Effect Of tDCS Application On P300 Potentials: A Randomized, Double Blind Placebo Controlled Study

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Abstract — **In this paper, we report the results of a study on the post-intervention effects of applying anodal transcranial direct current stimulation (A-tDCS) on the intensity of P300 potentials. Each of the eight subjects were given both 15 minutes sham and 1.5 mA tDCS in randomized order, in two separate experiments separated by 1 week. The interventions were double blinded. Post-intervention EEG was then recorded after each experiment while subjects were asked to perform a spelling task based on the "odd ball paradigm". Results show a 22% difference, in normalized signal power between tDCS and sham when recorded at 250ms-450ms with a paired *t-test p value* of 0.057.**

Keywords—Brain Computer Interface;tDCS; P300.

I. INTRODUCTION

Brain Computer Interfaces (BCI's) give their users communication and control channel that do not depend on the brain's normal output channels [1]. Some of the applications of Brain Computer Interfaces have typically been communication mediums [2-4] or transportation aids [5, 6] for people with severe neuro-muscular disabilities [7]. One of the major limitations for people with severe motor disabilities is the inability to communicate with ease. Consequently, early work on BCI focused on developing communication aids in the form of word spellers [3, 8, 9]. The concept of a BCI speller is based on a system that enables a direct brain to character translation. P300 event evoked potentials have been investigated for EEG spellers. These potentials are generated in the brain in response to external stimuli. It has been found that event related potentials produce more distinguishable signals than non-evoked potentials thus providing for higher accuracy rates [9].

It has been found that infrequent or particularly significant auditory, visual or somatosensory stimuli, when interspersed with frequent or routine stimuli, typically evoke a positive peak at about 300 ms in an EEG recording over the parietal cortex.[11]. This P300 response has thus been implemented in brain computer interfacing [10]. When undertaking a BCI using P300, a user is presented with an array of letters. The visual brightness of these characters are intensified in random sequence, either one character at a time, one row at a time, or as a random sequence of single rows and columns appearing simultaneously. A P300 response is recorded when the character under observation is intensified. The timing information of the response can then be used for character recognition.

However, P300 systems have had limited practical applications mostly because they assume brain EEG responses are identical in healthy subjects. Also, potential users of these spellers may have reduced neural activity in one or multiple areas of the brain due to illness or damage.

Recently, there has been a growing academic interest in neuro-stimulation techniques such as Trans-Cranial Direct Current Simulation (tDCS). tDCS is a non-invasive brain stimulation tool which has recently been used in neuro-scientific research. Recent studies have shown that it can assist in the facilitation of cognitive and motor processing as well as learning in the healthy brain [11]. It is a neuromodulatory technique that delivers low-intensity, direct current to cortical areas facilitating or inhibiting spontaneous neuronal activity [12].

It has been suggested that tDCS could be a highly promising technique in human neurorehabilitation, where (re-) learning, or at least preservation of motor and cognitive abilities, is of utmost importance. tDCS has several advantages that render it attractive for clinical use compared to invasive stimulation. The technique is, as stated, non-invasive and elicits only a slight tingling under the electrodes. The device is also easy to use and small allowing it to be attached to the patient in a rehabilitation session, and relatively inexpensive. Research has been published showing potential for tDCS for patients with neurodegenerative disease, movement disorders, epilepsy, and post-stroke language attention or executive deficits. The most promising and consistent results have been seen with post-stroke motor rehabilitation [11].

Studies have also demonstrated that tDCS can heighten the magnitude of alpha waves [18-20], and be used in conjunction with BCI [21]. A number of studies seem to suggest Event Related Desynchronisation (ERD), the phasic amplitude attenuation of the alpha rhythm that occurs in relation to an

This work was supported by the "Research and Innovation" Grant from HPC Wales and a Centenary Postgraduate Fellowship from the University of South Wales.

978-1-4799-5375-2/14/$31.00 ©2014 IEEE

event [13], can be slightly, but temporarily, amplified to heighten responsiveness using tDCS. It has also been suggested that there is a potentially beneficial effect of tDCS during rehabilitative motor training of patients who are suffering from subacute strokes [22]. However, the scale and effect duration of tDCS EEG potentials is still speculative. It is not clear, for instance, whether tDCS can influence the amplitude of P300 responses. If these can indeed be influenced, it may be worth considering tDCS in supportive intervention for locked-in patients using BCI. A modulation of Visual Evoked Potentials (VEPs) amplitude has been found both during and after tDCS, with effects dependent on the stimulation polarity and duration [23].

The study reported in this paper is a first step towards answering these questions, by looking initially at the effect of tDCS on P300 potentials on healthy subjects. The remainder of this paper is organized as follows; the experimental protocol is described in the next section then followed by a presentation of the results and conclusion.

II. METHOD

A. Subject selection

Eight healthy subjects (ages 22 ± 3 years, all right-handed) participated in this study after giving written informed consent. No subject had any history of neurological disease or had been receiving any acute or chronic medication affecting the central nervous system. The University of South Wales Ethical Committee approved the investigation.

B. tDCS application protocol

The tDCS was then fitted according to the procedure used by [24] for anodal stimulation. The anodal electrode was placed over the left M1, and the cathodal electrode over the right supraorbital area. Subjects sat in an armless chair, then using measurements of the distance between anion and nasion Cz was found, then 20% of the distance from Cz to the left pre-aurical point was found. This location, C3, was then gelled with EEG high conductivity gel. The temple was also gelled with the same. The tDCS pads were soaked in normal tap water and high conductivity get applied. The pads were placed on C3 and the frontal right lobe and both secured with a plastic band and netted cap.

Each subject underwent two experimental tDCS sessions, one real and one sham separated by a one-week interval. The order of sham and real tDCS was randomized and double blinded. The real tDCS consisted of 1.5mA current applied for 15min. The sham consisted of a dose of 1.5mA ramping up from 0mA to 1.5mA over 10s. 1.5mA was then driven for 8 seconds, before the tDCS automatically turned off. This was done to mimic the transient skin sensation at the beginning of actual tDCS without producing any conditioning effects on the brain [25].

Neither the investigator nor the participants were aware which of the dosages they were receiving. Participants were not informed that the dosage would be varied for each study (sham, 1.5mA), but were led to believe that the same dosage was being used for each study. They had given written informed consent with ethical approval being obtained for using stimuli up to a maximum dosage of 1.5mA for no longer than 20 minutes. The dosage was selected in each experiment by an independent investigator who either turned the sham button on or off based on a randomly generated binary number. The second investigator did not interact with experiment after applying the switch. The impedance value of the tDCS while operating was checked by the second investigator and remained between 4 kΩ and 9 kΩ for all participants, which was the recommend window given in the tDCS device instructions.

C. EEG measurement protocol

After the application of tDCS or sham stimulation, the EEG electrodes in the cap were connected to the participant using conductive gel. It took between 10 to 20 minutes to fit the cap and apply conductive gel to the electrodes. Once connected, the impedance of each electrode remained at a maximum of 20kΩ with a typical value being under 10kΩ throughout the experiment.

EEG signals were recorded from 14 Ag/AgCl disc electrodes (1 cm in diameter) with two reference electrodes at FCz and AFz to the international 10-20 system of electrode placement (Fz, F3, F4, F7, F8, Cz, C3, C4, Pz, P3, P4, P7, P8, Oz). The signal was pre-filtered (0.2-45Hz) with digital notch filters at 50Hz and 60Hz. The cap was centred on the scalp at Cz midway between the anion and nasion. Cz was checked for its equidistance to both left and right pre-aurical points.

D. P300 response measurement protocol

Subjects then sat in an armless chair with their eyes open facing a computer monitor placed approximately 0.7 m in front of them at eye level. They allowed both arms to dangle freely. They were asked to avoid any further muscular activity including blinking. The invigilator told them that if they do accidently blink or flinch they should ignore it and continue the study. They were told that the study would be repeated several times, and such artefacts would be removed. This was done so as to avoid participants feeling anxious if they accidently made any muscular motions during the study which could then have an effect on the remaining results.

A classic P300 speller, which contains all characters (A-Z), numbers from 0-9 and Space Bar was presented to the volunteer in 6×6 matrix form [26] . The volunteer was asked to spell the twenty letters in "THE QUICK FOX JUMPS" by focussing on the character inside the 6×6 matrix which they want to spell. Two sequences were used to select a character. In a sequence each row/column was intensified randomly. For each sequence there were 12 intensifications (6 rows + 6 columns), and therefore a total 24 intensifications were used to evoke a response for a character.

III. RESULTS

The following normalized measure was used to assess the P300 odd-ball response to intensified letters

$$NPR = \left[\frac{(P_{tl} - P_{ntl})}{P_{tl}}\right] \qquad (1)$$

Where *NPR* stands for the Normalized P300 Response.

P_{tl} is the average Oz channel power between 250ms-450ms after the target letter is intensified, averaged across 20 letters used.

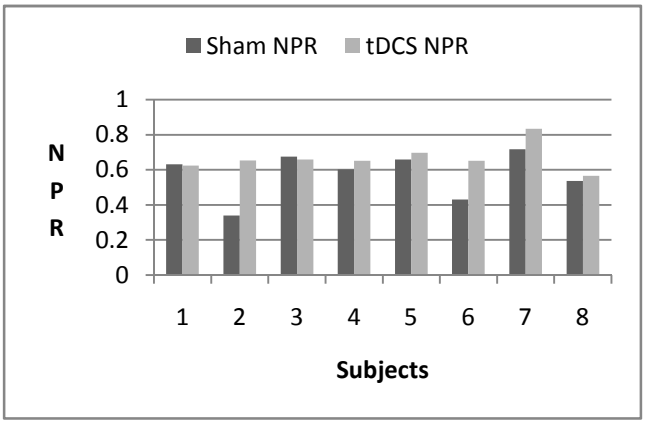

Fig. 1. Normalized P300 response across 8 subject with sham and tDCS.

P_{ntl} is the average Oz channel power between 250ms-450ms after a non-target letter is intensified, averaged across all non-target letters used.

NPR was separately calculated for each subject in both tDCS and sham cases. The data is summarized in figure 1.

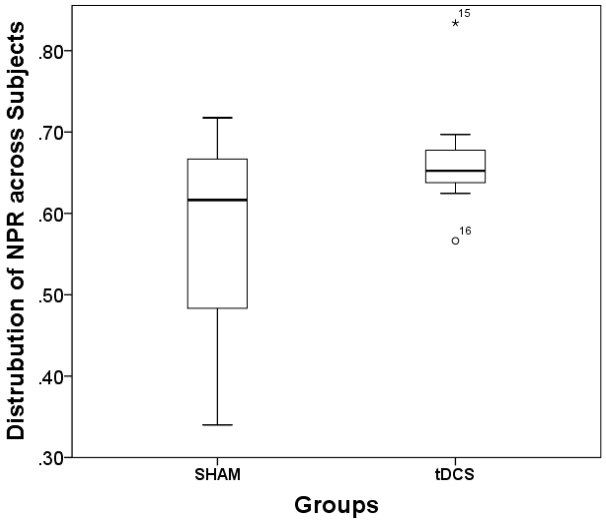

Fig. 2. Box plot showing Normalized P300 Response distribution of sham and tDCS across Oz Channel

It can be noted that there is an increase in the NPR with tDCS in all subjects except for two (subject 1 and 3) where the NPR remained on similar levels with a small decline. The average change in NPR across all subjects is a 22% increase with tDCS when compared to sham. The maximum change was observed on user 2 with a 91% increase. A paired sample t-test was calculated for the NPR values and gave a p-value of 0.059. The distribution of subject data is shown in figure 2. We note that tDCS exhibits higher average NPR with a small spread and fewer low values than sham. The difference between the two group averages when subjected to unpaired analysis using the ANOVA method produced a p-value of 0.102, which may be indicative of a trend but not statistically significant.

IV. Discussion

This paper has presented the results of a double blind placebo controlled experiments on the post-intervention effects of (A-tDCS) on the intensity of P300 potentials when subjects are performing BCI "odd-ball paradigm" spelling tasks. An overall trend of an increased normalized P300 response was noted with a paired t-test (p = 0.059).

Although this value moderately suggests a positive effect at this time it cannot be seen as conclusive. These findings suggest that more research is needed to determine the reliability of the effect seen here of tDCS on P300 potentials.

Regarding the security of the blinding, when questioned post-stimulation no subject in this study was able to distinguish between real and sham interventions. However, though the experiments were sham controlled and double blind, it is possible in principle that subjects may have had a different experience because of the nature of tDCS currents being applied. Any future studies could be made stronger by using a larger sample and improving the sham stimulus.

Acknowledgement

We would like to express our gratitude to Mr. John Starzewski from Neuradaptix Ltd. for facilitating the loan of part of the equipment used in this study.

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