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A vibrotactile P300-based BCI for consciousness detection and communication

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Abstract

Brain–computer interface (BCI) has been used for many years for communication in severely disabled patients. BCI based on electrophysiological signals has enabled communication, using auditory or visual stimuli to elicit event-related potentials (ERPs). The aim of this study was to determine whether patients with locked-in syndrome (LIS) could elicit a P300 wave, using a vibrotactile oddball paradigm for establishing somatosensory BCI-based communication. Six chronic LIS patients performed 2electroencephalography (EEG)-based vibrotactile P300 oddball tasks. After a simple mental counting task of the target stimuli, participants were instructed to answer 5 questions by counting the vibration on either the right wrist for “yes” or the left wrist for “no.” All participants were able to elicit a P300 wave using the vibrotactile oddball paradigm BCI task. In the counting task, 4 patients got accuracies of 100% (average above chance). In the communication task, one patient achieved 100% accuracy (average above chance). We have shown the feasibility of eliciting a P300 response using vibrotactile stimulation in patients with LIS. The present study provides evidence that this approach can be used for EEG-based BCI communications in this patient group. This is the first study to prove the feasibility of a BCI based on somatosensory (vibratory) stimulation in a group of braininjured patients. Furthermore, this approach could be used for the detection of consciousness in non-communicating patients due to severe brain injuries**.**

Key words. Brain Computer Interface. P300. Event-related potentials. Locked-in syndrome.

1. Introduction.

Brain computer interfaces (BCI) are being increasingly used and have successfully grown in very specific areas of neurology such as for the detection of consciousness in severely brain injured patients (for a review see Chatelle et al.[1] and Naci et al.[2]). This is in part due to the continuous improvement in the developed techniques and tests. BCIs have also been used to establish communication with conscious patients who have severe motor and language deficits due to brain lesions, which prevent them to use the motor system for expression [3].

A BCI is a system permitting communication between the brain and external environment, independent of any nerve or muscle, directly converting brain activity into a command signal for electronic devices [4]. It is based on cerebral activity measured by means of electrophysiological or neuroimaging techniques (electroencephalography – EEG, functional magnetic resonance imagery– fMRI, implanted electrodes, and functional near-infrared spectroscopy – fNIRS) in order to enable communication and control the environment. From these BCI techniques, electroencephalography offers the advantages of being easily accessible, transportable and low cost, beside a high temporal resolution which allows a communication in real time. Through the recording of evoked-related potentials (ERPs), it has been possible to establish the usefulness of some specific evoked responses both for diagnostic purposes and for communication[5-7].

The differentiation between altered states of consciousness as the vegetative state/unresponsive wakefulness syndrome (VS/UWS) and the minimally conscious state (MCS) remains a challenging task. In the VS/UWS, patients show preserved vegetative

nervous functioning (including sleep/awake cycles), but they do not show any voluntary response to commands nor verbalization [8, 9]. In the MCS, patients show

inconsistent but reproducible voluntary behaviors, indicating the persistence of some residual cognitive functions and therefore, consciousness [10]. A previous study has shown a rate of 40% error in the differentiation between VS/UWS and MCS [11].

Still more challenging is the differentiation of these states with a particular neurological condition in which, following a ventral pontine injury, the patient remains fully conscious but unable of move or speak. This condition is the locked-in syndrome (LIS), a term introduced by Posner to describe a clinical condition of quadriplegia and anarthria associated with ventral pons infarction[12]. The American Congress of Rehabilitation Medicine has defined the syndrome by: i) the presence of sustained eye opening, ii) preservation of cognitive skills, iii) severe hoarseness or hypophonia iv) quadriplegia or quadriparesis, v) a primary mode of communication using vertical or horizontal eyes movements or blinking [13]. Through the use of ERPs, the feasibility of performing a differential diagnosis between a VS/UWS and a complete LIS has been already been demonstrated[14].

P300 evoked potentials are the best studied ERPs (for a review see [15]. The P300, first described by Sutton [16] is a deflection in the EEG that occurs 200–700 ms after stimulus onset and is typically recorded over central-parietal scalp locations [17]. The response is evoked by attention to rare or surprising, task-relevant stimuli in a random series of stimulus events, by mean of a simple discrimination task.

One of the advantages of using this ERP component for BCI-systems, is not only the relative simplicity of the paradigms used to evoke this response, but also the possibility of using different sensory modalities (auditory, visual and somatosensory) to elicit it. In patients with brain injuries, it is important to have different ways to assess brain function due to the heterogeneity of the lesions and the consecutive deficits. In a cohort

of LIS patients, two thirds of them presented visual disturbances and almost a third had hearing impairments resulting from the injury (Lugo et al. in preparation).

To date, several studies have been conducted with auditory and visual modalities for a P300 based-BCI in disabled patients[17-19]. But so far, very few studies have been conducted on healthy subjects [20] -and to the best of our knowledge- none on patients having used the somatosensory modality for a BCI.

In this paper we present the results of a somatosensory P300-based BCI tested on LIS patients. The first objective of this study was to establish the feasibility of eliciting a P300 wave using a vibrotactile oddball paradigm in patients with LIS. The second objective was to use this paradigm for establishing communication with them.

2. Materials and methods

2.1 Subjects:

Six chronics (> 1 year since the diagnosis) LIS patients members of the French Association for the Locked-in Syndrome (ALIS) were evaluated (clinical data are shown in table 1). Four patients were evaluated at the Institutions where they live and two were evaluated at their homes. Only one subject (number 1) was naïf for BCI tests. Signed consent was obtained from all participants or their legal representatives. The study was approved by the Ethics Committee of the University of Liege and the Scientific Committee of ALIS.

2.2 ERP acquisition

The experiment was conducted in two parts. In the first, we tested the method to elicit a P300 response using vibrotactile stimulation in LIS patients according to the protocol already validated on healthy subjects by Ortner et al. (in preparation). In a second phase, we tried to establish a code of communication with the LIS patients using the obtained P300 vibrotactile response.

Experiment for eliciting the P300 wave. In this experiment two stimulators were used to produce non-target and target stimuli. The stimulators were placed on the wrist of each hand (except in the patient number 4 who has a loss of sensibility on the right hemibody, chest and left leg, therefore, the stimulator with the target was placed on the left wrist and the stimulator with the standard stimuli was placed on the neck). Both stimulators alternately produce a stream of short vibration pulses (duration 110ms, pause between two pulses: 40msec). An oddball paradigm was designed with 90% of pulses output from one of the stimulators (standard stimuli, left wrist) and 10% from the

other stimulator (target, right wrist). The sequence of stimuli on left and right wrist was random. Stimuli were delivered using a device consisting of an mechanical vibrator (g.VIBROstim; g.tec medical engineering GmbH, Austria) in a plastic sheath that ensures the sealing of the internal components. The contactors are powered by a g.STIMbox (g.tec medical engineering GmbH, Austria) that translates the order from the paradigm into voltage outputs that controls the vibrators (figure 1). The participants were asked to mentally focus and (if possible) to perform a mental count of the target stimuli on the right wrist. Five trials were performed for training a subject specific classifier with a linear discriminant analysis (LDA). Finally five trials with feedback were performed. During each trial 300 stimuli were delivered: 270 non-targets and 30 targets. One single trial lasted 45 seconds.

Experiment for testing communication. For this purpose three stimulators were used: one placed on the neck (acting as a distractor) and the others on each wrist (in the patient with loss of sensibility, the distractor was placed on the left scapula). The classifier was established on five training trials (300 stimuli by trial: 270 non-target and 30 target) where subjects were asked to concentrate on the right (R) or left (L) wrist (sequence: L, L, R, L, R). After this, five yes/no questions (with known answers by the examiner) were asked (sequence: yes, no, yes, yes, no) and the patient was instructed to count the vibration on the right wrist if the answer was “yes” and to count the vibration on the left wrist if the answer was “no”.

EEG recording: EEG was recorded using eight g.LADYbird electrodes mounted in a cap (g.GAMMAsys, g.tec medical engineering GmbH, Austria) following the international 10-20 electrode system at the positions Fz, FC1, FC2, C3, CZ, C4, CP1,

CP2. The reference electrode was at the left ear lobe and the ground electrode was placed at the AFz position.

2.3. Data analysis

Classification procedure

The experiment was conducted with a rapid prototyping platform (g.BCIsys, g.tec medical engineering GmbH, Austria) that acquires data, performs feature estimation and classification in real-time, controls the experimental paradigm and stores and visualizes the data. The data was sampled by the biosignal amplifier g.USBamp (g.tec medical engineering GmbH, Austria) with 256Hz with 24Bit and bandpass-filtered between 0.1Hz and 30Hz. The single trials for training and applying the LDA had a length of 700ms after stimulus onset and 100ms before. For each trial a baseline correction using the data 100ms before the stimulus onset was applied. Following that, the trials were separated according to their classes (e.g. neck, left hand, right hand). For each EEG channels every 12 samples were averaged resulting in 15 new sample points for the period of 700ms. Hence, 15 new samples x 8 channels = 120 features were feed into the LDA. After training the classifier with the data of the first run (five trials) a subject specific classifier was applied to the following five trials. The classifier selected the class having the highest sum of weighted parameters and presented then the class on the computer screen.

Statistical analysis

To establish the presence of a P300 wave, an ANOVA was done using the accepted target trials (kept targets trials after artefact rejection). The threshold for statistical significance was set at $p<0.05$. This analysis was performed over two groups of population, one for target trials and another for non-target trials. As the ANOVA test compares two populations with the same number of members, the bigger group, formed

by the non-target trials, was cut into subgroups of randomized trials, each one merged. At the end we got two groups with the same number of trials, one for the targets, one for the non-targets, free of artefacts. The ANOVA test was performed with a moving window of 13 samples (50ms) of both populations. Doing it, it was possible to get a significance value over time for the comparison of both populations. A P300 wave was accepted if a significant difference target / non-target was detected in at least two electrodes between 200 and 600 ms after the stimuli.

3. Results.

P300 response

According to the established criteria, it was possible to elicit a P300 wave in 5 out of 6 patients using the vibrotactile odd ball paradigm with two stimulators and in all the patients using three stimulators. Nevertheless, none of the patients showed the P3 wave in all four conditions (two contactors training, two contactors feedback, three contactors training and three contactors feedback). Also, differences in scalp topography and peaks of latency were found among the patients (table 2 shows electrodes location of the P3 wave for each patient in all the conditions and figures 2 and 3 show morphology and latency in the most representative locations only for the feedback runs). In patient number one with two stimulators, there was no evident P300 wave, but it was clearly present during the test with three stimulators. Patient number two showed a P300 in both conditions (two and three stimulators feedback) at about the same latency. Patient number three showed a P300 wave also in both conditions but, latency was shorter for the three contactors condition. Patient number four had a very early P300 component with a big area at the two contactors stimulation, which decreased significantly but was still present very early (at about 200 ms) at the three contactors condition. In patient number five, a very late P300 (at about 500 ms) was evident in both conditions, slightly later with three stimulators. Finally, in patient number 6, there was no significant P300 in the two stimulators feedback condition (this run was very noise as can be appreciated in figure 2) but it was possible to identify a significant difference during the feedback with three stimulators at about 200 ms.

Accuracies and communication test

In the test with two contactors, 4 out of 6 patients got accuracies of 100% (average 80%) and the number of stimuli needed to achieve this accuracy was between 7 and 20.

In the communication test, the grand average accuracy was 55.3%, and the number of stimuli was between 3 and 7. This does not mean that subjects needed fewer repetitions with three stimulators, it just means that the best performance was reached with less flashes (which was mostly not 100%). Table 3 shows the percentages of accuracies and the number of stimuli needed for each patient for each condition. Figure 4 shows the plots of the accuracies for patient 1 and patient 6. Patient number 1 reached his best performance (60%) with 4 flashes and did not improve with more flashes. But for example patient number 6 reached 100% of accuracy at only 7 flashes.

4. Discussion.

In the present paper, we established the feasibility of using a somatosensory (vibratory) stimulation to elicit a P300 wave in patients with cerebral injuries. This result is particularly important in the context of the evaluation of non-communicative patients, since it can be used as a diagnostic tool for differentiating patients with altered states of consciousness (VS/UWS) from those who are conscious but unable to speak or move due to their brain lesion (e.g. the LIS patients). The addition of the sensory modality for the evaluation of non communicative patients due to severe brain injuries helps to overcome the possible hearing and/or visual impairment, frequently found in LIS patients [21, 22]. In our sample, 5 out of 6 patients (83%) had a visual impairment due to the brain lesion.

The study also showed successfully that BCI technology can be used to identify if a patient is able to elicit a somatosenory P300 response. The BCI system gives an accuracy level that allows easily to identify if the target and non-target stimuli can be discriminated. If only the ERP waveform is investigated it is often difficult to see if the patient is following the task. Furthermore the BCI system also tells how many stimuli are required for reaching the highest classification accuracy and this is a very important predictor for the quality of the P300 response. If the P300 response is high then high classification accuracy will be reached after a few stimuli. If the P300 response is weak then more repetitions are needed. Also if the patients get tired the accuracy might drop down and this is a good indicator of how long the patient can use the system. This information can also be used to optimize other ERP experiments.

However, assessing the presence of an ERP in non-communicative patients is a difficult task. Generally, there are five criteria to evaluate an ERP component: polarity, latency,

duration, morphology, and topography, but these criteria must be critically revised in patients with severe neurological lesions, because the morphology, topography and latency can vary from normal subjects [23]. In our study we relied on the polarity, latency and topography to determine the presence of the P300 waveform. As shown in figures 2 and 3, P300 morphology and latency were highly variable among subjects. With respect to the morphology, it may vary not only in individual patients when compared to group studies [23], but also there could be a distortion caused by averaging: to the extent that the single trial wave-forms varies from trial to trial, the averaged ERP may provide a distorted view of the single-trial waveforms [24]. The automatic classification proposed in this paper circumvents the problem of the evaluation of the ERP.

P300 latency is thought to index brain classification speed, which is proportional to the time required to detect and evaluate a target stimulus [25]. In our sample, there is a high inter-subject variation of latency but always within the range of 200-500ms. In this regard, we note that the presence of a P300 with a longer latency relative to normal has been described in a LIS patient during the execution of an auditory paradigm[14]. Also physiological factors as body temperature, heart rate, fatigue and the intake of drugs, caffeine or alcohol, can affect the latency of the ERPs [26]

It must also be stressed that, the paradigm used to elicit the P300 wave in this study, was an active one since the beginning of the tests (the patients were asked to count the deviant stimuli since the first run). This can explains the presence of the waveform in most patients. It has already been shown that an active paradigm could evoke an ERP of bigger amplitude than a passive one in LIS patients[14].

The topography of the P300 wave, was detectable at the midline electrodes (Cz) in five out of six patients. This location has already been described as sufficient to show the

presence of the P300 in the auditory and visual modalities [26]. Nevertheless, in the previous pilot study with healthy subjects using identical stimulation, the best electrode set to check the P300 accuracy was Fz, FC1, FC2, C3, C4, CP1, CP2. (Ortner et al. in preparation). Although the neural generators of P300 are imprecisely delineated, several studies suggest that P3a and P3b generation stems from frontal and temporal/parietal activations [25]. In the case of LIS patients, lesions are mainly limited to the brainstem so, it is reasonable to expect a scalp distribution similar to healthy subjects.

In the communication tests, the accuracy percentages were not as satisfactory as in healthy controls. This seems difficult to explain in the context that, LIS patients, keep intact or almost intact cognitive abilities. Also in our sample, all the patients had a good education level (two of them at College level and the others a high school level) previous to the accident. Nevertheless, in LIS patients, a moderate and selective cognitive impairment that is not related to the location of the lesion has been shown[27]. Schnakers at al. also found in a cohort of 10 LIS patients, some impairment mainly in those patients with additional thalamic or cortical lesions[28]. Therefore, there could be some degree of a mild impairment in these patients, affecting the execution of the tasks. This points to that, even if fully conscious and with lesions mainly limited to the motor pathways (in our sample only patient 6 has lesions in other cerebral regions out of the brainstem, specifically the thalamus and the cerebellum), cognitive responses in LIS patients may not be completely alike those of healthy subjects as it could be expected.

However, a possible cognitive impairment present in some of the patients does not explain completely the low percentages of accuracy. Another reason for the poorer performance is the limited training time with the experimental setup. In previous tests

with healthy controls it was shown that classification accuracy improves to 100% after several repetitions of the tasks. The number of required repetitions is subject dependent. Some subjects are able to reach perfect classification accuracy after 1 run with 5 trials, others need more. Important is also to have good training data for the calculation of the classifier for the next real-time session. If the patient is not attending during some of the trials then the BCI system is mistrained and this limits the accuracy. Therefore, it is crucial to have very short training runs to keep the motivation of the patient during the experiment. The vibrotactile BCI with the P300 is very well suited for that because the training can be done quickly. This was also shown in a spelling system realized with a visual P300 paradigm that needs only 5 minutes of training to reach a grand average accuracy of 91% for 81 subjects [29].

A longer communication test could also improve the ratio of right/wrong answers and could be more suitable for patients, because the test was done following the protocol used on healthy controls in which the mean accuracy was 80% and assuming that LIS patients could have a similar response rate. As we have mentioned, this seems not necessarily true in view of the presence of cognitive differences in patients. A pre-training session could also significantly improve performances. In this regard it is interesting to note that the patient in our sample with better response rate (100%) had an involuntary training session (besides the initial training provided in the test). One of the contactors had fallen during the test of questions and it was necessary to repeat it completely. Additionally, this patient was given an additional track (the examiner's hand touched the arm where the patient had to count the stimuli) because the family reported that the patient had a slight confusion right / left (i.e., that it was difficult for the patient to locate where was that the right and where the left).

There were several limitations to this study. The main one was the size of the sample. A larger sample of LIS patients must be tested in order to validate these results and to establish some pattern regarding topography, amplitude and latency of the P300 wave in these patients. Another limitation was the lack of time to perform more training, this was because these patients have quite lengthy care routines (including those that were assessed in their homes) thus restricting the time for tests to a couple of hours. So it would be necessary to foresee at least two separate sessions in the next patients to be evaluated. Also, several runs should be done on different days to quantify the training effect and the fluctuations. Finally, despite excellent disposition and motivation of the patients, most of them showed signs of fatigue at the end of the session (the total duration of the session, including the placement of the electrodes was about 90 minutes).

In conclusion, we have shown the feasibility of eliciting a P300 response using vibrotactile stimulation in patients with brain injuries. The importance of this finding has to do in first place, with the possibility of using this type of evoked responses in the detection of consciousness in non communicating patients due to severe brain injuries. In the future, we will include patients in MCS and VS/UWS to study the presence/absence of a vibrotactile P300 which could be eventually used in a diagnostic battery. The proposed approach could be used as a communication tool in conscious patients but with severe motor and language disabilities (as LIS patients or patients with amyotrophic lateral sclerosis). This approach adds another sensory pathway for communication -besides the classic auditory and visual -, allowing better adaptation to individual patient deficits.

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Conflicts of interest

The authors declare no conflict of interest.

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Table 1. Clinical characteristics of the patients

Patient	Sex	Age	Time in LIS (years)	Etiology	Current Deficit	Auditory/visual impairment
1	F	47	4	Stroke (ischemic)	Quadriplegia, anarthria	Non
2	F	21	4	Stroke (ischemic)	Quadriplegia, anarthria	Decreased right visual field
3	M	46	16	Stroke (ischemic)	Quadriplegia, anarthria, lack of thermal sensitivity	Left ophthalmoplegia
4	M	33	12	Stroke (haemorrhagic)	Quadriplegia, anarthria lack of sensitivity at right hemibody, left leg and chest	Right hypoacusis, nystagmus, gaze paralysis (towards the left side)
5	F	48	5	Stroke (haemorrhagic)	Quadriplegia, anarthria	Gaze paralysis towards the left side, nystagmus
6	F	46	19	Stroke (ischemic)	Quadriplegia, anarthria, confusion right/left	Decreased visual field

Table 2. P300 wave electrodes location

	Two contactors (training)	Two contactors (feedback)	Three contactors (training)	Three contactors (feedback)
Patient 1	Fz, Cz	-	-	FC1,Fz, C3, Cz,C4, CP2
Patient 2	FC1, Cz, CP1, CP2	C3,Cz	FC2 C3, Cz, C4, CP1, CP2	C4 CP1, CP2
Patient 3	-	Fz, FC2, Cz, CP1, CP2	Fz, Cz, C4	FC1, Fz, C3, Cz, C4, CP1, CP2
Patient 4	FC1, FC2, C3,Cz,C4, CP1,CP2	FC1, C3, Cz, C4, CP1, CP2	CP1, CP2	Cz, CP1, CP2
Patient 5	FC2, Cz, C4, CP2	FC1, FC2, C3, Cz, C4, CP2	Fz, FC2, Cz, C4, CP1,CP2	FC2, CP2
Patient 6	C3, CP2	-	-	FC2, Cz, C4, CP2

Table 3. Percentages of accuracies and number of stimuli needed

	2 contactors		3 contactors	
	Accuracy (%)	**N° stimuli**	**Accuracy (%)**	**N° stimuli**
Patient 1	**100**	**12**	**60**	**4**
Patient 2	**20**	**2**	**20**	**4**
Patient 3	**100**	**20**	**40**	**3**
Patient 4	**100**	**20**	**60**	**7**
Patient 5	**60**	**2**	**40**	**4**
Patient 6	**100**	**7**	**100**	**7**
Average	**80**	**10.5**	**55.3**	**4.8**
STD	**33.5**	**8.2**	**27.3**	**1.7**

Figure 1. Prototype of the vibrotactile device

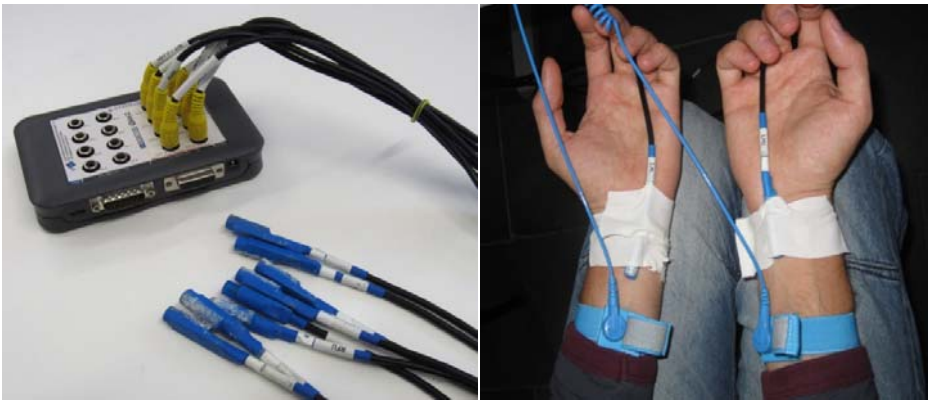

Figure 2. P300 wave with two stimulators for all patients in the feedback session. The green and blue area indicates a statistical difference ($p<0.05$, green: positive wave, blue: negative wave). On the right side the percentage of artifact free trials for target and non/target trials as well as artifact trials can be seen (1 equals 100%). The red line at zero indicates the start of the stimuli.

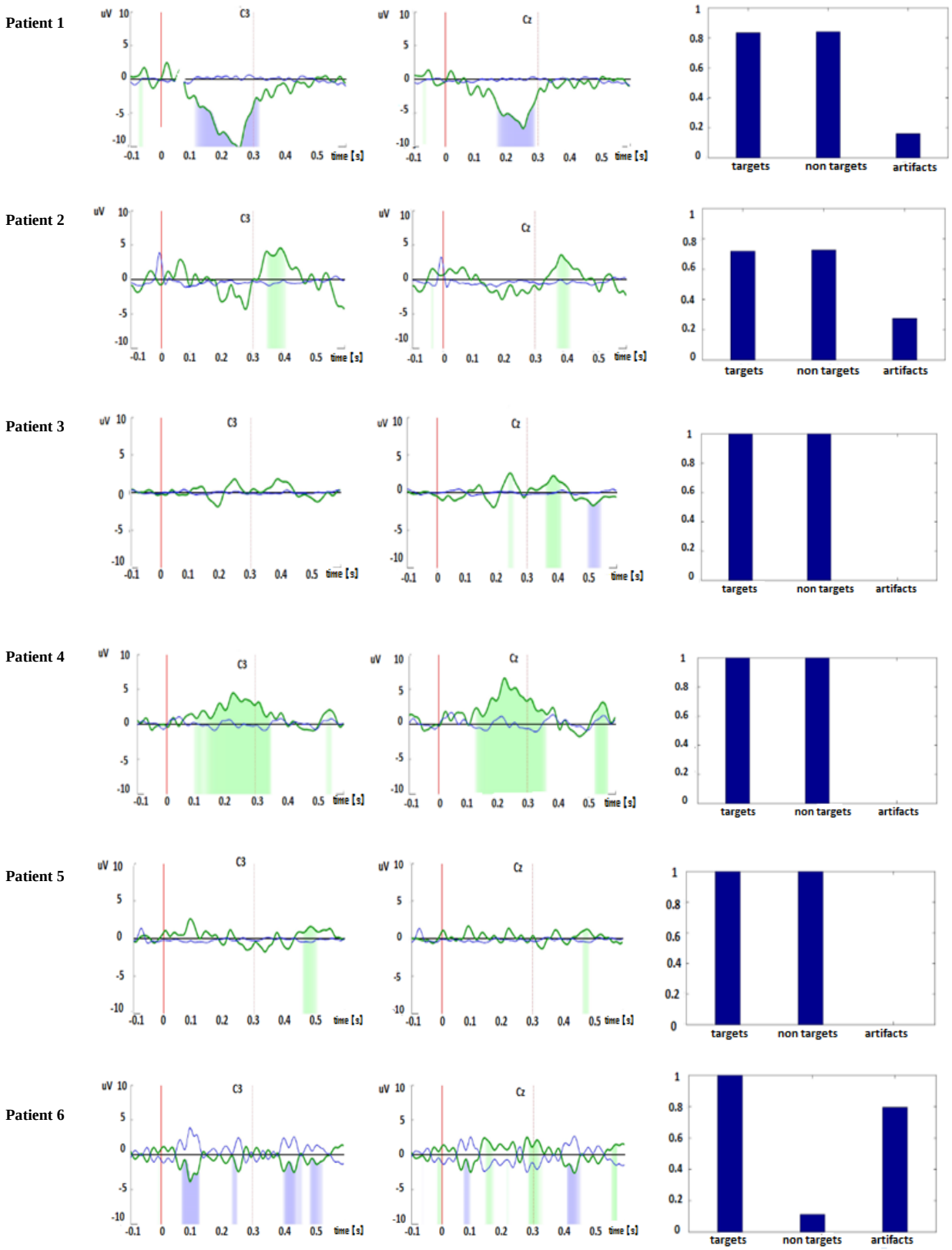

Figure 3. P300 wave with three stimulators for all patients in the feedback session.

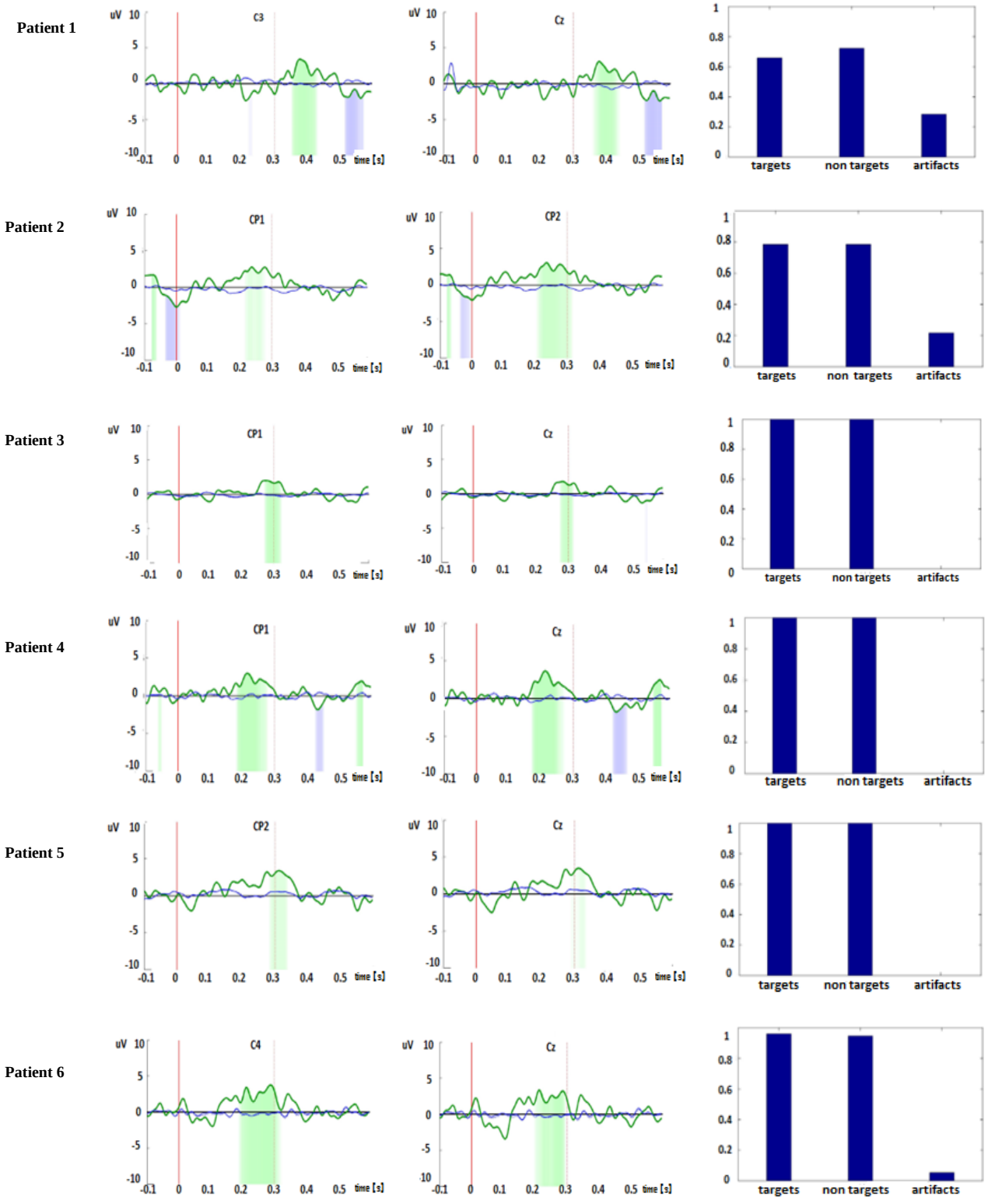

Figure 4. Percentage of accuracy in the communication test