The effect of dry needling in chronic stroke with a complex network approach: a case study

Abstract

Background: Dry Needling (DN) has been demonstrated to be effective in improving sensorimotor function and spasticity in patients with chronic stroke. Electroencephalogram (EEG) has been used to analyze if DN has effects on the central nervous system of patients with stroke. There are no studies on how DN works in patients with chronic stroke based on EEG analysis using complex networks. **Objective:** The aim of this study was to assess how DN works when it is applied in a patient with stroke, using the graph theory. **Methods:** One session of DN was applied to the spastic brachialis muscle of a 62-year-old man with right hemiplegia after stroke. EEG was used to analyze the effects of DN following metrics that measure the topological configuration: 1) network density, 2) clustering coefficient, 3) average shortest path length, 4) betweenness centrality, and 5) small-worldness. Measurements were taken before and during DN. **Results:** An improvement of the brain activity was observed in this patient with stroke after the application of DN, which led to variations of local parameters of the brain network in the delta, theta and alpha bands, and inclined towards those of the healthy control bands. **Conclusions:** This case study showed the positive effects of DN on brain network of a patient with chronic stroke.

Keywords: EEG. Stroke. Dry needling. Brain. Graph theory. Network.

Introduction

Stroke is one of the leading causes of disability with up to 70% of stroke patients experiencing moderate to severe dysfunction post-stroke which places a heavy physical and mental burden on patients and their families. Early post-stroke rehabilitation can improve recovery, minimize functional disability, and reduce the potential costs of long-term care [1].

Rehabilitation protocols in stroke patients usually combine different physiotherapy approaches with different medical treatments, such as oral antispastic drugs or botulinum toxin type A (BTX-A) infiltration to decrease spasticity and improve motor function. Moreover, in recent years, other non-pharmacological treatments such as dry needling (DN) have been demonstrated to be effective in improving sensorimotor function and spasticity in patients with chronic stroke [2] as well as demonstrating to be a cost-effective treatment [3]. In the case of DN, recent publications suggest that it may have central effects [4-6].

Electroencephalogram (EEG) has been used to analyze if interventions in stroke patients have effects on the central nervous system, as it provides continuous, real-time, non-invasive measurement of brain function, which offers new insights into the pathophysiology of the brain after a stroke [7-10]. Studies of brain network organization have adopted techniques used to quantitative analyze complex networks, largely based on graph theory, which provide a powerful way of quantifying the brain's structural and functional systems [11]. The low cost and availability of EEG, the simplicity, and the extraordinary sensitivity and specificity make this approach suitable for assessing the efficacy of therapeutic interventions [12].

However, to our knowledge, there are no studies on how DN works in patients with chronic stroke based on EEG analysis using complex networks. Therefore, the objective of this case study was to assess the effects of DN on brain network when it is applied in a patient post-stroke, using the graph theory.

Material and methods

Patient description and assessment

The patient was a 62-year-old man with chronic ischemic stroke as diagnosed by the neurologist. His stroke duration was two years since onset. He had right hemiplegia. The affected limb was in the Brunnstrom Recovery Stage 3 (marked spasticity with basic limb synergies performed voluntarily). Written consent was obtained before starting the measurements. Initial assessment was carried out with EEG, collecting data during 5 minutes in a resting mode in seated position with eyes closed, before and during DN. Data were compared with those of a healthy matched control (61-year-old). EEG data were recorded with 18 electrodes on the scalp at a sampling rate of 256 Hz. For recording, we used the 10-20 system and the electrodes Fp1, Fp2, F7, F3, Fz, F4, F8, T3, C3, Cz, C4, T4, P3, Pz, P4, T5, T6, O1.

Treatment

To perform the intervention, the patient was in supine position on his back. DN was performed in the approximate motor point of the brachialis muscle [13] for 60 seconds using a 50mm x 0.3 mm disposable sterile needle; DongBang AcuPrime Ltd, Korea. The needle was manipulated fast in and fast out, with a frequency of approximately 1Hz. The brachialis muscle was selected as it is shown the most limiting factor of the elbow extension in spasticity flexion pattern of elbow and the relevant target for spasticity treatment post stroke [13]. A point from distal 30% and 2 cm medial to a reference line connecting humerus lateral epicondyle to the coracoid process was needled for brachialis muscle [14].

Data analysis

Graph theory allows studying a complex real-world system by defining a network (or graph) as composed by a set of nodes (vertices) and the links (edges) between them, which models such system. Network structures exist in a wide range of different areas, such as technological and transportation infrastructures, social phenomena, biological and neural systems. Each network structure presents specific topological features which characterize a network's connectivity, interactions, and dynamic processes [15]. Therefore, a complex network's analysis relies on using measurements that can express its most relevant topological features to enable characterization of its complex statistical properties [16]. In the case of brain function studies, structural and functional brain networks can be defined from anatomical representations of the brain or from EEG electrodes, while links, depending on the data set, refers to anatomical, functional, or effective connections [17]. In this study, we considered a functional brain network using the electrodes as nodes of the graph and edges defined by analyzing the generalized partial directed coherence (GPDC) [18] between the signals of each pair of electrodes. EEG data was extracted in European Data Format and was processed in MATLAB with EEGLAB toolbox to generate the brain functional network and the association matrices. The analyzes were performed in python with NetworkX and SciPy to assess the effects of DN in this patient with stroke. Data below 45 Hz were considered for analysis.

Prior to data analysis, aberrant waves such as blink and electromyography signals were removed. GPDC relates each pair of electrodes by assigning a normalized signal coherence value between 0 and 1, thus nodes' association matrix defines a weighted link between all the nodes of the network. We converted the matrices from weighted to non-weighted directed by establishing a cut-off threshold of 0.15, removing the links between nodes with signal coherence below that threshold. Finally, 2700 unweighted directional matrices for each dataset were obtained corresponding to the processing of the EEG signals carried out on delta (below 4 Hz), theta (between 4 Hz to 8 Hz), alpha (between 8 to 13 Hz), beta (between 13 to 30 Hz), and gamma (between 30 and 45 Hz) bands.

For the assessment of the effects of DN in this patient with stroke, we used the following metrics that measure the topological configuration: 1) network density, 2) clustering coefficient, 3) average shortest path length, 4) betweenness centrality, and 5) small-worldness. Table 1 summarizes these key metrics.

Table 1. Network metrics

Parameter	Abbreviation	Formula	
Density	D	$D = \frac{2m}{n(n-1)}$	(1)
Average shortest path length	L	$L = \frac{1}{n(n-1)} \sum_{i \neq j} d_{ij}$	(2)
Local clustering coefficient	C_i	$C_i = \frac{1}{k_i(k_i-1)} \sum_{j,k} a_{ij} a_{jk} a_{ik}$	(3)
Global clustering coefficient	C	$C = \frac{1}{n} \sum_{i} C_i$	(4)
Betweenness centrality	B_C	$C_B(i) = \sum_{i \neq j \neq k} \frac{\sigma_{ij}(i)}{\sigma_{kj}}$	(5)
Small-worldness	SW	$SW = C/L$	(6)

Network density (D, formula 1) was obtained by the ratio of the number of network edges to the maximum possible number of network edges [19], with n as the number of nodes and m the number of edges. Values of D may range from 0 to 1. The closer D is to one, the more cohesive and denser the network, and the lower the number, the less cohesive the network.

Average shortest path length (L, formula 2) is defined as the average number of steps in the shortest paths for all node pairs in a network [20], where d_{ij} indicates the distance between node i and node j (the number of edges in the shortest path between both nodes).

Local clustering coefficient (C_i, formula 3) calculates the local cohesion of a node i with its neighbors [20], being k_j the number of nodes directly connected with node i, and a_{xy} terms indicate connections between pair of nodes (x, y) (they equal 1 if nodes are connected and 0 otherwise). Global clustering coefficient (C, formula 4), also called Network average clustering coefficient, provides an overall measure of the cohesion of the nodes in the whole network.

Centralities measure the relative importance of a node in a network, such as connecting directly or being available to others as well as being an intermediary between others. Infrastructural analysis to determine the characteristics of a network is derived from the concept of centrality, which is measured by a variety of criteria. In this analysis, we used betweenness centrality. Betweenness centrality (B_C, formula 5) determines which particular node is most among the nodes in the network [21]. In the formula, σ_{kj} is the number of shortest paths from node k to node j, and $\sigma_{kj}(i)$ is the number of those paths that pass through node i.

The measure of network small-worldness (SW, formula 6) is defined as the ratio between C and L [22,23]. The SW coefficient is used to describe the balance between the local connectedness and the global integration of a network. When SW is larger than 1, a network is said to have small-worldness properties. Small-worldness organization mixes short path length and high clustering.

Results

The results of the EEG analysis using complex dynamic networks are presented in figures 1 to 5, which show the variations of the metrics defined in Table 1 for each of the EEG bands. Each figure present 3 curves showing the changes in the network metrics considered from its maximum value to its minimum value. The green and blue lines show the changes in the network parameter considered for the patient before and during the DN treatment respectively, and the red line shows the parameter for the healthy subject as control.

Figure 1 shows the changes in network density, variations in the delta, theta, and alpha bands of the stroke case that are significantly different than those of the healthy control. As shown in figure 1, the values of the delta, theta and alpha bands in the stroke case are becoming closer to the healthy control during DN application. In the case of beta and gamma bands, the values are similar for both the stroke patient and the healthy control, although some changes also occurred in these bands during DN.

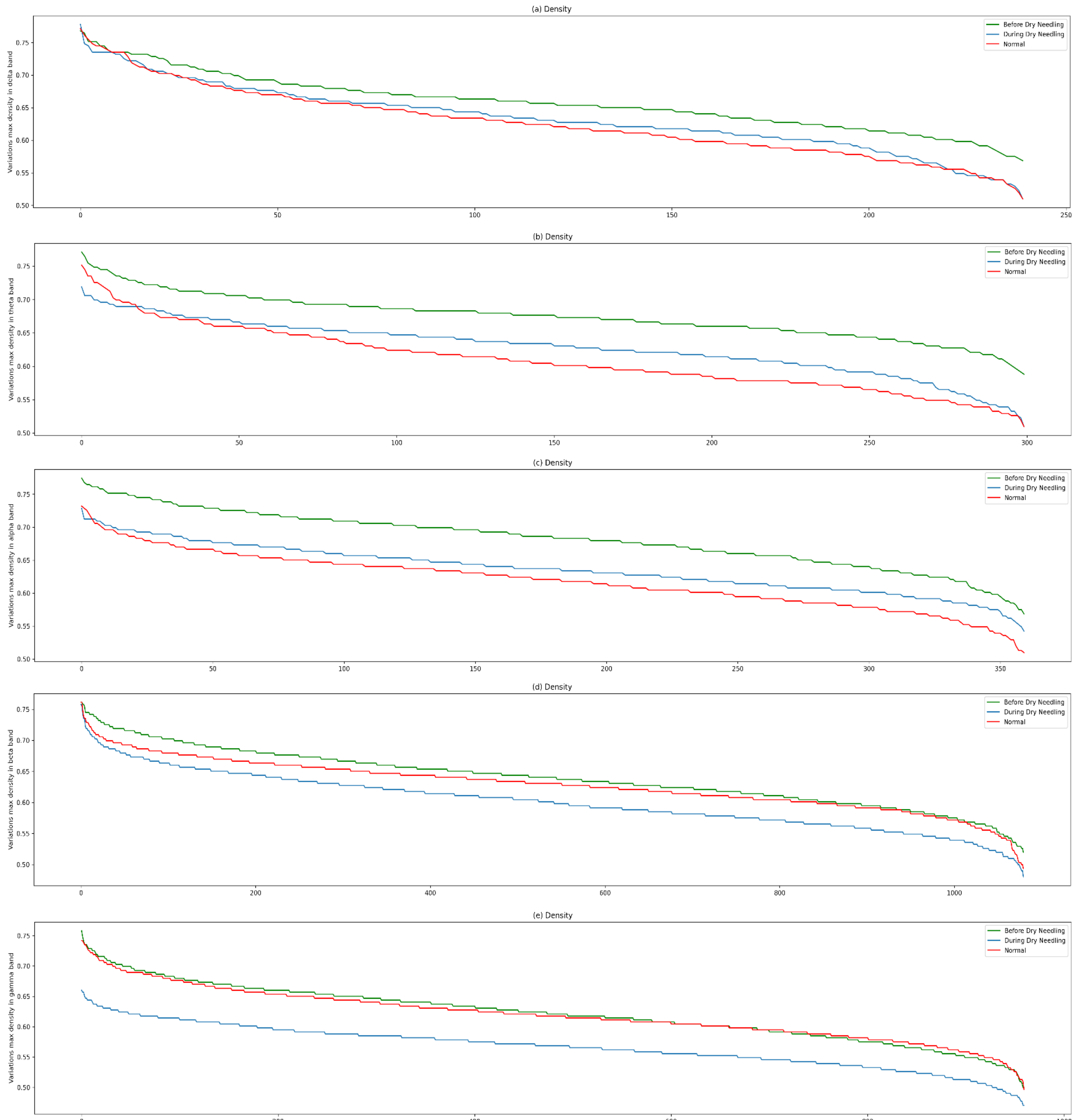

Figure 1. Variations in network density show delta (a), theta (b), and alpha (c) bands that becoming more similar to those of the healthy control during DN application. The beta (d) and gamma (e) bands show no significant differences between the stroke case and the healthy control.

Figure 2 on the average shortest path length shows that the variations in the stroke case are smaller than those of the normal case, with significant differences observed in the delta, theta and alpha bands. In the beta and gamma bands, there are no significant differences between the stroke case and the healthy control. In the delta, theta, and alpha bands, during DN application, the values of stroke case variations are becoming closer to normal. In the beta and gamma bands, although there is no difference between the stroke case and healthy control, performing DN increased the average shortest path length parameter values in these bands.

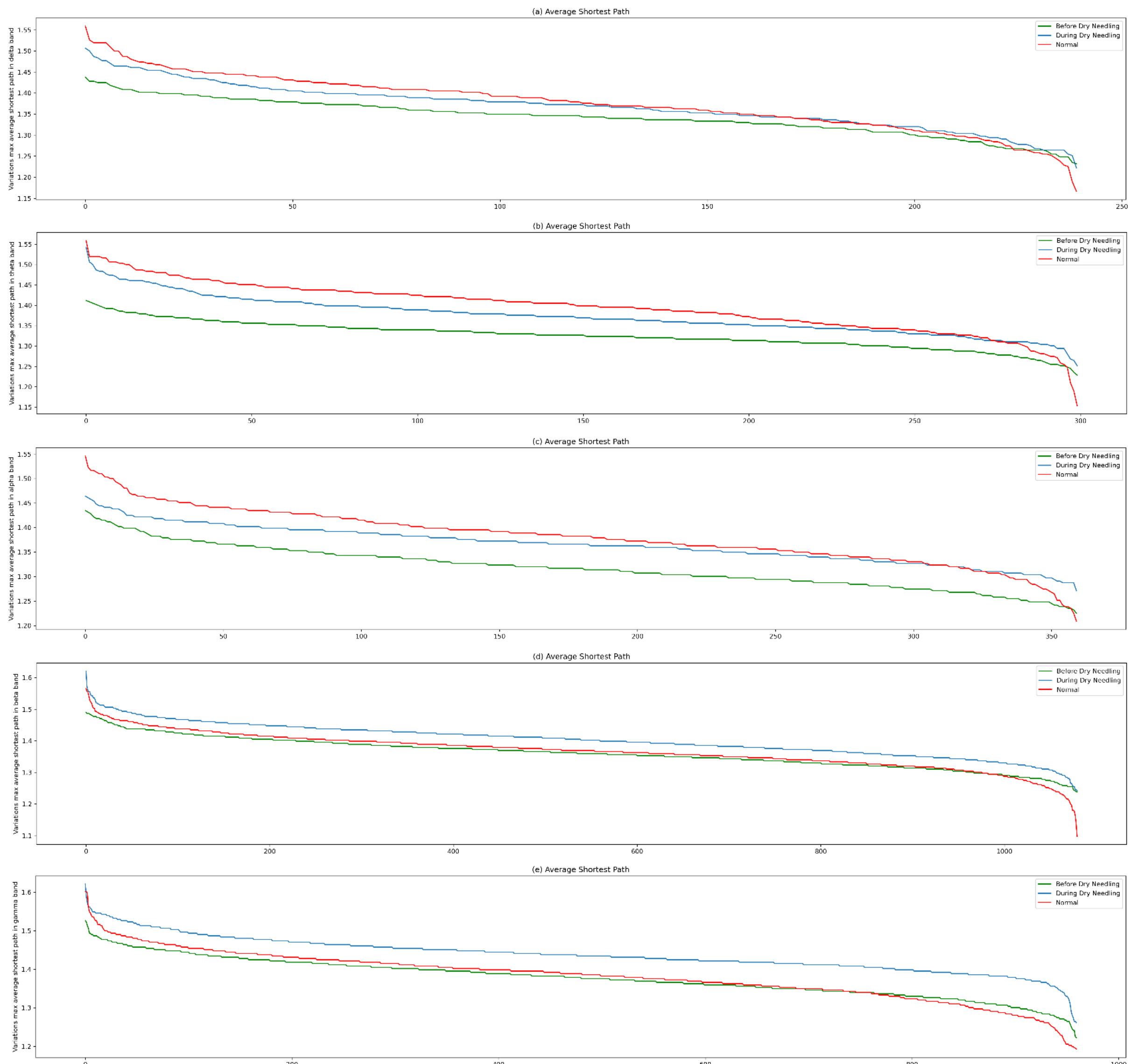

Figure 2. Variations in average shortest path show delta (a), theta (b), and alpha (c) bands becoming more similar to the healthy control during DN application. The beta (d) and gamma (e) bands show no significant differences between the stroke case and the healthy control.

Figure 3 shows the global clustering coefficient. In delta, theta, and alpha bands, there are significant differences between the stroke and the healthy control. During DN application, the global clustering coefficient parameter variations in the stroke case are becoming closer to normal. In beta and gamma bands, there are not much difference between the stroke case and the healthy control. In fact, DN caused changes in the structure of the stroke patient's brain network. The variations in Figure 3 are very similar to the density variations as shown in Figure 1.

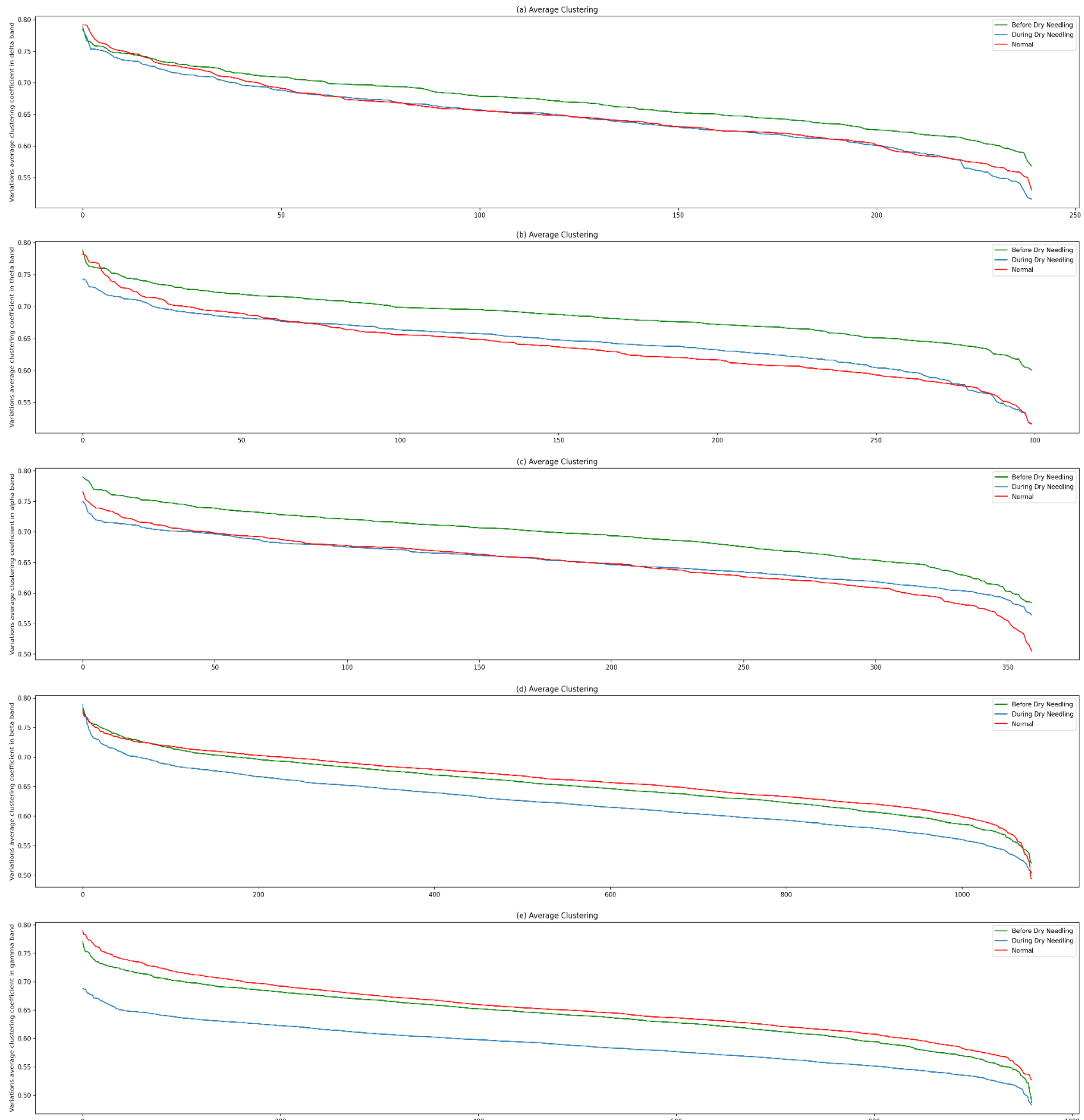

Figure 3. Variations in global clustering coefficient show delta (a), theta (b), and alpha (c) bands becoming more similar to the healthy control during DN application. The beta (d) and gamma (e) bands show no significant differences between the stroke case and the healthy control.

Figure 4 shows the betweenness centrality changes. The values of these variations in all bands show a lower value for the stroke case compared to those of the healthy control. In all bands, the betweenness centrality variations in the stroke case are becoming closer to normal during DN. In the delta, theta, and alpha bands, there are significant differences in maximum values of the variations in betweenness centrality between the stroke case (maximum value less than 0.1) and the healthy control (maximum value larger than 0.2). The betweenness centrality is the only parameter that shows differences in all bands between the stroke case and the healthy control.

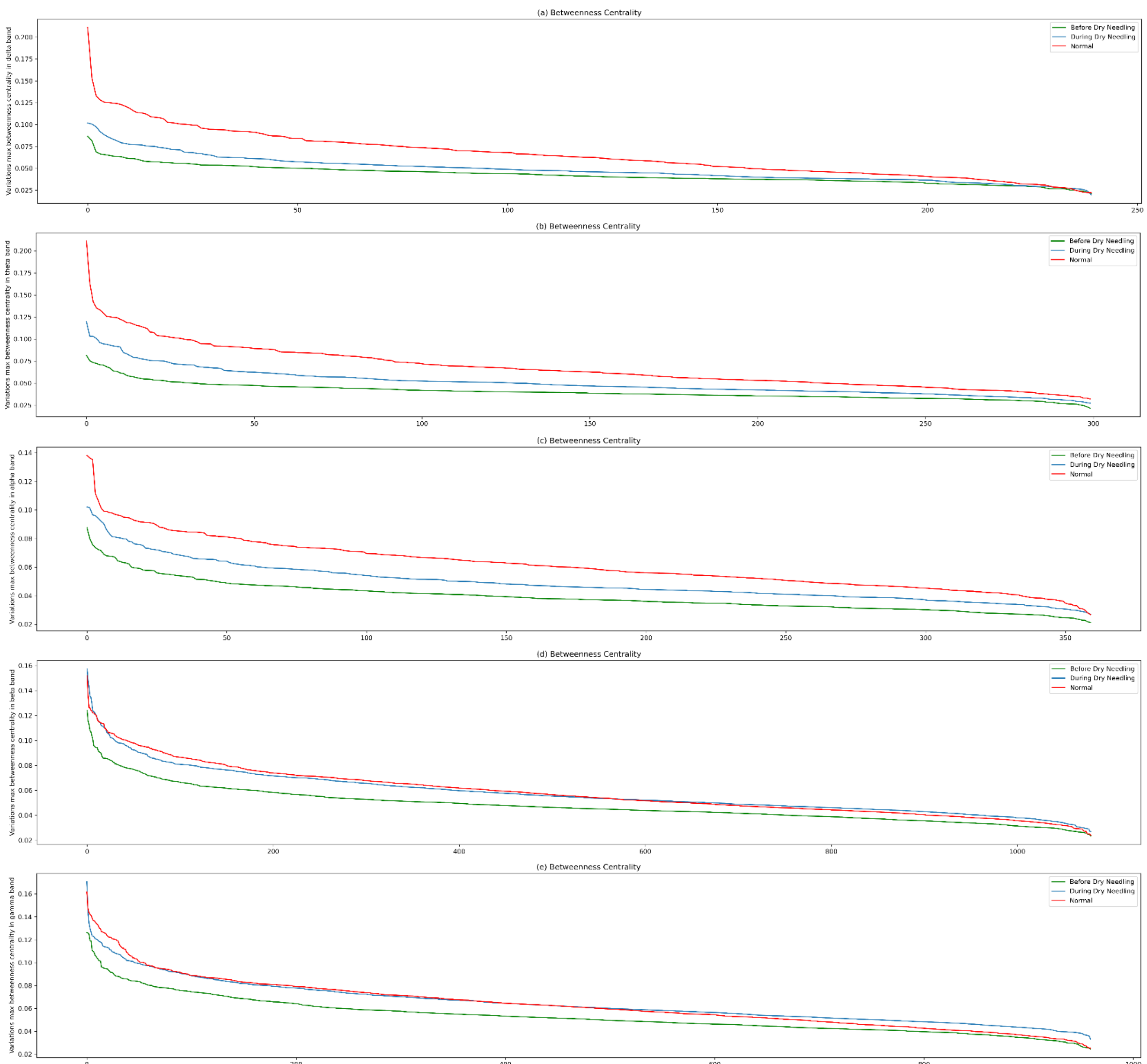

Figure 4. Variations in betweenness centrality show delta (a), theta (b), alpha (c), beta (d), and gamma (e) bands becoming more similar to the healthy control during DN application.

Figure 5 shows the small-worldness parameter. There were significant differences in small-worldness parameter variations in the patient with stroke and the healthy control in delta, theta, and alpha bands. In these bands, DN caused changes in the structure of the brain network in the stroke case towards normal. There were no differences in the beta and gamma bands between the stroke case and healthy control. In fact, DN caused changes in the structure of the stroke patient's brain network.

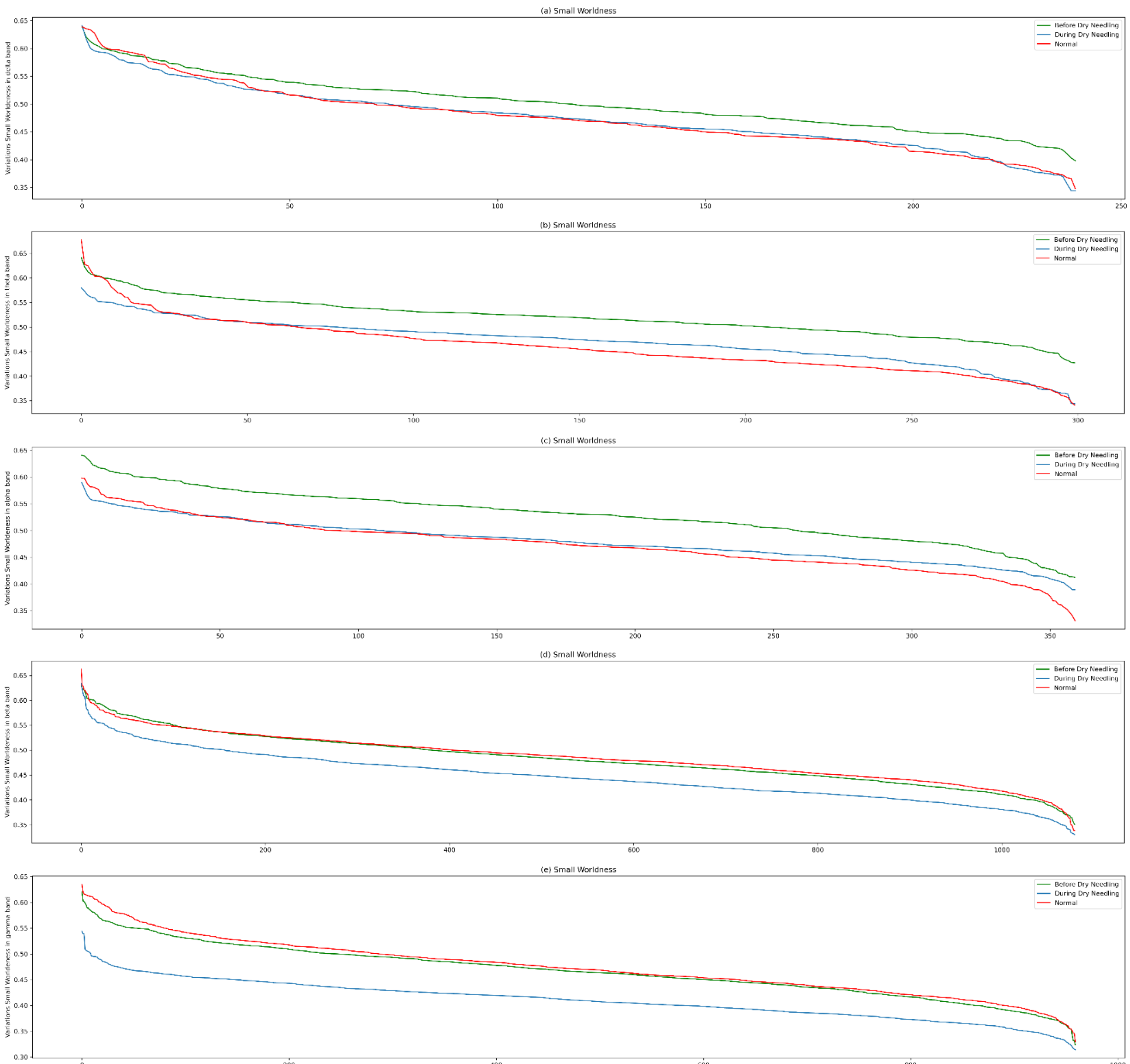

Figure 5. Variations in small-worldness show delta (a), theta (b), and alpha (c) bands becoming more similar to the healthy control during DN application. The beta (d) and gamma (e) bands show no significant differences between the stroke case and the healthy control.

Discussion

Stroke affects the whole brain and its network characteristics and therefore can be considered as a network disease. Many studies have been performed on the brain networks as well as on the effects of rehabilitation on patients with stroke. Network assessment to predict the treatment effects and to individualize rehabilitation is a promising approach to enhance the specific treatment effects and overall outcome after stroke [12].

We found that variations in network density, global clustering coefficient, and small-worldness were similar. The values of the parameters for the stroke case were higher than the values of the healthy control in the delta, theta, and alpha bands. During DN, the values of the stroke case parameters became closer to the values of the healthy control. The variations in average shortest path and betweenness centrality were the only variations where the healthy control had smaller values than the stroke case. In the case of the average shortest path variations, differences between the stroke case and the healthy control were seen only in delta, theta, and alpha bands, whereas the differences in betweenness centrality variations were in all bands. In all parameters except betweenness centrality, the beta and gamma bands had no differences between the stroke case and the healthy control. However, there were differences in all bands in the betweenness centrality parameter between the patient with stroke and the healthy control.

Among rehabilitation methods, DN impact positively on spasticity, pain, and range of motion in patients with stroke [24]. Our results in this patient with stroke showed that DN causes structural changes in the brain network, which is in line with other studies that have used and analyzed the EEG [29] and fMRI [6]. Calvo et al [25] showed that after the application of DN [DNHS technique] based on the measurement of quantitative EEG activity and EEG concordance, improvements in the regional brain activity occured. Mohammadpour et al [6] by using fMRI, showed that DN had a positive effect on the stroke patient's recovery. Absence of resting-state network rearrangement in beta and gamma bands is consistent with previous data [26, 27] considering that measurements with EEG were performed with closed eyes. A possible explanation could be that coherence in higher bands may be more involved in active (either motor or cognitive) tasks [28-30] and therefore, it might be better to study the effects of DN with open eyes for beta and gamma bands. However, we clearly observed the positive effects of DN in the delta, theta and alpha bands, which suggest performing DN in resting state could improve the structure of the brain network in this patient with stroke. There is a need for further study on the effects of DN on the structure of the brain network in patients with stroke using the EEG with eyes open. In the case of other interventions in stroke patients such as focal vibration, the authors reported binding power occurred in some central electrodes after focal vibration [31]. In fact, focal vibration as a rehabilitation method causes a cortical reorganization of the somatosensory representational maps. However, DN rebuilds the structure of the brain as shown in this patient with stroke, which has not been observed, to the best of our knowledge, in any other study.

The delta, theta and alpha bands are related to low frequency bands in EEG. With bregard to the large differences between the brain network of the stroke case and the healthy control on these bands before DN and significant improvements occurring during DN, we may conceptualize that the DN normalized the structure of the brain network of this patient with stroke in low frequency bands. Changes in resting state network were mainly detected in EEG low frequency bands, while no network rearrangement was found in beta and gamma bands except for betweenness centrality parameter which is consistent with previous findings [32].

Regarding high frequency bands of beta and gamma, there were no significant changes in the brain network structure in the studied parameters. Nevertheless, DN changed the structure of the brain network in this patient with chronic stroke. There were differences between the stroke case and the healthy control in high frequency bands and betweenness centrality parameter in the brain network. Considering the betweenness parameter, DN caused improvements even in high frequency bands such that they became similar to those of the healthy control network. The greatest difference between the stroke case and the healthy control was in the betweenness centrality parameter. Given that betweenness centrality plays an intermediate role in the network, it seems that DN could work through the creation of a network that maximizes the betweenness centrality in the nodes. This indicates that the betweenness centrality is an important parameter in the brain as it was modified in all bands in this patient with stroke.

Small-worldness organization of the brain networks [32-35] along with other measures from graph theory have been used to quantify the changes in brain connectivity and functional recovery in patients after stroke [36-39]. The results on the delta, theta, and alpha bands showed that the small-worldness variations in the patient with stroke were greater than those in the healthy control, which is consistent with the previous a reports for the theta band [40]. Accordingly, Caliandro et al. [32] found an increased segregation and a decreased integration in θ-band network consistent with a previous fMRI study [41].

This study has strength and limitations. The main strength is the innovation associated with using graph theory of complex network approach in the clinical context used for analysis of the effects of DN on the structure of the brain network. The main limitation is that this study was carried out only in one patient and therefore further study is needed to investigate whether DN is effective in improving the brain networks in stroke patients towards normal and whether there might be a cause-effect relationship. Future research should also examine how the brain network structure differs from normal in patients with chronic stroke. In this patient with stroke, the changes were not evaluated after the end of DN application. As well, clinical measures particularly muscle spasticity level and motor function were not assessed. Therefore, studies with larger sample sizes with rigorous design and follow-up should be carried out to investigate the effects of DN on the structure of the brain network and evaluate the associations with functional changes in patients with stroke.

In conclusion, this case study showed the positive effects of DN on brain network with the delta, theta and alpha bands becoming closer to the normal in density, average shortest path, global clustering coefficient, and small-worldness parameters in a patient with stroke. Further investigations in the context a well-design clinical trials are warranted.

References

[1] Duncan PW, Zorowitz R, Bates B, et al. Management of Adult Stroke Rehabilitation Care: a clinical practice guideline. Stroke. 2005;36(9):e100-e143. doi:10.1161/01.STR.0000180861.54180.FF

[2] Calvo S, Brandín-de la Cruz N, Jiménez-Sánchez C, Bravo-Esteban E, Herrero P. Effects of dry needling on function, hypertonia and quality of life in chronic stroke: a randomized clinical trial [published online ahead of print, 2021 Dec 13]. Acupunct Med. 2021;9645284211056347. doi:10.1177/09645284211056347

[3] Fernández-Sanchis D, Brandín-de la Cruz N, Jiménez-Sánchez C, Gil-Calvo M, Herrero P, Calvo S. Cost-Effectiveness of Upper Extremity Dry Needling in Chronic Stroke. Healthcare (Basel). 2022;10(1):160. Published 2022 Jan 14. doi:10.3390/healthcare10010160

[4] Ansari NN, Naghdi S, Fakhari Z, Radinmehr H, Hasson S. Dry needling for the treatment of poststroke muscle spasticity: a prospective case report. NeuroRehabilitation. 2015;36(1):61-65. doi:10.3233/NRE-141192

[5] Fakhari Z, Ansari NN, Naghdi S, Mansouri K, Radinmehr H. A single group, pretest-posttest clinical trial for the effects of dry needling on wrist flexors spasticity after stroke. NeuroRehabilitation. 2017;40(3):325-336. doi:10.3233/NRE-161420

[6] Mohammadpour F, Ali Oghabian M, Nakhostin Ansari N, Naghdi S, Dommerholt J. Effects of dry needling on post-stroke brain activity and muscle spasticity of the upper limb: a case report. Acupunct Med. 2021;39(1):69-71. doi:10.1177/0964528420920294

[7] Cohen BA, Bravo-Fernandez EJ, Sances A Jr. Automated electroencephalographic analysis as a prognostic indicator in stroke. Med Biol Eng Comput. 1977;15(4):431-437. doi:10.1007/BF02457998

[8] Cohen BA, Bravo-Fernandez EJ, Sances A Jr. Quantification of computer analyzed serial EEGs from stroke patients. Electroencephalogr Clin Neurophysiol. 1976;41(4):379-386. doi:10.1016/0013-4694(76)90100-0

[9] Juhász C, Kamondi A, Szirmai I. Spectral EEG analysis following hemispheric stroke: evidences of transhemispheric diaschisis. Acta Neurol Scand. 1997;96(6):397-400. doi:10.1111/j.1600-0404.1997.tb00305.x

[10] Luu P, Tucker DM, Englander R, Lockfeld A, Lutsep H, Oken B. Localizing acute stroke-related EEG changes: assessing the effects of spatial undersampling. J Clin Neurophysiol. 2001;18(4):302-317. doi:10.1097/00004691-200107000-00002

[11] Bullmore E, Sporns O. Complex brain networks: graph theoretical analysis of structural and functional systems [published correction appears in Nat Rev Neurosci. 2009 Apr;10(4):312]. Nat Rev Neurosci. 2009;10(3):186-198. doi:10.1038/nrn2575

[12] Guggisberg AG, Koch PJ, Hummel FC, Buetefisch CM. Brain networks and their relevance for stroke rehabilitation. Clin Neurophysiol. 2019;130(7):1098-1124. doi:10.1016/j.clinph.2019.04.004

[13] Genet F, Schnitzler A, Droz-Bartholet F, et al. Successive motor nerve blocks to identify the muscles causing a spasticity pattern: example of the arm flexion pattern. J Anat. 2017;230(1):106-116. doi:10.1111/joa.12538

[14] Park BK, Shin YB, Ko HY, Park JH, Baek SY. Anatomic motor point localization of the biceps brachii and brachialis muscles. J Korean Med Sci. 2007;22(3):459-462. doi:10.3346/jkms.2007.22.3.459

[15] Barrat A, Barthélemy M, Pastor-Satorras R, Vespignani A. The architecture of complex weighted networks. Proc Natl Acad Sci U S A. 2004;101(11):3747-3752. doi:10.1073/pnas.0400087101

[16] Costa LD, Rodrigues FA, Travieso G, Villas Boas PR. Characterization of complex networks: A survey of measurements. Advances in physics. 2007;56(1):167-242.

[17] Friston KJ. Functional and effective connectivity in neuroimaging: a synthesis. Human brain mapping. 1994;2(1-2):56-78.

[18] Baccala LA, Sameshima K, Takahashi DY. Generalized partial directed coherence. In2007 15th International conference on digital signal processing 2007 Jul 1 (pp. 163-166). IEEE.

[19] Barabasi AL, Albert R. Emergence of scaling in random networks. Science. 1999;286(5439):509-512. doi:10.1126/science.286.5439.509

[20] van Wijk BCM, Stam CJ, Daffertshofer A. (2010). Comparing brain networks of different size and connectivity density using graph theory. PLoS ONE. 2010; 5(10): e13701–e13701. doi:https://doi.org/10.1371/journal.pone.0013701

[21] Makarov VV, Zhuravlev MO, Runnova AE, Protasov P, Maksimenko VA, Frolov NS, Pisarchik AN, Hramov AE. Betweenness centrality in multiplex brain network during mental task evaluation. Physical Review E. 2018; 98(6): 062413. doi: https://doi.org/10.1103/PhysRevE.98.062413

[22] Onnela JP, Saramäki J, Kertész J, Kaski K. Intensity and coherence of motifs in weighted complex networks. Phys Rev E Stat Nonlin Soft Matter Phys. 2005;71(6 Pt 2):065103. doi:10.1103/PhysRevE.71.065103

[23] Rubinov M, Sporns O. Complex network measures of brain connectivity: uses and interpretations. Neuroimage. 2010;52(3):1059-1069. doi:10.1016/j.neuroimage.2009.10.003

[24] Valencia-Chulián R, Heredia-Rizo AM, Moral-Munoz JA, Lucena-Anton D, Luque-Moreno C. Dry needling for the management of spasticity, pain, and range of movement in adults after stroke: A systematic review. Complement Ther Med. 2020;52:102515. doi:10.1016/j.ctim.2020.102515

[25] Calvo S, Navarro J, Herrero P, Del Moral R, De Diego C, Marijuán PC. Electroencephalographic changes after application of dry needling [DNHS© technique] in two patients with chronic stroke. Myopain. 2015;23(3-4):112-7.

[26] Dubovik S, Pignat JM, Ptak R, et al. The behavioral significance of coherent resting-state oscillations after stroke. Neuroimage. 2012;61(1):249-257. doi:10.1016/j.neuroimage.2012.03.024

[27] Westlake KP, Hinkley LB, Bucci M, et al. Resting state α-band functional connectivity and recovery after stroke [published correction appears in Exp Neurol. 2012 Dec;238(2):100]. Exp Neurol. 2012;237(1):160-169. doi:10.1016/j.expneurol.2012.06.020

[28] Gerloff C, Bushara K, Sailer A, et al. Multimodal imaging of brain reorganization in motor areas of the contralesional hemisphere of well recovered patients after capsular stroke. Brain. 2006;129(Pt 3):791-808. doi:10.1093/brain/awh713

[29] 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. Anat Rec (Hoboken). 2009;292(12):2023-2031. doi:10.1002/ar.20965

[30] Jin SH, Lin P, Hallett M. Reorganization of brain functional small-world networks during finger movements. Hum Brain Mapp. 2012;33(4):861-872. doi:10.1002/hbm.21253

[31] Li W, Li C, Xu Q, Ji L. Effects of Focal Vibration over Upper Limb Muscles on the Activation of Sensorimotor Cortex Network: An EEG Study. J Healthc Eng. 2019;2019:9167028. Published 2019 May 27. doi:10.1155/2019/9167028

[32] Caliandro P, Vecchio F, Miraglia F, et al. Small-World Characteristics of Cortical Connectivity Changes in Acute Stroke. Neurorehabil Neural Repair. 2017;31(1):81-94. doi:10.1177/1545968316662525

[33] Wang L, Yu C, Chen H, et al. Dynamic functional reorganization of the motor execution network after stroke. Brain. 2010;133(Pt 4):1224-1238. doi:10.1093/brain/awq043

[34] Vecchio F, Caliandro P, Reale G, et al. Acute cerebellar stroke and middle cerebral artery stroke exert distinctive modifications on functional cortical connectivity: A comparative study via EEG graph theory. Clin Neurophysiol. 2019;130(6):997-1007. doi:10.1016/j.clinph.2019.03.017

[35] Vecchio F, Tomino C, Miraglia F, et al. Cortical connectivity from EEG data in acute stroke: A study via graph theory as a potential biomarker for functional recovery. Int J Psychophysiol. 2019;146:133-138. doi:10.1016/j.ijpsycho.2019.09.012

[36] Jiang L, Xu H, Yu C. Brain connectivity plasticity in the motor network after ischemic stroke. Neural Plast. 2013;2013:924192. doi:10.1155/2013/924192

[37] Rehme AK, Grefkes C. Cerebral network disorders after stroke: evidence from imaging-based connectivity analyses of active and resting brain states in humans. J Physiol. 2013;591(1):17-31. doi:10.1113/jphysiol.2012.243469

[38] Wu J, Quinlan EB, Dodakian L, et al. Connectivity measures are robust biomarkers of cortical function and plasticity after stroke. Brain. 2015;138(Pt 8):2359-2369. doi:10.1093/brain/awv156

[39] Van Kaam RC, van Putten MJAM, Vermeer SE, Hofmeijer J. Contralesional Brain Activity in Acute Ischemic Stroke. Cerebrovasc Dis. 2018;45(1-2):85-92. doi:10.1159/000486535

[40] Fanciullacci C, Panarese A, Spina V, et al. Connectivity Measures Differentiate Cortical and Subcortical Sub-Acute Ischemic Stroke Patients. Front Hum Neurosci. 2021;15:669915. Published 2021 Jul 1. doi:10.3389/fnhum.2021.669915

[41] Adhikari MH, Hacker CD, Siegel JS, et al. Decreased integration and information capacity in stroke measured by whole brain models of resting state activity. Brain. 2017;140(4):1068-1085. doi:10.1093/brain/awx021