A Brain Computer Interface for Audio-Visual Entrainment in Emotional Regulation: Preliminary Evidence of its Effects

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Abstract

Research on Brain-Computer Interfaces (BCIs) has significantly increased during the last few years. Here, we review the state-of-the-art of BCIs, looking at their components: signal acquisition, pre-processing or signal enhancement, feature extraction, classification and control interface. In order to translate this technology into useful clinical applications, data gathered in our laboratory using the Neuro-Upper(NU) prototype were also reported. The study proposes a BCI in which a NeuroskyMindwave® headset is connected to a EEG-based neuro-feedback computer so as to administer repetitive audio-visual stimulation or entrainment for regulating the emotional states of individuals with anxiety and depressive disorders. The application receives eight signals from the BCI analysis software and is settled on the self-regulation of the SSVEP amplitude as the effector device highlighting each lamp of the array corresponds to the eight brain signals detected. Seven subjects participated in the experiment to evaluate the system, and underwent a comprehensive clinical and neuropsychological assessment. Statistical analysis suggests a significant decrease in the symptomsof depression. Unexpectedly, however, important improvements were noted in outcome measures for cognitive function. The paper ends with a discussion of the challenges facing our BCI and concluding remarks on the future of the present technology.

KEYWORDS: Brain-Computer-Interface, Entrainment, Anxiety, Depression

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Introduction

Brain-Computer Interface (BCI) represents a rapidly emerging field of multidisciplinary research and applications integrating research from neurosciences, psychology, engineering, computer science, rehabilitation, and other health-care disciplines. A BCI is a computer-based system that acquires brain signals, analyzes and translates them into commands that are relayed to an output device to carry out the user's intentions. The most commonly studied signals are the electrical signals from brain activity measured from electrodes on the scalp, on the cortical surface, or in the cortex. A BCI is a system consisting of four successive components: 1) signal acquisition, 2) feature extraction, 3) feature translation, and 4) device output.These components are controlled by an operating protocol that defines the onset and timing of operation, the specifics of signal processing, the nature of the device commands, and the error of performance. A valid operating protocol allows a BCI system to be flexible and to serve the specific needs of the user. A BCI device may be used to replace or restore functions for people with neuromuscular disorders, and to improve rehabilitation in strokes, head trauma, and other similar disorders. At present, the impressive achievements of BCI research and development are confined to the laboratory. The future of BCI depends on progress in the field of: a) development of comfortable and stable signal-acquisition hardware; b) BCI validation; c) confirmation of BCI reliability for different user populations.

This paper presents the essential components of a BCI system and then shows how our trial attempts to translate this technology to practical and useful clinical applications reporting the data gathered in our laboratory with the prototype, Neuro-Upper (NU). Acquisition of brain signals is amplified to levels suitable for electronic processing, digitized and transmitted to a computer. After the signal is acquired, it has to be processed. This task is performed by the signal processing component which consists of two steps: feature extraction and feature translation/classification. The feature extraction process works in two ways: evaluation of the acquired signal, and identification of potential features or markers. This is achieved by the extraction algorithm which is helpful for uncovering the features that correlate most strongly with the subject's intent. These features are then sent to a classification algorithm and converted into the appropriate commands for the output device (i.e., commands that accomplish the user's intent). Feature extraction algorithms represent a difficult step in that, in order to detect features of interest, they deal with the source of the signal, which is often noisy and complex. For the discovery of these features, our device relies on time-frequency analysis using the Fourier transforms (FT). The commands from the feature translation algorithm control the last component, the effector device, which can be a computer cursor or a wheelchair. The operation of the device provides feedback to the user completing the control loop.

Among different brain imaging techniques that have been applied to BCI, the electroencephalogram (EEG) is the most commonly used, owing to the minimal risk involved and the relative convenience. In general, power spectrum analysis is typically used for decomposing the EEG signal into different frequency bands. This is useful in that it is accepted that specific bands of power in the EEG spectrum are linked to a broad variety of perceptual, sensorimotor, and cognitive operations. As far as BCI systems are concerned, the most important frequency activity in the EEG spectrum lies below 40 Hz. Investigations on EEG oscillations have particularly focused on alpha, theta, beta and gamma frequencies, and only recently on very slow activity. These oscillators are active usually in a random way. By application of sensory stimulation these generators may be coupled and act together in a coherent way. This synchronization and enhancement of EEG activity gives rise to ‘‘induced rhythms’’ (or ‘‘evoked’’); this is crucial to establish whether or not users can obtain power within distinct frequency bands in a voluntary manner. EEG variations, then, need to be noticed in order to be used as control signals.

The application of neuro-feedback for regulation purposes made use of computer software to show the visual and audio feedback according of brainwaves such as alpha, beta, or theta frequencies. One neuro-feedback method for depression involves reversing right frontal asymmetry associated with internalizing (depressive, anxious) symptomatology (Niv, 2013). The paradigm typically in use is that of evoked potentials. Evoked potentials or event-related potentials (ERPs) occur from perception to an external stimulus or set of stimuli. Sensory evoked potentials (SEPs) are electrical potentials recorded by the central nervous system;stimulating sense organs,SEPs are phase-locked to the stimulus. Therefore, SEPs can be enhanced. They can be interpreted as a reorganization of spontaneous brain oscillations in response to a stimulus. With repeated stimulation at short intervals, the brain's response to each subsequent stimulus is evoked before the response to the prior stimulus has finished. Instead of being permitted to return to a baseline state, a so-called steady-state response (SSVEP) is elicited (Middendorf, McMillan, Calhoun & Jones, 2000). SSVEP-based BCI is developed to translate EEG signals recorded from the individual into computer commands through recognizing the SSVEP by commonly using power spectral density analysis (PSDA). The typical setup for SSVEP-BCI is to have subjects observe flashing lights in the surrounding area (monitor or prosthetic device) allowing the BCI to correlate the observed light with a desired action (cursor control or robotic arm movement). VEPs can be generated from visual sensory stimulation to achieve neuronal synchronization with a similar frequency (or harmonic) to the flash of light presented. Another notable aspect of this field of research is that the colour of the visual stimuli is also known to affect the elicited SSVEP paradigms. A number of BCI studies have investigated which colours give raise strongest SSVEP (Falzon&Camilleri, 2013). Light therapy (Light-Emitting Diodes - LEDs) has also been show to produce beneficial cellular and physiological effects, particularly with the recent discovery of non-visual opsins (Pino & La Ragione, 2014).

SSVEPs were recently employed to show that patients suffering a major depressive disorder had low activation in the right temporo-parietal cortex when watching arousing stimuli, although they had normal occipital activation (Moratti et al., 2008), because of a deficit in the arousal of related brain structures, along with intact basic visual stimuli processing in patients with major depressive disorder. SSVEPs were also typically considered as a marker of anticipative anxiety. Some investigations indicated that the associations among psychometric measures of anxiety and depression and electroencephalogram (EEG) spectral power measures were positively correlated to alpha and negatively correlated to delta, regardless of cortical area (Knyazev et al., 2004). In high-anxiety subjects, alpha2 sub-band seems to be the most reactive while low-anxiety subjects tend to adjust to environmental changes by alpha3 power modification. Brain-computer interface-based therapy might provide a useful complement to standard treatment methods and might lower costs by reducing the need for the presence of a therapist (Shangkai, Yijun, Xiaorong&Bo, 2014). Principal treatments used today for anxiety and depression are pharmaceuticals and psychotherapy. Both approaches have limitations in terms of effectiveness, side effects, costs, or time required. Neuro-Upper (NU) is theBCI developed in our laboratory (by the second author) set on brain responses to exogenous repetitive visual and auditory stimuli. Synchronization of oscillatory activities in distributed neural assemblies is a well-studied mechanism. It can be thought of as a reflection of the cooperative and synchronous activity of neural assemblies with different EEG frequencies revealing synchronies related to different perceptual, motor or cognitive states. One property of oscillating elements is that they can be disturbed by an external periodic force becoming synchronized to this periodic event; in other words, the oscillating component starts to move with the same frequency as the external force. So, synchronization, entrainment, and locking are considered synonymous. The notion of driving brain oscillations by directly stimulating neuronal elements with rhythmic stimulation protocols has become increasingly popular (Thut, Schyns& Gross, 2011; Will & Berg, 2007). There are several headsets with scalp sensors connected up to a computer to create a system which intensifies attention and meditation via EEG-based neurofeedback (Shangkai, Yijun, Xiaorong&Bo, 2014). Controlled entrainment of brain rhythms may therefore prove highly advantageous for the study of human brain oscillation, and further research in this area may well lead to applications in rehabilitation or treatment of diseases. The ideal scenario to achieve this form of entrainment is to tune the frequency of the periodic force to the natural frequency of the to-be-entrained neuronal elements. Evoked potential generation is also of great interest for the study of entrainment. It is accepted that psychological disorders are characterized by alteration from typical circuitry in limbic, frontostriatal and prefrontal regions rather than neurochemistry (Menon, 2011), and that rather than specific regions of dysfunction, network involvement is frequent, as showed from frequent comorbidity. At least three neurocognitive networks have been indicated in relation to brain self-regulation pertinent to psychopathology posing that dysfunction in any one affects all three, as it happens for DMN and SN in depression (Chen, Chen & Dai, 2015). Music with certain rhythmic parameters is capable of triggering specific brain waves and physiological responses (Zatorre, 2003). Baroque music (60 bpm), for example, induces alpha rhythms and slows down heart and respiration rates, while music with driving rhythms or fast tempos (e.g., rock) stimulate beta waves and speed up heart and respiratory rate. When specific musical stimuli activate corresponding brain mechanisms, *global* extra-musical responses are generated, such as enhanced cortical synchrony (Juslin, Liljeström, Västfjäll, &Lundqvist, 2010). Neuromediators, endorphins, endocannabinoids, dopamine and nitric oxide are altered during the musical experience. Different forms of music activate distributedbrain regions in unique ways, and it has been shown that the brain responds predictably to different styles or pieces of music (Petsche et al., 1993) or voices (Loui, Bachori, Li, &Schlaug, 2013). Some findings indicated strong interactions between sensory and affective systems: the subcortical regions interact with the auditory sensory cortices to establish a potentially rewarding stimulus which is experienced for the first time as attractive. The auditory cortices are active in auditory sensory memory and imagery, extraction of sound relationships, and discrimination and organization of sound patterns making them an ideal placement for feedback regarding temporal predictions which, together with the right nucleus accumbens (Nacc), can contribute to the rewarding nature of music. Several neuroimaging studies have implicated emotion and reward circuits of the brain during pleasurable music listening, particularly the ventral striatum, indicating the involvement of dopaminergic mechanisms. It was evidenced that the intense pleasure experienced when listening to music is associated with dopamine activity in the mesolimbic reward system, including both dorsal and ventral striatum (Salimpoor, Benovoy, Larcher, Dagher&Zatorre, 2011). This effect need not be restricted to harmonic or metrical structure, but may also involve other features of music, including timbre, loudness changes or the integration of verbal content if present (Salimpoor, van den Bosch, Kovacevic, McIntosh, Dagher&Zatorre, 2013).Entrainment is most probable involved in periodic stimuli perception in primary auditory areas. Large and Kolen (1994) suggest that it is through synchronization that the perception of metrical structure occurs, and others (Clayton et al., 2005) propose that perception, attention and expectation are all rhythmic processes susceptible to entrainment. More recently, it was indicated that listening to simple periodic sounds elicits periodic responses at frequencies compatible with the periodicity of that sound giving evidence for a selective neuronal entrainment (Nozaradan, Peretz&Mouraux, 2012).Most of the studies indicate that such rhythmic stimulation may alter attention and perception by modifying communication in oscillatory networks through their entrainment. How stimulation parameters and ongoing oscillations interact to give rise to entrainment will need to be studied in detail. In addition, the duration of entrainment effects after stimulation will determine subsequent uses beyond basic research on brain oscillations. In our work we aimed at exploring real-time interactions with a BCI. The main purpose of the reported study was to show the effect of our laboratory-made device (NU) on brainwave patterns through audio-video entrainment in regulating emotional states of individuals with anxiety and depressive disorders. We hypothesized that participants would report increased feelings of wellbeing and relaxation after NU exposure, and that a decrease in salivary cortisol and 5-HIAA concentration would be observed.

Method

Participants

Recruitment process was carried out through notices in local newspaper. Twenty-one individuals responded to advertisements requesting people who experience depressive and anxiety symptoms; after some rounds of screening, the final group included seven participants (4 females). Those individuals who are potentially eligible will be invited to a face-to-face screening assessment including an elicitation of a medical history and medications for eligibility confirmation. To be eligible for the study, subjects must meet the inclusion and exclusion criteria. Individuals who exhibit any behavioral and psychological symptoms of dementia (at least one item of MMSE scoring <2) will be excluded from the study. Subjects will also be excluded if they have severe medical conditions which limit their abilities to complete the course of treatment. Concurrent psychotropic medication will be allowed without restriction, but any change in psychotropic prescriptions over the course of the treatment period will be monitored. Community-dwelling adults aged ≥ 18 years will be screened using the Hamilton Rating Scale for Depression (HAMS; Hamilton, 1960). Those who score between 8 and more with a diagnosis of depression or anxiety disturb will be screened for eligibility to the study. We included participants that met also the Diagnostic Statistical Manual of Mental Disorders-Fourth Edition Text Revision (DSM-IV-TR) criteria for one or more personality disorders.

Some form of personality disorder was diagnosed in almost all cases. Three participants had multiple comorbidities but only 3 were diagnosed primarily with avoidant personality disorder. Three patients had primary obsessive-compulsive disorder (with depressive or passive-aggressive personality disorders).One patient met criteria for paranoid disorder. Subjects were all right handed with mean age of 47.29 years (SD=14.98) and had no musical training. All subjects declared the absence of neurological illnesses, and were screened for the photosensitive epilepsy. They were right-handed as indicated by the Edinburgh Inventory (Oldfield, 1971). The experiment reported in this paper was performed in the Cognitive Psychology Laboratory of the Department of Neurosciences, University of Parma, Italy. All the details of the experimental procedures and the research targets of the VEP-based BCI paradigm were explained in detail to the seven users, who agreed voluntarily to participated in the study. Informed, written consent was obtained from all of the subjects.The research was conducted in accordance withThe World Medical Association Declaration of Helsinki - Ethical Principles for Medical Research Involving Human Subjects. Given that the experiment did not involve clinical tests, use of pharmaceuticals or medical equipment, did not involve the use of deception or involve participant discomfort in any other way, approval of Ethics Committee for Clinical Research of the University of Parma was deemed unnecessary, in accordance with the regulation of the local ethical committee of the University of Parma. All procedures were noninvasive and the subjects were free to withdraw at any time without any penalty. No one of the participants had previous experience in using a BCI.

Material and apparatus

Each participant is interviewed with the Structured Clinical Interview for DSM-IV-R Axis I Disorders (SCID-4-RV; APA, 2000) and prior to the inclusion into the study, undergoes a comprehensive clinical and neuropsychological assessment using the following tests: Spielberger State Trait Anxiety Inventory (STAI; Spielberger et al., 1983), Hamilton Rating Scale for Depression (HAMS; Hamilton, 1960), Wechsler Adult Intelligence Scale Revised (WAIS-R; Wechsler, 1981), Raven's Progressive Matrices (SPM; Raven, Raven & Court, 2003) and Mini Mental State Examination (MMSE; FolsteinFolstein& McHugh, 1975). Neuro-Upper used a NeuroSkyMindwave® headset (Fig. 2, b) measuring raw EEG activity data at a 512 Hz sampling rate. To reduce electrical interference generated by the human body, the device has a "base" contact, which is attached to the earlobe and allows the filtering of electrical waves produced by the body (noise).Despite the EEG data were collected using a single electrode BCI, yet the classification outcome was not far behind than multi electrode BCI (Lim & Chia, 2015). The apparatus of NU detects MindWave® electrical brain activity and decomposes the signal into eight outputs according to their frequency. There is evidence of at least two independent (lower and upper) alpha sub-bands. Values are assessed at a rate of 1Hz. A multi-colors paradigm was used with an application of higher flashing frequencies (40 Hz), comparing to the classical computer display (with limited refreshing rates allowing for at maximum 30 Hz stimulus generation) approaches.An array of colored lamps producing flickering light is used with direct mapping to the monitor of a personal computer. Microsoft Visual C # software is utilized to design the BCI, to measure brainwave signals when subjects listen to music, and the data for different frequency bands can be observed in real-time with the interface.

Fig. 1. a) Emotiv EPOC®neuroheadset, b) NeuroskyMindwave®

The frequency of light sources able to emit flashing light (eight PAR 56 Omnilux® lamps, 300 Watts, 26 x 23,5 x 22 cm each covered by colored gelatin sheets, also with color combination, see Fig. 2) is controlled by electronic circuits, which internally use micro-controllers providing the frequency of each brainwave and translating EEG feedback into flashing colors. Although red color has shown to receive an attentional advantage, blue light increases subjective alertness and performance, and blue, green and yellow are demonstrated possible candidates for use in SSVEP-BCI, as they have been associated with positive content, receiving experimental confirmation from laboratory studies (Elliot, 2015; Godinez Tello, Torres Muller, Ferreira & Freire Bastos, 2015). The array of lamps is placed about at 210 cm from the participants' seat. The challenge met by this software is the generation of the real time frequency to present visual repetitive stimuli on the computer screen to the user (e.g., feedback that shows real time brainwave activity). This application receives eight commands from BCI analysis software and is based on the self-regulation of SSVEP amplitude. BCI feedback is basically the user interface that translates data coming from the signal processing unit of the BCI into a visual representation on the screen to provide a second visual feedback to the user.

Figure 2: Neuro-Upper: the hardware system equipped with LED and the visual stimulation device used in the present study

Based on previous studies, play-lists of musical excerpts are arranged for different disorders. Play-lists without restrictions to the genre of music, which included classical, folk, jazz, electronica, rock, punk, techno and tango (see http://www.zlab.mcgill.ca/supplements/supplements_intro.html for samples) are maintained constant everyday for all the participants and changed only two times along the treatment period. The reward anticipatory phase, set off by temporal cues signaling that a potentially pleasurable auditory sequence is coming, can trigger expectations of euphoric emotional states and create a sense of waiting. This reward is completely abstract and may concern such factors as suspended expectations and a sense of resolution. The peak emotional response evoked by hearing the known sequence would represent the "consumatory" phase, representing fulfilled expectations and correct reward prediction. Salimpoor and collegues (Salimpoor, Benovoy, Larcher, Dagher&Zatorre, 2011) propose that each phases may involve dopamine release, but in different sub-circuits of the striatum with different connectivity and functional roles.Saliva samples were collected before and after NU treatment. Saliva samples were analyzed using an enzyme immunoassay.

Procedure

To avoid confounding effects due to the circadian and circaseptan rhythms of cortisol secretion, all experimental sessions took place at the same time for each participant. Subjects were comfortably seated in a chair in a dim room wearing the Mindwave® headset with eyes open and listen to the music. Musical excerpts are presented binaurally through earphones at a comfortable hearing level to each subject in sessions of 30 minutes for four consecutive months (five days for week). Participants were asked not to listen to those pieces anymore during the course of the study to ensure maximal responses during treatment. They were instructed to relax, avoid any unnecessary head or body movement. We record the EEGs of the subjects who are invited to listen to the music and observe the computer screen with their changing brain rhythms. Visual stimulation is delivered using a BCI stimulator (see Fig. 2), placed at 210 cm in front of the chair. Graphic waves patterns are rendered on the computer screen in the form of both bar histograms showing real-time frequency for each brainwave and flashing LED (Fig. 3). The participant receives a double feedback, one from the effector device which lights up each lamp, and the other by the dynamic vertical bars on the computer screen. Brainwave patterns are recorded continuously and saved for each participants. The procedure for each session takes approximately 40 minutes per subject. Treatment phase took place over about fifty sessions. Measurements post-treatment provide useful assessments of participants' progress.The same tests were administered on the final day of the program.

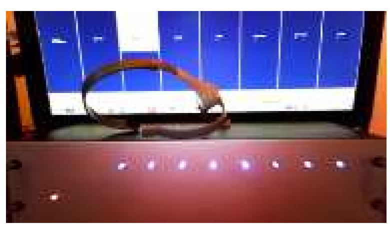

Figure 3: Graphics of brainwaves' real-time frequency showed to the subjects

Results

Data review included analysis of baseline and post-training scoring on the psychological tests administered. Statistical analysis utilized SPSS software version 20.0 (IBM Corporation, Armonk, New York).Our question was whether there was any significant difference in outcome measures between Pre and Post-treatment. The Wilcoxon rank-sum test was used to determine these differences. *P* values <.05 were considered significant.

Because the distribution of the cortisol concentration values deviated significantly from normality, the data was first log transformed to achieve normality. We then conducted a repeated measures analysis. However, no additional effect on salivary cortisol and 5-HIAA concentration associated specifically with exposure to NU sessions was detected. Figure 4 addresses this question by showing the results for the Hamilton Depression Rating Scale score, where significant differences were found (HAMS 19.71 versus 7.714, *P* = 0.022). State Trait Anxiety Inventory reported increasing levels of severity of anxiety (STAI-Y1 42.14 versus 53,*P* = 0.14; STAI-Y2 40.71 versus 48.14, *P* = 0.15, respectively). However, no difference is shown in the Mini Mental Status Examination (29.71 versus 29.57, *P* = 0.85) in which participants reached maximum score also at the baseline suggesting the absence of cognitive impairment. Notably, significant improvements were obtained in outcome measures for cognitive function. A significant increase was demonstrated for the Wechsler Adult Intelligence Scale III (QI total 117.9 versus 143.9, *P* = 0.016), both for Verbal (VIQ 104.1 versus 130.6, *P* = 0.016) and Performance (PIQ 104.1 versus 145.6, *P*= 0.016) scales respectively. Raven's Progressive Matrices scores also showed a significant gain from Pre-treatment and Post-treatment results (RPM 45.57 versus 48.14, *P* = 0.209).

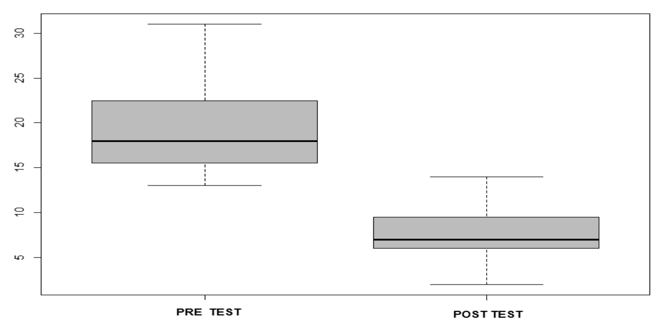

Figure 4. Hamilton Depression Rating Scale Pre- and Post-Treatment mean score

On average, forty-eight sessions of EEG were recorded. A frequency-domain-based method was implemented. We estimated the power spectra of *M* seconds of data, and the power values at the eight base frequencies were extracted. The power spectrum analysis is a kind of analysis technique that is used when the time-series signals change over time are transformed into the frequency field, and the signal aspect is evaluated by the degree of change in the frequency. A time-series analysis on median scores of spectral power for each sub-band was carried out (Fig. 5). Statistical analysis showed that some quantitative (median) values are rather stationary, precisely delta and theta bands, while the others showed a downward trend, confirming in part data from other studies (Kirsh& Nichols, 2013). Increased alpha correlates with improved relaxation and increased mental alertness or clarity. Beta-wave reductions between 20 and 30 Hz correlate with decreases in anxiety, ruminative thoughts, and obsessive/compulsive-like behaviors.

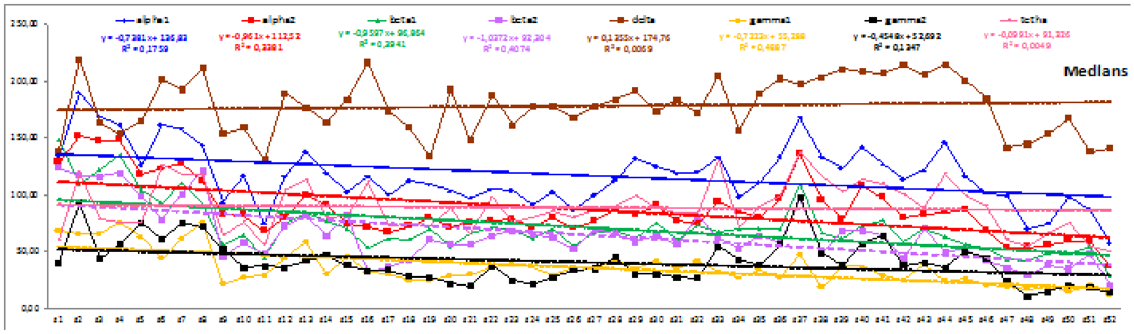

Figure 5. Mean trends for the frequency of the eight signals recorder during all training sessions

Conclusions

Interest in the BCI field is expected to increase, and BCI design and development will in all probability continue to bring benefits to the daily lives of people. Furthermore, recent results suggest that BCI device may find useful applications in the general population, and not just for people with severe disabilities. The present paper has indicated preliminary evidence from the trials using a methodology in which a combination of audio-visual entrainment and BCI is usedto treat anxiety and depressive symptoms. Despite methodological limitations (the absence of a control group) and the heterogeneity of the results (increase in anxiety scores), our findings supports the idea that a dis-regulation of brainwave patterns and abnormal connectivity may account for a wide range of the symptoms of these disorders, including emotional disturbances, and cognitive dysfunction, and that at least some of these disturbances can be alleviated by external manipulation or audiovisual entrainment. Real-time neurofeedback allows simultaneous acquisition, analysis, visualization, and feedback of brainwaves. The behavioral change produced by NU was demonstrated in depressive symptomatology remission, probably due to a modulation of the insular activity, that plays a central role in sensory integration, emotion, and cognition, or to generalized brain activation, as evidenced by the resulting improvement in cognitive ability (WAIS and RPM scores). The idea that dopamine can be released in anticipation of an abstract reward (a series of musical tones) has crucial implications for understanding how music has become pleasurable. A sense of anticipation may arise through familiarity with a specific piece and knowing that a particularly pleasant section is coming up. If music-induced emotional states can lead to dopamine release it may begin to explain why musical experiences are so valued. However, some data provide neuro-chemical evidence that intense emotional responses to music involve ancient reward circuitry (Salimpoor, Benovoy, Larcher, Dagher&Zatorre, 2011). Many symptoms seen in psychiatric conditions, such as anxiety, insomnia, and attention deficit disorders, are thought to be exacerbated by excess cortical activation. At the end of a NU session, most participants reported to feel more relaxed, yet alert, and have an increased sense of well-being. Zoefel and collegues (2010)showed that neurofeedback training significantly enhanced the cognitive performance when compared with a group who did not receive neurofeedback training. The significant reductions in depression symptomatology, as measured HAMS in the participants who completed about 50 sessions of NU, demonstrate another important mental-health dimension to the benefits that come from doing NU.

An important limitation of the present study was the real nature of the signals recorded, because it is likely that Mindwave® record non-brain signals, such as electro-oculographic signals from eye movements and blinks. So, in the future trials our aim is to improve NU using Emotive Epoch (Fig. 1, a) for the new adaptation of the device. Furthermore, although BCI training implies learning through operant conditioning, little is known of the deeper mechanism of learning using this methodology. Other studies will have to explore whether brain self-regulation persists if feedback is removed and whether the capability for self-regulation will persist in people with no psychological disorders showing the same pattern of increase in cognitive ability. Although our results are still empirical (given the limited number of participants and measurements available thus far) and the solidity of our claims requires further investigation and more data analysis, we believe that these first tentative results open the door for future applications of BCI both as a research tool and a new approach to therapy.

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