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FUNCTIONAL MAGNETIC RESONANCE IMAGING CASE SERIES

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ABSTRACT

This case series compares the functional magnetic-resonance imaging (fMRI) analysis of the increase in brain activation for three patients with chronic aphasia with their treatment outcomes and demographic variables. Each participant completed a word judgment task in a 3 Tesla MRI scanner before and after receiving an aphasia treatment. This treatment was formulated by Dr. Chaleece Sandberg and her colleague Dr. Swathi Kiran and involves the training of abstract words and the promotion of generalization to concrete words. BUMA15 and BUMA50 improved in trained abstract words and generalized to concrete words as a result of treatment. BUMA16 had a large effect size in trained abstract words but did not generalize to concrete words. The results for each patient will be discussed in terms of their brain activation, behavioral assessments, and lesion characteristics.

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I would like to thank my thesis advisor, Dr. Chaleece Sandberg. I could not have embarked on this academic journey without her knowledge, support, and encouragement!

Chapter 1

Introduction

Aphasia is a language disorder that can impair speech comprehension, speech production, and the ability to read or write. Aphasia results from a brain injury, such as a stroke or head trauma. This acquired language disorder affects an individual's ability to process language but not their intelligence. Although aphasia is common in older populations, it can affect a person of any age, race, or gender. There are multiple types of aphasia and they affect individuals differently depending on the location and magnitude of a lesion (National Aphasia Association, 2017).

There are many different types of treatments that have been proven effective for patients with aphasia. Treatments are often considered successful if patients improve on items that are directly trained (Sandberg & Kiran, 2014). However, clinical aphasiologists aim to improve communication beyond solely trained items. One way this can be attained is through treatments that promote generalization to untrained items. For this reason, there is a wealth of research on aphasia treatments that focus on generalization effects. A current area of research that may help improve generalization effects in treatment utilizes the difference in the cognitive processing of concrete and abstract words. Paivio (1991) explains in a review of the dual-coding theory that concrete words elicit image representations more than abstract words. The dual-coding theory (DCT) suggests that concrete words are represented in the semantic system with verbal and multi-modal sensory information such as visual information. However, abstract words are represented in the semantic system only with verbal information. This distinction leads to a difference in performance while processing concrete and abstract words, and it is referred to as the concreteness effect. The concreteness effect is the phenomenon that individuals can encode and retrieve concrete words more easily (Paivio, 1991). This concreteness effect can be manipulated in treatment in order to improve treatment outcomes by training more difficult items, in this case abstract words, and expecting generalization to easier items, as in concrete words (Kiran, Sandberg & Abbott, 2009; Sandberg & Kiran, 2014).

The concreteness effect can also be reversed, which creates a double dissociation between these two cognitive processes. In some disorders, individuals perform better on abstract word processing than on concrete word processing, and vice versa. Patterson, Nestor, and Rogers (2007) describes the double dissociation between abstract and concrete processing when comparing semantic dementia and aphasia. It has been shown that patients with aphasia due to a left hemisphere stroke exhibit the concreteness effect and process concrete words more easily. However, patients with semantic dementia have been known to process abstract words more easily because of damage to the frontotemporal region of the brain. Patterson et al. (2007) explains that patients with semantic dementia often have decently maintained cognition and memory of events, however they have trouble with vocabulary regarding everyday objects. This double dissociation supports the idea that abstract and concrete concepts are processed in different areas of the brain.

Treatment effects are most often studied behaviorally, but to see changes in brain activity, one of the most widely used neuro-imaging techniques is functional magnetic resonance imaging (fMRI) (Meinzer et al., 2012). Functional magnetic resonance imaging is used to analyze increases in neural activation due to treatment effects (Meinzer et al., 2012). It can be used to analyze treatment effects from direct training, as well as generalization effects. Additionally, patterns of activation can be interpreted by comparing the activation present during certain conditions. For example, when comparing abstract and concrete word processing, activation involved in abstract processing can be subtracted from concrete processing to determine what regions of the brain are preferential to concrete processing and vice versa (Wang, Conder, Blitzer, & Shinkareva, 2010; Binder, Desai, Graves, & Conant, 2009).

Based on what is known about abstract and concrete representations, we expect to see certain results in patients who receive this treatment. We expect to see regions involved in abstract word processing to increase activation due to direct training effects, such as the left middle temporal gyrus, left superior temporal gyrus, left inferior frontal gyrus pars orbitalis and pars triangularis. We also hope to see generalization effects, which would indicate regions involved in concrete word processing, such as the left middle frontal gyrus, left and right angular gyrus, left fusiform gyrus, left inferior temporal gyrus, left precuneus, and left posterior cingulate to have increased activation.

Additionally, every patient has a unique personal profile that will affect their results. Every participant is at a different point in the chronic stage and has different assessment scores and lesion characteristics, which will inevitably influence their response to treatment. The rewiring of the brain after stroke is variable from person to person. If a participant is further along in the recovery process, they may have developed certain compensatory strategies that others who are earlier in the chronic stage may not have developed. Also, participants with lower performance on assessments may have more room to improve whereas those with higher performance may have improved as much as they can already. Furthermore, patients may have varied lesion sites and sizes that impact their results. If a patient has a very large lesion, they have more regions with deficits, leaving fewer regions to compensate for the lost function. If a patient has a small lesion, less tissue is damaged, with the potential for more restoration and compensation of function. All of these factors affect how a patient responds in therapy, and it's important to take every aspect of a patient's profile into consideration when evaluating their improvement in treatment.

In this study, I am analyzing three participants with aphasia and their response to treatment. I will compare each participants' treatment and generalization effect sizes, increases in brain activation during a concrete and abstract word judgement task, their performance on various behavioral assessments, and their individual lesion characteristics. The purpose of this study is to take all of these factors into consideration to better understand what contributes to positive treatment outcomes in aphasia therapy. This case series will provide insight into individual variables that affect an individual's performance in therapy, that may not be brought to light solely by behavioral assessments.

Chapter 2

Methods

Participants

This case series involves three participants with aphasia (two males, one female). This data was collected at Boston University by Dr. Chaleece Sandberg and is a subset of data from a previous study by Sandberg, Bohland, and Kiran (2015).

BUMA16

Participant BUMA16 is a 56-year-old male with a lesion resulting from a left middle cerebral artery stroke. At the time of data collection, he was almost six and a half years post stroke, which is the most amount of time compared to the other participants. This participant has a lesion volume of 79.79 cc that has resulted in conduction aphasia. The following list of regions have been affected by this individual's lesion, including the middle frontal gyrus, which is involved in word retrieval, particularly in concrete word processing, and the rolandic operculum, which is involved in language processing. The insula lobe was affected by the lesion which is involved in self-referential processing and speech planning, as well as the precentral and postcentral gyrus which are involved in orofacial motor activity. The temporal pole which has been called the "semantic hub" of the brain due to its large involvement in semantic processing, along with the posterior portion of the superior temporal gyrus, which is commonly known as Wernicke's area. The anterior portion of the superior temporal gyrus has been shown to be involved in abstract processing. The middle temporal gyrus was affected by the lesion, which is responsible for semantic access, and seen particularly in abstract processing. The inferior temporal gyrus which is involved in object processing, seen in the "what" pathway, which is important for concrete word processing. The supramarginal gyrus which is involved in short term memory, the angular gyrus which is used for word recognition, particularly in concrete processing and the middle occipital gyrus which is important for vision (Price, 2012; Binder, Desai, Graves, & Conant, 2009; Kemmerer, 2015; See Appendix A for a complete list of regions and their functions and Appendix B for the corresponding abbreviations).

BUMA15

Participant BUMA15 is a 59-year-old male with a lesion to the left middle cerebral artery resulting in anomic aphasia. This participant has the largest lesion at 123.86 cc and at the time of data collection, he was less than two years post stroke, which is the least amount of time compared to the other two participants. Many of the regions affected by his lesion are similar to BUMA16, including the middle frontal gyrus, rolandic operculum, insula lobe, precentral gyrus and postcentral gyrus. The inferior frontal gyrus par triangularis, pars opercularis, and pars orbitalis were all affected by the lesion. These areas contain Broca's area and are important for both abstract and concrete word processing, and is preferentially active for abstract words. The superior temporal gyrus, middle temporal gyrus, supramarginal gyrus, and angular gyrus were all affected by the lesion. Additionally, the putamen, inferior parietal cortex, and superior parietal cortex were affected by the lesion. The putamen is a part of the basal ganglia and is involved in motor planning. The superior parietal cortex is a part of the dorsal attention network and the inferior parietal cortex contains the supramarginal gyrus, the angular gyrus, and is a part of the ventral attention network (Price, 2012; Binder et al., 2009; Kemmerer, 2015; Petersen & Posner, 2012; See Appendix A for a complete list of regions and their functions and Appendix B for the corresponding abbreviations).

BUMA50

Participant BUMA50 is a 57-year-old female with a lesion to the left middle cerebral artery resulting in conduction aphasia. This participant has the smallest lesion at 62.55 cc and she was slightly over three years post stroke at the time of data collection. All of the regions affected by the lesion overlap with the other participants including the middle frontal gyrus, the rolandic operculum, and the insula lobe. The inferior frontal gyrus pars triangularis and pars opercularis were affected by lesion. Additionally, the precentral gyrus, postcentral gyrus, supramarginal gyrus, and the inferior parietal cortex (See Appendix A for a complete list of regions and their functions and Appendix B for the corresponding abbreviations).

Assessments

Each participant completed a series of behavioral assessments including the Western Aphasia Battery (WAB), the Boston Naming Test (BNT), the Psycholinguistic Assessment of Language Processing in Aphasia (PALPA), the Pyramids and Palm Trees (PPT), and the Cognitive Linguistic Quick Test (CLQT). The Western Aphasia Battery assesses an individuals' type and severity of aphasia (Kertesz, 1982). The Boston Naming Test assesses an individual's confrontation naming ability for concrete words (Goodglass, Kaplan, & Weintraub, 1983). The Psycholinguistic Assessment of Language Processing in Aphasia identifies deficits in semantic processing for auditory and visual lexical decision making, semantic associations, as well as auditory and written synonym judgment tests in both high and low imageability words (Kay, Lesser, & Coltheart, 1992). These results provide information about participants' abilities understanding high imageability words, as in concrete words, and low imageability words, as in abstract words. The Pyramids and Palm Trees tests semantic knowledge for both picture recognition and for written word forms (Howard & Patterson, 1992). Lastly, the Cognitive Linguistic Quick Test determines the effect of cognitive deficits, such as attention, memory, visuospatial skills, and executive function, on language function (Helm-Estabrooks, 2001) (See Table 1 for individual scores and demographic information for each participant).

Table 1. Demographic and Diagnostic Information

Client ID	**BUMA50**	**BUMA16**	**BUMA15**
Age	57	56	59
Sex	Female	Male	Male
Years Post Stroke	3.2	6.3	1.9
Lesion Region	L MCA	L MCA	L MCA
Lesion Volume (in cc)	62.55	79.79	123.86
ROIs affected by lesion	MFG, IFGtri, IFGop, ROL, INS, preCG, PoCG, SMG, IPC	MFG, ROL, INS, PreCG, PoCG, TP, STG, MTG, ITG, SMG, AG, MOG	MFG, IFGtri, IFGorb, IFGop, ROL, INS, PreCG, PoCG, STG, MTG, SMG, AG, SPC, IPC, putamen
WAB			
Aphasia Quotient	99.2	77.7	78.6
Aphasia Type	Anomic	Conduction	Anomic
BNT	92%	87%	68%
PALPA			
Auditory Lexical Decision: High Imageability	100%	100%	98%
Auditory Lexical Decision: Low Imageability	100%	98%	98%
Visual Lexical Decision: High Imageability	100%	100%	100%
Visual Lexical Decision: Low Imageability	97%	100%	93%
Auditory Synonym Judgment: High Imageability	100%	90%	93%
Auditory Synonym Judgment: Low Imageability	97%	90%	77%
Written Synonym Judgment: High Imageability	100%	97%	87%
Written Synonym Judgment: Low Imageability	100%	83%	77%

Semantic Association: High Imageability	80%	DNT	73%
Semantic Association: Low Imageability	80%	DNT	87%
PPT			
Pictures	96%	98%	94%
Written Words	98%	96%	94%
CLQT			
Composite Severity	WNL	WNL	WNL
Composite Value	100%	90%	90%
Categorical Word Generation			
Concrete	30%	33%	17%
Abstract	10%	3%	3%

Treatment

The treatment each participant received was formulated by Dr. Chaleece Sandberg and Dr. Swathi Kiran (Sandberg & Kiran, 2014). This treatment uses a generative naming model with an established closed set of target concrete and abstract words for each trained context-category. Hospital and courthouse were the two context-categories, and ten abstract words were established as trained target words, and ten concrete words were untrained targets for generalization within each category. Twice a week participants received therapy during a two-hour session. Patients participated in tasks such as sorting words into their respective context categories (hospital, courthouse), selecting semantic features that apply to specific abstract words, answering yes/no questions, generating target words and synonyms, and generating words in a specific context-category. Participants were tested before, during and after treatment with a word generation task where they had two minutes to generate as many words as possible within each category (Sandberg & Kiran, 2014).

The Beeson & Robey (2006, 2008) calculation of effect size magnitude was used when determining treatment effects for these participants. BUMA15 has a large effect size for abstract items (12.07), and a small generalization effect size (4.62). BUMA50 has a small effect size for abstract items (5.82) and almost a medium effect size for generalization to concrete words (7.01). BUMA16 has a large effect size for trained items (17.53) but did not generalize to concrete words (-0.79) (See Table 2 for treatment and generalization effect sizes for each participant; See Table 3 for effect size and magnitudes).

Table 2. Effect Size for Target Items

Patient	Context-Category	Abstract	Concrete
BUMA16	Hospital	17.53	-0.79
BUMA15	Courthouse	12.07	4.62
BUMA50	Hospital	5.82	7.01

Table 3. Effect Size and Magnitude

Effect Size	Treatment	Generalization
Small	6.50	2.00
Medium	8.00	5.00
Large	9.50	8.00

fMRI Tasks and Stimuli

The task used in the fMRI is a word judgment task, where participants decide if a word is abstract or concrete (Sandberg & Kiran, 2013). The task consists of 50 abstract words and 50 concrete words that were taken from the Medical Research Council psycholinguistic database. All stimuli used during the word judgment task were balanced for their level of concreteness, imageability, and frequency (Frances & Kucera, 1983; Gilhooly & Logie, 1980). In the functional magnetic-resonance imaging scanner, participants used their left hand to make their selection with a single button press. For the control condition for this task, participants decided if a letter string was composed of consonants or vowels.

The task was implemented in an event-related design; therefore, stimuli were randomized for conditions (concrete, abstract, control). Scans were collected at Boston University Center for Biomedical Imaging in a 3 Tesla MRI scanner and each participant was scanned both before and after receiving treatment. High resolution T1-weighted images were collected for each participant providing a structural image of the brain, as well as blood-oxygen-level-dependent (BOLD) images.

Data Analysis

The functional magnetic resonance imaging (fMRI) analyses were completed at the individual level for each participant using SPM12 software. The first step in analyzing the data was preprocessing. Preprocessing is used to correct for slice timing differences, correct for movement in the scanner, remove slow baseline drifts, co-register structural and functional images, and spatially normalize structural and functional images (Sandberg et al., 2015). Realignment involves adjusting the head to compensate for movement in the scanner as well as correct for slice timing differences (Meinzer, Beeson & Cappa, 2012). Co-registration is the next step that overlays the functional data to the structural image. Realignment, slice-timing correction and co-registration are not affected by lesions, making these pre-processing steps for healthy and lesion brains similar (Meinzer et al., 2012). A high pass filter was also applied to filter out slow baseline drifts (Sandberg et al., 2015). Spatial normalization is the next step in pre-processing which is used to morph the structural and functional images to a normalized brain using the Montreal Neurologic Institute (MNI) template. Spatial smoothing was not applied to the functional images because although it increases statistical significance in group studies, it can cause a loss of certain activations when looking at the individual level (Sandberg et al., 2015; Meinzer et al., 2012).

Once pre-processing is completed, data is then entered into a General Linear Model (GLM) for individual analyses (Sandberg et al., 2015). The four conditions for this task include abstract words, concrete words, combined abstract and concrete words, and the control, which is letter strings. Only correct responses were included for each condition and the temporal derivative was included to compensate for stroke-related differences in the hemodynamic response (Sandberg et al., 2015). The contrasts of interest for this case series are post abstract > pre abstract, post concrete > pre concrete, post word > pre word, and post control > pre control. The results and discussion for this case series will focus on the post > pre contrasts for abstract and concrete words.

After the data were analyzed using the General Linear Model, to determine clusters with statistical significance, cluster-extent based thresholding was used. This method is the most popular to use for correcting for multiple comparisons (Woo, Krishnan & Wager, 2014). Woo, et al. (2014) suggests using an uncorrected, but stringent primary threshold at the voxel level, which is $p <.001$. Additionally, using an extent threshold at FDR $p<.05$ is considered best practice, therefore it was used for determining significance with this data.

Chapter 3

Results

Table 4, Table 5, and Table 6 below display the significant regions of increased activation and their corresponding MNI coordinates and t-values for each individual participant.

BUMA16

Participant BUMA16 was trained in the context category Hospital. This participant has the highest effect size in trained abstract words at 17.53. However, this is the only participant who did not generalize concrete words. BUMA16 has a generalization magnitude of -0.79.

BUMA16 showed increased activation for abstract words in areas significant for abstract processing such as the middle temporal gyrus. BUMA16 has 22.43% spared tissue in his left middle temporal gyrus, and showed increased activation in the right hemisphere homologue during the abstract condition. He showed an increase in activation in other areas involved in language processing such as the right lingual gyrus, which is involved in reading words and the left inferior parietal lobule which is involved in letter identity. Other areas involved in language processing had increased activation, such as the rolandic operculum, the middle frontal gyrus, which is involved in word retrieval, and the right and left precuneus, which is involved in speech comprehension like in narratives. Additional areas specific to short term memory and orofacial motor activity also showed an increase in activation. BUMA16 did not show increased activation in the left or right superior temporal gyrus during the abstract condition, which is often seen in abstract processing, however he has only 6.60% spared tissue in this area. He also did not show an increase in activation in the left inferior frontal gyrus par orbitalis or pars triangularis which is important in abstract processing, despite preserving 100% spared tissue in these regions.

During the concrete condition, BUMA16 had increased activation in many regions often seen in concrete processing. These include the left and right precuneus, the right and left middle frontal gyrus. He also had increased activation in other regions responsible for language processing like the left lingual gyrus, the right superior frontal gyrus which is the right hemisphere homologue for word selection, and the left middle frontal gyrus for word selection. Other regions with increased activation during the concrete condition are responsible for vision like the left and right cuneus and the left inferior occipital gyrus. The left and right middle cingulate had increased activation and these regions are involved in response selection and execution. Despite having 100% spared tissue in these regions that often involved in concrete processing, BUMA16 did not activate the left fusiform gyrus, the right angular gyrus, and the left posterior cingulate during the concrete condition (See Table 4 for BUMA16's regions of increased activation; See Figure 1 for axial slices of BUMA16's brain activation).

Red= abstract activation, Blue= concrete activation

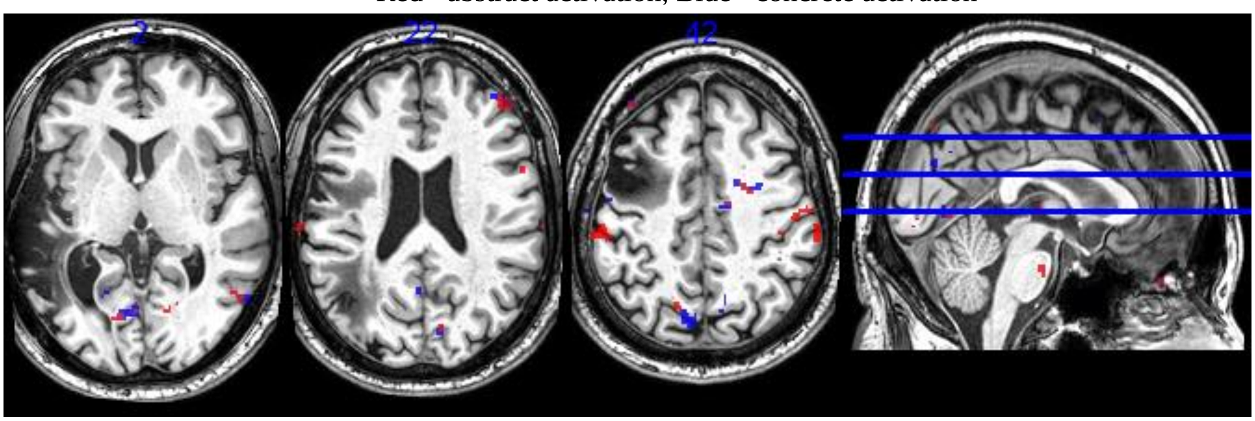

Figure 1. Axial Slices of BUMA16 Brain Activation

Table 4. Brain Activation for BUMA16

	Abstract Post-Pre		*Concrete Post-Pre*		*Word Post-Pre*		*Control Post-Pre*	
Regions	t-value	MNI coordinates	t-value	MNI coordinates	t-value	MNI coordinates	t-value	MNI coordinates
R Ling	3.72	14 -70 2						
R SMG	3.63	56 -30 46						
R ROL	3.66	62 0 8						
R MTG	3.60	54 -62 2			3.73	56 -62 6		
L CAL	4.18	0 86 -4			3.78	2 -88 -6		
L SMG	3.89	-54 -20 36			3.58	-52 -40 34		
L IPL	4.26	-54 -32 46			3.83	-34 -50 50	3.65	-54 -32 46
R PoCG	4.21	54 -14 50			4.21	54 -14 50	4.22	14 -52 72
L PoCG	3.56	-52 -16 16	3.96	-14 -38 76				
R PreCG	4.08	34 -20 48	3.91	32 -16 66	3.93	32 -16 66		
R PCN	3.17	8 -54 70	3.94	10 -62 46	3.83	10 -62 46		
L PCN	3.57	-10 -72 44	3.70	-6 -76 38	3.72	-10 -72 44		
R MFG	4.32	46 42 22	4.14	44 42 24	4.52	44 42 24	4.20	40 -2 58
L LING			4.04	-10 -72 2	4.23	-12 -74 2		
R CUN			4.52	22 -64 30	4.34	22 -64 30		
R SFG			3.80	14 -4 74	3.69	14 2 74	3.73	18 -10 74
L MCC			3.85	0 24 34				
L MFG			4.34	-36 50 26				
R MCC			3.60	4 -14 48				
L CUN			3.65	-6 -70 26				
L IOG			4.10	-48 -76 -14				

SMA					3.60	8 -10 78	3.57	8 -10 78
R TPOmid					4.16	46 14 -34		
L PreCG					3.39	-26 -20 70		
ITG					3.96	56 -42 -18		

BUMA15

Participant BUMA15 was trained in the context category Courthouse. A large effect size for trained abstract words is above 9.50 and BUMA15 has an effect size of 12.07. This participant's generalization magnitude is 4.62, which is in the small but almost medium range.

During the abstract condition, BUMA15 displayed increased activation in the right hemisphere homologue of the inferior frontal gyrus pars triangularis, which is important in abstract processing. He also showed increased activation in the left precuneus, left superior frontal gyrus, and the left superior medial frontal gyrus, which is a part of the default mode network and seen in concrete processing. The superior parietal lobule, which is involved in attention, was also activated.

During the concrete condition, the right inferior temporal gyrus was activated which is involved in object processing in the "what pathway", which is important in concrete processing. The right inferior frontal gyrus pars triangularis was activated again. Additionally, the right middle occipital gyrus was activated, which is involved in vision (See Table 5 for BUMA15's regions of increased activation; See Figure 2 for axial slices of BUMA15's brain activation).

Red= abstract activation, Blue= concrete activation

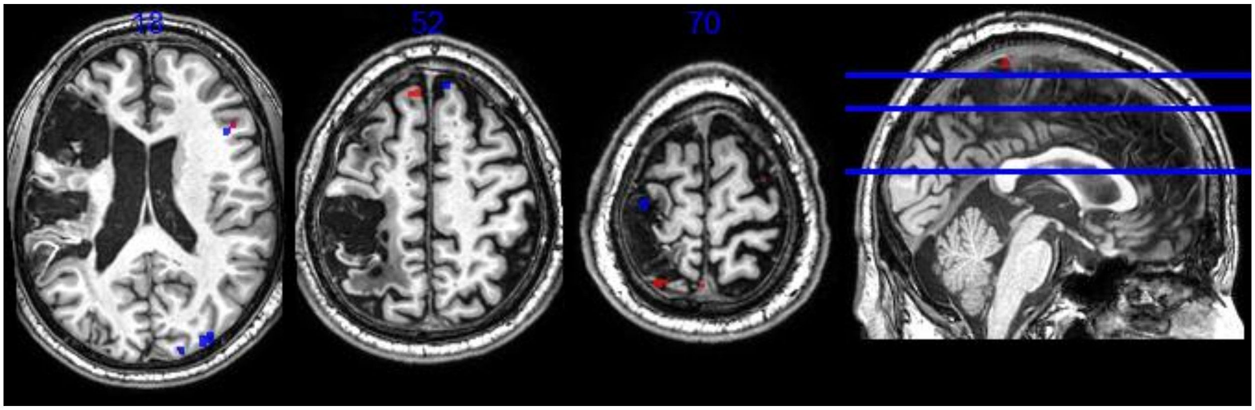

Figure 2. Axial Slices of BUMA15 Brain Activation

Table 5. Brain Activation for BUMA15

	Abstract Post-Pre		*Concrete Post-Pre*		*Word Post-Pre*		*Control Post-Pre*	
Regions	t-value	MNI coordinates	t-value	MNI coordinates	t-value	MNI coordinates	t-value	MNI coordinates
L PCN	3.61	-12 -56 74						
L SFG	3.60	-14 46 44						
L SFGmed	3.64	-6 42 52						
L SPL	3.68	-24 -60 70						
R IFGtri	4.56	46 22 14	4.16	44 20 12	4.86	44 20 12	4.73	42 20 12
R ITG			4.35	64 -58 -12				
R MOG			3.84	30 -92 18				
R OLF							3.58	16 12 -20
R PCN							3.71	2 -52 68
R SFG							4.46	30 -4 70
R SMG							3.73	54 -40 24
L MTG							4.50	-64 -52 -10

BUMA50

BUMA50 was trained in the context category Hospital. This participant has the smallest effect size in trained abstract words at 5.82. However, this participant has the largest generalization effect at 7.01, large being greater than 8.00.

During the abstract condition, BUMA50 showed increased activation in many regions of the brain known to be involved in abstract processing. She had an increase in activation in the right hemisphere homologue of the inferior frontal gyrus pars orbitalis and pars triangularis. This participant had increased activation in the right hemisphere homologue of the superior temporal gyrus, which is important in abstract processing. However, she did not have increased activation in the middle temporal gyrus which is also involved in abstract processing for semantic access. She had increased activation in the left fusiform gyrus, which is involved object processing and is a part of the "what" pathway. Other regions involved in language processing that were activated include the left rolandic operculum, the left insula which is involved in speech planning and self-referential processing and the left middle frontal gyrus which is involved in word retrieval. The right cerebellum VI was also activated which has been seen in retrieving words for speech production output and the right cerebellum crus I, which is involved in general cerebellar functions like motor coordination but also seen in language processing. Right hemisphere homologue for the superior parietal lobule which is involved in attention, the hippocampus which is important for memory, the left supramarginal gyrus for short term memory. Other regions activated are responsible for sensory motor functions, orofacial motor activity, articulatory planning, and auditory processing.

During the concrete condition, BUMA50 did not activate any of the major regions often seen in concrete processing. She did not activate the left middle frontal gyrus, left or right angular gyrus, left fusiform gyrus, left inferior temporal gyrus, the left precuneus or the left posterior cingulate. She showed an increase in activation in left cerebellum VI which is seen in retrieving words for speech production output. She also activated the left Heschl's gyrus which is the primary auditory cortex, the middle occipital gyrus, which is involved in vision, and the right postcentral gyrus which is involved in orofacial motor activity (See Table 6 for BUMA50's regions of increased activation; See Figure 3 for axial slices of BUMA50's brain activation).

Red= abstract activation, Blue= concrete activation

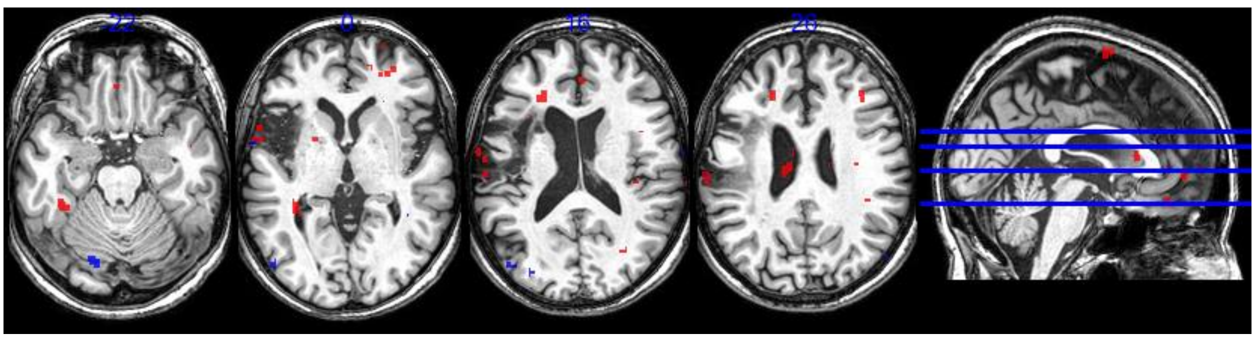

Figure 3. Axial Slices of BUMA50 Brain Activation

Table 6. Brain Activation for BUMA50

	Abstract Post-Pre		*Concrete Post-Pre*		*Word Post-Pre*		*Control Post-Pre*	
Regions	t-value	MNI coordinates	t-value	MNI coordinates	t-value	MNI coordinates	t-value	MNI coordinates
L PoCG	4.27	-58 -2 44						
L PreCG	3.96	-42 10 30						
SPL	3.91	-38 -46 68						
L ROL	4.18	-62 2 2						
L HP	3.74	-34 -20 -12						
L INS	4.02	-40 4 6						
L MFG	3.65	-26 26 32						
R IFGorb	4.29	34 30 -8						
R IFGtri	3.73	38 34 24						
R PoCG	4.03	46 -32 54						
R SFGmed	3.49	14 52 0						
L SMG	4.19	-66 -22 26						
R CBcr-1	5.09	48 -54 -30						
R CB-VI	4.30	40 -48 -26						
L PCL	3.94	-10 -26 82						
L FFG	5.26	-38 -42 -20						
R PCN	3.53	12 -62 30						
R STG	4.12	72 -18 8						

L IFGop	4.47	-60 -12 8						
L PCN	3.53	-8 -52 76						
SMA	4.27	-4 4 78						
R PreCG	4.45	20 -18 80	5.44	20 -18 80				
L HES	4.27	-62 -12 8	4.10	-62 -12 8				
L MOG			3.89	-48 -80 0				
L CB-VI			5.91	-18 -78 -22				
L SPL					3.84	-26 -64 70	4.52	-24 -60 72
L ACC							4.54	2 38 14
L IOG							4.10	-54 -72 -6
R CUN							3.82	14 -88 18
R IPL							5.16	50 -48 54
R SOG							3.86	22 -90 26
R ORBsup							4.87	22 66 -2

Chapter 4

Discussion

BUMA16

This participant has the lowest Aphasia Quotient at 77.7 and it had been almost six and half years since his stroke at the time of data collection, which is the longest time post stroke of the three participants. He was within normal limits on the Boston Naming Test at 87%. The BNT is a confrontation naming task for concrete words and therefore should be easier than a generative naming task used in therapy. His scores on the Psychological Assessment of Language Processing in Aphasia were within normal limits; however, for low imageability words in the written synonym judgement section, his score was 83%, and in high imageabilty words, it was 97%. This shows he has more difficulty with abstract concepts. He also has the highest score of the three participants for categorical word generation for concrete concepts at 33% and the lowest score on abstract concepts at 3%. Most notably, BUMA16 is the only participant who did not generalize from therapy. It is possible it was due to his low aphasia quotient, although another participant had an aphasia quotient only one point higher who successfully generalized. However, he did have the largest effect size for trained abstract words. Therefore, his low categorical word generation score for abstract words did not hinder his ability to attain the largest treatment effect size in abstract words compared to the other participants. Additionally, he has a 33% on the categorical word generation for concrete concepts, which still provides plenty of opportunity for improvement.

During the concrete condition of the fMRI task, BUMA16 showed increased activation in two regions important for concrete processing, the left precuneus and left middle frontal gyrus, as well as each of their right hemisphere homologues. This suggests this participant was increasing use of the regions normally used in concrete processing, but it did not assist with concrete word retrieval during therapy. Also, despite having 100% spared tissue in three major regions involved in concrete processing, the right angular gyrus, the left fusiform gyrus, and the left posterior cingulate, he did not show increased activation in any of these areas after treatment. This could indicate BUMA16 is not being efficient in his neural activation. It is possible the word generation task was more taxing and therefore he wasn't employing his concrete network to the fullest. However, the activation being analyzed is only the increase in activation from post minus pretreatment. It is possible BUMA16 was activating these areas to the best of his ability prior to therapy, and was unable to engage these regions any more.

Additionally, this may suggest that the left fusiform gyrus may be crucial in object processing, and if its activation isn't increased after treatment, it may prevent a participant from generalizing to concrete words. Binder et al. (2009) explains the potential importance of the mid-fusiform gyrus in, "retrieving knowledge about the visual attributes of concrete objects", because it is close to object perception areas (p. 11). The angular gyrus is another pivotal contributor to concrete processing as it's known to be involved in integrating complex information and knowledge retrieval. Its close proximity to visual, spatial, auditory and somatosensory association areas makes it potentially vital in supramodal integration for high level language processing (Binder et al., 2009). BUMA16 did not display increased activation in either the left or right angular gyrus, or the left fusiform gyrus, which all may contribute to him not generalizing from treatment. Overall, BUMA16 shows that he is increasing engagement of some of the concrete network, but not it in its entirety.

BUMA15

This participant has the largest lesion and it had been the least amount of time post stroke at the time of data collection, which was less than two years. This participant's Aphasia Quotient was 78.6 and BUMA15 has the lowest score on the Boston Naming Test at 68%. This participant had the most difficulty with the Psycholinguistic Assessment of Language Processing in Aphasia (PALPA), particularly with low imageability words, as in abstract words because they are more difficult to visualize. On the auditory synonym judgment portion of the PALPA, BUMA15 received a 93% for high imageability words and a 77% for low imageability words. For the written synonym judgment portion, this participant received an 87% for high imageability words and a 77% for low imageability words. These scores are suggesting a strong concreteness effect in this participant. During the categorical word generation task, BUMA15 received the lowest score for concrete words at 17% and also received the lowest score for abstract words, like BUMA16, which was 3%.

After treatment, BUMA15 had a large effect size for abstract words and successfully generalized to concrete words. This participant showed increased activation in the right inferior frontal gyrus pars triangularis in every condition. BUMA15 has only 2.60% spared tissue in the left inferior frontal gyrus pars triangularis, therefore appears to have been activating his right hemisphere homologue in order to compensate for damage to Broca's area. This compensation seems to be aiding his ability to process both abstract and concrete concepts.

Despite having the largest lesion and being the oldest participant, BUMA15 has had the least amount of time since his stroke and was able to respond well to therapy both in the trained and untrained items. He had the most predictable pattern of activation, as he displayed increased activation in regions important for abstract and concrete processing during their respective conditions. His improvement from treatment may reflect the idea that a participant with the most room to improve will do so in the way it's hoped. BUMA15 did not show many regions increase in activation, however this may indicate he is using these areas as effectively as he can, which proved to be successful given his effect sizes.

BUMA50

BUMA50 has the smallest lesion at 62.55 cc and an aphasia quotient at 99.2, which is the highest compared to the other two participants. She also has the highest BNT score at 92% and the highest scores on the Psychological Assessment of Language Processing in Aphasia compared to the other participants. Her only scores on the PALPA lower than a 97% were an 80% in the semantic association section for both high and low imageability words. Although her assessment scores were the best, BUMA50 has the lowest treatment effect size, but also the highest generalization effect size. BUMA50's behavioral assessment scores were not enough to predict her treatment effect size, which is why it's important to assess a participant's change in brain activation in conjunction with behavioral assessments.

BUMA50 showed a considerable amount of increased activation in the abstract condition, but far less for the concrete condition. It's possible she was efficiently utilizing resources for the concrete condition, therefore she did not require a large increase in activation. Her large generalization effect size is most likely associated with her sparing 100% of tissue in the majority of the regions involved in concrete processing like the left fusiform gyrus, left and right angular gyrus, the left inferior temporal gyrus, the left precuneus and the left posterior cingulate. In the abstract condition, it appears BUMA50 is employing the right hemisphere in order to compensate for any deficits she may have in regions involved in abstract processing. She only has 51.35% spared tissue in the left inferior frontal gyrus pars triangularis and showed increased activation in the right hemisphere homologue. She also only has 59.31% spared tissue in the left superior temporal gyrus and also showed increased activation in the right hemisphere homologue in the abstract condition. It's possible her small effect size in trained abstract words is due to damage in regions that are important for abstract word processing. However, BUMA15 only has 2.60% spared tissue in the left inferior frontal gyrus pars triangularis and still showed a large treatment effect size. BUMA16 also has 22.43% spared tissue in the left middle temporal gyrus and 6.60% spared tissue in the left superior temporal gyrus and showed a very large treatment effect size. BUMA50's assessment scores and lesion characteristics are still not supporting why she did not perform strongly in the trained abstract items.

It's possible BUMA50 is showing more increased activation in the right hemisphere because of the Hemispheric Asymmetry Reduction in Old Adults (HAROLD) model, which explains older adults need to engage their right hemisphere more for language processes that once could be accomplished primarily by the left hemisphere (Cabeza, 2001). She showed increased activation in the right hemisphere homologue of the inferior frontal gyrus pars orbitalis, even though she has 100% spared tissue in the left pars orbitalis. It's possible BUMA50 was still utilizing as much of the left inferior frontal gyrus pars orbitalis as she could, and still had to rely on right hemisphere compensation. Cabeza (2001) explains that as adults age, their neural activation becomes less asymmetric. BUMA50 may have already been relying on her right hemisphere due to aging effects, so her increased activation after treatment displays this also.

Overall, BUMA50 shows a large amount of increased activation during the abstract condition for only having a very small treatment effect size, which may indicate her abstract processing is less efficient than her concrete processing. Whether she is recruiting the right hemisphere because of the HAROLD model or due to the amount of lesioned tissue in regions important in abstract processing, Turkeltaub (2011) explains that recruitment of certain areas in the right hemisphere may prevent recovery, rather than facilitate it. Overactive compensatory strategies may inhibit certain neural functions and it is possible BUMA50 is demonstrating this. Although BUMA50 has the smallest lesion, a high aphasia quotient and the largest generalization effect size, her increase in brain activation during the abstract condition appears inefficient in light of her direct training effect size, particularly in comparison to her increased activation during the concrete condition in light of her generalization effect size.

Conclusion

We expected to see increases in activation in regions involved in abstract and concrete processing associated with treatment and generalization effect sizes in participants after they received this treatment. In BUMA15, typical patterns of activation were observed as he increased engagement in regions appropriate in abstract and concrete word processing, but only when necessary. He displayed an adaptive strategy to reorganizing his neural activation as a result of treatment. BUMA16 displayed interesting results as he had a large treatment effect size for trained abstract words, but did not generalize to concrete words. Although BUMA15 and BUMA16 have similar aphasia quotients, BUMA16 showed more of a partial adaptive strategy to his neural organization as he did not appear to utilize his entire concrete network. This could not have been predicted from his behavioral assessments because his score on the Boston Naming Test is within normal limits. BUMA50 has the largest generalization effect size of the three participants, but has a very small treatment effect size for trained abstract words. She has an unexpectedly large amount of increased activation during the abstract condition, which may indicate she was inefficiently processing abstract words. This could not have been predicted solely based on her behavioral assessment scores because she scored so highly on the sections of the PALPA targeting low imageability words. Out of the three participants, based on behavioral assessments alone, we most likely would predict BUMA50 would perform the best in treatment because she has the highest aphasia quotient, BNT score and PALPA scores. However, she showed possibly the most maladaptive reorganization because her increased activation in the abstract condition did not associate with a higher treatment effect size. In conclusion, behavioral assessments alone are not enough to accurately assess effect sizes in treatment. To provide a fuller understanding of how individual participants respond to treatment, fMRI data should be analyzed in conjunction with behavioral data. In the future, more case studies should be used to evaluate how individual characteristics influence improvement in therapy in order to create the most effective treatments for patients with aphasia.

Appendix A

Regions and Corresponding Functions

Regions	**Function**
Inferior Temporal Gyrus	object processing/"what" pathway
L ACC	decision making/inhibitory control
L Calcarine Gyrus	primary visual cortex
L Cerebelum (VI)	retrieving words for speech production output
L Cuneus	vision
L Fusiform Gyrus	object processing/"what" pathway
L Heschls Gyrus	primary auditory
L Hippocampus	memory
L IFG (p. Opercularis)	Broca's Area
L Inferior Occipital Gyrus	vision
L Inferior Parietal Lobule	letter identity
L Insula Lobe	self-referential processing/speech planning
L Lingual Gyrus	reading words
L MCC	response selection and execution
L Middle Frontal Gyrus	word retireval
L Middle Occipital Gyrus	vision
L Middle Temporal Gyrus	semantic access
L Paracentral Lobule	sensory motor cortex
L Postcentral Gyrus	orofacial motor activity
L Precentral Gyrus	orofacial motor activity
L Precuneus	narratives (speech comprehension)
L Rolandic Operculum	language processing
L Superior Frontal Gyrus	word selection
L Superior Medial Frontal Gyrus	concrete processing/DMN
L Superior Parietal Lobule	attention
L SupraMarginal Gyrus	short term memory
R Cerebelum (Crus 1)	motor coordination, language processing
R Cerebelum (VI)	retrieving words for speech production output
R Cuneus	vision
R IFG (p. Orbitalis)	right homologue for Broca'a Area
R IFG (p. Triangularis)	right homologue for Broca'a Area

R Inferior Parietal Lobule	right homologue for letter identity
R Inferior Temporal Gyrus	object processing/"what" pathway
R Lingual Gyrus	right homologue for reading words
R MCC	right homologue for response selection and execution
R Medial Temporal Pole	right homologue for sentence meaning, semantic hub
R Middle Frontal Gyrus	right homologue for word retrieval
R Middle Occipital Gyrus	“where” pathway, visual processing
R Middle Temporal Gyrus	right homologue for semantic access
R Olfactory cortex	olfaction
R Postcentral Gyrus	orofacial motor activity
R Precentral Gyrus	orofacial motor activity
R Precuneus	right homologue for narratives (speech comprehension)
R Rolandic Operculum	right homologue for language processing
R Superior Frontal Gyrus	right homologue for word selection
R Superior Medial Frontal Gyrus	concrete processing/DMN
R Superior Occipital Gyrus	visual processing/"where" pathway
R Superior Orbital Gyrus	decision making/inhibitory control
R Superior Parietal Lobule	attention
R Superior Temporal Gyrus	right homologue for abstract processing
R SupraMarginal Gyrus	short term memory
Supplementary Motor Area	articulatory planning, sub-vocal rehearsal

All regions’ functions cited from Binder et al. (2009), Price (2012), Kemmerer (2015), and Petersen & Posner (2012).

Appendix B

Regions and Corresponding Abbreviations

Abbreviation	Regions
ACC	Anterior Cingulate Cortex
CAL	Calcarine Gyrus
CBcr-1	Cerebelum (Crus 1)
CB-VI	Cerebelum (VI)
CUN	Cuneus
FFG	Fusiform Gyrus
HES	Heschls Gyrus
HP	Hippocampus
IFGop	Inferior Frontal Gyrus (p. Opercularis)
IFGorb	Inferior Frontal Gyrus (p. Orbitalis)
IFGtri	Inferior Frontal Gyrus (p. Triangularis)
IOG	Inferior Occipital Gyrus
IPL	Inferior Parietal Lobule
ITG	Inferior Temporal Gyrus
INS	Insula Lobe
LING	Lingual Gyrus
TPOmid	Medial Temporal Pole
MCC	Middle Cingulate Cortex
MFG	Middle Frontal Gyrus
MOG	Middle Occipital Gyrus
MTG	Middle Temporal Gyrus
OLF	Olfactory cortex
PCL	Paracentral Lobule
PoCG	Postcentral Gyrus
PreCG	Precentral Gyrus
PCN	Precuneus
ROL	Rolandic Operculum
SFG	Superior Frontal Gyrus
SFGmed	Superior Medial Frontal Gyrus
SOG	Superior Occipital Gyrus
ORBsup	Superior Orbital Gyrus
SPL	Superior Parietal Lobule
STG	Superior Temporal Gyrus
SMA	Supplementary Motor Area
SMG	SupraMarginal Gyrus

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