Clinical EEG and Neuroscience
2019, Vol. 50(6) 429–435

DOI: 10.1177/1550059419840246
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Treatment of Medial Medullary Infarction Using a Novel iNems Training: A Case Report and Literature Review

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Abstract

Objective. We describe the case of a 66-year-old Japanese male patient who developed medial medullary infarction along with severe motor paralysis and intense numbness of the left arm, pain catastrophizing, and abnormal physical sensation. We further describe his recovery using a new imagery neurofeedback-based multisensory systems (iNems) training method. *Clinical Course and Intervention*. The patient underwent physical therapy for the rehabilitation of motor paralysis and numbness of the paralyzed upper limbs; in addition, we implemented iNems training using EEG activity, which aims to synchronize movement intent (motor imagery) with sensory information (feedback visual information). *Results*. Considerable improvement in motor function, pain catastrophizing, representation of the body in the brain, and abnormal physical sensations was accomplished with iNems training. Furthermore, iNems training improved the neural activity of the default mode network at rest and the sensorimotor region when the movement was intended. *Conclusions*. The newly developed iNems could prove a novel, useful tool for neurorehabilitation considering that both behavioral and neurophysiological changes were observed in our case.

Keywords

medial medullary infarction, motor imagery, brain machine interface, neurorehabilitation, EEG

Received December 22, 2018; revised February 6, 2019; accepted February 20, 2019.

Introduction

One type of recently developed neurorehabilitation[1] has focused on promoting the recovery of sensory cranial nerve function in response to movement and sensory disorders in patients with stroke. This type of neurorehabilitation uses “motor imagery” as a stimulus aiming at regaining sensorimotor function and has been garnering attention as a method that allows patients to form an image of physical movement without executing the movement, that is, to form a neurological foundation toward executing a movement.[2]

Patients with numbness after stroke reportedly experience reduced motor skills and brain capacity for work, depression,[3] and a decrease in self-esteem,[4] which may result in catastrophizing. Although the efficacy of mirror therapy,[5] pharmacological approaches,[6] and repetitive transcranial magnetic stimulation[7] are reportedly effective for central poststroke pain, the effect is short-lasting and there are reports suggesting that it is ineffective for brainstem infarction.[8] Therefore, we developed a novel sensorimotor imagery neurofeedback systems training method based on EEG activity (Supplementary Data 1, available in the online version of the article, and Figures 1 and 2) that allows the patient to synchronize movement intent (motor imagery) with sensory information (feedback visual information) from the afflicted limb, called imagery neurofeedback-based multisensory systems (iNems).

We present the case of a patient who developed medial medullary infarction, that is, Dejerine syndrome, which may involve various neurological symptoms.[4] Furthermore, we describe the implementation of our novel technique, iNems, which was used to alleviate the patient’s behavioral and neurophysiological symptoms.

Case Presentation

Case Introduction

The patient was a 66-year-old Japanese man who had developed right-medial medullary infarction (Figure 1). At the time of onset, the patient presented with severe motor paralysis of the left upper limb, intractable stuttering, and intense numbness. Approximately 2 months after onset, the patient started

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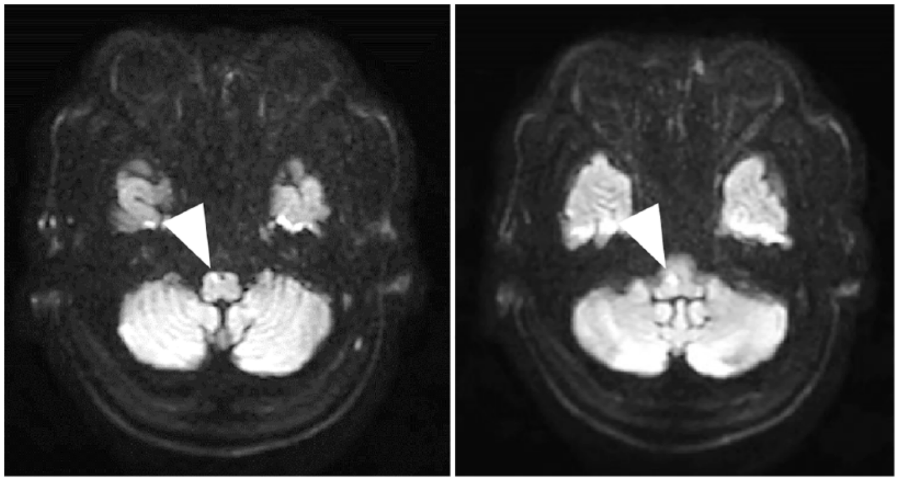
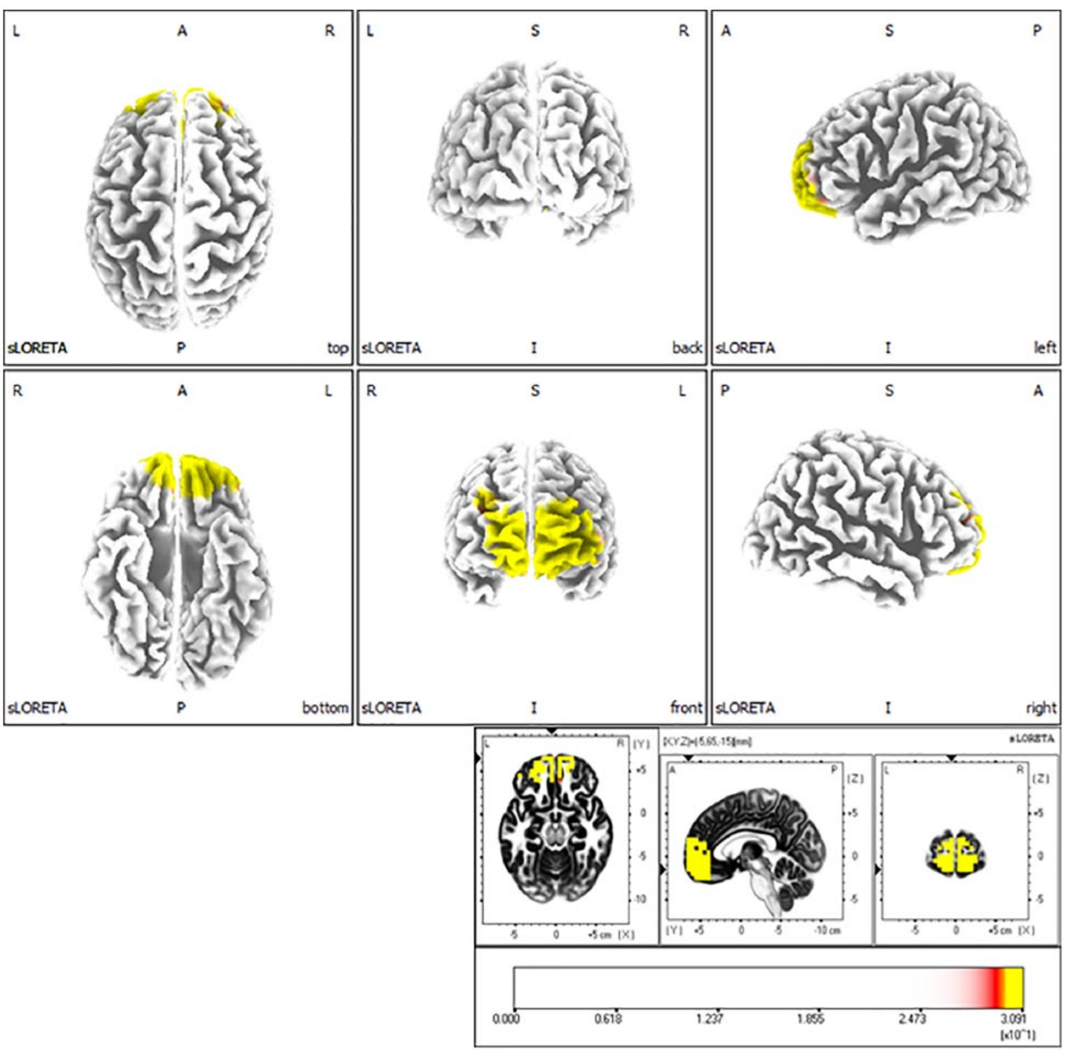


Figure 1. Findings of magnetic resonance diffusion weighted imaging at the time of infarction onset. Infarction identified in the right-medial medulla oblongata on head magnetic resonance imaging (part marked by ∇).



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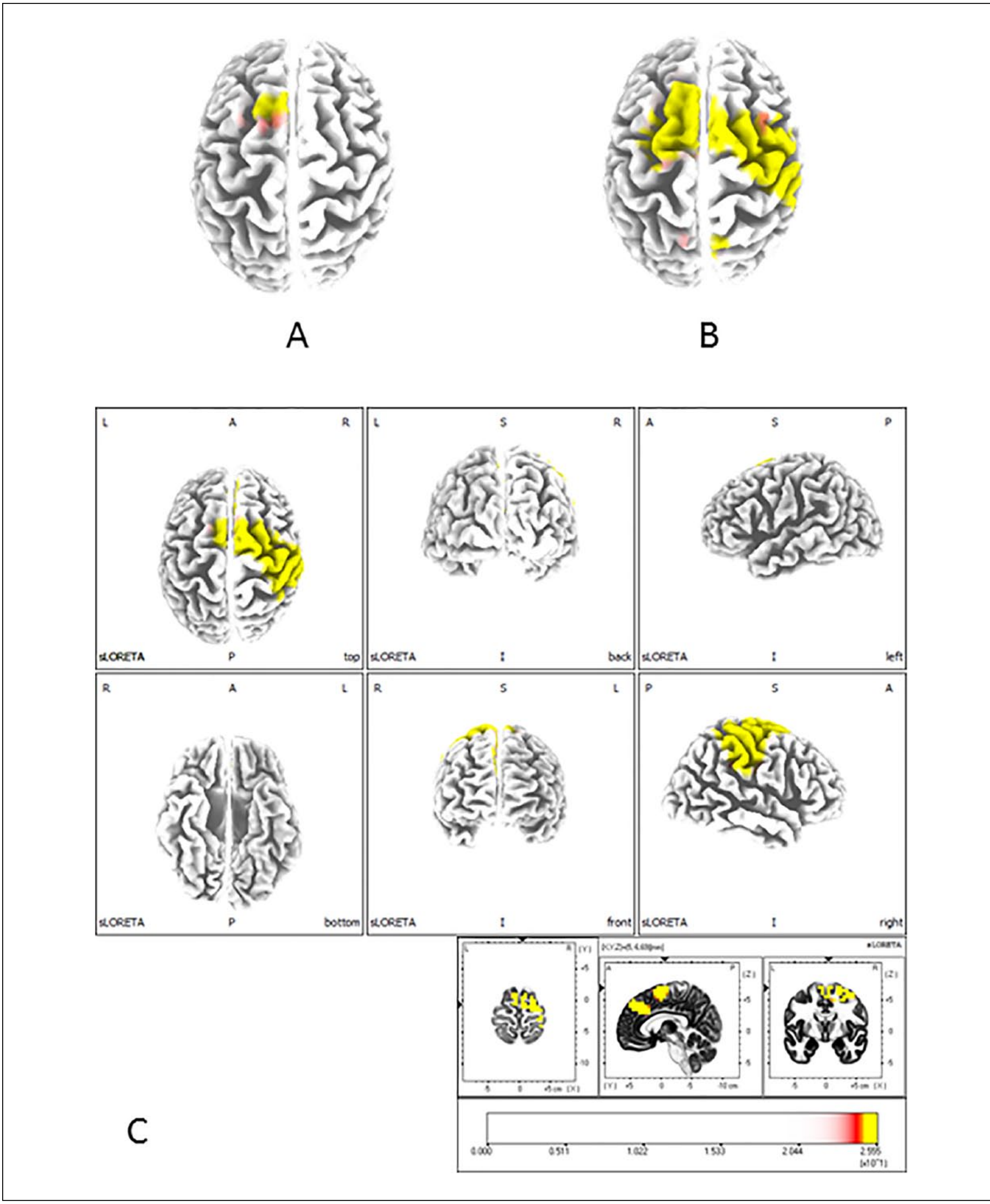

Figure 2. (1) Comparison of the status of brain function in the alpha (α) wave band while at rest. The neural activity in the medial prefrontal cortex (Brodmann area 24) was higher at the end than at the start of training. (2) Comparison of the status of brain function in the sensorimotor region in the mu (μ) wave band during motor imagery formation. (A) Neural activity at the start of the training. (B) Neural activity after 6 weeks. (C) The neural activity in the right sensorimotor-related region was higher at the end than at the start of training.

receiving physical therapy for 3 hours per day, 5 days per week. Rehabilitation during hospitalization primarily consisted of upper and lower limb functional practice (eg, range of motion [ROM]-ex) and practice of daily routine motion, wheelchair operation, walking, and dressing. Approximately 6 months after onset, the patient was discharged to the special elderly nursing home affiliated with this hospital. Concerning the final assessment of the patient at discharge, the upper limb Fugl-Meyer Assessment (FMA)[9,10] score, at 14/66, had changed compared with the initial assessment. The numbness in the paralyzed upper limb, at 7/10, as measured with the Numerical Rating Scale (NRS) (where 0 = none and 10 = severe), signified that numbness had persisted at a level higher than that immediately after the infarction onset. In assessing numbness using the Pain Catastrophizing Scale (PCS), which is an assessment of the cognitive aspects of pain, the patient scored 11/20 for rumination, 10/20 for helplessness, and 4/12 for magnification, which led to suspicion of pain catastrophizing. In addition, the patient often remarked on the paralyzed limb in a manner suggestive of decline in physical representation, such as "I don't feel that I am moving it myself" and "I don't feel that it is my own hand." Therefore, we considered that that patient had experienced a decline in the sense of agency, that is, "I am carrying out the movement myself," and the sense of ownership, that is, "This is my own body." For this reason, we proceeded to evaluate the sense of agency as "I am moving the hand" and sense of ownership as "This is my own hand" using the NRS (where 0 = not at all and 10 = definitely), and the results were 7/10 for sense of agency and 5/10 for sense of ownership, which confirmed the decline in physical representation. We also used the Bath Complex Regional Pain Syndrome body perception disturbance scale (BPDS) to evaluate abnormal physical sensations in the paralyzed upper limb and obtained a score of 42/57.

Method of Intervention

iNems Training. We focused on the fact that this patient, in addition to motor paralysis and numbness, presented with decline in physical representation in the brain (Supplementary Data 2). Therefore, we devised a training system (iNems) that is capable of sensing scalp-recorded nerve activity. We added iNems training to the existing rehabilitation program (upper and lower limb functional practice and practice of daily routine motion, walking, and dressing). iNems training was performed for 10 minutes per day, 5 days per week, for 6 weeks.

Evaluation of the iNems Training

Neural Activity at Rest and While Imagining Fingertip Movement on the Paralyzed Side. The neural activity at rest was measured for 2 minutes using electroencephalography (Neurofax; Nihon Kohden, Inc, Tokyo, Japan) (Supplementary Data 3). Brain activity during motor imagery was determined by calculating the change in neural activity by subtracting the data at the end of the intervention from the data at the start of intervention. Regarding the subtraction method, data from 18 electrode sites measured at the start and after the intervention were calculated in text format using EEG FOCUS (Nihon Kohden, Inc, Tokyo, Japan), an EEG software program, and the brain activity data were obtained by subtracting the data at the start of the intervention from the postintervention data.

Mental and Physical Function. In line with the initial evaluation prior to iNems training, responses to questions on sense of agency, sense of ownership, and numbness intensity were scored using the NRS, and the FMA, passive ROM of the finger (index finger), PCS, and BPDS were administered prior to the final training of each week. The number of times the imagery switched from an image of the finger-flexed position to an image of the finger-extended position during the iNems training was recorded as the number of times that the desired motor imagery was accomplished. After completion of each training, we carried out assessments with "yes" or "no" responses to evaluate the consistency of whether successful imagining and feedback by imagery switching happened "without deviation or discomfort" and whether "the image switched as a result of imagination" with regard to whether neural activity related to motor imagery was reflected.

Ethical Consideration

This case was reported with the approval of the Watanabe Hospital Ethics Committee (Approval No. H29-01) and after sufficient explanation of the summary of the case report was provided to the patient and his written consent was secured.

Results

Scalp-Recorded Nerve Activity at Rest and During Motor Imagery

There was higher activity in the medial prefrontal cortex in the α wave band during rest at the end of the intervention compared with the initial assessment (Figure 2-1). The neural activity in the nu (μ) wave band at the time of motor imagery of the paralyzed fingers showed higher activity in the right sensorimotor-related region, mainly in the supplementary motor cortex, at the end than at the start of the intervention (Figure 2-2).

Mental and Physical Function (Table 1)

The paralyzed upper-limb FMA improved from 9/66 at the start of intervention to 14/66 at the end of the intervention. While the ROM of the finger was at the metacarpophalangeal joint (MP), 90°; proximal interphalangeal joint (PIP), 55°; and distal interphalangeal joint (DIP), 25° at the start of intervention, PIP and DIP improved into the movable region of 95° and 60°, respectively, at the end of the intervention. For the paralyzed upper limb, the sense of agency as measured with the NRS improved from 7 to 10, while the sense of ownership improved from 5 to 10. Numbness, as measured with the NRS, remained unchanged at 7/10 even after 6 weeks. With regard to PCS, the

Table 1. Evaluation of Mental and Physical Status.

	Start of Intervention	6 Weeks Later
FMA (U/E)	9/66	14/66
ROM of index finger		
Left MP	90°	90°
PIP	55°	95°
DIP	25°	60°
Numbness (NRS)	7/10	7/10
PCS		
Rumination	11/20	3/20
Helplessness	10/20	6/20
Magnification	4/12	0/12
Sense of self-agency (NRS)	7/10	10/10
Sense of self-ownership (NRS)	5/10	10/10
BPDS	42/57	2/57
HDS-R	24/30	24/30

Abbreviations: FMA, Fugl-Meyer Assessment; ROM, range of motion, MP, metacarpophalangeal joint; PIP, proximal interphalangeal; DIP, distal interphalangeal; NRS, Numerical Rating Scale; PCS, Pain Catastrophizing Scale; BPDS, The Bath CRPS body perception disturbance scale; HDS-R, Hasegawa Dementia Rating Scale–Revised.

rumination score decreased from 11 to 3, helplessness, from 10 to 6; and magnification, from 4 to 0, showing improvement in pain catastrophizing. The BPDS improved from 42 to 2.

Degree of Success in Motor Imagery Formation

During the first week of iNems training, the mean number of times in 10 minutes that motor imagery was accomplished was 9.4 ± 6.6 (0 times on the first day), but this gradually increased through training to reach 66.2 ± 6.2 times in 10 minutes during the last week, 6 weeks later. The patient answered "yes" to questions concerning the integrity of training, after all training sessions were conducted.

Discussion

Concerning the higher neural activity in the medial prefrontal cortex in terms of the α wave band at the end than at the start of the intervention, this area is considered related to forming a plan of action[11] and is considered the central area of the default mode network (DMN), which is active at rest. Baliki et al[12] reported that disruption of the DMN is the root of cognitive and behavioral disorders associated with chronic pain[12] This suggests that the DMN is associated with chronic pain and pain catastrophizing. As we found improvement on the PCS after 6 weeks, we considered that the results concerned scalp-recorded nerve activity reflecting neurophysiological changes associated with PCS improvement.

Furthermore, with regard to the increased neural activity from the bilateral supplementary motor cortex to the lesioned sensorimotor cortex, the supplementary motor cortex is a region that controls central motor imagery creation and the activity of the motor cortex[13]; therefore, the increased neural activity in this region increased the activity of the sensorimotor cortex that controls the paralyzed side, thereby improving motor function. Furthermore, this region plays a part in the mirror neuron system (MNS).[14] The attenuation of mu rhythms reflects elevated neural activity and is associated with MNS activity as a downstream indication.[15] This system is known to play a role in the mapping of motor information that is visually input to a brain region without actually executing a movement and is largely involved in the execution of motor intention.[16] Frenkel-Toledo et al[17] examined the association between the MNS and mu wave suppression in stroke patients by observing their movements and reported that mu wave suppression was milder in the impaired hemisphere compared with the normal hemisphere. This suggests that the motor function state of the brain is deeply associated with mu waves that serve as a marker of MNS activity. The elevation of activity in the supplementary motor area through iNems training suggested the possibility that a neural base for movement execution had been formed. Hence, we considered that the FMA score and the ROM improved as a result of successful motor imagery-formation increase.

We identified improvements in the patient's sense of agency and ownership with regard to the paralyzed fingers. To raise the sense of agency, it is important to match in the brain the predictive information that would evoke movement (efferent copy) with the actual sensorimotor information.[18] Conversely, the sense of ownership reportedly arises from "multisensory integration between vision and somatosensation etc."[19] In addition, MNS activation occurs only when the subject engages in a goal-oriented activity, that is, when the subject performs a purposive, meaningful action through the observation of movements.[20] Moreover, MNS activation occurs when there are interactions between prediction or intention and actual sensory information.[21] In this study, the patient was able to carry out the training without consistency issues, while exhibiting improved MNS activity, including the supplementary motor cortex, which is responsible for the occurrence of the sense of agency and ownership.[22] We considered that in training, the actively created intent to move and the visual information fed back were compared and resulted in learning. Additionally, considering that the PCS score improved and as it is known that pain catastrophizing during the acute phase reduces the frequency of afflicted-limb use,[23] there is a strong relationship between the PCS and the assessment of the sense of agency and ownership. Since the posterior insular cortex, which is regarded as the area responsible for chronic pain,[24] is associated with changes in the sense of ownership,[25] it appears that the PCS score also improved along with improvement in the sense of ownership.

Regarding the improvement in the BPDS score, because the patient carried out training with active and visual awareness of the paralyzed limb, we considered that distortion of the body image may have improved along with the improvement in the patient's sense of agency and ownership, ultimately leading to BPDS improvement. Conversely, as to the fact that no change was observed in the intensity of numbness, since the imaging findings for this case suggested significant influence of organic damage to this upstream pathway, the iNems training may have not been sufficient to effect change.

Conclusion

iNems training may improve the patient's motor function and reduce pain symptoms, which we believe may result from changes in brain activity at rest and scalp-recorded nerve activity in the sensorimotor region associated with these improvements. iNems training, which takes advantage of the characteristics of brain waves with high time resolution, resulted in behavioral changes to the paralyzed upper limb and in neurophysiological changes, which suggested that it may be used as a novel neurorehabilitation tool. However, in the future, it would be necessary to further examine this training protocol by reestablishing the intervention period, frequency, and difficulty to address the lack of therapeutic effect on numbness.

Author Contributions

TK contributed to conception and design; contributed to acquisition, analysis, and interpretation; drafted manuscript; gave final approval; agrees to be accountable for all aspects of work ensuring integrity and accuracy. OK contributed to design; contributed to acquisition and analysis; drafted manuscript; agrees to be accountable for all aspects of work ensuring integrity and accuracy. HN contributed to conception; contributed to interpretation; critically revised manuscript; agrees to be accountable for all aspects of work ensuring integrity and accuracy. TU contributed to design; contributed to analysis; agrees to be accountable for all aspects of work ensuring integrity and accuracy. SM contributed to design; contributed to interpretation; critically revised manuscript; gave final approval; agrees to be accountable for all aspects of work ensuring integrity and accuracy.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

Supplemental Material

Supplemental material for this article is available online.

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