FEASIBILITY OF TASK-SPECIFIC BRAIN-MACHINE INTERFACE TRAINING FOR UPPER-EXTREMITY PARALYSIS IN PATIENTS WITH CHRONIC HEMI Paretic STROKE

Atsuko NISHIMOTO, OTR1,*, Michiyuki KAWAKAMI, MD, PhD1,*, Toshiyuki FUJWARA, MD, PhD2, Miho HIRAMOTO, OTR1, Kaoru HONAGA, MD, PhD3, Kaoru ABE, OTR3, Katsuhiro MIZUNO, MD, PhD1, Junichi USHIBA, PhD4,5 and Meigen LIU, MD, PhD1

From the 1Department of Rehabilitation Medicine, Keio University School of Medicine, 2Department of Rehabilitation Medicine, Juntendo University Graduate School of Medicine, 3Department of Rehabilitation Medicine, Keio University Hospital, 4Department of Biosciences and Informatics, Faculty of Science and Technology, Keio University, and 5Keio Institute of Pure and Applied Sciences (KiPAS), Kanagawa, Japan *These authors contributed equally to this work.

**Objective:** Brain-machine interface training was developed for upper-extremity rehabilitation for patients with severe hemiparesis. Its clinical application, however, has been limited because of its lack of feasibility in real-world rehabilitation settings. We developed a new compact task-specific brain-machine interface system that enables task-specific training, including reach-and-grasp tasks, and studied its clinical feasibility and effectiveness for upper-extremity motor paralysis in patients with stroke.

**Design:** Prospective before-after study.

**Subjects:** Twenty-six patients with severe chronic hemiparetic stroke.

**Methods:** Participants were trained with the brain-machine interface system to pick up and release pegs during 40-min sessions and 40 min of standard occupational therapy per day for 10 days. Fugl-Meyer upper-extremity motor (FMA) and Motor Activity Log-14 amount of use (MAL-AOU) scores were assessed before and after the intervention. To test its feasibility, 4 occupational therapists who operated the system for the first time assessed it with the Quebec User Evaluation of Satisfaction with assistive Technology (QUEST) 2.0.

**Results:** FMA and MAL-AOU scores improved significantly after brain-machine interface training, with the effect sizes being medium and large, respectively ($p < 0.01, d = 0.55; p < 0.01, d = 0.88$). QUEST effectiveness and safety scores showed feasibility and satisfaction in the clinical setting.

**Conclusion:** Our newly developed compact brain-machine interface system is feasible for use in real-world clinical settings.

**Key words:** electroencephalogram; cerebrovascular disease; hand function; rehabilitation.

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Correspondence address: Toshiyuki Fujiwara, Department of Rehabilitation Medicine, Juntendo University Graduate School of Medicine, 2-1-1 Hongo, Bunkyo, Tokyo 113-8421, Japan. E-mail: tofuj@xc5.so-net.ne.jp

**ORIGINAL REPORT**

**STROKE**

Stroke is one of the most prevalent neurological conditions worldwide, especially among elderly adults. It has been reported that 30–66% of all stroke patients with hemiparesis have poor arm function 6 months post-stroke (1). Motor recovery relates to: restoration of function in neural tissue that was initially lost; restoration of the ability to perform movement in the same way as before injury; and successful task completion as typically performed by individuals who are not disabled. Types of motor compensation in these 3 areas include the acquisition by neural tissue of a function that it did not have before the injury; performance of a movement in a new way; and successful task completion by using different techniques (2, 3). It has been reported that the major portion of recovery of upper-extremity (UE) motor impairment occurs over the first few months after stroke (4). However, some newly developed approaches for rehabilitation have also improved UE motor function in patients with chronic stroke (5–7).

Recently, a brain-machine interface (BMI) has been developed as a new rehabilitation tool for patients with severe UE paresis (8–14). A BMI detects the increased sensorimotor cortical activity following patient’s attempting UE motor activities and provides associated actions with external devices, such as a motor-driven orthosis by functional neuromuscular electrical stimulation (15). Due to such BMI actions, patients begin to exercise UE movement by themselves, even though no volitional signs on EMG or kinematics are found in the innate condition. Several clinical studies have tested the clinical efficacy of BMI-based exercise as motor rehabilitation after stroke and spinal cord injury (16).

BMI is thought to be a novel tool for rehabilitation of patients with severe paresis, for which no intervention has so far been convincingly shown to be effective. A randomized, controlled trial showed that BMI training improved UE motor function even in patients with chronic stroke and severe UE impairment (11). Kawakami and colleagues (17) reported that significant functional recovery from stroke could be induced with BMI training followed by Hybrid Assistive Neuromuscular Dynamic Stimulation (HANDS) therapy in patients with chronic and severe hemiparesis (Fugl-Meyer upper extremity motor (FMA)-gain 14.6
points). There have been, however, some limitations to clinical application of BMI systems. Most of them were set up in the laboratory and cannot be used in general clinical areas (i.e. therapy rooms). In addition, most of the BMI training in previous reports mainly aimed at improving paretic finger extension (10, 11). To make their paretic UE useful in real-life activities of daily living (ADL), it is necessary to restore hand grip-and-release function combined with arm-reaching function (18).

A new compact BMI system that enables task-specific training, including reach-and-grasp tasks was developed, and applied to a clinical rehabilitation setting. The aim of this study was to investigate the feasibility of this compact BMI system in clinical rehabilitation.

**MATERIAL AND METHODS**

**Participants**

Patients were recruited from the outpatient rehabilitation clinics of Keio University Hospital. They were included in this study if they met the following criteria: (i) a unilateral subcortical stroke not involving the sensorimotor cortex as confirmed with brain magnetic resonance imaging (MRI) or computed tomography (CT); (ii) age between 20 and 80 years; (iii) time from stroke onset longer than 180 days; (iv) ability to extend the paretic hand to the height of the nipple; (v) no severe proprioceptive deficit in the affected UE; (vi) no motor improvement during the 30 days prior to starting the intervention, as confirmed by both the patients and their physicians; (vii) no cognitive deficits as determined by a Mini-Mental State Examination score > 25; (viii) no pacemaker or other implanted stimulator; and (ix) no history of seizures within the past 2 years and no use of anticonvulsants at least for 1 month before the intervention.

From 2011 to 2013, 50 patients were seen at the outpatient clinic to be evaluated for eligibility for this study. Twenty-four patients were excluded because they did not meet the inclusion criteria, and 26 patients were enrolled in the study. The study purpose and procedures were explained to the participants, and written, informed consent was obtained from each patient. This study was approved by the institutional ethics review board. This study was registered as a clinical trial with the University Hospital Medical Information Network in Japan (UMIN Critical Trial Registry UMIN000002121).

**Electroencephalographic recording**

The experiment consisted of BMI training and brain activity assessment using electroencephalography (EEG). EEG was performed with Ag-AgCl1 electrodes (1 cm in diameter), at C3 and the left ear in patients with right hemiparesis, and at C4 and the right ear in patients with left hemiparesis, according to the international 10–20 system (18). An additional electrode was placed at a position 2.5 cm anterior to C3 or C4. A ground electrode was placed on the forehead, and the reference electrode was placed on either A1 or A2 (ipsilateral to the affected hemisphere). EEGs were recorded in a bipolar manner. The signals were digitized at 256 Hz using a bio signal amplifier (g.MOBILab+, G.tec Medical Engineering GmbH, Graz Austria).

**Event-related desynchronization quantification**

As a feature representing the increased excitability of the ipsilesional sensorimotor cortex, event-related desynchronization (ERD), which is a diminution of the alpha band (8–13 Hz) of the mu rhythm amplitude, was calculated as follows, and used as a trigger signal for BMI actions. The ERD was expressed as the percentage of the power decrease related to the 1-s reference interval before the direction of intention. The ERD at a certain frequency was calculated for each time and frequency according to the following equation:

\[
ERD(f, t) = \frac{(R(f) - A(f, t))/R(f)}{100} \%
\]

where \(A(f, t)\) is the power spectrum density of the EEG at a certain frequency \(f\) [Hz] and time \(t\) [s] since the imagery task was started, and \(R(f)\) is the power spectrum at the same frequency \(f\) [Hz] of the baseline period.

The physiological relevance of the mu rhythm and its ERD on EEG have been reported previously; the mu rhythm amplitude is inversely correlated with the blood oxygen level-dependent signal of the sensorimotor cortex (19), corticospinal tract excitability (20), disinhibition of intra-cortical inhibition in the primary motor cortex (20), and spinal motoneuronal excitability (21). Operating the BMI through this EEG feature is therefore interpreted as an up-conditioning of the ipsilesional cortico-muscular pathway involved in motor control.

**Task-specific brain-machine interface training**

BMI training was carried out for approximately 40 min for 10 days. All of the participants received 40 min of standard occupational therapy per day, which consisted of gentle stretching exercises, active muscle re-education exercises, and introduction to bimanual activities in their daily lives.

The participants wore a headset with 2 brush-type electrodes that recorded the ipsilesional mu rhythm (Fig. 1a). With this headset electrode system, it is easy to set the electrode on C3 or C4 (i.e. the corticocerebral motor area) to record the EEG by adjusting the headset to the relative positions of both ears. It takes only 5 min to set the electrodes. The motor-driven orthosis was attached to the affected hand to achieve finger extension movement at the metacarpophalangeal and proximal interphalangeal joints. The affected forearm was placed on a balanced forearm orthosis (Fig. 1b). The participants were seated in front of a desk. Thirty pegs were set on the desk peg board. Participants were asked to pick up a peg with the affected hand with the orthosis (Fig. 1c). A star-shaped cursor began to move at a fixed rate from left to right across the monitor over an 8-s period. Participants were instructed to rest for 5 s and then to either imagine extending their affected fingers or remain relaxed for the next 3 s, depending on the task cue on the monitor. If the mu ERD was detected after the cue instruction to imagine finger extension, the star-shaped cursor moved down on the screen as visual feedback, and then the motor-driven hand orthosis extended the affected fingers and stimulated the extensor digitorum communis muscle (EDC) by electrical stimulation weaker than its motor threshold (frequency 100 Hz, pulse width 200 μs) for 3 s (Fig. 2). If ERD was not detected after the cue, which meant that the motor imagery was not successfully performed, the orthosis did not move, and electric stimulation was not applied.
Feasibility of the newly developed BMI system for professional users

The time needed to set up this BMI training system every day was measured, and the mean time calculated. Four occupational therapists who had not operated the BMI system previously were asked to set up and operate the system, and a questionnaire survey with the Quebec User Evaluation of Satisfaction with Assistive Technology 2.0 (QUEST 2.0) (22) was conducted after the intervention. The QUEST survey comprises 12 satisfaction items whose scores range from 1 (very satisfied) to 5 (not satisfied at all). The QUEST 2.0 was used to evaluate the usability of a BMI-based system in a previous report (23). The time needed for each therapist to set up the system was also measured.

Outcome measures

The following clinical assessments were conducted one day before (pre) and the day after the intervention (post). The number of times that a participant...
produced appropriate ERD (number of ERD detections) during BMI training was reported each day.

**Clinical assessments**

UE motor function was assessed with the FMA (range 0–66 points, total score) (24, 25). The FMA consists of test A (shoulder/elbow/forearm: 36 points, A score), test B (wrist: 10 points, B score), test C (hand/finger: 14 points, C score), and test D (coordination: 6 points, D score). The D score was excluded because not all of the patients in this study could touch their nose with their index finger fully extended, and they had no voluntary finger extension. The FMA was assessed according to the scoring manual (26), and the validity and reliability of this method have been confirmed previously (25, 27). It was reported that the estimated clinically important difference of the UE-FM scores ranged from 4.25 to 7.25 points in individuals with stable, mild to moderate UE hemiparesis (28). However, the minimal clinically important difference (MCID) for patients with severe hemiparesis remains to be shown. Because it was considered that a greater than 10% change in FM motor scores may represent a clinically meaningful improvement based on clinical experience (29), it is conceivable that the MCID for severe hemiparesis is lower than that for mild hemiparesis. A minimal detectable change of 3.2 points was reported in 31 patients with stroke (30).

UE disability in ADL was assessed with the Motor Activity Log-14 (MAL), which uses a structured interview (31). MAL includes 14 items, scored on an 11-point amount of use scale (range 0–5) to rate how much the arm is used (MAL-AOU) and an 11-point quality of movement scale (range 0–5) to rate how well the participants are using their affected upper extremity (31). We selected only the MAL-AOU score in this study because it was difficult for patients with a severely paretic hand to change the quality of movements. High construct validity and reliability have been demonstrated in patients with chronic stroke (31, 32).

The capability to pick-up and release pegs with the reaching task was assessed by the number of pegs picked up and released in 1 min (peg number). Participants tried to pick up from the board and release pegs out of the board as many times as possible for 1 min (board: width 300 mm × 250 mm × height 25 mm; peg: diameter 21 mm, height 70 mm; 30 pegs were set on the board).

FMA and MAL-AOU were assessed by an independent assessor who did not know which patients were recruited for this study to receive the BMI training. This assessor scored all of the participants with stroke who were admitted to the department during the study period, including participants not recruited for this study, and the peg number was assessed by an occupational therapist who was not engaged in the BMI training.

**RESULTS**

### Feasibility of the newly developed BMI system for professional users

All patients were fully compliant with the BMI training programme with no adverse events. For all participants, there was no interruption in training due to any cause including fatigue. Skilled BMI system users could set it up in approximately 10 min, while the 4 therapists who set it up for the first time could do so within 15 min. They all answered “more than somewhat satisfied” for the weight, facility, safety, and effectiveness, and 3 therapists answered “more than somewhat satisfied” for the size and ease of adjustment (Table I). They felt that it would be easy to operate the system after operating it continuously.

### Effect of BMI training

Table II shows the patients’ clinical characteristics (age, time from onset of stroke, sex, type of stroke, paretic side, lesion). Twenty-six patients were included in the current analyses. The mean age of all patients was 50.3 years (SD = 11.1,
range = 25–72 years), and their mean time from stroke onset was 1,421.5 days (SD = 1,318.1). Twelve patients had hemiparesis affecting their right UEs.

After the BMI training, Wilcoxon signed-rank testing showed significant differences in the FMA-total, FMA-A score, FMA-C score, MAL-AOU score, and peg number (Table III). The effect sizes for FMA-total, FMA-A score, and peg number were moderate. The effect size for the FMA-C score was small, and the MAL-AOU score showed a large effect size. FMA-gain was 3.3 (SD = 2.9).

**Table II. Clinical characteristics of participants**

<table>
<thead>
<tr>
<th>Age, years</th>
<th>Stroke type</th>
<th>Stroke lesion</th>
<th>Paretic side</th>
<th>Time from onset of stroke, days</th>
</tr>
</thead>
<tbody>
<tr>
<td>49</td>
<td>CI</td>
<td>Corona radiata</td>
<td>Left</td>
<td>262</td>
</tr>
<tr>
<td>53</td>
<td>CH</td>
<td>Putamen</td>
<td>Right</td>
<td>1,050</td>
</tr>
<tr>
<td>66</td>
<td>CI</td>
<td>MCA</td>
<td>Right</td>
<td>3,046</td>
</tr>
<tr>
<td>52</td>
<td>CH</td>
<td>Putamen</td>
<td>Left</td>
<td>635</td>
</tr>
<tr>
<td>65</td>
<td>CH</td>
<td>Putamen</td>
<td>Right</td>
<td>5,391</td>
</tr>
<tr>
<td>50</td>
<td>CH</td>
<td>Putamen</td>
<td>Left</td>
<td>3,611</td>
</tr>
<tr>
<td>55</td>
<td>CH</td>
<td>Putamen</td>
<td>Right</td>
<td>491</td>
</tr>
<tr>
<td>47</td>
<td>CH</td>
<td>Putamen</td>
<td>Left</td>
<td>732</td>
</tr>
<tr>
<td>72</td>
<td>CI</td>
<td>Corona radiata</td>
<td>Left</td>
<td>2,866</td>
</tr>
<tr>
<td>45</td>
<td>CH</td>
<td>Putamen</td>
<td>Left</td>
<td>873</td>
</tr>
<tr>
<td>71</td>
<td>CI</td>
<td>Corona radiata</td>
<td>Left</td>
<td>169</td>
</tr>
<tr>
<td>46</td>
<td>CH</td>
<td>Putamen</td>
<td>Right</td>
<td>773</td>
</tr>
<tr>
<td>42</td>
<td>CH</td>
<td>Thalamus</td>
<td>Right</td>
<td>739</td>
</tr>
<tr>
<td>53</td>
<td>CH</td>
<td>Putamen</td>
<td>Left</td>
<td>736</td>
</tr>
<tr>
<td>25</td>
<td>CH</td>
<td>Putamen</td>
<td>Right</td>
<td>983</td>
</tr>
<tr>
<td>51</td>
<td>CH</td>
<td>Putamen</td>
<td>Right</td>
<td>566</td>
</tr>
<tr>
<td>36</td>
<td>CI</td>
<td>MCA</td>
<td>Left</td>
<td>3,077</td>
</tr>
<tr>
<td>48</td>
<td>CH</td>
<td>Putamen</td>
<td>Right</td>
<td>2,468</td>
</tr>
<tr>
<td>43</td>
<td>CH</td>
<td>Putamen</td>
<td>Left</td>
<td>454</td>
</tr>
<tr>
<td>64</td>
<td>CI</td>
<td>MCA</td>
<td>Left</td>
<td>915</td>
</tr>
<tr>
<td>63</td>
<td>CH</td>
<td>Putamen</td>
<td>Left</td>
<td>605</td>
</tr>
<tr>
<td>41</td>
<td>CH</td>
<td>Putamen</td>
<td>Right</td>
<td>532</td>
</tr>
<tr>
<td>52</td>
<td>CH</td>
<td>Putamen</td>
<td>Left</td>
<td>1,018</td>
</tr>
<tr>
<td>43</td>
<td>CH</td>
<td>Putamen</td>
<td>Right</td>
<td>629</td>
</tr>
<tr>
<td>38</td>
<td>CH</td>
<td>Putamen</td>
<td>Left</td>
<td>772</td>
</tr>
</tbody>
</table>

CI: cerebral infarction; CH: cerebral hemorrhage; MCA: middle cerebral artery.

**Table III. Changes in clinical assessment scores**

<table>
<thead>
<tr>
<th></th>
<th>Pre-BMI Median (IQR)</th>
<th>Post-BMI Median (IQR)</th>
<th>Effect size</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>FMA-A</td>
<td>14.5 (12.25–17.75)</td>
<td>17.0 (14.0–22.0)</td>
<td>&lt; 0.01</td>
<td>0.51</td>
</tr>
<tr>
<td>FMA-B</td>
<td>0 (0–0)</td>
<td>0 (0–0)</td>
<td>0.53</td>
<td>0.16</td>
</tr>
<tr>
<td>FMA-C</td>
<td>2.0 (1.0–3.0)</td>
<td>3.0 (2.0–4.0)</td>
<td>&lt; 0.01</td>
<td>0.30</td>
</tr>
<tr>
<td>FMA-total</td>
<td>17.5 (14.0–22.75)</td>
<td>19.5 (17.25–25.75)</td>
<td>&lt; 0.01</td>
<td>0.55</td>
</tr>
<tr>
<td>Peg number</td>
<td>5.0 (4.0–7.0)</td>
<td>7.0 (5.0–10.5)</td>
<td>&lt; 0.01</td>
<td>0.68</td>
</tr>
<tr>
<td>MAL-AOU</td>
<td>2.0 (0–2.0)</td>
<td>4.0 (2.0–7.0)</td>
<td>&lt; 0.01</td>
<td>0.88</td>
</tr>
</tbody>
</table>

Effect sizes were calculated using Cohen’s d statistic and an effect size less than 0.5 was regarded as small, 0.5–0.8 as medium and above 0.8 as large. Pre-BMI: before brain-machine interface training; post-BMI: after brain-machine interface training; FMA: Fugl-Meyer upper extremity score; A, shoulder/elbow/forearm; R, 36 points; B, wrist, 10 points; C, hand/finger, 14 points; MAL-AOU: motor activity log amount of use; peg number: number of pegs picked up and released in 1 min; IQR: interquartile range.

**DISCUSSION**

Feasibility of the newly developed BMI system for professional users

When using a new rehabilitation device in clinical settings, it is necessary to consider the time to set up the system, the space required for its operation, and its usability from the point of view of therapists (23). Our results showed that the QUEST effectiveness and safety scores were comparable to or better than those of Morone’s report (23). This indicates that our BMI system is feasible for use in real clinical situations.

Task-specific BMI training on upper extremity limb in patients with severe score

To our knowledge, this is the first study to demonstrate the efficacy of task-specific BMI training for severe UE paresis. In previous reports, the FMA score of severe arm paresis was defined as 35 or less (35, 36). All participants in this study met this definition. There was improvement in UE function, peg pick-up and release task performance, and the amount of use of the paretic hand in their ADL. The gain in FMA in this report was comparable to that in previous reports, (10, 11) even though the hand paralysis of our participants was more severe.

**Table IV. Correlations between total number of event-related desynchronization (ERD) detections and changes in clinical assessment scores**

<table>
<thead>
<tr>
<th></th>
<th>Spearman’s rank correlation coefficient</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>FMA-total gain</td>
<td>0.24</td>
<td>0.26</td>
</tr>
<tr>
<td>MAL-AOU gain</td>
<td>0.11</td>
<td>0.59</td>
</tr>
<tr>
<td>Peg number gain</td>
<td>0.50*</td>
<td>0.02</td>
</tr>
</tbody>
</table>

FMA: Fugl-Meyer upper extremity score; MAL-AOU: motor activity log-14 amount of use.

**Figure 1.** Example of brain activity captured from electrode (A) and its corresponding BMI output (B). (A) Brain activity from left posterior region of the brain showing desynchronization as indicated by a decrease in voltage. (B) Corresponding BMI output showing an increase in the EMG signal, indicating a release of the hand. (C) Brain activity from the left anterior region showing synchronization as indicated by an increase in voltage. (D) Corresponding BMI output showing a decrease in the EMG signal, indicating a grasp of the hand.
In addition, there was significant improvement in peg pick-up and release task performance and the amount of use of the affected UE in daily life assessed with the MAL-AOU. To the best of our knowledge, the MCID of MAL-AOU had not been reported previously. The present data showed a large effect size for MAL-AOU. Although it is necessary to further investigate whether this result is due to the characteristics of the measurement method, we are considering the following 2 hypotheses: (i) since participants were severely paralysed and had not used the paralysed hand before the intervention, the use frequency of the paralysed hands was likely to increase because the “learned non-use” was improved by the intervention; (ii) our BMI training might affect not only arm function but also use of the paretic hand in their ADL, because our system consists of task-specific tasks (i.e. pinch and release). Task-specific BMI training induced task-specific improvements of hand function and reaching function of the paretic UE. Picking up and releasing objects while reaching are basic UE movements in ADL. These improvements may have increased the MAL-AOU score.

In this study, there was a significant correlation between the total number of ERD detections (successful trials) during the BMI training and peg numbers. It was supposed that electrical stimulation and actual paretic finger movement triggered by motor intention increased motor cortex excitability. The increase in motor cortex excitability might be dose-dependent.

Kasashima-Shindo et al. (14) reported that the accuracy rate of ERD detection increased significantly after BMI training. Shindo and colleagues (10) found that increased cortical excitability in the affected hemisphere was confirmed by transcranial magnetic stimulation after BMI training. Li and co-workers (12) also suggested that the activation of the affected sensorimotor cortex and the parietal lobe may contribute to effective motor function improvement assessed with the action research arm test in stroke patients. In addition to these previous reports, our results might support a relationship between the change in brain activity (especially neural excitation in the affected hemisphere) and functional recovery.

Study limitations

In this study, we cannot convincingly discuss the effectiveness of the BMI intervention because the number of patients treated was small, and there was no age-matched control or sham treatment group. Furthermore, our protocol included not only BMI training but also occupational therapy. Therefore, one cannot differentiate the effects brought about by the 2 interventions. In previous randomized, controlled trials, the BMI training group showed a greater improvement in the paretic UE than the control group (11–13). The pilot data presented here provide a basis for designing and conducting a larger scale trial with more rigorous study design, including masking and randomization, to test the task-specific BMI training effects. This research was performed as a phase 1–2 clinical trial. However, the effect was not large. Thus, this protocol might need revision before moving to stage 3 trials.

Conclusion

Our newly developed compact BMI system is feasible for use in real-world clinical settings, and BMI training is potentially a useful technology in rehabilitation, not only to substitute for lost functions, but also to induce brain plasticity and improve paresis. According to the phased approach to the development of clinical rehabilitation evidence (37), the present study was positioned as a phase 1–2 clinical trial. The present study confirmed that the proposed treatment was clinically feasible from the perspective of both efficacy and safety, and it ensured that the effects of the treatment are in the desired direction. The results now encourage us to compare its effectiveness with that of existing standardized treatments. A phase 3 clinical trial with a larger sample is needed for further development of clinical BMI interventions.

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