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A multimodal analysis to explore upper limb motor recovery at 4 weeks after stroke: insights from EEG and kinematics measures.

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Abstract:	Background: Stroke is a leading cause of death and disability worldwide and there is a very short period of increased synaptic plasticity, fundamental in motor recovery. Thus, it is crucial to acquire data to guide the rehabilitation treatment. Promising results have been achieved with kinematics and neurophysiological data, but currently few studies integrate these different modalities. Objectives: We analysed the role of kinematic and electroencephalography (EEG) measures in predicting motor recovery four weeks after stroke. Methods: 26 patients were considered. Among them, 20 patients also performed the EEG study, beyond the kinematic analysis, at 4 weeks. We explored the correlations between standardised clinical scales, kinematic data and EEG measures. Results: We found interesting correlations between the Fugl-Meyer Assessment-Upper Extremity, movement duration, smoothness measures and velocity peaks. Moreover, EEG measures showed a tendency for the healthy hemisphere to vicariate the affected one in patients characterized by better clinical conditions. Conclusions: These results suggest the relevance of early kinematic and EEG biomarkers to predict post-stroke recovery. We emphasise the importance of integrating clinical data with kinematic and EEG analyses from the early stroke stages, in order to guide rehabilitation strategies to best leverage the short period of increased synaptic plasticity.

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Key-words: Stroke, Motor recovery, FMA-UE, EEG, Kinematic, Upper Limb

Short title: EEG, kinematics and stroke motor recovery

List of abbreviations: EEG: Electroencephalography; qEEG: quantitative Electroencephalography; FMA-UE: Fugl-Meyer Assessment - Upper Extremity; DAR:

delta/alpha ratio; DTABR: delta+theta/alpha+beta ratio; BSI: Brain Simmetry Index; dirBSI: Diretional Brain Simmetry Index; PSD: Power Spectral Density; ARAT: Action Research Arm Test; TMS: Transcranial Magnetic Stimulation; NIHSS: National Institutes of Health Stroke Scale; MRI: Magnetic Rensonance Imaging; CNS: Central Nervous System; ROM: Range of Motion; M1: primary motor cortex; MEP: Motor Evoked Potentials; FDI: first dorsal interosseous muscle; RMT: Resting Motor Threshold; UE: Upper Extremity; ICA: Independent Component Analysis; AH: Affected Hemisphere; UH: Unaffected Hemisphere; #PV: Peak Velocity.

Availability of data and materials: the dataset used for the data analysis is available on reasonable request to the corresponding author.

1. Introduction

Stroke is a leading cause of worldwide death and disability [1]. Given the difficulties in post-stroke rehabilitation, a great deal of research has been carried out attempting to identify biomarkers capable of predicting motor recovery, often assessed by standardised clinical scales [2,3]. Depending on stroke location, different prognostic and therapeutic implications arise, leading to different rehabilitation considerations [4]. Thus, one of the most important objectives is the search for individualised and tailor-made biomarkers in post-stroke rehabilitation [5], also considering that standardised measurement scales are not always able to describe the complexity of the individual condition. Therefore, in addition to the clincal assessements, it is crucial to identify other sources of information enabling improved patient characterization, to guide rehabilitation.

Electroencephalography (EEG), in particular quantitative EEG (qEEG), is a non-invasive, easy-to-apply, repeatable and low-cost method that can provide useful information on the changes that occur in cortical activity following stroke. Generally stroke patients show power in slow EEG rhythms, particularly in the theta and delta bands [6]. EEG recordings can be made at rest (i.e. resting state) or while performing mental or motor tasks. In this work, we

analyzed resting state recordings and focused our analysis on the delta-alpha ratio (DAR) and the Brain Symmetry Index (BSI) parameters that can be extracted from the EEG. The DAR measures the ratio between slow (lesional) and faster (physiological) rhythms, with research showing that subacute stroke survivors show increased DAR values compared to healthy individuals, at least in the early post-stroke phase [7], driven by increased delta activity in the acute/subacute period that tends to normalize in the chronic period [8]. Delta+theta/alpha+beta ratio (DTABR) is linked to DAR but is additionally sensitive to theta and beta activity, which may sometimes be informative [7]. The BSI evaluates the asymmetry between the spectral powers obtained from the two hemispheres [9] and it could be a useful measure for assessing the reorganisation of cortical areas after stroke, in particular by evaluating the intervention of the healthy hemisphere to vicariate impaired functions of the damaged one [10]. Directional BSI (dirBSI) provides information not only on the asymmetry between the spectral powers obtained from the hemispheres, but also to take the direction of this asymmetry into account [8]; dirBSI = 0 represents perfect symmetry, positive values (0-1) represent higher power in the affected hemisphere, vice versa for negative values. Therefore, for stroke survivors a positive value corresponds to higher power in the affected hemisphere compared to the unaffected one. Measures of qEEG are of great interest during stroke recovery, since stroke patients undergo a structural and functional brain reorganisation, in order to recover impaired functions through the modification of cortical-subcortical networks [10,11].

The time interval for neuroplasticity to support recovery is very limited and it is therefore essential to start rehabilitation early after stroke [11]. Recently, considerable support has been provided by the possibility of integrating clinical and neurophysiological data with kinematic analyses, which allow to get useful information on movement characteristics. Indeed, kinematic parameters make it possible to analyse the quality of movements, highlighting the strategies and motor patterns used in order to distinguish between true motor recovery and compensation, in the impossibility of achieving the former instead of the latter

[12]. Here, we evaluate the potential association between clinical assessments, reaching task kinematic data and qEEG measures in predicting recovery four weeks after stroke.

2. Methods

We describe a cross-sectional observational clinical study, conducted between April 2019 and April 2021. Subjects with first diagnosis of stroke admitted to our University Hospital were recruited. Subjects were evaluated and interviewed to determine the presence of inclusion and/or exclusion criteria, were informed about the study procedures, and informed consent was then requested. Inclusion criteria were: 18 years or older; first cerebral stroke (ischemic or haemorrhagic) verified by brain imaging; evaluation within 7 days since stroke with the PREP2 algorithm [13] for upper limb paresis. Exclusion criteria were: cerebellar stroke or bilateral cerebral stroke, any medical and neurological conditions that may interfere with the ability to safely complete the study or to comprehend, severe cardiopulmonary, renal, or hepatic disease and pregnancy. All participants signed their informed consent.

2.1. Procedures

2.1.1 Clinical and instrumental evaluations

Data were collected at 3-7 days (T0) and 4 weeks (T1) from the acute cerebrovascular event. According to the PREP2 algorithm [13], the National Institutes of Health Stroke Scale (NIHSS), the SAFE Score and Transcranial Magnetic Stimulation (TMS) were collected at T0. The Action Research Arm Test (ARAT), the FMA-UE, the kinematics and resting state EEG were collected at 4 weeks (T1) after stroke onset, respectively.

NIHSS is an important predictor for outcome, consisting of a scale that is useful in quantifying the overall severity [14]. ARAT is an observational test used to determine the function of the upper limb [15]. FMA-UE is a commonly used scale in the rehabilitation field, widely recognised in terms of validity and reliability for upper limb impairment, in particular about the quantification of the influence of pathological synergies on the current motor activity [16,17].

Single-pulse TMS on the primary motor area (M1) was used to study the excitability of the cortico-spinal tract by electromyographically recording the Motor Evoked Potentials (MEPs) of the first dorsal interosseous muscle (FDI) of both hands at baseline as a possible prognostic factor. The resting motor threshold (RMT, i.e. the lowest stimulation intensity capable of inducing 5/10 MEPs with a peak-to-peak amplitude of at least 50 μV) was recorded for each hemisphere. Ten TMS pulses were delivered with a figure-of-eight coil connected to a MagStim 200 monophasic stimulator with an intensity of 120% RMT. The presence of MEP is an early prognostic factor of functional recovery as it provides information on the state of the cortico-spinal tract [18]. Finally, EEG was recorded during resting state, 3 minutes with eyes open, 3 minutes with eyes closed. During the 'open eyes' portion subjects had to fix a white cross on a black background. Participants were instructed to remain seated, trying not to move for the entire duration of the recording.

2.1.2 Kinematic Recording and Data Analysis

Kinematics was acquired with the subjects seated on a bench with no back support, with hip and knee flexed at 90°. The patient was asked to perform two different movements: Reach Up and Reach Out (see Figure 1). During the second movement, subjects had placed in front of them a table with a target-can on it (weight about 300 grams) placed in coincidence with the midline of the subject at a distance equal to the length of the entire upper limb. Each movement, performed with the impaired limb, was repeated 5 times and of these trials the three best performances were maintained. During each trial, study participants were instructed to perform the movements at a self-selected speed. A 14-camera motion capture system (Vicon, Oxford Metrics Ltd., Oxford, UK) was used to track reflective markers placed on the upper body during the movement. Nexus 2.8.1 software (Vicon, Oxford Metrics Ltd, Oxford, UK) was used to derive motion kinematics from the position data of the reflective upper extremity (UE) markers. The start and end of the target reaching movements were identified using the marker located metacarpophalangeal joint of the index finger; events were manually verified. Joint angles were estimated using Nexus software 2.8.1 via a

standard biomechanical model [19] in which the anatomical joints are represented as universal joints. The data were then imported into MATLAB (R2019a, The Math- Works Inc., Natick MA, USA) and custom scripts were used to assess the several kinematic parameters. The marker placed on metacarpophalangeal joint of the index finger was used to derive movement duration (total and relative to first and second phase), maximum velocity, first and second phase peak velocity, numbers of peak velocities and logarithm of the a-dimensional jerk [20] as measures of smoothness. Movement duration and smoothness gave information about precision and efficiency of the movement; peak velocity provided information about movement planning. Finally, a subset of markers placed on the UE and trunk were used to estimate the range of motion of the shoulder and elbow. Compensatory movements were captured by estimating trunk displacement in the transverse plane and sagittal plane.

INSERT FIGURE 1 HERE

2.1.3 EEG Recordings and Data Analysis

The EEG was recorded using the BrainAmp System (Brain Products, Munich, Germany), with a 32-channel headset with electrodes placed according to the International 10-20 System, acquisition frequency of 1000 Hz, using the FCz electrode as the reference channel. Data were stored on hard disk for further analysis. A 50-Hz notch filter was applied online to eliminate external noise (mains power frequency at 50 Hz), and impedances were checked before the start of each session and considered acceptable if less than 20 KΩ. The signal was recorded and monitored through a computerized system (Brain Vision Recorder, Brain Products, Munich, Germany). Vertical and horizontal electro-oculographic signals were recorded using electrodes above and below the paretic hemisoma and from the external canthi. Analysis was conducted using Matlab in combination with FieldTrip [21]. EEG data were filtered offline with a 0.5–45 Hz band-pass second order Butterworth filter. Channels that showed no data or very poor data quality were rejected, while short artifactual epochs in single channels were interpolated as a weighted average of the surrounding electrodes, followed by a new reference to the remaining average. After that, ocular and muscolar

artifacts were manually removed using independent component analysis (ICA) [22]. Power spectral density (PSD) was computed with a Fast Fourier Transform (FFT) for each channel using a Hanning window with 2s window length, without zero padding or overlap. From the average power spectra, the related PSD across the following frequency bands was computed: delta (1–4 Hz), theta (4–8 Hz), alpha (8–13 Hz) and beta (13– 35 Hz) [7]. DAR and DTABR were computed as the ratios of the absolute power band relative to each band of interest both as total average and by splitting affected hemisphere (AH) from unaffected hemisphere (UH) [6]. dirBSI was computed as decribed by Saes and his group [8]. and it was determined in the whole range 1-35 Hz and separately for delta, theta, alpha and beta.

2.2 Statistical Analysis

Baseline (T0) characteristics were reported as median and interquartile range, mean and standard deviation or frequency and percentage. The free software Jamovi (Jamovi, 1.6) [23] was used for the statistical analysis. In particular, we wanted to investigate the relationship between the extracted kinematic features and the scores related to the clinical evaluation and then its relationship with the calculated EEG parameters. Spearman's correlation was used to identify any significant correlation trend considering the whole group and separately for the subgroup with identified EEG and kinematic assessment. The level of statistical significance was set at $p < 0.05$.

3. Results

58 patients were enrolled up to November 2021 and 26 patients were considered for this study. This included the majority of those who completed the upper limb kinematic analysis protocol at 4 weeks and for whom it was possible to reconstruct and analyse the recorded tests (without technical issues). The inability to complete the above described movements led to the exclusion of patients with more severe motor deficit. Among the 26 patients considered, 20 patients also performed the EEG at 4 weeks (11 men and 9 women, average age about 65 years).

In some patients (n=5), it was not possible to perform all the evaluations because of clinical instability or limitations due to Covid-19 restrictions; other subjects were not included because of the presence of excessive artefacts in the EEG analysis that compromised data processing (n=1). It was decided to exclude patients who had only performed EEG and not kinematic analysis.

The following analysis was based on a sample of 26 subjects, whose characteristics are outlined in Table 1.

INSERT TABLE 1 ABOUT HERE

The sample consisted of 15 men and 11 women, with an average age of about 67 years. About 80% were affected by an ischaemic stroke, while the situation was homogeneous about the affected hemisphere. Mean NIHSS at admission was 8.25; mean FMA-UE and ARAT values at one month were 52 and 44, respectively. 9 patients underwent TMS: 8 of these showed MEPs, 1 did not.

The results are illustrated mainly by means of graphs, in which values obtained from the clinical assessment (FMA-UE) were correlated with kinematic parameters (measured during Reach Up and Reach Out movements) and EEG measures, collected according to the above-mentioned time-points. We chose kinematic measures crucial in the stroke patient: movement duration (total, and relative to first and second phase); peak velocity; peak velocity of the first and second movement phase (see Figure 1); number of peak velocity (#PV) and logarithm a-dimensional jerk (Jerk), as measures of smoothness; shoulder and elbow range of motion; trunk displacement (trunk flexion/extension).

For both the Reach-up and the Reach-out, it was possible to highlight that the first movement phase had a shorter duration than the second one, and that the duration of the movement (both total and relative to the sub-phases) strongly correlated with the FMA-UE: on average, patients with lower FMA-UE values took longer to complete the movement. On the contrary, the maximum speed (PV) recorded in Reach Up and Reach Out correlated poorly with FMA-

UE. The correlation between FMA-UE and smoothness measures was stronger: for Reach Up and Reach Out, the R^2 of the number of velocity peaks (#PV) was equal to 0.5872 and 0.5084, respectively, while the R^2 of the logarithm a-dimensional jerk (Jerk) was equal to 0.5921 and 0.7159, respectively. Considering the data for joint angles, presented as absolute ROM in the sagittal plane only, patients showed no clear correlation with FMA-UE. See Figure 2 and Figure 3, which show data for Reach Up and Reach Out movements (where not otherwise specified, p-values < 0.05).

INSERT FIGURE 2 AND FIGURE 3 ABOUT HERE

In the EEG subgroup, relative band power analysis of the EEG rhythms of each patient showed a clear predominance of alpha rhythm.

INSERT FIGURE 4 ABOUT HERE

Figure 4 shows the DAR and the DTABR. The DAR was higher than 1 considering the bihemispheric EEG recording, and even higher considering only the affected hemisphere. The total average DTABR also showed a value between 1 and 2. According to Finnigan and co-workers, it would be appropriate to consider an overall DAR or DTABR value of around 1 or less as normal, while values above 2 would be abnormal [6].

INSERT FIGURE 5 ABOUT HERE

In Figure 5, it can be seen that the dirBSI was positive for the delta and theta bands, and negative for the alpha and beta rhythms. In particular, positive values found in the delta and theta bands indicated higher spectral power in the affected hemisphere for these measures, while negative values for the alpha and beta rhythms denoted higher spectral power in the healthy hemisphere. Of note, the dirBSI beta correlated negatively with the average maximum velocity, with higher spectral power on the beta-band in the affected hemisphere corresponding to lower average maximum velocities. Data analysis about ARAT did not show any significant correlation.

4. Discussion

To our knowledge, a limited number of studies investigated post-stroke upper limb motor recovery by integrating multiple data modalities. The correlation between standardised clinical scales, kinematic data and qEEG measures allowed the investigation of motor recovery from multiple perspectives. These data are fundamental to tailor the care for the individual patient, but also to better understand the dynamics of motor recovery.

Despite numerous advances in diagnosis, early treatment and outcome prediction, stroke is still the leading cause of long-term disability [24]. Cortical plasticity and functional reorganisation are crucial in post-stroke motor recovery, where it is important to distinguish between phenomena mediating true restitution and those mediating compensation. As neural repair is mostly completed in the first five weeks after stroke, this interval is a critical period from a rehabilitation perspective [25,26].

Clinical and instrumental data provide different and complementary information for a correct patient assessment. Regarding instrumental data, qEEG analysis provides neurophysiological measures about the functional status of the cerebral cortex and the motor system, while kinematic analysis offers objective information on the quality of movements and its modifications over time [27,28]. While clinical data are often insufficient to predict recovery, the combination of multiple measures and the skilful integration of the aforementioned methods can help plan the patient's tailored rehabilitation [29].

This study highlights some interesting aspects in relation to both kinematic and qEEG measures. In recent years, interest in kinematics data in the context of post-stroke recovery has increased significantly, although a standardised methodology is still lacking, as evidenced by recent numerous literature reviews and roundtables [30-34]. Since some works have shown a good correlation between kinematic parametrics and motor outcome assessment scales, such as the FMA-UE [35], our study also investigated the same correlation. In our dataset, movement duration (total and relative to each sub-phases)

strongly correlated with upper limb motor impairment (FMA-UE) in the reaching tasks and patients with lower FMA-UE values took longer on average to complete the movement. Similarly, we found a strong correlation between FMA-UE and smoothness measures (number of velocity peaks and logarithm a-dimensional jerk). Furthermore, the average total duration of movements correlated with smoothness in a positive manner. Indeed, smoothness measures are important parameters in post stroke motor recovery and are commonly used to assess the quality of movement of the paretic upper limb during reaching movements [20,33]. In fact, fluid movements are characteristic of healthy, well-trained motor behaviour [36] and movement fluidity increases with neurodevelopment [37], motor learning [38,39], and motor recovery after stroke [40].

Peak velocity positively correlated with upper limb motor impairment and movement duration and this finding is consistent with a previous study, highlighting that movement duration is closely related to peak velocity, whereas the timing with which peak velocity is reached (time to peak velocity) provides information on movement construction [35]. In healthy people, peak velocity is reached during the final moments of the first half of the total time in the reaching phase, indicating an efficient movement with few corrections in the deceleration phase towards the target. Conversely, the reaching movements in stroke patients are characterised by a longer movement duration with a smaller peak velocity recorded prior to the first half of the movement, followed by a long deceleration phase [35,41]. Therefore, it is possible to hypothesise that speed profiles reflect the effectiveness of motor control and are an index linked to movement strategy.

Analyses on joint angles demonstrated weak correlations with FMA-UE, as expected: even healthy subjects, while describing similar movement trajectories, demonstrate the relative variability that certain functional movements may have for different motor strategies at the individual subject level (particularly in shoulder intra-extrotation and abduction-adduction, elbow flexion-extension and prone-supination) [42]. Thus, in stroke patients, an even greater variability of joint angles makes comparative analyses difficult [43]. More clinically relevant,

however, is the intra-subject monitoring of changes in these kinematic parameters over time, which is why our study focused on these measures.

Considering qEEG measures, we found a predominance of alpha rhythm, consistently with the current literature [44]. While an unaltered alpha activity has been associated with healthy brain activity [45], hemispheric strokes are associated with an increase in oscillations in the delta and theta band [6,46,47]. The DAR had a value higher than 1 considering the bihemispheric EEG recording, and even higher considering only the affected hemisphere. This finding is coherent with current evidence showing that subacute stroke survivors show increased DAR values compared to healthy individuals [7,48], at least in the early post-stroke phase. Indeed, delta activity is higher in the acute/subacute period and it shows a trend towards normalisation in the chronic period. Consistently, DAR in chronic stroke survivors does not differ significantly from healthy individuals [8]. Thus, discrepancies in DAR may be caused by a difference in the stroke timeframe assessment.

The overall mean DTABR value highlighted a value between 1 and 2. According to Finnigan et al, an overall DAR or DTABR value of about 1 or less would be normal, while values above 2 are pathological [6]. Since most of the subjects included had a mild level of impairment, this result seems consistent with the previous interpretation.

Agius Anastasi et al. examined the role of BSI in poststroke patients and proved correlations between this EEG measure and some functional scales [9]. Our study did not show results consistent with this interpretation, but it should be pointed out that Saes et al. found significant negative correlations between BSI and FMA-UE only in patients with more pronounced asymmetry differences in the delta and theta frequency bands (i.e. patients with a poor outcome), who were scarcely represented in our sample [8]. About the directionality of interhemispheric asymmetries, positive dirBSI values found in the delta and theta bands indicate higher spectral power in the affected hemisphere for these frequency bands, while negative values for the alpha and beta rhythms denote higher spectral power in the contralateral hemisphere [8]. Few works analyse the changes of this EEG measure in the

post-stroke recovery, so it is difficult to make comparisons between different studies. However, Saes et al. showed that, in the most severely affected stroke survivors, the affected hemisphere generated more power than the contralateral, especially in the delta and theta frequency band [8]. Numerous studies have shown that the beta rhythm is the one most closely linked to motor activity [49]. In the present study, dirBSI beta showed a negative correlation with the average maximum velocity during reaching tasks. This means that higher spectral power on the beta-band in the affected hemisphere (dirBSI beta > 0) corresponded to lower mean maximum velocities, whereas higher spectral power on the beta-band in the contralateral hemisphere (dirBSI beta < 0) corresponded to higher mean maximum velocities. A study of Thibaut et al., shows that motor function correlates positively with beta rhythm in the central regions of the uninjured hemisphere, while it correlates negatively with beta rhythm in the affected hemisphere; furthermore, lower values of the FMA-UE are observed when beta activity is higher in the affected hemisphere in comparison to the healthy one [50]. Of note, Thibaut et al. use the beta ratio (the ratio between the beta value in the two hemispheres), whereas we analysed the dirBSI beta (the ratio between the difference between the two beta values in the two hemispheres, out of the total). Even considering the differences between the parameters studied (beta ratio vs dirBSI beta) and between the study populations (chronic vs subacute), the results of the two studies seem to be consistent. Thus, considering maximal speed as an index related to motor control that correlates positively with FMA-UE, we might suggest a functional tendency to "lateralisation" when the spectral power on the beta band was higher in the unaffected hemisphere, because these patients were vicariating the affected hemisphere with the healthy one.

This study has some limitations: the limited sample size; the availability of clinical, EEGs and kinematics data recorded only 4 weeks after stroke, which do not allow to follow the evolution over time; the lack of a control group; the majority of patients have mild haemiparesis, which is compatible with the possibility of performing kinematic analysis of functional movements.

However, it implies exclusion of severe patients who would have given further heterogeneity and information especially from the EEG point of view.

5. Conclusions

The identification of biomarkers (both kinematic and/or neurophysiological) of early motor recovery is crucial for the choice of the best rehabilitation treatment and future research should focus on distinguishing between this measure and compensation indices, in order to create suitable assessment scales [25]. Moreover, future studies are needed to better characterize the possible correlations between kinematic parameters and EEG data (possibly monitoring their evolution over stroke timeframe) to deepen the pattern of post stroke motor recovery. In conclusion, this study emphasises the importance of integrating information from different sources for correct clinical assessment of stroke patients and, consequently, appropriate choice of the most suitable rehabilitation treatment.

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All figures can be printed in black/white, the use of colour is not essential.

Figure 1. Movement performed with the impaired limb

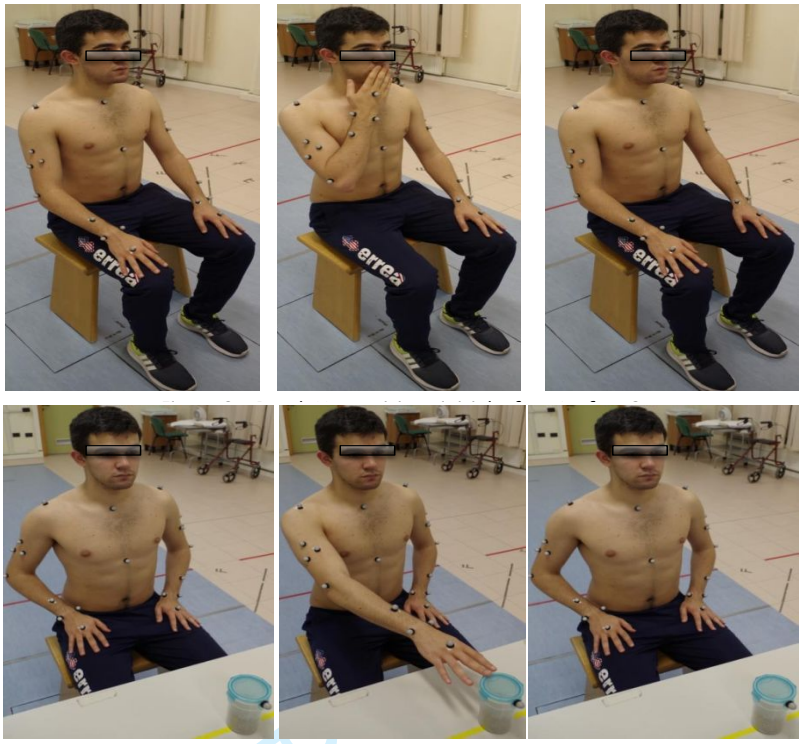

Figure 1: Reach Up (above): Starting position with the hand resting at the distal third of the thigh. The subject is asked to: bring the hand toward the mouth, going to touch the lips with the hand turned palm up (Step 1); return to starting position (Step 2). Reach Out (below): Initial position with the hand resting at the root of the thigh. Set up the table in front of the subject, with the jar on top. Subject is asked to: reach out and touch the lid of the jar with the hand (Step 1); return to the initial position (Step 2).

Figure 2: correlation between FMA and kinematic data of Reach-Up movement

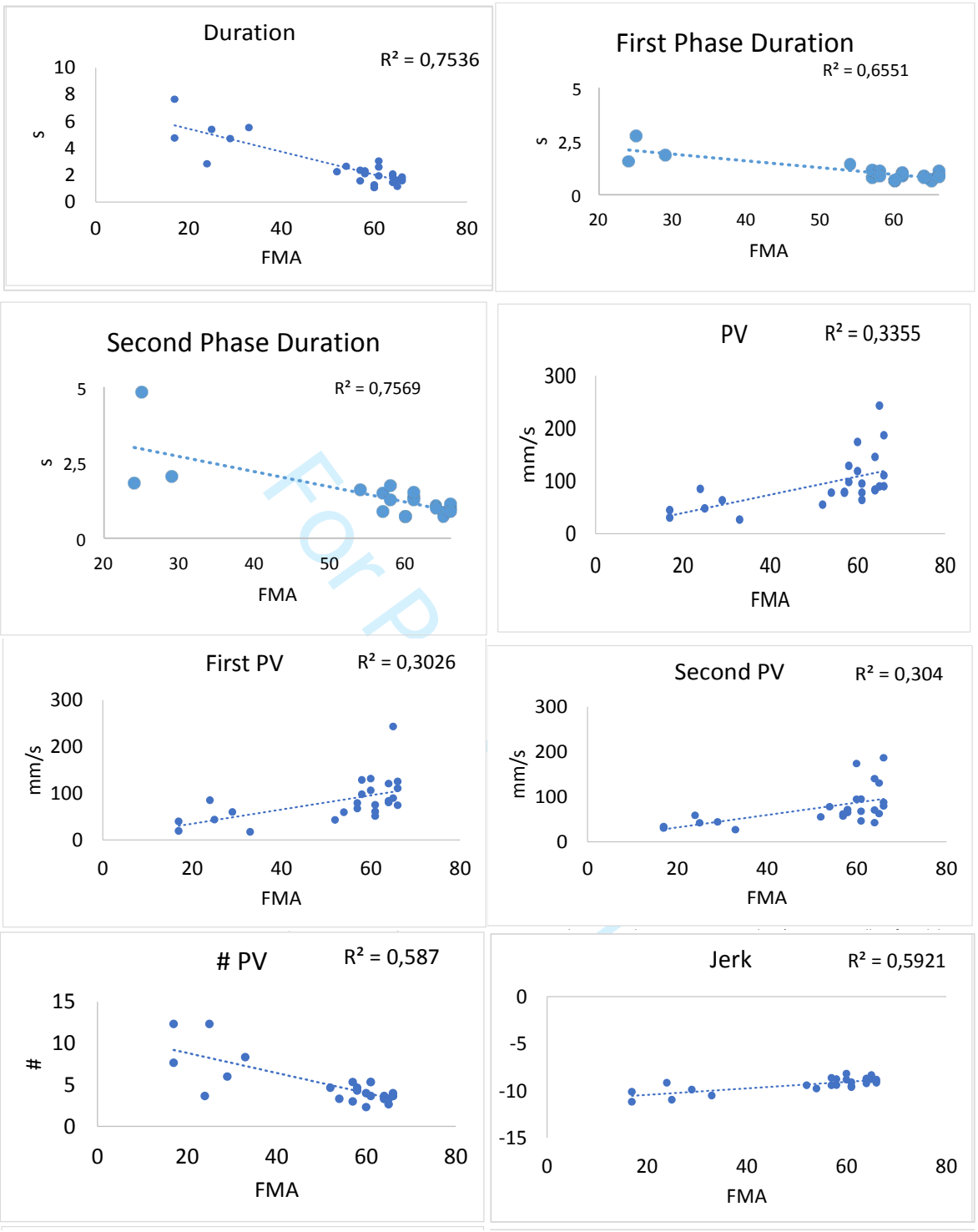

Figure 2. Reach Up: correlation between FMA and, in the order: total movement duration, duration of the first movement phase, duration of the second movement phase, peak velocity (PV), PV in the first and second phase of the movement, number of peak velocities (# PV) and log adimensional jerk (Jerk).

Figure 3: correlation between FMA and kinematic data of Reach-Out movement

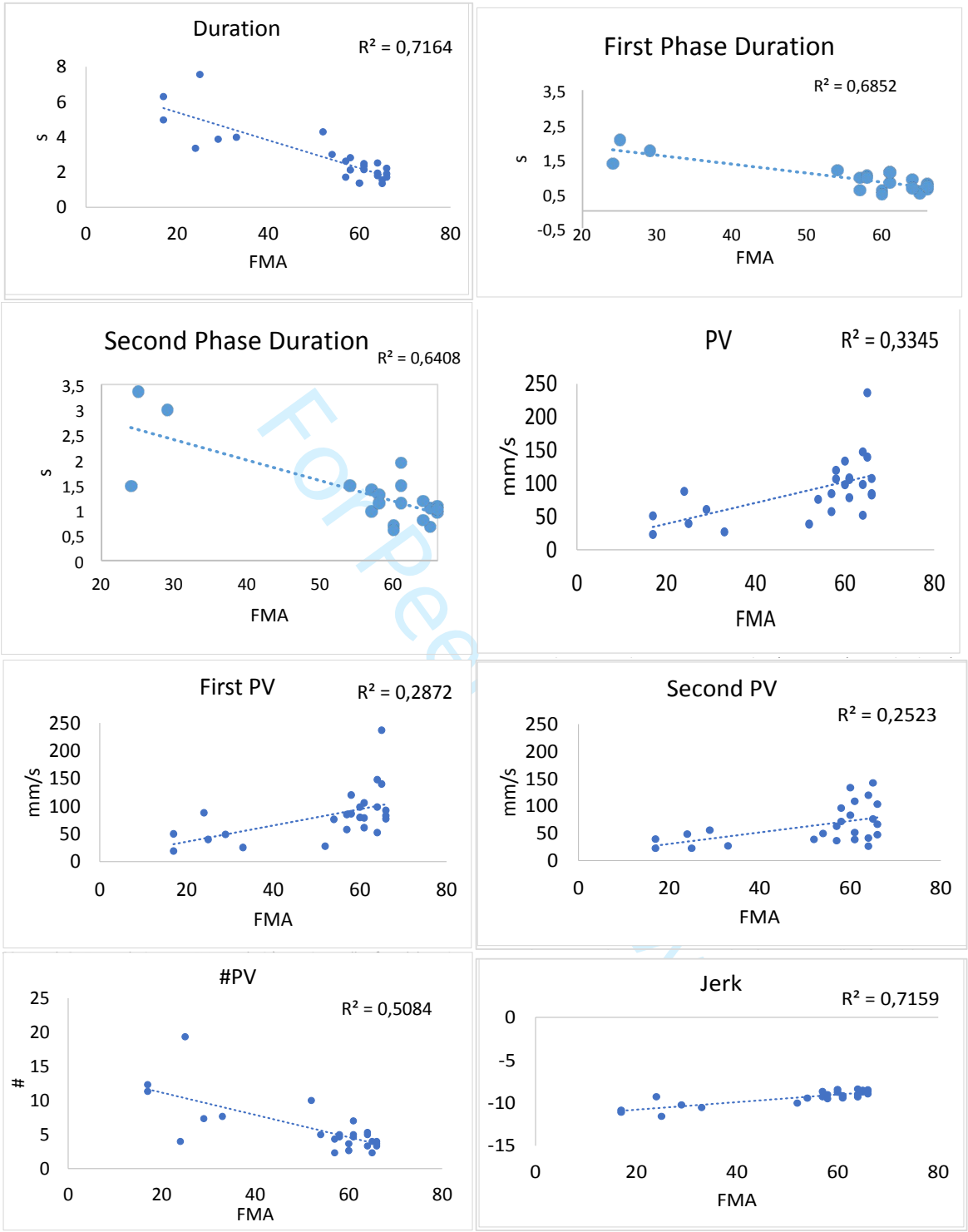

Figure 3, Reach Out: correlation between FMA and, in the order: total movement duration, duration of the first movement phase, duration of the second movement phase, peak velocity (PV), PV in the first and second phase of the movement, number of peak velocities (# PV) and log adimensional jerk (Jerk).

Figure 4: DAR and DTABR in EEG measures

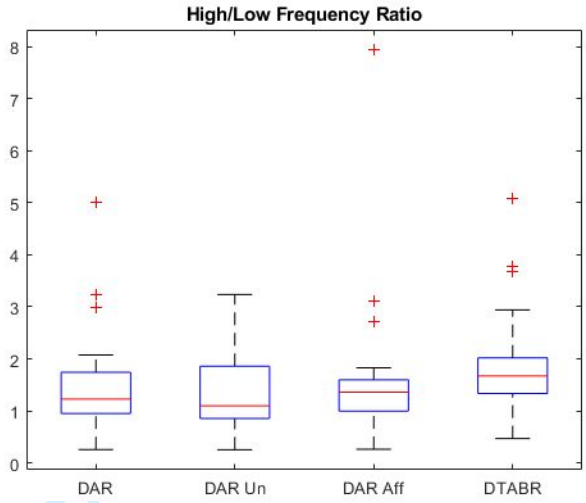

Figure 4: Boxplot with values of the delta/alpha ratio (DAR) and delta+theta/alpha+beta ratio (DTABR).

Figure 5: dirBSI in EEG measures

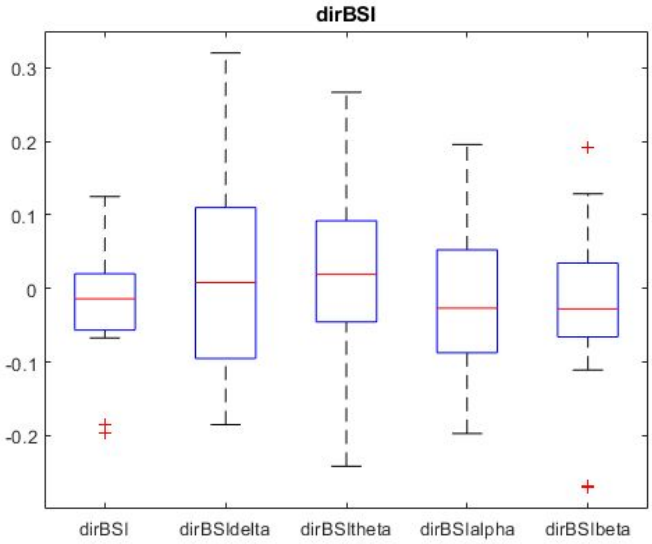

Figure 5: Boxplot with dirBSI values, determined over the entire range 1-35 Hz and separately for δ (1-4 Hz), θ (4-8 Hz), alpha (8-12 Hz) and β (12-30 Hz). dirBSI = 0 represents perfect symmetry, positive values (0-1) represent higher power in the affected hemisphere, vice versa for negative values.

Table 1. Participants Characteristics at Baseline

	Stroke patients (n = 26)
Age, years	66.5 (59.5 – 74.25)
Gender, no, male (%)	15 (57.7)
Time since stroke, days	9.5 (5-11)
Affected hemisphere, no. left (%)	13 (50)
MEPs, n(%)	7(26.9)*
Ischemic stroke (%)	20 (77)
NIHSS	7 (5-11.5)
ARAT 4th week	52 (44-56.5)
FMA-UE 4th week	52.16 (16.7)

Table 1. Baseline characteristics were reported as median and interquartile range, mean and standard deviation or frequency and percentage. FMA-UE: Fugl-Meyer Assessment - Upper Extremity; ARAT: Action Research Arm Test; NIHSS: National Institutes of Health Stroke Scale; MEPs: Motor Evoked Potentials

Reporting checklist for cross sectional study.

Based on the STROBE cross sectional guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the STROBE cross sectionalreporting guidelines, and cite them as:

von Elm E, Altman DG, Egger M, Pocock SJ, Gotzsche PC, Vandenbroucke JP. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: guidelines for reporting observational studies.

		Reporting Item	Page Number
Title and abstract			
Title	#1a	Indicate the study's design with a commonly used term in the title or the abstract	1
Abstract	#1b	Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background / rationale	#2	Explain the scientific background and rationale for the investigation being reported	3-5
Objectives	#3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	#4	Present key elements of study design early in the paper	5
Setting	#5	Describe the setting, locations, and relevant dates, including periods of	5

		recruitment, exposure, follow-up, and data collection	
Eligibility criteria	#6a	Give the eligibility criteria, and the sources and methods of selection of participants.	5
	#7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5-6
Data sources / measurement	#8	For each variable of interest give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group. Give information separately for for exposed and unexposed groups if applicable.	5-8
Bias	#9	Describe any efforts to address potential sources of bias	5-8
Study size	#10	Explain how the study size was arrived at	5
Quantitative variables	#11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why	5-8
Statistical methods	#12a	Describe all statistical methods, including those used to control for confounding	8
Statistical methods	#12b	Describe any methods used to examine subgroups and interactions	8
Statistical methods	#12c	Explain how missing data were addressed	8
Statistical methods	#12d	If applicable, describe analytical methods taking account of sampling strategy	8
Statistical methods	#12e	Describe any sensitivity analyses	8
Results			
Participants	#13a	Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed. Give information separately for for exposed and unexposed groups if applicable.	8-9
Participants	#13b	Give reasons for non-participation at each stage	9
Descriptive data	#14a	Give characteristics of study participants (eg demographic, clinical,	8-9

		social) and information on exposures and potential confounders. Give information separately for exposed and unexposed groups if applicable.	
Descriptive data	#14b	Indicate number of participants with missing data for each variable of interest	9
Outcome data	#15	Report numbers of outcome events or summary measures. Give information separately for exposed and unexposed groups if applicable.	9-11
Main results	#16a	Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	9-11
Main results	#16b	Report category boundaries when continuous variables were categorized	9-11
Discussion			
Key results	#18	Summarise key results with reference to study objectives	11-15
Limitations	#19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias.	15
Interpretation	#20	Give a cautious overall interpretation considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence.	11-15
Generalisability	#21	Discuss the generalisability (external validity) of the study results	15
Other Information			
Funding	#22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	3