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THE EFFECT OF 10 VIBRO-TACTILE P300 BCI SESSIONS IN PATIENTS WITH MINIMALLY CONSCIOUS STATE

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ABSTRACT: It has been shown that brain-computer interface (BCI) technology can help in assessing the cognitive abilities of patients with minimally conscious state (MCS) and can provide a platform for communication. In this study the effects of a vibro-tactile BCI oddball paradigm with three different stimulation location (VT3) were investigated. Seven MCS patients performed 10 VT3 P300 BCI sessions over 10 days with 8-12 runs each day. Changes in the classification accuracies over the 10 days were investigated. Coma Recovery Scale – Revised (CRS-R) was assessed before and after the 10 sessions. The average classification accuracy in the best sessions was 80±15%. Four out of seven patients showed an improvement in the CRS-R score of 2 to 7 points. This study shows the importance of repeated BCI measures in assessing MCS patients. The improvement in the CRS-R score is an important fact which should be considered in future studies.

INTRODUCTION

Some patients diagnosed with disorders of consciousness (DOC) recover to a chronic state of poor responsiveness to stimuli. Nevertheless these patients show evidence of awareness of themselves and their environment, depending on their motor control and cognitive abilities [1]. The fluctuations in responsiveness in these patients is a challenge for the diagnosis[2]. Behavioral tests such as the Glasgow Coma Scale or the Coma Recovery Scale – Revised (CRS-R) are commonly used tools to determine the diagnosis of these patients [2]–[5]. The limitation of using these scores is their dependence on voluntary motor control.

Alternatively, brain-computer interfaces (BCIs) have shown promising results in providing a platform for assessment and communication for DOC patients [6]–[8]. BCI systems rely on different neurophysiological phenomena and can thereby utilize different approaches like transient evoked potentials, for example the P300, a positive amplitude rising 300ms after the stimulus in the EEG signal [9]. Other techniques include slow cortical potentials and mu or beta rhythms [10], [11].

Visual P300 paradigms yielded high accuracies in patients with motor paralysis [12], [13]. However, DOC patients do not always have control of eye movements, which may cause difficulties in orienting attention to a specific location in the visual field. Therefore, we here chose to focus on a vibro-tactile paradigm.

The current study investigated the changes in the CRS-R score before and after ten sessions of a vibro-tactile P300 BCI paradigm with three stimulators used in seven MCS patients. Also, the changes in the classification accuracies during the training were explored. Our principal aim was to seek the possibility that training with a vibro-tactile BCI paradigm could facilitate recovery. Our secondary aim was to show that one or only a few sessions would not be sufficient for evaluating a patient's cognitive capabilities and that these results cannot be used potentially for BCI-based communication.

MATERIALS AND METHODS

Sample

This study included data acquired from 7 different MCS patients in a stable chronic stage. Patient Nr. 1 and 2 were located at the University of Palermo, Italy (PA) and patient Nr. 3-7 at the Shanghai Rehabilitation Hospital 3, China (SH). The following inclusion criteria were used: patients had to be over 18 years old, and diagnosed with MCS state according to the CRS-R scale administered by experienced neurologists. The CRS-R Score was measured the day before and after the 10 VT3 BCI sessions.

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Table 1 presents the patients' demographic data. We are presenting 7 MCS patients (Median age: 60; Min: 39; Max: 69).

Table 1: *Patients' demographic and CRS-R data. (A) Age (years); (B) Sex (M: Male, F: Female); (C) Diagnosis (CH: Cerebral Hemorrage, ENC: Mitochondrial Encephalopathy, TBI: Traumatic Brain Injury, HT: Hematoma, SH: Subdural hematoma); (D) Clinical State Before; (E) CRS-R before; (F) CRS-R after; (G) Δ CRS-R*

#	A	B	C	D	E	F	G
1	39	F	CH	MCS	11	11	0
2	30	F	ENC	MCS	12	14	2
3	66	M	TBI	MCS	7	9	2
4	60	M	CH	MCS	7	6	-1
5	56	M	HT	MCS	7	9	2
6	69	M	Anoxia	MCS	13	12	-1
7	61	F	SH	MCS	7	14	7

Brain-computer interface system

For data acquisition the mindBEAGLE system (Guger Technologies OG, Austria) was used. The gel-based EEG electrodes g.LADYbirds (Guger Technologies OG, Austria) were used. The electrodes were connected to a biosignal amplifier (g.USBamp, g.tec medical engineering GmbH, Austria). The amplifier has a 24-bit resolution combined with a high oversampling rate to increase the signal-to-noise ratio. The amplifier was connected to a computer using a USB cabel, and the EEG data were recorded with a sampling rate of 256 Hz. The EEG signal is presented for visual inspection on a monitor during the measurement. The data are stored in floating point format for later data analysis.

A bandpass filter between 0.1-30 Hz was used to filter the EEG signal. This was done to remove baseline shifts and eliminate most EEG artifacts. The electrode positions for recording were FCz, C3, Cz, C4, CP1, CPz, CP2 and Pz according to the extended international 10-20 electrode system. The reference electrode was mounted on the right earlobe, while the ground electrode was placed on the forehead. This system relies on P300 and motor imagery BCI approaches, and step-by-step explanations of system operation can be found in [7], [9]. In this study only the vibro-tactile P300 approach was used.

Paradigm

Three vibro-stimulators were placed on the left and right wrist of the patient. A third stimulator was placed on the foot to act as an additional distractor. The paradigm consists of 480 stimuli per run, with 60 groups of 8 stimuli. Via earbuds the patients were instructed to silently count vibro-tactile pulses on either their left or right wrist. All vibrotactile stimuli lasted 100 ms with a 100 ms pause between stimuli. The whole paradigm required around 2.5 minutes per run. Patient 1 and Patient 2 participated in 10 sessions over 10 consecutive days. For Patient 1 and Patient 2 each session consisted of 12 VT3 runs. Patient 3-7 participated in 10 sessions over 10 consecutive days. For Patient 3-7 one session consisted of 8 VT3 runs.

Data Analysis

Data segments of -100 ms to 600 ms around each stimulus were extracted and the EEG signal was averaged and baseline corrected. Trials with a signal amplitude +/- 100 µV were rejected from further processing. An automatic artifact detection was used during the run so the trial number varied.

To calculate the classification accuracy, the following steps were done. The target and nontarget trials are randomly assigned into two equal sized pools. One pool is used to train a classifier, and the other pool is used to test the classifier. The classifier is tested on an increasing number of averaged stimuli out of the test pool. At first, it is tested on only one target and seven nontarget stimuli. If the classifier detected the target stimulus correctly, the resulting accuracy is 100 %; otherwise, it is 0 %. This process is repeated for two averaged target stimuli and 14 averaged nontarget stimuli, for three nontarget stimuli and 21 target stimuli, and so on until the full test pool is used. This produces a plot of 30 single values (for 30 target stimuli in the test pool), each one either 100 % or 0 %. The averaging of 10 single plots results in values ranging from 0 % to 100 %. From these plots we selected the median value, the maximum value and first value on the x-axis the plot reached the maximum percentage. The accuracy value represents how well the data could be discriminated by the classifier, with a high value indicating a good separability of the EEG data.

The EPs from target and nontarget trials are averaged for all channels separately. Examples of EPs are shown in Figure 1. For each sample point, a Kruskal Wallis test ($p<0.05$) is done to find statistical differences between target and nontarget trials. A Wilcoxon rank sum test was performed to test the significance of the classification accuracies.

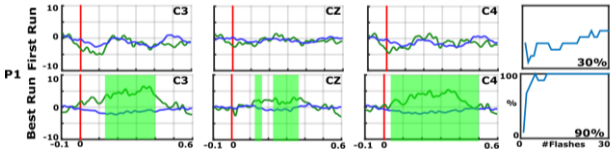

Figure 1: *EP's and classification accuracies of patient P1 in the first session compared to the best session on the electrodes C3, CZ and C4.*

A Wilcoxon rank sum test was performed to test both the significance of the classification accuracies and the significance of the CRS-R score. The factor was the timing of measurement (first run vs best run) for the classification accuracy and the timing of measurement (before vs after) for the CRS-R score.

RESULTS

Classification Accuracy

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The results are shown in Figure 2. The classification accuracy in the first run ranged between 30% and 100% (Mean: 49%) cross all seven patients. The best classification accuracy of each patient yielded from 60% to 100% (Mean: 80%). Notably, P6 and P7 reached 100% in the best run. The median accuracy over 10 days ranged from 10% to 40% (Mean: 21%). A Wilcoxon rank sum test was performed on each single classification accuracy and revealed a significant difference between the accuracies in the first run compared to the accuracies in the best run ($p < 0.01$).

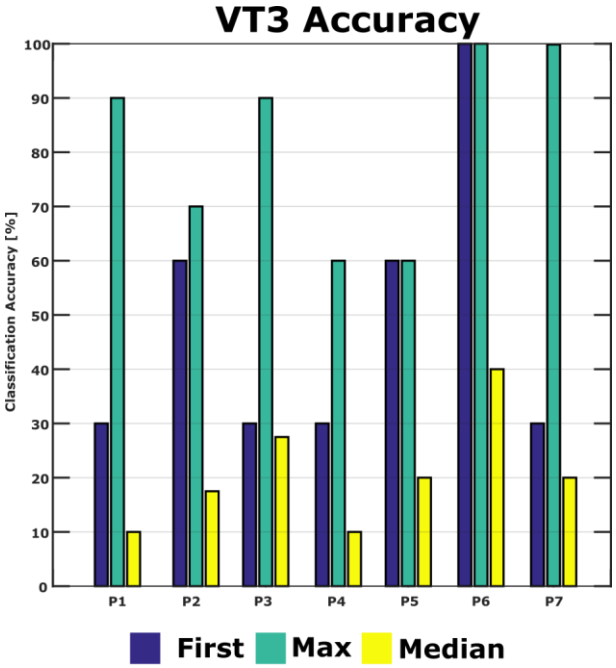

Figure 2: *Classification accuracies of all 7 MCS patients. Blue bars indicate the classification accuracies of the first run. Cyan bars indicate the best classification accuracy and the yellow bars show the median classification accuracy over all sessions.*

CRS-R score

Table 1 shows the total CRS-R scores of each patient before and after the 10 sessions. It shows also the delta of the CRS-R scores, i.e. the difference between the pre- and post- scores. The change in CRS-R score is on average 1.6 points (Max: 7; Min: 0). Specifically, 4 out of 7 patients (P1, P2, P5, P7) showed an improvement of two point or more after the VT3 BCI sessions. P1, P2 and P5 changed with a total improvement of 2 points. P7 showed the biggest improvement of 7 points. 1 patient did not show a change of the CRS-R score (P1) and 2 patients showed a decline in the score by 1 point (P4, P6). Of these 4 patients with improvement in CRS-R, 3 improved in auditory function, 3 in visual function, 2 in motor function, 1 in oromotor/verbal function, 2 in communication and 2 in arousal.

The Wilcoxon rank sum test revealed a significant difference in the CRS-R score before and after the 10 VT3 P300 BCI sessions ($p < .01$).

DISCUSSION

In this study the changes in the CRS-R score before and after ten VT3 P300 BCI sessions and the changes in the classification accuracies were investigated.

During the 10 VT3 P300 BCI sessions, the classifier resulted in accuracies of 60% or higher in the best runs of the patients. This is an indicator that the patients are able to follow commands as tested with the active P300 VT3 paradigm, according to the study by Guger et al[14].. This study also showed that a single session is not sufficient to assess command following in MCS since these patients have large fluctuations. By comparing the grand average accuracy of 49% in the first run with the grand average accuracy of 80% in the best run, the importance of repeated measurements are highlighted. This difference could be attributed to many factors in MCS patients, like motor or language impairments and vigilance fluctuations[15]. The best run is even in the range of healthy controls (N=6) who achieved 83 % classification accuracy after one VT3 run [16]. This highlights the importance of repeated testing of DOC patients to show command following [14]. It also shows that MCS patients can reach results similar to healthy controls.

An improvement in the CRS-R score was observed in 4 out of 7 MCS patients. In 3 patients the score improved for 2 points, in 1 patient it improved 7 points. We do not currently claim that the improvement was caused by the VT3 paradigm and that there is a causal link between the CRS-R scores and vibrotactile results. Although this should be investigated in future studies. In the past, studies indicated large-scale cerebral networks exist in MCS patients [17], [18]. These findings indicate that there might be residual functional capacity in some patients that could be supported by therapeutic interventions. Schiff et al. also showed activity in the postcentral gyrus during bilateral tactile stimulation of the hands[18]. A prior work reported that the repetition of behavioural assessments in DOC can influence the clinical diagnosis [19].

Following limitations of this study are listed. Firstly, the sample size of 7 MCS patients is too small. For the future, the effect on the CRS-R score will be investigated on more patients and compared to a control group. Secondly, CRS-R score that was used to measure the changes, was assessed only once on the day before and after the VT3 paradigm. Wannez et al. showed in a study that ingle CRS-R score evaluations are not reliable in about 35% of the patients [19], which may reflect fluctuations in conscious awareness and/or arousal that would also increase BCI performance variability. In the future repeated CRS-R score measurements will be done before and after the experiment to minimize the chance of fluctuations in the level of consciousness.

CONCLUSION

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A tactile P300 BCI was performed on 7 MCS patients over ten consecutive days, showing significant changes in the CRS-R. 4 patients showed high classification accuracy and therefore are potential to use a BCI for communication. In the future the possible recovery effects of vibro-tactile P300 BCI paradigms will be further explored.

CONFLICT OF INTEREST

The authors AH, NM, RX, RO and CG belong to g.tec medical engineering GmbH. The other authors declare no conflict of interest.

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NM, AH and YM recorded the data. RX, JJ, RO, FC, KM and CG contributed to study design, scientific protocols, and review/analysis of results. AH reviewed results and was primarily responsible for writing, and all authors discussed the results and implications. This research was supported by the EC SME Phase 2 project ComaWare, the Eurostars project ComAlert (Grant number E19361) and and the Marie Skłodowska-Curie grant DoCMA (agreement No 778234).

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