Effect of Post-Stroke Motor Training on EEG Movement-Related Cortical Potentials

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Research

Keywords: EEG, stroke rehabilitation, motor training, neuroplasticity, robot-assisted therapy, movement-related cortical potentials

Posted Date: August 2nd, 2020

DOI: https://doi.org/10.21203/rs.3.rs-50667/v1

Abstract

Background

Rehabilitation of post-stroke patients with motor impairments promotes re-learning of lost motor functions through the brain neuroplasticity. Monitoring of electroencephalogram (EEG) signals has the potential to show neuroplasticity changes that take place during motor training.

Methods

In this study, an EEG-derived time-domain pattern namely movement-related cortical potential (MRCP) was deployed to assess the effect of motor training in seven post-stroke patients. Patients were divided into two groups; group A comprising four subjects with supratentorial lesions and group B consisting of three subjects with infratentorial lesions. Both groups participated in motor training with an AMADEO hand rehabilitation device. During pre and post-training periods, EEG signals at eight selected electrodes were recorded. In addition, hand-kinematic parameters, and clinical tests were measured at the beginning and the end of all training sessions.

Results

The negative peak of the MRCP signals decreased at all electrodes and reached significance in seven of eight electrodes for group A after 12 training sessions, while it was decreased at all electrodes and reached significance in two of eight electrodes for group B after 24 sessions according to paired t-test ($p < 0.05$). Moreover, these MRCP changes correlated with improvements in kinematic parameters and clinical test results for both groups.

Conclusions

This study shows that robot-assisted training that improves clinical outcomes is associated with MRCP pattern changes. Subjects with infratentorial strokes improved slower clinically compared to subjects with supratentorial strokes. This was consistent with the longer rehabilitation required for this group of patients to produce significant changes in MRCP. The reduction of negative peaks of the MRCP signal indicates that neurological pathways are established and less cortical resources are needed for motor tasks. This study demonstrates the significance of EEG as a practical and low-cost tool in detecting patterns associated with brain neuroplasticity in the course of motor re-learning.

Ethics Approval

The procedures performed in this study were approved by the University of Wollongong Ethics Committee (Ethics application number: 2014/400) on 03/07/2017.

Introduction

According to the recent annual report of the World Stroke Organization, approximately 14 million people had their first-time stroke in 2019 and 80 million people lived with the impact of stroke globally (1). The effects of stroke vary among patients and it depends on the type of stroke, the brain part that is damaged, and the amount of damage caused by it. Generally, stroke results in changes in the level of consciousness, changes in behavioral styles, and impairment of cognition, perception, language, sensory, and motor skills. Motor skills impairment is the predominant effect of the stroke. Specifically, the impairment of hand functions limits the independence of stroke survivors.

After the stroke, re-learning of lost motor functions is achieved with training strategies such as physiotherapy (2, 3), constraint-induced movement therapy (4, 5), mirror-box therapy (6, 7), virtual reality therapy (8, 9), and robot-assisted therapy (10, 11). All these types of training strategies promote the mechanism of neuroplasticity. The neuroplasticity is a neurological adaption in the brain where new neural pathways are established, existing pathways are reinforced and adjacent surviving neuronal tissues assume the role of the damaged neuronal tissues (12, 13).

The effect of rehabilitation training on brain activities helps to better understand the mechanism of recovery after stroke which in turn can facilitate the development of advanced rehabilitation training strategies. Many technologies are used in the literature to determine the effect of various motor training. Examples include electroencephalography (EEG) (14–24), magnetoencephalography (MEG) (25), functional magnetic resonance imaging (fMRI) (26, 27), functional infrared spectroscopy (fNIRS) (28, 29), transcranial magnetic stimulation (TMS) (30, 31) and transcranial direct-current stimulation (tDCS) (32). Among these technologies, EEG is a low-cost, safe, and user-friendly method of recording brain activity that has been a popular choice in the literature to determine training effects on brain activities during motor tasks.

There are two types of EEG-derived patterns that are associated with movement and have been used to assess the effect of motor training. One of these patterns is known as event-related desynchronization/event-related synchronization (ERD/ERS). ERD is a frequency-specific power decrease mostly in alpha (8–13 Hz) and beta (13–30 Hz) frequency bands of EEG during the preparation of a movement until its onset which then increases after motor execution denoted by ERS (33). The other EEG-derived pattern appears in a time-domain called movement-related cortical potential (MRCP). MRCP is a slow event-related potential that appears in the delta frequency band of EEG as a direct-current shifts up to 2 s before cue-based as well as self-initiated movements (34). MRCP has three pre-movement components, which have been widely addressed in the literature that could indicate the effect of motor training (18–24). The first pre-movement component is a slow decrease in the cortical potential that starts around 2 s before movement onset (in this paper it is called Bereitschaftspotential 1 (BP1)). The second pre-movement component is a steeper decrease in cortical potential and starts at about 0.5 s before movement onset (termed as Bereitschaftspotential 2 (BP2)). The third pre-movement component of the MRCP is the lowest negative potential near the movement onset (defined as the negative peak (Npeak)).

In the literature, the variations in the amplitude of MRCP components due to motor training or skill acquisition have been reported with conflicting results. For instance, Taylor (18) observed that the amplitude of MRCP increased with the improvement in response time after single-session training of finger motor tasks. Lang et al. (19) demonstrated an increase in the MRCP amplitude with improvement in task performance during a visual-motor activity. Niemann et al. (20) observed a significant decrease in the amplitude at some electrodes during a complex hand movement task performed by healthy participants. Some other studies also reported a decrease in the amplitude of the MRCP after the subjects achieved competency in motor task with practice (21–24). Notably, all these studies demonstrate the effects of various motor training protocols in healthy participants on the MRCP signal. Moreover, these studies overlook the factor of stroke lesion location during motor training design and analysis of the results, although several authors reported that the post-stroke recovery during motor skills acquisition after rehabilitation training depends upon the lesion location (35–39).

This study focuses on the motor training effect occurring in post-stroke patients using the MRCP signal. It also aims to investigate the effect of different lesion locations on the MRCP signal after the stroke patients completed the rehabilitation training. By establishing the effect of motor training on MRCP features with post-stroke patients, this study can be a stepping-stone in guiding therapists to adjust the difficulty of rehabilitation training to continually challenge the subjects, induce higher degrees of brain neuroplasticity, and to enhance consequent therapeutic outcomes.

In the approach deployed in this research, post-stroke patients underwent robot-assisted motor training of their affected hand with the help of an AMADEO rehabilitation device. An EEG acquisition system extracted MRCP signals during pre and post-training protocols. The improvements in hand motor skills after the training were determined using clinical tests and hand-kinematic parameters measurement. The clinical tests included the Fugl–Meyer Assessment (FMA) for upper extremity and Motor Assessment Scale (MAS). The hand-kinematic parameters consisted of hand strength measured during flexion (force-flexion), hand strength measured during extension (force-extension), and hand range of movement (HROM). Also, variations in MRCP features were correlated with improvements in hand motor skills in this paper.

Compared to the previous work, the study presented in this paper is novel and unique. The MRCP signal has been deployed previously but only for healthy subjects in non-clinical applications. For example, Wright et al. (23) observed a reduction in the amplitude of MRCP features when participants learned to play guitar after five weeks of training. Jochumsen et al. (24) reported reduced MRCP features' amplitude when healthy participants completed 6 training sessions of simulated laparoscopic surgery training with their non-dominant hand. In this study, the MRCP signal is used to demonstrate the effect of designed robot-assisted training in post-stroke patients and identifying the effect of stroke lesion location on the rehabilitation process. The results produced by the study are validated by benchmarking against standard clinical methods and procedures.

This paper is structured as follows. The material and method section provides details of equipment used in the experimental work, participants' information, pre and post-training protocols, motor training protocols as well as data processing details and statistical analysis. The analysis of the EEG data, the clinical test results, the hand-kinematic parameters' results for both groups A and B, and extended study of group B are provided in the following section. The discussion section highlights the main findings, implications, and limitations of the study. At the end of the paper, some conclusions are drawn and future potential of the work is discussed.

Materials And Method

AMADEO Hand Rehabilitation Device

Robot-assisted therapy is widely investigated and coming into clinical practice for the rehabilitation of post-stroke patients (40, 41). AMADEO (Tyromotion GmbH, Graz, Austria) is a state-of-the-art rehabilitation device designed for fine motor skill improvement in patients with spinal cord injury and stroke (42). It is gaining significant interest in both research and clinical communities (41). AMADEO is specially designed for distal upper-extremity motor recovery of patients (43). It has five degrees of freedom that allow passive, assistive as well as the active movement (with the help of 2D interactive games) of fingers and thumb. Many studies have used AMADEO for post-stroke rehabilitation. For instance, Xianwei et al. (44, 45) used AMADEO for fine finger motor recovery of post-stroke patients. A novel algorithm incorporating assist-as-needed, integrated into AMADEO demonstrated a 35% increase in the hand movement after multi-session training. The same research group studied the effect of 18 sessions of motor training with AMADEO on stroke patients and showed significant improvements in finger strength, range of hand movement, and coordination (46).

In this study, an AMADEO standard therapy program is used for motor training of patients' stroke affected hands. The force-flexion, force-extension, and HROM parameters (termed as hand-kinematic parameters) of all patients during pre and post-training protocols were measured using the AMADEO assessment tool.

EEG Acquisition System

EEG signals were acquired during pre and post-training protocols to extract the MRCP signal for self-paced hand movements. The EEG signal was recorded using 32-channel Ag/AgCl Quick-Cap (Compumedics-Neuroscan) according to the 10–20 electrode positioning system. The Grael 4K EEG amplifier was configured for a sampling frequency of 2048 Hz, bandwidth DC-2048 Hz, resolution 24-bit, and input range of 600 mVpp. The FPz electrode was used as a ground electrode and a separate electrode was placed on the ipsilateral earlobe as a reference. The impedance of each electrode was set below 5 kΩ. The EEG acquisition software used in this study is CURRY 8X (Compumedics-Neuroscan), which allows both offline and online data processing.

Participants

The following inclusion criteria were designed for recruiting participants:

(1) Range of age: 50–85

(2) Clinical stroke within 6 months to enrolment and MRI scan evidence of stroke consistent clinical presentation

(3) Stroke lesion location isolated to either supratentorial or infratentorial region

(4) Major impairment: hand motor (fine finger motor) deficits

(5) Impairment level: motor abilities suggested by MAS score (Sect. 7, hand movements, 1–5)

(6) Good cognition: suggested by widely adopted Rowland Universal Dementia Assessment Scale or Mini-Mental State Examination score of 26 or more out of 30 (47)

(7) Ability to understand verbal instructions in English

Based on the inclusion criteria, four post-stroke patients having supratentorial stroke lesion, and three patients with stroke in infratentorial regions were identified. All patients were right-hand dominant and had an ischemic stroke. The characteristics of all stroke patients are listed in Table 1. Every patient also received standard care at a local hospital, in addition to our intervention protocol. The participants gave their written informed consent before the experiment commencement.

Table 1
Basic characteristics of each stroke patient based on inclusion criteria

Category	Stroke Patient (Gender)	Age (Years)	Stroke Lesion Location	Onset Duration (Months)	Affected Hand	MAS-Hand Movement Test Score (0–6)
Group A	SP1 (Male)	82	Left motor cortex	3	Right	2
	SP2 (Male)	81	Left thalamic and internal capsule	2	Right	3
	SP3 (Male)	67	Left internal capsule	2	Right	2
	SP4 (Female)	51	Right basal ganglia	1.3	Left	4
Group B	SP5 (Female)	64	Left pons	4	Right	1
	SP6 (Male)	60	Left ponto-medullary junction	3	Right	1
	SP7 (Female)	63	Right pons	6	Left	1

The MAS-hand movement test scores in Table 1, acquired at the beginning of the motor training program, indicate that the patients in group A had better baseline finger movements while group B patients had limited finger movements consistent with the location of the lesion in their brain stem.

Motor Training Protocol

AMADEO standard therapy programs were used for motor training of the affected hand for both groups A and B. AMADEO allows four basic training programs which include Continuous Passive Motion (CPM), CPMplus, Assistive therapy, and Active therapy programs. In the beginning, the HROM for each patient was set according to the AMADEO protocol to the maximum potential range depending on each patient's hand size. The duration of each training session was 30 minutes and patients received three training sessions weekly up to four weeks (12 training sessions). The total training duration for each patient was 360 minutes in one month. However, patient SP7 completed 10 motor training sessions instead of 12 due to personal circumstances. The specific training programs for groups A and B are presented in Table 2.

Table 2
Motor training program for groups A and B

Category	Training Program
Group A	1) CPM training mode for 5 minutes; 2) CPMplus training mode for 5 minutes; 3) Assistive training mode for 10 minutes; and 4) Active training mode (2D interactive games) for 10 minutes.
Group B	1) CPM training mode for 10 minutes; 2) CPMplus training mode for 10 minutes; and 3) Assistive training mode for 10 minutes.

Although the total duration of motor training for group A was designed to be the same as for group B, active training mode was included only in group A training protocol because stroke patients in group B were unable to play the 2D games with their initial finger movements. At first, it was decided to compare the results of four weeks of training for both groups. However, it was anticipated that group B participants might require longer training-period due to lesion location in their brain stem (48).

Pre and Post-Training Protocols

Three baseline measurements were recorded for each patient in both groups A and B:

(1) The EEG signal was acquired while the subjects were asked to perform self-paced simple hand grasping movements with their affected hand in 8 to 10 blocks of 10 trials each. The time gap between any two trials was randomly varied from 8 s to 10 s. Patients focused their vision on a cross-mark to avoid random eye-movement artifacts. On each movement trial, a digital trigger was manually sent to the acquisition software (CURRY 8X, Compumedics-Neuroscan) to divide the continuous EEG data recording into epochs of 10 s duration.

(2) The clinical tests namely FMA test (wrist and hand sections only) (49) as well as the MAS tests (50), for both hand movement and advanced hand movements, were applied to assess the current hand motor abilities of patients. These clinical tests were denoted as FMA-wrist, FMA-hand, MAS-hand movements, and MAS-advanced hand movements in this paper.

(3) The force-flexion, force-extension, and HROM parameters for the affected hand were measured using the assessment tool on the AMADEO hand rehabilitation device.

These three measurements were repeated on day 13 after completion of 12 training sessions.

Data Processing and Statistical Analysis

Eight single EEG electrodes were used for the analysis (FC3, FC4, C3, C4, CP3, CP4, Cz, and CPz). In the literature, the C3, Cz, and C4 electrodes are commonly used to extract MRCP signals for hand motor tasks (18–24). In addition, five other electrodes (FC3, FC4, CP3, CP4, and CPz) were also explored in this experiment. The positions of all these selected electrodes in 32-channels Quick-Cap are shown in red color in Fig. 1. EEG signals from each selected electrode were first passed through a notch filter (49–51 Hz) to remove any power line noise. They were then passed through a low-pass filter with 5 Hz cut-off frequency and a high-pass filter with a 0.5 Hz cut-off because MRCP signals lie in the 0.5–5 Hz delta band range (51). The filtered EEG data were then divided into epochs using event triggers. The duration of these epochs was set from − 5 s to 5 s and where 0 s was the onset of the movement. MRCP has the lowest potential around the movement onset point (24, 34). The independent component analysis (ICA) algorithm was employed to remove eye-related artifacts from EEG data (52). These 10 s epochs are termed long epochs. Short epochs were then formed starting from − 3 s to 1 s.

Epoch data were averaged to obtain global MRCP signals at all eight electrode sites. For those patients who performed the movement with their right hand, odd number electrodes (FC3, C3, and CP3) were contralateral channels and even number electrodes (FC4, C4, and CP4) were ipsilateral channels. The reverse was true for the patients who performed the left-hand movement. For group analysis, these electrodes were designated contralateral FC (CLFC), contralateral C (CLC), and contralateral CP (CLCP) to indicate the contralateral representation for both right and left-hand movements. Similarly, to represent the ipsilateral side of both hand movements, the electrodes were designated ipsilateral FC (ILFC), ipsilateral C (ILC), and ipsilateral CP (ILCP). The electrodes Cz and CPz are central channels and therefore do not need to have their labels based on ipsilateral or contralateral positions. Hence, the electrodes used in the analysis were CLFC, CLC, CLCP, ILFC, ILC, ILCP, Cz, and CPz. The amplitude of the Npeak feature using averaged MRCP signals was extracted from the eight electrodes using a MATLAB toolbox called ‘visualEEG’ (53).

Along with EEG data analysis, clinical tests, hand force, and HROM measurements were also analyzed. The clinical tests (FMA-wrist, FMA-hand, MAS-hand movements, and MAS-advanced hand movements) were performed three times by each patient and the best scores were recorded according to the general rule of administration for these clinical tests. Whereas force-flexion, force-extension, and HROM parameters were also measured three times but their average values were used during analysis of the results.

Statistical significance was calculated in all three measurements (MRCP signal features, clinical tests, as well as hand-kinematic parameters) using a two-tailed paired t-test. The significant level of the t-test is reported at the alpha value of $p < 0.05$.

Results

EEG Data Analysis Results

In this section, results obtained from EEG data analysis for groups A and B are presented. For both groups, visible MRCP signals were obtained using the patients' data at all eight selected electrodes during pre and post-training periods. The averaged pre and post-training MRCP signals at all selected electrodes (ILFC, ILC, ILCP, CLFC, CLC, CLCP, Cz, and CPz) for group A and group B are shown in Fig. 2 and Fig. 3 respectively. The MRCP signals at all electrode sites are plotted for the time interval -1 to 1 s for better visualization of the changes that occur in the MRCP signals during motor training. For group A, visual inspection of the MRCP plots indicates that the post-training values of Npeak of MRCP signals are prominently decreased at all selected electrodes compared to their corresponding pre-training values. Whereas, MRCP plots for group B shows that the post-training Npeak values are considerably increased at ipsilateral electrodes (ILFC, ILC, ILCP), slightly decreased at contralateral electrodes and one of the central electrode (CLFC, CLC, CLCP, CPz) but remains the same at Cz central electrode.

Figure 4 (a) shows the column chart representation of the mean absolute pre and post-data values of the Npeak features of the MRCP signal with error bars for each electrode position for group A. The error bars were calculated using the standard deviation (SD) values for all eight electrodes. The Npeak amplitude at all eight electrode positions decreased compared to pre-training values. The application of paired t-test on Npeak values of group A revealed that its post-training values were statistically significant at ILC (p=0.005), ILCP (p=0.03), CLFC (p=0.035), CLC (p=0.027), CLCP (p=0.019), Cz (p=0.035) as well as CPz (p=0.014) compared to pre-training values as indicated by a '*' symbol in Fig. 4 (a). However, the decrease in post-training Npeak amplitude was not statistically significant at ILFC (p=0.118). Hence, it was concluded that group A participants showed a statistically significant decrease in Npeak amplitude in seven of eight selected electrodes after completion of training.

For group B, Fig. 4 (b) represents the bar-chart representation for mean absolute pre and post-training values for Npeak amplitude. An increase in all ipsilateral electrodes (ILFC, ILC, and ILCP) for post-training Npeak values was observed compared to their pre-training values. On the other hand, Npeak amplitudes at all contralateral and central electrodes (CLFC, CLC, CLCP, Cz, and CPz) either remained constant or decreased after the training. However, these changes were not statistically significant at any electrode's position ($p > 0.05$).

Clinical Tests Results

FMA-wrist, FMA-hand, MAS-hand movements, and MAS-advanced hand movements' tests were executed on day 0 and day 13 of the designed robot-assisted training for each stroke patient in group A and group B. These clinical tests were used to determine the physical improvements in the hand motor abilities of the patients.

Table 3 shows the average values for four clinical tests of group A in the mean (± SD) form. The paired t-test was applied between pre and post-training values on all four clinical tests. The significant change is indicated by bold values and a '*' symbol on the values in Table 3. For group A, FMA-wrist (p = 0.006),

FMA-hand ($p = 0.043$) as well as MAS-hand movements ($p = 0.035$). However, the MAS-advanced hand movement clinical test did not show statistically significant improvement ($p = 0.252$).

Table 3
Average clinical tests results for group A after 4 weeks of motor training (mean (± SD))

Assessment Period	FMA-Wrist Score (0–10)	FMA-Hand Score (0–14)	MAS-Hand Movements Score (0–6)	MAS-Advanced Hand Movements Score (0–6)
Pre-training (Week 0)	6.5 (± 2.4)	8.3 (± 2.6)	2.8 (± 1)	3.3 (± 2.8)
Post-training (Week 4)	**8.3 (± 2.1)***	**12 (± 1.2)***	**4.5 (± 1.3)***	4.3 (± 1.5)

For group B, the average clinical test results are presented in Table 4 in the form of the mean (± SD). The paired t-test was applied and the significance level is indicated as bold values and a '*' symbol on the values in Table 4. The paired t-test revealed that only the FMA-hand test ($p = 0.035$) showed statistically significant improvement for the patients in group B. Whereas, the FMA-wrist test ($p = 0.27$), MAS-hand movements test ($p = 0.423$) and MAS-advanced hand movements test did not show statistically significant improvements.

Table 4
Average clinical tests results for group B after 4 weeks of motor training (mean (± SD))

Assessment Period	FMA-Wrist Score (0–10)	FMA-Hand Score (0–14)	MAS-Hand Movements Score (0–6)	MAS-Advanced Hand Movements Score (0–6)
Pre-training (Week 0)	1.3 (± 1.2)	2.7 (± 1.5)	0.7 (± 0.6)	0.3 (± 0.6)
Post-training (Week 4)	2.7 (± 2.5)	**5.7 (± 2.1)***	1 (± 1)	0.3 (± 0.6)

Results for Hand-Kinematic Parameters

The AMADEO assessment tool allows the measurement of force-flexion, force-extension, and average HROM of fingers and thumb. To find the changes in these hand-kinematic parameters after the training, force-flexion, force-extension, and HROM were calculated at the pre and post-training periods for group A and group B.

For group A, Table 5 shows the mean (± SD) values of force-flexion, force-extension, and HROM obtained during pre and post-training protocols. The statistical significance levels between pre and post-values of all three kinematic parameters were calculated using the paired t-test. The pre and post-values of all these

kinematic parameters for hand movement recovery (force-flexion, $p = 0.028$; force-extension, $p = 0.048$; HROM; $p = 0.039$) showed statistically significant improvements.

Table 5
Average hand-kinematic parameters' results for group A after 4 weeks of motor training (mean (± SD))

Assessment Period	Force-Flexion (N)	Force-Extension (N)	HROM (%)
Pre-training (Week 0)	38.9 (± 14)	6.9 (± 8)	52.8 (± 34.9)
Post-training (Week 4)	**59.1 (± 8.4)***	**19.6 (± 8)***	**89.4 (± 15.9)***

Table 6 presents the average force-flexion, force-extension, and HROM values obtained from the AMADEO assessment tool for group B. Application of paired t-test between pre and post-values of all three kinematic parameters showed that improvements were not statistically significant.

Table 6
Average hand-kinematic parameters' results for group B after 4 weeks of motor training (mean (± SD))

Assessment Period	Force-Flexion (N)	Force-Extension (N)	HROM (%)
Pre-training (Week 0)	15.1 (± 15.9)	2.1 (± 2.6)	11.9 (± 18.3)
Post-training (Week 4)	31.1 (± 30.3)	5.6 (± 6.4)	39.7 (± 34.4)

Extended Training of Group B and its Results

Apart from the FMA-hand score, the above results revealed that 4 weeks of motor training did not have a significant effect on MRCP Npeak amplitude or other clinical tests and hand-kinematic parameters' results for post-stroke patients in group B. Therefore, it was decided to extend the training period for all participants in group B for another 4 weeks to determine whether the extension of the hand motor training affects MRCP Npeak feature, clinical tests, and hand-kinematics parameters.

The three brain stem stroke patients in group B underwent another phase of motor training that consisted of 4 weeks (12 sessions, 3 sessions per week) of advanced training protocols using the AMADEO device. During this extended training, patients received four levels of training each day consisting of CPM training mode for 5 minutes, CPMplus training mode for 5 minutes, Assistive training mode for 10 minutes, and Active training mode for 10 minutes. In this way, group B participants received two-phases of training using the AMADEO robot in which the second phase of training was slightly more intense compared to the first phase as it included training on active therapy. Moreover, the same three assessment procedures were conducted at the end of 8 weeks of the designed robot-assisted training of

hand as performed during the beginning of training (week 0) and at the end of the first phase of training (week 4).

The results obtained from the data analysis of week 8 were compared to that obtained during week 0 and week 4 to measure the effect of extending the training on MRCP Npeak amplitude and physical improvement in hand motor skills. Figure 5 shows the averaged MRCP signal plots at all eight electrodes, extracted from EEG data acquired before the rehabilitation training (week 0), at the end of the first phase of training (week 4) and after the completion of both phases of training (week 8) for brain stem stroke patients of group B. Visual inspection of the plots reveal that averaged Npeak amplitude of MRCP signal was decreased at week 8 with respect to corresponding value at week 0 for all electrode positions. Whereas, as stated above, the Npeak amplitude at week 4 was increased at ipsilateral electrodes, slightly decreased at contralateral and CPz electrodes, and remained the same at the Cz electrode compared to week 0.

To assess the significance of these variations, the MRCP Npeak feature was analyzed. The Npeak feature of the MRCP signal was extracted from the acquired EEG data after completion of two-phase training of group B. Figure 6 shows the bar-chart representation of average Npeak amplitudes at all eight electrodes for group B. A consistent decrease in average Npeak amplitude was observed for all selected electrodes after a total of 8 weeks of training when it is compared with week 0. When the paired t-test was applied, a significant change in Npeak was obtained at CLC ($p = 0.01$) and CPz ($p = 0.04$) electrodes. The significance level is indicated by a '*' symbol in Fig. 6. In contrast to these results, change in Npeak amplitude at all eight electrodes was not consistently decreased after the first 4 weeks of motor training compared to week 0. These results of MRCP Npeak analysis suggest that 4 weeks of rehabilitation is not a sufficient time to obtain consistent EEG signal changes for the brain stem stroke patients in group B. This outcome is consistent with clinical observations that patients with brain stem strokes are typically slower to recover motor function than patients with supratentorial strokes (48).

Table 7 shows the average results of FMA-wrist, FMA-hand, MAS-hand movements, and MAS-advanced hand movements' clinical tests. The two-tailed paired t-test was applied between their pre-training (week 0) and post-training 1 (week 4) values as well as between the pre-training (week 0) and post-training 2 (week 8) values. The results are presented in the form of the mean (± SD) and the significant change between these tests is indicated by bold values and a '*' symbol on the values. It is observed that only the FMA-hand test shows a significant change in all patients when they complete the first phase (4 weeks) of the intervention protocol. However, after 8 weeks of training, the patients show statistically significant improvement in two clinical tests i.e. FMA-hand ($p = 0.015$) and MAS-hand movements ($p = 0.038$).

Table 8 shows values for three hand-kinematic parameters which include force-flexion, force-extension, and HROM for group B during the pre-training, post-training 1, and post-training 2 periods. The values are presented in mean (± SD) and the statistical significance change is indicated by bold values and a '*' sign on the values. According to Table 8, none of the kinematic parameters show any significant change after motor training in the first phase (4 weeks). Whereas, a statistically significant improvement in all the

force-flexion ($p = 0.036$), force-extension ($p = 0.041$), and HROM ($p = 0.046$) parameters were observed when the patients completed their 8 weeks of training (two-phases of training).

Table 7
Average clinical tests results for group B after two-phases of training (mean (± SD))

Assessment Period	Clinical Tests Results			
	FMA-Wrist Score (0–10)	FMA-Hand Score (0–14)	MAS-Hand Movements Score (0–6)	MAS-Advanced Hand Movements Score (0–6)
Pre-training (Week 0)	1.3 (± 1.2)	2.7 (± 1.5)	0.7 (± 0.6)	0.3 (± 0.6)
Post-training 1 (Week 4)	2.7 (± 2.5)	**5.7 (± 2.1)***	1 (± 1)	0.3 (± 0.6)
Post-training 2 (Week 8)	3.7 (± 2.3)	**8 (± 2.6)***	**2.3 (± 0.6)***	1.3 (± 0.6)

Table 8
Average hand-kinematic parameters' results for group B after two-phases of training (mean (± SD))

Assessment Period	Hand-Kinematic Parameters' Results		
	Force Flexion (N)	Force Extension (N)	HROM (%)
Pre-training (Week 0)	15.1 (± 15.9)	2.1 (± 2.6)	11.9 (± 18.3)
Post-training 1 (Week 4)	31.1 (± 30.3)	5.6 (± 6.4)	39.7 (± 34.4)
Post-training 2 (Week 8)	**42.2 (± 24.9)***	**13.9 (± 6.8)***	**64.6 (± 24.8)***

Clinical tests and hand-kinematic parameters' results show that group B patients regained significant motor recovery of hand functions after 8 weeks of robot-assisted training and this was associated with a significant change in the Npeak of the MRCP at two sites. As mentioned before, these outcomes are consistent with clinical observations for this category of patients (48).

Discussion

The main purpose of this study was to investigate possible changes in the features of the MRCP signal when two groups of post-stroke patients with different lesion locations receive robot-assisted rehabilitation training for their impaired hand using AMADEO robot.

The EEG data analysis revealed that all participants in both groups A and B were able to generate MRCP signals during the self-paced motor task of their affected hand at all eight selected electrode positions.

The MRCP signal's Npeak was investigated for group A and group B separately to explore whether it is increased or decreased after the completion of 12 robot-assisted motor training sessions. Npeak amplitude for group A showed a statistically significant decrease after four weeks of training. Group B participants showed a statistically significant decrease in the Npeak at CLC and CPz electrodes after 24 training sessions.

To determine motor and functional improvements in hand motor skills, the clinical tests, and hand-kinematic parameters were analyzed. According to the results of clinical tests obtained after four weeks of robot-assisted training, group A showed statistically significant improvement in three out of four clinical tests. Whereas, group B showed improvement in only one clinical test after the first four weeks of training and in two clinical tests after eight weeks of training. The analysis of hand-kinematic parameters showed that post-stroke patients in group A gained significant improvements in all force-flexion, force-extension, and HROM values after completion of four weeks of the motor training program. Group B showed significant improvement in all the hand-kinematic parameters after completing 8 weeks of robot-assisted training.

The reported results reveal that the Npeak amplitude of the MRCP signal is decreased consistently in patients with supratentorial strokes (group A) after four weeks of training while it is decreased consistently in patients with brain stem strokes (group B) after eight weeks of training. These Npeak changes of both groups also correlate with improvements in clinical tests and hand-kinematic parameters' results. These results suggest that 4 weeks of rehabilitation is not sufficient time to induce significant MRCP signal changes for the brain stem stroke patients who comprise group B. This outcome is consistent with the clinical observation that patients with brain stem strokes are typically slower to recover motor function than patients with supratentorial strokes (48).

The decrease in MRCP Npeak amplitude after the designed robot-assisted motor training reflects that neurological pathways become more established so that fewer cortical resources are needed for motor planning and execution of tasks. This hypothesis is supported by studies in healthy participants available in the literature (20–24). However, further investigations are required to validate the occurrence of neuroplasticity.

To the best of our knowledge, this study is the first attempt to use the MRCP signal as an assessment tool to determine the effect of motor training in actual stroke patients. EEG is an easy and cost-effective method to assess changes in brain activation during functional motor activities (24). The results of this study indicate that EEG has future potential in clinical utility for stroke rehabilitation.

A larger number of participants in the study would have strengthened our confidence in the results. However, the number of potential participants was limited by the clinical availability of suitable participants within the time frame of the study. Participants in the study were relatively heterogeneous with regard to the length of time from stroke to onset of the intervention (see Table 1). It may be the case that with a more homogeneous group of participants more uniform and statistically significant data

could have been extracted. However, our inclusion criteria had to be wide; otherwise, clinical availability would have not allowed us to recruit a sufficient number of participants.

Conclusion

This paper demonstrated the feasibility of using the EEG signal as an assessment parameter for the determination of motor training outcomes for stroke patients with different lesion locations. We found that there was a statistically significant decrease in the Npeak amplitude of the MRCP signals for stroke patients with supratentorial lesions and they also demonstrated associated significant improvements in hand-kinematic parameters and clinical test outcomes after four weeks of training. While the infratentorial (brain stem) stroke patient showed a statistically significant decrease in Npeak as well as a significant improvement in kinematic parameters and clinical tests after eight weeks of training. We conclude that MRCP could be used as an assessment tool to determine motor training effects in both supratentorial and infratentorial strokes. Moreover, this technology has real potential as a practical and inexpensive therapeutic tool that could be used by therapists to detect neuroplasticity responses during stroke rehabilitation, and allow them to adjust the intensity of training challenges accordingly to enhance neuroplasticity responses and therefore therapeutic outcomes.

Abbreviations

EEG
Electroencephalogram
MRCP
Movement-related cortical potential
MEG
Magnetoencephalography
fMRI
Functional magnetic resonance imaging
TMS
Transcranial magnetic stimulation
tDCS
Transcranial direct-current stimulation
ERD
Event-related desynchronization
ERS
Event-related synchronization
BP1
Bereitschaftspotential 1
BP2
Bereitschaftspotential 2

Npeak
Negative peak
FMA
Fugl–Meyer assessment
MAS
Motor assessment scale
CPM
Continuous passive motion
HROM
Hand range of movement
ICA
Independent component analysis
SD
Standard deviation

Declarations

Ethics approval and consent to participate

The study was approved by the University of Wollongong Ethics Committee (Ethics application number: 2014/400), and all procedures performed under the approved study protocol. The written informed consent was obtained from all the participants before the experiment commencement.

Consent for publication

All the participants involved in the study provided their written informed consent for publication.

Availability of data and materials

The data collected during this study are available from the corresponding author on reasonable request

Competing interests

All authors declare no competing interest related to the research presented in this article

Author’s contributions

All authors were involved in the design of the experimental protocol. MB carried out the experiments. FN, GN, and HD supervised the study. GM recruited suitable participants. MB analyzed the collected data and interpreted the results. MB, GN, FN, and GM wrote and drafted the manuscript. All authors read and approved the final manuscript.

Acknowledgment

This research is jointly supported by The University of Wollongong and Higher Education Commission Pakistan. We thank Imran Khan Niazi, Research Fellow at Center for Chiropractic Research at New Zealand College of Chiropractic, who provided insight and expertise in designing the experimental protocol and interpretation of results. We thank the Departments of Rehabilitation and Neurology in the Illawarra Shoalhaven Local Health District with EEG development and recruitment of participants. We also thank the UOW Statistical Consulting Centre for providing help with the statistical analysis.

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Figures

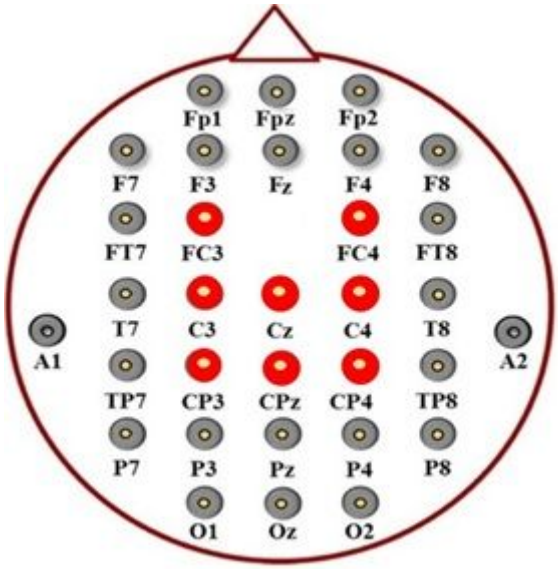

Figure 1

Positions of selected electrodes for this experiment

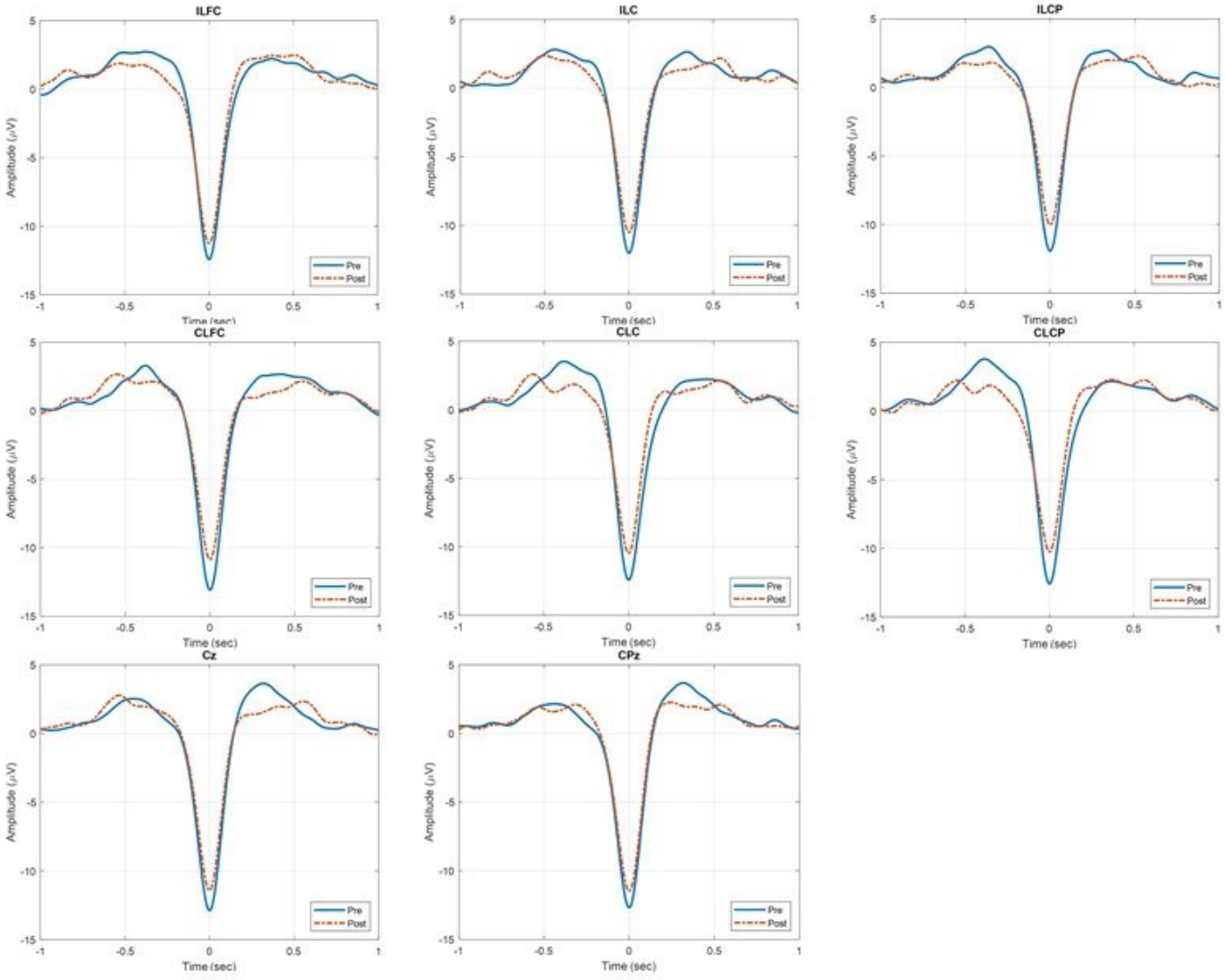

Figure 2

Average MRCP signals for group A at all channels over multiple-session training

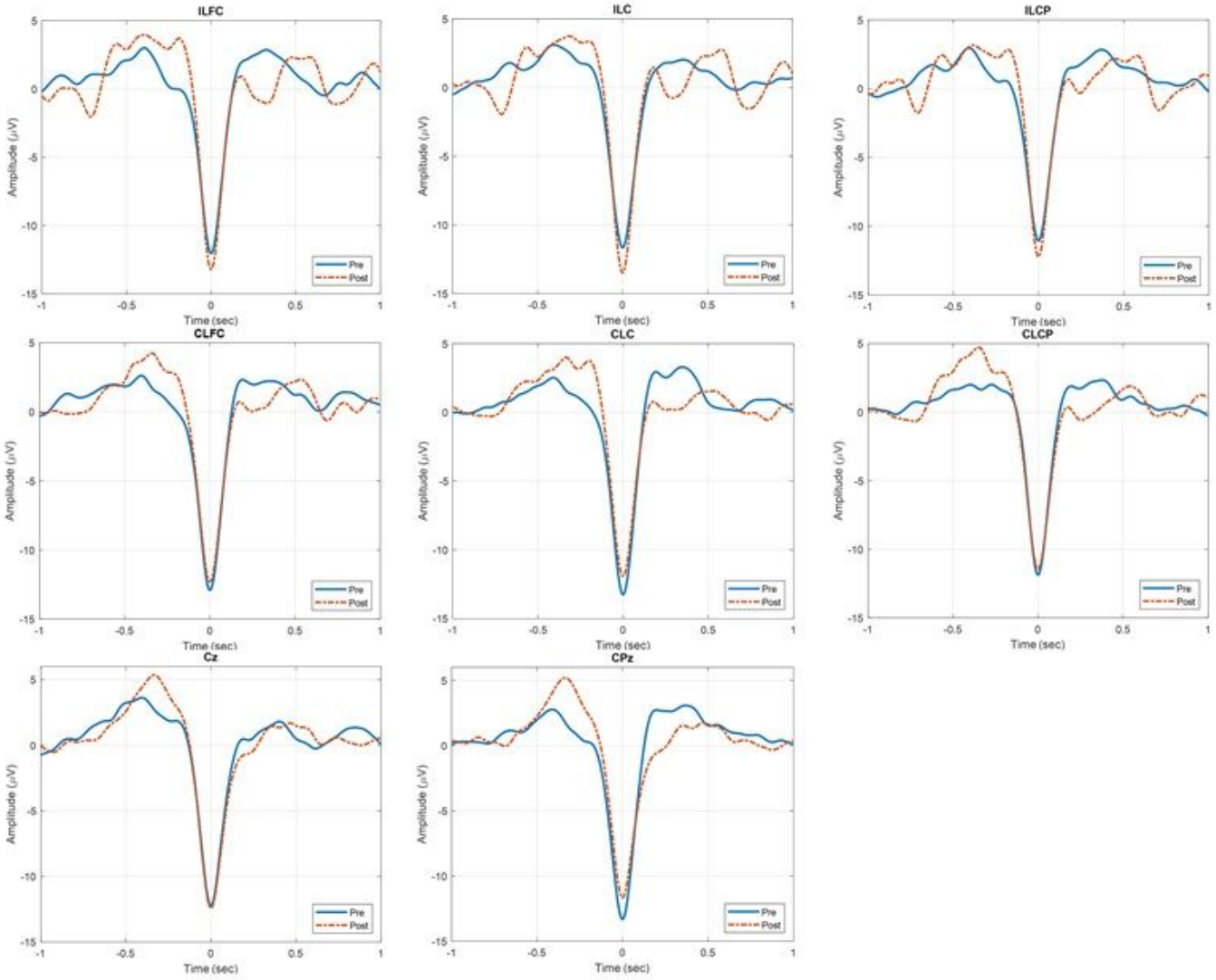

Figure 3

Average MRCP signals for group B at all channels over multiple-session training

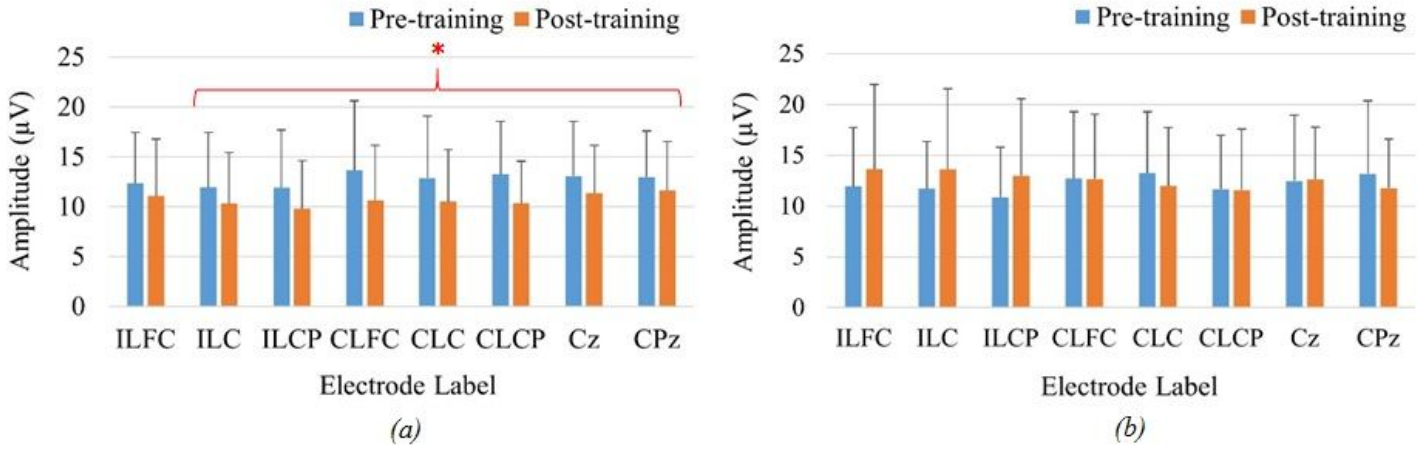

Figure 4

Mean absolute Npeak amplitude at pre-training and post-training periods (a) group A, (b) group B

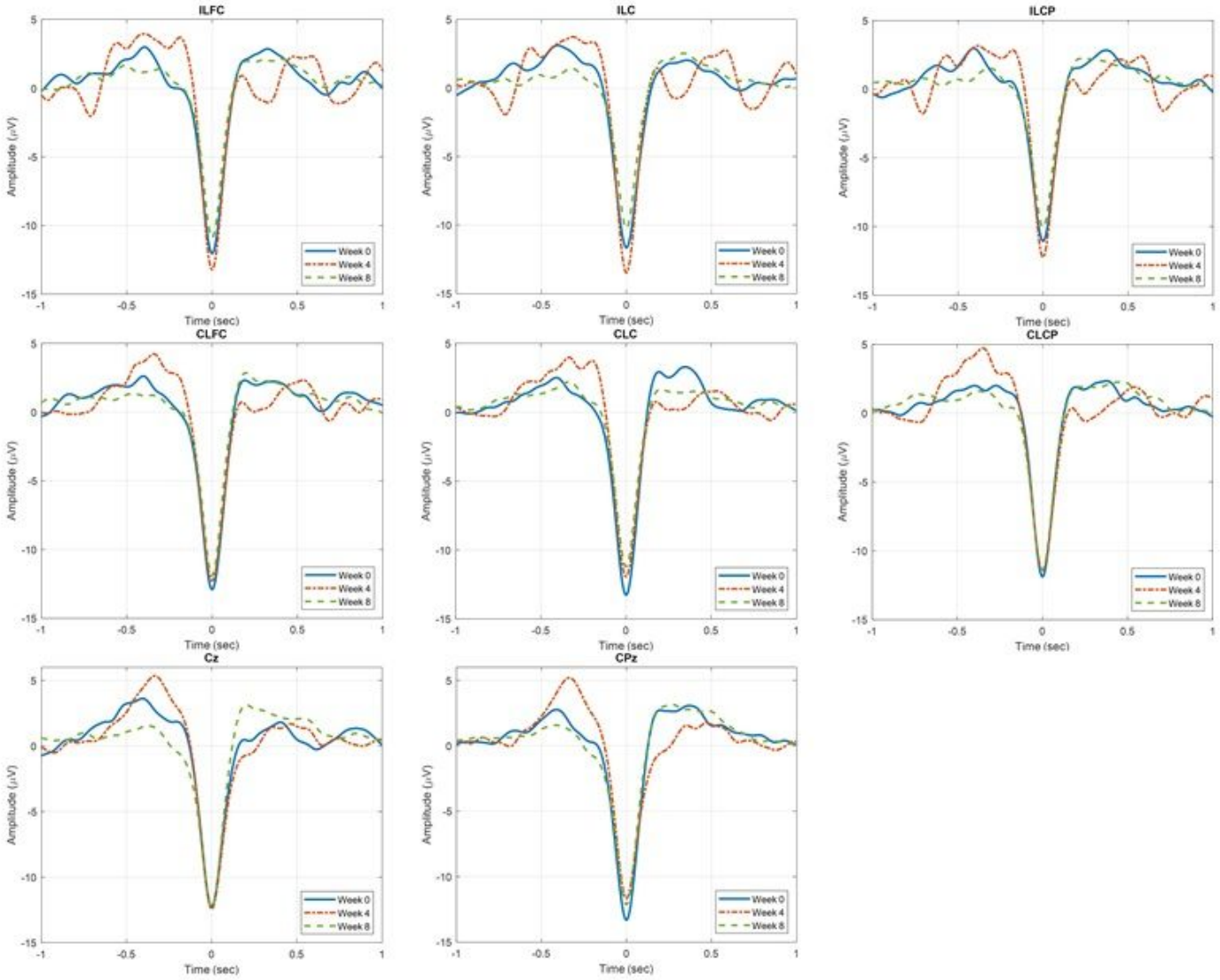

Figure 5

Average MRCP signals for group B after extended training at all channels over multiple-session training

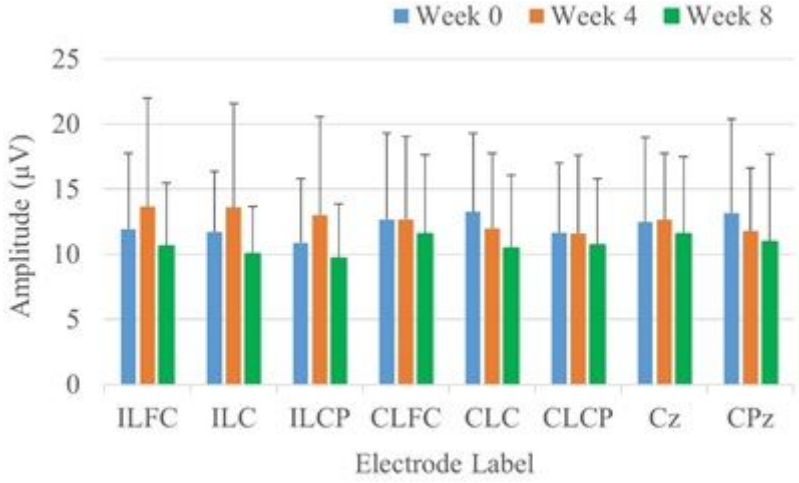

Figure 6

Mean absolute Npeak amplitude at week 0, week 4 and week 8 for group B