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Altered Modulation of the Movement-Related Beta Desynchronization with Force in Stroke – a Pilot Study

Didier Allexandre, *Member, IEEE*, Vikram Shenoy Handiru, *Member, IEEE,* Armand Hoxha, Danit Mark, Easter S. Suviseshamuthu, *Member, IEEE*, Guang H. Yue, *Member, IEEE*

***Abstract*— Conventional therapy improves motor recovery after stroke. However, 50% of stroke survivors still suffer from a significant level of long-term upper extremity impairment. Identifying a specific biomarker whose magnitude scales with the level of force could help in the development of more effective, novel, highly targeted rehabilitation therapies such as brain stimulation or neurofeedback. Four chronic stroke participants were enrolled in this pilot study to find such a neural marker using an Independent Component Analysis (ICA)-based source analysis approach, and investigate how it has been affected by the injury. *Beta* band desynchronization in the ipsilesional primary motor cortex was found to be most robustly scaling with force. This activity modulation with force was found to be significantly reduced, and to plateau at higher force than that of the contralesional (unaffected) side. A rehabilitation therapy that would target such a neuromarker could have the potential to strengthen the brain-to-muscle drive and improve motor learning and recovery.**

***Clinical Relevance*— This study identifies a neural marker that scales with motor output and shows how this modulation has been affected by stroke.**

I. Introduction

Nearly 800,000 people experience a new or recurrent stroke each year [1] in the US alone, with long-term, chronic upper extremity (UE) impairment affecting 40-70% of stroke survivors with devastating personal, social, and economic cost [2]–[5]. Conventional therapy improves motor recovery, but nearly 50% of patients still suffer from a significant level of impairment after rehabilitation [5], [6]. A plausible reason for the limitation of conventional therapies could be that they are premised on peripheral training to impact the central loss of function. , and thus require constant, repetitive, and intense effort to trigger sufficient neuroplasticity changes to achieve motor recovery [4] presenting a significant challenge to motivation, engagement, and compliance [7]. Neurofeedback (NF) and brain computer interface (BCI) are promising new approaches that can improve rehabilitation therapy through the goal of increasing excitability and neuroplasticity of the brain to improve motor learning and functional recovery [4], [8]–[11].

One potential limitation of conventional NF/BCI is the modulation of a biomarker chosen based on its discriminant (such as between rest and motor imagery (MI)) rather than its therapeutic capability, which may not always lead to functional gain [12]. The main concern is that motor-related EEG activity modulations are widespread throughout the brain and may be associated with various processes (based on the frequency band and location of activity) [13], [14], that may not be directly related to motor execution. Furthermore, most classifiers and approaches are binary where the NF algorithm training tries to maximize differentiation between two states such as between motor imagery and rest [15]. The identification and use of a specific biomarker whose magnitude scales with the level of motor output —the mental effort required to produce force in a motor task [16], could have greater benefit. However, it remains unclear if brain activity scales with force. While some have found such a relationship in terms of *alpha/beta* desynchronization, cortico-muscular coherence, or cortical potential [17]–[20], others have not during movement [21]. Furthermore, no studies have previously investigated how this brain-force linear relationship is affected by stroke given that the brain activities are diminished or altered [22], [23].

In this current pilot study, we seek to find a neural marker that scales with force and investigate how this is affected by the stroke injury by comparing this brain-force relationship in the affected vs. unaffected side.

II. Methods

A. Participants

Four chronic stroke survivors (2 male, 2 female, age 58 ±9 years) 2-3 years post-injury (ischemic or hemorrhagic) participated in the study. Three participants had a lesion in the right and one in the left hemisphere (Fig. 1). Inclusion criteria were age between 18-70 years, stroke onset at least six months, hand hemiparesis with some residual fingers flexion. Patients with severe wrist spasticity scores >3 (Modified

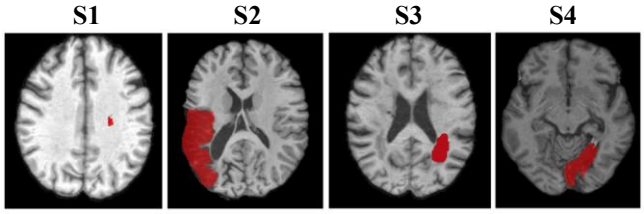

Figure 1. Lesion location for all 4 participants. The lesion in red as a binary mask was extracted using the LINDA (Lesion Identification with Neighborhood Data Analysis) toolbox [31] on a T1-weighted MRI scan.

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D. Allexandre, V. Shenoy Handiru, A. Hoxha, D. Mark, S.E. Selvan, G.H. Yue are with the Center for Mobility and Rehabilitation Engineering Research at Kessler Foundation, West Orange, NJ, USA

D. Allexandre, V. Shenoy Handiru, S.E. Selvan G.H. Yue are also affiliated with the Department of Physical Medicine and Rehabilitation, Rutgers New Jersey Medical School, Newark, NJ, USA

Corresponding author is D. Allexandre (phone: 973-324-3541; e-mail: dallexandre@kesslerfoundation.org).

Ashworth Scale) were excluded. The study was approved by the Kessler Foundation Institutional Review Board. Hand function was evaluated with the 9-hole-peg test (9HPT) [24] and Box and Blocks Test (BBT) [25].

B. Experimental Procedure

First, the 9HPT and BBT was administered for both the affected and unaffected hand. Participants then participated in a handgrip task, where they were first asked to perform 3 to 5 trials of Maximum Voluntary Contraction (MVC) for each hand using a handgrip dynamometer (Vernier, OR, USA) with 1 min rest between contractions. Then, participants were asked to perform a series of handgrip contractions for 5s at 10%, 30%, and 50% MVC, first for the left and then the right hand. Trials appeared in random order with an inter-trial rest period varying between 5-30s to avoid fatigue. Throughout the task, EEG brain activity (64-channel ActiCAP slim, BrainAmp Brain Products, Munich, Germany), and EMG hand muscle activity (16ch ExG BrainAmp) were continuously recorded at 1000Hz from the main handgrip flexor/extensor (Extensor Digitorum (ED), Flexor Digitorum Superficialis (FDS), Flexor Digitorum Profundus (FDP), and Flexor Dorsal Interosseous (FDI)).

C. Data Processing and Outcome Measurements

EMG data was bandpass filtered (1-125Hz) using a fourth-order Butterworth filter, and the root-mean-square envelope was computed using a moving 250ms average time window.

Using the EEGLAB toolbox [26], EEG data were band-pass filtered (1-50Hz) using a fourth-order Butterworth filter, average referenced after rejecting and interpolating bad channels, and downsampled to 250Hz before further analysis. The ASR Toolbox was used to clean the data. After epoching the data, independent components (IC) representing independent EEG source signals were extracted using Infomax and their equivalent dipole location was computed using DIPFIT with a standard circular MNI head model.

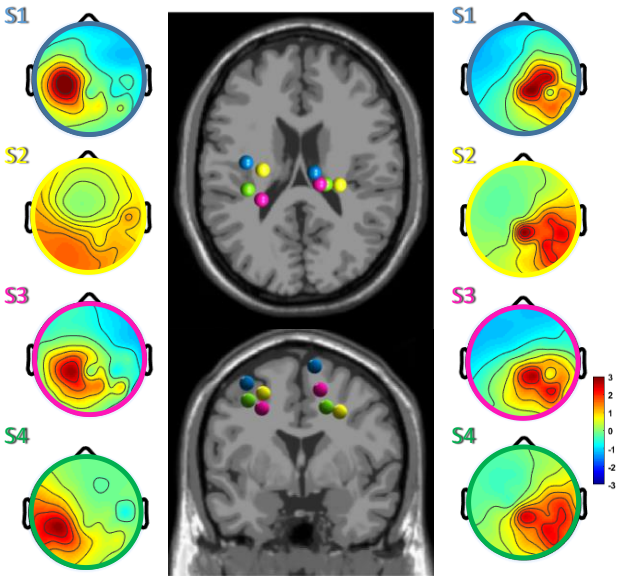

Figure 2. Dipole locations (middle) and corresponding normalized scalp topograhic electric field maps (left and right plot) for the left and right hemisphere sensorimotor source components for each participant. Dipole sphere and corresponding scalp map are color coded for each participant.

ICs were subsequently classified using the IClabel plugin [27]. ICs labeled as brain signals localized within the brain and which explained more than 85% of scalp variance were retained. ICs were consistently found in temporal, occipital, parietal, sensorimotor, and premotor areas. EEG power spectrum density (PSD) for frequencies between 1-50Hz was subsequently computed (in dB) with respect to the common baseline across the three force level conditions, which we found critical to eliminate variations in baseline values that could mask the EEG-force relationship. Finally, the force-brain activity (PSD) relationship was computed using a linear least-square fit across trials and force levels for all frequencies and brain components, to find the component and frequency band whose activity most consistently scale with force.

D. Statistical Analysis

Comparisons between affected vs. unaffected hand were performed using a simple paired t-test with a significant α level set at 0.05.

III. RESULTS

The 9HP and BBT results in Table 1 show significant mild to moderate impairment in hand function in the affected vs. unaffected hand. MVC was significantly less in the affected than the unaffected hand (341±135 vs 163 ±106N, p=0.08).

TABLE I. FUNCTIONAL MEASURES

Participant	9HPT (s)		BBT (boxes/min)	
	Unaffected	Affected	Unaffected	Affected
S1	26.6	No peg	42	3
S2	22.3	No peg	56	16
S3	25.3	48	46	32
S4	23.9	128	58	30
Mean (std)	**24.3±2.0**	**79±44**	**50±8**	**20±13**
p-value	**NA**		**0.02**	

Activity (with respect to baseline) in the low *beta* frequency band (10-20Hz) for the left and right sensorimotor (M1) was found to be most consistently (across participants and hemispheres) scaling with force among all brain components analyzed. Fig. 2 shows the results of the IC decomposition and the sensorimotor sources location (M1) and scalp activation for each participant. Fig. 3 illustrates the increasing modulation of force, muscle (FDI), and EEG *beta* band desynchronization as the target force increases (10%, 30%, 50% MVC) as shown for an exemplary participant S1.

Across all participants, peak desynchronization corresponding to the maximum brain-force scaling occurs in the low *beta* band with frequencies ranging from 13 to 21Hz. As illustrated in Fig. 4, this EEG power peak desynchronization showed a consistent scaling with force. Furthermore, the ipsilesional source desynchronization is consistently and significantly lower than that of the contralesional side. They both show an increased desynchronization at larger force, which plateaus for the ipsilesional source at 30% MVC (red).

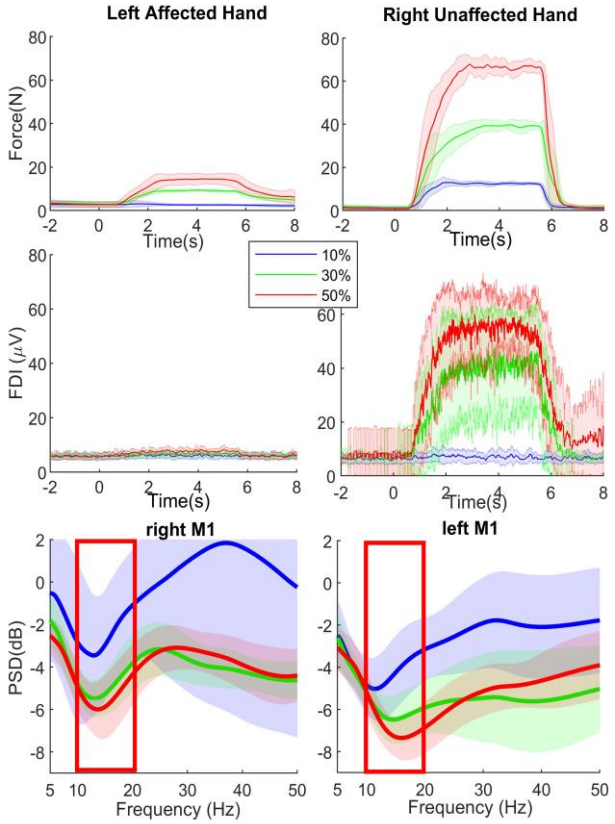

Figure 3. Force, EMG (FDI), and EEG power for an exemplary participant (S1) for the left and right affected hand contraction at 10%, 30% and 50% MVC shown respectively in blue, green, and red. The right ipsilesional (left contralesional) M1 EEG source activity controlling the left (right) hand is shown on the left (right). These results illustrate the lower activity on the left affected compared to right unaffected hand contraction at each level of force amplitude.

IV. DISCUSSION

As previously observed in the healthy and older population [17]–[20], we were able to find a neural marker that scales with force in stroke survivors. This relationship was not only found in the contralesional side for handgrip contraction of the unaffected hand, but also in the ipsilesional side during contraction of the affected hand. This was only consistently found for ICs in the sensorimotor area and low *beta* (10-20Hz), highlighting the critical role of these brain sources and frequency band in driving motor output. The physiological role of *beta* desynchronization remains poorly understood. Evidence suggests that it reflects the release of background cortical inhibition involved in gating motor commands and somatosensory inputs during movement execution [28], [29]. *Beta* band cortico-muscular coherence, a measure of the brain to muscle drive has also been shown to scale with force supporting the role of M1 brain source within the *beta* band in driving motor output [30]. As indicated previously [22], [23], due to the stroke, we observed a marked decrease in brain activity in the ipsilesional M1 ICs. The ipsilesional reduction in *beta* desynchronization during movement and the resulting decrease in overall MVC force compared to the contralateral unaffected brain region are consistent with its role in driving motor output. It is noteworthy that the

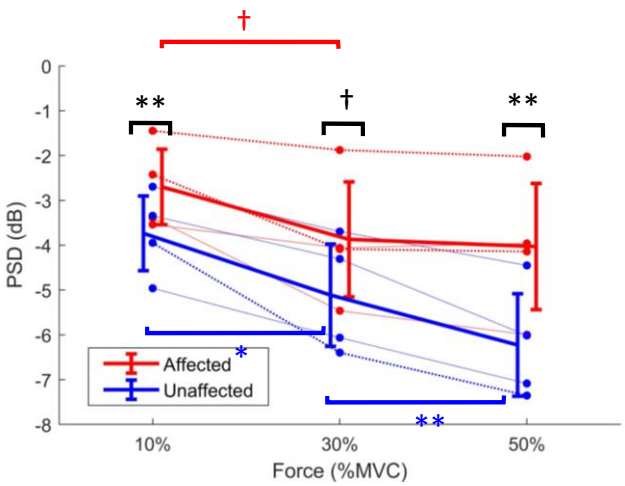

Figure 4. EEG-force relationship for the ipsilesional (affected) and contralesional (unaffected) sensorimotor dipole sources when contracting the affected and unaffected hand respectively at various force intensities. Results for each participant are shown in dotted line and average results for each condition in solid line. † p<0.1, * p<0.05, ** p<0.01.

ipsilesional EEG-force relationship plateaus at higher force output, another reflection of the loss in motor drive.

The small sample size is a major limitation of the current study. Irrespective, results remain strong and consistent across all four participants. Findings should be confirmed in a larger and more representative sample.

V. CONCLUSION

A biomarker that scales with force was found in the ipsilesional primary motor cortex. The linear relationship was altered suggesting a potential role in reducing cortical drive, and force output to the affected hand. The modulation of such a marker using brain stimulation or neurofeedback could potentially strengthen the brain to muscle drive, enhancing neuroplasticity and motor recovery.

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