Journal of Systems and Integrative Neuroscience

Commentary Article ISSN: 2059-9781

Protocol creation in neurofeedback training: multimodal assessments, target measures and automation

Francesco Amico[1]* and Slav Danev[2]

[1]Department of Psychiatry, Trinity Centre for Health Sciences, St. James Hospital, James's Street, Dublin 8, Ireland

[2]Medeia Inc, 7 W. Figueroa Street, Suite 215 Santa Barbara, CA 93101, United States

Abstract

Neurofeedback training (NFT) is a learning-based form of neurotherapy that has been shown to non-invasively induce changes in brain activity. Discovered over fifty years ago, NFT methods have since then been highly improved and are now employed to treat a wide range of neurological and psychiatric disorders. Of all the methods developed, NFT based on the preliminary analysis of electroencephalogram and on the evaluation of symptoms presented is a relatively affordable method that has been adopted by hundreds of clinics around the world.

The present article aims at remarking the importance of creating evidence-based NFT protocols, following the preliminary and combined evaluation of electrophysiological, psychomotor and behavioral data, rather than relying on "out of the box" protocols. In this context, a number of target measures of brain activity are critically discussed and hands-on equipment is recommended as a solution to effectively guide assessments, protocol creation and delivery of NFT.

Introduction

Neurofeedback training (NFT) is form of therapy originally discovered and developed by neuroscientist M. Barry Sterman and biologist Wanda Wyrwicka, during a research project at NASA [1-3]. Using electroencephalography (EEG), the two scientists found that cats trained to press a lever in exchange for a food reward entered a state of increased attention while waiting for the reward. During the waiting period, a distinct rhythm, an activity pattern that later became known as sensorimotor rhythm (SMR), was repeatedly observed in the cats' EEGs. The experiments eventually demonstrated that the EEG of animals can be non-invasively manipulated employing operant conditioning paradigms, and that the EEG changes resulting from the repeated exposure to the training reflected enhanced attention.

During further research at the University of California, on behalf of the United States Air Force, Dr. Sterman and collaborators set up to test the cognitive effects of monomethylhydrazine (MMH), a chemical contained in rocked fuel. They found that, while MMH had epileptogenic effects when injected into cats, previous training of the animals in an operant conditioning paradigm was associated with a decreased likelihood for epilectiform EEG patterns to occur. In particular, while seizures normally started to appear in the EEG waveform 40–70 min after the injection of the chemical, they were delayed or not present only in the cats that had received SMR conditioning [4]. In subsequent research, Sterman and colleagues discovered that the risk of seizures could be diminished in human epilepsy patients who learned to increase their SMR. Since then, thanks to more recent technological advances, neurofeedback has been adopted by hundreds of private clinics around the world as a non-invasive intervention for a wide range of neurological and psychiatric disorders [5].

The main purpose of EEG-NFT is to assist the individual in self-regulating EEG activity that appears as deviant when compared to normative activity. The intervention is based on the hypothesis proposing that non-normative brain functioning is responsible for behavioral anomalies. EEG changes are sought through the enhancement or inhibition of specific, atypical activity during an operant conditioning paradigm, where optimal activity in one or more frequency bands is sought using immediate positive reinforcement [6-9]. The process starts with the acquisition of EEG at rest, followed by real-time or offline data analysis [10] to determine activity in specific frequency bands. Next, a neurofeedback training protocol [8] is created to target frequencies that are found to be deviant from normative standards. The patient is then required to perform a task (e.g., watch a movie or play a video game), during which raw EEG activity and threshold values are used to form a positive feedback loop that is then employed as a reward when a desired mental state is reached (e.g., the video plays without interruptions or a specific action in a video game is enabled) [11-14].

Since when NFT became commercially available to clinics, a wide range of methods and training protocols have been developed to suit different conditions, demographics, and related EEG imbalances [11-13,15]. More recently, considerable and well meaning effort has been put on suggesting "one fits all" protocols that may seem attractive to busy practitioners [16]. In this context, the present paper aims at remarking that NFT protocols always need to be tailored to the patient on the basis of preliminary electrophysiological, psychomotor and interview-based assessments, which should be used as a guide for both frequency training and electrode placing. Reassuringly, while until a few years ago, multimodal assessments required expensive equipment that most neurofeedback clinics could not afford, a growing number

Correspondence to: Dr. Francesco Amico – address: Department of Psychiatry, Trinity Centre for Health Sciences, St. James Hospital, James's Street, Dublin 8, Ireland, E-mail: amicof@gmail.com

Keywords: *neurofeedback training, protocol creation, multimodal assessments, automated technology*

Received: July 29, 2022; **Accepted:** August 06, 2022; **Published:** August 08, 2022

of highly sophisticated applications and devices are today available to the average practitioner, overall providing the technical means to potentially increase the efficacy of NFT interventions [16].

Going beyond interviews and standard questionnaires

The diagnostic value of assessments based on standardized interviews and questionnaires administered by qualified clinical staff has been long established [17-20]. On the other hand, although useful in a wide range of clinical settings, clinical interviews and the administration of rating scales may have some disadvantages e.g., misinterpretation of subtle differences in meanings of words, objective and subjective biases and difficulties in reliably assessing the intensity of symptoms [21].

In the context of NFT protocol creation, the evaluation of symptoms gathered through standardized interviews and questionnaires provides a rationale to guide the search and selection of relevant functional anomalies in the brain, employing both neurocognitive tests and EEG-based methods. This process can assist the NFT practitioner in the critical interpretation of relevant deviant brain activity and, in some cases, also reveal additional disturbances that were missed during the clinical assessment. For example, in children clinically diagnosed with unusual subtypes of attention deficit hyperactivity disorder (ADHD), the combined analysis of quantitative EEG (qEEG) profiles and neurocognitive performance has revealed anomalies that were suspected to reflect depression [22]. Moreover, the analysis of qEEG maps can be critical to unify apparently unrelated symptoms and behaviors into a common disorder, as it is the case of girls with ADHD displaying comorbidity for atypical depression [23,24], social isolation and avoidance [23,25], screen addiction [26], social media or relational obsessive behaviors [27,28], rebellious and oppositional behaviors [29], poor response to medication (for symptoms that are not directly related to ADHD, see [30]), or substance use disorders [31].

The analysis of qEEG maps can also play an important role in the detection of brain anomalies before the manifestation of the related symptoms. For example, individuals who show hypoactivation in the left frontal region of the brain (frontal asymmetry) could be more at risk to developing anxiety and depression [32,33] and individuals at risk for suicide may exhibit frequency-specific anomalies in both frontal and central brain regions [34]. There is also evidence that the ratio between low frequency (theta, 4-8 Hz) and high frequency (beta, 12-30 Hz) EEG activity at rest (theta/beta ratio or T/B ratio) is a measure of attentional control and resilience under stressful conditions [35]. Additionally, although it may change with the reference used, age, and type of task performed [36], peak alpha frequency (PAF), a measure of cognitive performance [37], has been shown to reflect greater anxiety in persons with post-traumatic stress [38].

Finally, It is well established that the analysis of event related potentials (ERP) can offer key insights into both sensory and cognitive processing, with hundreds of studies suggesting a role of specific ERP components in the diagnosis and management of a wide range of neurological and psychiatric disorders [39]. Of high clinical importance, is the N100 component for example, a negative deflection peaking between 90 and 200 ms elicited by any discernible auditory stimulus. The N100 measure is frequently used to assess cognitive functions and has been shown to be altered in patients from multiple clinical populations, including patients with traumatic brain injury (TBI), ADHD, schizophrenia and multiple sclerosis [e.g., 40,41-44].

Another widely studied ERP component is the P300 measure (a positive going deflection appearing in the EEG 250-500 ms after the presentation of rare target stimuli) [45], which has been shown to be altered in patients with cortical synaptic transmission deficits. The P300 deflection consists of two components: 1) a P3a component appearing in the EEG 250-280 ms after stimulus presentation, thought to originate from stimulus-driven frontal attention mechanisms during task processing and 2) a P3b component, with peak latency falling in the 250-500 ms time window after stimulus presentation, originating in the temporal-parietal region and thought to be associated with attention and subsequent memory processing [45]. Similarly, the P200 component (a positive deflection in the EEG waveform that peaks between 150 and 275 ms after stimulus onset) has been shown to offer valuable insights into cognitive processing. The P200 component is elicited by both auditory and visual stimuli and is thought to reflect the recruitment of attention as well as perceptual processing [46,47].

ERP investigations also include the acquisition of the minimal time needed to respond to a stimulus or reaction time (RT), which is considered a basic measure of psychomotor activity and processing speed, found to be altered in patients with impaired brain function, including patients with dementia, Parkinson's disease (PD), TBI and affective disorders [e.g., 48-50].

Below are some examples of how multimodal investigations have contributed over the years to provide target measures that can potentially improve the diagnostic process in neurology and psychiatry, which hopefully will offer an overview of the methodological resources that are already available to physicians and clinics.

Affective disorders: One of the most discussed EEG activity patterns in patients with affective disorders [51,52] is the change in prefrontal alpha (8-13 Hz) asymmetry (PFA) [53]. In particular, while in normal persons alpha power is greater in the left prefrontal region, changes in this balance are thought to reflect altered emotion processing [54,55]. It has also been proposed that PFA is linked to both affective valence (negative or positive) and motivation [56], with several studies indicating a link between higher relative left hemispheric activity, approach (positive) motivation [57,58], positive affect [33,59] and lower vulnerability to negative stimuli [59-61]. Other research indicates that higher relative PFA in the left-hemisphere is associated with the ability to adapt to challenges [62,63], and that changes in this balance may increase the risk for emotion dysregulation [64]. Hence, rather than being indicative of a given emotional state, PFA reflects the ability to modulate emotion under changing environmental conditions.

In patients with affective disorders, the previously mentioned theta/beta ratio, has been found to be proportionally associated to greater vulnerability to stress. Moreover, the inter-individual variance of the theta/beta ratio at rest could reflect different predispositions to responding to environmental challenges through the modulation of attentional control [35] and as such, offer an insight into cognitive performance anxiety. Increases in the theta/beta ratio have also been found to predict the disruptive effects of acute psychosocial stress [65], and there is evidence that increased slow wave/fast wave ratios may be linked to lower motivation or reward efficacy [66], risk taking and increased impulsiveness [66,67]. Importantly, treatment with noradrenaline or dopamine agonists normalizes the theta/beta ratio [66,68], which supports the notion that it reflects the prefrontal modulation of attentional control and suggests that changes in this measure should be monitored throughout interventions in persons with affective disorders.

Another measure that has been found to be altered at rest in patients with emotional disturbances is cordance, an algorithm that for

a given frequency, is computed combining absolute power (the amount of activity at a given electrode site) and relative power (the percentage of EEG activity relative to the total frequency spectrum). Cordance has been shown to be an estimate of antidepressant treatment response or remission with 70% or greater accuracy [69]. The cutoff point is determined as 0.30 and while it is most frequently employed for theta and beta frequency bands, cordance investigations have also been recommended for all other frequencies bands. In general, low cordance is an indicator of unresponsiveness to antidepressive treatment [70], which suggests that NFT protocols targeting cordance should also be considered in patients with affective disorders, especially if NFT is combined with pharmacotherapy.

A wealth of data also indicates that ERPs and RTs are altered in patients with affective disorders. For example, P300 deflections elicited during performance of attention tasks exhibit lower amplitude in patients with depression when compared with healthy controls, which has been suggested to reflect cognitive deficits [71]. On the other hand, increased P300 amplitude has been detected in patients with depression following the presentation of emotional (pleasant or unpleasant) stimuli, compared to neutral stimuli [72,73].

Importantly, ERP investigations can play a role in suicide prevention. Studies comparing patients with suicidal ideation and patients who attempted suicide found that the latter group was characterized by enhanced P200 amplitudes in response to the presentation of negative stimuli, which may reflect abnormal early semantic monitoring of depressogenic information. This could suggest that, among suicide attempters, enhanced attendance to negative information may facilitate, at least in some cases, the transition from ideation to action [74].

Cognitive impairment: Several studies indicate a link between EEG alpha band activity and cognitive performance [75-78]. Further, PAF (the discrete frequency with the highest magnitude within the alpha band) has been found to be reduced in persons with cognitive impairment, when compared with healthy matched controls [79]. Interestingly, reductions in theta absolute power were associated with improvements in cognitive functions in healthy elderly individuals [80] and cognitive amelioration has been shown in older adults with mild cognitive impairment (MCI) using a NFT protocol that combined SMR enhancement and theta/beta ratio reduction [81].

In general, ERP studies have shown normal latency and amplitude of the early "sensory" components (e.g., N100 and P200) in elderly individuals and in patients with Alzheimer's disease (AD) [82] but there is evidence that they may be increased also in patients with subcortical dementias such as Huntington's disease and PD [83]. Also, RTs recorded during performance of cognitive tasks are generally increased in patients with cognitive impairment and their analysis can contribute to differentiate between different types of dementias [84-86].

In AD, P300 latency has been shown to be considerably increased (~2 standard deviations above the mean of normal older individuals). Importantly, the clinical value of the P300 latency measure can be enhanced when neurospychological data are also considered. For example, Goodin [87] found that in patients with equivocal dementia, greater P300 latencies increased the likelihood of developing a dementing illness. One study even showed that altered P300 latencies more reliably predicted disease progression over one year than either the Cognitive Abilities Screening Instruments (CASI) or Mini Mental State Exam, in both AD and MCI patients [88]. The P300 measure can also be very useful in quantifying the effects of cognitively enhancing drugs, such as cholinesterase inhibitors, in addition to standardized rating instruments [89], suggesting that clinicians should include routine P300 measurements to more objectively monitor the effects of pharmacotherapy in their patients.

ADHD: A recent metareview of ADHD studies carried out on a total sample of 2268 children and adolescents aged between 4 and 18 years found that qEEG was used as a diagnostic aid in 62.5% of the studies [90]. Several studies have also reported on the ability of qEEG measures to differentiate between a participant with ADHD and a healthy control [91-93]. In particular, Markovska-Simoska and colleagues reported that when using the theta/beta ratio as a discriminant measure, qEEG was significantly more accurate at differentiating un-medicated ADHD children from healthy controls than a diagnosis reached by a qualified clinician [93].

Further, analyzing the theta/beta ratio in a mixed clinical sample of children exhibiting a wide range of behavioral and mood issues, Coolidge, *et al.* [94] found that qEEG had a sensitivity of 50% and a specificity of 36% at differentiating ADHD from other non-ADHD disorders [94]. Importantly, when qEEG was used to guide NFT for the treatment of children and adolescents with ADHD, a decrease of the theta/beta ratio was associated with lower irritability, lethargy, stereotypy, hyperactivity, and inappropriate speech, as measured by the Aberrant Behavior Checklist [95]. Finally, studies monitoring how qEEG changed after treatment with methylphenidate reported lower theta/beta ratio and increased relative beta power at rest or during the performance of a cognitive task [96,97].

Extensive ERP research has also shown several anomalies in ADHD patients [98]. In particular, ERP amplitude/latency and performance data from an auditory oddball task were able to distinguish AD/HD (both major subtypes) children from healthy controls with 73% accuracy. Button press RT, N100, P200, P300 latency to standard stimuli, and P300 amplitudes to target and standard stimuli were the measures that most contributed to classification. Accuracy was also found to be lower (59%) in adolescents, with P300 amplitudes and latencies to target and standard stimuli having the most weight in group classification [99].

Autism*:* Several studies have revealed qEEG anomalies in autism spectrum disorder (ASD). For example, during the visualization of human faces, ASD youth exhibited higher beta and gamma absolute power compared to healthy controls [100]. In a study where the qEEG profiles of 20 youth with ASD were compared with healthy controls while at rest, Coben, *et al.* [101] found a reduction in relative delta seen most predominantly in the left frontal and vertex regions. They also detected higher relative theta in ASD patients when compared to healthy controls in frontal and posterior regions, and lower absolute beta in the posterior region. These results might be in line with the results of a study where a higher theta/beta ratio was found in ASD youth when compared with healthy controls [102].

Coherence has also been found to be altered in ASD. For example, Coben, *et al.* [101] reported reduced coherence across multiple electrodes and across the scalp in ASD youth. Specifically, they found lower delta and theta coherence at short-medium inter-electrode distances and lower delta coherence at long inter-electrode distances.

Finally, several studies have shown abnormal ERP latencies and amplitudes in autism compared to controls, although results may vary across studies [103]. In particular, it has been shown that children with autism have significantly shorter latencies of the P1, N1, P2 and P3 components, while task performance may not be affected when compared with healthy controls [104,105].

Epilepsy: At the first medical examination or at an outpatient clinic, the diagnosis of epilepsy usually relies on the symptoms reported by family and caregivers. Questions on febrile convulsions, developmental delay and infections of the central nervous system are typically asked [106]. Laboratory markers can also help determine whether an unwitnessed event was of epileptic nature. In particular, prolactin testing helps differentiate epileptic from psychogenic non-epileptic seizures in adults and adolescents, elevations in creatine kinase levels are commonly detected after generalized tonic-clonic seizures, and investigations of metabolic markers such as ammonia and lactate have also been proposed as postictal blood tests. Also, analyzing blood postictally may help ascertain whether symptomatic seizures are linked to endocrine, metabolic, toxic or infectious etiologies [107].

Neuropsychological examinations are also needed to explore the link between seizures and brain function. For example, epileptic seizures in the frontal or temporal lobe can be associated with altered motor coordination and planning, disruption of emotion processing and impaired cognitive functions [108,109].

Standard EEG investigations during wakefulness, sleep, photic stimulation and hyperventilations can help identify the type of epileptiform activity, pointing towards specific syndromes and prognostics. For example, the presence of generalized slow wave activity, 3 Hz spike-wave complexes or rolandic discharges may be indicative of underlying cerebral abnormality [106]. However, while the visual analysis of standard EEG continues to be the most common approach to EEG assessment in epilepsy, the analysis of qEEG is increasingly becoming more popular among neurologists [110]. Several adult and pediatric studies have determined the accuracy of the qEEG method for seizure detection and also demonstrated its ability to characterize different epilepsy subtypes [e.g., 111,112]. In particular, qEEG sensitivity for seizure diagnosis has been shown to range between 43% and 72%, with asymmetry correlating with focal seizures in almost all patients [111].

In addition to resting state methods, ERP investigations can reveal cognitive changes that may be associated with the epileptogenesis process, frequency of seizures, lesions and anti-epileptic treatments. A number of studies have remarked the role of the P300 component in the diagnosis and monitoring of epilepsy. For example, the auditory P300 latency can be significantly increased in both adults and children with idiopatic generalized epilepsy and a positive correlation between P300 latencies and RTs has been found. Also, reductions of the P300 amplitude have been demonstrated during performance of an auditory continuous performance task in patients with absence seizures [for a full review of P300 anomalies in epilepsy, see 113].

Finally, the combination of structural and functional magnetic resonance imaging (MRI) may improve the accuracy of detecting epileptogenic brain regions and investigations using glucose positron emission tomography (PET) combined with high-resolution MRI can reveal hypometabolism associated with subtle cortical malformations [114].

Stroke: The most common symptoms that suggest a stroke are seizure, conversion disorder (disruption of normal signal transmission involving the central and the peripheral nervous systems), migraine headache, and hypoglycemia [115]. Neuroimaging is always required to localize the insult, differentiate ischemic stroke from intracerebral hemorrhage, and to investigate other conditions other than stroke. Acute hemorrhage is easily detectable by computerized tomography (CT) and subtle ischemic changes can be detected by a CT in some cases as early as a few hours after the stroke onset [116]. However, the resolution power of CT can be limited in certain regions of the brain (e.g., the posterior fossa), and other imaging techniques including MRI may be needed to carry out further investigations [117].

Stroke patients often exhibit qEEG anomalies. In particular, the theta/beta ratio is significantly increased in the damaged hemisphere [118]. Also, patients may exhibit power reduction in the alpha frequency band in both the damaged and spared hemispheres [119]. Moreover, the delta/alpha ratio (DAR) and the alpha asymmetry index have been found to be increased after stroke [119]. Importantly, the DAR has been recently proposed as a predictor of clinical outcome in patients with acute ischemic stroke after endovascular treatment [120], with greater DAR predicting a poor clinical outcome [121].

Cognitive impairment and often depression are detected within the first year after stroke and neuropsychological assessments can reveal deficits in executive functioning, mental processing speed, visual perception, and construction ability in both subacute and chronic patients [122-127]. In this context, it has been shown that the latency of the P300 component is abnormally increased after stroke, and that patients where P300 latency anomalies persist are more at risk for reinfarction [128].

TBI: A range of resting EEG measures have been found to be altered in patients with TBI. In particular, reductions in alpha frequency expressed as PAF have been found [129] when compared with healthy controls. Moreover, increased frontal midline theta power and reduced frontal beta power have been shown to correlate with executive attention impairment in TBI subjects [130], a pattern that could reflect reduced excitatory synaptic activity in the medial frontal neuronal population [131].

One of the most observed impairments associated with brain injury is the reduction of cognitive processing speed [132-134], which is thought to reflect diffuse axonal damage and altered functional connectivity between the left and right hemisphere [135]. Patients with brain injury are over 1.5 times slower than healthy controls, as measured by RTs [132] and patients with faster RTs exhibit greater level of alpha power synchronization over the midline fronto-central region, suggesting prefrontal down-regulation [136].

Patients with TBI may exhibit decreased P200 amplitude, when compared to healthy controls, which has been linked to reduced accuracy in stimulus classification [137]. Further, the P300 component can show significant changes even in mild cases of TBI or in asymptomatic patients with history of concussion [138-140].

Substance abuse: Substance abuse has been linked to a wide range of qEEG anomalies, which however strictly depend on the substance in question, whether the patient is still currently using it, the chronicity of use, and on the current stage of withdrawal. For example, while higher theta power has been widely shown in alcoholics when compared with healthy controls [141-143], other research has found decreased low frequency activity, which was interpreted as a sign of cortical atrophy [144].

In substance abuse patients, ERP investigations may prove valuable for assessing cognitive/reward processing or heightened attention/motivation toward drug cues. For example, a larger occipital NoGo N170 associated to alcohol cues [145] and longer N200 latencies [146] have been found to be predictive of relapse in patients with history of alcohol abuse. Other studies have remarked the utility of ERP investigations for predicting treatment completion [147-149], generally reporting reduced P3a/P3b in treatment non-completers.

Sleep disorders: The first step to clinically investigate sleep disturbances is to acquire an accurate and detailed history from the patient, bed partner or family member [150]. Laboratory tests include the polysomnogram (PSG), multiple sleep latency test, maintenance of wakefulness test (MWT), actigraphy, electrocardiogram (ECG), and EEG. Depending on the clinical diagnosis, additional tests may be required to investigate transcutaneous CO_2 or end-tidal gas, extremity muscle activity, motor activity movement, penile tumescence, oesophageal pressure, gastroesophageal reflux, snoring and continuous blood pressure [151,153].

Research employing qEEG indicates a link between greater sleepiness and increased relative power in slow (delta and theta) frequencies [153], as well as decreased relative power in the alpha frequency band [154]. On the other hand, insomnia has been linked to generalized hyperarousal, reflected by an increase in high beta power as well as a decrease in delta and sigma power in anterior scalp locations [155], although an increase in slow frequency activity has also been found in frontal areas [156].

Key information on sleep disturbances also emerges from ERP research indicating amplitude increases in P200 during non-rapid eye movement sleep that may be followed by the onset of P300-like and late negative (N350 and N550) deflections [157]. Anomalies in ERP measures have been shown to be linked to altered psychomotor activity. For example, sleep deprivation is generally associated with slower RTs [158] and in patients with insomnia, response inhibition deficits are associated with decreased NoGo P300 amplitudes [159].

Software developments in EEG recording and neurofeedback technology: Since their first stages of development [160], EEG methods and technology have swiftly evolved, and a plethora of highly sophisticated applications now allow researchers and clinicians to easily record, process and analyze EEG signals [161]. State-of-the-art EEG technology today allows not only for resting state recordings, qEEG mapping and analysis but also for the automated detection and interpretation of ERPs elicited during performance of readily available and customizable behavioral tasks [162-163]. Appropriately trained staff can quickly generate detailed reports based on well-established markers of brain activity, which also offers the opportunity to evaluate the effects of psychological, neurobehavioral and pharmachological interventions on specific non-normative EEG measures of brain activity. This has laid down new avenues in neurotherapy, and has helped clinicians formulate more informed, objective and targeted treatment plans for their patients.

Moreover, NFT technology has been dramatically advanced over the last decade, and a wide range of platforms are today available to clinics and research labs. However, while many of these applications can implement qEEG-based neurofeedback training protocols, they offer little or no support for neuropsychological and psychomotor evaluations. Also, the interpretation of the outputs generated is often time consuming and, in many cases, requires dedicated staff. In this context, Brainview by Medeia is a state-of the-art FDA-cleared EEG computer-based system that incorporates the most up-to-date technological advances in the field of EEG recording and processing. The built-in software can carry out routine 1 to 19 channel recordings (sampling rate: 200, 500, or 1000 Hz), assessments of EEG waveforms in multiple frequency bands (alpha, beta, theta and gamma), during resting state, and also extract a range of ERPs generated during performance of behavioral paradigms (e.g., visual/auditory oddball). The system is capable of i) "automatic" artifact (blinks, pulse artifact, MR gradient artifact, ballisto-cardiogram, and bad blocks) detection and removal via fast Fourier transforms (FFT), wavelet and independent component analysis (ICA), as well as ii) feature extraction, iii) frequency-based analysis and iv) time-to-frequency domain transformations. The software can also perform qEEG mapping, statistical comparisons with a normative database (provided with the package) and also carry out source localization based on the implementation of the eLORETA algorithm. Reports can be customized to provide at-a-glance results that allow the clinician to easily detect deviant (out of range) EEG and ERP activity. Finally, the Brainview application also allows to deliver 1 to 19 channel-qEEG-guided- surface/cross-frequency surface and s/eLORETA Z score NFT, implementing protocols based on the preliminary evaluation of electrophysiological/neurobehavioral data gathered during resting state or behavioral task performance, and on the symptoms/complaints that may emerge from self-administered questionnaires and/or interviews.

Conclusions

NFT is a non-invasive, learning-based intervention that allows to target selective EEG imbalances in the brain, gradually facilitating functional changes in the central nervous system using a normative system as a reference. Since its first discovery, NFT has been developed and employed as a standalone or complementary intervention for a wide range of neurological and psychiatric conditions/disorders.

While several attempts have been made to devise standard intervention protocols for each condition, research suggests that preliminary evaluations of electrophysiological and psychomotor activity should always be carried out in order to formulate ad hoc training protocols. In this context, recent advances in EEG signal acquisition and processing offer clinicians the opportunity to easily gather and analyze neurobehavioral data from their patients and customize NFT protocols targeting non-normative EEG and the symptoms that may emerge from self-assessments/interviews. The present paper recommends the use of applications that allow for the automated detection and interpretation of electrophysiological and neurobehavioral data, to improve targeting in NFT. We suggest that technology of this kind might also contribute to decrease the overall cost of treatment plans and eventually make NFT more accessible to the general population.

Acknowledgements

We wish to thank the anonymous reviewers who took the time to read the manuscript and suggest improvements.

Authors' Contributions

Mr. Danev recommended the topic and supervised the project. Dr. Amico researched the literature and wrote the manuscript.

Funding Sources

The present paper was entirely funded by Medeia Inc.

Competing Interest

Mr. Danev represents Medeia Inc.; Dr. Amico has received honoraria from Medeia Inc. to research and write the manuscript. A Medeia Inc. product is mentioned on the paper.

References

1. Wyrwicka W, Sterman MB (1968) Instrumental conditioning of sensorimotor cortex EEG spindles in the waking cat. *Physiology and Behavior* 3: 703-707. [Crossref]
2. Sterman MB, Wyrwicka W, Roth S (1969) Electrophysiological correlates and neural substrates of alimentary behavior in the cat. *Ann N Y Acad Sci* 157: 723-739. [Crossref]
3. Sterman MB, Wyrwicka W (1967) EEG correlates of sleep: evidence for separate forebrain substrates. *Brain Res* 6: 143-163. [Crossref]
4. Sterman MB (1976) Effects of brain surgery and EEG operant conditioning on seizure latency following monomethylhydrazine intoxication in the cat. *Exp Neurol* 50: 757-65. [Crossref]
5. Sitaram R (2019) Author Correction: Closed-loop brain training: the science of neurofeedback. *Nat Rev Neurosci* 20: 314.
6. Research, I.I.S.f.N.a. Definition of Neurofeedback. 2010; Available from: https://www.isnr.org/neurofeedback-introduction.
7. Sitaram R (2017) Closed-loop brain training: the science of neurofeedback. *Nat Rev Neurosci* 18: 86-100. [Crossref]
8. Enriquez-Geppert S, Huster RJ, Herrmann CR (2017) EEG-Neurofeedback as a Tool to Modulate Cognition and Behavior: A Review Tutorial. *Front Hum Neurosci* 11: 51. [Crossref]
9. Sherlin LH (2011) Neurofeedback and basic learning theory:Implications for research and practice. *Journal of Neurotherapy* 15: 292-304.
10. Thatcher RW (2014) score neurofeedback: Clinical applications. 2014, San Diego, CA: Academic Press Inc.
11. Bagdasaryan J, Quyen Mle V (2013) Experiencing your brain: neurofeedback as a new bridge between neuroscience and phenomenology. *Front Hum Neurosci* 7: 680. [Crossref]
12. Gruzelier JH (2014) EEG-neurofeedback for optimising performance. III: a review of methodological and theoretical considerations. *Neurosci Biobehav Rev* 44: 159-182. [Crossref]
13. Rogala J (2016) The Do's and Don'ts of Neurofeedback Training: A Review of the Controlled Studies Using Healthy Adults. *Front Hum Neurosci* 10: 301. [Crossref]
14. Vernon D, Frick A, Gruzelier JH (2004) Neurofeedback as a Treatment for ADHD: A Methodological Review with Implications for Future Research. *Journal of Neurotherapy* 8: 53-82. [Crossref]
15. Rajabi S, Pakize A (2020) Effect of combined neurofeedback and game-based cognitive training on the treatment of ADHD: A randomized controlled study. *Appl Neuropsychol Child* 9: 193-205.
16. Marzbani H, Marateb HR, Mansourian M (2016) Neurofeedback: A Comprehensive Review on System Design, Methodology and Clinical Applications. *Basic Clin Neurosci* 7: 143-158.
17. Berrios GE (1999) The History of Mental Symptoms: Descriptive Psychopathology Since the Nineteenth Century. 1999, Springer.
18. WHO, The ICD-10 Classification of Mental and Behavioral Disorders: Diagnostic Criteria for Research. 10th edition ed., W.H. Organization, Editor. 1993: Geneva, Switzerland.
19. Guha MJRR (2014) Diagnostic and statistical manual of mental disorders: DSM-5. 2014.
20. McHugh RJJ (2005) Striving for coherence: *psychiatry's efforts over classification* 293: 2526-2528. [Crossref]
21. Hall JA (2011) Clinicians' accuracy in perceiving patients: its relevance for clinical practice and a narrative review of methods and correlates. *Patient Educ Couns* 84: 319-324. [Crossref]
22. Byeon J (2020) A novel quantitative electroencephalography subtype with high alpha power in ADHD: ADHD or misdiagnosed ADHD? *PLoS One* 15: e0242566. [Crossref]
23. Nandi A, Beard JR, Galea S (2009) Epidemiologic heterogeneity of common mood and anxiety disorders over the lifecourse in the general population: a systematic review. *BMC Psychiatry* 9: 31.
24. Young S (2020) Females with ADHD: An expert consensus statement taking a lifespan approach providing guidance for the identification and treatment of attention-deficit/hyperactivity disorder in girls and women. *BMC Psychiatry* 20: 404. [Crossref]
25. Elkins IJ (2011) The impact of attention-deficit/hyperactivity disorder on preadolescent adjustment may be greater for girls than for boys. *J Clin Child Adolesc Psychol* 40: 532-545.
26. Tateno M (2018) Internet Addiction and Attention-Deficit/Hyperactivity Disorder Traits among Female College Students in Japan. *Soa Chongsonyon Chongsin Uihak* 29: 144-148.
27. Schou Andreassen C (2016) The relationship between addictive use of social media and video games and symptoms of psychiatric disorders: A large-scale cross-sectional study. *Psychol Addict Behav* 30: 252-262.
28. Ohan JL, Johnston C (2007) What is the social impact of ADHD in girls? A multi-method assessment. *J Abnorm Child Psychol* 35: 239-250.
29. Tung I (2016) Patterns of Comorbidity Among Girls With ADHD: A Meta-analysis. *Pediatrics* 138(4).
30. Kok FM (2020) The female side of pharmacotherapy for ADHD-A systematic literature review. *PLoS One* 15: e0239257.
31. Ottosen C (2016) Gender Differences in Associations Between Attention-Deficit/Hyperactivity Disorder and Substance Use Disorder. *J Am Acad Child Adolesc Psychiatry* 55: 227-34 e4.
32. Coan JA, Allen JJ, McKnight E (2006) A capability model of individual differences in frontal EEG asymmetry. *Biol Psychol* 72: 198-207. [Crossref]
33. Thibodeau R, Jorgensen RS, Kim S (2006) Depression, anxiety, and resting frontal EEG asymmetry: a meta-analytic review. *J Abnorm Psychol* 115: 715-29. [Crossref]
34. Lee SM, Jang KI, Chae JH (2017) Electroencephalographic Correlates of Suicidal Ideation in the Theta Band. *Clin EEG Neurosci* 48: 316-321.
35. Putman Y (2014) EEG theta/beta ratio as a potential biomarker for attentional control and resilience against deleterious effects of stress on attention. *Cogn Affect Behav Neurosci* 14: 782-791.
36. Osaka M (1984) Peak alpha frequency of EEG during a mental task: task difficulty and hemispheric differences. *Psychophysiology* 21: 101-105.
37. Grandy TH (2013) Peak individual alpha frequency qualifies as a stable neurophysiological trait marker in healthy younger and older adults. *Psychophysiology* 50: 570-582. [Crossref]
38. Wahbeh H, Oken BS (2013) Peak high-frequency HRV and peak alpha frequency higher in PTSD. *Appl Psychophysiol Biofeedback* 38: 57-69.
39. Campanella S (2021) Use of cognitive event-related potentials in the management of psychiatric disorders: Towards an individual follow-up and multi-component clinical approach. *World J Psychiatry* 11: 153-168. [Crossref]
40. Gonzalez-Heydrich J (2015) Early auditory processing evoked potentials (N100) show a continuum of blunting from clinical high risk to psychosis in a pediatric sample. *Schizophr Res* 169: 340-345.
41. Onitsuka T, Oribe N, Kanba S (2013) Neurophysiological findings in patients with bipolar disorder. *Suppl Clin Neurophysiol* 62: 197-206. [Crossref]
42. Bauer EA, Wilson KA, MacNamara A (2020) Cognitive and Affective Psychophysiology, in Reference Module in Neuroscience and Biobehavioral Psychology. Elsevier.
43. Gilbert DL (2019) Transcranial Magnetic Stimulation in Attention Deficit Hyperactivity Disorder, in Neurotechnology and Brain Stimulation in Pediatric Psychiatric and Neurodevelopmental Disorders, L.M. Oberman, Enticott, G., Editor. 2019, Academic Press. 115-146.
44. Jones S (2005) Electrophysiological Correlates of Relapse, Remission, Persistent Sensorimotor Deficit, and Long-Term Recovery Processes in Multiple Sclerosis, in Multiple Sclerosis as A Neuronal Disease, S.G. Waxman, Editor. 2005, Academic Press. 227-239.
45. Polich J (20078) Updating P300: an integrative theory of P3a and P3b. *Clin Neurophysiol* 118: 2128-2148.
46. Key A, Dove GO, Maguire MJ (2005) Linking brainwaves to the brain: an ERP primer. *Dev Neuropsychol* 27: 183-215.
47. Freunberger R (2007) Visual P2 component is related to theta phase-locking. *Neurosci Lett* 426: 181-186.
48. Waninger S (2018) Event-related potentials during sustained attention and memory tasks: Utility as biomarkers for mild cognitive impairment. *Alzheimers Dement (Amst)* 10: 452-460.
49. Chang Y (2016) Event-Related Potentials in Parkinson's Disease Patients with Visual Hallucination. *Parkinsons Dis*: 1863508. [Crossref]
50. Proudfit GH (2015) Depression and Event-related Potentials: Emotional disengagement and reward insensitivity. *Curr Opin Psychol* 4: 110-113. [Crossref]

51. Gainotti G (1972) Emotional behavior and hemispheric side of the lesion. Cortex. *A Journal Devoted to the Study of the Nervous System and Behavior* 8: 41-55.

52. Robinson RG (1984) Mood disorders in stroke patients. Importance of location of lesion. *Brain* 107: 81-93.

53. Davidson RJ, Tomarken AJ (1989) Laterality and emotion: An electrophysiological approach, in Handbook of Neuropsychology, B.J.G. (Eds.), Editor. 1989, Elsevier: Amsterdam. 419-441.

54. Allen JJB (2003) The state and trait nature of frontal EEG asymmetry in emotion. In in The Asymmetrical Brain K.H.R.J.D. (Eds.), Editor. 2003, MIT Press: Carmbridge. 565-615.

55. Hagemann D (2002) Does resting electroencephalograph asymmetry reflect a trait? an application of latent state-trait theory. *J Pers Soc Psychol* 82: 619-641. [Crossref]

56. Harmon-Jones E, Gable A (2018) On the role of asymmetric frontal cortical activity in approach and withdrawal motivation: An updated review of the evidence. *Psychophysiology* 55.

57. Coan JA, Allen JJ (2003) Frontal EEG asymmetry and the behavioral activation and inhibition systems. *Psychophysiology* 40: 106-114. [Crossref]

58. Harmon-Jones E, Allen JJB (1997) Behavioral activation sensitivity and resting frontal EEG asymmetry: Covariation of putative indicators related to risk for mood disorders. *Journal of Abnormal Psychology* 106: 159-163.

59. Tomarken AJ, Davidson RJ, Henriques JB (1990) Resting frontal brain asymmetry predicts affective responses to films. *J Pers Soc Psychol* 59: 791-801.

60. Henderson HA, Fox NA, Rubin KH (2001) Temperamental contributions to social behavior: the moderating roles of frontal EEG asymmetry and gender. *J Am Acad Child Adolesc Psychiatry* 40: 68-74. [Crossref]

61. Nash K, Inzlicht M, and McGregor I (2012) Approach-related left prefrontal EEG asymmetry predicts muted error-related negativity. *Biol Psychol* 91: 96-102.

62. Baeken C (2014) One left dorsolateral prefrontal cortical HF-rTMS session attenuates HPA-system sensitivity to critical feedback in healthy females. *Neuropsychologia* 57: 112-121.

63. Koslov K (2011) Asymmetry in resting intracortical activity as a buffer to social threat. *Psychol Sci* 22: 641-649.

64. Davidson RJ (1998) Anterior electrophysiological asymmetries, emotion, and depression: conceptual and methodological conundrums. *Psychophysiology* 35: 607-614. [Crossref]

65. Putman C (2018) EEG theta/beta ratio in relation to fear-modulated response-inhibition, attentional control, and affective traits. Biol Psychol 83: 73-78.

66. Schutter DJ, Van Honk J (2005) Electrophysiological ratio markers for the balance between reward and punishment. *Brain Res Cogn Brain Res* 24: 685-690. [Crossref]

67. Massar SA (2012) Baseline EEG theta/beta ratio and punishment sensitivity as biomarkers for feedback-related negativity (FRN) and risk-taking. *Clin Neurophysiol* 123: 1958-1965.

68. Clarke AR (2003) Effects of stimulant medications on the EEG of children with Attention-Deficit/Hyperactivity Disorder Predominantly Inattentive type. *Int J Psychophysiol* 47: 129-137.

69. Hunter AM, Cook IA, Leuchter AF (2007) The promise of the quantitative electroencephalogram as a predictor of antidepressant treatment outcomes in major depressive disorder. *Psychiatr Clin North Am* 30: 105-124. [Crossref]

70. Leuchter AF (1999) Relationship between brain electrical activity and cortical perfusion in normal subjects. *Psychiatry Res* 90: 125-140.

71. Luck SJ, Kappenman ES (2011) The Oxford handbook of event-related potential components. 2011: Oxford university press.

72. Johnston VS, Miller DR, Burleson MHJ (1986) Multiple P3s to emotional stimuli and their theoretical significance 23: 684-694.

73. Radilova JJANS (1982) The late positive component of visual evoked response sensitive to emotional factors. 2: 334-337.

74. Auerbach R, Stewart JG, Johnson SL (2017) Impulsivity and Suicidality in Adolescent Inpatients. *J Abnorm Child Psychol* 45: 91-103.

75. Anokhin A, F. Vogel F (1996) EEG alpha rhythm frequency and intelligence in normal adults. *Intelligence* 23: 1-14.

76. Klimesch W (1997) Brain oscillations and human memory: EEG correlates in the upper alpha and theta band. *Neurosci Lett* 238: 9-12. [Crossref]

77. Neubauer A, Freudenthaler H, furtscheller G (1995) Intelligence and spatio-temporal patterns of eventrelated desynchronization. *Intelligence* 20: 249-267.

78. Neubauer AC (2005) Intelligence and neural efficiency: further evidence of the influence of task content and sex on the brain-IQ relationship. *Cogn Brain Res* 25: 217-225. [Crossref]

79. Garces Y (2013) Brain-wide slowing of spontaneous alpha rhythms in mild cognitive impairment. *Front Aging Neurosci* 5: 100.

80. Becerra J (2012) Neurofeedback in healthy elderly human subjects with electroencephalographic risk for cognitive disorder. *J Alzheimers Dis* 28: 357-367.

81. Marlats F (2020) SMR/Theta Neurofeedback Training Improves Cognitive Performance and EEG Activity in Elderly with Mild Cognitive Impairment: A Pilot Study. *Front Aging Neurosci* 12: 147.

82. Goodin DS (1987) M.J.J.A.o.N.O.J.o.t.A.N.A. Aminoff, and t.C.N. Society, Electrophysiological dfierences between demented and nondemented patients with *Parkinson's disease* 21: 90-94.

83. Goodin DS, Aminoff MJ (1986) Electrophysiological differences between subtypes of *dementia* 109: 1103-1113. [Crossref]

84. Van Deursen JA (2009) Response speed, contingent negative variation and P300 in Alzheimer's disease and MCI. *Brain Cogn* 69: 592-599. [Crossref]

85. Dixon RA (2007) Neurocognitive markers of cognitive impairment: exploring the roles of speed and *inconsistency* 21: 381.

86. Gorus E (2008) Reaction times and performance variability in normal aging, mild cognitive impairment. *Alzheimer's disease* 21: 204-218.

87. Goodin DSJE (1990) Neurophysiology, Clinical utility of long latency 'cognitive'event-related potentials (P3): *the pros* 76: 2-5.

88. Lai CL (2010) The role of event-related potentials in cognitive decline Alzheimer's disease 121: 194-199.

89. Werber EA (2003) The clinical use of P300 event related potentials for the evaluation of cholinesterase inhibitors treatment in demented patients. *J Neural Transm* (Vienna) 110: 659-669.

90. McVoy M (2019) A systematic review of quantitative EEG as a possible biomarker in child psychiatric disorders. *Psychiatry Res* 279: 331-344.

91. Fonseca LC (2008) Epileptiform abnormalities and quantitative EEG in children with attention-deficit/hyperactivity disorder. *Arq Neuropsiquiatr* 66: 462-467. [Crossref]

92. Kim JW (2015) Theta-phase gamma-amplitude coupling as a neurophysiological marker of attention deficit/hyperactivity disorder in children. *Neurosci Lett* 603: 25-30.

93. Markovska-Simoska S, Pop-Jordanova N (2017) Quantitative EEG in Children and Adults with Attention Deficit Hyperactivity Disorder: Comparison of Absolute and Relative Power Spectra and Theta/Beta Ratio. *Clin EEG Neurosci* 48: 20-32.

94. Coolidge FL, Starkey MT, Cahill BS (2007) Comparison of a parent-rated DSM-IV measure of attention-deficit/hyperactivity disorder and quantitative EEG parameters in an outpatient sample of children. *J Clin Neurophysiol* 24: 348-351.

95. Hillard B (2013) Neurofeedback training aimed to improve focused attention and alertness in children with ADHD: a study of relative power of EEG rhythms using custom-made software application. *Clin EEG Neurosci* 44: 193-202.

96. Song DH (2005) Effects of methylphenidate on quantitative EEG of boys with attention-deficit hyperactivity disorder in continuous performance test. *Yonsei Med J* 46: 34-41.

97. Isiten HN (2017) Medication Effects on EEG Biomarkers in Attention-Deficit/Hyperactivity Disorder. *Clin EEG Neurosci* 48: 246-250.

98. Johnstone SJ, Barry RJ, Clarke AR (2013) Ten years on: a follow-up review of ERP research in attention-deficit/hyperactivity disorder. *Clin Neurophysiol* 124: 644-657.

99. Smith JL, Johnstone SJ, Barry RJ (2003) Aiding diagnosis of attention-deficit/hyperactivity disorder and its subtypes: discriminant function analysis of event-related potential data. *J Child Psychol Psychiatry* 44: 1067-1075.

100. Paula CAR (2017) High-Frequency EEG Variations in Children with Autism Spectrum Disorder during Human Faces Visualization. Biomed Res Int, 2017. 2017: 3591914.

101. Coben R (2008) EEG power and coherence in autistic spectrum disorder. *Clin Neurophysiol* 119: 1002-1009.

102. Chan AS, Leung WW (2006) Differentiating Autistic Children with Quantitative Encephalography: A 3-Month Longitudinal Study. *J Child Neurol* 21: 392-399.

103. Jeste SS, Nelson CA (2009) 3rd, Event related potentials in the understanding of autism spectrum disorders: an analytical review. *J Autism Dev Disord* 39: 495-510.

104. Martineau J (1984) Evoked potentials and P300 during sensory conditioning in autistic children. 1984.

105. Courchesne E (1984) Autism: processing of novel auditory information assessed by event-related brain potentials 59: 238-248.

106. Oguni H (2004) Diagnosis and treatment of epilepsy. *Epilepsia* 45: 13-16.

107. Nass RD (2017) The role of postictal laboratory blood analyses in the diagnosis and prognosis of seizures. *Seizure* 47: 51-65.

108. Exner C (2002) Neuropsychological performance in frontal lobe epilepsy. *Seizure* 11: 20-32.

109. Patrikelis E, Angelakis, Gatzonis S (2009) Neurocognitive and behavioral functioning in frontal lobe epilepsy: a review. *Epilepsy Behav* 14: 19-26.

110. Sansevere AJ, Hahn CD, Abend NS (2019) Conventional and quantitative EEG in status epilepticus. *Seizure* 68: 38-45.

111. Goenka A, Boro A, Yozawitz E (2018) Comparative sensitivity of quantitative EEG (QEEG) spectrograms for detecting seizure subtypes. *Seizure* 55: 70-75.

112. Williamson CA (2014) Sensitivity of compressed spectral arrays for detecting seizures in acutely ill adults. *Neurocrit Care* 20: 32-39.

113. Sowndhararajan K (2018) Application of the P300 Event-Related Potential in the Diagnosis of Epilepsy Disorder: *A Review Sci Pharm* 86: 10. [Crossref]

114. Juhasz C and John F (2020) Utility of MRI, PET, and ictal SPECT in presurgical evaluation of non-lesional pediatric epilepsy. *Seizure* 77: 15-28.

115. Yew KS (2015) E.M. Cheng, Diagnosis of acute stroke. *Am Fam Physician* 91: 528-536.

116. Wityk RJ, Beauchamp NJ (2000) Jr., Diagnostic evaluation of stroke. Neurol Clin, 2000. 18: 357-378.

117. Bryan RN (1991) Diagnosis of acute cerebral infarction: comparison of CT and MR imaging. *AJNR Am J Neuroradiol* 12: 611-620.

118. Kopruner V, Pfurtscheller G, Auer LM (1984) Quantitative EEG in normals and in patients with cerebral ischemia. *Prog Brain Res* 62: 29-50. [Crossref]

119. Kanna S, Heng J (2009) Quantitative EEG parameters for monitoring and biofeedback during rehabilitation after stroke, in 2009 IEEE/ASME International Conference on Advanced Intelligent Mechatronics. 2009, IEEE: Singapore.

120. Wang Y (2021) Quantitative EEG provides early prediction of poor outcome in acute ischemic stroke after endovascular treatment: a preliminary study. *Neurol Res* 43: 831-837.

121. Leon-Carrion J (2009) Delta-alpha ratio correlates with level of recovery after neurorehabilitation in patients with acquired brain injury. *Clin Neurophysiol* 120: 1039-1045. [Crossref]

122. Leśniak M (2008) Frequency and prognostic value of cognitive disorders in stroke patients. 26: 356-363.

123. Nys G (2005) The prognostic value of domain-specific cognitive abilities in acute first-ever. *stroke* 64: 821-827.

124. Stephens S (2004) Neuropsychological characteristics of mild vascular cognitive impairment and dementia after stroke. 19: 1053-1057.

125. Hochstenbach JB (2003) Cognitive recovery after stroke: a 2-year follow-u 2003. 84: 1499-1504.

126. Hosking SG (2000) Depression at 3 months poststroke in the elderly: predictors and indicators of prevalence. 7: 205-216.

127. Ayerbe L (2013) The natural history of depression up to 15 years after stroke: the South London Stroke Register. 44: 1105-1110.

128. Stahlhut L (2014) The impact of stroke on cognitive processing - a prospective event-related potential study. *J Neurol Sci* 339: 157-63.

129. Angelakis E (2004) Peak alpha frequency: an electroencephalographic measure of cognitive preparedness. *Clin Neurophysiol* 115: 887-897. [Crossref]

130. Shah SA (2017) Executive attention deficits after traumatic brain injury reflect impaired recruitment of resources. *Neuroimage Clin* 14: 233-241.

131. McWilliams J and Schmitter-Edgecombe M (2008) Semantic memory organization during the early stage of recovery from traumatic brain injury. *Brain Inj,* 22: 243-253.

132. Ferraro FR (1996) Cognitive slowing in closed-head injury. *Brain Cogn 32*: 429-400.

133. Mathias JL, Beall JA, Bigler ED (2004) Neuropsychological and information processing deficits following mild traumatic brain injury. *J Int Neuropsychol Soc* 10: 286-297.

134. Mathias JL and Wheaton (2007) Changes in attention and information-processing speed following severe traumatic brain injury: a meta-analytic review. *Neuropsychology* 21: 212-223.

135. Felmingham KL, Baguley IJ, Green AM (2004) Effects of diffuse axonal injury on speed of information processing following severe traumatic brain injury. *Neuropsychology* 18: 564-571.

136. Garavan H (2002) Dissociable executive functions in the dynamic control of behavior: inhibition, error detection, and correction. *Neuroimage* 17: 1820-1829. [Crossref]

137. Hampton A and Weber-Fox C (2008) Non-linguistic auditory processing in stuttering: evidence from behavior and event-related brain potentials. J Fluency Disord, 2008. 33: 253-273.

138. Theriault M (2009) Electrophysiological abnormalities in well-functioning multiple concussed athletes. *Brain Inj* 23: 899-906.

139. Moore RD, Lepine J, Ellemberg D (2017) The independent influence of concussive and sub-concussive impacts on soccer players' neurophysiological and neuropsychological function. *Int J Psychophysiol* 112: 22-30.

140. Baillargeon A (2012) Neuropsychological and neurophysiological assessment of sport concussion in children, adolescents and adults. Brain Inj 26: 211-220. [Crossref]

141. Bauer LOJN (2001) Predicting relapse to alcohol and drug abuse via quantitative electroencephalography 25: 332-340.

142. De Bruin EA (2004) Abnormal EEG synchronisation in heavily drinking students. 115: 2048-2055.

143. Rangaswamy M (2003) Theta power in the EEG of alcoholics. 27: 607-615.

144. Coutin-Churchman (2006) Clinical correlates of quantitative EEG alterations in alcoholic patients. *Clin Neurophysiol* 117: 740-751.

145. Matheus-Roth C (2016) Occipital event-related potentials to addiction-related stimuli in detoxified patients with alcohol dependence, and their association with three-month relapse. 16: 1-12.

146. Glenn SW, Sinha R, Parsons OAJA (1993) Electrophysiological indices predict resumption of drinking in sober alcoholics. 10: 89-95.

147. Anderson NE (2011) P3a amplitude predicts successful treatment program completion in substance-dependent individuals. 46: 669-677.

148. Fink BC (2016) Brain potentials predict substance abuse treatment completion in a prison sample. 6: e00501.

149. Wan L (2010) Association of P3 amplitude to treatment completion in substance dependent individuals. 177: 223-227.

150. Abad VC and Guilleminault C (2003) Diagnosis and treatment of sleep disorders: a brief review for clinicians. *Dialogues Clin Neurosci* 5: 371-388.

151. Kushida CA (2005) Practice parameters for the indications for polysomnography and related procedures: an update for 2005. *Sleep* 28: 499-521.

152. Keenan SAJSDM (1994) Polysomnographic technique: an overview. 1994: 79-94.

153. D'Rozario AL (2017) Quantitative electroencephalogram measures in adult obstructive sleep apnea - Potential biomarkers of neurobehavioural functioning. *Sleep Med Rev* 36: 29-42.

154. Xiromeritis AG (2011) Quantitative spectral analysis of vigilance EEG in patients with obstructive sleep apnoea syndrome: EEG mapping in OSAS patients. *Sleep Breath* 15: 121-128.

155. Marzano C (2008) Quantitative electroencephalogram (EEG) in insomnia: a new window on pathophysiological mechanisms. *Curr Pharm Des* 14: 3446-3455. [Crossref]

156. OH DY, Park SM, and Choi SW (2020) Daytime Neurophysiological Hyperarousal in Chronic Insomnia: A Study of qEEG. *J Clin Med* 9.

157. Campbell K (2010) Event-related potentials as a measure of sleep disturbance: a tutorial review. *Noise Health* 12: 137-153.

158. Colrain IM and Campbell KB (2007) The use of evoked potentials in sleep research. *Sleep Med Rev* 11: 277-293.

159. Zhao W (2018) Response Inhibition Deficits in Insomnia Disorder: An Event-Related Potential Study with the Stop-Signal Task. *Front Neurol* 9: 610.

160. Collura TF (1993) History and evolution of electroencephalographic instruments and techniques. *J Clin Neurophysiol* 10: 476-504.

161. Borck C (2005) Writing brains: tracing the psyche with the graphical method. *Hist Psychol* 8: 79-94.

162. Gevins A (1998) The future of electroencephalography in assessing neurocognitive functioning. *Electroencephalogr Clin Neurophysiol* 106: 165-172. [Crossref]

163. Gevins A (1999) Electroencephalographic imaging of higher brain function. *Philos Trans R Soc Lond B Biol Sci* 354: 1125-1133. [Crossref]