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Electroencephalographic markers of robot-aided therapy in stroke patients for the evaluation of upper limb rehabilitation

Patrizio Sale[a,*], Francesco Infarinato[a,*], Claudio Del Percio[a], Roberta Lizio[a], Claudio Babiloni[a,b], Calogero Foti[c] and Marco Franceschini[a]

Stroke is the leading cause of permanent disability in developed countries; its effects may include sensory, motor, and cognitive impairment as well as a reduced ability to perform self-care and participate in social and community activities. A number of studies have shown that the use of robotic systems in upper limb motor rehabilitation programs provides safe and intensive treatment to patients with motor impairments because of a neurological injury. Furthermore, robot-aided therapy was shown to be well accepted and tolerated by all patients; however, it is not known whether a specific robot-aided rehabilitation can induce beneficial cortical plasticity in stroke patients. Here, we present a procedure to study neural underpinning of robot-aided upper limb rehabilitation in stroke patients. Neurophysiological recordings use the following: (a) 10–20 system electroencephalographic (EEG) electrode montage; (b) bipolar vertical and horizontal electrooculographies; and (c) bipolar electromyography from the operating upper limb. Behavior monitoring includes the following: (a) clinical data and (b) kinematic and dynamic of the operant upper limb movements. Experimental conditions include the following: (a) resting state eyes closed and eyes open, and (b) robotic rehabilitation task (maximum 80 s each block to reach 4-min EEG data; interblock pause of 1 min). The data collection is performed before and after a program of 30 daily rehabilitation sessions. EEG markers include the following: (a) EEG power density in the eyes-closed condition; (b) reactivity of EEG power density to eyes opening; and (c) reactivity of EEG power density to robotic rehabilitation task. The above procedure was tested on a subacute patient (29 poststroke days) and on a chronic patient (21 poststroke months). After the rehabilitation program, we observed (a) improved clinical condition; (b) improved performance during the robotic task; (c) reduced delta rhythms (1–4 Hz) and increased alpha rhythms (8–12 Hz) during the resting state eyes-closed condition; (d) increased alpha desynchronization to eyes opening; and (e) decreased alpha desynchronization during the robotic rehabilitation task. We conclude that the present procedure is suitable for evaluation of the neural underpinning of robot-aided upper limb rehabilitation. ***International Journal of Rehabilitation Research*** **00:000–000 Copyright © 2015 Wolters Kluwer Health, Inc. All rights reserved.**

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Background

The incidence of stroke in Italy varies from 250 to 300/100 000. About 130 000 Italians suffer from first-ever stroke each year and 50 000 from recurrent stroke (Indredavik *et al.*, 1998, 1999, 2009; Blinzler *et al.*, 2010; Mishra *et al.*, 2010). It is the leading cause of permanent disability in developed countries; treatments of stroke survivors are aimed at a faster and more efficient motor recovery (Franceschini *et al.*, 2012). The effects of stroke may include sensory, motor, and cognitive impairment as well as a reduced ability to perform self-care and participate in social and community activities (Mayo *et al.*, 1999). The acute phase immediately following a stroke event is a time of extreme dynamic evolution in a patient's condition. In the following days (10–60 days), the clinical state of a certain patient could place him/her on one of several possible recovery paths, thus providing quantitative clues to late prognosis (Wevers *et al.*, 2009; Langhorne *et al.*, 2011). Up to 60% of patients with stroke have poor dexterity in the upper extremity late after onset (Veerbeek *et al.*, 2011; Sale and Franceschini, 2012).

Numerous studies have shown that ascertaining the effectiveness of rehabilitative interventions on conditions leading to long-term disability, such as stroke, is a complex task because the outcome depends on many interacting factors (Semprini *et al.*, 2009; Langhammer and Lindmark, 2012; Sale *et al.*, 2012; Fazekas, 2006, 2013; Huang *et al.*, 2012). The use of robotic systems in upper limb motor rehabilitation programs has already been shown to provide safe and intensive treatment to patients with motor impairments because of a neurological injury. Several studies have shown the advantages of robotic

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therapy in chronic poststroke patients for delivering repetitive training, thus facilitating high-intensity and volume training, even if no consistent influence on functional abilities was found and evidence of better results providing intensive treatments, both robotic and conventional rehabilitative techniques, was found (Mehrholz *et al.*, 2008; Bovolenta *et al.*, 2009; Lo *et al.*, 2010; Bovolenta *et al.*, 2011). The robot-aided therapy was shown to be well accepted and tolerated by all patients. Previous studies have shown a significant decrease in motor impairment in the paretic upper limb after the robot-aided treatment both in chronic and in subacute patients on the shoulder and elbow joints (Posteraro *et al.*, 2009, 2010; Bovolenta *et al.*, 2011; Mazzoleni *et al.*, 2011; Zollo *et al.*, 2011; Leon *et al.*, 2014; Sale *et al.*, 2014a, 2014b, 2014c).

The above-mentioned studies suggest that robot-aided treatment is a useful approach to improve motor performance in stroke patients. However, it is not known whether a specific robot-aided rehabilitation can induce beneficial cortical plasticity in stroke patients. In the last few years, several studies have shown that quantitative analysis of electroencephalographic (EEG) rhythms in awakening patients at rest (eyes closed) is a low-cost, easy to perform, and widely available neurophysiological approach for the study of cortical activity in stroke patients. Specifically, previous studies have shown that compared with normal elderly individuals, stroke patients were characterized by a higher amplitude of delta rhythms (1–4 Hz), often accompanied by a decrease in alpha rhythms (8–12 Hz) particularly at electrodes overlying the ischemic regions (Murri *et al.*, 1998; Fernández-Bouzas *et al.*, 2000; Luu *et al.*, 2001). It has also been reported that the amplitude of resting EEG rhythms can aid monitoring of brain pathophysiology and prediction of stroke evolution (Cuspineda *et al.*, 2007; Finnigan *et al.*, 2004, 2007). Indeed, a relationship was found between amplitude of EEG delta rhythms and delta/alpha ratio acquired within 8 and 15 h after stroke and Institutes of Health Stroke Scale Scores (NIHSSS) at 30 days after stroke (Finnigan *et al.*, 2004, 2007). Similarly, the global power of EEG data acquired within 72 h after stroke onset was significantly correlated with Rankin scale scores at 3 months after stroke (Cuspineda *et al.*, 2007). More recently, the efficacy of an EEG-based motor imagery brain–computer interface technology system coupled with MIT-Manus was investigated, showing the correlation of the revised brain symmetry index with motor improvements indexed by the Fugl-Meyer Assessment of Motor Recovery After Stroke (FM) score (Ang *et al.*, 2014).

The present study aimed to describe a methodological approach to study the neural underpinning of robot-aided upper limb rehabilitation in stroke patients. To address this issue, we recorded EEG data from a postacute and a chronic stroke patient during resting state and a robotic rehabilitation task before and after a program of 30 daily rehabilitation sessions to show that this methodological approach allows the recording of high-quality EEG data. The quality of the EEG data was evaluated by the rate of artifact-free EEG epochs and by the features of dominant alpha rhythms (about 8–12 Hz) during resting state and the robotic rehabilitation task. It is noteworthy that because of the limited number of observations, we could not test specific hypotheses, namely, the modulation of EEG cortical activity after robot-aided therapy. For this reason, we report exclusively the global cortical activity of two stroke patients before and after the rehabilitation program.

Methods

Patients

A 56-year-old male patient, with chronic stroke-related lesions, partial anterior circulation infarct in the right hemisphere (August 2009), left hemiparesis with a moderate/severe upper limb impairment, and moderate disability (Barthel Index 61/100), and a 75-year-old female patient, with subacute stroke-related lesions, left hemisphere right hemiparesis with a severe upper and lower limb impairment, and severe disability at the admission (Barthel Index 2/100) were recruited. The chronic patient had experienced the acute event at least 2 years before the study (time from onset of neurological damage 21 months) and the subacute stroke patient had experienced the acute event at least 29 days before the study. Both patients provided their informed consent according to the Declaration of Helsinki. They were free to withdraw from the study at any time. The procedure was approved by the local Institutional Ethics Committee.

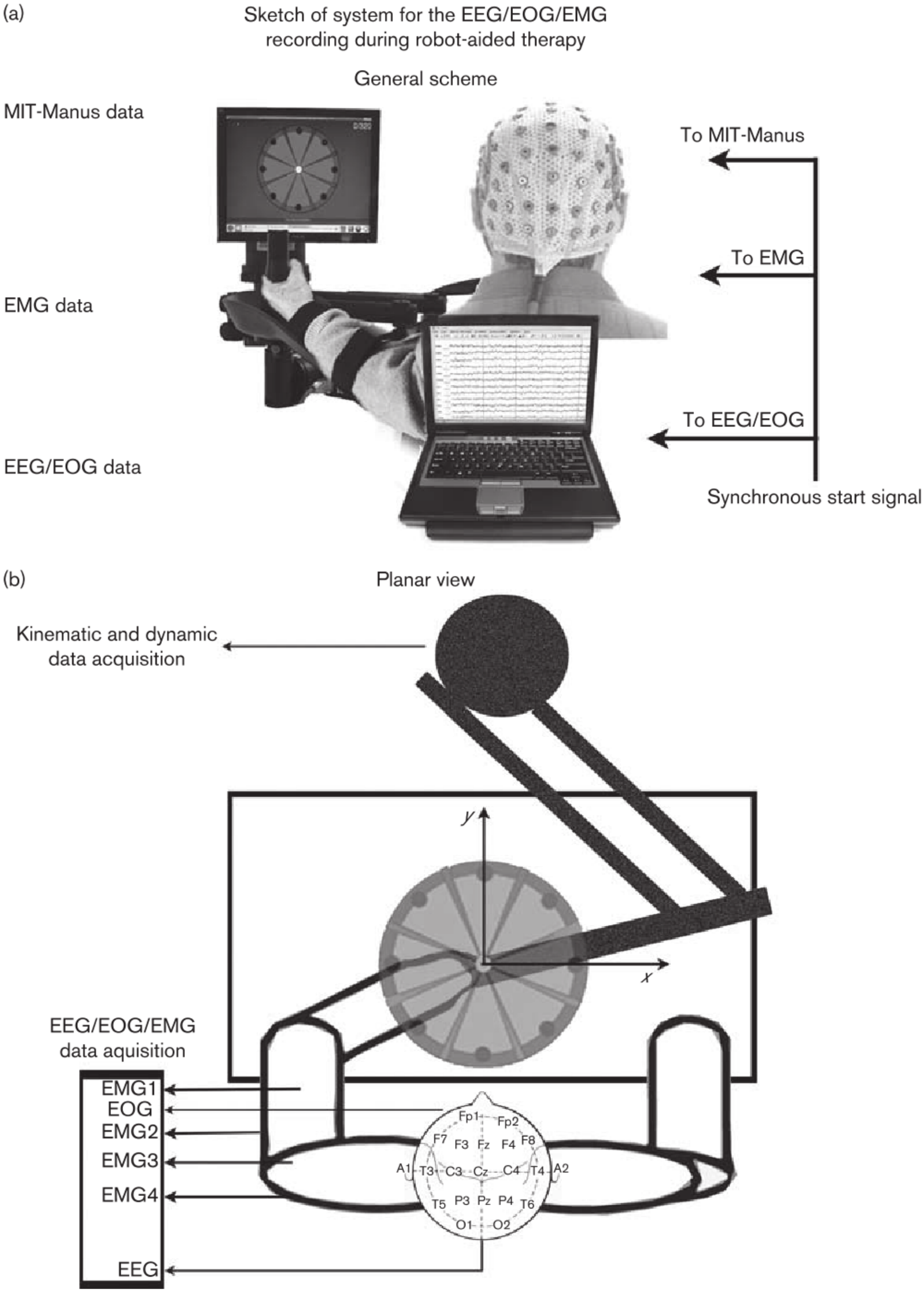
Design of the system for simultaneous recording of electrophysiological, kinematic, and dynamic data during the robotic rehabilitation task

Figure 1a plots the general scheme of the system for the simultaneous recording of electrophysiological, kinematic, and dynamic data during a robot-aided session of motor rehabilitation. Figure 1b shows in planar view the schematization of the data acquisition.

The system is composed of several interconnected items. It is noteworthy that these items are commercial products whose technical features and quality are well known (they were licensed by European community regulatory agencies at the time they were approved for commercialization, etc.). The novelty of the present methodological approach is their interconnection for new scientific purposes.

Specifically, the patient performed the robotic motor rehabilitation with the InMotion2 robotic machine (MIT-Manus InMotion2; Interactive Motion Technologies Inc., Boston, Massachusetts, USA), a robot designed for clinical and neurological applications (Krebs

Fig. 1



(a) general scheme of the system for the simultaneous recording of electrophysiological, kinematic, and dynamic data during a robot-aided session of motor rehabilitation. (b) Planar view of the schematization of the data acquisition. EEG, electroencephalography; EMG, electromyography; EOG, electrooculography.

et al., 1998). The InMotion2 robotic machine supports the execution of reaching movements in the horizontal plane through an 'assist as needed' control strategy, which is described below. The robot can guide the movement of the upper limb of the patients and record end-effector physical quantities such as the position, velocity, and applied forces. During the robot-aided session of motor rehabilitation, the patient wore an EEG caps including 19 electrodes placed according to a 10–20 system connected to a multichannel amplifier box (BrainAmp; Brain Products GmbH, München, Germany) that also received the individual bipolar electrooculographic (EOG) and electromyographic (EMG) signals. A synchronous start signal was given to allow the simultaneous recording of electrophysiological, kinematic, and dynamic indices and to start the rehabilitation session. Of note, in the above system, the patients were electrically decoupled to satisfy international safety guidelines and to record high-quality EEG–EOG–EMG signals.

Rehabilitative treatment

The robot-aided therapy session consisted of performing exercises with the InMotion2 robotic machine. Specifically, the rehabilitative treatment consisted of a total of 30 sessions lasting 45 min each, 5 days a week, for a total period of 6 weeks; the rehabilitative protocol designed by us consisted of exercises aimed at improving both movement type (i.e. the joints involved, with a proximal–distal progression) and mode of execution of the movement itself, with progression from passive movement to free movement.

Each patient sat in front of the monitor handling a robotic manipulandum with the plegic arm. They were asked to perform eight blocks of point-to-point movements on an imaginary scheme placed on the table under the manipulandum from the center to eight outbound targets distributed along a circle at a distance of 0.14 m (clockwise repetitions). Patients were required to move at a self-paced speed. A visual feedback of the target and of every movement was displayed continuously (25 Hz) on the monitor. The robot was completely passive while the position and force sensors recorded the patients' kinematic and force data.

Each session included (i) a series of 16 assisted clockwise repetitions to each robot target (training test); (ii) a series of 16 unassisted clockwise repetitions to each robot target (Record); and (iii) three series of 320 assisted clockwise repetitions (Adaptive). At the end of each Adaptive series, the patient is asked to perform a further series of 16 unassisted clockwise movements (Record).

Clinical data

Each patient underwent an upper limb evaluation by an experienced blinded physical therapist not involved in the rehabilitation treatment team. This evaluation was performed before (T0) and after (T1) the rehabilitative treatment.

The upper limb evaluation included the following measures: the Fugl-Meyer test of the upper limb (FM) (Fugl-Meyer *et al.*, 1975), the Box and Block test (BBT) (Mathiowetz *et al.*, 1985), the Modified Ashworth Scale of shoulder and elbow (AS); (Bohannon and Smith, 1987), range of motion (ROM), Motricity Index (MI); (Collin and Wade, 1990), and the modified Barthel index (mBI).

Kinematic and dynamic data recordings

Kinematic and dynamic performance indices were extracted from position and force data recorded with the InMotion2 robot. In particular, hand position, velocity, and interaction force were recorded online during all evaluation tasks. Biomechanical data were recorded from the robotic system before starting the therapy and at the end of the therapy during the recorded series of exercises. The low impendence of the system facilitates the residual movement of more severely impaired patients: if the patient is not able to reach the target, after an adjustable time threshold, set here at t equal to 5 s, the blinking cursor to be reached automatically moves from one target to another. Kinematics parameters are recorded even if the patient performs the movement partially, without reaching the target.

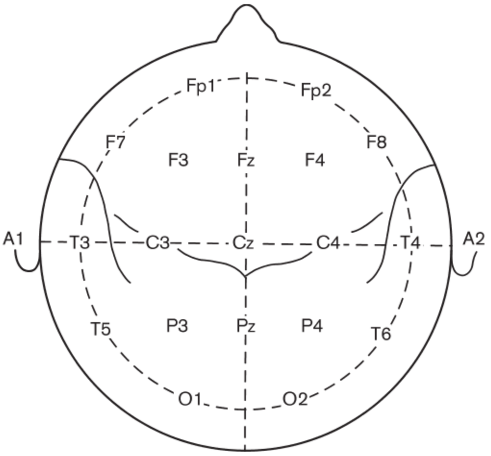
Upon demonstration of competency and understanding by the patient, minimal feedback was provided. Verbal encouragement and environmental distraction was kept to a minimum. The list of kinematic and dynamic indices can be found in Krebs *et al.* (1998) and Sale *et al.* (2014a).

Electrophysiological data recordings

EEG data were recorded continuously (bandpass: 0.01–100 Hz, sampling rate: 512 Hz; BrainAmp; Brain Products GmbH) from 19 scalp electrodes (cap) positioned according to the 10–20 system (see Fig. 2). The electrical reference was located between the Fz and Cz electrodes, and the ground electrode was located between the Cz and Pz electrodes. Electrode impedance was maintained below 5 kΩ. In parallel, we performed the recording of vertical and horizontal bipolar EOG data (bandpass: 0.1–100 Hz; sampling rate: 512 Hz) for the monitoring of blinking and eye movements.

Furthermore, surface EMG activity (bandpass: 0.1–100 Hz; sampling rate: 512 Hz) of the biceps, triceps, anterior deltoid, and posterior deltoid of the plegic arm was recorded using pairs of surface electrodes (8-mm

Fig. 2



Electroencephalographic electrode montage.

diameter; Ag–AgCl) placed 16 mm apart (center-to-center) on the skin overlying the respective muscles. Low impedance of the surface EMG electrodes (< 5 kΩ) at the skin–electrode interface was obtained by shaving, abrading, and cleaning the skin with alcohol. Special focus was placed on the standardization of the experimental procedure (electrode position) to reduce the susceptibility of surface EMG to cross-talk (Kellis, 1998).

EEG–EOG–EMG data collection was performed before (T0) and after (T1) the rehabilitative treatment. In both sessions, EEG–EOG–EMG data were collected during: (a) eyes-closed (3 min) and eyes-open (3 min) resting state, and (b) robotic rehabilitation task. The robotic rehabilitation task consisted of a series of 16 unassisted clockwise repetitions to each robot target (clockwise test). The number of repetitions of the task was such as to reach at least 4-min of EEG–EOG–EMG data. The interseries pause was 1 min.

Electroencephalography–electrooculography–electromyography data processing

Recorded EEG–EOG–EMG data were segmented into single epochs lasting 2 s. The EEG–EOG–EMG epochs with ocular, muscular, and other types of artifact were preliminarily identified using a computerized automatic procedure (Moretti *et al.*, 2003). The EEG epochs contaminated by ocular artifacts were then corrected by an autoregressive method (Moretti *et al.*, 2003). Finally, two expert electroencephalographists manually confirmed this automatic selection and correction, with special attention to residual contaminations of the EEG epochs because of head, trunk, and eye movements. Therefore, only the EEG epochs totally free from artifact residuals were included in the subsequent analyses. These EEG epochs referred to a common average reference for further analyses.

Frequency analysis of alpha rhythms

For the analysis of the EEG power density spectrum, artifact-free EEG epochs were analyzed by a standard Fast Fourier Transform approach using the Welch technique and the Hanning windowing function (1 Hz frequency resolution). EEG relative power density was obtained by normalizing the EEG absolute power density at each frequency bin and electrode for the mean of the EEG absolute power density across all frequency bins and electrodes. For the determination of the alpha sub-bands, the individual alpha frequency (IAF) peak was identified on resting EEG data according to the literature guidelines (Klimesch *et al.*, 1996, 1998, 1999). The IAF is defined as the frequency within the 6–13 Hz range of the EEG spectrum showing the maximum power. With reference to the IAF, the alpha sub-bands of interest were as follows: low-frequency alpha band as IAF − 2 Hz to IAF and high-frequency alpha band as IAF to IAF + 2 Hz. The IAF value was 10 Hz for the postacute stroke patient and 7 Hz for the chronic stroke patient.

Reactivity of electroencephalography power to eyes opening and to the robotic rehabilitation task

For the analysis of the reactivity of EEG power density to eyes opening, the difference in power density in the eyes-open minus the eyes-closed resting state was computed. Negative values of EEG power difference indexed a decrease in power density in the eyes-open compared with the eyes-closed condition, whereas positive values of the EEG power difference indexed an increase in power density in the eyes-open compared with the eyes-closed condition.

For the analysis of the reactivity of EEG power density to the robotic rehabilitation task, the difference in power density in the robotic rehabilitation task minus the eyes-open resting state was computed. Negative values of EEG power difference indexed a decrease in power density in the robotic rehabilitation task compared with the eyes-open condition, whereas positive values of EEG power difference indexed an increase in power density in the robotic rehabilitation task compared with the eyes-open condition.

Topographic maps

Topographic maps (256 colours) of (a) the EEG power density in the eyes-closed condition, (b) the reactivity of EEG power density to eyes opening, and (c) the reactivity of EEG power density to the robotic rehabilitation task at the two alpha sub-bands were calculated on a 3D cortical model using a spline interpolating function (Babiloni *et al.*, 1996). This model is based on the magnetic resonance data of 152 patients digitized at the Brain Imaging Centre of the Montreal Neurological Institute.

Results

Clinical outcomes

The robot-assisted therapy was well accepted and tolerated by two patients. The results from clinical outcome measures showed a decrease in motor impairment in the paretic upper limb after the robot-aided treatment in both subacute and chronic stroke patients. In particular, improvements after the rehabilitative treatment were found on the FM, BBT, ROM, MI, and mBI, whereas a decrease was found on the AS.

Table 1 summarizes the results of the mentioned clinical before (T0) and after (T1) the rehabilitative treatment. The gain (difference between evaluation at T1 and T0) is also reported.

Kinematic and dynamic results

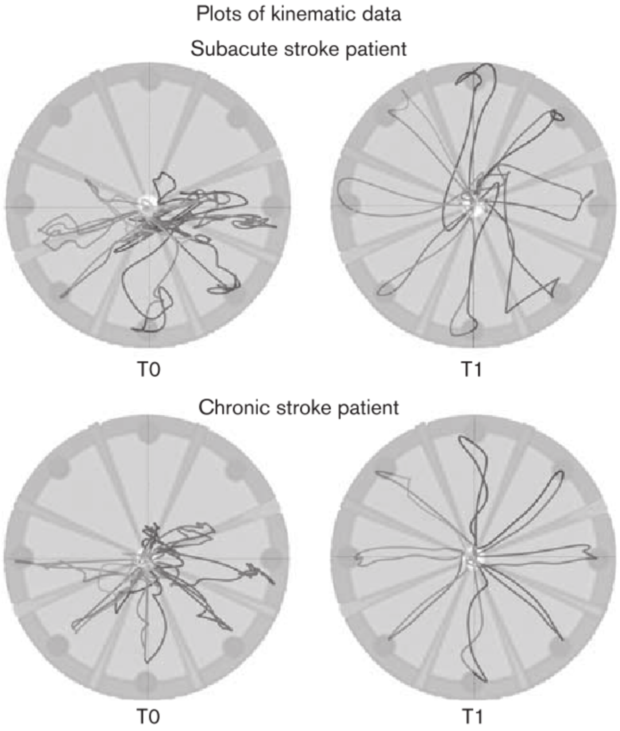
Figure 3 shows the plot of motion trajectories of the subacute and chronic stroke patients during a point-to-point evaluation task before (T0) and after (T1) the

Table 1 Impairment and functional evaluations performed before (T0) and after (T1) the rehabilitative treatment for postacute and chronic strike patients

	T0	T1	Gain
Postacute stroke patient			
FM	29	44	15
BBT	10	10	0
AS shoulder	2	1	−1
AS elbow	2	1	−1
ROM	760	820	60
MI	70	70	0
mBI	2	39	37
Chronic stroke patient			
FM	8	30	22
BBT	0	1	1
AS shoulder	3	2	−1
AS elbow	3	2	−1
ROM	660	820	160
MI	1	53	52
mBI	61	89	28

The gain (difference between evaluation at T1 and T0) is also reported.
AS, Modified Ashworth Scale (minimum 0, maximum 5); BBT, Box and Block test; FM, Fugl-Meyer test of the upper limb (minimum 0, maximum 66); mBI, Modified Barthel Index (minimum, 0 maximum 100); MI, Motricity Index; ROM, range of motion.

Fig. 3



Plot of motion trajectories for chronic and subacute stroke patients during a point-to-point evaluation task before (T0) and after (T1) the rehabilitative treatment.

rehabilitative treatment when the EEG and EMG signals were simultaneously recorded.

The gain toward more linear trajectories secondary to the motor improvement on ROM and other motor parameters that augment the capability of extending the arm toward the recovery of a full planar movement is clear.

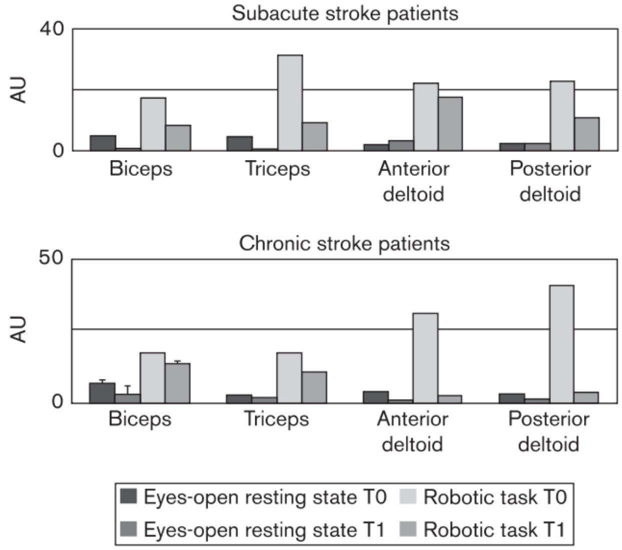
Electromyography results

The quality of the EMG data was confirmed by the features of EMG activity. Indeed, the analysis of EMG activity showed typical features of human muscle activity during resting state and engaging epochs. Figure 4 shows the mean amplitude of rectified EMG activity for the subacute and chronic stroke patients. In particular, the rectified EMG activity refers to biceps, triceps, anterior deltoid, and posterior deltoid of the plegic arm before (T0) and after (T1) the rehabilitative treatment for the eyes-open resting state condition and the robotic rehabilitation task. As expected, the amplitude of the rectified EMG activity was stronger for the motor robotic rehabilitation task compared with the eyes-open resting state. Furthermore, after the rehabilitation program, both patients were characterized by a decrease in EMG activity during the motor robotic rehabilitation task, as a sign of a more fine and simple movement of the plegic arm after the rehabilitation treatment.

Electroencephalography results

The quality of the EEG data was confirmed by the high rate (>80%) of artifact-free EEG epochs. Indeed, for the postacute stroke patient, the percentage of artifact-free EEG epochs was more than 90% for the eyes-closed and

Fig. 4



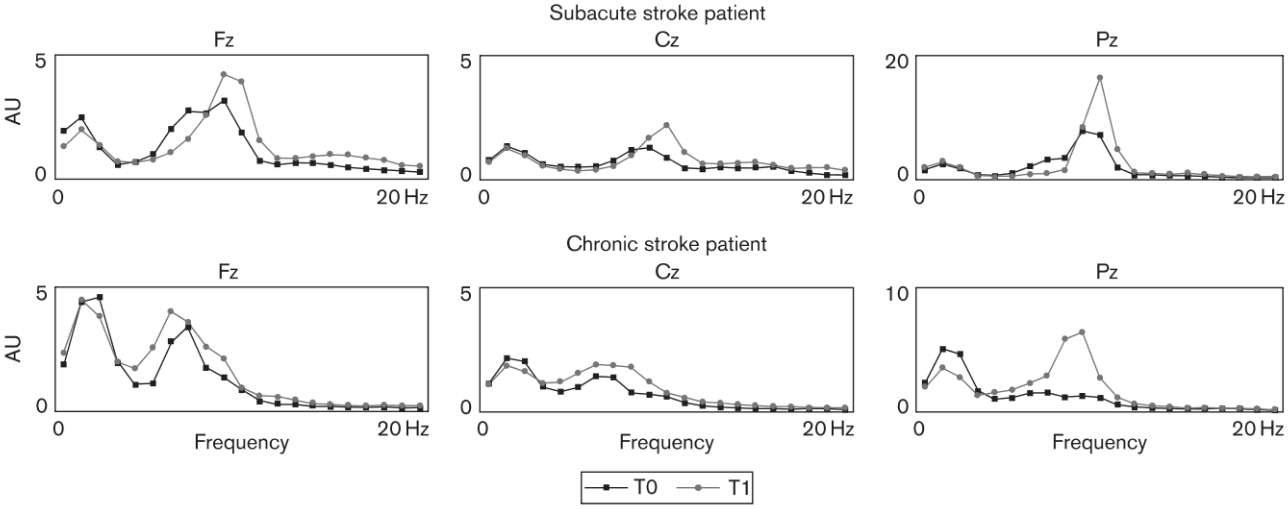
Mean amplitude of rectified EMG activity for the subacute and chronic stroke patients. In particular, the rectified EMG activity refers to the biceps, triceps, anterior deltoid, and posterior deltoid of the plegic arm before (T0) and after (T1) the rehabilitative treatment for the eyes-open resting state condition and the robotic rehabilitation task. EMG, electromyography.

eyes-open resting condition, and more than 80% for the robotic rehabilitation. For the chronic stroke patient, the percentage of artifact-free EEG epochs was more than 90% for the eyes-closed and eyes-open resting condition, and more than 85% for the robotic rehabilitation task.

Furthermore, the quality of the EEG data was also confirmed by the features of EEG spectra. Indeed, the analysis of EEG power density spectrum showed typical features of human cortical oscillatory activity during resting state and engaging epochs. Figure 5 shows the normalized EEG power density spectra in the eyes-closed resting state for the subacute and chronic stroke patients. In particular, the normalized EEG power density spectra refer to the frequency range between 0 and 20 Hz at the three electrodes of interest (Fz, Cz, Pz) before (T0) and after (T1) the rehabilitative treatment. In both patients, dominant EEG power density values were observed at the alpha band (8–12 Hz) in the posterior cortical regions. Furthermore, values of EEG power density at lower frequency bands were highest in the anterior cortical regions (delta, 1–4 Hz; theta, 4–8 Hz). Moreover, values of EEG power density at high-frequency bands were negligible overall (beta, 14–20 Hz). Finally, after the rehabilitation program, both patients showed reduced delta rhythms (1–4 Hz) and increased alpha rhythms (8–12 Hz). Figure 6 show the reactivity of normalized EEG power density to eyes-opening (i.e. difference of EEG power density in eyes-open minus eyes-closed resting state) for the subacute and chronic stroke patients. In particular, the reactivity of normalized EEG power density to eyes opening refers to the frequency range between 0 and 20 Hz at the three electrodes of interest (Fz, Cz, Pz) before (T0) and after (T1) the rehabilitative treatment. In both patients, maximal negative values (i.e. maximal reactivity to eyes-opening) were observed at the alpha band. Furthermore, after the rehabilitation program, both patients showed an increased reactivity to eyes opening at the alpha band. Figure 7 shows the reactivity of normalized EEG power density to the robotic rehabilitation task (i.e. difference in EEG power density in the robotic rehabilitation task minus the eyes-open resting state) for the subacute and chronic stroke patients. In particular, the reactivity of normalized EEG power density to the robotic rehabilitation task refers to the frequency range between 0 and 20 Hz at the three electrodes of interest (F3, C3, P3 for subacute stroke patient; F4, C4, P4 for the chronic stroke patient) before (T0) and after (T1) the rehabilitative treatment. In both patients, maximal negative values (i.e. maximal reactivity to the robotic rehabilitation task) were observed at the alpha band (8–12 Hz). Furthermore, after the rehabilitation program, both patients showed a decreased reactivity to the robotic rehabilitation task at the alpha band.

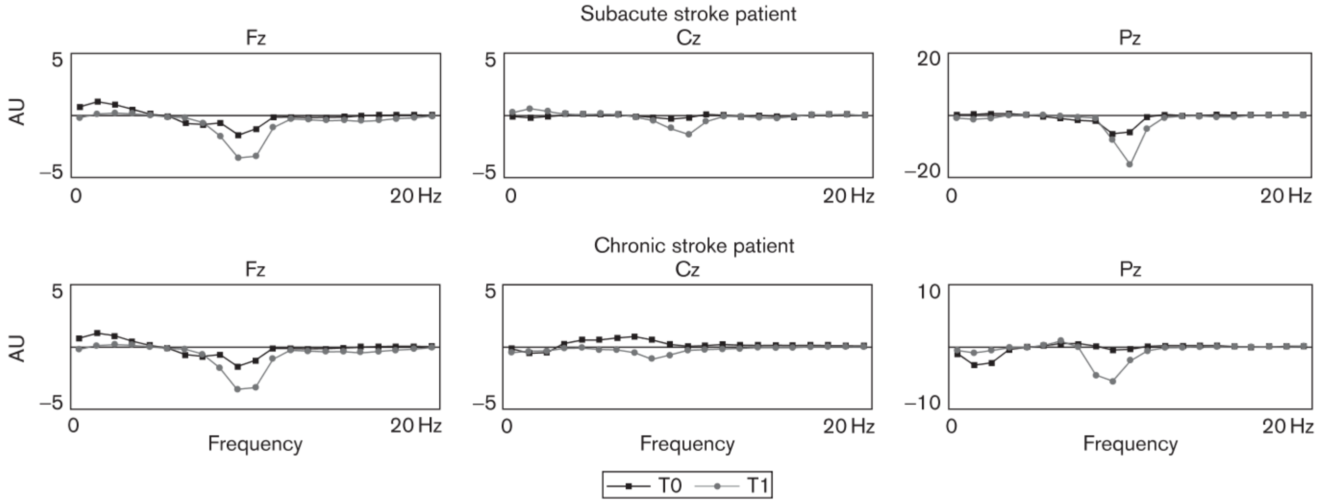
For illustrative purposes, Fig. 8 maps fine topographical details of the normalized low-frequency and high-frequency alpha EEG power density in the eyes-closed resting state before (T0) and after (T1) the rehabilitative treatment for the subacute and chronic stroke patients. After the rehabilitation program, both patients were characterized by a decrease in low-frequency and high-frequency alpha EEG power density. Figure 9 maps the fine topographical details of the reactivity of normalized low-frequency and high-frequency alpha EEG power

Fig. 5



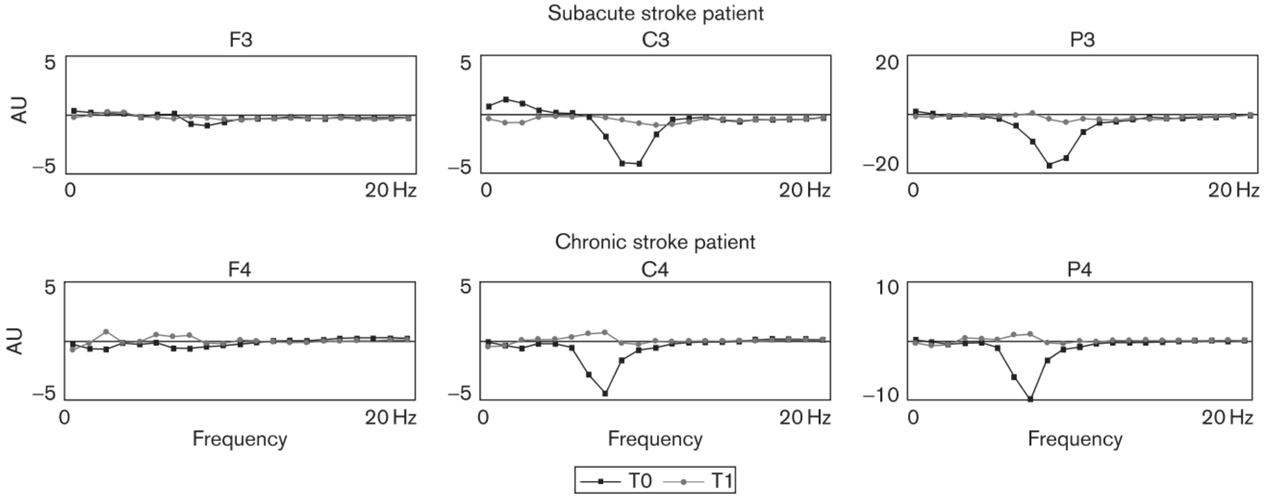
Normalized EEG power density spectra in the eyes-closed resting state for the subacute and chronic stroke patients. In particular, the normalized EEG power density spectra refer to the frequency range between 0 and 20 Hz at the three electrodes of interest (Fz, Cz, Pz) before (T0) and after (T1) the rehabilitative treatment. EEG, electroencephalography.

Fig. 6



Reactivity of normalized EEG power density to eyes-opening (i.e. difference of EEG power density in eyes-open minus eyes-closed resting state) for the subacute and chronic stroke patients. In particular, the reactivity of normalized EEG power density to eyes opening refers to the frequency range between 0 and 20 Hz at the three electrodes of interest (Fz, Cz, Pz) before (T0) and after (T1) the rehabilitative treatment. EEG, electroencephalography.

Fig. 7

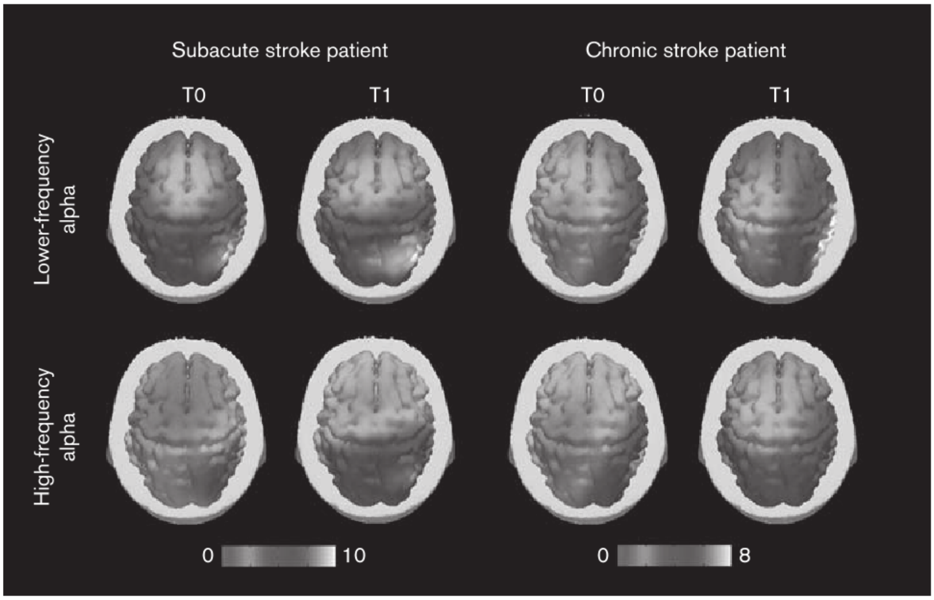


Reactivity of normalized EEG power density to the robotic rehabilitation task (i.e. difference of G power density in the robotic rehabilitation task minus the eyes-open resting state) for the subacute and chronic stroke patients. In particular, the reactivity of normalized EEG power density to eyes opening refers to the frequency range between 0 and 20 Hz at the three electrodes of interest (F3, C3, P3 for the subacute stroke patient; F4, C4, P4 for the chronic stroke patient) before (T0) and after (T1) the rehabilitative treatment. EEG, electroencephalography.

density to eyes-opening before (T0) and after (T1) the rehabilitative treatment for the subacute and chronic stroke patients. After the rehabilitation program, both patients were characterized by an increased reactivity of low-frequency and high-frequency alpha EEG power. Figure 10 maps the fine topographical details of the reactivity of normalized low-frequency and high-frequency alpha EEG power density to the robotic rehabilitation task before (T0) and after (T1) the rehabilitative treatment for the subacute and chronic stroke patients. After the rehabilitation program, both patients were characterized by a decreased reactivity of low-frequency and high-frequency alpha EEG power.

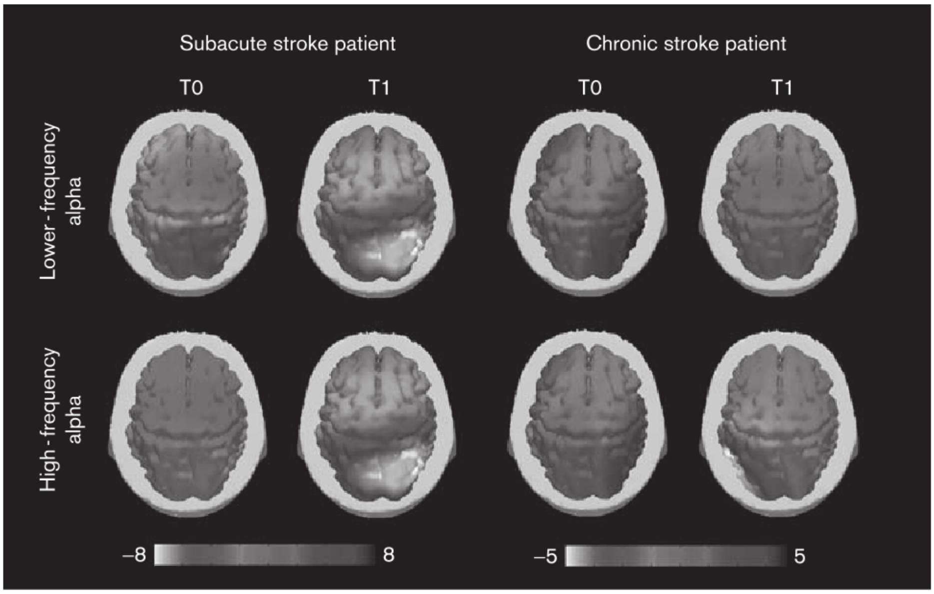
It is noteworthy that the limited number of patients in the present study did not allow statistical analysis or conclusions, and should be considered as a preliminary

Fig. 8



Topographical distribution of normalized low-frequency and high-frequency alpha electroencephalography power density in the eyes-closed resting state before (T0) and after (T1) the rehabilitative treatment for the subacute and chronic stroke patients. Black and White scale: maximum alpha EEG power density is coded in white. The maximal value is reported under the maps.

Fig. 9



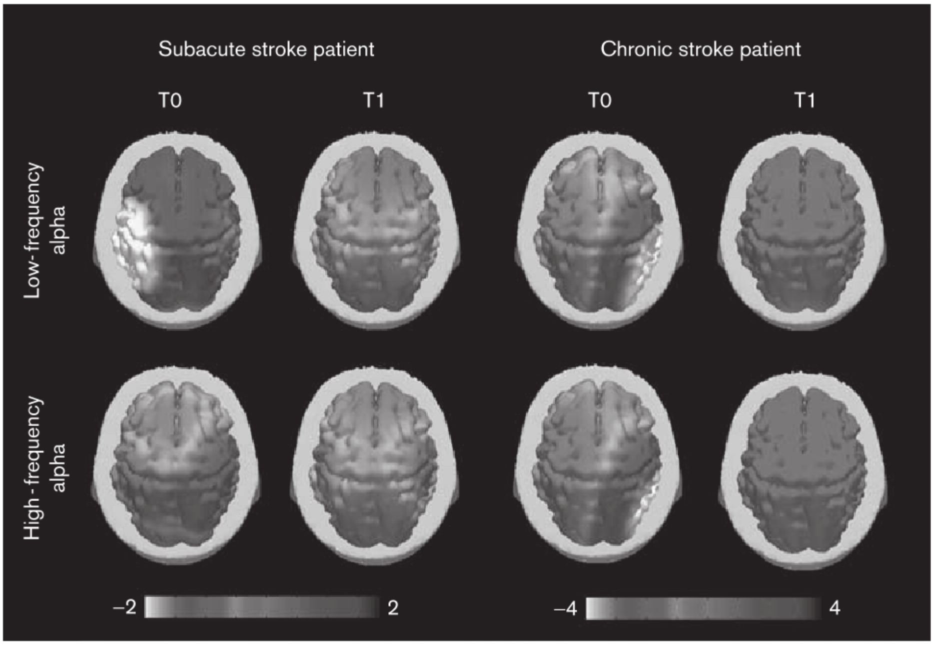
Topographical distribution of the reactivity of normalized low-frequency and high-frequency alpha electroencephalography power to eyes opening before (T0) and after (T1) the rehabilitative treatment for the subacute and chronic stroke patients. Black and White scale: minimum and maximum values are coded in white and gray, respectively. The maximal value is reported under the maps.

descriptive finding to be quantitatively evaluated in future studies using a larger data sample (more stroke patients) with a proper data analysis design. This is beyond the scope of the present methodological study.

Discussion

In the present study, we present a new procedure to study neural underpinning of robot-aided upper limb rehabilitation in stroke patients. In particular, we propose

Fig. 10



Topographical distribution of the reactivity of normalized low-frequency and high-frequency alpha electroencephalography power to the robotic rehabilitation task before (T0) and after (T1) the rehabilitative treatment for the subacute and chronic stroke patients. Black and White scale: minimum and maximum values are coded in white and gray, respectively. The maximal value is reported under the maps.

a system for the EEG–EOG–EMG recording in stroke patients during a robotic rehabilitation task. This system was designed to obtain safe recording conditions, high-quality EEG–EOG—EMG data, triggering signals to track the task, and to align EEG segments to motor performance, user-friendly visualization, and management of the EEG–EOG–EMG–control data during the signal acquisition and subsequent analysis. These EMG data can be used to identify the motor performance of stroke patients, thus potentially enabling the investigation of the relationships between EEG dynamics and different modes of motor performance. It is noteworthy that the proposed system consists of commercial hardware and software items whose technical features and quality are well known (i.e. they were licensed by European community regulatory agencies). The novelty of the present methodological approach is their interconnection for a new scientific purpose. For this reason, we did not go into in-depth technical details of these items, but focused on the quality of EEG signals.

The quality of the EEG data was evaluated by the rate of artifact-free EEG epochs and by the features of dominant alpha rhythms (about 8–12 Hz) during both the resting state (eyes closed and eyes open) and the robotic rehabilitation task. The results showed high-quality EEG data recorded in the two patients with about 80% of artifact-free EEG epochs during robotic performance (i.e. the patients were trained to minimize head, neck, forelimb, and trunk movements during their performance). Overall, the relatively high percentage of artifact-free EEG epochs represents a good first index of the quality of the EEG recordings. Furthermore, the analysis of EEG power density spectrum showed typical features of human cortical EEG oscillatory activity during resting state and engaging events. During the eyes-closed resting state, dominant EEG power density values were observed at the alpha band (8–12 Hz) in the posterior cortical regions. Furthermore, values of EEG power density at lower frequency bands were maximal in the anterior cortical regions (delta, 1–4 Hz; theta, 4–8 Hz). Finally, values of EEG power density at high-frequency bands were overall negligible (beta, 14–20 Hz). Compared with the eyes-closed resting state, the eyes-open resting state was characterized by a decrease in alpha power density values in amplitude in several cortical regions. Similarly, compared with the eyes-open resting state, the robotic task was characterized by a decrease in alpha power density values in amplitude in several cortical regions.

To illustrate possible future neurophysiological applications, after the rehabilitation program, we observed (a) reduced delta rhythms (1–4 Hz) and increased alpha rhythms (8–12 Hz) during the resting state eyes-closed condition; (b) increased alpha desynchronization to eyes opening; and (c) decreased alpha desynchronization during the robotic rehabilitation task. It can be speculated that a specific robot-aided rehabilitation can modulate cortical activity during resting state and a motor task in stroke patients.

Conclusion

Future studies with more stroke patients and a proper statistical design will enable the quantification of the relationships between cortical activity and robotic rehabilitation. In conclusion, the present methodological approach appeared to be suitable for EEG–EOG–EMG recordings in stroke patients during a robotic rehabilitation task, thus providing a new avenue to the study the neural underpinning of robot-aided upper limb rehabilitation in stroke patients.

Acknowledgements

Conflicts of interest

There are no conflicts of interest.

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