Alteration in Resting-State Brain Activity in Stroke Survivors Following Repetitive Finger Stimulation

Dorothy He[1]*, William A. Sikora[2]*, Shirley A. James[3], Jordan N. Williamson[4], Louis V. Lepak[5], Carolyn F. Cheema[5], Evgeny Sidorov[6], Sheng Li[7], Yuan Yang[4,5,8,9,10#]

[1]University of Oklahoma Health Sciences Center, College of Medicine, Oklahoma City, Oklahoma

[2]University of Oklahoma, Stephenson School of Biomedical Engineering, Norman, Oklahoma

[3]University of Oklahoma Health Sciences Center, Hudson College of Public Health, Oklahoma City, Oklahoma

[4]University of Illinois Urbana-Champaign, Department of Bioengineering, Urbana, Illinois, USA

[5]University of Oklahoma Health Sciences Center, Department of Rehabilitation Sciences, Tulsa, Oklahoma

[6]University of Oklahoma Health Sciences Center, Department of Neurology, Oklahoma City, Oklahoma

[7]UT Health Huston McGovern Medical School, Department of Physical Medicine and Rehabilitation, Houston, Texas

[8]Carle Foundation Hospital, Clinical Imaging Research Center, Stephenson Family Clinical Research Institute, Urbana, Illinois, USA

[9]Beckman Institute for Advanced Science and Technology, University of Illinois Urbana-Champaign, Urbana, IL 61820, USA

[10]Northwestern University, Department of Physical Therapy and Human Movement Sciences, Chicago, Illinois, USA

*Shared primary authorship

Corresponding author: Yuan Yang - yuany@illinois.edu

All authors declare they have no conflicts of interest.

Data Availability Statement

The data that support the findings of this study are available on request from the corresponding author.

Funding

The team is supported by The Oklahoma Center for the Advancement of Science and Technology (OCAST) Health Research Program HR21-164, the American Heart Association (932980), National Science Foundation (2401215), Oklahoma Shared Clinical and Translational Resources (U54GM104938) with an Institutional Development Award from National Institute of General Medical Sciences.

Abstract

Objective – This quasi-experimental study examined the effect of repetitive finger stimulation on brain activation in eight stroke and seven control subjects, measured by quantitative electroencephalogram (qEEG).

Methods – We applied five minutes of two Hz repetitive bilateral index finger transcutaneous electrical nerve stimulation (TENS), and compared differences pre and post TENS using qEEG metrics delta/alpha ratio (DAR) and delta-theta/alpha-beta ratio (DTABR).

Results –Between group differences pre and post-stimulation were significantly different in the DAR ($z=-2.88$ with $p=0.0040$) and the DTABR variables ($z=-3.90$ with $p<.0001$). Significant decrease in the DAR and DTABR variables after the TENS was detected only in the stroke group (DAR diff = 3.87 $p=.0211$), (DTABR diff = 1.19, $p=.0074$).

Conclusions – The decrease in qEEG metrics in the stroke group may indicate improved brain activity following TENS. This finding may pave the way for a future novel therapy based on TENS and qEEG measures to improve brain recovery after stroke.

Keywords: stroke, DAR, EEG, DTABR, sensory stimulation, finger stimulation

- What is Known
    - DAR and DTABR serve as indicators of post-stroke impairment in the acute phase.
- What is New
    - Repetitive finger stimulation leads to changes in DTABR and DAR scores for stroke survivors.

Introduction

With a mean global lifetime risk of 24.9%, stroke ranks as the leading cause of significant morbidity in the US, and the fifth leading cause of death.[1] Approximately 795,000 people experience a new or recurrent stroke each year.[1] Stroke can cause a variety of impairments including hemiparesis, hemisensory loss, cognitive dysfunction, altered speech, and altered oral-motor function.[1] These impairments lead to functional disability including depression, social isolation, and the inability to resume vocational pursuit. Three percent of males and two percent of females living in the United States report long-term disability due to stroke.[1]

Up to 88% of acute and 75% of chronic stroke survivors experience upper extremity motor impairment, and research suggests motor impairment is linked to sensory impairment.[2] Sensory function has also been correlated to position-cortical coherence, a measure of motor function that compares the degree of wrist perturbation with cortical activity.[3] Transcutaneous electrical nerve stimulation (TENS), even without motor recruitment, is beneficial to motor return.[4] In a previous study, subjects who received two hours of median and ulnar peripheral nerve stimulation at 1 Hz to their involved hands experienced enhanced training effects as measured by the Jebsen-Taylor Hand Function Test (JTHFT).[5] Finger stimulation intervention lasting 90 minutes, four days a week, for six weeks has been associated with improvement in motor performance.[1,3] Despite these findings, the neural mechanisms and objective measurements of post-stroke sensory-motor interaction remain unclear.

Electroencephalogram (EEG) is a non-invasive technology that measures electrical activity in the brain using electrodes attached to the surface of the scalp. Quantitative EEG (qEEG) is a revised form of EEG that processes, transforms, and analyzes EEG signals using complex mathematical algorithms.[6] Delta-alpha ratio (DAR) and Delta-theta/Alpha-beta ratio (DTABR) are established

qEEG metrics representing ratios of the power of each frequency band on resting-state EEG recordings. When measured in subjects 24 hours after stroke, brain activity in delta (1-3 Hz) and/or theta (4-7 Hz) band(s) increases, and alpha (8-12 Hz) and/or beta (13-30 Hz) activity decreases, leading to increased DAR and DTABR values.[7] These acute brain changes, as measured by EEG readings, can persist during stroke recovery and have been associated with the severity of disability when compared to the Modified Rankin Scale.[7] The existing literature indicates elevated DTABR and DAR in acute stroke patients are useful measures of the degree of post-stroke motor impairment.[8,9] Other studies have explored a possible negative association between DTABR, DAR, and cognition in a 90-day period after stroke.[10] These results imply resting-state EEG metrics contain unique information about motor impairment.[11] MRI and CT scans are useful for identifying structural characteristics of the lesion such as location and size, which are clinically important for diagnosing stroke and identifying interventions for acute stroke, but do not offer insight into the underlying mechanisms of recovery. The qEEG, similar to other emerging imaging modalities such as functional MRI, attempts to explore the changes in brain activity that occur during stroke recovery and therefore offers a different type of information.[12] In addition, qEEG can be used to enhance our understanding of the pathophysiology underlying various neurological diseases in a way that routine assessments based on gross observation may not. For example, the qEEG indices have been studied as a diagnostic tool for Parkinson's disease and schizophrenia, and as a way of measuring responses to therapy.[13] This early phase study in stroke may pave the way for future longitudinal studies to develop qEEG as a diagnostic tool for post-stroke recovery of brain activity.

The primary aim of this study was to determine the effect of repetitive finger stimulation on brain activity using qEEG metrics. A secondary aim of this study was to explore the correlation

between qEEG measures and motor function during stroke recovery. We hypothesized that elevated DAR and DTABR have the potential to demonstrate the response to tactile stimulation in patients in stroke recovery. We further hypothesized somatosensory input to distal peripheral nerves would improve brain activity in the sensorimotor area as reflected by decreased DAR/DTABR.

Methods

Participants

Eight stroke survivors (three female) with ages ranging from 57-75 years, and a mean time after stroke of 3.333 years, and seven age-similar healthy controls (five female) with an age range between 52-77 years participated in this study (Table 1). Study subjects had unilateral stroke lesions confirmed by a physician through magnetic resonance imaging, computed tomography scan, or radiological report at least three months prior to the study. Additional inclusion criteria included unilateral hemiparesis with substantial upper extremity involvement, absence of significant sensory deficits in the non-hemiplegic upper extremity, and the ability to provide informed consent. Subjects were excluded from the study if they had motor or sensory involvement in the non-affected limbs, severe atrophy or joint contracture in the hemiplegic upper extremity, significant concurrent medical problems including cardiorespiratory impairment, history of epilepsy or seizures, or brainstem lesions. The study was approved by the internal review board (IRB) of the University of Oklahoma Health Sciences Center (IRB # 12550). All participants provided written informed consent to be included in the study. This quasi-experimental study conforms to Transparent Reporting of Evaluations with Non-randomized Designs (TREND) guidelines and reports the required information accordingly (see Supplementary Checklist)

Experimental Protocol

A licensed physical therapist administered the upper extremity portion of the Fugl-Meyer Motor Assessment (FMA-UE)[14,15] Research personnel recorded a resting-state, 3-minute, continuous EEG for all participants using the BrainVision Recorder EEG System (Brain Vision LLC, Morrisville, NC) before and after 2 Hz repetitive transcutaneous electrical nerve stimulation (TENS) in the index finger. Previous studies indicate a 3-minute resting state EEG recording is capable of predicting stroke recovery.[16] Finger stimulation was also provided to the control group to assess its floor effect.

Each participant was fitted with an EasyCap electrode cap (EASYCAP GmbH, Woerthsee-Etterschlag, Germany) using 64 electrodes in the 10-10 system. We utilized a sampling rate of 1000 Hz to collect EEG data. We also used a 60 Hz notch filter to mitigate interference by the electrical grid. During each recording, we asked participants to sit quietly, with hands and arms supported, eyes open, and without excessive blinking.

Following the three-minute resting-state EEG recording, participants received repetitive index finger TENS using a Digitimer DS7A Constant Current Stimulator (DigitimerLtd, Welwyn Garden City, UK). Electrodes were placed with the positive and ground termini on the distal and intermediate phalanges, respectively. The stimulus was delivered in the form of a square wave with a duration of 200μs with the current normalized to twice the sensory threshold for each subject. Each trial lasted one minute and consisted of 120 individual stimuli delivered at 2 Hz. Each hand received five trials interspersed with 30-second rests. The order of hand stimulation was randomized across subjects. This design standardizes the intervention across subjects regardless of the side of the lesion. The resting-state EEG recording was repeated post-stimulation.

Preprocessing

EEG data was preprocessed using the EEGLAB v. 2020.0 toolbox in MATLAB (EEGLAB v. 2020.0, Swartz Center for Computational Neuroscience).[17] We applied a common average reference and visually inspected the data for artifact removal.[18]

DTABR and DAR

DTABR and DAR are expressed as follows:

$$DTABR = \frac{\delta+\theta}{\alpha+\beta} \quad (1)$$

$$DAR = \frac{\delta}{\alpha} \quad (2)$$

where θ, δ, α and β represent the power for each respective frequency band, calculated using the fast Fourier transform (FFT) in MATLAB.[19] DTABR and DAR were calculated for each subject before and after finger stimulation. Only the sensorimotor channels were included in the calculations (C1, C3, C5, CP1, CP3, C2, C4, C6, CP2, CP4, CP6)[20] to test whether finger TENS can improve brain activity at the sensorimotor area.

Statistical analysis

We calculated summary statistics for each continuous variable in the study. We utilized Proc Univariate to check for a normal distribution within the means of the DAR and DTABR outcome variables. We utilized generalized estimating equation analysis to determine within group and between group mean differences in the outcome variables DAR and DTABR over time, and then checked for interactions between group and time. We analyzed pre-post outcome assessment differences using Generalized Estimating Equations (GEE) because this technique unbiased

estimation of population-averaged regression coefficients despite possible misspecification of the correlation structure. We then used Proc Glimmix to determine the correlation between upper extremity Fugl-Meyer scores, and both DTABR and DAR measures. We plotted scalp topographies, averaging the logarithmic power at each channel for the stroke group to demonstrate the difference after finger stimulation for each frequency band. We completed all statistical analyses using SAS 9.4 (Carey, NC) with an alpha = 0.05.

Results

Prior to stimulation, mean DAR values were significantly higher in the stroke group (12.00) compared to the control group (4.60) (p=.0126) according to GEE. Following stimulation, while mean DAR values were higher in the stroke group (8.13) compared to the control group (2.54), the difference was not significant (p=.0627, see Figure 1).

Prior to stimulation, DTABR values were significantly higher in the stroke group (4.15) compared to the control group (2.96) (p=.0028). Following stimulation, while mean DTABR values in the stroke group (1.50) approached those of the control group (1.03) (p=.0085), they were still significantly different (see Figure 1).

Within group differences. The stroke group mean DAR demonstrated a significant decrease (mean change =3.87, p=.0211) after the repetitive TENS, while the control group DAR did not (mean change=2.06, p=.1880). The stroke group mean DTABR demonstrated a significant decrease after the intervention (mean change = - 1.19, p=.0074), while the control group DTABR did not (mean change = - 0.47, p=.1978) (Table 2).

Between group differences. The mean difference in the DAR value between pre- and post-TENS was significantly higher in the stroke group (3.87, 95% CI = 0.78, 6.96) compared to the control

group (2.06, 95% CI = -1.33, 5.44) (p=.0040). The mean difference in the DTABR was also significantly higher in the stroke group (1.19, 95% CI = 0.43, 1.94) compared to the control group (0.47, 95% CI = -0.32, 1.26) (p=.0002). The lack of interaction in either variable between group and time (DAR p=.3053, DTABR p=.0880) indicated the groups did not change significantly differently over time (Table 2, 3, and 4).

Correlation between qEEG measures and motor impairment. Figure 2 shows the relation between pre-stimulation qEEG ratios (DAR and DTABR) and Fugl-Meyer (FMA-UE) scores (DAR: $R^2 = 0.376$, $P = 0.106$; DTABR: $R^2 = 0.4754$, $P = 0.0585$). We did not observe a statistically significant correlation between elevated DAR/DTABR values and the Fugl-Meyer standardized assessment of movement.

Discussion

We found that somatosensory input to distal peripheral nerves significantly decreased DAR/DTABR values in stroke subjects, but not in controls. The difference between pre vs. post intervention on the control group was not statistically significant. The range of difference was within the range of experimental error and individual differences. Additionally, decreases in DAR/DTABR were significantly greater in stroke subjects compared to controls. However, while the p-value suggested a difference in the impact of intervention between the stroke group and the control group~~s~~, the lack of interaction between group and time indicates the groups did not change at different rates over time.

DTABR and DAR values are potential tools for mapping stroke recovery, and measuring changes following intervention, particularly because EEG is a noninvasive way to measure brain activity. Previous studies have found lower DAR and DTABR values can differentiate the degree

of severity following a stroke.[21-23] While our data showed no correlation between FM-UE and qEEG values, changes in qEEG values do suggest that the brain may be capable of demonstrating neural plasticity in stroke recovery. The qEEG metrics could be advantageous in a clinical setting and provide additional information, regarding the change of brain activity, to the anatomical change in the brain reflected by MRI or CAT scans.

We did not observe a statistically significant correlation between elevated DAR/DTABR values and the Fugl-Meyer standardized assessment of movement, an indicator of post-stroke movement impairment (DAR: $R^2 = 0.38$, $P = 0.11$; DTABR: $R^2 = 0.48$, $P = 0.06$); however, this may be a reflection of the accuracy of the Fugl-Meyer measures rather than the EEG values.[24]

Scalp topography illustrating the power spectrum density difference between pre- and post-TENS for each frequency band demonstrates increased oscillatory activity in the beta and gamma bands (Figure 3). Previous studies suggest that beta oscillations are associated with voluntary movement.[25-29] A study of functional connectivity in the brain before and during finger extension shows that stroke subjects demonstrate decreased functional connectivity compared to healthy controls, and these changes are especially prominent within higher frequency (beta and gamma) bands.[25] A similar study with older adults found that EEG functional connectivity in the beta band is most predictive of motor performance.[28] During an actual motor task, beta band power tends to decrease relative to the resting state. In one study, changes in alpha and beta band activity in the primary sensorimotor cortex were associated with the contralateral leg swing phase during gait.[23] Studies have documented that decreased power in the beta band is associated with increased local excitability in the sensorimotor cortex during the swing phase (movement), while increased power was found in the double-support or stance phase of gait.[29] Proprioceptive feedback during brain-computer interface (BCI) training also produces increased

beta band power in the motor cortex.[27] In our study, the beta band power was recorded during rest, rather than with task activity, suggesting increased resting state beta band power may correlate with improved motor function. This is an interesting finding compared to previous studies which document changes in beta band power during a motor task and increased beta band functional connectivity in the resting state. A potential next step might involve exploring the usefulness of EEG in determining the effectiveness of interventions during stroke recovery. Additional studies investigating the frequency of stimulation needed to achieve results would also be helpful. Other studies investigating transcranial direct current stimulation (tDCS) in motor recovery using treatment schedules of five or six stimulation sessions per week, with sessions lasting ten to twenty-five minutes, demonstrated improvement.[30] A similar frequency might be used for finger stimulation to explore its clinical value as a part of our future work.

Limitations

Significant decreases in DTABR and DAR values after finger stimulation indicate the potential for finger stimulation or other similar sensory input to alter the activation in the brain. This study was exploratory and only investigated resting-state brain activity. Future studies could attempt to correlate clinical sensory assessments pre and post-TENS with the brain changes documented here. A power analysis using our effect size would ensure a sample size with sufficient power to document change. The current single session study only allows the pre- vs. post-intervention comparison. Future study will be conducted to explore the within-person variability over time.

One of the main goals of this study was to explore whether qEEG can be an indicator or predictor for impairments in stroke. Therefore, we only assessed the correlation between pre-intervention qEEG values and UE-FMA scores. The other goal of this study was to investigate the changes in resting-state brain activity as reflected by qEEG after finger stimulation.

Therefore, we did not collect post-intervention upper extremity Fugl-Meyer scores. We acknowledge the limitation of using UE-FMA as not specific to hand function but rather reflecting the overall impairment of the upper extremity. In the future, we will use more specific hand function clinical measures such as the Wolf Motor Function Test (WMFT) and Action Research Arm Test (ARAT) and include post-intervention assessment to explore the effects of finger stimulation as a potential therapeutic intervention for improving motor function.

Conclusion

We observed decreased qEEG metrics following TENS repetitive finger stimulation. Studies with a larger sample size are needed to confirm these findings. Additional research demonstrating the usefulness of DTABR and DAR as chronic-phase indicators is needed to develop qEEG biomarkers for stroke rehabilitation. The use of TENS as a supplemental intervention for motor function recovery could be further assessed with qEEG biomarkers and other clinical measures.

Conflict of Interest

The authors report that this research was conducted in the absence of any known commercial or financial relationships that could be potential conflicts of interest.

Author Contributions

D.H. conducted the data analysis and drafted the manuscript. W.S. collected the data. S.J. reviewed the results and conducted data analysis. L.L. and C.C. conducted participant recruitment and screening. Y.Y. contributed to conceptualization, problem solving, and guidance during the conduction of the study. All authors participated in editing the manuscript.

Funding

This work is supported by NIH/NICHD R01HD109157. The team is also supported by The Oklahoma Center for the Advancement of Science and Technology (OCAST) Health Research Program HR21-164, the American Heart Association (932980), National Science Foundation (2401215), Oklahoma Shared Clinical and Translational Resources (U54GM104938) with an Institutional Development Award from National Institute of General Medical Sciences.

Acknowledgments

Authors would like to thank Mr. Runfeng Tian, for his assistance with data collection and preprocessing.

290 References

291 1. Tsao CW, Aday AW, Almarzooq ZI, et al. Heart Disease and Stroke Statistics—2022
292 Update: A Report From the American Heart Association. *Circulation*.
293 2022;145(8)doi:10.1161/cir.0000000000001052
294 2. Coscia M, Wessel MJ, Chaudary U, et al. Neurotechnology-aided interventions for upper
295 limb motor rehabilitation in severe chronic stroke. *Brain*. 2019;142(8):2182-2197.
296 doi:10.1093/brain/awz181
297 3. Campfens SF, Zandvliet SB, Meskers CGM, Schouten AC, Van Putten MJAM, Van Der
298 Kooij H. Poor motor function is associated with reduced sensory processing after stroke.
299 *Experimental Brain Research*. 2015;233(4):1339-1349. doi:10.1007/s00221-015-4206-z
300 4. Sharififar S, Shuster JJ, Bishop MD. Adding electrical stimulation during standard
301 rehabilitation after stroke to improve motor function. A systematic review and meta-analysis.
302 *Ann Phys Rehabil Med*. Sep 2018;61(5):339-344. doi:10.1016/j.rehab.2018.06.005
303 5. Celnik P, Hummel F, Harris-Love M, Wolk R, Cohen LG. Somatosensory Stimulation
304 Enhances the Effects of Training Functional Hand Tasks in Patients With Chronic Stroke.
305 *Archives of Physical Medicine and Rehabilitation*. 2007;88(11):1369-1376.
306 doi:10.1016/j.apmr.2007.08.001
307 6. Livint Popa L, Dragos H, Pantelemon C, Verisezan Rosu O, Strilciuc S. The Role of
308 Quantitative EEG in the Diagnosis of Neuropsychiatric Disorders. *J Med Life*. Jan-Mar
309 2020;13(1):8-15. doi:10.25122/jml-2019-0085
310 7. Finnigan SP, Walsh M, Rose SE, Chalk JB. Quantitative EEG indices of sub-acute
311 ischaemic stroke correlate with clinical outcomes. *Clinical Neurophysiology*.
312 2007;118(11):2525-2532.
313 8. Ajčević M, Furlanis G, Miladinović A, et al. Early EEG Alterations Correlate with CTP
314 Hypoperfused Volumes and Neurological Deficit: A Wireless EEG Study in Hyper-Acute
315 Ischemic Stroke. *Ann Biomed Eng*. Sep 2021;49(9):2150-2158. doi:10.1007/s10439-021-02735-
316 w
317 9. Finnigan S, Wong A, Read S. Defining abnormal slow EEG activity in acute ischaemic
318 stroke: Delta/alpha ratio as an optimal QEEG index. *Clin Neurophysiol*. Feb 2016;127(2):1452-
319 1459. doi:10.1016/j.clinph.2015.07.014
320 10. Popa LL, Iancu M, Livint G, et al. N-Pep-12 supplementation after ischemic stroke
321 positively impacts frequency domain QEEG. *Neurol Sci*. Feb 2022;43(2):1115-1125.
322 doi:10.1007/s10072-021-05406-9
323 11. Saes M, Meskers CGM, Daffertshofer A, van Wegen EEH, Kwakkel G. Are early
324 measured resting-state EEG parameters predictive for upper limb motor impairment six months
325 poststroke? *Clinical Neurophysiology*. 2021/01/01/ 2021;132(1):56-62.
326 doi:https://doi.org/10.1016/j.clinph.2020.09.031
327 12. Mandeville ET, Ayata C, Zheng Y, Mandeville JB. Translational MR Neuroimaging of
328 Stroke and Recovery. *Transl Stroke Res*. Feb 2017;8(1):22-32. doi:10.1007/s12975-016-0497-z
329 13. Cantor DS, Chabot R. QEEG studies in the assessment and treatment of childhood
330 disorders. *Clin EEG Neurosci*. Apr 2009;40(2):113-21. doi:10.1177/155005940904000209
331 14. Fugl-Meyer AR, Jääskö L, Leyman I, Olsson S, Steglind S. The post-stroke hemiplegic
332 patient. 1. a method for evaluation of physical performance. *Scand J Rehabil Med*. 1975;7(1):13-
333 31.

15. Moore JL, Raad J, Ehrlich-Jones L, Heinemann AW. Development and Use of a Knowledge Translation Tool: The Rehabilitation Measures Database. *Archives of Physical Medicine and Rehabilitation*. 2014/01/01/ 2014;95(1):197-202. doi:https://doi.org/10.1016/j.apmr.2013.09.010
16. Wilkinson CM, Burrell JI, Kuziek JW, Thirunavukkarasu S, Buck BH, Mathewson KE. Predicting stroke severity with a 3-min recording from the Muse portable EEG system for rapid diagnosis of stroke. *Scientific Reports*. 2020;10(1):1-11.
17. Delorme A, Makeig S. EEGLAB: an open source toolbox for analysis of single-trial EEG dynamics including independent component analysis. *J Neurosci Methods*. Mar 15 2004;134(1):9-21. doi:10.1016/j.jneumeth.2003.10.009
18. Tsuchimoto S, Shibusawa S, Iwama S, et al. Use of common average reference and large-Laplacian spatial-filters enhances EEG signal-to-noise ratios in intrinsic sensorimotor activity. *Journal of Neuroscience Methods*. 2021/04/01/ 2021;353:109089. doi:https://doi.org/10.1016/j.jneumeth.2021.109089
19. Sheorajpanday RV, Nagels G, Weeren AJ, van Putten MJ, De Deyn PP. Reproducibility and clinical relevance of quantitative EEG parameters in cerebral ischemia: a basic approach. *Clin Neurophysiol*. May 2009;120(5):845-55. doi:10.1016/j.clinph.2009.02.171
20. Vlaar MP, Solis-Escalante T, Dewald JPA, et al. Quantification of task-dependent cortical activation evoked by robotic continuous wrist joint manipulation in chronic hemiparetic stroke. *Journal of NeuroEngineering and Rehabilitation*. 2017/04/17 2017;14(1):30. doi:10.1186/s12984-017-0240-3
21. Wang Y, Liu D, Liu J, et al. Quantitative EEG provides early prediction of poor outcome in acute ischemic stroke after endovascular treatment: a preliminary study. *Neurol Res*. Oct 2021;43(10):831-837. doi:10.1080/01616412.2021.1939237
22. Schleiger E, Sheikh N, Rowland T, Wong A, Read S, Finnigan S. Frontal EEG delta/alpha ratio and screening for post-stroke cognitive deficits: the power of four electrodes. *Int J Psychophysiol*. Oct 2014;94(1):19-24. doi:10.1016/j.ijpsycho.2014.06.012
23. Finnigan SP, Rose SE, Walsh M, et al. Correlation of quantitative EEG in acute ischemic stroke with 30-day NIHSS score: comparison with diffusion and perfusion MRI. *Stroke*. Apr 2004;35(4):899-903. doi:10.1161/01.STR.0000122622.73916.d2
24. Hsieh YW, Wu CY, Lin KC, Chang YF, Chen CL, Liu JS. Responsiveness and validity of three outcome measures of motor function after stroke rehabilitation. *Stroke*. Apr 2009;40(4):1386-91. doi:10.1161/strokeaha.108.530584
25. De Vico Fallani F, Astolfi L, Cincotti F, et al. Evaluation of the Brain Network Organization From EEG Signals: A Preliminary Evidence in Stroke Patient. *The Anatomical Record*. 2009;292(12):2023-2031. doi:https://doi.org/10.1002/ar.20965
26. Stolk A, Brinkman L, Vansteensel MJ, et al. Electrocorticographic dissociation of alpha and beta rhythmic activity in the human sensorimotor system. *Elife*. Oct 9 2019;8doi:10.7554/eLife.48065
27. Halme HL, Parkkonen L. The effect of visual and proprioceptive feedback on sensorimotor rhythms during BCI training. *PLoS One*. 2022;17(2):e0264354. doi:10.1371/journal.pone.0264354
28. Samogin J, Rueda Delgado L, Taberna GA, Swinnen SP, Mantini D. Age-Related Differences of Frequency-Dependent Functional Connectivity in Brain Networks and Their Link to Motor Performance. *Brain Connect*. Apr 1 2022;doi:10.1089/brain.2021.0135

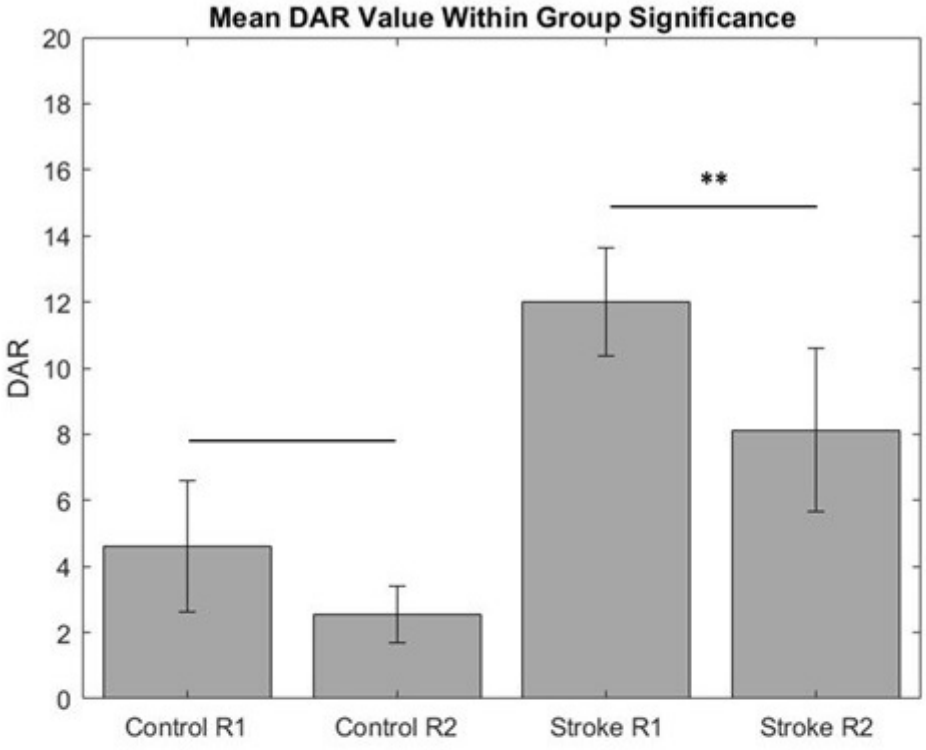
29. Zhao M, Bonassi G, Samogin J, et al. Frequency-dependent modulation of neural oscillations across the gait cycle. *Hum Brain Mapp*. Aug 1 2022;43(11):3404-3415. doi:10.1002/hbm.25856
30. Lefaucheur JP, Antal A, Ayache SS, et al. Evidence-based guidelines on the therapeutic use of transcranial direct current stimulation (tDCS). *Clin Neurophysiol*. Jan 2017;128(1):56-92. doi:10.1016/j.clinph.2016.10.087

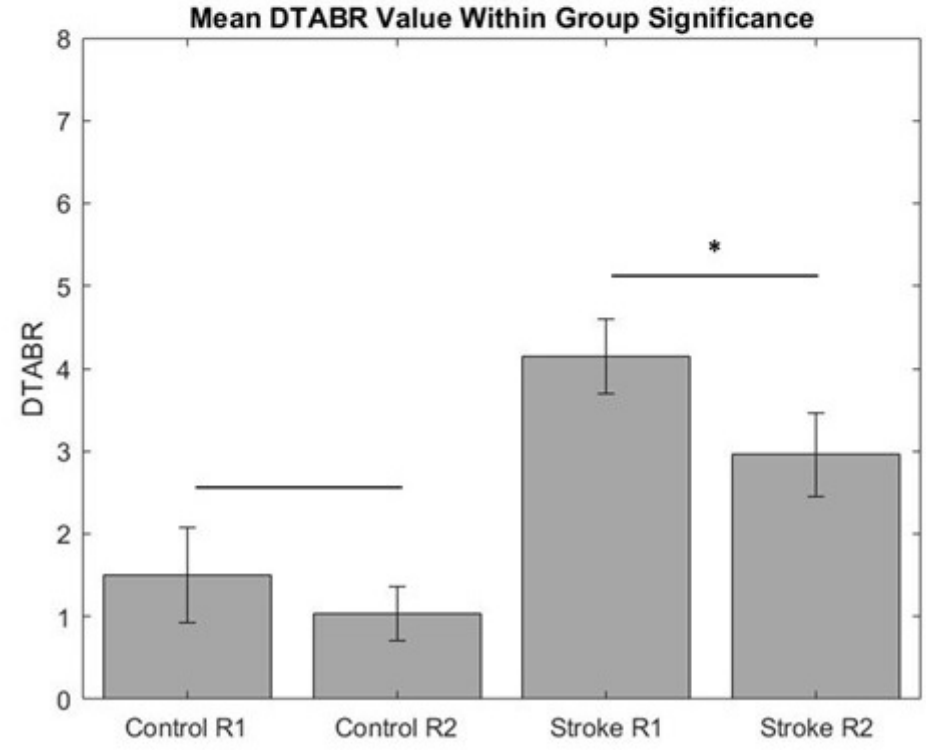
Figure Legends

FIG. 1. Delta-Alpha Ratio (DAR) and Delta-Theta-Alpha-Beta Ratio (DTABR) in the stroke and the control groups. R1: pre-TENS, R2: post-TENS, * indicates *P* value in the range of 0.01-0.05, ** indicates *P* value in the range of 0-0.01.

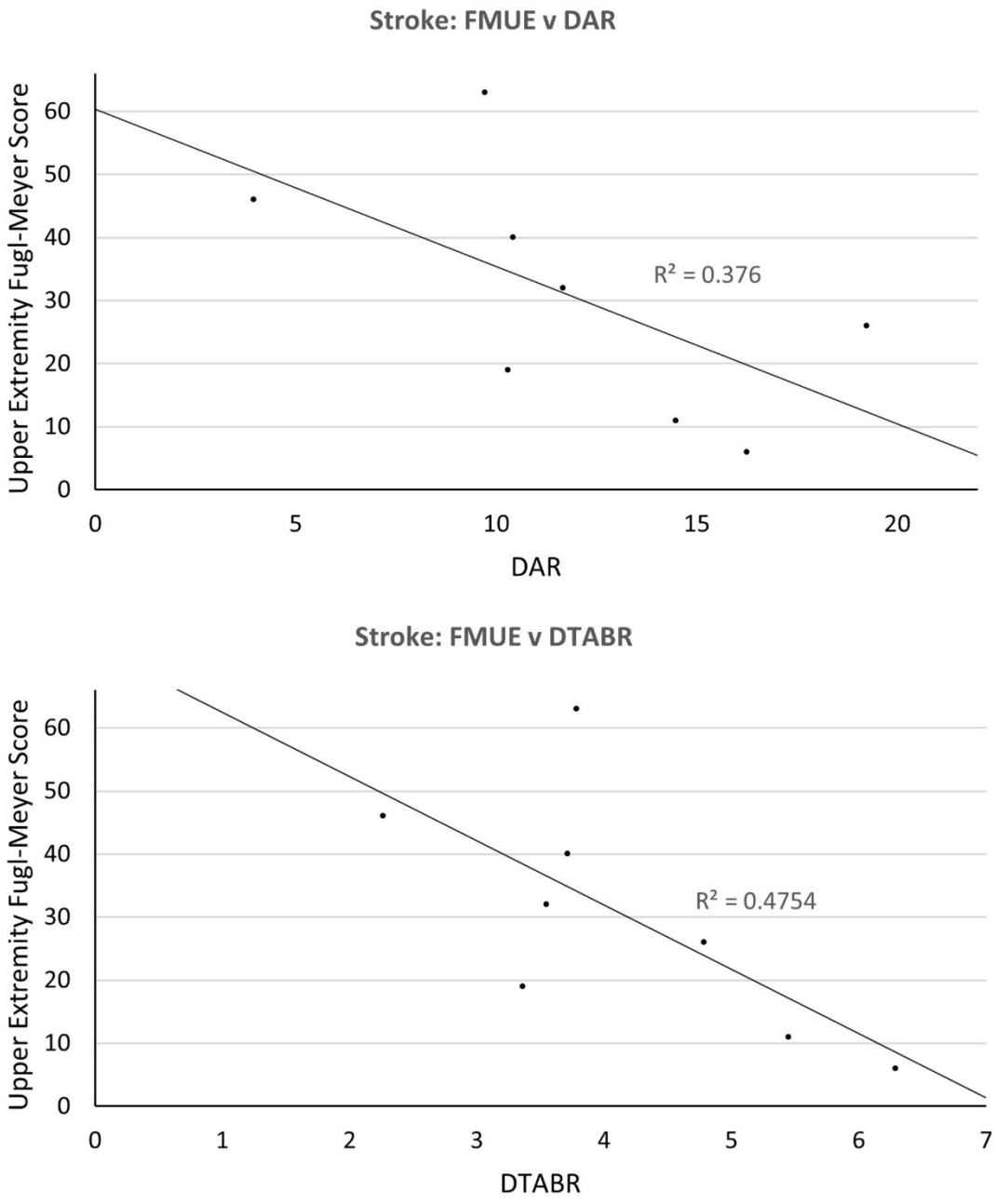
FIG. 2. Linear regression between Delta-Alpha Ratio (DAR, top) and Delta-Theta-Alpha-Beta Ratio (DTABR, bottom) with Upper Extremity Fugl-Meyer scores.

FIG. 3. Difference in power after finger stimulation (R2 – R1). Positive values (an increase in activation) are indicated by red, and negative values are indicated by blue ends of the spectrum. The plots have been normalized and averaged across subjects with the lesion hemisphere presented on the left.


Mean DAR Value Within Group Significance
DAR
20
18
16
14
12
10
8
6
4
2
0
**
Control R1
Control R2
Stroke R1
Stroke R2

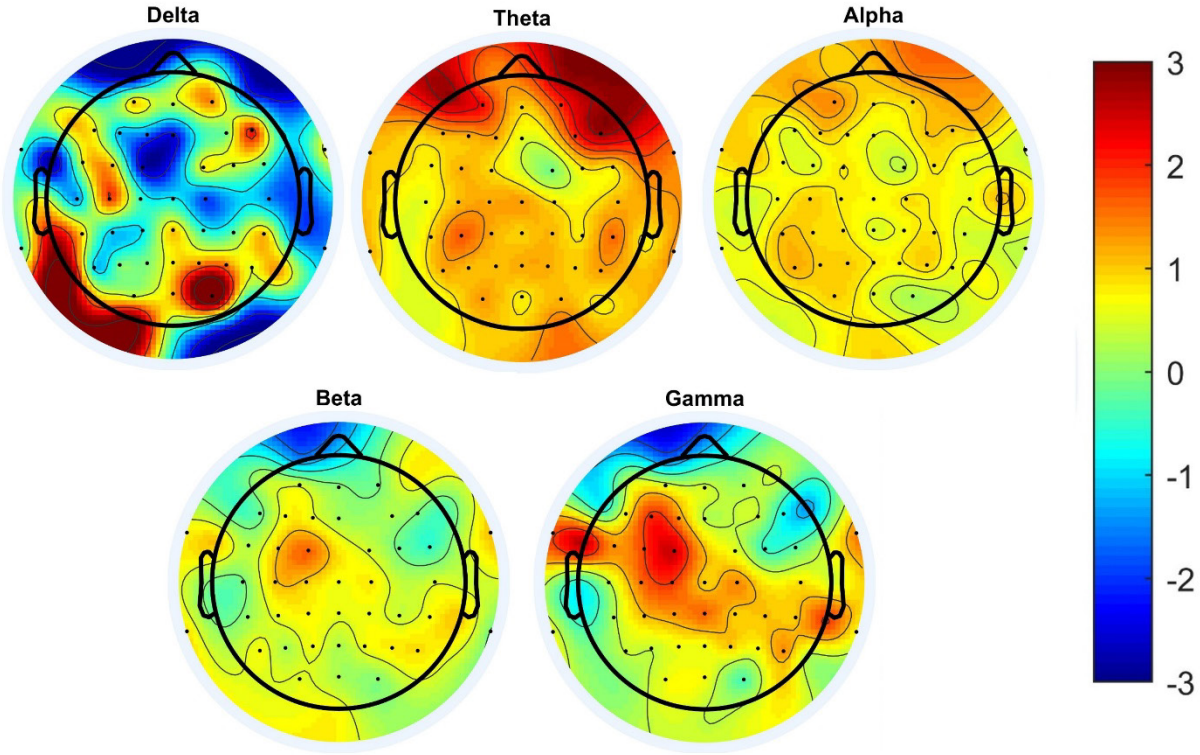

Mean DTABR Value Within Group Significance
DTABR
8
7
6
5
4
3
2
1
0
*
Control R1
Control R2
Stroke R1
Stroke R2

398 Figure 1


Stroke: FMUE v DAR
Upper Extremity Fugl-Meyer Score
60
50
40
30
20
10
0
0
5
10
15
20
DAR
R² = 0.376
Stroke: FMUE v DTABR
Upper Extremity Fugl-Meyer Score
60
50
40
30
20
10
0
0
1
2
3
4
5
6
7
DTABR
R² = 0.4754

399 Figure 2

400 Figure 3



401