Clinical trial design to validate a BCI-supported task-specific training in neurorehabilitation after stroke: lesson from experience

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Abstract. The present study aimed to evaluate the efficacy of mental training of motor skills (motor imagery, MI) supported by an EEG-based BCI device, whose development and implementation was based on neurorehabilitation principles, in promoting hand function recovery after stroke. The validation procedure of such BCI application was designed as a rehabilitation stage II pilot trial with two endpoints: primarily, to demonstrate the efficacy this BCI-based MI training as an adjunctive intervention in post-stroke rehabilitation and, secondarily to foster the transfer of BCI technology into clinical practice. Sixteen stroke patients were enrolled and randomized in two programme groups: i) a BCI-based MI training programme group and a MI training programme control group. Both groups of patients received a similar usual care treatment. The results showed a significant improvement of some of the outcome measures in the intervention group (MI-based BCI training) with respect to the control group. Yet, two important biases in the randomization process were found and corrective actions were discussed.

Keywords: EEG-based BCI, Stroke, Rehabilitation, Motor Imagery

1. Introduction

Motor Imagery (MI) was proposed to enhance arm motor recovery after stroke. Yet, unambiguous evidence are currently available about the efficacy of such covert motor practice [Ietswaart et al. 2011; Zimmermann-Schlatter et al. 2008]. EEG-based BCIs operated by MI can provide a valuable method to support mental motor practice by allowing for direct monitoring of the patient’s adherence to such task-specific training. Furthermore, BCI paradigms based on neurofeedback mechanisms offer a unique strategy to favor activity-dependent plasticity. For this reason a BCI-driven rehabilitation device was developed to encourage recovery of hand function after stroke [Pichiorri et al. 2011]. As such, the implemented BCI-based rehabilitation device requires two actors: the patients who is provided with an enriched visual feedback congruent with his MI task (imagery of affected hand movements) and performance, and the therapist who monitors patient’s performance by means of the instant BCI feedback of the patient’s EEG sensorimotor rhythm modulation occurring over the stroke lesioned hemisphere. Here we report how the validation of this BCI technology format was conducted in accordance with the guidelines to demonstrate efficacy of new motor rehabilitation interventions and to foster their translation in clinical practice.

2. Material and Methods

Sixteen first-ever unilateral cortical/subcortical stroke patients, (mean age 60.3±9.1; time form event between 6 weeks and 1 year) were consecutively recruited at the Fondazione Santa Lucia, upon their admission for post-stroke rehabilitation treatment. Exclusions criteria were: concomitant chronic disabling pathologies, orthopedic injuries that could impair reaching or grasping, severe spasticity, Mini-Mental State Examination score < 24 and cognitive deficits that needs rehabilitation after a neuropsychological evaluation. Patients were randomly assigned to the BCI-based MI training group (BCI; n=8) or MI control group (CTRL; n=8) group. The BCI technology and the training session details are reported elsewhere [Pichiorri et al. 2011]. The MI intervention in both groups lasted 4 weeks, with weekly training sessions (3 times per week) according to standardized practices in an “add-on” to usual care. Functional pre- and post- intervention assessments were performed by a physician who was concealed to allocation. The primary outcome measure was the arm section of the Fugl-Meyer scale (arm F-M). A minimal clinically important difference for this scale (MCID) was described to 7 points. Secondary outcome measures included the European Stroke Scale (ESS) and the arm MRC (arm section of the Medical Research Council Scale). The study protocol was approved by the local Ethical Committee and patients signed the informed consent before entering in the study. The
study design was a stage 2 (“Development-of-Concept Trials”) pilot study of phase III trials for motor intervention [Dobkin et al. 2009].

3. Results

Randomization was partially successful since no significant group differences at baseline were found on the primary (arm F-M, see Table 1) and secondary outcome measures (ESS, arm MRC) or other demographic factors (mean age was 56.3±9.1 in the BCI group and 57.7±13.6 in the control group; time from event was 5.2±4.3 months in the BCI group and 2.3±0.7 in the control group, not significant). Table 1 summarizes the results for the primary and secondary outcome measures. Regarding the primary outcome measure arm F-M, a mean change of 9.3 (+45%) was observed exceeding the MCID of 7 with respect to an improvement of 5.62 (+9%) observed in control group. Indeed the arm F-M MCID score was achieved in 4 patients in the BCI Group and only 2 patients in the Control Group.

**TABLE 1**: Average scores for outcome measures. Mann Whitney U test was used to compare the two groups at baseline (’pre’ columns). Sign Test was used to assess changes from baseline to post-training in each group (‘raw’).

<table>
<thead>
<tr>
<th></th>
<th>F-M* (⁄66)</th>
<th>ESS (…/100)</th>
<th>MRC* (⁄80)</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>pre</td>
<td>post</td>
<td>p</td>
</tr>
<tr>
<td>BCI</td>
<td>Avg</td>
<td>20.6</td>
<td>29.9</td>
</tr>
<tr>
<td></td>
<td>SD</td>
<td>16.2</td>
<td>22.2</td>
</tr>
<tr>
<td>CTRL</td>
<td>Avg</td>
<td>29.4</td>
<td>35.0</td>
</tr>
<tr>
<td></td>
<td>SD</td>
<td>22.7</td>
<td>24.1</td>
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<tr>
<td>p</td>
<td>&gt; 0.05</td>
<td>-</td>
<td>&gt; 0.05</td>
</tr>
</tbody>
</table>

* = only upper limb function items are considered

4. Discussion

To our knowledge this is the first randomized controlled trial (RCT) carried out to evaluate the efficacy of the mental training of motor skills (motor imagery, MI) supported by an EEG-based BCI device to promote recovery of hand function after stroke. Our findings highlight the possible efficacy of such BCI technology-based approach.

Two possible biases were however found in the randomization procedure. The first regarded the side of the brain lesion, being the BCI group composed by 7 patients with a right hemispheric and 1 with left hemispheric stroke, while the CTRL group contained all left hemispheric lesions. The second possible confounding factor was the time from event. Although, no significant difference was observed at baseline between the two groups (probably due to high standard deviations), it has to be pointed out that the “BCI-based MI training” contained 3 chronic patients (more than 3 months form event) while in the “MI training control” group all patients were in the subacute phase. A key point for further large RCT aiming to consolidate the clinical benefit of the BCI-supported MI practice in subacute stroke will be to employ a randomization procedure with the stratification to adjust time onset and lesion side.

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References


