Exploring the Interplay of Prosody, Language Skills, and Brain Connectivity:

A Stroke Resting State fMRI Study

by

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ABSTRACT

This thesis explores the interplay of aphasia symptoms and brain connectivity using resting-state functional Magnetic Resonance Imaging (MRI). The research presented here is a step towards understanding the neural basis of linguistic prosody in particular, and its relationship with language impairments in post-stroke aphasia. This study focuses on examining the functional connectivities of the frontal-parietal control network and the dorsal attention networks with specific regions within traditional language networks, as a growing body of research suggests that prosodic cues in speech may recruit control and attention networks to support language processing. Using resting-state fMRI, the present study examined the functional connectivity of the frontal parietal control and dorsal attention networks with traditional language regions in 28 participants who have experienced a stroke-related language impairment (i.e. aphasia) and 32 matched neurotypical adults. Overall, the study reveals significant functional connectivity differences of the frontoparietal control and dorsal attention networks between the stroke and control groups, indicating that individuals with aphasia have brain connectivity differences beyond the traditional language networks. Multiple regression analyses were then used to determine if functional connectivities of the frontoparietal control and dorsal attention networks within themselves and with traditional language regions could predict aphasia symptoms, as measured by the Western Aphasia Battery (WAB). Overall, the regression results indicate that greater functional connectivity between the frontoparietal control and dorsal attention networks with traditional language regions is associated with improved language abilities, with different connectivities predicting different types of aphasia symptoms (e.g. speech, naming / word finding, auditory comprehension, overall impairment). Altogether this study contributes to the understanding of the neural bases of language impairments post-stroke, highlighting the intricate connections between language and other cognitive networks, which may be mediated by prosody.

DEDICATION

This achievement holds profound significance for me, as I dedicate it firstly to my father, whose physical absence doesn't diminish the impact he has had on my journey. Every step I've taken, every milestone reached, I believe resonates with his spirit, filling me with the belief that I've made him proud. To my beloved Samarth, for always being there, supporting me, and for believing in me. You have been my anchor through every challenge and triumph. I owe this achievement to you, for your faith in me has always propelled me towards greatness. My dear mother, your strength, bravery, and boundless kindness inspire me every day. I strive to emulate your resilience as I pursue my dreams, knowing that without your unwavering support, I wouldn't stand where I am today. And to my brother and sister, who always had my back. I love you all with all that I have in me. You are the pillar of strength in my life, each one of you play an important part in my life, and I am truly grateful for this achievement.

ACKNOWLEDGMENTS

I would like to express my gratitude to my advisor for the opportunity to work on my research project and for their guidance and support throughout my journey. I would also like to sincerely thank my committee members for helping me develop my research and providing valuable guidance and encouragement throughout my studies.

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INTRODUCTION

Language is one of the most defining networks of human cognition and communication. Language has captivated the curiosity for researchers of learning the language areas in understanding the processes that underlie our ability for communication. Over the years, extensive research in the language realm, researchers have illuminated several facets of language processing, unveiling the neural mechanisms that facilitate our ability to comprehend and produce language. Friederici & Wartenburger (2010), stated "*Language is the quintessential human cognitive faculty, and understanding its neural underpinnings is crucial for unraveling the mysteries of the human mind*." Extensive research carried in the field of language processing has made notable progress in identifying the critical mechanisms behind the ability to produce and comprehend language. However, there remains a need to explore the relationship between language impairments (e.g. post-stroke aphasia) prosody (intonation, melody of speech, and rhythm), each playing a pivotal role in effective communication (Levinson, 2016).

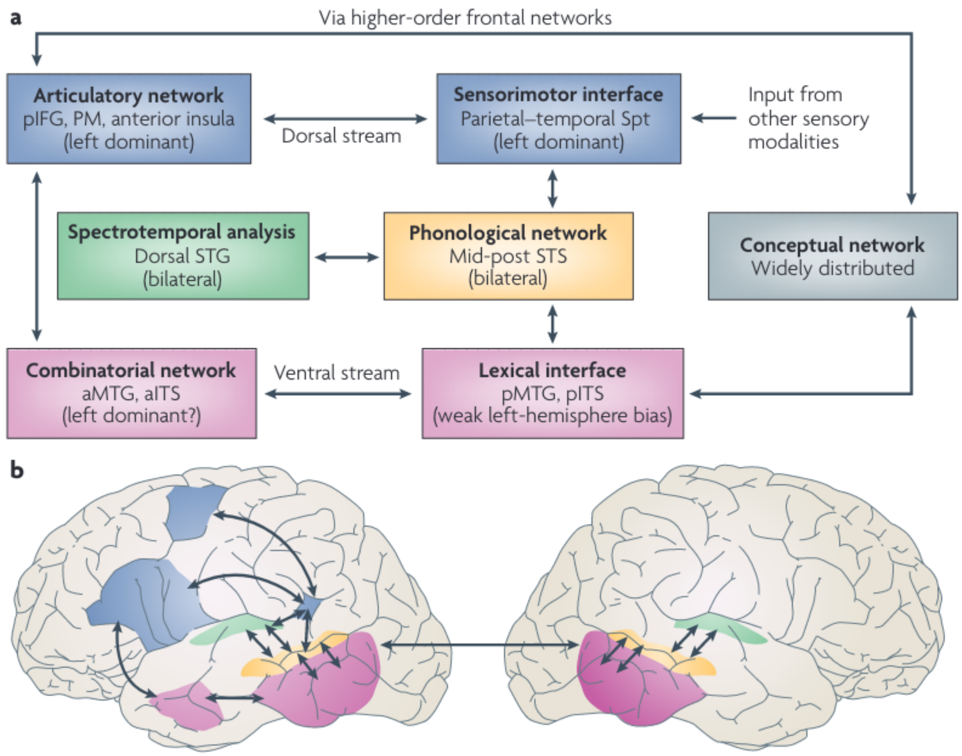
THE RELEVANCE OF PROSODY

In the language network, prosody plays a pivotal role in enhancing our linguistic abilities and interactions. Prosody refers to rhythm, melody and intonation of rhythm in spoken language and, it serves a very important role because it provides support for emotional tone, intent, and subtlety in speech (Xu, 2019). Yet, the neuroanatomy supporting linguistic prosody is poorly understood. However, there is strong growing evidence that attention and cognitive control networks may interact with traditional fronto-temporal language networks via prosody (e.g. LaCroix et al. 2020). The frontal-parietal control network is involved in many functions, including attention, working memory, and executive functions (Fedorenko & Thompson-Schill, 2014), which are functions known to support language processes, particularly in difficult or degraded situations. In addition to this, the larger language network includes important areas such as Broca's and Wernicke's regions closely related to comprehending and producing languages (Rogalsky & Hickok, 2011; Fedorenko & Thompson-Schill, 2014).

LANGUAGE AND COGNITIVE MODELS OF INTEREST

In the literature, the arguably predominant neuroanatomical model of speech is the dual-stream language network, proposed by Hickok & Poeppel (Hickok & Poeppel, 2004 & 2007), and refined by others. This network consists of two main pathways: the dorsal stream, responsible for mapping sound to articulatory gestures; and the ventral stream, involved in mapping sound to meaning. Here is a simplified diagram of the dual-stream language network given below in Figure 1:

Figure 1: Dual-stream Language Network



Alongside the dual-stream language network, there are other well-defined networks that may be relevant to language processing, that we investigate in the present study. One of these is the frontal-parietal control network, which is known to play a key role specifically in cognitive tasks such as auditory perception, attention and working memory and is often involved in regulating attention and decision-making during language tasks (Smith et al., 2013). The core regions that comprise the frontal-parietal control network include, among others, the superior frontal sulcus (SFS), the dorsolateral prefrontal cortex (DLPFC), and the inferior parietal lobule (IPL) (Corbetta & Shulman, 2002). These regions help control focus on specific stimuli or features, which is essential in processing and understanding auditory stimuli such as speech.

Fedorenko et al., (2010) suggest that this network is important in higher-level language processing since it is engaged in syntactic and semantic processing during sentence comprehension. Additionally, Baddeley (2003), found that Frontal-Parietal Control Language Network integrates to working memory processes, which is important for maintaining and processing auditory information like speech perception or spoken language. In addition, the frontal- parietal control network involves cognitive processing of language. This network is known to be involved in attention and regulatory processes when performing a language task (Fedorenko & Thompson-Schill, 2014).

Another important network is the dorsal attention network, specifically the regions include superior parietal lobule (SPL) and the frontal eyelids (FEF), which is primarily responsible for directing attention to relevant stimuli and coordinating sensory information processing (Corbetta & Shulman, 2002). The Dorsal Attention Network interacts with traditional language areas, predominantly in the left hemisphere, although emotional prosody engages distributed neural networks across both hemispheres including the dorsal attention network (Corbetta & Shulman, 2002). Altogether, the literature suggests that the frontal-parietal control network and dorsal attention network may be responsible for higher-order language-related tasks as well as low-level auditory processing.

Prosody as a Potential Link between Language and Cognitive Networks

The neuroanatomy of prosody perception and production has been studied, but most studies focus on emotional prosody in the right hemisphere, not linguistic prosody which is known to be supported by the left hemisphere (Sammler et al., 2015). It is crucial to understand the neural bases of linguistic prosody in order to understand how it interacts with other language and attention systems.

One of the main regions in the study of prosody is the right hemisphere, which is majorly involved in processing emotional and intonation of speech. Damage to the right hemisphere, particularly the right superior temporal gyrus (STG), has been shown in lesion studies (Ross et al., 1997) to be associated with deficits in the perception and interpretation of emotional prosody, resulting in difficulties recognizing emotional tone and speech rhythm. Furthermore, multiple neuroimaging studies have discovered that superior temporal sulcus (STS) in the right hemisphere is involved in processing of auditory social cues in speech, providing evidence that it is a key area in emotional prosody perception (Sammler et al., 2015).

According to (Sheppard et al., 2020), the neuroanatomy of prosody combines an interesting foundation in the areas of the brain involved for its function. The superior temporal gyrus (STG) in the right hemisphere, an area associated with auditory perception, has also been shown to be important for the processing of prosodic sound characteristics. In addition, (Belin et al., 2000), found that the superior temporal sulcus (STS) in the right hemisphere, has greater neural activity when recognizing the emotional and behavioral aspects of prosody. This investigation delves further into the research gaps in the literature focusing on the relationship between prosody, basic language measures and the functional connectivity within the language network. The left hemisphere of the brain plays a crucial role in processing prosody, the rhythmic and intonational aspects of speech that convey emotional nuances and meaning.

According to research, the left hemisphere is predominantly involved for the processing of linguistic prosody, and it has been found that patients suffering from left-hemisphere-damaged (LHD) showed sensitivity to prosodic cues, but they had unexpected responses compared to neurotypical individuals (NC) without brain pathology and the insensitivity of right-hemisphere-damaged (RHD) patients to sentence prosody (Baum & Dwivedi, 2003). However, research indicates the complexity of these theories explaining how prosodic elements are processed in a structural sentences' framework, highlighting the task-related and cue-related hypotheses (Baum & Pell, 1999).

Other investigations into prosody perception following brain damage reveal a complex picture, suggesting a role for both hemispheres in prosody comprehension (Baum & Pell, 1999). Studies indicate right hemisphere dominance in emotional prosody perception, while left hemisphere involvement is more pronounced in perceiving linguistic prosody (Baum & Pell, 1999). Additionally, findings from tonal language speakers suggest a crucial left hemisphere involvement in processing linguistic elements like lexical stress and phonemic tone (Liang & Du, 2018). Overall, while lateralization trends exist, the comprehensive understanding of prosody's neural bases suggests the involvement of both hemispheres, with their roles varying across different linguistic and emotional aspects of prosody comprehension.

The intricate relationship between comprehension impairments, prosody, and lesion to the left hemisphere indicate that prosody may facilitate speech processing when traditional language networks have been compromised, if adequate frontal and parietal attention resources are available (LaCroix, Blumenstein, et al., 2020). MRI analyses also have identified critical neural correlates within the left hemisphere that contribute to linguistic prosody, particularly the left inferior parietal lobe (LaCroix, Blumenstein, et al., 2020).

Overall, these findings underscore the multifaceted nature of prosody and its neural underpinnings, indicate that linguistic prosody may help facilitate the interactions between frontoparietal control and attention networks with traditional language areas, predominantly in the left hemisphere, while emotional prosody involves more distributed neural networks across both hemispheres.

RESEARCH GAPS AND THE PRESENT STUDY

This thesis builds upon previous research that emphasized the vital importance of prosody in supporting language in difficult or degraded situations, potentially as a way to engage a larger network outside of traditional areas of language processing, including both the frontal-parietal control and dorsal attention networks. The primary objective of the present study is *to determine how performance on basic language measures and aphasia symptoms may be related to the functional connectivity between traditional language areas and the frontal-parietal control and dorsal attention networks*, *specifically.* We seek to answer these questions by examining resting-state fMRI functional connectivity in 28 left hemisphere stroke participants who acutely received an aphasia diagnosis, and 32 matched neurotypical control participants**.** Overall, we hypothesize that the stroke participants will exhibit lower functional connectivity within frontoparietal control and dorsal attention networks, and between these networks and traditional language areas compared to the control group. Furthermore, we predict that the connectivity of these control and attention networks with traditional areas associated with aphasia will predict aphasia symptoms and severity, as measured by the Western Aphasia Battery (WAB). Our specific hypotheses include:

Hypothesis 1: Stronger connectivity between the frontal-parietal network and dorsal attention network as well as the left inferior frontal gyrus; a core component of the larger language network responsible for syntactic processing, will be associated with greater speech production and auditory comprehension abilities, as measured by the spontaneous speech and auditory verbal comprehension subtests of the Western Aphasia Battery (WAB).

Hypothesis 2: It is predicted that stroke participants with greater performance on the repetition and auditory verbal comprehension WAB subtests will show greater functional connectivity between the frontal-parietal network and dorsal attention network, as well as the left posterior superior temporal gyrus; a critical region involved in auditory speech processing and sensorimotor integration for speech.

Hypothesis 3: Stroke participants with greater frontoparietal network connectivity with the left supramarginal gyrus will have greater performance on the WAB subtests of naming, and repetition, as engagement of these networks with the supramarginal gyrus may improve attention to phonological and other information.

Hypothesis 4: Stroke participants with stronger connectivity between the frontal-parietal network and the left superior frontal gyrus will exhibit strong performance on the spontaneous speech production subtest due to increased speech fluency, implying a connection between superior frontal pitch control regions and cognitive control.

METHODOLOGY

Participants:

Stroke Group: Twenty-eight adults who experienced a left hemisphere stroke and presented acutely with speech impairments were by our collaborators at the University of South Carolina. One of the stroke patients had a large lesion that excluded the regions of interest, making it impossible to identify any regions for testing. As a solution, we reset the matrix for that patient, setting all values across columns and rows to 0. Stroke participants ranged between 35-78 years. The inclusion criteria included individuals with chronic stroke (within 6 months prior to testing), right-handedness before the stroke, native speakers of American English, aged 18 years or older, and with no prior history of neurological disease, head trauma, or psychiatric disturbances.

Neurotypical Control Group: Thirty-two neurotypical adults, aged between 29 to 79 years, who were right-handed, native speakers of American English, and without a history of neurological disease, head trauma, or psychiatric disturbances, were recruited from the greater Phoenix, Arizona area.

IMAGE ACQUISITION

Stroke Group: The stroke group's MRI data were obtained using a 3T Siemens scanner at Prisma Health Richland Hospital. A T2 structural image was obtained with the following parameters: echo time (TE) = 57 ms, image size: [176 256 256], and voxel size = 1 × 1 × 1 mm. Resting-state fMRI data were collected using EPI with the following parameters: one 11-minute run, 427 total volumes, repetition time (TR) = 1650 ms, Percent Phase FOV = 100, and 2-mm slice thickness.

Control Group: For the control group, MRI data were obtained using a 3T Phillips Ingenia MRI scanner equipped with a 32-channel radiofrequency head coil situated at the Keller Center for Imaging Innovation at the Barrow Neurological Institute in Phoenix, Arizona. A T1 image was acquired with the following parameters: field of view (FOV) = 270 × 252, repetition time (TR) = 6.74 s, echo time (TE) = 3.10 ms, flip angle = 9 degrees, and voxel size = 1 × 1 × 1 mm. Resting-state fMRI data were collected using single-shot EPI with the following parameters: one 10-minute run, 197 total volumes, TR = 3000 ms, FOV = 217 × 217, matrix = 64 × 62, slice thickness = 3.39 mm, and in-plane resolution = 3.39 × 3.39 mm.

BEHAVIORAL DATA COLLECTION

The language skills of the stroke group were assessed using the Western Aphasia Battery-Revised (WAB). In subsequent analyses, we utilized the WAB's aphasia quotient to measure overall aphasia severity, along with the scores from the following subtests: Spontaneous Speech, Auditory Verbal Comprehension, Repetition, and Naming and Word Finding. Lower scores indicate greater impairment / more severe aphasia.

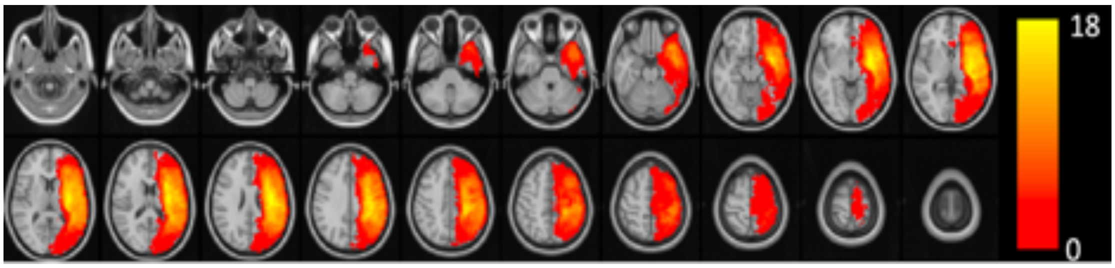
DATA ANALYSIS

MRI Data Processing:

The preprocessing of all resting-state fMRI data was conducted using Statistical Parametric Mapping 12 (SPM) (https://www.fil.ion.ucl.ac.uk/spm). To ensure the magnetization reached a steady state and subjects adapted to the environment, the first two time points of each run were discarded. Slice timing was adjusted to compensate for the interleaved acquisition in the remaining 187 volumes for the control group and 427 volumes for stroke survivors. Following that, realignment was performed to rectify head motion by utilizing the six standard head motion parameters. Subsequently, the structural image (i.e., T1-weighted image for the control group and T2-weighted image for the stroke group) was realigned to the mean functional image. Diffeomorphic anatomical registration through exponentiated Lie algebra normalization (DARTEL) (Ashburner, 2007) was employed to segment the structural image into white matter, grey matter, and cerebral spinal fluid, and to normalize it to the Montreal Neurological Institute (MNI) template. Using the standard parameters derived from DARTEL for the structural image, the functional images underwent spatial normalization to MNI space.

Additionally, nuisance covariates such as WM signal, CSF signal, and head motion parameters were regressed out from the functional signal. Subsequently, band-pass filtering between 0.01 and 0.1 Hz and spatial smoothing with an 8mm FWHM Gaussian kernel were applied to facilitate group analyses. For the processing of the stroke group's fMRI data, we implemented an additional step of cost function masking (Andersen et al., 2010; Brett et al., 2001) to mitigate the risk of distorted peri-lesion tissue affecting normalization. This mask was generated through manual delineation of the chronic stroke lesion observed on the T2-weighted images by researchers proficient in neuroanatomy and lesion mapping techniques.

Figure 2: Lesion Overlap Map of Stroke Group



NETWORK IDENTIFICATION

To investigate the functional connectivity of language networks with the frontoparietal and dorsal attention networks, we first defined the nodes of the language network via regions of interest (ROI) identified in previous task-based fMRI research conducted by Labache (Labache et al., 2019) as our lab has done in previous work (Zhu et al., 2023).

To identify and define the nodes in the Frontal Parietal Control Network (FPC) and Dorsal Attention Network (DA), as listed in Table 1, (Gao & Lin, 2012), a systematic methodological approach was adopted. Initially, a comprehensive review of existing literature was conducted to ascertain brain regions associated with attentional processes. These studies employed experimental paradigms specifically designed to engage either Dorsal Attention Network (DA) or Frontal Parietal Control Network (FPC). The MNI coordinates sourced from the work Gao and Lin (2012) were used as reference points. For instance, in their paper regions involved in executive control and attention were categorized under frontal parietal control (FPC), whereas those associated with top-down attentional control were categorized as part of the dorsal attention network (DA). Finally, each node within the networks was used as a reference for the present study. For example, nodes in the DA encompasses regions responsible for directing attentional resources, such as the frontal eye fields and intraparietal sulcus, while nodes within the FPC involved areas responsible for executive control and task monitoring, such as the dorsolateral prefrontal cortex and anterior cingulate cortex.

TABLE 1: BRAIN REGIONS AND MNI COORDINATES

Brain Regions	**MNI Coordinates/Nodes**	**Abbreviation (in Labache et.al., 2019)**	**Category**
Superior temporal sulcus - 4	-56.5 -48.4 13.4	STS4	Dorsal
Supra Marginal gyrus - 7	-55.2 -51.7 25.5	SMG7	Dorsal
Superior temporal gyrus – 4	-58.7 -23.3 3.7	T1_4	Ventral
Middle temporal gyrus - 4	-53.1 -59.4 7.0	T2_4	Ventral

Middle temporal gyrus - 3	-61.0 -35.0 -4.8	T2_3	Ventral
Superior temporal sulcus - 3	-54.7 -33.0 -1.7	STS3	Ventral
Angular gyrus - 2	-37.5 -70.4 39.5	AG2	Ventral
Inferior frontal pars triangularis gyrus - 1	-49.4 25.6 4.7	F3t	Dorsal
Inferior frontal pars opercularis gyrus - 1	- 42.2 30.5 -16.9	F3O1	Dorsal
Brain Regions	**MNI Coordinates**	**Abbreviation in Gao & Lin, 2012)**	**Category**
Anterior Cingulate Cortex	3, 31, 27	ACC	Frontal Parietal Control
Left Dorsal Lateral Prefrontal Cortex	-50, 20, 34	ldlPFC	Frontal Parietal Control
Right Dorsal Lateral Prefrontal Cortex	46, 14, 43	rdlPFC	Frontal Parietal Control
Left Frontal Eye Lids	-25, -8, 50	lFEF	Dorsal Attention

Right Frontal Eye Lids	27, -8, 50	rFEF	Dorsal Attention
Left Intra Parietal Sulcus	-27, -52, 57	lIPS	Dorsal Attention
Right Intra Parietal Sulcus	24, -56, 55	rIPS	Dorsal Attention

All the functional connectivity analyses were performed using in-house scripts executed in MATLAB. Functional connectivity was computed between the different regions of interest (ROI) using the nodes from the task-based fMRI work by Labache (Labache et al., 2019) to identify the nodes in the dorsal and ventral streams with the peak coordinates from the two tasks used by Labache (Labache et al., 2019). The nodes were defined as a 6mm radius sphere around the peak coordinates. One of the stroke patients had a large lesion that excluded the regions of interest, making it impossible to identify any regions for testing. As a solution, we reset the matrix for that patient, setting all values across columns and rows to 0. We then calculated the Pearson correlation coefficients between each pair of nodes; correlation coefficients were then Fisher transformed. To explore possible functional reorganization in the right hemisphere in response to left dorsal stream damage, we also included potential right dorsal stream nodes using the homologue coordinates of the left hemisphere's dorsal stream's nodes.

STATISTICAL ANALYSES BETWEEN GROUPS

We conducted independent-samples t-tests using Excel to compare the stroke versus control groups on the following functional connectivities measures, determined by our hypotheses. First, t-tests were computed for within the dual-stream language network, within the frontoparietal network, and within the dorsal attention network. Then, functional connectivity between the following language nodes and were computed: left inferior frontal gyrus between frontal parietal control and dorsal attention, left posterior superior temporal gyrus between frontal parietal control and dorsal attention, the left supramarginal gyrus between frontal parietal control and the left superior frontal gyrus between frontal parietal control. An FDR correction was employed to manage false positives, maintaining significance at $p<0.05$.

REGRESSION ANALYSIS OF FUNCTIONAL CONNECTIVITY TO PREDICT STROKE GROUP PERFORMANCE

The functional connectivities within the frontal-parietal control and dorsal attention networks as well as between them and the traditional language regions also were used as predictors in multiple regression models (lm command in R) to predict each stroke participant's performance on each WAB behavioral measure. The selection of the predictors included to predict each measure from the WAB, were based on previous lesion-symptom mapping and task-based fMRI research (Baldo, Arévalo, Patterson, & Dronkers, 2013; Fridriksson et al., 2018; Kertesz, 2022; Kümmerer et al., 2013; Shulman et al., 1997; Thye & Mirman, 2018). Lesion size, age, sex and education years were also included in each model as covariates. We also applied a reduction of predictor variables using Akaike Information Criterion based elimination in R (step order) to remove the predictors or covariates that contribute little to each model – a standard procedure to remove predictors that are not related to the response variable that could lead to an inflated prediction error (Hastie & Pregibon, 1992).

RESULTS

The independent sample t-tests computed between the control and stroke groups to compare the mean functional connectivity within the Dorsal Attention Network and Frontal Parietal Networks, respectively, yielded no significant differences frontal-parietal control: ($t = 1.08$, $p = 0.56$) and dorsal attention: ($t = 2.43$, $p = 0.09$).

Figure 3: Group Functional Connectivity within Frontal Parietal Control Network:

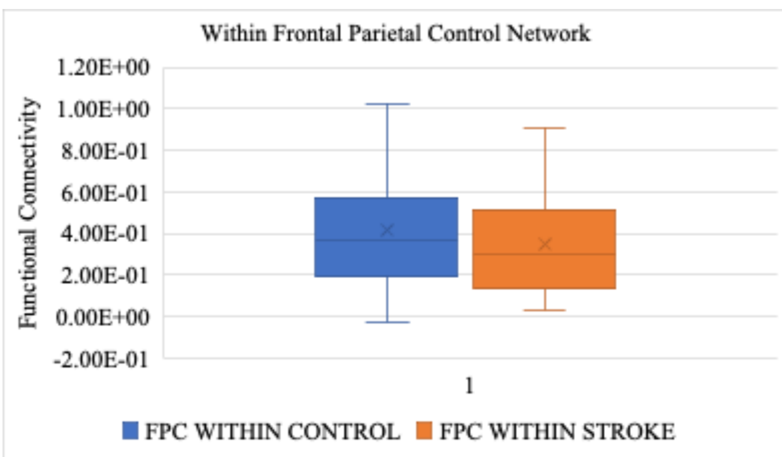
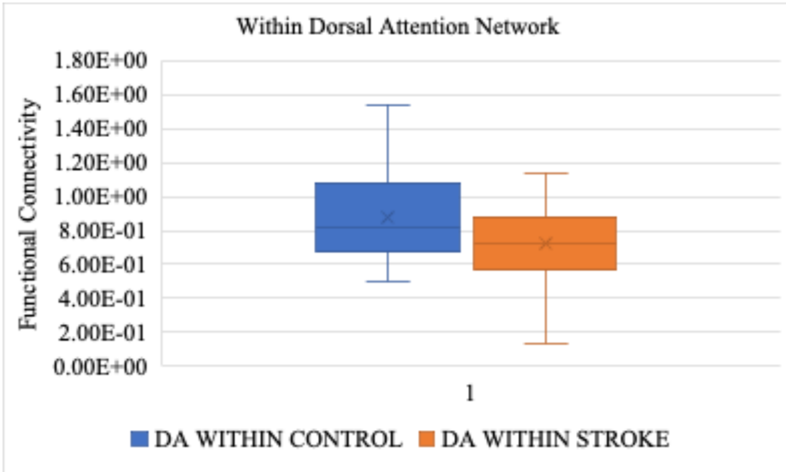


Figure 4: Group Functional Connectivity within Dorsal Attention Network:



Then, the t-tests comparing the stroke and control groups regarding the functional connectivity of the frontoparietal control network with regions within traditional language networks yielded the following results: The functional connectivity of the frontal-parietal control network with the left inferior frontal gyrus was significantly stronger in the control than in the stroke group ($t = 2.95$, $p = 0.03$), as was functional connectivity between the frontal-parietal control network and the left supramarginal gyrus ($t = 4.01$, $p = 0.001$). The frontal-parietal network - left posterior superior temporal gyrus between-group t-test also trended in the same direction but did not reach significance ($t = 2.38$, $p = 0.09$). There was no significant difference between groups regarding functional connectivity of the frontal-parietal control network and the left superior frontal gyrus ($t = 0.29$, $p = 0.77$).

Figure 5: Significant group difference for functional connectivity between Frontal Parietal Control Network and Left Inferior Frontal Gyrus:

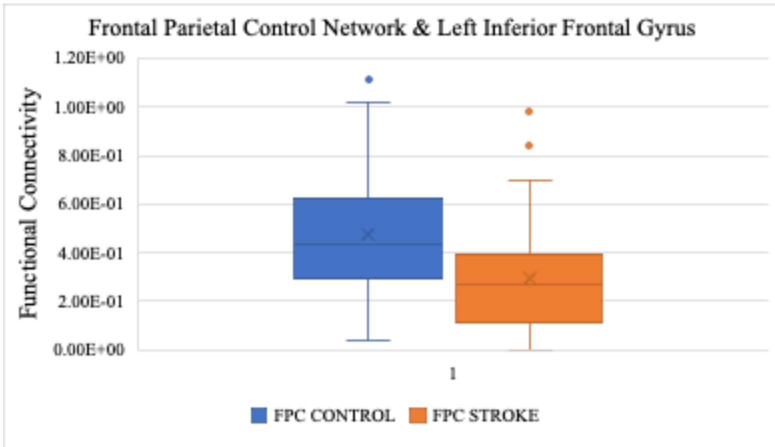


Figure 6: No significant difference between groups for Frontal Parietal Control Network - Left Posterior Superior Temporal Gyrus functional connectivity:

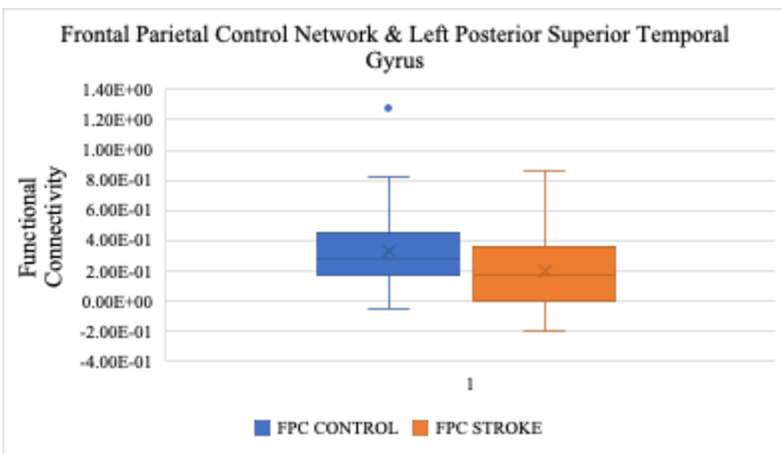


Figure 7: Significant between group difference for Frontal Parietal Control Network - Left Supramarginal Gyrus functional connectivity:

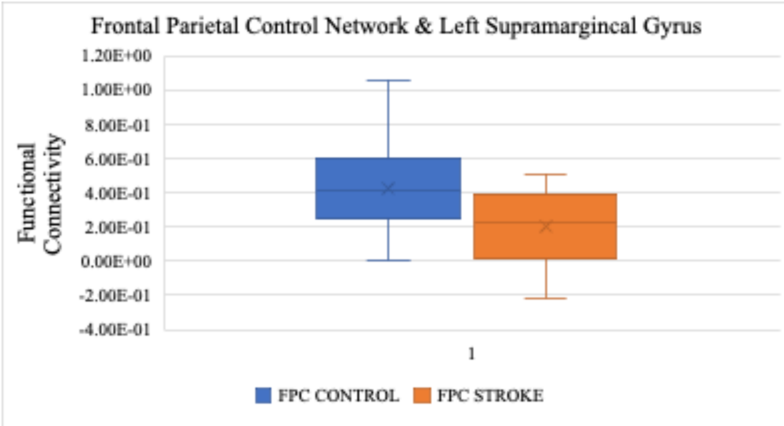
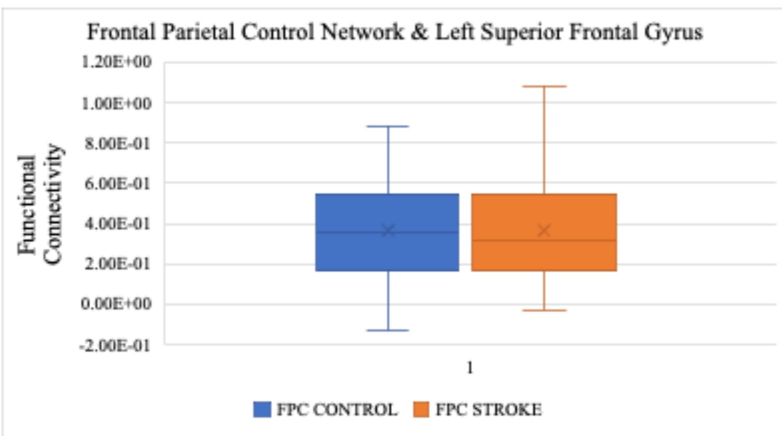


Figure 8: No significant group difference for Frontal Parietal Control Network - Left Superior Frontal Gyrus functional connectivity:



Finally, t-tests comparing the stroke and control groups regarding the functional connectivity of the dorsal attention network with regions within traditional language networks yielded the following results: There was no significant group difference for the functional connectivity of the dorsal attention network and the left inferior frontal gyrus (t = 1.73, p = 0.26). However, the control group exhibited significantly stronger functional connectivity than the stroke group between the dorsal attention network and the left posterior superior temporal gyrus (t = 4.68, p = 0.00).

Figure 9: No Significant Group Difference for Dorsal Attention Network - Left Inferior Frontal Gyrus Functional Connectivity:

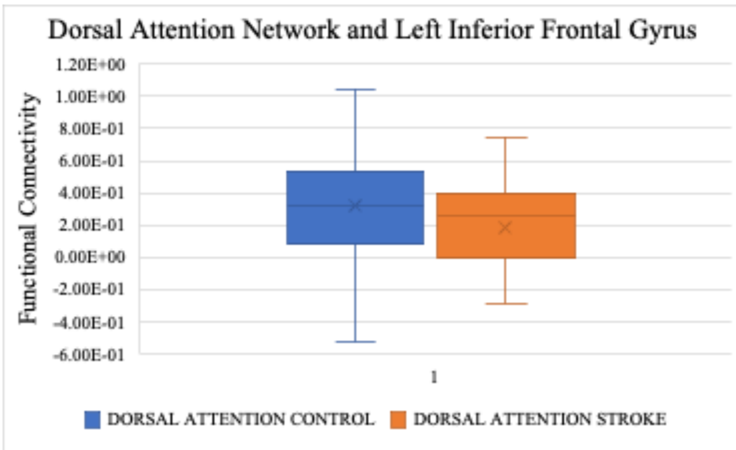


Figure 10: Significant Group Difference for Dorsal Attention Network - Left Posterior Superior Temporal Gyrus Functional Connectivity:

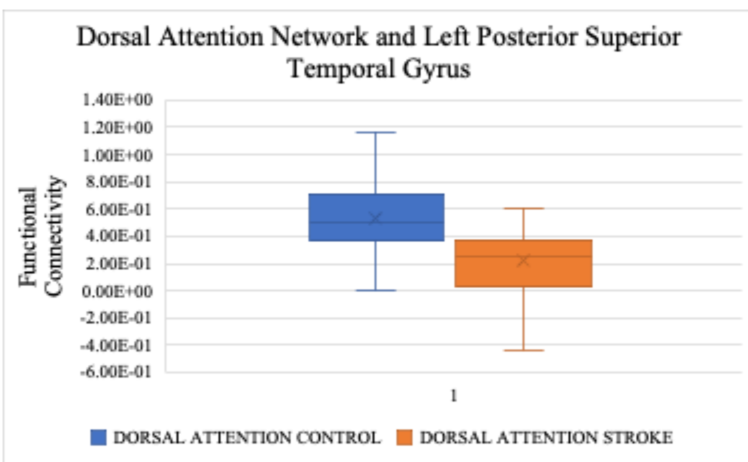


Table 2 represents all the results from the regression models predicting WAB performance in the stroke group from frontoparietal control and dorsal attention network functional connectivity, both within each network respectively, and with specific nodes of the language network. Significant results are summarized here; see **Table 2** for full results: **Spontaneous Speech's** significant positive predictor (i.e. greater functional connectivity was related to better performance) was dorsal attention - left inferior frontal gyrus ($\beta = 7.65$, $t = 2.27$, $p < 0.05$), Education ($\beta = 0.79$, $t = 3.0$, $p < 0.01$). The significant negative predictor (i.e. greater functional connectivity was related to lower performance) was the dorsal attention - left supramarginal gyrus ($\beta = -8.94$, $t = -2.33$, $p < 0.05$) and lesion size ($\beta = -0.00$, $t = -4.177$, $p < 0.001$) were also significant predictors. **Auditory Verbal Comprehension Score's** significant positive predictor (i.e. greater functional connectivity was related to better performance) was dorsal attention - left inferior frontal gyrus ($\beta = 2.98$, $t = 2.44$, $p < 0.05$) and education ($\beta = 0.24$, $t = 2.54$, $p < 0.05$). The significant negative predictor (i.e. greater functional connectivity was related to lower performance) were frontal parietal control - left inferior frontal gyrus ($\beta = -2.51$, $t = -2.11$, $p < 0.05$), dorsal attention - left supramarginal gyrus ($\beta = -5.06$, $t = -4.02$, $p < 0.001$), and lesion size ($\beta = -0.00$, $t = -4.12$, $p < 0.001$). **Naming and Word Finding's** significant positive predictor (i.e. greater functional connectivity was related to better performance) were dorsal attention - left posterior superior temporal gyrus ($\beta = 3.76$, $t = 2.16$, p

< 0.05), within the dorsal attention network ($\beta = 4.90$, $t = 3.49$, $p < 0.01$), and education ($\beta = 0.46$, $t = 3.405$, $p < 0.01$). The significant negative predictor (i.e. greater functional connectivity was related to lower performance) was dorsal attention - left supramarginal gyrus ($\beta = -6.00$, $t = -3.20$, $p < 0.01$), and lesion size ($\beta = -0.00$, $t = -3.80$, $p < 0.01$). **Repetition's** significant positive predictor (i.e. greater functional connectivity was related to better performance) was only education ($\beta = 0.37$, $t = 2.31$, $p < 0.05$) and the significant negative predictor (i.e. greater functional connectivity was related to lower performance) was only lesion size ($\beta = -0.00$, $t = -3.22$, $p < 0.01$). **Aphasia Quotient's** significant positive predictor (i.e. greater functional connectivity was related to better performance) were dorsal attention - left inferior frontal gyrus ($\beta = 33.23$, $t = 2.35$, $p < 0.05$), within the dorsal attention network within ($\beta = 27.89$, $t = 2.32$, $p < 0.05$), and education, ($\beta = 3.93$, $t = 3.46$, $p < 0.01$. The significant negative predictor (i.e. greater functional connectivity was related to lower performance) were frontal parietal control - left posterior superior temporal gyrus ($\beta = -33.41$, $t = -2.13$, $p < 0.05$), dorsal attention - left supramarginal gyrus ($\beta = -46.50$, $t = -2.88$, $p < 0.01$), and lesion size ($\beta = -0.00$, $t = -4.403$, $p < 0.001$).

Table 2: The Regression Model using the Functional Connectivity Predictors

Dependent	FPC-lpSTG	FPC-SMG	FPC-lIFG	FPC-within	FPC-lSFG	DA-lIFG	DA-within	DA-lSMG	DA-lpSTG	F-test

Variable										
SS	β= -7.180, t = -1.926, p= 0.0683	β= -9.496, t = -1.935, p = 0.0673	-	-	-	**β = 7.65, t = 2.27, p = 0.034**	β= 4.783, t = 1.675, p = 0.109	**β = -8.94, t = -2.33, p = 0.030**	-	**F (7/20) = 6.101, p<0.01**
AVC	-	-	**β = -2.513, t = -2.113, p = 0.047**	-	-	**β = 2.978, t = 2.441, p = 0.024**	β= 1.340, t = 1.329, p = 0.198	**β = -5.062, t = -4.025, p = 0.0006**	-	**F (7/20) = 7.198, p<0.01**
NWF	β = -3.373, t = -1.869, p = 0.076	β = -3.933, t = -1.602, p = 0.124	-	-	-	-	**β = 4.903, t = 3.488, p = 0.002**	**β = -6.002, t = -3.206, p = 0.004**	**β = 3.763, t = 2.157, p = 0.043**	**F (7/20) = 8.735, p<0.01**
RS	β = -4.426, t = -1.999, p = 0.059	β = -4.082. t = -1.4, p = 0.176				β = 3.975, t = 1.987, p = 0.060	β = 2.196, t = 1.295, p = 0.210	β = -3.919, t = -1.718, p = 0.101	-	**F (7/20) = 3.833, p<0.01**
AQ	**β = -33.41, t = -2.134, p = 0.045**	β= -3.629, t = -1.760, p = 0.093	-	-	-	**β = 33.23, t = 2.35, p = 0.029**	**β = 27.89, t = 2.325, p = 0.030**	**β = -46.50, t = -2.882, p = 0.009**	-	**F (7/20) = 7.778, p<0.01**

The first column in the Table above, represents the dependent variables from the Western Aphasia Battery, the following columns are the independent variables contributing to functional connectivity and the last column is the F-test of the regression model. Dependent Variables: SS = Spontaneous Speech, AVC = Auditory Verbal Comprehension, AQ = Aphasia Quotient NWF = Naming and Word Finding, RP = Repetition. Independent Variable: DA_lIFG = Dorsal Attention left Inferior Frontal Gyrus, DA_lSMG = Dorsal Attention left Supra Marginal Gyrus, FPC_lIFG = Frontal Parietal Control left Inferior Frontal Gyrus, FPC_lpSMG = Frontal Parietal Control left posterior Supra Marginal Gyrus, DA_within = Dorsal Attention within Network, DA_lpSTG = Dorsal Attention left posterior Superior Temporal Gyrus. The significant predictors are written in bold. The dash indicates the functional connectivity is not included in the regression model for the specific dependent variables.

DISCUSSION

The purpose of this study was to investigate the relationship between aphasia symptoms and functional connectivity of the frontal-parietal control and dorsal attention networks with traditional language regions. Our findings generally supported our hypotheses, revealing that aphasia participants do not have significantly reduced functional connectivity within the frontal-parietal control or dorsal attention networks, but do exhibit lower connectivity between these networks and traditional language regions, particularly between the left inferior frontal gyrus and frontal parietal control network, the left supramarginal gyrus and frontal parietal control network, and between the dorsal attention network and the left posterior superior temporal gyrus. Our regression analysis indicates that the analysis prioritized identifying predictors of aphasia symptoms. Notably, the functional connectivity of the dorsal attention network was implicated as a significant predictor for multiple aphasia measures, particularly the within dorsal network connectivity and the dorsal attention network's connectivity with the left inferior frontal gyrus (lIFG). This suggests an association between the dorsal attention network and aphasia symptoms, indicating their importance in understanding aphasia symptoms and its severity. More broadly, our findings suggest that functional connectivity analyses can provide valuable insights into the coordination and integration of cognitive control and attention networks with traditional language networks, as previously hypothesized (Fedorenko & Thompson-Schill, 2014; Corbetta & Shulman, 2002).

Our investigation of the functional connectivity of the left inferior frontal gyrus with the frontal parietal control network revealed significantly lower functional connectivity in the stroke than the control group, suggesting that frontal-parietal control resources may not be as available to individuals with aphasia, particularly in relation to functions of the inferior frontal gyrus, which include speech production and lexical selection (Fedorenko et al., 2010). Conversely, our other frontal language ROI, the left superior frontal gyrus, did not exhibit lower functional connectivity with the frontal-parietal control network in the stroke group, suggesting that the frontal-parietal control / dorsal-stream language region interactions are not all reduced in individuals with aphasia.

Our examination of a potential group difference between the left posterior superior temporal gyrus and the frontal parietal control network did not reveal a significant result. This suggests that the left posterior superior temporal gyrus, known to be critical for phonological processing and speech perception, does not have reduced support from cognitive control processes. However, we did find significantly lower functional connectivity in the stroke group compared to the control group between the left posterior superior temporal gyrus and the dorsal attention network, as well as between the left supramarginal gyrus and the frontal-parietal control network. These findings suggest that perhaps there is coordinated involvement of attention-related processes with receptive speech regions that may be contributing to speech perception impairments in individuals with aphasia (Ross et al., 1997).

The significant group differences related to regions previously implicated in prosody processing, such as the left inferior frontal gyrus and left supramarginal gyrus, with the frontal-parietal control network highlight the possibility that coordination of these cognitive control regions during language tasks may be impaired in individuals with aphasia, and that the distinct findings in the frontal-parietal control and dorsal attention networks highlights the differential roles of these networks in supporting language processing and impairments. The frontal parietal control network findings are consistent with prior research highlighting the role of the frontal parietal control network in sentence comprehension and working memory, which are nearly universally impaired in individuals with aphasia (Rogalsky & Hickok, 2011).

The regression analysis provides further evidence for the predictive value of functional connectivity within cognitive networks (and their interactions with traditional language regions) for post-stroke language performance (Zhu et al., 2023). The present study extends the analysis beyond the traditional language networks, exploring the significance of predictors in the frontal-parietal control and dorsal attention networks, and between these networks and traditional language regions. Specifically, examining the predictors for each subtest and aphasia quotient, it is evident that the previous study done by (Zhu et al., 2023) and the present study identified the left inferior frontal gyrus (lIFG) as significant predicting the symptoms of aphasia symptoms. The present study adds to this previous work by providing evidence that the connectivity outside of the dual-stream language network, notably between the dorsal stream (which the lIFG is a part of) and the dorsal attention network are significant predictors of overall aphasia severity and specific aphasia symptoms. In the ventral stream particularly the left posterior superior temporal gyrus (lpSTG), we found that functional connectivity between it and the dorsal attention network was a significant predictor of the naming / word finding subtest. This finding seemingly contradicts the lack of findings of ventral stream connectivity predicting aphasia performance in Zhu et al., (2023); but perhaps our finding suggests that connectivity not within the left ventral stream, but rather between the left ventral stream and cognitive resources is advantageous to individuals with aphasia. Overall, our regression findings suggest that understanding the connectivity of brain networks beyond traditional language regions is crucial for predicting language outcomes post-stroke. These findings underscore the importance of considering both structural (traditional approaches in aphasia to map deficits to structural damage) and functional neural correlates (e.g. the present study's functional connectivity measures) in understanding language impairments following stroke and emphasize the utility of resting-state fMRI in assessing functional connectivity in clinical populations.

The findings suggest that the dorsal attention network's connectivity, both within itself and with traditional language regions, serves as a significant predictor of aphasia severity and offers a compelling avenue for exploring the relationship between prosody and language impairments. Given the dorsal attention network's acknowledged involvement in directing attentional resources towards relevant stimuli, it is plausible that disruptions in its connectivity could affect the allocation of attention to prosodic cues during language processing. Specifically, impaired connectivity between the dorsal attention network and regions critical for prosody processing, such as left posterior superior temporal gyrus (lpSTG), may prevent individuals with aphasia from effectively integrating prosodic information into their comprehension and production of speech.

Moreover, the observed differences in functional connectivity patterns between lpSTG and the dorsal attention network between control and stroke groups suggests a potential link between prosodic impairments and aphasia. This raises intriguing questions regarding the specific roles of prosody in the context of attentional allocation and cognitive control during language tasks. Further investigations into how disruptions in dorsal attention network connectivity affect the processing of prosodic features such as intonation and rhythm, could provide valuable insights into the mechanisms underlying aphasia and inform the development of targeted interventions aimed at improving prosody-related language impairments in individual's post-stroke. The present study has the potential to increase our understanding of aphasia symptoms and contribute to the development of effective diagnostic and therapeutic strategies by shedding light on the interconnectedness between prosody, attentional mechanisms and language impairments.

LIMITATIONS AND FUTURE RESEARCH DIRECTIONS

Limitations in this study include small sample size, which may limit the generalizability of the findings, and relying solely on ROI's based analyses might overlook contributions from other brain regions involved in language processing. Future research should explore additional factors that may influence the relationship between language skills and brain connectivity, such as effects of lesion location, cognitive training and rehabilitation techniques. Additionally, examining the longitudinal effects of network changes on post-stroke language processing will provide further insights into the mechanisms underlying language recovery and the development of targeted interventions. Explicit measures of prosody should also be examined. Longitudinal studies tracking changes in prosody abilities, frontoparietal control and dorsal attention network connectivity, and language skills over time could provide valuable insights into how these cognitive networks support language recovery and impairments during stroke recovery.

CONCLUSION

Overall, the findings of this study provide compelling evidence that frontoparietal control and attention networks contribute to language abilities after a stroke, in particular via their interactions with traditional language circuitry. We propose that these networks may be contributing via prosodic processes, which require cognitive control and attention resources. More broadly, this study contributes to a deeper understanding of the neural basis of human communication and cognition. Future research should explore the longitudinal effects of control and attention network changes on post-stroke language processing and investigate potential interventions targeting functional connectivity of attention and control networks, and/or prosody, to improve language outcomes in clinical populations.

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APPENDIX

ASU IRB

ASU Knowledge Enterprise Development

APPROVAL: MODIFICATION AND CONTINUATION

Corianne Reddy
CHS: Health Solutions, College of
480/965-0576
Corianne.Rogalsky@asu.edu

Dear Corianne Reddy:

On 3/20/2024 the ASU IRB reviewed the following protocol:

Type of Review:	Modification and Continuing Review
Title:	Structural Correlates of Speech and Music
Investigator:	Corianne Reddy
IRB ID:	STUDY00000422
Category of review:	(7)(a) Behavioral research (7)(b) Social science methods
Funding:	Name: HHS: National Institutes of Health (NIH), Grant Office ID: pending, Funding Source ID: subcontract of NIH DC009659; Name: HHS: National Institutes of Health (NIH), Funding Source ID: subcontract of NIH DC R01 DC009659; Name: American Heart Association, Grant Office ID: 13840; Name: HHS: National Institutes of Health (NIH), Funding Source ID: subcontract of NIH DC03861; Name: Arizona Board of Regents, Grant Office ID: Start-up funds awarded to Dr. Rogalsky; Name: Grammy Foundation, Grant Office ID: Pending
Grant Title:	None
Grant ID:	None
Documents Reviewed:	None

The IRB approved the protocol from 3/20/2024 to 6/19/2024 inclusive. Three weeks before 6/19/2024 you are to submit a completed Continuing Review application and required attachments to request continuing approval or closure.

If continuing review approval is not granted before the expiration date of 6/19/2024 approval of this protocol expires on that date. When consent is appropriate, you must use final, watermarked versions available under the “Documents” tab in ERA-IRB.

In conducting this protocol you are required to follow the requirements listed in the INVESTIGATOR MANUAL (HRP-103).

Sincerely,

IRB Administrator

cc:

Ayoub Daliri
Lamees Al-Hassan
Surbhi Haridas Mendhe
Isabelle Ugarte
Visar Berisha
Saraching Chao
Madilyn Majors
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