A Vibrotactile P300-Based Brain–Computer Interface 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 2 electroencephalography (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 brain-injured patients. Furthermore, this approach could be used for the detection of consciousness in non-communicating patients due to severe brain injuries.

Keywords
Brain–computer interface, P300, event-related potentials, locked-in syndrome

Introduction
BCIs 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 al¹ and Naci et al²). This is in part due to the continuous improvement in 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 using 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 (EEG, functional magnetic resonance imaging [fMRI], implanted electrodes, and functional near-infrared spectroscopy [fNIRS]) to enable communication and control the environment. Of these BCI techniques, EEG offers the advantages of being easily accessible, transportable, low cost, and a high temporal resolution, which allows communication in real time. Through the recording of eventERPs, it has been possible to establish the usefulness of specific evoked responses for diagnosis and communication.⁵ ⁷

The differentiation between altered states of consciousness, such as the vegetative state/unresponsive wakefulness syndrome (VS/UWS) and the minimally conscious state (MCS), remains a challenging task. VS/UWS patients show preserved vegetative nervous functioning (including sleep/awake cycles), but not any voluntary response to commands or verbalization.⁸ ⁹ MCS patients show inconsistent but reproducible voluntary behaviors, indicating the persistence of some residual cognitive functions and, therefore, consciousness.¹⁰ A previous study showed 40% error in differentiating between VS/UWS and MCS.¹¹

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Full-color figures are available online at http://eeg.sagepub.com
Table 1. Clinical Characteristics of the Patients.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Gender</th>
<th>Age (Years)</th>
<th>Time in Locked-in Syndrome (Years)</th>
<th>Etiology</th>
<th>Current Deficit</th>
<th>Auditory/Visual Impairment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Female</td>
<td>47</td>
<td>4</td>
<td>Stroke (ischemic)</td>
<td>Quadriplegia, anarthria</td>
<td>None</td>
</tr>
<tr>
<td>2</td>
<td>Female</td>
<td>21</td>
<td>4</td>
<td>Stroke (ischemic)</td>
<td>Quadriplegia, anarthria</td>
<td>Decreased right visual field</td>
</tr>
<tr>
<td>3</td>
<td>Male</td>
<td>46</td>
<td>16</td>
<td>Stroke (ischemic)</td>
<td>Quadriplegia, anarthria, lack of thermal sensitivity</td>
<td>Left ophthalmoplegia</td>
</tr>
<tr>
<td>4</td>
<td>Male</td>
<td>33</td>
<td>12</td>
<td>Stroke (hemorrhagic)</td>
<td>Quadriplegia, anarthria lack of sensitivity at right hemibody, left leg and chest</td>
<td>Right hypoacusis, nystagmus, gaze paralysis (toward the left side)</td>
</tr>
<tr>
<td>5</td>
<td>Female</td>
<td>48</td>
<td>5</td>
<td>Stroke (hemorrhagic)</td>
<td>Quadriplegia, anarthria</td>
<td>Gaze paralysis toward the left side, nystagmus</td>
</tr>
<tr>
<td>6</td>
<td>Female</td>
<td>46</td>
<td>19</td>
<td>Stroke (ischemic)</td>
<td>Quadriplegia, anarthria, confusion right/left</td>
<td>Decreased visual field</td>
</tr>
</tbody>
</table>

More challenging is the differentiation of these states in a neurological condition following a ventral pontine injury, in which the patient remains fully conscious but unable to move or speak. This condition is LIS, a term introduced by Posner to describe a clinical condition of quadriplegia and anarthria associated with ventral pons infarction. The American Congress of Rehabilitation Medicine has defined the syndrome by (a) the presence of sustained eye opening, (b) preservation of cognitive skills, (c) severe hoarseness or hypophonia, (d) quadriplegia or quadriaparesis, and (e) a primary mode of communication using vertical or horizontal eye movements or blinking. Through the use of ERPs, the feasibility of performing a differential diagnosis between a VS/UWS and a complete LIS has been demonstrated.

P300 evoked potentials are the best studied ERPs (for a review, see Fazel-Rezai et al.). The P300, first described by Sutton et al., is a deflection in the EEG that occurs 200 to 700 ms after stimulus onset and is typically recorded over central–parietal scalp locations. The response is evoked by attention to rare or surprising, task-relevant stimuli in a random series of stimulus events, by means 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. unpublished data).

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

Materials and Methods

Subjects

Six chronic (>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 2 were evaluated at their homes. Only 1 subject (number 1) was naïve 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.

Event-Related Potential Acquisition

The experiment was conducted in 2 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. (unpublished data). 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, 2 stimulators were used to produce non-target (standard) and target stimuli. The stimulators were placed on each wrist (except in 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 110 ms, pause between 2 pulses = 40 ms). 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 wrists was random. Stimuli were delivered using a mechanical vibrator (g.VIBROstim; g.tec Medical Engineering GmbH, Schiedlberg, Austria) in a plastic sheath that ensures...
the sealing of the internal components. The contactors were powered by a g.STIMbox (g.tec Medical Engineering GmbH, Schiedlberg, Austria) that translates the order from the paradigm into voltage outputs that control 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, 5 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, 3 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 5 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, 5 yes/no questions (with known answers by the examiner) were asked (sequence: yes, no, yes, no, yes) 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 8 g.LADYbird electrodes mounted in a cap (g.GAMMAsys, g.tec Medical Engineering GmbH, Schiedlberg, Austria) following the International 10-20 Electrode System at the positions Fz, FC1, FC2, C3, CZ, C4, CP1, and CP2. The reference electrode was at the left ear lobe and the ground electrode was placed at the AFz position.

**Data Analysis**

**Classification Procedure.** The experiment was conducted with a rapid prototyping platform (g.BCIsys, g.tec medical engineering GmbH, Schiedlberg, Austria) that acquires data, performs feature estimation and classification in real time, controls the experimental paradigm and stores and visualizes the data. The data were sampled by the biosignal amplifier g.USBamp (g.tec medical engineering GmbH, Schiedlberg, Austria) with 256 Hz with 24 Bit and bandpass-filtered between 0.1 Hz and 30 Hz. The single trials for training and applying the LDA had a length of 700 ms after stimulus onset and 100 ms before. For each trial a baseline correction using the data 100 ms before the stimulus onset was applied. Following that, the trials were separated according to their classes (eg, neck, left hand, right hand). For each EEG channel every 12 samples were averaged resulting in 15 new sample points for the period of 700 ms. Hence, 15 new samples × 8 channels = 120 features were feed into the LDA. After training the classifier with the data of the first run (5 trials), a subject specific classifier was applied to the following 5 trials. The classifier selected the class having the highest sum of weighted parameters and then presented the class on the computer screen.

**Statistical Analysis.** To establish the presence of a P300 wave, an analysis of variance (ANOVA) was done using the accepted target trials (kept targets trials after artifact rejection). The threshold for statistical significance was set at $P < .05$. This analysis was performed over 2 groups, one for target trials and another for non-target. As the ANOVA test compares 2 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 2 groups with the same number of trials, one for targets and one for non-targets, free of artifacts. The ANOVA test was performed with a moving window of 13 samples (50 ms) of both populations. 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 2 electrodes between 200 and 600 ms after the stimuli.

**Results**

**P300 Response**

According to established criteria, it was possible to elicit a P300 wave in 5 out of 6 patients using the vibrotactile oddball paradigm with 2 stimulators, and in all the patients using 3 stimulators. Nevertheless, none of the patients showed the P3 wave in all 4 conditions (2 contactors training, 2 contactors feedback, 3 contactors training, and 3 contactors feedback). Also, differences in scalp topography and peaks of latency were found among the patients. Table 2 shows electrode locations of the P3 wave for each patient in all conditions, and Figures 2 and 3 show morphology and latency in the most representative locations only for the feedback runs. In patient number 1 with 2 stimulators, there was no evident P300 wave, but it was clearly present with 3 stimulators. Patient number 2 showed a P300 in both conditions (2 and 3 stimulators feedback) at about the same latency. Patient number 3 showed a P300 wave also in both conditions, but latency was shorter for the 3 contactors. Patient number 4 had a very early P300 component with a big area under 2 contactors stimulation, which decreased significantly but was still present very early (at about 200 ms) under 3 contactors. In patient number 5, a very late P300 (at about 500 ms) was evident in both conditions, slightly later with 3 stimulators. Finally, in patient number 6, there was no significant P300 in the 2 stimulator feedback (this run was very noisy as can be appreciated in Figure 2), but it was
Table 2. P300 Wave Electrodes Location.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Two Contactors (Training)</th>
<th>Two Contactors (Feedback)</th>
<th>Three Contactors (Training)</th>
<th>Three Contactors (Feedback)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient 1</td>
<td>Fz, Cz</td>
<td>—</td>
<td>FC1, Fz, C3, Cz, C4, CP1, CP2</td>
<td>FC1, Fz, C3, Cz, C4, CP1, CP2</td>
</tr>
<tr>
<td>Patient 2</td>
<td>FC1, Cz, CP1, CP2</td>
<td>Fz, FC2, Cz, CP1, CP2</td>
<td>C3, Cz</td>
<td>—</td>
</tr>
<tr>
<td>Patient 3</td>
<td>—</td>
<td>Fz, FC2, Cz, CP1, CP2</td>
<td>FC1, C3, Cz, C4, CP1, CP2</td>
<td>C4, CP1, CP2</td>
</tr>
<tr>
<td>Patient 4</td>
<td>FC1, FC2, C3, C4, CP1, CP2</td>
<td>C3, Cz</td>
<td>FC1, C3, Cz, C4, CP1, CP2</td>
<td>C4, CP1, CP2</td>
</tr>
<tr>
<td>Patient 5</td>
<td>FC2, Cz, C4, CP2</td>
<td>Fz, FC2, Cz, C4, CP1, CP2</td>
<td>—</td>
<td>FC2, Cz, C4, CP2</td>
</tr>
<tr>
<td>Patient 6</td>
<td>C3, CP2</td>
<td>—</td>
<td>FC1, Fz, C3, Cz, C4, CP1, CP2</td>
<td>—</td>
</tr>
</tbody>
</table>

Figure 2. P300 wave with 2 stimulators for all patients in the feedback session. The green and blue areas indicate a statistical difference (P < .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.

Accuracies and Communication Test

In the test with 2 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 3 stimulators; it just means that the best performance was reached with fewer flashes (which was mostly not 100%). Table 3 shows the percentage accuracy, and the number of stimuli needed for each patient for each condition. Figure 4 shows the plots of accuracies for patients 1 and 6. Patient number 1 reached his best performance (60%) with 4 flashes and did not improve with more flashes. But patient number 6 reached 100% of accuracy at only 7 flashes.
Discussion

In the present article, 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 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 overcome the possible hearing and/or visual impairment, frequently found in LIS patients. 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 identify whether a patient is able to elicit a somatosensory P300 response. The BCI system's accuracy makes it easy to determine if the target and non-target stimuli can be discriminated. If only the ERP waveform is investigated, it is often difficult to see whether 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, 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 difficult. Generally, there are 5 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 morphology, topography and latency can vary from normal subjects. 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 with group studies, but there could also be a distortion...

Figure 3. P300 wave with 3 stimulators for all patients in the feedback session.
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Figure 4. Percentage of accuracy in the communication test for patient 1 (upper plot) and patient 6 (lower plot).

Table 3. Percentages of Accuracies and Number of Stimuli Needed.

<table>
<thead>
<tr>
<th></th>
<th>Two Contactors</th>
<th>Three Contactors</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Accuracy (%)</td>
<td>No. of Stimuli</td>
</tr>
<tr>
<td>Patient 1</td>
<td>100</td>
<td>12</td>
</tr>
<tr>
<td>Patient 2</td>
<td>20</td>
<td>2</td>
</tr>
<tr>
<td>Patient 3</td>
<td>100</td>
<td>20</td>
</tr>
<tr>
<td>Patient 4</td>
<td>100</td>
<td>20</td>
</tr>
<tr>
<td>Patient 5</td>
<td>60</td>
<td>2</td>
</tr>
<tr>
<td>Patient 6</td>
<td>100</td>
<td>7</td>
</tr>
<tr>
<td>Average</td>
<td>80</td>
<td>10.5</td>
</tr>
<tr>
<td>Standard deviation</td>
<td>33.5</td>
<td>8.2</td>
</tr>
</tbody>
</table>

caused by averaging: to the extent that the single trial waveforms vary from trial to trial, the averaged ERP may provide a distorted view of the single-trial waveforms. The automatic classification proposed in this article circumvents the problem of the evaluation of the ERP.

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

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 explain the presence of the waveform in most patients. It has already been shown that an active paradigm evokes an ERP of bigger amplitude than a passive one in LIS patients.

The topography of the P300 wave was detectable at the midline electrodes (Cz) in 5 out of 6 patients. This location has already been described as sufficient to show the presence of the P300 in auditory and visual modalities. Nevertheless, in the previous pilot study with healthy subjects using identical stimulation, the best electrode set for P300 accuracy was Fz, FC1, FC2, C3, C4, CP1, and CP2 (Ortner et al, unpublished data). Although the neural generators of P300 are imprecisely delineated, several studies suggest that P3a and P3b generation stems from frontal and temporal/parietal activations. In the case of LIS patients, lesions are mainly limited to the brainstem, therefore, 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 (2 of them at college level and the others at high school level) previous to the accident. Nevertheless, in LIS patients, moderate and selective cognitive impairment, not related to the location of the lesion, has been shown. Schnakers at al also found in a cohort of 10 LIS patients, some impairment mainly in those patients with additional thalamic or cortical lesions. Therefore, there could be some degree of a mild impairment in these patients, affecting the execution of the tasks. Even if fully conscious, and with lesions mainly limited to the motor pathways (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 like those of healthy subjects.

However, a possible cognitive impairment present in some patients does not explain completely the low 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, using 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. An additional track was given to this patient (the examiner’s hand touched the arm where the patient had to count the stimuli) because the family reported that the patient had slight confusion about right/left side (ie, that it was difficult for the patient to locate where was 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 the pattern of topography, amplitude, and latency of the P300. Another limitation was the lack of time for more training; this was because these patients have quite lengthy care routines (including those who were assessed in their homes) thus restricting the time for tests to a couple of hours. Therefore, it would be necessary to have at least 2 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 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 with severe motor and language disabilities (such 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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