1, ground A2).

### Results

This investigation is in progress. Changes in behavioral and neurophysiologic parameters will be presented at the time of the conference.

#### Conclusion

Treatment implications, study limitations, and future directions in research will be addressed.

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#### **Neurofeedback & the Performing Arts**

John Gruzelier Goldsmiths, University of London

We have conducted 8 controlled studies of neurofeedback (NF) for enhancing creativity in the arts. The first studies with conservatoire musicians disclosed that whereas sensorymotor rhythm (SMR) and beta1 benefited anxiety as did other popular diverse interventions without impacting performance ratings of experts, alpha-theta (A/T) training benefited all three music domains—musicality, communication, technique—especially musicality to include interpretative imagination, professionally significant changes (Egner & Gruzelier, 2003). A/T was historically designed to facilitate creativity through inducing hypnagogia, a borderline waking state associated with creative insights, through putative facilitation of neural connectivity (Gruzelier, 2009). Subsequent studies examined novice singing in conservatoire instrumentalists. A/T again benefited instrumental performance, extending to novice singing including creative improvisation. SMR had a suggestive impact on novice singing, subsequently examined with 11-year-old children with benefits on improvisation (creativity, communication); A/T benefited technique in prepared performance, creativity, and communication in improvisation. Dance performance was examined contrasting A/T and heart rate variability (HRV) training. Both improved dancing in competitive university ballroom dancers compared with controls. In contemporary dancers, A/T increased cognitive creativity, whereas HRV reduced anxiety. Finally, university actors were examined with SMR with the NF training-display depicting a rendering of an auditorium seen from the stage. The 2D laptop rendition was compared with a 3D VR version. Immersive VR was the more successful in facilitating brain rhythm control and acting. However, both were superior to control in inculcating a flow state in acting. The more successful NF outcome may follow greater immersion in performance during training with SMR via a visual representation or with A/T through imagination. Mechanisms and methods will be discussed along with pedagogical implications for the performing arts and optimal performance (Gruzelier, in press).

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## Alpha Activity Training Using a Novel System Enhances Relaxation and Cognition

performance and perception. Oxford, UK:

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Fifty healthy participants took part in a doubleblind placebo-controlled study in which they were given auditory alpha activity training, random beta training, or no training at all. A novel wireless electrode system was used for training, involving water-based electrodes mounted in an audio headset. Training was applied roughly at central electrodes and comprised 15 sessions of three 8-min training periods each, alternated with cognitive tasks (Flanker task, Stop task, Stroop task, N-Back task). Posttraining measurement using a conventional full-cap EEG system revealed an increase in alpha activity at posterior sites in the alpha group only, which persisted until a follow-up 3 months later. About twice as many participants in the alpha training group mentioned that the training was relaxing, in comparison to the other two groups. Behavioral measures of stress and relaxation suggested effects of alpha activity training and subjective relaxation reflecting the alternation of training periods and cognitive tasks within a session was correlated with alternations in alpha power. Alpha training led to faster learning of cognitive tasks, but the end result of training was the same for all groups. Results suggest that alpha activity training using our novel system is feasible and may represent a step forward in the ease of instrumental conditioning of brain rhythms.

## The Effects of Neurofeedback in Autism: Results of a Blinded Randomized Trial Using a Skin Conductance Biofeedback Control Group

*Mirjam Kouijzer* Radboud University

### Introduction

The results of a study investigating the effects of neurofeedback in autism spectrum disorders (ASD) will be presented. A blinded and randomized trial using skin conductance (SC) biofeedback as a control group was performed to prevent the outcomes of the study from attention and expectancy biases.

#### Method

The present study included three research groups: an EEG biofeedback group, a SC biofeedback group, and a waiting list control group. All participants (N = 41) were pretested with 19-channel EEG and executive function tasks, and parents and teachers filled out behavior questionnaires measuring ASD symptoms. Then, the EEG and SC biofeedback groups had identical sessions of EEG or SC biofeedback and were blinded for the type of feedback they received. The EEG biofeedback group inhibited delta and theta power at centro-frontal scalp locations while SC was recorded. Participants in the SC biofeedback group inhibited SC while theta power was recorded. After 40 biofeedback sessions, all participants were retested with 19-channel EEG and executive function tasks, and parents and teachers filled out behavior questionnaires again. Six months later, a

final collection of data was completed to investigate long-term effects of the treatment.

## Results

Seven of 13 participants of the EEG biofeedback group successfully reduced delta and theta power and were named as EEG responders. Six of 13 participants showed no effect in EEG, the so-called EEG nonresponders. In the SC biofeedback group, 8 of 12 participants reduced SC and were named SC responders. Four participants showed no reduction of SC and were called SC nonresponders. EEG responders showed a long-term improvement in cognitive flexibility, whereas no such improvement was found in other participants. No effects were found in ASD symptoms as rated by parents or teachers. The 19-channel EEG recordings of EEG responders showed a reduction of delta power at Pz immediately after treatment ended but not after 6 months.

## Low Voltage EEG Is Associated with the BDNF Val66Met Polymorphism in Depression

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Low voltage alpha power is known as a highly heritable and deviating electroencephalography (EEG) trait (Enoch et al., 2008). Psychiatric diseases, like ADHD and alcoholism, both contain a higher prevalence of low voltage EEG (Arns et al., 2008; Bierut et al., 2002). Because of these pathological characteristics, the low-voltage EEG is useful to investigate the effects of the Brain-Derived Neurotrophic Factor (BDNF) gene. BDNF Val66Met polymorphism produces the protein BDNF, which has an important role in growth and plasticity of neurons. Therefore the BDNF polymorphism has been supposed to play a role in psychiatric diseases and particularly depression (Duman, 2006). As such, the BDNF gene expression has been attenuated in depression (Chourbaji, 2011).

The BDNF polymorphism has been earlier related to EEG patterns in depression (Bulgin et al., 2008), whereas the BDNF protein directly affects neuronal activity (Bolton et al., 2000). Moreover, etiology of depression probably has been mediated via lower alpha power (Gatt et al., 2008).

The aim of the study was to compare the association between BDNF and low voltage in depressed patients (N = 96) and matched healthy controls (N = 100). We performed multivariate logistic regression analyses and found a strong and stable association in depression. Carriers of the Met/Met BDNF allele in depression were more likely to exhibit a low voltage EEG in depression, compared to carriers of the Val/Val allele. In healthy subjects, we found no such association.

These findings suggest an important gene–environment interaction of the BDNF Met allele with depressive state. Future neurogenetic research directions should focus on deviating EEG patterns and consider the gene– environment interaction with disease. Epigenetic mechanisms leading to a low-voltage EEG may be of great interest for exploring BDNF effects on brain functioning and its relation to depression.

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## The Effects of QEEG-Informed Neurofeedback in ADHD

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The application of neurofeedback in the treatment of attention deficit/hyperactivity disorder (ADHD) has been well investigated, and a recent meta-analysis concluded that neurofeedback has demonstrated a large effect size (ES) on impulsivity and inattention (Arns, de Ridder, Strehl, Breteler, & Coenen, 2009). Other recent studies however have failed to

find an effect of neurofeedback against a "placebo" condition (Lansbergen, van Dongen-Boomsma, Buitelaar, & Slaats-Willemse, 2010; Perreau-Linck, Lessard, Levesque, & Beauregard, 2010). Most published studies have used a single treatment protocol for all subjects. The Monastra, Monastra, and George (2002) study had to be excluded from the meta-analysis due to contributing too much to the heterogeneity of variance. They employed preselection of subjects based on a deviating theta/ beta ratio, which resulted in a larger ES as compared to most other studies. In the present open-label study we therefore investigated the effects of selecting and personalizing a neurofeedback protocol based on the individual QEEG of subjects and hypothesized that this would improve treatment outcome. Twentyone patients with a primary diagnosis of ADHD were included in this study. Diagnosis was confirmed using the MINI. At intake, every 10th session and outtake an ADHD rating scale and a sleep questionnaire were assessed to monitor treatment progress. For nonresponders and dropouts a last-observation carried forward procedure was used. One to two protocols were selected from 5 standard protocols and were personalized based on the individual QEEG. At outtake 76% patients could be considered a responder (>50% decrease on 1 or more subscales of the ADHD rating scales), 14% a nonresponder, and 10% a dropout. The ES on inattention was 1.78 and for Impulsivity/Hyperactivity was 1.22. The presented results are similar to the results from Monastra et al. (2002) and substantially larger than the ES obtained in the metaanalysis. These results show promise for personalizing well-established neurofeedback protocols (such as central SMR/Theta and Frontocentral theta/beta) based on the individual EEG. However, these results require further replication employing larger sample sizes, randomization, and adequate control groups.

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## Waking Brain Rhythms in CFS: Implications for a Model of CNS Dysfunction

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#### Introduction

This study investigated the electrophysiological profiles of spontaneous brain activity in CFS at rest and during a "fatigue-inducing" cognitive performance task, with the aim of relating the findings to an empirical database of normal (healthy) brain function. The implications of any discrepancies were explored within an existing model of brainwave patterns found in central nervous system (CNS) disorder(s).

#### Methods

The brain signatures of CFS screened patients (n = 30) admitted to a UK-based clinic were assessed using a full-head 19 channel quantitative EEG (electroencephalography) during 5 min of eyes open/closed at rest and while performing a 20-min Visual Continuous Performance Task. Following spectral and topographical analysis, the data were compared to the Russian Academy of Sciences Human Brain Institute normative database for statistically significant differences. In addition, associations between the data and symptom severity scales were also investigated.

#### Results

As a first replication of preceding research in the eyes-closed condition, a large proportion (>80%) of the patients presented significant slow-wave power abnormalities in the delta (2–4 Hz), theta (4–7 Hz), and alpha (8–11 Hz) wavebands. However, this was found to be intermixed with an even larger proportion (>90%) of persistent global and/or focal elevated fast-wave beta (>15 Hz) power during eyes opened and fatigue-inducing conditions, indicative of EEG hyperactivity in this waveband range. Collective evidence exists that beta hyperactivity can be brought on by stress, infection, and toxicity while also being implicated in disorders of CNS overarousal. Moreover, it has been directly linked to sleep inefficiency during EEG sleep-stage polysomnography of disorders such as Insomnia.

#### Conclusion

We report findings of disrupted "faster" (>15 Hz) brain rhythms in CFS during eyesopen and induced mental fatigue conditions, suggestive of cortical hyperarousal at both rest and during cognitive load. This may explain why cognitive dysfunction worsens with extended workload as the system "burns out." This may provide an early link between recent evidence of sleep dysfunction in CFS and general EEG hyperactivity and support a "cumulating sleep-debt model" whereby sequelae of reduced CNS sleep efficiency could directly lead to mental fatigue via disruption of synaptic homeostasis while indirectly leading to physical fatigue.

## Loreta Neurofeedback—First Clinical Results

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This presentation reviews the first results of sLoreta based Neurofeedback (LNFB) in clinical applications in a neurofeedback practice in Switzerland. Patients were trained with 1-, 2- or 4-channel NFB with BioExplorer and had additional LNFB training on the anterior cingulate and BA 41 for tinnitus.We analysed the efficacy of LNFB while training on the anterior cingulate (BA 32) as a region that receives inputs from several sensory areas and which therefore plays a critical role in information processing, modulation of attention, executive functions, emotional control, and monitoring (error detection). In addition to BA 32, patients with tinnitus were trained on primary auditory cortex BA 41. A 19-channel EEG was recorded during LNFB with Mitsar and Braintuner Software. All subjects had a QEEG at the beginning of their therapy. We compared QEEG data from the LNFB training sessions with the data from the QEEG at the beginning of therapy.

The subjects were (a) 12-year-old boy with increased theta in frontal-central cortex; (b) 14-year-old boy with increased frontal midline theta; (c) 14-year-old boy with alphaexcess in central (mu rhythms) and parietal regions; (d) 57-year-old man with depression, alpha-excess over whole cortex and alphaasymmetry; and (e) 42-year-old woman with Results showed significant tinnitus. а reduction in theta activity in Subjects A and B and in alpha-activity in Subjects C and D. Subject E reported that tinnitus decreased significantly. In conclusion, LNFB seems to be a very effective way for neurofeedback training. The EEG patterns showed significant changes, although the training time was much shorter than in conventional neurofeedback. This makes LNFB practicable for clinical applications. The additional time needed for the montage of the full cap is counterbalanced by the shorter training time.

## The Effects of Slow and Fast rTMS of the Dorsolateral Prefrontal Cortex in Depression and Neurophysiological Predictors of Treatment Outcome

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The application of rTMS in Depression has been investigated intensively over the last years. Several meta-analysis have demonstrated that compared to placebo the effects of fast rTMS (>5 Hz) to the left dorsolateral prefrontal cortex (DLPFC) has antidepressant effects (ES = 0.39; Schutter, 2009) and that slow rTMS (>1 Hz) over the right DLPFC also has antidepressant effects (ES = 0.63; Schutter, 2010). Given that previous studies have all employed double-blind placebo controlled studies and investigated the effects or rTMS as a mono-treatment, in this study we investigated the effects of fast and slow rTMS in Depression combined with psychotherapy in an open-label study in clinical practice. Ninety patients with a primary diagnosis of depression or dysthymia were included in this study. All subjects underwent neurophysiological testing before treatment (eyes open and eyes closed EEG, oddball ERP) and several rating scales were assessed. The BDI was used to assess response to treatment. Thirty-three patients received slow rTMS over the right DLPFC (1 Hz) and 57 patients received fast rTMS over the left DLPFC (10 Hz). The results demonstrated that 79.9% of all patients could be considered a responder (remission or >50%decrease in BDI score) to treatment after on

average 20.56 sessions (responders). On average there was a 77.2% decrease in depressive symptoms after treatment (BDI) and the within subject Hedges' D ES = 1.72. There was no significant difference, F(1, 88) = 1.477, p = .862, for response rates between fast rTMS (76.8%) and slow rTMS (81.8%). For 39 responders, more than 6-month follow-up data were available, demonstrating that after 6 months 61.5% of these responders could still be classified a responder. These long-term effects are likely to be mainly due to the combination of rTMS with psychotherapy, as the results of rTMS have often been found to last 3 to 6 months. EEG and ERP predictors for treatment response of this whole sample are currently being further analyzed and these results will be reported.

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## Assessing Effects of Neurofeedback on Emotional Interference

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#### Introduction

Forty students received seven NFB sessions of 30 min each. Four conditions were trained, based on SMR neurofeedback at Cz: visual and auditive feedback (VFAF), visual feedback and auditive placebo (VFAP), visual placebo and auditive feedback (VPAF), visual and auditive placebo (VPAP). An operant response task was administered both before and after NFB sessions. In between presentations of pictures from the International Affective Picture System, subjects were to press a keyboard with their left

### Results

SMR and theta increased over time in a repeated measures design, no interaction effects with condition were found. SMR (5.0 and 5.7 uV) and theta (11.1 and 11.9uV) were not significantly different before and after NFB. In the operant response task, a main effect of time was found for errors in the negativevalence pictures: After NFB the number of correct responses was decreased. A Condition  $\times$ Time interaction effect was found for reaction time: Whereas in the VPAP condition a decrease of reaction time was found with negative-valence pictures, in the VFAF condition the decrease was smaller or the reaction time even increased. No interaction effects were found for errors.

#### Discussion

In spite of lack of objective support for changes in EEG, neurofeedback appears to have affected emotional interference. The increased response time may be due to a decrease in impulsivity. Another possible explanation may be increased activity of the pulvinar due to NFB, thus enhancing the affective strength of the negative-valence pictures shown. Subjects were not asked for their beliefs about the condition they were in. This leaves room for methodological factors influencing the results.

### Alpha EEG Indices of Musical Performance Ability in Different Age Musicians and Nonmusicians

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#### Introduction

Previous investigations showed that individual alpha EEG activity indices were associated with

fluency and creativity in musical performance (Bazanova et al., 2003). Thus changes in EEG alpha activity during development may help to understand the maturation of musical performing ability.

#### **Methods**

We used different age groups to study technique, rhythm, and originality in musical performance, pitch, tactile sensitivity, and individual alpha EEG activity indices (peak frequency (IAPF), bandwidth (IABW), amplitude suppression (IAAS) with eyes open recording) in 251 healthy children and adolescents ages 3 to 20 years with different musical experience.

### Results

Pitch and the differential tactile sensitivity threshold decreased, whereas technique and rhythm in musical performance expert estimations, IAPF, and IAAS increased with age. These changes were larger for nonmusicians than musicians. Originality in musical performance and IABW did not differ in different age groups.

## Conclusion

Increases in musical performance quality, pitch, and tactile sensitivity sharpen with age and were associated with increasing IAPF and IAAS, and may be interpreted in terms of a reorganization of the EEG toward a higher frequency oscillatory scale and higher activation, which reflects maturation of "top down" control.

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## The Benefits and Feasibility of Neurofeedback with Children in School

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The feasibility of conducting neurofeedback in the school setting and effects on music performance, attention, and school/home experience were examined in 11-year-olds in a deprived part of London. This followed our demonstration in elite conservatoire musicians of professionally significant improvements in music performance in musicality, communication, and technique, especially musicality including interpretative imagination (Egner & Gruzelier, 2003), and in attention (Egner & Gruzelier, 2001, 2004). In school children, alongside rehearsed vocal or instrumental music performance, we also examined creative musical improvisation, sustained attention, and ADHD levels of inattention. Thirty-three 11-year-olds selected for musical potential and behavioral issues were randomised to alpha/theta (A/T) or sensory-motor rhythm (SMR) 10-session training or to a nointervention control. Performances were filmed, randomised for order and group, and rated by teacher assessors for Creativity, Communication, and Technique. With training T/A and SMR/beta ratios were increased but not SMR/theta. Improvements were seen in prepared music performance with A/T: Technique—vocal quality, diction, pitch, instrument control; Communication confidence, posture, engagement, enjoyment; and in creative improvisation with both A/T and SMR: Creativity-imagination, wellstructured performance, appropriateness to title, and expression (dynamics and articulation): Communication-engagement with audience, enjoyment. In attention there was a highly significant improvement in the global attention index d' following A/T, and a tendency with SMR. Nineteen of 33 were in the ADHD range. On a structured questionnaire 19 of 22 trained children reported improved well-being at school or home, and carry-over to the classroom-8 SMR and

6 A/T including science, math, physical education, performing arts, and English. Logistical, methodological, and pedagogic implications will be discussed together with the value of neurofeedback as an integral part of curriculum planning. Thanks to NESTA and ARK for support.

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## The Influence of Baseline and Mean Maximum Amplitude in the Ability to Control SMR

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The exact contingencies necessary to produce successful outcomes using neurofeedback are yet to be confirmed (Vernon, 2005). Furthermore, it has yet to be established whether individual electrophysiological features can influence the ability to self-regulate electrophysiological variables. The present study aimed to investigate the role of baseline EEG and mean maximum amplitudes on the ability to self-regulate sensorimotor rhythm (SMR; 12–15 Hz) as measured by the percentage of time spent above the threshold. Twelve adults

without any psychological or neurological disorders participated in 10 neurofeedback training sessions to increase SMR amplitude, which consisted of a 2-min baseline recording, followed by  $5 \times 6$ -min periods separated by 1-min breaks. The threshold was set at 0.8 times SMR baseline mean amplitude (Ros et al., 2009). Correlations between mean baseline amplitude and mean percentage time above threshold across all sessions, indicated a marginally significant correlation (r = -.55,p = .06). Individual analyses showed this directional relationship was true for all participants and significant for 6. Correlation between mean maximum amplitude and mean percentage time above threshold was not significant (r = .01, p = .98). Individual analyses showed no pattern in the data. Results indicate the ability to maintain SMR above threshold is not influenced by the maximum amplitude during training. However, ability to learn to control SMR might be dependent on baseline amplitude, which has important implications regarding threshold setting. Thresholds have been decided according to baseline levels so as to adjust the degree of difficulty to the natural levels shown by the individual before each training session. The present results suggest that adjusting the threshold level according to a higher baseline, for example, might increase the difficulty in maintaining SMR amplitude above threshold. Future research could investigate baseline amplitude and its predictive value regarding self-regulation of brain activity.

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Is Neurofeedback Able to Improve Behavior and Academic Performance in Children with Attention Deficit/Hyperactivity Disorder? A Comparison with Pharmacological Intervention

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Neurofeeedback is a promising alternative treatment to pharmacological intervention for Attention Deficit/Hyperactivity Disorder (ADHD). We present the preliminary findings of a study that aims to analyze the efficacy of neurofeedback in the improvement of behavior and academic performance of children with ADHD. This randomized and controlled study compares neurofeedback treatment with pharmacological standard intervention, using multiple measures at different periods of time. Neurofeedback treatment consisted of 40 sessions (2 per week) of a theta/beta training protocol. Data presented here corresponds to 8 children (7-12 years old) who were randomly assigned to neurofeedback or medication. Participants were assessed before and after the treatment by their fathers, mothers, and teachers in terms of inattention, hyperactivity, behavioral problems, negative impact of ADHD in family life, and academic performance. The assessments were collected at the following periods: pretreatment asssessment, posttreatment and two follow-up assessments. Results show a decrease in behavioral problems and an increase in some areas of academic performance after both treatments. In the follow-up assessments we observe a small increase of the

10 measures of behavioral problems in the neurofeedback group and in the medication group as well. In addition, academic performance decreases in two different areas for both treatments through the follow-ups. The results are only preliminary due to the sample size. Nevertheless, these findings suggest that neurofeedback has a similar tendency of improvement as medication for the treatment of ADHD.

### Is Artifact Rejection Enhanced if EOG Signals Are Included in ICA Decomposition?

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During the last decade, many Artifact Rejection techniques, based on Independent Component Analysis (ICA), were proposed (Jung et al., 1998; Papadelis, Braun, & Bamidis, 2011). One of their major drawbacks is that ICA is not able to completely separate the signals derived from the eye movements and blinks, with the signals originated from the prefrontal cortex. This leads to the bidirectional contamination phenomenon (Papadelis et al., 2011). A lot of discussion has been held in various scientific fora and newsletters, suggesting that if the electrooculographic (EOG) signals are included during the decompositions procedure, then the ICA separates more properly the aforementioned signals. Despite this, until now there has not been any scientific evidence supporting this practice. This study comes to shed light on this assumption, by comparing the portion of cerebral activity included in the artifactual independent components (ICs) extracted by ICA, including or not the EOG signals during the decomposition procedure. In more details, the artificially contaminated dataset described in Papadelis et al. (2011) decomposed using the extended was INFOMAX ICA algorithm (Jung et al., 1998)

two times, one with and one without using the EOG signals. To quantify the portion of neural signals included into the artifactual ICs, Artifact to Signal Ratio (ASR; Papadelis et al., 2011) was adopted. ASR was computed for all artifactual ICs extracted with both procedures. Then a one-way analysis of variance was used to investigate if there was a statistically significance between their mean values. Results suggested that the ASR  $(-4.40 \text{ dB} \pm 4.58)$ was enhanced when the EOG signals were included in ICA, whereas the mean ASR for the artifactual ICs extracted without using the EOG signals is  $-5.19 \, \text{dB} \pm 5.54$ . Despite the ostensibly difference of the ASR values, there is not a statistically significant difference among them (F = 0.592, p < .44). So it seems that when the EOG signals are included during the ICA decomposition, ICA separates more properly the ocular artifacts. But until now, there is not any clear evidence proposing for sure the use of EOG signals in ICA.

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## Method of EEG Operant Conditioning for Children with Learning Disabilities

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#### Introduction

EEG operant conditioning (neurofeedback) has been developed and used as a form of

integrative therapy particularly for children with learning disabilities. This method is based on the neuronal conditioning of specific cerebral EEG activity.

### Methods

More than 240 EEG records were analysed from Cz, C3 and C4 scalp areas of 12 children (8 to 12 years old) with learning disabilities during 20 sessions of neurofeedback training. A standard protocol of sensorimotor SMR frequency band (12–15 Hz) enhancing with concurrent reduction of theta (3–6 Hz) activity was applied. Two-channel EEG module 2E (BrainMaster Technologies, Inc.) with standard software was used. Linear (Pearson) correlation analysis of the power of different EEG frequency bands at the same scalp area during neurofeedback training sessions for each child was performed.

#### Results

Correlation analysis during successful neurofeedback training (of the responders only) revealed significant (p > .05) positive correlations between the power of the SMR band and the power of the alpha2 (10–12 Hz) and beta1 (15–20 Hz) frequency bands. There were significant negative correlations between the SMR and low frequency (theta and delta) bands as well as nonsignificant correlations between SMR and alpha1 (8–10 Hz) activities.

### Conclusions

- 1. Standard neurofeedback SMR training increases the peak frequency of the brain's dominant alpha rhythm. These findings suggest that different neurofeedback protocols, namely, SMR power or alpha peak frequency enhancing, both have the similar neurophysiological correlates associated with enhancing of the cortical arousal.
- 2. Preliminary results of the correlation analysis during SMR neurofeedback training reveal the following new neurofeedback protocols for future approbation: (a) If there is reduced left hemisphere cortical arousal and increased right hemisphere arousal

the training protocol could contain SMR or beta1 enhancement at C3 and alpha1 enhancement at C4 with concurrent suppression of theta activity, and (b) if there is reduced right hemisphere arousal and increased left hemisphere arousal the training protocol could contain SMR or beta1 enhancement at C4 and alpha1 enhancement at C3 with concurrent suppression of theta activity.