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Cognitive control and language network connectivity associated with language production in aphasia

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Cognitive control and language network connectivity associated with language production in aphasia

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Tables

Table 1

Inter-rater Reliability Measures

Reliability	
Measure	Reliability
	Point-to-Point
CIU	86.87%
	ICC
CIU	0.995
Duration	0.997
Total Utterances	0.889
MLU Utterances	0.896
MLU Words	0.857
MLU Morhemes	0.869
FREQ Types	0.996
FREQ Tokens	0.978
Words per Minute	0.975
Verbs per Utterance	0.799
Density	0.593
Noun_Verb	0.866
Open_Closed	0.425
Open_Class	0.954
Closed_Class	0.981
Retracing	0.795
Repetition	0.92
Semantic Paraphasias	0.233
Phonological Paraphasias	0.623
Mixed Paraphasia	.
Omission	0.882
Abandoned Utterance	0.798
Circulocution	.

Table 2

Patient Demographics

PAR	Age	Gender	Educatio	MPO	LV (cm3)	Aphasia Type	AQ	WAB Content	WAB Fluency	AOS	AOS Severity
DIS001	70	M	13	52	80.7	AN	86	10	9	0	1
DIS003	72	M	11	156	34.34	AN	81.3	9	5	1	3
DIS006	54	M	16	36	59.25	AN	75.1	7	8	1	5
DIS007	71	M	13	17	32.46	CO	73.7	9	6	0	2
DIS008	58	M	15	10	27.14	WE	68.3	8	6	0	1
DIS009	71	M	11	16	1.46	AN	91.6	9	8	0	1
DIS010	57	M	13	58	70.4	AN	86.4	9	6	0	1
DIS011	77	M	15	81	140.34	CO	60.5	5	5	1	6
DIS012	70	M	19	27	55.26	AN	80.8	9	5	1	3
DIS014	48	M	15	13	62.37	BR	41.6	3	2	1	5
DIS015	67	M	11	84	171.11	CO	75.3	8	5	1	3
DIS017	76	M	15	120	158.57	BR	39.6	3	2	1	6
DIS018	67	M	16	21	20.96	NL	97.3	10	10	0	2
DIS023	50	M	17	14	46.43	AN	72.5	5	7	0	1
DIS024	59	M	11	69	132.88	AN	80.7	8	6	0	1
DIS025	55	F	19	92	16.44	NL	98.7	10	10	0	1
DIS026	71	M	13	11	212	TS	66.6	3	6	0	1
DIS027	73	M	17	26	297.2	BR	50	5	4	0	1
DIS031	64	M	19	23	56.22	BR	62.8	7	2	1	3
DIS047	45	F	17	37	161.54	BR	36.9	3	4	0	1
DIS052	74	F	21	5	1.29	NL	96	10	9	0	1

Table 3

Language Measure Results from Picture Description Task

PAR	**CIU**	**Retracing**	**Repetition**	**Filled Pauses**	**Unfilled Pauses**	**Semantic Paraphasia**	**Omission**	**Abandoned Utterance**	**Circumlocution**
DIS001	92	9	15	11	1	3	0	0	0
DIS003	89	4	5	17	5	0	0	1	0
DIS006	81	10	0	25	12	4	0	1	0
DIS007	80	17	13	27	12	3	0	4	0
DIS008	23	10	4	10	8	2	0	1	0
DIS009	78	0	0	5	1	0	0	1	0
DIS010	52	2	2	1	4	1	0	0	0
DIS011	13	1	0	13	6	0	0	0	0
DIS012	31	12	3	15	7	3	0	2	0
DIS014	8	1	0	4	29	0	0	1	0
DIS015	21	3	0	5	16	3	0	0	0
DIS017	0	0	4	0	13	0	0	0	0
DIS018	31	2	0	11	1	0	0	0	0
DIS023	45	6	1	9	13	3	0	2	0
DIS024	55	0	1	6	6	2	0	0	0
DIS025	118	8	1	7	12	4	0	0	0
DIS026	58	1	3	11	34	1	0	3	0
DIS027	27	10	6	3	36	1	0	2	0
DIS031	18	3	4	21	33	0	0	0	0
DIS047	4	2	4	3	5	8	0	0	0
DIS052	91	9	1	19	14	3	0	0	0

Table 4

Significant NBS and FDR Correlations for Network Edges and Language Measures

Network	**Measure**	**NBS**
FPN	CIU	**Significant**
FPN	Semantic Paraphasia	ns
FPN	Abandoned Utterance	ns
FPN	Density	ns
FPN	Unfilled Pauses	ns
FPN	% Noun	ns
FPN	% Preposition	ns
FPN	%Present Participle	ns
FPN	Repetitions	ns
FPN	Retrace	**Significant**
FPN	TTR	ns
LN	CIU	ns
LN	Semantic Paraphasia	ns
LN	Abandoned Utterance	ns
LN	Density	ns
LN	Unfilled Pauses	ns
LN	% Noun	ns
LN	% Preposition	ns
LN	%Present Participle	ns
LN	Repetitions	ns
LN	Retrace	ns
LN	TTR	ns

Table 5

Summary of Significant Language Measure Correlations

	Predictor	**NBS**	
		CIU	**Retrace**
Network			
FPN	Frontal_Inf_Tri_L1 to Frontal_Sup_Orb_R2	3.02	
FPN	Frontal_Inf_Tri_L1 to Precentral_L2	3.39	
FPN	Temporal_Inf_R1 to Precentral_L2	3.58	3.06
FPN	Frontal_Inf_Tri_L1 to Frontal_Mid_L2	3.19	
FPN	Precentral_R1 to Frontal_Mid_L2	3.15	
FPN	Frontal_Inf_Tri_L1 to Frontal_Mid_R1	3.26	
FPN	Frontal_Inf_Tri_L1 to Frontal_Mid_R2	3.1	
FPN	Precentral_L2 to Angular_R1	4.05	
FPN	Precentral_L2 to Parietal_Inf_L3	3.1	
FPN	Precentral_L1 to Frontal_Mid_Orb_R2	3.96	
FPN	Frontal_Inf_Tri_L1 to Frontal_Mid_Orb_R2	3.98	
FPN	Frontal_Mid_L1 to Frontal_Sup_Medial_L2	3.31	
FPN	Frontal_Mid_R2 to Frontal_Sup_Medial_L2	3.47	
FPN	Parietal_Inf_L1 to Temporal_Inf_R1		
FPN	Precentral_L2 to Angular_R2		
FPN	Parietal_Inf_L1 to Frontal_Sup_Medial_L2		
FPN	Parietal_Inf_L1 to Frontal_Sup_Orb_R2		3.53
FPN	Parietal_Inf_L1 to Frontal_Mid_R1		3.25
FPN	Frontal_Inf_Tri_L1 to Parietal_Inf_R1		3.04

FPN	Frontal_Sup_Orb_R2 to Parietal_Inf_R1		3.32
FPN	Frontal_Inf_Tri_L1 to Parietal_Inf_L2		3.03
FPN	Parietal_Inf_L1 to Angular_R1		3.05
FPN	Frontal_Sup_Orb_R2 to Parietal_Inf_L3		3.09
FPN	Angular_R1 to Parietal_Inf_L3		3.01
FPN	Parietal_Inf_L3 to Frontal_Inf_Tri_L2		3.19

Figures

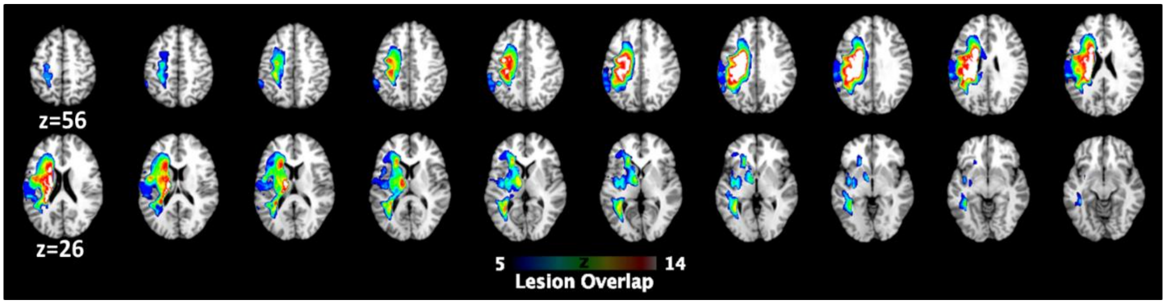

Figure 1. Lesion overlap lap; blue indicates few patients had lesions in that area; red/white indicates many patients had lesions in that area. The main brain structures with lesions in multiple patients include the caudate nucleus (body and tail), premotor cortex, and extending into the

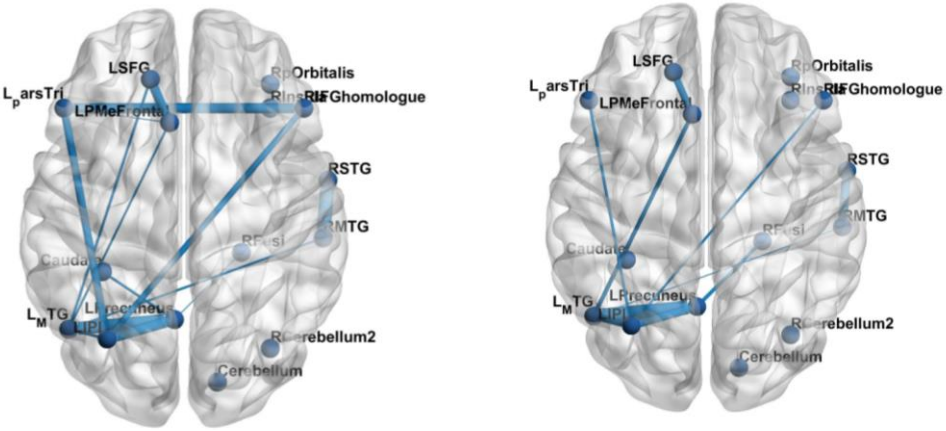

Figure 2: LN Edges in HC (left) and PWA (right) at 1000 permutations, T=9, p<.001

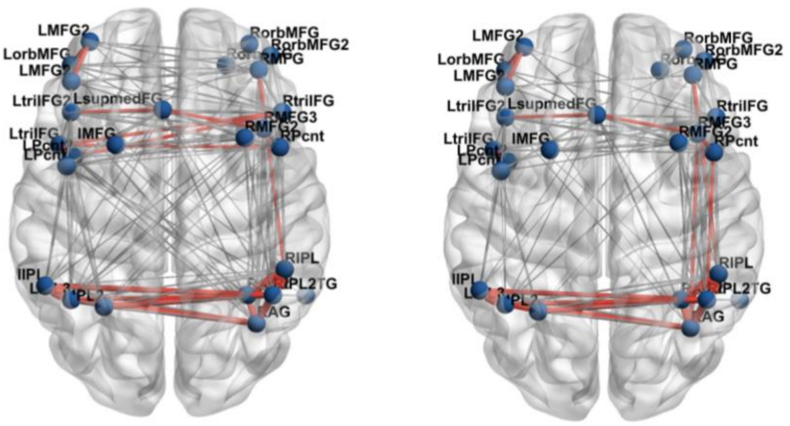

Figure 3: FPN edges for HC (left) and PWA (right). NBS at 1000 permutations, T=9, p<.001. Threshold for edges shown in red is T=15.

FPN HC > PWA Significant Edges	**t value**
Frontal_Inf_Tri_L1 to Precentral_R1	3.17
Precentral_R1 to Precentral_L2	3.57
Frontal_Mid_R1 to Frontal_Inf_Tri_L2	3.17
LN HC > PWA Significant Edges	**t value**
L_parsTri to RIFGhomologue	3.51

Figure 4. Summary of significant between group differences. FDR at 1000 permutations, $p = .050$

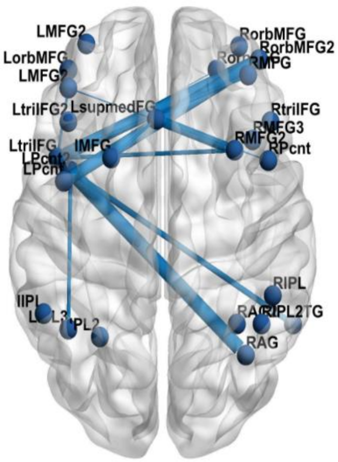

Figure 5. *FPN CIU Correlations. NBS at 1000 permutations, t(20)>3, p= .014 , Cohen's d=.951*

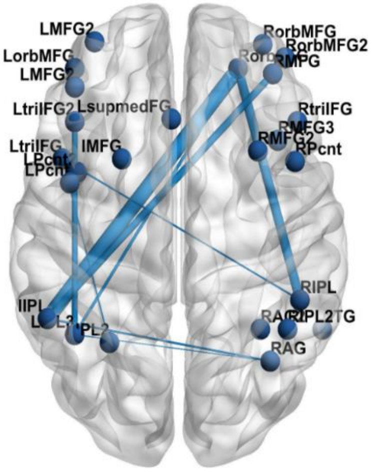

Figure 6 FPN Retracing correlation. NBS permutations=1000, t(20)>3, p<.19, Cohen's d=.998

Abstract

Aphasia is the breakdown of language comprehension and production due to an acquired brain injury of the left hemisphere. Investigation of the neurological underpinnings of aphasia have advanced from post-mortem investigation of specific regions in the 1800s to the utilization of brain imaging technology to understand brain networks. These approaches have helped us to appreciate the reorganization of the brain and its networks post stroke, particularly as it relates or is modified for adequate versus impaired performance. Research into neuroplastic changes can elucidate differences between healthy and lesioned brains. Furthermore, identification of adaptive (or maladaptive) neuroplastic changes can also inform diagnostics or aid in monitoring the neuroplastic effects of evidence-based treatment. This study utilized resting state functional MRI to characterize graph theory metrics of language (LN) and cognitive control networks (frontoparietal, FPN) in 21 persons with aphasia (PWA) and 18 healthy controls (HC). This study further investigated the relationship between strength of connectivity and semantic access and errors in PWA during a picture description task. When comparing resting state network connectivity of the LN in PWA vs. HC, many edges (10/14) and node degree hubs (3/3) were common to both groups for the LN, suggesting that an inherent network that remains relatively intact even post-stroke. Analyses yielded similar results for resting state FPN network connectivity with common edges and node degree hubs. When investigating correlations between network edges and language measures, correlations between FPN edges and CIU's and retracing suggested the importance of right hemisphere and 'healthy' edge integrity.

Keywords: Aphasia, Graph Theory, Language, Picture Description, resting-state fMRI

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Aphasia is a breakdown of language comprehension and production due to an acquired brain injury, typically a left hemisphere stroke. Understanding aphasia is complex given the multifactorial nature of language and the dynamic brain networks likely underlying it. This study aims to utilize graph theory approach to investigate the neurobiological underpinnings of aphasia in multiple brain networks. Though the investigation of aphasia is not a new venture, the use of graph theory to do so is a fairly recent undertaking of researchers.

To approach understanding the complexity of the neurobiological underpinnings of aphasia, early 19th century research noted that language impairment is linked to the brain lesion observed post-mortem. In this way, Paul Broca and Carl Wernicke each found left hemisphere regions responsible for language production and comprehension, the anterior inferior frontal gyrus and posterior temporal area respectively (Tremblay & Dick, 2016). Lichtheim extended the approach to include study of connections between regions, and for example found that damage to the arcuate fasciculus connecting Broca's and Wernicke's areas also results in language impairment. Study of the connections between regions has truly advanced our understanding of the neurobiology of language by elucidating that there are many connections between regions and that damage to any of these can result in language deficits (Tremblay & Dick, 2016).

Current models of language provide a framework in which multiple regions are involved in isolated language processes to perform language processing. For example, the dual stream model proposed by Hickock and Poeppel (2004), based initially on a ventral/dorsal stream model that exists for visual attention, proposes a ventral ("what") or dorsal ("where") stream for processing incoming auditory stimuli. In this model, language processes are simplified, in that brain region-to-task specific processes are outlined. The dorsal stream begins with auditory input to the phonological network (bilateral mid-posterior STS). The model proposes that this information is then processed in the sylvian parietotemporal area (spt, sensorimotor interface; Hickock and Poeppel, 2004), where it is translated from sensory codes to the motor system, and follows a dorsal connection to an articulatory network in the posterior inferior frontal gyrus (IFG), premotor cortex (PM) and the anterior insula. The dorsal pathway is responsible for mapping sensory/phonological representations to articulatory representations. This pathway is critical for performance of a task such as repetition.

The ventral stream is the “what” pathway, mapping auditory input to meaning, and is also the focus of this study, in particular the brain regions involved for semantics. This pathway begins at the decoding level at the spt, traveling in a ventral direction to the phonological network (superior temporal sulcus [STS] and the superior temporal gyrus (STG)). Once the auditory signal is processed for its spectral and temporal components and a phonological frame is formed in the STG, it is thought to then be linked to semantic information by further processing involving the posterior middle temporal gyrus (pMTG), posterior inferior temporal sulcus (pITS), and the combinatorial network (anterior [aMTG], anterior [aITS]). This pathway is essential for performing any task requiring lexical retrieval. While both streams are involved in different aspects of language production, they are also heavily integrated and work in conjunction for language comprehension and production. The value of this model is that it specifies some roles that brain regions have in different aspects of language, and adds to the argument that different aspects of language involve different regions. However, it still may not adequately account for natural or connected language processing as a whole.

Advances in neuroimaging technology have allowed for the investigation of the neurobiology of language *in vivo* (in contrast to the anatomical studies of Broca/Wernicke/Lichtheim), in both healthy and acquired brain injury populations. There are a multitude of approaches used to study brain-behavior relationships. While some researchers investigate behavioral outcomes secondary to brain lesions or damage to structural connections, others seek this answer in healthy participants by investigating functional connectivity. Such approaches include static measures of brain physiology that characterize gray and white matter structure (magnetic resonance imaging, MRI) or the integrity of white matter connections between regions (e.g., using diffusion tensor imaging, DTI). These imaging approaches investigate brain structure and can be correlated with language measures acquired outside of the scanner to establish brain structure-to-language behavior associations. In addition, dynamic brain function acquired during task performance using functional MRI (fMRI) can be used to identify regions or networks activated during those specific tasks. Task-based fMRI allows for observation of brain activity during task performance, while the participant is actively ‘doing’ language. In this way, the brain regions, or networks of brain regions, are identified as they interact to accomplish a task. Resting state fMRI is also helpful in providing information about brain region/network connectivity, as regions and networks are known to interact even at rest (Smith et al. 2009). For example, the nodes of a central executive network are correlated at rest and together correspond to cognitive paradigms requiring executive functions (e.g., Smith et al., 2009). Therefore, tasks are not always required to appreciate network connectivity. The benefit of utilizing resting state fMRI data in people with aphasia is that it does not rely on the participant’s ability to comprehend or execute a task based in language (Balaev et al., 2016).

Therefore, resting state data allows for comparison of network connectivity in healthy controls versus people with aphasia that is not biased by task performance.

The variety of imaging techniques has led to findings regarding language and its neurological underpinnings, such as the specificity of brain regions for semantics, identification of networks activated during semantic tasks, and the connectivity of semantically-involved regions coherently oscillating at rest. However, it is important to note that no single imaging measure is the best predictor of language measures. In fact, Pustina and colleagues found that a stacked multimodal prediction (STAMP) from three sources (structural connectivity, lesion maps, and functional connectivity) best predicted performance on sentence comprehension, sentence repetition, picture naming, and aphasia severity scores (Pustina et al., 2017). These measures included graph theory metrics: *node degree* – the number of connections or edges to which a node is connected, *betweenness* – a measure of centrality, *local efficiency* – the inverse of path length, and *local transitivity* – a measure of segregation for each modality. In addition to graph theory metrics, other predictions for severity of aphasia included values of raw pairwise connectivity and lesion size. For a semantically involved task (picture naming), the strongest predictors of performance were local efficiency in DTI, local transitivity in DTI, and the betweenness and pairwise connectivity in resting state fMRI.

Structural Imaging Findings Relating to Semantics/Language

Structural imaging data has provided information regarding the specificity of some brain regions relative to certain language functions. For example, Halai and colleagues (2017) correlated brain lesion volumes with participant performance on language factors identified through principal component analysis (PCA). The semantic component (the factor including type:token ratio [TTR] for the ‘Cookie Theft’ description, word to picture matching, Boston

Naming Test performance, Cambridge 64-item naming, and a 96-synonym judgement) was correlated to damage of the left anterior middle temporal gyrus, anterior temporal fusiform cortex, and posterior inferior temporal gyrus (Halai et al., 2017). These data suggest that access to semantic information for tasks requiring both production and comprehension of content is reliant on a spatially diffuse area of the left temporal cortex.

Similarly, Fridriksson and colleagues (2017) demonstrated degraded connections between grey matter regions within the left hemisphere dorsal/ventral streams in individuals with aphasia and found that semantic errors on the Philadelphia Naming Test correlated with extent of damage to the left middle temporal gyrus (MTG), as well as to the left middle occipital gyrus, left globus pallidus, and left angular gyrus. Semantic errors also negatively correlated with white matter integrity connecting the left superior occipital gyrus (SOG) and left thalamus, left MTG and left SOG, and left STG and left SOG. These findings demonstrate that damage to specific brain regions, particularly left temporal areas, or regions involved in a network with them (i.e., the ventral stream), correlate with poorer performance on semantically-involved tasks such as naming, synonym judgement, word to picture matching, and ratios such as TTR. These findings help to confirm that the left temporal lobe is involved in semantics.

While the above studies have investigated the relationship between left temporal regional damage and language performance, further structural investigation has found correlations between right hemisphere integrity and stronger language performance as well. For example, Hope et al. (2016) found positive correlations between structural change in the brain and improvement in a spoken object naming task. These positive correlations were found in the right middle temporal gyrus, suggesting that the right hemisphere may play a role in adaptation or recovery in people with aphasia (PWA). Additionally, Balaev et al.(2016) found a negative correlation between gray matter volumes in the right supramarginal gyrus (SMG) and aphasia severity. This finding suggests a potential importance of the right hemisphere in adaptive neuroplasticity in PWA, as increased volumes in the right hemisphere correlated with less severe aphasia. These structural studies have identified regions likely involved with semantics, specifically, diffuse left temporal regions, and some right hemisphere regions potentially resultant from adaptive neuroplasticity. However, language and its subcomponents are not likely represented in focal areas, but rather in several connected regions representing networks.

Task-based fMRI Studies Relating to Semantics/Language:

fMRI studies have found networks involved in semantic language tasks/processing. For example, Humphreys et al. (2014) identified a semantic network by investigating task-related activations in semantic tasks (synonym judgement, semantic association, and category judgement across visual and auditory modalities) versus non-semantic tasks (number judgement, stimulus matching, and auditory decision). They found certain regions that were specifically active for processing semantic information that included the left fronto-temporo-parietal region (left fusiform gyrus, left middle temporal gyrus, left temporal pole, bilateral IFG, right middle orbital gyrus, and left precentral gyrus, left putamen, and bilateral superior parietal cortex).

Resting State fMRI and Language:

Resting state fMRI studies have investigated differences in functional connectivity in healthy controls versus people with aphasia. For example, Balaev et al. (2016) found group differences between PWA and HC in terms of resting state functional network connectivity (rsFNC) between the auditory network and the posterior Default Mode Network (DMN), and between the posterior DMN and right frontoparietal network. Both network associations were poorly correlated in people with aphasia (PWA) compared with healthy controls. Furthermore, investigation of functional connectivity between right hemisphere regions involved with these networks found right superior frontal gyrus (SFG) connectivity in the posterior DMN in PWA only. These functional connectivity differences between groups were hypothesized to result from both left hemisphere lesions (decrease in auditory network-posterior DMN functional connectivity), as well as compensatory plasticity (increase in right hemisphere region connectivity).

Additionally, resting state fMRI studies have found that functional connectivity amongst regions of the language network correlate with language performance in PWA. For example, Ramage et al. (2020) found correlations between left IFG-left middle frontal gyrus, and right posterior MTG and right IFG correlated with higher Word Finding and WAB-R Naming scores. These findings are in line with other studies discussed regarding the role of the MTG and IFG in semantics (Fridriksson et al., 2017; Halai et al., 2017; Hickock & Poeppel, 2004; Humphreys et al., 2014). Not only are they identified in structural imaging as being important, but their resting state connectivity with other regions also correlates with semantic performance in PWA. The involvement of the right hemisphere regions in PWA for both language-identified ROIs and in the posterior DMN again suggest the potential for a compensatory role of the right hemisphere post-stroke.

Cognitive Control

Baleav et. al’s (2016) findings introduce investigation into networks other than the language network for the study of the neurobiology of language in PWA. That is, in addition to a language network, there is also a potential role for cognitive control networks in language processing, particularly when the language task requires more cognitive effort. Several studies have investigated the relationship between executive function and language networks, particularly for complex language tasks. For example, a multiple domain (MD) network (bilateral frontal, parietal, opercular and cingulate cortex) that is known to support cognitive tasks and is related to cognitive control, working memory, and goal directed behavior becomes engaged when individuals are comprehending sentences (e.g., Diachek et al., 2020). These authors found that the language network alone was active for passive auditory comprehension of sentences, but that the MD becomes engaged when additional cognitive effort is needed for sentence comprehension tasks (picture-sentence matching, sentence rating, or answering comprehension questions). Similarly, Humphreys et al. (2015) found that activity of a semantic network and the DMN during task performance overlapped considerably, but also varied depending on stimulus type, task difficulty, modality, and the semantic nature of the tasks. For example, bilateral angular gyrus (common to both networks) was deactivated for all tasks, but more strongly deactivated for non-semantic tasks. Therefore, while cognitive control networks are engaged for language tasks, they are not part of the core language network. Rather, cognitive control networks are recruited for more complex tasks. Thus, overlap between these two networks exist, but is modulated depending on the nature of the linguistic task.

These collective findings suggest that there is an inseparable role of cognitive control systems to support cognitively effortful or complex language tasks in HC and PWA. Connected language or natural discourse requires more cognitive control network involvement, given their multiple demands. This is supported by Aylahya et al. (2020), as story retelling correlates with a slower speech rate (inferred as an index of increased processing demands) and increased lexical diversity compared to other narrative tasks that are considered less demanding. Investigation of the relationship between cognitive control and language networks will lead to a deeper understanding of the brain's role in language production and comprehension, as well as of how these networks interact or change post-stroke.

Graph Theory

One method for investigating neural connectivity in both language and cognitive control networks is graph theory. Graph theory is an approach to investigating complex neural network properties. Though graph theory dates back to the 18th century, its application to neural networks is fairly new. Network analysis describes properties of complex systems such as neural networks (Rubinov & Sporns, 2009). A network is defined as a mathematical representation of a complex system in the real world and consists of nodes (brain regions in imaging application) and edges (connections between two nodes). For functional imaging, connectivity pertains to the magnitude of temporal correlations between nodes. Some of the properties that graph theory can output include node degree, as described above per Pustina et al. (2017).

Network-based statistics (NBS) is a statistic used to characterize and contrast networks (Zalesky 2010). NBS is a method that is used with mass univariate testing, controlling for family-wise error (FWE) in order to identify functional connections. In functional connectivity imaging, the strength of the connections between nodes is measured as a value of temporal correlation. NBS can identify group differences in a single edge (e.g., weaker connection in one group) or a disconnected subnetwork (e.g., a set of all the disconnections).

Networks can also be characterized by the density and length of edges. Node degree is the number of connections or edges to which a node is connected. A node with a high degree indicates that it is a hub of connectivity and more integrated with the other nodes of the network, whereas a node with low degree is more segregated.

These measures provide more information about how networks within the brain interact with each other, and where certain ‘hubs’ or nodes with many edges are. These graph theory measures are used in this study to investigate differences in connectivity between PWA and HC, node degree measures for PWA and HC, and correlation of these two to language measures.

The present study will utilize graph theory metrics (network-based statistics, node degree) to characterize rsfMRI data of the language network (LN) and the fronto-parietal network (FPN) in persons with aphasia (PWA) relative to healthy controls (HC). As well, correlations between these graph theory metrics, or combination of metrics, and semantic content in connected language production will help to identify which are potential predictors of language in PWA. The long-range goal, if specific metrics are found to predict semantic performance/content, is to determine the role of brain imaging in diagnostics, or the potential for brain imaging to be used to track progress in semantic interventions for PWA.

Aims and Hypotheses:

1. Characterize graph theory metrics of language networks in PWA to controls.
    a. PWA will have more dysconnections (pairs of nodes showing weaker association in the group) in the LN compared to healthy controls.
        i. Hypothesis a_0- PWA and HC will not differ for number of dysconnections.
    b. Node degree will indicate differing hub structure in the LN by group, with right hemisphere nodes having higher summed node degree than left in the PWA group. The opposite will be true in the HC.
        i. Hypothesis b_0 – no group or laterality differences in node degree for the LN.

2. LN/FPN functional connectivity strength will correlate with measures of semantic content produced in connected language of PWA.
    a. Stronger LN connectivity particularly in the middle temporal gyri (MTG), superior temporal gyri (STG) and angular gyri, will correlate with better semantic access.
        i. Hypothesis 2_0- there is no correlation between LN connectivity strength and semantic access during connected language.
    b. More connectivity strength in FPN will correlate with better semantic access during connected language.
        i. Hypothesis 2_0- no correlation
    c. Higher node degree in LN nodes; specifically the middle temporal gyri (MTG), superior temporal gyri (STG) and angular gyri, will associate with the importance of these nodes in connectivity for semantic access during language production.
        i. Hypothesis 2_0- no correlation

Methods

Participants:

21 right-handed individuals with chronic left-hemisphere stroke and aphasia (PWA) were included in speech-language assessments, providing audio-recorded language samples and resting-state functional MRI. 18 healthy, age-matched controls also underwent functional MRI. Inclusion criteria were: 18-75 years of age, right-handedness, native English speaker, and no contraindications for undergoing an MRI. Furthermore, to be eligible, participants had no history of uncorrected hearing, vision or other sensory impairments; cognitive impairments (assessed with the Mini Mental State Exam in HC and Raven's Colored Progressive Matrices in PWA); premorbid speech, language or reading impairments; or substance abuse. All subjects gave written consent to participate in the study per the Sydney Local Health District Human Research Ethics Committee.

Speech and language measures:

PWA underwent speech and language testing to diagnose and determine severity of dysarthria, apraxia, and severity and type of aphasia. The battery included: Western Aphasia Battery-Revised, the Motor Speech Examination, Raven's Progressive Colored Matrices, Apraxia Battery for Adults-increasing word length, Psycholinguistic Assessments of Language Processing in Aphasia (PALPA)-auditory word discrimination, and connected speech samples for a Story Retell Procedure (c.f., Ballard et al., 2016; New et al., 2015 for full test battery description). For the present study, the picture description subtest of the WAB, in which patients were instructed to describe the 'Picnic Scene' in their own words, was analyzed using CHAT/CLAN (Macwhinney, 2010). In addition to the morpho-syntax analysis of CHAT/CLAN (e.g., type token ratio; and words per minute), coding for the following variables was included (Casilio et al. 2019; Mack et al. 2015;Tochadse et al., 2018):

1. Semantic paraphasia: a real word that is semantically related but not phonologically related to the target word
2. Filled pause: when words are used as fillers (i.e. um, uh, hm) preceding a target word
3. Unfilled pause: a period of silence lasting for longer than .9 seconds
4. Circumlocutions: a description of a target word without an attempt to produce the name
5. Abandoned utterance: Utterances that are left incomplete. The speaker may stop talking, attempt to gesture, move on with another utterance/idea, or conclude the utterance vaguely (e.g. shrug, "you know") (Casilio et al. 2019)
6. Omissions: words not used in a place that they should be (Casilio et al. 2019)

Additionally, as in Nicholas & Brookshire (1993), transcriptions were also coded for correct information units (CIU's) which are defined as a measure evaluating the communicative informativeness of PWA in connected language.

CLAN Transcription

Audio language samples were transcribed by two graduate students using CHAT conventions in CLAN. The two graduate students transcribed 100% of the samples independently in three blocks of 7 transcriptions. Raters were previously trained and established reliability following each of the three transcription blocks. EVAL (MacWhinney, 2010) was run for each transcription to output measures and scores for various morphosyntax measures.

After each transcription block was completed, interrater reliability was analyzed using a two-way, random intraclass correlation coefficient (ICC) with absolute agreement.

Disagreements were then discussed and resolved, and consensus transcriptions were created. Furthermore, the transcription and coding rules were updated if necessary. For example, it was determined after block 2 that semantic paraphasias followed by a correction should be double coded as a semantic paraphasia and a subsequent retracing. Coders corrected this in the block 2 consensus transcriptions as well as the block 1 transcriptions, and implemented this rule for the transcription of block 3.

Consensus samples were then separated into C-units (main clause + its dependent clauses) (Miller, Andriacchi & Nockerts, 2016) . The end of an utterance/C-unit was determined by the following: complete structure (main clause and all its dependent clauses) coordination conjunctions (used to connect two main clauses): For, And, Nor, But, Or, Yet, So; or a terminal intonation contour (Ratner & Brundage, 2020).

Correct Information Units

Correct information units (CIUs) were manually counted by the same raters. Correct information units were counted using guidelines from Nicholas & Brookshire (1993). Research assistants met to review the guidelines and practice on a sample. They then individually coded 7 training transcriptions, and met to establish reliability and consensus. Any disagreements were discussed, and rules or examples were updated for the next set. When the two research assistants could not come to agreement, then an expert third party was consulted to make a final decision. For example, after some discussion, the words ‘sandcastle’ and ‘flagpole’ were determined to be one CIU each. Following this decision, all previous transcriptions were corrected to reflect this if needed. Additionally, the same process was completed for the determination that in the case of an unintelligible noun any article preceding it or contraction attached to it was still counted as a CIU. Following the completion of each block, both ICC and point-to-point reliability were calculated. Consensus transcripts were created after disagreements were discussed and with the most updated set or rules.

It is noteworthy that though the guidelines from Nicholas & Brookshire (1993) were used, certain rules were re-evaluated for consistency's sake (see appendix A). For example, root words were counted as CIU's despite an inaccuracy of plural /s/ use.

ICC interrater reliability for EVAL variables is reported in Table 1.

Pause Analysis

Both filled and unfilled pauses are indicative of word finding/semantic difficulties and were thus investigated in this study. Filled pauses were defined to be filler words such as: uh, um, mhm, hm, and were manually coded in CLAN. Unfilled pauses were instances of silence lasting longer than a predetermined duration, and were investigated by one graduate student using Praat software in conjunction with a script from Speech Corpus Toolkit (SpeCT) was used (v1.102.2). This script uses a long sound audio to run intensity analyses. The output of this script includes a raw number of silences and a text grid, where utterance and silence (unfilled pause) boundaries are indicated. The parameters for marking these unfilled pauses can be defined by the users. The settings for this study included all default settings with the exceptions of minimum duration, maximum intensity, and boundary margin. Minimum duration was changed from .39 to .9 seconds. Maximum intensity for a silence was 65 db SPL. The boundary margin was decreased to .01. Thus, an unfilled pause was defined to be a minimum duration of .9 seconds and a maximum intensity of 65 db SPL.

The same student reviewed each text grid to discard and counted pauses that were outside of the picture description (spontaneous speech before or after the task), or pauses that were counted as more than one because of coughing or other miscellaneous sounds that were not utterances.

Image acquisition/Preprocessing

A Philips 3T TX MRI scanner was utilized to acquire T-1-weighted structural and resting state echo-planar imaging fMRI data. Blood oxygen-level dependent contrast was used in the acquisition of 216 resting state echo-planar images.

Structural scans were normalized to Montreal Neurological Institute space in SPM 8 ((http://www.fil.ion.ucl.ac.uk/spm)). The "unified segmentation" algorithm was utilized. In the PWA, "lesion" was added to segmentation as an extra tissue class separate from gray/white/cerebrospinal fluid (Seghier et al., 2008). Segmentation output images were smoothed with an 8mm isotropic kernel full width at half maximum. Each voxel identified the probability of tissue belonging to a specific class. This tissue class image was utilized to calculate and determine lesion volumes with the automated lesion identification algorithm (ALI toolbox) in SPM8. The calculated lesion volumes (cm^3) were included in analyses.

Head movement was corrected for in echo-planar images with a two-pass procedure of affine registration in SPM8. Mean echo-planar images for subjects were created and normalized spatially to the Montreal Neurological Institute (MNI) template. Images were smoothed using a 5mm full width at half-maximum Gaussian kernel. False correlations were accounted for by removing variance associated with motion and physiological noise. Data was then bandpass filtered, frequencies between 0.01 and 0.08 Hz were preserved.

ROI Selection.

Two networks were investigated in this study: the language network (LN) and frontoparietal network (FPN). The LN nodes were defined utilizing an automated meta-analysis of 871 brain imaging studies (http://neurosynth.org/decode; Yarkoni et al., 2011). These 871 studies were those grouped into Topic 44, which included coding for keywords: semantic, word, words, priming, processing, repetition, language, lexical, verbal, naming, fluency, verbs, task, production, nouns, meaning, picture, decision, effect, verb, semantically, noun, association. The list of studies included in Topic 44 are reported in Appendix B. The convergence of topics in this group of studies on lexical-semantics indicated it as a viable language network for the purposes of this study. ROIs for the FPN were those proposed by Power and colleagues (Power et al. 2011) including the dorsolateral prefrontal cortex, inferior parietal lobule, precuneus, middle cingulate cortex, dorsal frontal cortex, and intraparietal sulcus. The time series for each of the ROIs were extracted by creating 5mm spherical binary masks around the coordinates for the LN and FPN networks using Response Exploration for Neuroimaging Datasets (REX; Duff, 2008) for each subject.

Graph Theoretical Analyses

The Network Based Statistic (NBS; Zalesky et al., 2010) was used to assess the main effect of group (HC vs. PWA) and the relationship between network connectivity and several language measures. This graph theory method allows for more control over family-wise error (FWE) while identifying connections (or edges) in a graph. Cohen's *d* was used to calculate effect sizes for t-tests.

From the time series extracted for each node for each participant, correlation matrices for each subject and network were created and then concatenated. These concatenated matrices were utilized to create a design matrix to be used in NBS. Comparisons between groups for the LN and FPN were assessed with NBS corrections for multiple comparisons and statistical threshold set at $t > 2$, and $p < .05$ with 1,000 permutations. If contrasts did not reach significance with NBS, then the false discovery rate was utilized. NBS was also utilized to investigate the relationships between network functional connectivity and several language measures in the PWA group.

In addition, node degree was also calculated for each network and group. Node degree can be utilized to identify “hubs”, or nodes with a multitude of connections to other nodes within networks.

Results

Participants. Demographics for the PWA sample are reported in Table 2, and language measures gained are reported in Table 3. **Figure 1** displays the results from the lesion overlap map. In PWA, the regions of greatest overlap were: left caudate, left inferior parietal lobule, left precentral gyrus, left mid frontal gyrus, and left post central gyrus. The greatest number of patients with a lesion in the same region was 14, while smallest number of patients that had a lesion in the same region was 5.

Group Differences Within the Resting State Networks

Language Network.

Characteristics of the LN differed by group in a few ways (**Figure 2)**. First, while the LN was defined by Neurosynth included 15 nodes, the significant network identified in PWA LN had 10 nodes and 10 edges, $t(20)>9$, $p < .001$Cohen's $d = 3.89$, and in HC LN had 11 nodes and 14 edges in the $t(17)>9$, $p < .001$ Cohen's $d = 3.01$. Thus, not all nodes of the LN were significantly connected to the rest of the network at rest in either group. It is noteworthy that all 10 LN edges in the PWA group were also present in the HC group. The commonality of these edges suggests the existence of an inherent network of nodes and edges present in both groups.

The only statistically significant between-group difference was the stronger connectivity of the left pars triangularis- rIFG homologue edge in the HC relative to PWA, $t = 3.51$, $p = .05$. No statistically significant edges are noted to be stronger in PWA compared to adults. **Figure 4** summarizes between group findings for both FPN and LN. However, while the groups did not differ significantly, the strength of those edges differed by group with: 4 being stronger in the HC (left pars triangularis-left IPL; left MTG-right MTG; right STG-right MTG; LIPL- right IFG homologue) and 6 being stronger in PWA (left MTG-left PMeFrontal; left MTG-leftIPL; left PMeFrontal-left SFG; left MTG-left precuneus; left IPL-left precuneus; right fusi-left precuneus). In addition to the 10 common edges, the HC had significant connections between the left pars triangularis-left posterior medial frontal, left middle temporal gyrus (MTG)-left superior frontal gyrus (SFG), left caudate nucleus-left precuneus, and left pars triangularis - right inferior frontal gyrus homologue (rIFG). These edges are noted to involve mostly left-sided nodes, with the exception of the rIFG.

In regard to node degree, the ‘hubs’ or nodes with the most edges relative to the network for healthy controls included left MTG (5), left inferior parietal lobule (4), and left precuneus (4). Node degree hubs in PWA included those same nodes: left MTG (4), left inferior parietal lobule (4), and left precuneus (3). The overlap in common node degree hubs between both groups suggests an innate, consistent network, with similar regions that are maximally connected within the network that is intact for both HC and PWA.

Frontoparietal Network.

Figure 3 presents the resting state edges for the FPN for PWA and HC. The FPN for patients had 102 edges, $t(20)>9$, $p<.001$, Cohen’s $d= 1.337$, and the healthy control network had 125 edges, $t(17) > 9$, $p < .001$, Cohen’s $d= 1.146$. When investigating significant edges with $t > 15$, HC had 20 edges and PWA had 19. Of these, with 10 edges being common to both groups. It is noteworthy that all 10 common edges were stronger in the PWA. No group differences existed with NBS, but there was stronger connectivity of the left frontal inferior gyrus-right precentral, right precentral – left precentral2, and right middle frontal gyrus – left inferior frontal gyrus (pars triangularis) in the HC relative to the PWA, $t(38) > 3.17$, $p = .05$. Between group differences were also assessed with FDR correction three edges in the FPN were statistically stronger in HC when compared to PWA, Cohen's *d*=1.907. Of these three, one is noted to be a significant edge in the HC resting state FPN network (left frontal inferior gyrus-right precentral). All three edges in this network involved left-right node connections.

Of the edges significant only in the healthy controls, 2 involved left-sided nodes only, and 7 involved left-right connections. In the PWA, unique edges consisted of 3 left-sided, 3 right-sided, and 4 left-right edges. **Table C** in the appendix presents FPN edges for both HC and PWA, in which edges common to both groups is bolded. In HC, the hubs for node degree included the right inferior triangularis (18), and the right angular gyrus (18). For PWA, the hubs for node degree included the right inferior triangularis (16), and right angular gyrus (16) as well.

When visually inspecting only the strongest edges in each group ($t > 15$ as in Figure 3), it is evident that the posterior bilateral edges were strongest in PWA, as well as with the right-hemisphere posterior-anterior edges, but fewer strong anterior bilateral edges are noted. The HC, in contrast, had a larger number of strong bilateral and anterior-posterior edges.

Correlations with Language Measures

NBS was initially run to investigate whether there were any significant results ($t > 3$ with $p = .05$). **Table 4** describes where significant results were found, if any. Two language measure correlations (CIUs and retracing) for the FPN were significant. **Table 5** summarizes the results of the NBS analyses run to correlate edges with language measures.

Figure 5 presents the 12 edges of the FPN that correlate with CIU in PWA, $t(20) > 3$, $p = .014$, Cohen's $d = .951$. In general, significant nodes appear to involve left parietal regions and right anterior and posterior regions. 10 edges are noted to involve left-right connections, while two involve left sided nodes only. In this, the left inferior triangularis is noted to be the 'hub' for node degree with 6 connections. Thus, the integrity of this node may indicate a more intact network for semantics. Furthermore, five of these 10 edges were noted to be edges significant in HC resting state FPN networks. These edges all involved the left frontal inferior gyrus, left precentral gyrus, or left frontal superior medial.

Figure 6 presents the 10 edges of the FPN that correlate with retracing in PWA, $t(20) > 3$, $p<.19$, Cohen's $d=.998$. Six edges are noted to involve left-right connections, while 2 edges involve only left sided nodes, and 1 edge involves only right-sided nodes. Furthermore, six of these edges are noted to be present in the HC resting state network. In this, hubs are noted to be found in the left frontal inferior triangularis (3), left parietal inferior-1 (3), right frontal superior orbitalis (3) and left parietal inferior (3).

Discussion

This study analyzed rsfMRI data in HC and PWA to 1.) characterize graph theory metrics of language and cognitive control networks and 2.) investigate correlations between these networks' functional connectivity strength and measures of semantic content produced in connected language of PWA. Findings included relatively common network connectivity between HC and PWA, particularly in the language network, indicative of relatively spared intrinsic connections within each network that may be resilient even post-stroke. Additionally, correlations between FPN edges and language measures were suggestive of the importance of intactness of the 'healthy' network connections (connections present in the healthy controls) as well as the right hemisphere for the informativeness of picture descriptions. As well, the FPN appears to play an important role in aspects of language production that may require more cognitive demand, for example for detecting and correcting conveyance of information (i.e., retracing).

Resting State Network Connectivity

Characterization of graph theory metrics of the language network and frontoparietal (cognitive control) network in PWA and HC indicated edges that were common to both groups. In the LN, which encompasses largely left hemisphere nodes, there were only four edges that were significant in the HC that were not also present the PWA. Thus, the commonality of edges within the language network in the PWA is suggestive that inherent or innate connections of the language cortex can survive, at least at rest, post-stroke. The four edges absent in the PWA group relative to HC were potentially present within the damaged cortex in the left hemisphere. In particular, the L pars triangularis-RIFG homologue edge statistically differed between groups

(HC>Patients), as was the case in Ramage et al. (2020) and New et al. (2015). Both of those studies conducted similar analyses with similar regions using this same data set. These studies found a negative correlation between this connection and expert severity ratings of apraxia of speech (AOS) (New et al., 2015). This measure does not directly relate to language measures investigated in the current study. However, the presence and severity of AOS can contribute to performance in a picture description task (i.e., motor planning difficulties may contribute to pausing, retracing, or repetition), and thus can provide a fuller picture of overall performance. Therefore, the first hypothesis: PWA will have more dysconnections (pairs of nodes showing weaker association in the group) in the language network compared to healthy controls, is supported because HC have 4 additional unique edges. However, the commonality of most edges is noteworthy.

In regard to the FPN, there were again edges that were strongly present in both groups that may indicate preserved integrity of inherent or innate connectivity of this network. However, there were nine edges present in the HC that were not present in the PWA. Of those nine, seven were bilateral edges and two involved only left-hemisphere nodes. As with the LN, the absence of these edges in the PWA may be attributed to post-stroke damage, as the PWA FPN is noted to have fewer bilateral parietal connections (see Figure 3).

Node Degree

In regard to the second hypothesis: Node degree will indicate differing hub structure in the language network by group, with right hemisphere nodes having higher summed node degree than left in the PWA group. Though lesion location affected node degree in frontal regions of the left hemisphere, nodes and their degrees were very similar across groups. Therefore, this hypothesis was not supported. The nodes most involved in network connectivity were the same for each group, with subtle differences in general node degree. This finding, evaluated with node degree, suggests that even when there is lesioned tissue in the left hemisphere, the same ‘hubs’ of connectivity existed in both PWA and HC. These findings regarding node degree appear to be slightly different than other studies that have investigated node degree in focally damaged brains. For example, Nomura et al. (2010) investigated the effects of focal brain damage to two cognitive control networks using rsfMRI data. They found that network damaged correlated with decreased functional connectivity for that network, yet spared the network that did not have a lesion. Though the present study also investigated rsfMRI data for multiple networks, lesions were noted to occur with nodes of both networks. However, findings from Nomura et al. (2010) would encourage further investigation into how these networks are interacting with each other. Furthermore, these investigators found that simulated lesions in the same networks from HC data resulted in less severe changes in functional connectivity than the actual lesioned data. These findings suggest that the diminishing connectivity in patients with lesions is evidence of diaschisis, as damage to specific areas appears to result in decreased connectivity in functionally connected non-lesioned areas. These results may explain some of the subtle differences in node degree found between groups.

Tao & Rapp (2021) found that fMRI of post-stroke patients differed in network properties relative to a healthy control group with a simulated lesion (node subtraction). Researchers hypothesized that neuroplasticity post-stroke was responsible for the reorganization of local hubs in the lesioned data that was not reflected in the simulated lesion data. Therefore, the similarities in LN hubs in these data despite focal damage to the left hemisphere may be due to neuroplastic changes that occur in the stroke recovery process.

Language Measure Correlations

We also investigated whether LN and FPN functional connectivity strength associated with language measures of semantic content produced in PWA. Somewhat surprisingly, these analyses revealed that there were only correlations of language variables to FPN edges, specifically CIUs and retracing. There were no significant correlations with LN edges. Therefore, the hypothesis that stronger LN connectivity particularly in the middle temporal gyri (MTG), superior temporal gyri (STG) and angular gyri, will correlate with better semantic access was not supported. However, the hypothesis that more connectivity strength in the FPN will correlate with better semantic access during connected language, was supported because of its correlations with CIUs and retracing.

CIU's are indicative of intact semantic performance, along with other language processes. For example, in order to produce a CIU, individuals must recognize the features in the picture and make semantic associations amongst the elements. However, syntactic processes are also needed to generate the concept the participant wishes to convey, and encode that concept into a grammatically correct message. Therefore, production of CIUs is an involved task that requires several processes. While we had anticipated that intactness and connectedness of the LN would correlate with CIU production, it was the FPN in which edge strength associated with CIUs. Stronger edges connecting left parietal to right anterior and posterior nodes associated with production of a larger number of CIUs (see Figure 5) . The hub for these edges, or node most involved in the edges associating with CIUs, was the left anterior pars triangularis, Brodmann area 45 and a considerable portion of Broca's area. In regard to the pars triangularis specifically, Foundas et al. (1996) found that leftward asymmetry of the pars triangularis on volumetric magnetic resonance imaging scales was suggestive of this left hemisphere node's role in language. Therefore, integrity of this area may indicate a more intact network for semantics and language.

Retracing in connected language tasks suggests a certain level of self-monitoring for errors and self-correction. Retracing was noted in transcripts involving several different processes. For example, retracing (coded as [//]) was utilized after word fragments ("the boy has uh a &+ka [//] uh a &+flor [//] like a &+kl [//] &+ff [//] &+fos [//] floss yeah"). This type of retracing may be involved with motor planning or phonological representations, as the participant appeared to be monitoring auditorily and retracing inaccurate attempts at the target phonological string. Additionally, retracing has also been noted following whole words ("oh the neighbor's making [//] catching a fish for dinner"). This type of retracing is indicative of monitoring of word choice, as the participant appears to retrace following an inaccurate verb selection. Therefore, retracing can involve varied language processes (phonology vs. semantics), but still requires self-monitoring for errors in both aspects.

Nine edges of the FPN correlated with the frequency of retracing, six of which involved bilateral nodes. Hubs for the subset of edges associated with retracing included the left pars triangularis, left inferior parietal lobule, and right pars orbitalis. In particular the left inferior triangularis connectivity may suggest that the integrity of this node correlates with stronger language/semantic performance. The involvement of the FPN, a cognitive control network, in retracing suggests domain general functioning to monitor and correct language production on-line. This is opposed to considering retracing to be involved as a core language function. These findings align with Diachek et al. (2020) who found increased involvement of a multiple demand network in language comprehension tasks that were hypothesized to require more cognitive control with increasing demands for attention, memory, or syntax processing. While the present study did not manipulate the complexity of the stimuli as exquisitely, picture description is also complex and cognitively demanding (c.f., Aylahya et al., 2020). Therefore, because picture description requires more connected language, it may be more cognitively demanding and require more cognitive control for the monitoring of errors as well as the to accommodate the increased cognitive demand in the task when compared to less cognitively demanding tasks such as naming.

The hypothesis that higher node degree in language network nodes would associate with the importance of these nodes in connectivity for semantic access during language production was not supported. Specifically, we hypothesized that the middle temporal gyri (MTG), superior temporal gyri (STG) and angular gyri node degrees would correlate with semantic measures, given their documented roles in semantic processing (Fridriksson et al., 2017; Halai et al., 2017; Hickock & Poeppel, 2004; Humphreys et al., 2014), but these nodes did not have higher node degree in either group for the language measure correlations. Rather, regions such as the left pars triangularis, left inferior parietal lobule, and right pars orbitalis of the FPN appear to correlate with measures as hubs with increased CIUs or retracing.

Overall, both groups had relatively similar connectivity for both networks. These similarities also appear to impact language performance, as the integrity of existing ‘healthy’ edges in PWA correlates with successful language. Furthermore, important nodes in both resting state networks and their correlations to successful language production include the left anterior triangularis, which has long been established to be pertinent to language function. However, its presence in both the LN and FPN is noteworthy, and future directions include investigating the interaction between these networks themselves. Additional future directions include investigation of graph theory metrics such as resilience or modularity with these data to identify node connectivity, as well as its connectedness with other networks, and would thus reveal more information regarding the interactions between different networks.

The noted correlations between language measures and the FPN, which is primarily thought to be a cognitive control network, provide evidence of the increased demand of a picture description task that may require more domain general functioning in addition to core language function.

Limitations

Limitations for this study included the small sample size. This sample size may have contributed to the limitations with running NBS as opposed to FDR. Additionally, the small sample size paired with the heterogeneity in the sample related to lesion location may also affect the power of analyses run.

Additionally, in all analyses run, lesions were not taken into account. For example, lesion volume was not controlled for. In future analyses, lesion masking, or excluding nodes in which there is a loss of gray matter in several participants may be necessary.

Furthermore, eight of the 21 PWA were noted to have a comorbid diagnosis of AOS. At the connected language level, AOS could have effects on instances of pausing, repetition, and retracing. Therefore, future studies should control for presence of AOS.

Conclusion:

Language and cognitive control networks were investigated in this study. Graph theory metrics were characterized for both healthy controls and people with aphasia, revealing relatively similar patterns of connectivity in both networks, despite the left hemisphere damage in the PWA group. Furthermore, several edges were correlated with language measures indicative of successful language performance. Some of these edges were pre-established in the resting state networks in HC, or both groups, while others appeared to be new and indicative of neuroplasticity. The correlation between FPN network edges and language measures may be indicative of the role of higher-level cognition in more demanding tasks such as a picture description, as well as the increased role in cognitive control to compensate for damage to language centers in the brain.

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Appendix

A. *Rules Amended for CIU coding:*

Nicholas & Brookshire (1993) provided the example that if a picture showed one boy and one girl arriving and the utterance was “The boys and girls are arriving”, then ‘boys’ and ‘girls’ would **not** be counted because of the inaccuracy of the plural. However, this rule was amended so that despite an inaccuracy of plural, the root word would still be counted as a CIU.

B. Language Network Neurosynth Studies

Title	Authors	Journal	Loading
The functional neuroanatomy of morphology in language production.	Koester D, Schiller NO	NeuroImage	0.786
Dissociation of automatic and strategic lexical-semantics: functional magnetic resonance imaging evidence for differing roles of multiple frontotemporal regions.	Gold BT, Balota DA, Jones SJ, Powell DK, Smith CD, Andersen AH	The Journal of neuroscience : the official journal of the Society for Neuroscience	0.593
The interaction of lexical semantics and cohort competition in spoken word recognition: an fMRI study.	Zhuang J, Randall B, Stamatakis EA, Marslen-Wilson WD, Tyler LK	Journal of cognitive neuroscience	0.588
Brain activity during automatic semantic priming revealed by event-related functional magnetic resonance imaging.	Copland DA, de Zubicaray GI, McMahon K, Wilson SJ, Eastburn M, Chenery HJ	NeuroImage	0.584
Repetition suppression and semantic enhancement: an investigation of the neural correlates of priming.	Raposo A, Moss HE, Stamatakis EA, Tyler LK	Neuropsychologia	0.576
Auditory processing of different types of pseudo-words: an event-related fMRI study.	Raettig T, Kotz SA	NeuroImage	0.576
Task and semantic relationship influence both the polarity and localization of hemodynamic modulation during lexico-semantic processing.	Kuperberg GR, Lakshmanan BM, Greve DN, West WC	Human brain mapping	0.573
Neural correlates of semantic priming for ambiguous words: an event-related fMRI study.	Copland DA, de Zubicaray GI, McMahon K, Eastburn M	Brain research	0.561

Functional dissociations in top-down control dependent neural repetition priming.	Klaver P, Schnaidt M, Fell J, Ruhlmann J, Elger CE, Fernandez G	NeuroImage	0.557
Neuroanatomically separable effects of imageability and grammatical class during single-word comprehension.	Bedny M, Thompson-Schill SL	Brain and language	0.55
Brain activation during automatic and controlled processing of semantic relations: a priming experiment using lexical-decision.	Rossell SL, Bullmore ET, Williams SC, David AS	Neuropsychologia	0.544
Effect of language task demands on the neural response during lexical access: a functional magnetic resonance imaging study.	Gan G, Buchel C, Isel F	Brain and behavior	0.533
Converging evidence from fMRI and aphasia that the left temporoparietal cortex has an essential role in representing abstract semantic knowledge.	Skipper-Kallal LM, Mirman D, Olson IR	Cortex; a journal devoted to the study of the nervous system and behavior	0.518
The role of semantics and grammatical class in the neural representation of words.	Vigliocco G, Warren J, Siri S, Arciuli J, Scott S, Wise R	Cerebral cortex (New York, N.Y. : 1991)	0.512
Brain activation during masked and unmasked semantic priming: commonalities and differences.	Ulrich M, Hoenig K, Gron G, Kiefer M	Journal of cognitive neuroscience	0.507
Suggestion-Induced Modulation of Semantic Priming during Functional Magnetic Resonance Imaging.	Ulrich M, Kiefer M, Bongartz W, Gron G, Hoenig K	PloS one	0.502

Neural correlates of generating visual nouns and motor verbs in a minimal phrase context.	Khader PH, Jost K, Mertens M, Bien S, Rosler F	Brain research	0.493
Neural processing of nouns and verbs: the role of inflectional morphology.	Tyler LK, Bright P, Fletcher P, Stamatakis EA	Neuropsychologia	0.491
Common and dissociable activation patterns associated with controlled semantic and phonological processing: evidence from FMRI adaptation.	Gold BT, Balota DA, Kirchhoff BA, Buckner RL	Cerebral cortex (New York, N.Y. : 1991)	0.491
Connectivity among semantic associates: an fMRI study of semantic priming.	Wible CG, Han SD, Spencer MH, Kubicki M, Niznikiewicz MH, Jolesz FA, McCarley RW, Nestor P	Brain and language	0.49
Processing of zero-derived words in English: an fMRI investigation.	Pliatsikas C, Wheeldon L, Lahiri A, Hansen PC	Neuropsychologia	0.487
Dissociating stimulus-driven semantic and phonological effect during reading and naming.	Mechelli A, Josephs O, Lambon Ralph MA, McClelland JL, Price CJ	Human brain mapping	0.485
Top-down influences on lexical selection during spoken word production: A 4T fMRI investigation of refractory effects in picture naming.	de Zubicaray G, McMahon K, Eastburn M, Pringle A	Human brain mapping	0.48
Developmental changes in the neural correlates of semantic processing.	Chou TL, Booth JR, Burman DD, Bitan T, Bigio JD, Lu D, Cone NE	NeuroImage	0.476
Automatic top-down processing explains common left occipito-	Kherif F, Josse G, Price CJ	Cerebral cortex (New York, N.Y. : 1991)	0.476

temporal responses to visual words and objects.			
The effect of sublexical and lexical frequency on speech production: An fMRI investigation.	Shuster LI	Brain and language	0.475
Functional MRI evidence for a role of frontal and inferior temporal cortex in amodal components of priming.	Buckner RL, Koutstaal W, Schacter DL, Rosen BR	Brain : a journal of neurology	0.473
Common and segregated neural substrates for automatic conceptual and affective priming as revealed by event-related functional magnetic resonance imaging.	Liu H, Hu Z, Peng D, Yang Y, Li K	Brain and language	0.473
Distributed cortical networks for syntax processing: Broca's area as the common denominator.	Heim S, Opitz B, Friederici AD	Brain and language	0.472
Neural correlates of abstract verb processing.	Rodriguez-Ferreiro J, Gennari SP, Davies R, Cuetos F	Journal of cognitive neuroscience	0.458
Emotional valence of words modulates the subliminal repetition priming effect in the left fusiform gyrus: an event-related fMRI study.	Luo Q, Peng D, Jin Z, Xu D, Xiao L, Ding G	NeuroImage	0.457
Neural correlates of semantic competition during processing of ambiguous words.	Bilenko NY, Grindrod CM, Myers EB, Blumstein SE	Journal of cognitive neuroscience	0.457
Neural systems underlying lexical competition: an eye tracking and fMRI study.	Righi G, Blumstein SE, Mertus J, Worden MS	Journal of cognitive neuroscience	0.456
Neural circuits subserving the retrieval of stems and grammatical	de Diego Balaguer R, Rodriguez-Fornells	Human brain mapping	0.454

features in regular and irregular verbs.	A, Rotte M, Bahlmann J, Heinze HJ, Munte TF		
The effect of word concreteness on recognition memory.	Fliessbach K, Weis S, Klaver P, Elger CE, Weber B	NeuroImage	0.454
The impact of semantic reference on word class: an fMRI study of action and object naming.	Saccuman MC, Cappa SF, Bates EA, Arevalo A, Della Rosa P, Danna M, Perani D	NeuroImage	0.453
The effect of lexical priming on sentence comprehension: an fMRI study.	Newman SD, Ratliff K, Muratore T, Burns T Jr	Brain research	0.453
Broca's area in the human brain is involved in the selection of grammatical gender for language production: evidence from event-related functional magnetic resonance imaging.	Heim S, Opitz B, Friederici AD	Neuroscience letters	0.451
Neural representations of nouns and verbs in Chinese: an fMRI study.	Li P, Jin Z, Tan LH	NeuroImage	0.445
Neural systems for word meaning modulated by semantic ambiguity.	Chan AH, Liu HL, Yip V, Fox PT, Gao JH, Tan LH	NeuroImage	0.442
Independent distractor frequency and age-of-acquisition effects in picture-word interference: fMRI evidence for post-lexical and lexical accounts according to distractor type.	de Zubicaray GI, Miozzo M, Johnson K, Schiller NO, McMahon KL	Journal of cognitive neuroscience	0.438
Dopaminergic neuromodulation of semantic processing: a 4-	Copland DA, McMahon KL,	Cerebral cortex (New York, N.Y. : 1991)	0.437

T FMRI study with levodopa.	Silburn PA, de Zubicaray GI		
The effect of word imagery on priming effect under a preconscious condition: An fMRI study.	Lee JS, Choi J, Yoo JH, Kim M, Lee S, Kim JW, Jeong B	Human brain mapping	0.433
The neural substrate of naming events: effects of processing demands but not of grammatical class.	Siri S, Tettamanti M, Cappa SF, Della Rosa P, Saccuman C, Scifo P, Vigliocco G	Cerebral cortex (New York, N.Y. : 1991)	0.43
Age-related neural reorganization during spoken word recognition: the interaction of form and meaning.	Shafto M, Randall B, Stamatakis EA, Wright P, Tyler LK	Journal of cognitive neuroscience	0.429
Repetition priming without identification of the primes: evidence for a component process view of priming.	Lin CY, Ryan L	NeuroImage	0.422
The impact of affect and frequency on lexical decision: the role of the amygdala and inferior frontal cortex.	Nakic M, Smith BW, Busis S, Vythilingam M, Blair RJ	NeuroImage	0.42
Dissociative neural correlates of semantic processing of nouns and verbs in Chinese--a language with minimal inflectional morphology.	Yu X, Law SP, Han Z, Zhu C, Bi Y	NeuroImage	0.419
The neuronal infrastructure of speaking.	Menenti L, Segaert K, Hagoort P	Brain and language	0.419
The past tense debate: is phonological complexity the key to the puzzle?	Oh TM, Tan KL, Ng P, Berne YI, Graham S	NeuroImage	0.415
Functional neuroanatomy of contextual acquisition of concrete and abstract words.	Mestres-Misse A, Munte TF, Rodriguez-Fornells A	Journal of cognitive neuroscience	0.414

Grammatical categories in the brain: the role of morphological structure.	Longe O, Randall B, Stamatakis EA, Tyler LK	Cerebral cortex (New York, N.Y. : 1991)	0.412
Phonological repetition-suppression in bilateral superior temporal sulci.	Vaden KI Jr, Muftuler LT, Hickok G	NeuroImage	0.412
Repetition enhancement and perceptual processing of visual word form.	Lebreton K, Villain N, Chetelat G, Landeau B, Seghier ML, Lazeyras F, Eustache F, Ibanez V	Frontiers in human neuroscience	0.411
An fMRI examination of the effects of acoustic-phonetic and lexical competition on access to the lexical-semantic network.	Minicucci D, Guediche S, Blumstein SE	Neuropsychologia	0.41
Effective connectivity of the left BA 44, BA 45, and inferior temporal gyrus during lexical and phonological decisions identified with DCM.	Heim S, Eickhoff SB, Ischebeck AK, Friederici AD, Stephan KE, Amunts K	Human brain mapping	0.409
Specialisation in Broca's region for semantic, phonological, and syntactic fluency?	Heim S, Eickhoff SB, Amunts K	NeuroImage	0.407
Neural responses to morphological, syntactic, and semantic properties of single words: an fMRI study.	Davis MH, Meunier F, Marslen-Wilson WD	Brain and language	0.406
Recruitment of anterior and posterior structures in lexical-semantic processing: an fMRI study comparing implicit and explicit tasks.	Ruff I, Blumstein SE, Myers EB, Hutchison E	Brain and language	0.405
Neuroimaging-guided rTMS of the left inferior frontal gyrus	Thiel A, Haupt WF, Habedank B,	NeuroImage	0.402

interferes with repetition priming.	Winhuisen L, Herholz K, Kessler J, Markowitsch HJ, Heiss WD		
Phonological neighborhood effects in spoken word production: an fMRI study.	Peramunage D, Blumstein SE, Myers EB, Goldrick M, Baese-Berk M	Journal of cognitive neuroscience	0.399
Conceptual control across modalities: graded specialisation for pictures and words in inferior frontal and posterior temporal cortex.	Krieger-Redwood K, Teige C, Davey J, Hymers M, Jefferies E	Neuropsychologia	0.396
Imaging implicit morphological processing: evidence from Hebrew.	Bick AS, Frost R, Goelman G	Journal of cognitive neuroscience	0.395
Left cytoarchitectonic area 44 supports selection in the mental lexicon during language production.	Heim S, Eickhoff SB, Friederici AD, Amunts K	Brain structure & function	0.394
Cerebellar involvement in verb generation: an fMRI study.	Frings M, Dimitrova A, Schorn CF, Elles HG, Hein-Kropp C, Gizewski ER, Diener HC, Timmann D	Neuroscience letters	0.393
Structural correlates of semantic and phonemic fluency ability in first and second languages.	Grogan A, Green DW, Ali N, Crinion JT, Price CJ	Cerebral cortex (New York, N.Y. : 1991)	0.392
Effects of representational distance between meanings on the neural correlates of semantic ambiguity.	Grindrod CM, Garnett EO, Malyutina S, den Ouden DB	Brain and language	0.392
Written distractor words influence brain activity during overt picture naming.	Diaz MT, Hogstrom LJ, Zhuang J, Voyvodic JT, Johnson MA, Camblin CC	Frontiers in human neuroscience	0.391

Speaking words in two languages with one brain: neural overlap and dissociation.	Liu H, Hu Z, Guo T, Peng D	Brain research	0.39
A repetition suppression effect lasting several days within the semantic network.	Meister IG, Buelte D, Sparing R, Boroojerdi B	Experimental brain research	0.389
Common prefrontal regions coactivate with dissociable posterior regions during controlled semantic and phonological tasks.	Gold BT, Buckner RL	Neuron	0.386
Visuospatial complexity modulates reading in the brain.	Rao C, Singh NC	Brain and language	0.386
Insight into the neurophysiological processes of melodically intoned language with functional MRI.	Mendez Orellana CP, van de Sandt-Koenderman ME, Saliasi E, van der Meulen I, Klip S, van der Lugt A, Smits M	Brain and behavior	0.382
Neural correlates of continuous causal word generation.	Wende KC, Straube B, Stratmann M, Sommer J, Kircher T, Nagels A	NeuroImage	0.381
Neural differences in the mapping of verb and noun concepts onto novel words.	Mestres-Misse A, Rodriguez-Fornells A, Munte TF	NeuroImage	0.38
Neural correlates of morphological decomposition in a morphologically rich language: an fMRI study.	Lehtonen M, Vorobyev VA, Hugdahl K, Tuokkola T, Laine M	Brain and language	0.377
Are abstract action words embodied? An fMRI investigation at the interface between language and motor cognition.	Sakreida K, Scorolli C, Menz MM, Heim S, Borghi AM, Binkofski F	Frontiers in human neuroscience	0.375

Modeling activation and effective connectivity of VWFA in same script bilinguals.	Boukrina O, Hanson SJ, Hanson C	Human brain mapping	0.374
Semantic memory: distinct neural representations for abstractness and valence.	Skipper LM, Olson IR	Brain and language	0.373
Lion - tiger - stripes: Neural correlates of indirect semantic priming across processing modalities.	Sass K, Krach S, Sachs O, Kircher T	NeuroImage	0.372
Changes in functional connectivity within the fronto-temporal brain network induced by regular and irregular Russian verb production.	Kireev M, Slioussar N, Korotkov AD, Chernigovskaya TV, Medvedev SV	Frontiers in human neuroscience	0.372
The determiner congruency effect in language production investigated with functional MRI.	Heim S, Friederici AD, Schiller NO, Ruschemeyer SA, Amunts K	Human brain mapping	0.371
Neural correlates of rhyming vs. lexical and semantic fluency.	Kircher T, Nagels A, Kirner-Veselinovic A, Krach S	Brain research	0.37
Incongruent abstract stimulus-response bindings result in response interference: FMRI and EEG evidence from visual object classification priming.	Horner AJ, Henson RN	Journal of cognitive neuroscience	0.37
Priming words with pictures: neural correlates of semantic associations in a cross-modal priming task using fMRI.	Kircher T, Sass K, Sachs O, Krach S	Human brain mapping	0.367
This is your brain on Scrabble: Neural correlates of visual word recognition in competitive Scrabble players as	Protzner AB, Hargreaves IS, Campbell JA, Myers-Stewart K, van Hees S,	Cortex; a journal devoted to the study of the nervous system and behavior	0.367

measured during task and resting-state.	Goodyear BG, Sargious P, Pexman PM		
Predication drives verb cortical signatures.	Hernandez M, Fairhall SL, Lenci A, Baroni M, Caramazza A	Journal of cognitive neuroscience	0.364
Neuroimaging the short- and long-term effects of repeated picture naming in healthy older adults.	MacDonald AD, Heath S, McMahon KL, Nickels L, Angwin AJ, Hees SV, Johnson K, Copland DA	Neuropsychologia	0.363
Segregating semantic and syntactic aspects of processing in the human brain: an fMRI investigation of different word types.	Friederici AD, Opitz B, von Cramon DY	Cerebral cortex (New York, N.Y. : 1991)	0.362
Demand on verbal working memory delays haemodynamic response in the inferior prefrontal cortex.	Thierry G, Ibarrola D, Demonet JF, Cardebat D	Human brain mapping	0.362
Taxonomic and thematic categories: Neural correlates of categorization in an auditory-to-visual priming task using fMRI.	Sass K, Sachs O, Krach S, Kircher T	Brain research	0.362
Priming picture naming with a semantic task: an fMRI investigation.	Heath S, McMahon K, Nickels L, Angwin A, MacDonald A, van Hees S, Johnson K, Copland D	PloS one	0.361
A supramodal brain substrate of word form processing--an fMRI study on homonym finding with auditory and visual input.	Balthasar AJ, Huber W, Weis S	Brain research	0.359

Hippocampal dysfunction during free word association in male patients with schizophrenia.	Kircher T, Whitney C, Krings T, Huber W, Weis S	Schizophrenia research	0.358
Optimally efficient neural systems for processing spoken language.	Zhuang J, Tyler LK, Randall B, Stamatakis EA, Marslen-Wilson WD	Cerebral cortex (New York, N.Y. : 1991)	0.358
Distinct functional connectivity of the hippocampus during semantic and phonemic fluency.	Glikmann-Johnston Y, Oren N, Hendler T, Shapira-Lichter I	Neuropsychologia	0.357
An event-related fMRI investigation of phonological-lexical competition.	Prabhakaran R, Blumstein SE, Myers EB, Hutchison E, Britton B	Neuropsychologia	0.356
Brain activation and lexical learning: the impact of learning phase and word type.	Raboyeau G, Marcotte K, Adrover-Roig D, Ansaldo AI	NeuroImage	0.356
Processing concrete words: fMRI evidence against a specific right-hemisphere involvement.	Fiebach CJ, Friederici AD	Neuropsychologia	0.354
Argument structure and morphological factors in noun and verb processing: an fMRI study.	Garbin G, Collina S, Tabossi P	PloS one	0.353

For presentation purposes the appendix includes the first 100 of 868 studies utilized in this meta-analysis.

C. *FPN Resting State Connectivity*

Healthy Controls		People with Aphasia	
Edge	t-value	Edge	t-value
Parietal_Inf_R1 to Parietal_Inf_R2.	**39.45**	**Parietal_Inf_R1 to Parietal_Inf_R2.**	**41.31**
Parietal_Inf_L1 to Parietal_Inf_L3.	**34.83**	**Parietal_Inf_L1 to Parietal_Inf_L3.**	**39.39**
Parietal_Inf_R1 to Angular_R2.	**29.41**	**Parietal_Inf_R1 to Angular_R2.**	**31.75**
Frontal_Inf_Tri_L1 to Precentral_L2.	25.22	**Parietal_Inf_R2 to Angular_R1.**	**26.89**
Parietal_Inf_R2 to Angular_R1.	24.72	**Angular_R1 to Angular_R2.**	**24.85**
Parietal_Inf_L2 to Angular_R2.	22.71	Frontal_Inf_Tri_L1 to Precentral_L2.	24.84
Angular_R1 to Angular_R2.	**22.7**	**Parietal_Inf_R2 to Angular_R2.**	**24.08**
Parietal_Inf_R2 to Angular_R2.	**22.67**	**Frontal_Mid_L3 to Frontal_Mid_Orb_L1.**	**21.56**
Angular_R1 to Parietal_Inf_L3.	22	Parietal_Inf_L2 to Angular_R2.	21.49
Parietal_Inf_L1 to Parietal_Inf_R2.	20.19	Angular_R1 to Parietal_Inf_L3.	21.26
Frontal_Mid_L3 to Frontal_Mid_Orb_L1.	**18.14**	**Parietal_Inf_R2 to Parietal_Inf_L3.**	**19.59**
Frontal_Mid_L2 to Frontal_Mid_L3.	17.42	Parietal_Inf_L1 to Parietal_Inf_R2.	19.12
Parietal_Inf_R2 to Parietal_Inf_L3.	**17.37**	Precentral_R1 to Frontal_Mid_R3.	17.49
Frontal_Mid_R1 to Parietal_Inf_R1.	**15.66**	Parietal_Inf_L2 to Parietal_Inf_L3.	17.33
Frontal_Inf_Tri_R1 to Frontal_Inf_Tri_L1.	15.55	Frontal_Mid_L2 to Frontal_Mid_L3.	16.3
Frontal_Inf_Tri_L1 to Precentral_R1.	15.34	**Frontal_Mid_R1 to Parietal_Inf_R1.**	**16.28**
Frontal_Mid_R3 to Frontal_Sup_Medial_L2.	15.12	Angular_R1 to Frontal_Mid_R3.	15.38
Frontal_Inf_Tri_L2 to Frontal_Sup_Medial_L2.	**15.12**	**Frontal_Inf_Tri_L2 to Frontal_Sup_Medial_L2.**	**15.34**
Frontal_Inf_Tri_R1 to Precentral_L2.	15.02	Precentral_R1 to Parietal_Inf_R2.	15.29
Precentral_R1 to Frontal_Mid_R3.	14.88	Frontal_Mid_R3 to Frontal_Sup_Medial_L2.	15.01
Precentral_R1 to Frontal_Inf_Tri_L2.	14.79	Parietal_Inf_R2 to Frontal_Mid_R3.	14.78
Frontal_Mid_L1 to Frontal_Mid_R2.	14.63	Frontal_Inf_Tri_R1 to Frontal_Mid_R3.	14.63

Frontal_Mid_R1 to Frontal_Mid_Orb_R2.	14.53	Frontal_Mid_R1 to Frontal_Mid_Orb_R2.	14.59
Frontal_Inf_Tri_R1 to Frontal_Mid_R1.	14.52	Frontal_Mid_L1 to Frontal_Mid_R2.	14.36
Parietal_Inf_L2 to Parietal_Inf_L3.	14.52	Frontal_Inf_Tri_R1 to Angular_R1.	14.35
Precentral_L1 to Frontal_Sup_Medial_L2.	14.38	Parietal_Inf_R1 to Angular_R1.	14.35
Frontal_Inf_Tri_L1 to Parietal_Inf_L2.	14.34	Parietal_Inf_L1 to Angular_R1.	13.99
Frontal_Inf_Tri_R1 to Angular_R1.	13.8	Frontal_Sup_Orb_R2 to Frontal_Mid_Orb_R1.	13.98
Parietal_Inf_R1 to Parietal_Inf_L2.	13.77	Frontal_Inf_Tri_R1 to Frontal_Inf_Tri_L1.	13.85
Parietal_Inf_L1 to Angular_R1.	13.75	Frontal_Inf_Tri_R1 to Frontal_Mid_R1.	13.8
Parietal_Inf_R1 to Angular_R1.	13.6	Frontal_Inf_Tri_R1 to Precentral_L2.	13.59
Precentral_R1 to Frontal_Sup_Medial_L2.	13.58	Parietal_Inf_L2 to Angular_R1.	13.58
Precentral_R1 to Parietal_Inf_R2.	13.39	Parietal_Inf_R1 to Parietal_Inf_L2.	13.52
Parietal_Inf_L2 to Angular_R1.	13.39	Angular_R1 to Frontal_Mid_Orb_R2.	13.41
Frontal_Inf_Tri_R1 to Precentral_R1.	13.38	Frontal_Inf_Tri_R1 to Parietal_Inf_R1.	13.1
Frontal_Mid_L2 to Frontal_Mid_R1.	13.21	Precentral_R1 to Frontal_Sup_Medial_L2.	13.09
Frontal_Inf_Tri_L1 to Frontal_Inf_Tri_L2.	12.9	Parietal_Inf_L3 to Angular_R2.	12.79
Angular_R1 to Frontal_Mid_R3.	12.84	Frontal_Inf_Tri_R1 to Precentral_R1.	12.71
Precentral_L1 to Precentral_L2.	12.82	Precentral_L1 to Parietal_Inf_L1.	12.69
Precentral_L1 to Parietal_Inf_L1.	12.78	Parietal_Inf_R2 to Frontal_Mid_R2.	12.64
Frontal_Inf_Tri_R1 to Frontal_Inf_Tri_L2.	12.68	Precentral_L1 to Frontal_Sup_Medial_L2.	12.45
Frontal_Mid_L2 to Frontal_Inf_Tri_L2.	12.57	Frontal_Mid_R2 to Frontal_Mid_R3.	12.23
Frontal_Mid_R1 to Parietal_Inf_R2.	12.52	Frontal_Mid_R2 to Frontal_Sup_Medial_L2.	12.17
Parietal_Inf_L3 to Angular_R2.	12.5	Frontal_Mid_L2 to Frontal_Mid_Orb_L1.	12.1
Frontal_Inf_Tri_R1 to Parietal_Inf_R1.	12.38	Frontal_Inf_Tri_R1 to Angular_R2.	11.99

Temporal_Inf_R1 to Parietal_Inf_R1.	12.18	Temporal_Inf_R1 to Angular_R2.	11.99
Frontal_Inf_Tri_R1 to Frontal_Mid_R3.	12.17	Frontal_Mid_R2 to Angular_R1.	11.96
Frontal_Mid_L2 to Frontal_Mid_Orb_L1.	11.97	Parietal_Inf_R1 to Parietal_Inf_L3.	11.96
Precentral_R1 to Precentral_L2.	11.96	Frontal_Inf_Tri_L1 to Precentral_R1.	11.9
Precentral_L1 to Frontal_Inf_Tri_L2.	11.91	Precentral_R1 to Frontal_Inf_Tri_L2.	11.9
Frontal_Inf_Tri_R1 to Frontal_Mid_Orb_L1.	11.9	Precentral_L1 to Precentral_L2.	11.88
Angular_R1 to Frontal_Mid_Orb_R2.	11.82	Angular_R1 to Frontal_Sup_Medial_L2.	11.82
Angular_R1 to Frontal_Inf_Tri_L2.	11.82	Temporal_Inf_R1 to Parietal_Inf_R1.	11.78
Frontal_Mid_R1 to Angular_R2.	11.8	Parietal_Inf_L2 to Parietal_Inf_R2.	11.78
Frontal_Mid_R2 to Frontal_Sup_Medial_L2.	11.71	Frontal_Mid_R3 to Angular_R2.	11.71
Precentral_L1 to Parietal_Inf_L3.	11.66	Frontal_Mid_L2 to Frontal_Inf_Tri_L2.	11.59
Frontal_Mid_R3 to Frontal_Inf_Tri_L2.	11.49	Parietal_Inf_R2 to Frontal_Sup_Medial_L2.	11.54
Frontal_Inf_Tri_L1 to Angular_R2.	11.43	Precentral_R1 to Parietal_Inf_R1.	11.47
Precentral_L1 to Parietal_Inf_R2.	11.38	Frontal_Inf_Tri_L1 to Frontal_Inf_Tri_L2.	11.47
Frontal_Inf_Tri_R1 to Angular_R2.	11.37	Parietal_Inf_R1 to Frontal_Mid_R3.	11.46
Frontal_Inf_Tri_R1 to Frontal_Mid_L3.	11.34	Frontal_Mid_R1 to Angular_R2.	11.44
Angular_R1 to Frontal_Sup_Medial_L2.	11.29	Frontal_Inf_Tri_L1 to Parietal_Inf_L2.	11.33
Parietal_Inf_R2 to Frontal_Mid_R3.	11.25	Frontal_Inf_Tri_R1 to Parietal_Inf_R2.	11.29
Parietal_Inf_L2 to Parietal_Inf_R2.	11.21	Precentral_L1 to Frontal_Inf_Tri_L2.	11.14
Precentral_L1 to Frontal_Mid_R2.	11.16	Frontal_Mid_R2 to Frontal_Inf_Tri_L2.	11.14
Frontal_Mid_R2 to Angular_R1.	11.15	Precentral_R1 to Angular_R1.	11.09
Frontal_Mid_R2 to Frontal_Mid_R3.	11.13	Parietal_Inf_R2 to Frontal_Mid_Orb_R2.	11.03
Parietal_Inf_R2 to Frontal_Sup_Medial_L2.	11.09	Frontal_Mid_L3 to Frontal_Sup_Medial_L2.	11

Parietal_Inf_R2 to Frontal_Mid_R2.	11.08	Frontal_Mid_R1 to Parietal_Inf_R2.	10.92
Frontal_Inf_Tri_R1 to Parietal_Inf_L2.	11	Frontal_Mid_L2 to Frontal_Mid_R1.	10.75
Frontal_Mid_R1 to Frontal_Mid_L3.	10.97	Frontal_Inf_Tri_R1 to Frontal_Sup_Medial_L2.	10.66
Frontal_Mid_L3 to Frontal_Mid_Orb_R2.	10.91	Frontal_Mid_Orb_L1 to Frontal_Sup_Medial_L2.	10.66
Frontal_Mid_Orb_L1 to Frontal_Mid_Orb_R2.	10.89	Precentral_L1 to Frontal_Mid_R2.	10.57
Frontal_Mid_R1 to Frontal_Mid_Orb_L1.	10.85	Parietal_Inf_L3 to Frontal_Mid_R3.	10.53
Precentral_L1 to Frontal_Mid_R3.	10.84	Angular_R1 to Frontal_Inf_Tri_L2.	10.48
Parietal_Inf_L3 to Frontal_Mid_Orb_R2.	10.83	Frontal_Inf_Tri_R1 to Frontal_Mid_Orb_L1.	10.42
Parietal_Inf_L3 to Frontal_Mid_R3.	10.82	Parietal_Inf_L3 to Frontal_Mid_Orb_R2.	10.36
Frontal_Inf_Tri_R1 to Parietal_Inf_R2.	10.8	Precentral_R1 to Angular_R2.	10.31
Precentral_R1 to Parietal_Inf_R1.	10.74	Parietal_Inf_L3 to Frontal_Sup_Medial_L2.	10.12
Parietal_Inf_R1 to Parietal_Inf_L3.	10.61	Frontal_Inf_Tri_R1 to Frontal_Mid_R2.	10.04
Frontal_Mid_R1 to Frontal_Inf_Tri_L2.	10.61	Parietal_Inf_L1 to Parietal_Inf_L2.	10.02
Frontal_Mid_L2 to Frontal_Sup_Medial_L2.	10.57	Parietal_Inf_L3 to Frontal_Inf_Tri_L2.	9.92
Temporal_Inf_R1 to Parietal_Inf_R2.	10.5	Frontal_Mid_R3 to Frontal_Inf_Tri_L2.	9.7
Precentral_R1 to Angular_R1.	10.5	Frontal_Inf_Tri_R1 to Frontal_Mid_L3.	9.68
Precentral_L2 to Parietal_Inf_L2.	10.45	Temporal_Inf_R1 to Parietal_Inf_R2.	9.67
Precentral_L1 to Angular_R1.	10.45	Parietal_Inf_L1 to Frontal_Sup_Medial_L2.	9.6
Frontal_Mid_Orb_L1 to Frontal_Sup_Medial_L2.	10.44	Frontal_Mid_L2 to Frontal_Sup_Medial_L2.	9.6
Parietal_Inf_L3 to Frontal_Inf_Tri_L2.	10.43	Parietal_Inf_L1 to Frontal_Inf_Tri_L2.	9.48
Frontal_Inf_Tri_R1 to Frontal_Sup_Medial_L2.	10.39	Frontal_Mid_Orb_L1 to Frontal_Inf_Tri_L2.	9.46
Precentral_R1 to Parietal_Inf_L2.	10.31	Parietal_Inf_R1 to Frontal_Mid_R2.	9.36

Parietal_Inf_R2 to Frontal_Mid_Orb_R2.	10.27	Frontal_Inf_Tri_R1 to Frontal_Mid_Orb_R2.	9.33
Precentral_L2 to Angular_R1.	10.25	Frontal_Inf_Tri_L1 to Frontal_Mid_Orb_R2.	9.32
Precentral_L1 to Temporal_Inf_R1.	10.23	Frontal_Inf_Tri_R1 to Parietal_Inf_L2.	9.28
Frontal_Mid_R1 to Angular_R1.	10.23	Frontal_Mid_R3 to Frontal_Mid_Orb_R2.	9.25
Precentral_L2 to Angular_R2.	10.14	Frontal_Inf_Tri_R1 to Frontal_Inf_Tri_L2.	9.24
Precentral_R1 to Angular_R2.	10.13	Angular_R1 to Frontal_Mid_Orb_L1.	9.2
Frontal_Inf_Tri_L1 to Frontal_Mid_Orb_R2.	10.1	Temporal_Inf_R1 to Angular_R1.	9.19
Parietal_Inf_L3 to Frontal_Sup_Medial_L2.	9.98	Precentral_L1 to Parietal_Inf_L3.	9.19
Temporal_Inf_R1 to Angular_R2.	9.97	Precentral_L1 to Frontal_Mid_L2.	9.17
Precentral_L2 to Frontal_Inf_Tri_L2.	9.96	Parietal_Inf_L1 to Frontal_Mid_Orb_R1.	9.15
Parietal_Inf_L1 to Frontal_Mid_R2.	9.95	Parietal_Inf_R2 to Frontal_Inf_Tri_L2.	9.15
Precentral_L1 to Precentral_R1.	9.86	Frontal_Mid_R1 to Angular_R1.	9.05
Parietal_Inf_L1 to Frontal_Sup_Medial_L2.	9.85		
Frontal_Inf_Tri_L1 to Angular_R1.	9.82		
Parietal_Inf_R2 to Frontal_Inf_Tri_L2.	9.82		
Frontal_Mid_R2 to Parietal_Inf_L3.	9.79		
Precentral_R1 to Frontal_Mid_R1.	9.78		
Parietal_Inf_L1 to Frontal_Inf_Tri_L2.	9.78		
Frontal_Mid_Orb_R2 to Frontal_Inf_Tri_L2.	9.77		
Parietal_Inf_L1 to Parietal_Inf_R1.	9.67		
Frontal_Inf_Tri_R1 to Frontal_Mid_L2.	9.66		
Frontal_Inf_Tri_L1 to Frontal_Mid_Orb_L1.	9.65		
Parietal_Inf_R1 to Frontal_Inf_Tri_L2.	9.63		

Precentral_L2 to Frontal_Mid_R3.	9.61		
Precentral_R1 to Parietal_Inf_L3.	9.47		
Frontal_Mid_L3 to Frontal_Sup_Medial_L2.	9.45		
Angular_R1 to Frontal_Mid_Orb_L1.	9.44		
Frontal_Inf_Tri_R1 to Parietal_Inf_L3.	9.41		
Precentral_L2 to Frontal_Sup_Medial_L2.	9.39		
Frontal_Inf_Tri_R1 to Frontal_Mid_Orb_R2.	9.35		
Precentral_L2 to Parietal_Inf_L3.	9.31		
Parietal_Inf_L1 to Frontal_Mid_R1.	9.1		
Frontal_Mid_Orb_L1 to Frontal_Inf_Tri_L2.	9.05		
Parietal_Inf_R1 to Frontal_Sup_Medial_L2.	9.05		
Parietal_Inf_L3 to Frontal_Mid_L3.	9.01		