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Quantitative EEG for Predicting Upper-limb Motor Recovery in Chronic Stroke Robot-assisted Rehabilitation

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***Abstract*— Stroke is a leading cause for adult disability, which in many cases causes motor deficits. Despite the developments in motor rehabilitation techniques, recovery of upper limb functions after stroke is limited and heterogeneous in terms of outcomes, and knowledge of important factors that may affect the outcome of the therapy is necessary to make a reasonable prediction for individual patients. In this study, we assessed the relationship between quantitative electroencephalographic (QEEG) measures and the motor outcome in chronic stroke patients that underwent a robot-assisted rehabilitation program to evaluate the utility of QEEG indices to predict motor recovery. For this purpose, we acquired resting-state electroencephalographic signals from which the Power Ratio Index (PRI), Delta/Alpha Ratio (DAR), and Brain Symmetry Index (BSI) were calculated. The outcome of the motor rehabilitation was evaluated using upper-limb section of the Fugl-Meyer Assessment. We found that PRI was significantly correlated with the motor recovery, suggesting that this index may provide useful information to predict the rehabilitation outcome.**

***Index Terms*— Chronic Stroke, Robot-assisted Rehabilitation, Quantitative Electroencephalography (QEEG), Outcome Prediction**

I. Introduction

STROKE is one of the leading causes of long-term disability in adults [1]–[3]. It occurs when blood flow to an area of the brain is cut off, and brain cells deprived of oxygen begin to die. When brain cells die, the abilities controlled by that area of the brain, such as memory and muscle control, can be partially or totally lost. How a person is affected by stroke depends on where the stroke occurs in the brain and how much the brain is damaged [4]. Approximately two thirds of the stroke patients require rehabilitation and most of them present residual and disabling long-term deficits due to impaired motor function [5].

When the damage is in the motor areas of the brain, it can produce devastating motor deficits particularly for the upper limb. Upper limb weakness and loss of function is a significant problem among survivors [6], [7]. In many cases, the severe disabilities affect their daily living activities, including activities of self-care, such as eating, washing and dressing, resulting in the loss of independence and causing major changes in the quality of life. Hence, rehabilitation of the impaired upper limb is of critical importance. Upper limb rehabilitation is generally focused on improving independent function on various daily activities, and it is considered effective if patients are able to transfer motor and functional improvements to their living environments [8].

Physical therapy involving repetitive limb movement can stimulate damaged brain areas and lead to partial or full motor function recovery [9]–[13]. Moreover, it has been shown that upper limb exercises applied with functional tasks are more effective in improving functions and daily living activities compared to simple repetitive upper extremity exercises [14]. In traditional rehabilitation therapies, patients perform repetitive limb movements with the help of the physiotherapist. This approach, however, requires extensive training periods for patients, and intensive labor for therapist.

Recently, robot-assisted rehabilitation has been used to promote motor recovery in stroke patients as an alternative to traditional therapy, and several studies have shown that it can be effective in both subacute and chronic patients [15]–[17]. Robot-based systems have the advantage to allow programmable movement patterns, control of movement repetitions, and real-time position and force measurement. Robots can be programmed to perform a wide variety of motions including functional movements, which allows the patient to perform autonomous and repetitive training on tasks simulating activities of daily living, even without the help of the therapist. Robot-based systems have also the advantage of possible cost reduction by automating the therapy procedure, allowing the therapist to work with many patients at the same time.

To date, most of the robotic systems have been developed for

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controlled supervised hospital-settings, requiring clinic visits for patients, and making it inconvenient or unaffordable for many patients. Recent studies have shown the feasibility of developing low-cost, easily transportable, wearable, automated and customizable robot-assisted rehabilitation system for home based rehabilitation [18]–[21]. Novel strategies also include the use of biofeedback, virtual reality, and haptics to improve patient motivation, engagement and adherence to the treatment [18], [22]–[27].

Despite the developments in motor rehabilitation techniques [28], recovery from stroke is heterogeneous in terms of outcomes, which means that not all stroke patients achieve the same degree of motor recovery. A variety of clinical factors influences the efficacy of the therapy, including age, stroke severity, infarct location, and related complications. Patients, families, healthcare workers, and insurance providers often enquire the clinician for a prediction of the duration and efficacy of the rehabilitation program. Knowledge of important factors that may affect the outcome of the therapy is necessary to make a reasonable prediction for individual patients. Thus, there is a need for reliable markers to predict the efficacy of the therapy according to the individual level and type of impairment.

In the acute phase, the most powerful predictors of functional recovery are the initial severity of the stroke and the patient's age [29], [30]. Other factors, such as the presence of finger extension and shoulder abduction within 72 hours after stroke can be used to predict functional recovery [31] in the acute phase. In the chronic phase, however, predicting the outcome of the therapy is more challenging as the motor recovery is not always related to the extent of the initial damage, and many complex dynamic neuroplasticity processes may occur since the initial stroke lesion. Hence, predicting motor function, particularly in the chronic phases, requires the use of complementary techniques. Different studies have shown that neuroimaging and neurophysiological techniques can provide useful information to predict clinical outcomes [32]–[35]. Among these, electroencephalography (EEG) is a low cost, noninvasive, and versatile technique to assess cortical function reorganization [35], suitable for measuring brain activity in both acute and chronic phases.

The EEG is typically described in terms of rhythmic activity, and it is generally divided into frequency bands known as delta (1-4 Hz), theta (4-8 Hz), alpha (8-12 Hz) and beta (12-30 Hz). EEG is very sensitive in detecting abnormalities of cerebral rhythms that are typical of stroke. In particular, quantitative EEG (QEEG) indices based on the relationship between the power of slow (i.e. 1-7 Hz) and fast (i.e. 8-30 Hz) brain activity, estimated by resting-state EEG power spectrum analysis, have been shown to be useful to characterize the brain status after stroke. Several EEG studies in patients with acute stroke have shown that QEEG indices can offer valuable information for clinical decision-making, providing predictors of clinical outcomes [34], [36]–[40]. Specifically, the relationship between the power bands by means of the Power Ratio Index (PRI) [37], and the delta/alpha ratio (DAR) [41], as well the characterization of brain asymmetry via the Brain Asymmetry Index (BSI) [39], [40], [42], [43], have been used to predict and monitor the evolution of stroke in the acute phase. In this phase, an increase in PRI, DAR and BSI have been related to poorer functional outcomes, and can be associated with the severity of the initial damage.

Most of the prior studies, however, have examined the QEEG predictors in the acute phase, and there are currently few studies investigating the relationship between the QEEG indices and the functional outcome after neurorehabilitation in chronic patients [35], [44]–[48]. Moreover, only one previous study investigated the QEEG indices as predictors of the rehabilitation outcomes in chronic patients; specifically, in that case, rehabilitation was multidisciplinary including both motor and cognitive functions [47]. On the other hand, regarding robot-assisted motor rehabilitation, several studies have examined EEG power modulations in alpha and beta bands during movement [49]–[51], and have explored the effects of rehabilitation using robot devices [48], but, to our knowledge, none of the previous studies has examined the QEEG indices as predictors of motor recovery.

To fill this gap, the present study aimed to evaluate the possible relationship between the QEEG indices and the motor recovery measure in chronic stroke patients that underwent a robot-assisted motor rehabilitation program to evaluate the utility of QEEG indices to predict motor recovery, and guide rehabilitation strategies in chronic stroke patients.

II. Materials and Methods

A. Patients

Ten post-stroke patients in the chronic phase were recruited for the study. All patients had monolateral upper-limb deficits. The demographic and clinical characteristics of the patients are listed in Table 1. Written informed consent was obtained from each subject before inclusion in the study. The study was reviewed and approved by the local Ethics Committee at Como Valduce Hospital and was conducted in compliance with the Declaration of Helsinki.

B. Rehabilitation System and Protocol

The Mitsubishi Pa10-7 robot (Fig. 1) was used to perform upper-limb rehabilitation training sessions, based on the intensive execution of Reaching Movement (RM) and Hand-to-Mouth Movement (HtMM) robot-assisted functional movements. The RM consisted in the flexion of the shoulder on the sagittal plane up to 90°, coupled with the complete extension of the elbow, mimicking the gesture of reaching for an object. The HtMM consisted in slightly flexing the shoulder while flexing the elbow to simulate the gesture of bringing objects to the mouth. These two movements were chosen because they resemble common actions performed during everyday life, like reaching for a desired object or eating, and because they engage most of the upper limb joints (mainly shoulder and elbow for the RM, and elbow and wrist for the

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TABLE I
DEMOGRAPHIC AND CLINICAL DATA

Patient	Gender	Age	Years from Stroke	Handedness	Impaired hand	Type of Stroke	FMA_{T0}	FMA_{T1}
A	Male	74	1	Right	Left	Hemorrhagic	56	57
B	Male	49	2	Right	Right	Ischemic	36	44
C	Male	51	10	Right	Left	Ischemic	11	12
D	Male	67	1	Right	Right	Ischemic	61	65
E	Male	31	4	Right	Left	Ischemic	17	17
F	Male	66	6	Right	Left	Ischemic	48	57
G	Female	46	14	Right	Right	Ischemic	61	64
H	Male	56	13	Left	Right	Hemorrhagic	46	50
I	Female	36	4	Right	Right	Ischemic	48	57
J	Male	81	2	Left	Left	Ischemic	40	47

HtMM). Moreover, the RM trains movements directed away from the body, while HtMM movements towards the body; this particular feature is supposed to encourage the role of proprioception in motor recovery.

Patients interacted with the robot through the handle mounted as end-effector. Further, during the HtMM movement, patients had to actively orientate the robot handle, which was provided with a revolute joint to promote the correct orientation of the hand.

Robot paths were rigidly imposed, i.e., the robot handle followed the predefined path and motion law regardless of the forces applied by the patient. Robot paths were created and customized to meet each patients' needs; motion laws mimicked bell-shaped, physiological-like velocity profiles, executed smoothly [52] and at quasi-physiological velocity.

The rehabilitation protocol consisted of 12 training sessions, each one lasting 40 minutes. Patients performed 3 sessions per week, thus the rehabilitation treatment lasted 4 weeks. Each session consisted in 20 minutes of intensive repetition of the RM and 20 minutes of intensive repetition of the HtMM. Patients were asked to change their level of engagement and participation every five movements by alternately relaxing during movement and actively participating. The operator, a specialized physiotherapist, could monitor on video the forces of interaction between the patient and the robot and, if necessary, could encourage the patient to try to participate more.

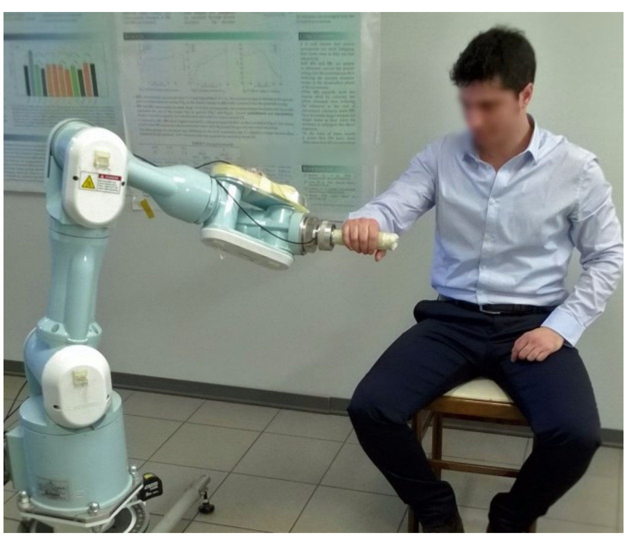

Fig. 1. The Mitsubishi Pa10-7 robot platform

C. Patient Clinical Evaluation

Clinical evaluations were performed by a physical therapist before treatment (T0) and after one month of treatment (T1), using the Fugl-Meyer Assessment (FMA) [53], [54]. The FMA is a stroke-specific, performance-based impairment scale, belonging to the body function domain of the ICF model, designed to assess motor functioning, balance, sensation and joint functioning in patients with post-stroke hemiplegia. Specifically, in this study, we used only the upper extremity motor section of the FMA (scale 0-66, 66=no motor deficits), and, accordingly to previous studies [55]–[57], the primary measure of motor recovery ΔFMA was calculated as difference between the FMA measures at T1 (FMA_{T1}) and T0 (FMA_{T0}). Considering the variability in FMA_{T0} of the participants in this study, and with the twofold aim of keeping track of FMA_{T0} and preventing ceiling effects on mild patients, a secondary measure of the motor recovery, the ΔFMA% was also used, defined as the difference between the FMA measures at T1 and T0, divided by the FMA measure at T0. Such index expresses the amount of motor recovery relative to the condition at the beginning of the therapy (T0), or, more precisely, the percentage of increase (decrease) of the FMA score at the end of the rehabilitative treatment (T1) with respect to the clinical status at T0.

D. EEG Recordings

Resting state EEG recordings were performed before treatment (T0) and after treatment (T1), with the subject in a comfortable supine position. Patients were asked to keep the eyes closed and remain awake and relaxed for 3 minutes while the EEG was recorded. The signals were acquired using a cap with 64 Ag/AgCl scalp monopolar electrodes placed according to the International 10/20 system. Impedances were kept below 5 kΩ. The online reference electrode was placed between Cz and Cpz. The EEG data were acquired using a Synamps 2/RT EEG system (Neuroscan) with a sampling frequency of 1 kHz.

For one of the patients (patient G), the EEG signal at T1 had many artifacts, and therefore only the EEG signal at T0 was considered for the analysis.

In order to assess the reliability of the QEEG measures, in six patients we performed an additional EEG recording approximately one hour after the first acquisition, under the same conditions as above and by the same operator. This was done at both T0 and T1, thus a total of twelve measures was considered for the reliability analysis.

E. EEG Data Analysis

Data analysis was performed offline in Matlab (R2015a, Mathworks, Natick, MA, USA) using the EEGLAB toolbox (Swartz Center for Computational Neuroscience, San Diego, CA, USA, http://sccn.ucsd.edu/). The EEG data were re-sampled at 500 Hz, bandpass filtered (Least-square linear-phase FIR filter: 1) lowpass filter: cutoff frequency=45 Hz, filter order=33; 2) highpass filter: cutoff frequency=0.5 Hz, filter order=3000), and re-referenced to the common average reference. The ear channels (M1 and M2), bad channels and segments containing gross artifacts (identified by visual inspection), were excluded from further analysis (in the worst case, 4 channels were eliminated, thus 58 were considered for the analysis). Then, the signals were epoched into contiguous epochs of 1024 data points (approximately 88 epochs), and those exceeding ±100 µV were automatically rejected (worst case: 69 epochs were considered for the subsequent analysis). Other artifacts (e.g. ocular artifacts, muscle artifacts, lost electrode connections) were removed using Independent Component Analysis (ICA) [58]. The ICA decomposition was performed using the logistic infomax ICA algorithm [59], implemented in EEGLAB. The selection of the artefactual components was guided by automated rejection methods (ADJUST [60]; FASTER [61]; MARA [62]; SASICA [63]), and supervised by an expert user via visual inspection.

Power spectral density was calculated for each channel using Welch's periodogram with Hamming window without overlap. As done in previous studies [38], [64], [65], the absolute power was summed across the delta (0.98-3.91 Hz), theta (4.39-7.32 Hz), alpha (7.81-12.21 Hz), and beta (12.70-29.79 Hz) bands. The relative power values for each frequency band were calculated as the ratio of summed absolute band-power to total summed power across the 0.98–29.79Hz range. All the indices were initially calculated for each channel, and then averaged across all electrodes.

The absolute band-power values were used to calculate the following quantitative indices:

1) *Power Ratio Index (PRI)* [66]: the ratio of "slow" to "fast" activity defined as the ratio of delta-plus-theta to alpha-plus-beta absolute power:
$$PRI = \frac{\delta + \theta}{\alpha + \beta} \tag{1}$$
2) *Delta/Alpha Ratio (DAR)* [41]: defined as the ratio of delta to alpha absolute power:
$$DAR = \frac{\delta}{\alpha} \tag{2}$$

The power spectral density for each channel was also used to calculate the pairwise derived Brain Symmetry Index (pdBSI) [40], which estimates the global asymmetry along homologous channel pairs (right and left), in the 1–25 Hz range averaged for frequency range and the number of channel pairs:
$$pdBSI = \frac{1}{NM}\sum_{j=1}^{M}\sum_{i=1}^{N}\left|\frac{R_{ij} - L_{ij}}{R_{ij} + L_{ij}}\right| \tag{3}$$
with R_{ij} and L_{ij} being the power spectral density from right and left channels of a homologous channel pair (with i=1,2,…M) at frequency j=1,2,…,N. For our specific settings, M=27, which corresponds to the total number of channel pairs. All the QEEG indices where calculated for T0 and T1, to verify if there were any changes in the brain activity before and after treatment.

F. Statistical Analysis

Assuming a Spearman's rank correlation coefficient of 0.7 ± 0.1 between the QEEG indices at T0 and motor outcome, the recommended sample size was 9-19 subjects to achieve statistical power of 80% with a significance level of 0.05. Power analysis was performed using the QFAB Bioinformatics, ANZMTG Statistical Decision Tree, Power Calculator, v 1.0.

Because of the small sample size, nonparametric tests were used for multivariate analysis. Non-parametric Spearman's rank correlation coefficients were calculated to assess the correlation between the QEEG indices and outcome measures (ΔFMA and ΔFMA%), as well as the correlation between the values at T0 and T1. The comparisons between the QEEG values before and after treatment were performed using the Wilcoxon signed-rank test. The intraclass correlation coefficient (ICC) was used to assess the reliability of the QEEG measures. In all analysis, the level of significance was set at 0.05. The statistical analysis was performed using the Statistics and Machine Learning Toolbox of Matlab (R2015a, Mathworks, Natick, MA, USA).

III. Results

The correlation analysis between QEEG indices at T0 and motor outcome showed a significant negative correlation between PRI_{T0} and the ΔFMA (ρ=-0.77, P=0.009, Fig. 2(a)). DAR_{T0} also showed a negative relationship with ΔFMA, but was not statistically significant (ρ=-0.61, P=0.06, Fig. 2(b)). Similarly, we also observed a significant negative correlation between PRI_{T0} and the ΔFMA% (ρ=-0.69, P=0.03, Fig. 2(d)), and a trend to a negative correlation between DAR_{T0} and ΔFMA% (ρ=-0.54, P=0.11, Fig. 2(e)). As regards to the $pdBSI_{T0}$, it did not correlate with neither the ΔFMA (ρ=-0.02, P=0.97, Fig. 2(c)), nor the ΔFMA% (ρ=-0.04, P=0.91, Fig. 2(f)).

FMA_{T0} was not correlated with PRI_{T0} (ρ=-0.19, P=0.60), DAR_{T0} (ρ=-0.012, P=0.97), nor $pdBSI_{T0}$ (ρ=0.45, P=0.19); analogously, FMA_{T1} was not correlated with PRI_{T1} (ρ=-0.24, P=0.51), DAR_{T1} (ρ=-0.08, P=0.83), nor $pdBSI_{T1}$ (ρ=0.42, P=0.22). There was no statistical correlation between

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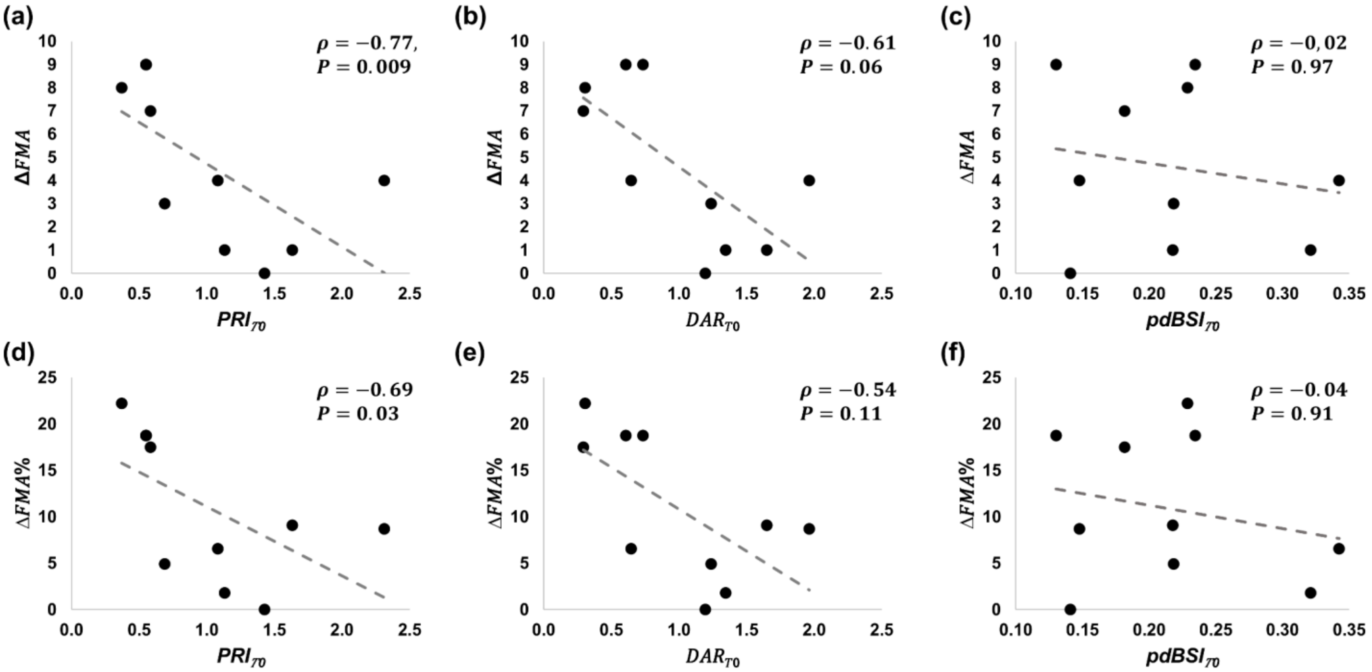

Fig. 2. Scatterplot showing the correlation between QEEG indices at T0 (PRI_{T0}, DAR_{T0}, and $pdBSI_{T0}$) and the clinical outcomes (ΔFMA and ΔFMA%): (a) PRI_{T0} vs ΔFMA; (b) DAR_{T0} vs ΔFMA; (c) $pdBSI_{T0}$ vs ΔFMA; (d) PRI_{T0} vs ΔFMA%; (e) DAR_{T0} vs ΔFMA%; (f) $pdBSI_{T0}$ vs ΔFMA%. The Spearman correlation coefficient (ρ) and the P-value are indicated in each subfigure.

FMA_{T0} and ΔFMA (ρ=0.19, P=0.60), nor between FMA_{T0} and ΔFMA% (ρ=-0.23, P=0.53), suggesting that motor improvements were not related to initial condition (Fig. 3). In addition, the ΔFMA and ΔFMA% were not correlated with neither the age of the patients (ρ=0.12, P=0.74; ρ=-0.049, P=0.89) nor the time since injury (ρ=-0.052, P=0.89; ρ=0.009, P=0.98).

We also tested whether the relative powers in each frequency band were correlated with the ΔFMA. We found a negative correlation between the ΔFMA and the relative power of the delta (ρ=-0.62, P=0.06) and theta (ρ=-0.68, P=0.03) bands, and a positive correlation between ΔFMA and the relative power of the alpha band (ρ=0.61, P=0.06). The relative power in the beta band did not correlate with the ΔFMA (ρ=0.14, P=0.7).

Fig. 4 shows the individual relative power values for each frequency band obtained from the analysis of the EEG signals at T0 and T1. When comparing the relative band powers between T0 and T1, we found no significant changes (P>0.5 for all bands). Consequently, the comparison between T0 and T1 for PRI and DAR indices did not show any significant variation.

The ICCs (95% CI) for PRI and DAR were 0.97 (0.92 to 0.99) and 0.96 (0.88 to 0.99), respectively, indicating good agreement between measurements.

IV. Discussion

Several studies have shown that the QEEG indices, in particular DAR, provide useful information to predict the functional recovery in acute stroke patients [34], [36], [38], and that they are useful to differentiate between stroke patients in the acute phase and healthy controls [64]. On the other hand, its usefulness in the chronic phase of stroke is still not well elucidated.

Currently, only few clinical studies have investigated the relationship between the QEEG indices and the functional outcome after neurorehabilitation in chronic patients [35], [44]–[48], and, to our knowledge, only one study has explored the utility of DAR and PRI indices as predictors of functional outcome [47]. In that study, the authors examined the relationship between three QEEG indices (DAR, PRI and BSI) and their association with the functional outcome of a multidisciplinary rehabilitation program on motor and cognitive functions. Their results showed that DAR index was correlated with the rehabilitation outcome, suggesting that it could play a role in predicting multidisciplinary rehabilitation outcomes. Nevertheless, none of the previous studies has reported the correlation between the above-mentioned QEEG indices and the motor recovery resulting from robot-assisted rehabilitation. To the extent of our knowledge, the present study is the first to evaluate the QEEG indices as predictors of motor recovery in chronic stroke patients that underwent a robot-assisted rehabilitation program.

Robot-assisted therapy has been shown to be promising in the rehabilitation of the upper limb in chronic stroke patients [15]–[17]. Robot systems allow the patients to train autonomously on tasks simulating activities of daily living [50]. Personalized therapy involving robot systems and virtual reality can be used to promote repetition, task oriented training, with appropriate feedback and motivation for under-supervised environments such as the home [18], [20], [27], [67], [68], making this approach an attractive alternative to traditional therapy. Predicting the possible success of the robotic

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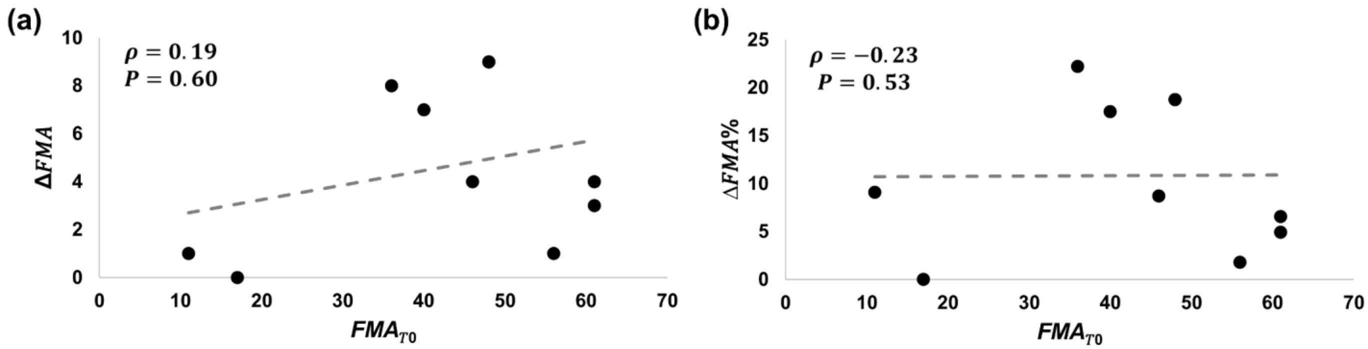

Fig. 3. Scatterplot showing the correlation between (a) FMA_{T0} vs ΔFMA; (b) FMA_{T0} vs ΔFMA%. The Spearman correlation coefficient (ρ) and the P-value are indicated in each subfigure.

intervention becomes essential to select the possible candidates for the therapy, and to optimize the treatment according to the individual level and type of impairment. Within this context, our study investigated the QEEG indices as an objective automatic tool for predicting the motor recovery and supporting the treatment decision making.

In this study, we examined a group of chronic stroke patients to evaluate the relationship between the QEEG indices and the motor outcomes after one month of robot-assisted rehabilitation. The correlation analysis showed a trend to negative relationship between the QEEG indices (PRI and DAR) and both measures of the motor outcome (ΔFMA and ΔFMA%), suggesting that high PRI and DAR values are associated to poorer outcomes in patients that underwent robot-assisted therapy. Although the results of this study suggest that PRI and DAR values might be useful to predict the motor recovery, the statistical power of this study is low because of small sample size, and therefore our results should be considered as exploratory and deserve further investigation. Given the small size of our sample, we did not adjust the P-values for multiple comparisons, which increases the probability of type I error.

The results of the present study are in line with the previous report on chronic patients [47]. As in the previous report, DAR and PRI correlated with the clinical outcomes, and no significant results were found regarding the pdBSI. Yet, there are some differences between this study and the previous report that should be elucidated. First, the previous study examined non-acute acquired brain injury patients (including traumatic brain injury and stroke, more than 6 months post-injury), whereas in the present study we studied a small population of patients in the chronic phase of stroke (including patients at more than one year from the stroke event). Second, in the previous study, patients underwent six months of comprehensive and multidisciplinary neurorehabilitation program, whereas in this study the rehabilitation was only focused on the motor recovery of patients that went through four weeks of robot-assisted motor therapy.

Third, in the previous study the Functional Independence Measure + Functional Assessment Measure (FIM+FAM), a multi-dimensional outcome assessment scale which probe cognitive, behavioral, mobility, locomotion, self-care, communication and physical functions, was used to measure the outcome of the therapy, whereas in this study we used the FMA, which is focused on the motor outcome of the upper limb. The FMA is one of the most widely used quantitative measures of motor impairment [46] and it is applied both in clinical and in research environment to determine disease severity, to describe motor recovery, and to plan and assess treatment. Even in the robotic rehabilitation field, it has often been employed as a primary outcome measure [55], [56], [69]. The FMA has reliable psychometric measures, such as excellent test-retest reliability [70] and excellent interrater/intrarater reliability [71]. These features make the FMA the most suitable clinical scale for the designed work. Some studies suggest that a 10% recovery on the baseline of the FMA scale (6-7 points) is considered as clinically meaningful [69], but the magnitude of change in the FMA that is necessary to produce real-world effects for chronic patients may be smaller, especially for those with severe impairment [69]. Thus, in the literature, many studies suggest to take into account also initial condition (FMA_{T0}) and the percentage of motor recovery in respect to the initial condition [72] for refined evaluation of motor recovery [73]. The previous study proposed a percentage of recovery potential index (PRP), indicating the amount of percentage recovery in respect to the possible achievable recovery. However, applied to the FMA, PRP may penalize severe and moderate impaired patients with respect to mild ones, whose motor recovery may show as 'very high' while not being associated to remarkable daily-life benefits because of ceiling effects [74] that intrinsically characterizes the PRP index.

Lastly, the previous study [47] used a slightly different asymmetry index, the mean BSI (mBSI) defined as the mean of the absolute value of the difference in mean hemispheric power in the frequency range from 1 to 25 Hz. In this study we used the pdBSI, which has been introduced [40] as a slightly refinement of the revised BSI (rBSI), previously proposed by [43]. The pdBSI evaluates asymmetry along homologous, interhemispheric channels pairs instead of a global asymmetry as evaluated by the rBSI. Despite of the slightly differences in the definition of mBSI and pdBSI, our results are in line with [47], with no significant correlations between the pdBSI (or mBSI) and the clinical outcomes. In [47], the authors attributed the lack of significant results regarding mBSI to the possible

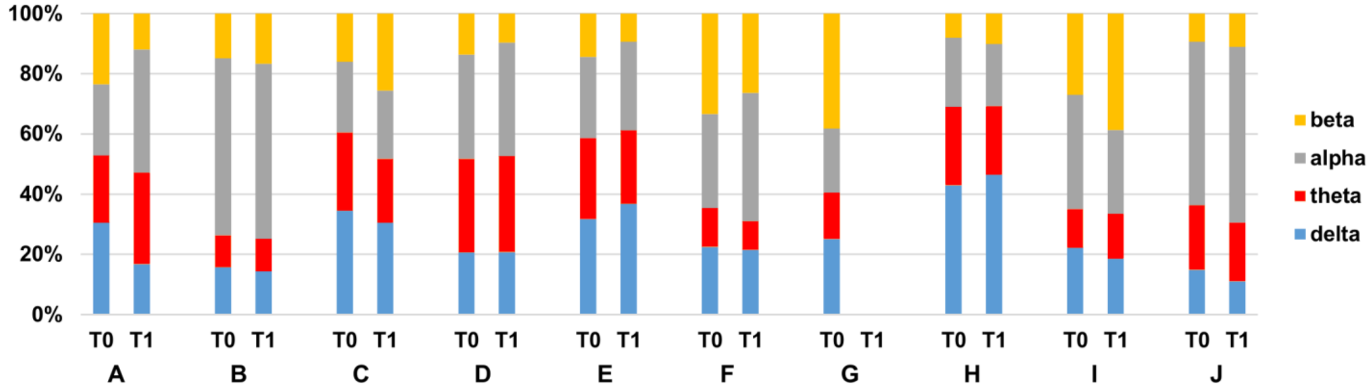

Fig. 4. Bar graphs plotting relative power values for each of the four classical frequency bands in each patient before (T0) and after (T1) treatment.

interaction between the calculation of the index and the QEEG patterns of some patients (e.g. some patients could show similar impairment in homologous electrodes). Additionally, the authors also mentioned that the presence of breach rhythms in a given location might produce asymmetry between that location and the homologous pair, not necessarily related to brain damage. This effect is attenuated in PRI and DAR, because both are calculated as the average of all scalp channels.

Other previous studies have reported that asymmetry index are sensitive in acute [39], [75] and subacute [40] stages to early brain changes and provide prognostic information. In [39] the authors showed that pdBSI obtained within 6 hours of stroke onset reflects early neurological outcome, while pdBSI from EEGs obtained between 6 and 72 hours after symptom onset correlate with functional outcome at month 6, suggesting that functional outcome is revealed once the brain changes are more or less stabilized. However, they did not find any significant correlation between the pdBSI from EEGs obtained between 72 hours and 7 days after symptom onset and the functional outcome at month 6, suggesting that pdBSI might be especially useful as a marker of acute stroke, and should be pursued as soon as feasible to obtain prognostic information. Additionally, they suggested that the effects of stroke are local in the 72 first hours and become more global on longer times scales, and, in fact, they found that PRI (which is a global measure) obtained between 72 hours and 7 days after symptom onset showed higher correlation with the functional outcome at month 6 than the pdBSI. Moreover, in a more recent study [38], the authors compared subacute DAR and pdBSI, and reported that only DAR had significant correlations with functional outcomes.

There are only a few studies reporting the asymmetry indices in chronic stroke patients [47], [76], and the results are inconsistent. In [76], the authors showed a significant correlation between rBSI and FMA improvements, and suggested that rBSI may be used as a prognostic measure for stroke rehabilitation. On the contrary, we and [47] found no significant correlation between pdBSI (or mBSI) and the outcomes of the rehabilitation therapy. Nevertheless, it is worth noting that the asymmetry index used in [76] (i.e. rBSI) is slightly different to the one used in the present study (i.e. pdBSI), but more importantly the experimental conditions of both studies were very different. In particular, in [76], rBSI was computed while patients were performing a task (Motor imagery brain computer interface with robotic feedback), whereas in our study, pdBSI was based on resting-state EEG signal. Given the inconsistent results found in literature, additional studies are necessary to investigate the potential value of the asymmetry indices (e.g. pdBSI, mBSI and rBSI) as a prognostic measure for chronic stroke rehabilitation.

Despite the differences mentioned above, both the study presented in [47] and the present study indicate that there is a tendency of better outcomes for patients that have low DAR and PRI values. In this study, reduced delta and theta activity and increased alpha and beta activity seemed to be associated with favorable outcomes, suggesting that better clinical outcomes come from higher frequency bands in brain activity, which can be related to better reactivity and receptiveness of the patient [77]. Our findings are also consistent with the results of previous studies in acute stroke patients [34], [36]–[40], in which decreases in delta activity and increases in alpha activity were associated with better outcomes. Previous studies [47], [64] showed a stronger correlation between DAR and the functional outcome, whereas in this study, the stronger correlation was found for PRI. This observation, together with the significant negative correlation between the relative power in the theta band and the motor recovery found in this study, suggests that theta band might also add value to the prediction when pure motor recovery is considered. However, this particular finding deserves further investigation in order to provide a solid pathophysiological interpretation.

A recent study [64] showed that DAR could be used to differentiate acute stroke patients from healthy controls, and in particular a threshold of 3.7 demonstrated maximal accuracy for classifying all participants as acute stroke or control. In this study, all of the chronic stroke patients had DAR values lower than 3, and the relative power values for each of the four classical frequency bands bear a closer resemblance to the reported [64] bandpowers for the control participants than for the acute stroke patients. Given that DAR values of the chronic stroke patients examined in this study, as well as their relative band-powers, were in the range of values previously reported for healthy subjects [64], we did not expect substantial changes in the QEEG measures before and after treatment, and in fact, our results showed no significant changes. Our results suggest that PRI and DAR (based on resting-state eyes-closed EEG signal) in chronic patients are stable, even after motor rehabilitation.

In this study, we did not expect to find a correlation between the QEEG indices and a neurologic recovery in chronic patients, but rather to show that QEEG could be useful to assess the tendency of a chronic patient to improve (re-learn) the execution of upper limb movements. Our results are in line with a previous study [78], which suggested that enhanced alpha bandpower may be related to better movement performance, and better reactivity and receptiveness [77]. Following this line of reasoning, a patient with high alpha power (thus low PRI and DAR) could be more receptive to relearn movement, and make better use of the therapy, and thus, pre-therapy (T0) QEEG indices could be useful to predict the outcome of motor rehabilitation.

The main limitation of the present study is the small number of subjects due to the complexity and length of the study protocol (i.e. patient selection, evaluation pre-treatment, robot-assisted rehabilitation, evaluation post-treatment). Nevertheless, it is worth noting that, even if small, the sample of this study was diverse and covered a wide range of FMA values (11-61, pre-treatment), as well as years after stroke (1-14), and thus, it could be considered as representative of the chronic stroke patient population. Despite of the small sample size, we believe our results showed interesting trends on chronic patients, and are still appealing considering the lack of studies in this field of research, and the contradictory results found in the literature. Our results showed interesting tendencies that have not been investigated before on chronic patients, which are usually considered as having low potential improvement. Yet, the results of this study should be considered as a first exploratory insight about the predictive use of QEEG indices in the motor rehabilitation outcomes in chronic stroke patients, and prospective experiments with a bigger sample size are needed to confirm our results.

Finally, the purpose of the present study was to demonstrate that simple QEEG indices could predict the outcomes of motor rehabilitation in chronic stroke patients. PRI and DAR indices are simple numerical values that are easy to calculate, and relatively straightforward to interpret, and thus may provide valuable information for clinical decision-making. However, further complementary EEG measures, such as those derived from resting-state connectivity analysis should provide a more comprehensive overview of brain status, and additional prospective studies shall evaluate its usefulness to predict the success of rehabilitation in chronic stroke patients.

V. Conclusion

The results of this study suggest that QEEG indices may be useful to predict motor outcomes, offering valuable information for clinical decision-making. This kind of information is of critical importance when selecting the possible candidates for robot-assisted rehabilitation. While the results of this study suggest that patients with low PRI e DAR values are more prone to motor improvements, further studies in larger samples are needed to validate the role of QEEG in predicting motor recovery.

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References

[1] World Health Organization, “The global burden of disease: 2004 update,” Geneve, Switzerland, 2008.
[2] R. L. Harvey, C J. Stain, J. Winstein, G. F. Wittenberg, and R. D. Zorowitz, "Stroke Recovery and Rehabilitation," 2nd Ed. Demos Medical Publising, 2014.
[3] World Health Organization, “World health report 2003,” Geneva, Switzerland, 2003.
[4] C. Warlow, J. van Gijn, M. Dennis, J. Wardlaw, J. Bamford, G. Hankey, P. Sandercock, G. Rinkel, P. Langhorne, C. Sudlow, and P. Rothwell, "Stroke: practical management," 3rd Ed. Blackwell Publishing Ltd, Oxford, UK, 2008.
[5] National Institute of Neurological Disorders and Stroke, “Post-Stroke Rehabilitation,” NIH Publication n° 14-1846, 2014.
[6] D. T. Wade, R. Langton-Hewer, V. A. Wood, C. E. Skilbeck, and H. M. Ismail, “The hemiplegic arm after stroke: measurement and recovery,” *J. Neurol. Neurosurg. Psychiatry*, vol. 46, no. 6, pp. 521–524, Jun. 1983.
[7] A. Sunderland, D. Tinson, L. Bradley, and R. L. Hewer, “Arm function after stroke. An evaluation of grip strength as a measure of recovery and a prognostic indicator,” *J. Neurol. Neurosurg. Psychiatry*, vol. 52, no. 11, pp. 1267–1272, Nov. 1989.
[8] C. A. Trombly and H. Ma, “A synthesis of the effects of occupational therapy for persons with stroke, Part I: Restoration of roles, tasks, and activities,” *Am. J. Occup. Ther.*, vol. 56, no. 3, pp. 250–259, May-Jun 2002.
[9] A. R. Luft, S. McCombe-Waller, J. Whitall, L. W. Forrester, R. Macko, J. D. Sorkin, J. B. Schulz, A. P. Goldberg, and D. F. Hanley, “Repetitive bilateral arm training and motor cortex activation in chronic stroke: a randomized controlled trial,” *JAMA*, vol. 292, no. 15, pp. 1853–1861, Oct. 2004.
[10] B. E. Fisher and K. J. Sullivan, “Activity-dependent factors affecting poststroke functional outcomes,” *Top. Stroke Rehabil.*, vol. 8, no. 3, pp. 31–44, 2001.
[11] J. D. Schaechter, “Motor rehabilitation and brain plasticity after hemiparetic stroke,” *Prog. Neurobiol.*, vol. 73, no. 1, pp. 61–72, May 2004.
[12] L. Oujamaa, I. Relave, J. Froger, D. Mottet, and J.-Y. Pelissier, “Rehabilitation of arm function after stroke. Literature review,” *Ann. Phys. Rehabil. Med.*, vol. 52, no. 3, pp. 269–293, Apr. 2009.
[13] P. Langhorne, F. Coupar, and A. Pollock, “Motor recovery after stroke: a systematic review,” *Lancet. Neurol.*, vol. 8, no. 8, pp. 741–754, Aug. 2009.
[14] G. Bin Song, “The effects of task-oriented versus repetitive bilateral arm training on upper limb function and activities of daily living in stroke patients,” *J. Phys. Ther. Sci.*, vol. 27, no. 5, pp. 1353–1355, May 2015.
[15] S. Masiero, M. Armani, and G. Rosati, “Upper-limb robot-assisted therapy in rehabilitation of acute stroke patients: focused review and results of new randomized controlled trial,” *J. Rehabil. Res. Dev.*, vol. 48, no. 4, pp. 355–366, 2011.
[16] G. B. Prange, M. J. A. Jannink, C. G. M. Groothuis-Oudshoorn, H. J. Hermens, and M. J. Ijzerman, “Systematic review of the effect of robot-aided therapy on recovery of the hemiparetic arm after stroke,” *J. Rehabil. Res. Dev.*, vol. 43, no. 2, pp. 171–184, Mar-Apr 2006.
[17] R. Colombo, F. Pisano, A. Mazzone, C. Delconte, S. Micera, M. C. Carrozza, P. Dario, and G. Minuco, “Design strategies to improve patient

motivation during robot-aided rehabilitation," *J. Neuroeng. Rehabil.*, vol. 4, p. 3, Feb. 2007.
[18] T. G. Sugar, J. He, E. J. Koeneman, J. B. Koeneman, R. Herman, H. Huang, R. S. Schultz, D. E. Herring, J. Wanberg, S. Balasubramanian, P. Swenson, and J. A. Ward, "Design and control of RUPERT: A device for robotic upper extremity repetitive therapy," *IEEE Trans. Neural Syst. Rehabil. Eng.*, vol. 15, no. 1, pp. 336–346, Sep. 2007.
[19] P. Poli, G. Morone, G. Rosati, and S. Masiero, "Robotic technologies and rehabilitation: new tools for stroke patients' therapy," *Biomed Res. Int.*, vol. 2013, p. 153872, 2013.
[20] M. J. Johnson, X. Feng, L. M. Johnson, and J. M. Winters, "Potential of a suite of robot/computer-assisted motivating systems for personalized, home-based, stroke rehabilitation," *J. Neuroeng. Rehabil.*, vol. 1, p. 4-6, Mar. 2007.
[21] M. Malosio, M. Caimmi, G. Legnani, and L. M. Tosatti, "LINarm: A low-cost variable stiffness device for upper-limb rehabilitation," in *IEEE Int. Conf. Intell. Robot. Syst.*, Chicago, IL, USA, 2014, pp. 3598–3603.
[22] I. Sharp, J. Patton, M. Listenberger, and E. Case, "Haptic/graphic rehabilitation: integrating a robot into a virtual environment library and applying it to stroke therapy," *J. Vis. Exp.*, vol. 54, e3007, 2011.
[23] A. Mirelman, B. L. Patritti, P. Bonato, and J. E. Deutsch, "Effects of virtual reality training on gait biomechanics of individuals post-stroke," *Gait Posture*, vol. 31, no. 4, pp. 433–437, Apr. 2010.
[24] D. De Santis, J. Zenzeri, M. Casadio, L. Masia, A. Riva, P. Morasso, and V. Squeri, "Robot-assisted training of the kinesthetic sense: enhancing proprioception after stroke," *Front. Hum. Neurosci.*, vol. 8, p. 1037, Jan. 2015.
[25] S.-C. Yeh, S.-H. Lee, R.-C. Chan, S. Chen, and A. Rizzo, "A virtual reality system integrated with robot-assisted haptics to simulate pinch-grip task: Motor ingredients for the assessment in chronic stroke," *NeuroRehabilitation*, vol. 35, no. 3, pp. 435–449, 2014.
[26] S. Ueki, Y. Nishimoto, M. Abe, H. Kawasaki, S. Ito, Y. Ishigure, J. Mizumoto, and T. Ojika, "Development of virtual reality exercise of hand motion assist robot for rehabilitation therapy by patient self-motion control," in *Conf. Proc. IEEE Eng. Med. Biol. Soc.*, Vancouver, BC, Canada, 2008, pp. 4282–4285.
[27] A. Mastropietro, S. Arlati, S. Mrakic-Sposta, L. Fontana, C. Franchin, M. Malosio, S. Pittaccio, C. Gramigna, F. Molteni, M. Sacco, and G. Rizzo, "Quantitative EEG and Virtual Reality to Support Post-stroke Rehabilitation at Home," in *Innovation in Medicine and Healthcare*, 2016, pp. 147–157.
[28] L. Brewer, F. Horgan, A. Hickey, and D. Williams, "Stroke rehabilitation: recent advances and future therapies," *QJM*, vol. 106, no. 1, pp. 11–25, Jan. 2013.
[29] M. P. Alexander, "Stroke rehabilitation outcome. A potential use of predictive variables to establish levels of care," *Stroke*, vol. 25, no. 1, pp. 128–134, Jan. 1994.
[30] R. Teasell, N. Hussein, R. Viana, M. Madady, S. Donaldson, A. McClure, and M. Richardson, "Stroke Rehabilitation Clinician Handbook," *Heart and Stroke Foundation*, London, Canada, 2015.
[31] R. H. M. Nijland, E. E. H. van Wegen, B. C. Harmeling-van der Wel, G. Kwakkel, and EPOS Investigators, "Presence of finger extension and shoulder abduction within 72 hours after stroke predicts functional recovery: early prediction of functional outcome after stroke: the EPOS cohort study," *Stroke*, vol. 41, no. 4, pp. 745–750, Apr. 2010.
[32] C. Calautti and J.-C. Baron, "Functional Neuroimaging Studies of Motor Recovery After Stroke in Adults A Review," *Stroke*, vol. 34, no. 6, pp. 1553–1566, Jun. 2003.
[33] C. Granziera, A. Daducci, D. E. Meskaldji, A. Roche, P. Maeder, P. Michel, N. Hadjikhani, A. G. Sorensen, R. S. Frackowiak, J. P. Thiran, R. Meuli, and G. Krueger, "A new early and automated MRI-based predictor of motor improvement after stroke," *Neurology*, vol. 79, no. 1, pp. 39–46, Jul. 2012.
[34] S. P. Finnigan, S. E. Rose, M. Walsh, M. Griffin, A. L. Janke, K. L. McMahon, R. Gillies, M. W. Strudwick, C. M. Pettigrew, J. Semple, J. Brown, P. Brown, and J. B. Chalk, "Correlation of Quantitative EEG in Acute Ischemic Stroke with 30-Day NIHSS Score: Comparison with Diffusion and Perfusion MRI," *Stroke*, vol. 35, no. 4, pp. 899–903, Apr. 2004.
[35] C. Gerloff, K. Bushara, A. Sailer, E. M. Wassermann, R. Chen, T. Matsuoka, D. Waldvogel, G. F. Wittenberg, K. Ishii, L. G. Cohen, and M. Hallett, "Multimodal imaging of brain reorganization in motor areas of the contralesional hemisphere of well recovered patients after capsular stroke," *Brain*, vol. 129, no. 3, pp. 791–808, Mar. 2006.
[36] S. Finnigan and M. J. A. M. van Putten, "EEG in ischaemic stroke: Quantitative EEG can uniquely inform (sub-)acute prognoses and clinical management," *Clin. Neurophysiol.*, vol. 124, no. 1, pp. 10–19, Jan. 2013.
[37] S. P. Finnigan, M. Walsh, S. E. Rose, and J. B. Chalk, "Quantitative EEG indices of sub-acute ischaemic stroke correlate with clinical outcomes," *Clin. Neurophysiol.*, vol. 118, no. 11, pp. 2525–2532, Nov. 2007.
[38] E. Schleiger, N. Sheikh, T. Rowland, A. Wong, S. Read, and S. Finnigan, "Frontal EEG delta/alpha ratio and screening for post-stroke cognitive deficits: the power of four electrodes," *Int. J. Psychophysiol.*, vol. 94, no. 1, pp. 19–24, Oct. 2014.
[39] R. V. A. Sheorajpanday, G. Nagels, A. J. T. M. Weeren, M. J. A. M. van Putten, and P. P. De Deyn, "Quantitative EEG in ischemic stroke: Correlation with functional status after 6months," *Clin. Neurophysiol.*, vol. 122, no. 5, pp. 874–883, May 2011.
[40] R. V. A. Sheorajpanday, G. Nagels, A. J. T. M. Weeren, M. J. A. M. van Putten, and P. P. De Deyn, "Reproducibility and clinical relevance of quantitative EEG parameters in cerebral ischemia: a basic approach," *Clin. Neurophysiol.*, vol. 120, no. 5, pp. 845–855, May 2009.
[41] J. Claassen, L. J. Hirsch, K. T. Kreiter, E. Y. Du, E. S. Connolly, R. G. Emerson, and S. A. Mayer, "Quantitative continuous EEG for detecting delayed cerebral ischemia in patients with poor-grade subarachnoid hemorrhage," *Clin. Neurophysiol.*, vol. 115, no. 12, pp. 2699–2710, Dec. 2004.
[42] M. J. A. M. van Putten, J. M. Peters, S. M. Mulder, J. A. M. de Haas, C. M. A. Bruijninckx, and D. L. J. Tavy, "A brain symmetry index (BSI) for online EEG monitoring in carotid endarterectomy," *Clin. Neurophysiol.*, vol. 115, no. 5, pp. 1189–1194, May 2004.
[43] M. J. A. M. van Putten, "The revised brain symmetry index.," *Clin. Neurophysiol.*, vol. 118, no. 11, pp. 2362–2367, Nov. 2007.
[44] A. Muralidharan, J. Chae, and D. M. Taylor, "Extracting attempted hand movements from EEGs in people with complete hand paralysis following stroke," *Front. Neurosci.*, vol. 5, no. MAR, pp. 1–7, Mar. 2011.
[45] M. J. Fu, J. J. Daly, and M. C. Cavusoglu, "Assessment of EEG event-related desynchronization in stroke survivors performing shoulder-elbow movements," in *Proceedings 2006 IEEE International Conference on Robotics and Automation,* Orlando, FL, USA, 2006, pp. 3158–3164.
[46] M. Simis, D. Doruk, M. Imamura, R. Anghinah, L. Morales-Quezada, F. Fregni, and L. R. Battistella, "Neurophysiologic predictors of motor function in stroke," *Restor. Neurol. Neurosci.*, vol. 34, no. 1, pp. 45–54, Oct. 2015.
[47] J. Leon-Carrion, J. F. Martin-Rodriguez, J. Damas-Lopez, J. M. Barroso y Martin, and M. R. Dominguez-Morales, "Delta-alpha ratio correlates with level of recovery after neurorehabilitation in patients with acquired brain injury," *Clin. Neurophysiol.*, vol. 120, no. 6, pp. 1039–1045, Jun. 2009.
[48] P. Sale, F. Infarinato, C. Del Percio, R. Lizio, C. Babiloni, C. Foti, and M. Franceschini, "Electroencephalographic markers of robot-aided therapy in stroke patients for the evaluation of upper limb rehabilitation," Int. J. Rehabil. Res., vol. 38, no. 4, pp. 294–305, Dec. 2015.
[49] G. Pfurtscheller and F. H. Lopes da Silva, "Event-related EEG/MEG synchronization and desynchronization: basic principles," *Clin. Neurophysiol.*, vol. 110, no. 11, pp. 1842–1857, Nov. 1999.
[50] M. Caimmi, E. Visani, F. Digiacomo, A. Scano, A. Chiavenna, C. Gramigna, L. Molinari Tosatti, S. Franceschetti, F. Molteni, and F. Panzica, "Predicting Functional Recovery in Chronic Stroke Rehabilitation Using Event-Related Desynchronization-Synchronization during Robot-Assisted Movement," *Biomed Res. Int.*, vol. 2016, article ID 7051340, 2016.
[51] E. Formaggio, S. F. Storti, I. Boscolo Galazzo, M. Gandolfi, C. Geroin, N. Smania, L. Spezia, A. Waldner, A. Fiaschi, and P. Manganotti, "Modulation of event-related desynchronization in robot-assisted hand performance: brain oscillatory changes in active, passive and imagined movements," *J. Neuroeng. Rehabil.*, vol. 10, no. 1, p. 24, Feb. 2013.
[52] M. Caimmi, N. Pedrocchi, A. Scano, M. Malosio, F. Vicentini, L. M. Tosatti, and F. Molteni, "Proprioceptivity and upper-extremity dynamics in robot-assisted reaching movement," in P*roc. IEEE RAS EMBS Int. Conf. Biomed. Robot. Biomechatronics*, Rome, Italy, 2012, pp. 1316–1322.
[53] A. R. Fugl-Meyer, L. Jääskö, I. Leyman, S. Olsson, and S. Steglind, "The post-stroke hemiplegic patient. 1. a method for evaluation of physical performance," *Scand. J. Rehabil. Med.*, vol. 7, no. 1, pp. 13–31, 1975.
[54] D. J. Gladstone, C. J. Danells, and S. E. Black, "The fugl-meyer assessment of motor recovery after stroke: a critical review of its measurement properties," *Neurorehabil. Neural Repair*, vol. 16, no. 3, pp.

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232–240, Sep. 2002.

[55] C. G. Burgar, P. S. Lum, A. M. E. Scremin, S. L. Garber, H. F. M. Van der Loos, D. Kenney, and P. Shor, "Robot-assisted upper-limb therapy in acute rehabilitation setting following stroke: Department of Veterans Affairs multisite clinical trial," *J. Rehabil. Res. Dev.*, vol. 48, no. 4, pp. 445–458, 2011.

[56] P. S. Lum, C. G. Burgar, P. C. Shor, M. Majmundar, and M. Van der Loos, "Robot-assisted movement training compared with conventional therapy techniques for the rehabilitation of upper-limb motor function after stroke," *Arch. Phys. Med. Rehabil.*, vol. 83, no. 7, pp. 952–959, Jul. 2002.

[57] K. J. Sullivan, J. K. Tilson, S. Y. Cen, D. K. Rose, J. Hershberg, A. Correa, J. Gallichio, M. McLeod, C. Moore, S. S. Wu, and P. W. Duncan, "Fugl-Meyer assessment of sensorimotor function after stroke: standardized training procedure for clinical practice and clinical trials," *Stroke*, vol. 42, no. 2, pp. 427–432, Feb. 2011.

[58] T. P. Jung, S. Makeig, C. Humphries, T. W. Lee, M. J. McKeown, V. Iragui, and T. J. Sejnowski, "Removing electroencephalographic artifacts by blind source separation," *Psychophysiology*, vol. 37, no. 2, pp. 163–178, Mar. 2000.

[59] A. J. Bell and T. J. Sejnowski, "An information-maximization approach to blind separation and blind deconvolution," *Neural Comput.*, vol. 7, no. 6, pp. 1129–1159, Nov. 1995.

[60] A. Mognon, J. Jovicich, L. Bruzzone, and M. Buiatti, "ADJUST: An automatic EEG artifact detector based on the joint use of spatial and temporal features," *Psychophysiology*, vol. 48, no. 2, pp. 229–240, Feb. 2011.

[61] H. Nolan, R. Whelan, and R. B. Reilly, "FASTER: Fully Automated Statistical Thresholding for EEG artifact Rejection," *J. Neurosci. Methods*, vol. 192, no. 1, pp. 152–162, Sep. 2010.

[62] I. Winkler, S. Haufe, and M. Tangermann, "Automatic Classification of Artifactual ICA-Components for Artifact Removal in EEG Signals," *Behav. Brain Funct.*, vol. 7, no. 1, p. 30, Aug. 2011.

[63] M. Chaumon, D. V. M. Bishop, and N. A. Busch, "A practical guide to the selection of independent components of the electroencephalogram for artifact correction," *J. Neurosci. Methods*, vol. 250, pp. 47–63, Jul. 2015.

[64] S. Finnigan, A. Wong, and S. Read, "Defining abnormal slow EEG activity in acute ischaemic stroke: Delta/alpha ratio as an optimal QEEG index," *Clin. Neurophysiol.*, vol. 127, no. 2, pp. 1452–1459, Feb. 2016.

[65] R. Yuvaraj, M. Murugappan, N. Mohamed Ibrahim, M. Iqbal, K. Sundaraj, K. Mohamad, R. Palaniappan, E. Mesquita, and M. Satiyan, "On the analysis of EEG power, frequency and asymmetry in Parkinson's disease during emotion processing," *Behav. Brain Funct.*, vol. 10, no. 1, p. 12, Apr. 2014.

[66] K. Nagata, K. Tagawa, S. Hiroi, F. Shishido, and K. Uemura, "Electroencephalographic correlates of blood flow and oxygen metabolism provided by positron emission tomography in patients with cerebral infarction," *Electroencephalogr. Clin. Neurophysiol.*, vol. 72, no. 1, pp. 16–30, Jan. 1989.

[67] S. Comani, L. Velluto, L. Schinaia, G. Cerroni, A. Serio, S. Buzzelli, S. Sorbi, and B. Guarnieri, "Monitoring Neuro-Motor Recovery From Stroke With High-Resolution EEG, Robotics and Virtual Reality: A Proof of Concept," *IEEE Trans. Neural Syst. Rehabil. Eng.*, vol. 23, no. 6, pp. 1106–1116, Nov. 2015.

[68] Y. Shakya and M. J. Johnson, "A mobile robot therapist for under-supervised training with robot/computer assisted motivating systems," in *Conf. Proc. IEEE Eng. Med. Biol. Soc.*, Vancouver, BC, Canada, 2008, pp. 4511–4514.

[69] A. C. Lo, P. D. Guarino, L. G. Richards, J. K. Haselkorn, G. F. Wittenberg, D. G. Federman, R. J. Ringer, T. H. Wagner, H. I. Krebs, B. T. Volpe, C. T. Bever, D. M. Bravata, P. W. Duncan, B. H. Corn, A. D. Maffucci, S. E. Nadeau, S. S. Conroy, J. M. Powell, G. D. Huang, and P. Peduzzi, "Robot-assisted therapy for long-term upper-limb impairment after stroke," *N. Engl. J. Med.*, vol. 362, no. 19, pp. 1772–1783, May 2010.

[70] T. Platz, C. Pinkowski, F. van Wijck, I.-H. Kim, P. di Bella, and G. Johnson, "Reliability and validity of arm function assessment with standardized guidelines for the Fugl-Meyer Test, Action Research Arm Test and Box and Block Test: a multicentre study," *Clin. Rehabil.*, vol. 19, no. 4, pp. 404–411, Jun. 2005.

[71] P. W. Duncan, M. Propst, and S. G. Nelson, "Reliability of the Fugl-Meyer assessment of sensorimotor recovery following cerebrovascular accident," *Phys. Ther.*, vol. 63, no. 10, pp. 1606–1610, Oct. 1983.

[72] S. J. Page, G. D. Fulk, and P. Boyne, "Clinically important differences for the upper-extremity Fugl-Meyer Scale in people with minimal to moderate impairment due to chronic stroke," *Phys. Ther.*, vol. 92, no. 6, pp. 791–798, Jun. 2012.

[73] E. Zarahn, L. Alon, S. L. Ryan, R. M. Lazar, M.-S. S. Vry, C. Weiller, R. S. Marshall, and J. W. Krakauer, "Prediction of motor recovery using initial impairment and fMRI 48 h poststroke," *Cereb. Cortex*, vol. 21, no. 12, pp. 2712–2721, Dec. 2011.

[74] H.-F. Mao, I.-P. Hsueh, P.-F. Tang, C.-F. Sheu, and C.-L. Hsieh, "Analysis and comparison of the psychometric properties of three balance measures for stroke patients," *Stroke*, vol. 33, no. 4, pp. 1022–1027, Apr. 2002.

[75] M. J. A. M. van Putten and D. L. J. Tavy, "Continuous quantitative EEG monitoring in hemispheric stroke patients using the brain symmetry index," *Stroke*, vol. 35, no. 11, pp. 2489–2492, Oct. 2004.

[76] K. K. Ang, K. S. G. Chua, K. S. Phua, C. Wang, Z. Y. Chin, C. W. K. Kuah, W. Low, and C. Guan, "A Randomized Controlled Trial of EEG-Based Motor Imagery Brain-Computer Interface Robotic Rehabilitation for Stroke," *Clin. EEG Neurosci.*, vol. 46, no. 4, pp. 310–320, Oct. 2014.

[77] W. Klimesch, "α-band oscillations, attention, and controlled access to stored information," *Trends Cogn. Sci.*, vol. 16, no. 12, pp. 606–617, Dec. 2012.

[78] T. Meyer, J. Peters, T. O. Zander, B. Schölkopf, and M. Grosse-Wentrup, "Predicting motor learning performance from Electroencephalographic data," *J. Neuroeng. Rehabil.*, vol. 11, p. 24, Jan. 2014.