Title

Mitigating Sentence Comprehension Difficulty in Individuals with Aphasia

Author

Akhavan, Niloofar

Publication Date

2022

Peer reviewed|Thesis/dissertation

UNIVERSITY OF CALIFORNIA SAN DIEGO
SAN DIEGO STATE UNIVERSITY

Mitigating Sentence Comprehension Difficulty in Individuals with Aphasia

A Dissertation submitted in partial satisfaction of the requirements
for the degree Doctor of Philosophy

in

Language and Communicative Disorders

by

Niloofar Akhavan

Committee in charge:

San Diego State University

Professor Tracy Love, Chair
Professor Henrike K. Blumenfeld, Co-Chair
Professor Phillip Holcomb
Professor Stephanie Riès

University of California San Diego

Professor Timothy T. Brown
Professor Seana Coulson

2022

The Dissertation of Niloofar Akhavan is approved, and it is acceptable in quality and form for publication on microfilm and electronically.

Co-chair

Chair

University of California San Diego

San Diego State University

2022

DEDICATION

This dissertation is dedicated to my parents, Maryam and Alireza, for their love and limitless encouragement throughout my life. I have no words to thank them for all the dreams and sacrifices they had to let go, just to give me the opportunity at achieving mine.

TABLE OF CONTENTS

LIST OF FIGURES

LIST OF TABLES

ACKNOWLEDGEMENTS

I would like to express my sincere gratitude to my advisor, Dr. Tracy Love, for her support, patience, and encouragement throughout my PhD studies. She has set an example of excellence as a mentor and a leader. I thank her for creating a pleasant and challenging research environment where I could develop my thinking and research skills. My heartfelt appreciation goes to Dr. Henrike K. Blumenfeld for many ways in which she kindly supported me throughout the past years. She was always available to support and advice on any problem, technical or life matter.

I would like to thank Dr. Seana Coulson, Dr. Timothy Brown and Dr. Phillip Holcomb for their guidance and comments as my dissertation committee member. I would like to especially thank Dr. Stephanie Riès for her invaluable advice and guidance on my research studies throughout the past years.

I would like to express my gratitude to Dr. Tilbe Göksun and Dr. Nazbanou Nozari, my advisors during my master’s studies who played important roles in the path I took.

I own loving thanks to Carey Baker and Noelle Abbott, for being my dearest friends and lab mates over the past years. I am grateful for having Yusheng Wang, Jonathan Robinson Anthony, Jacob Momsen, and Christina Sen as my friends and colleagues. Every moment of spending time with these people was precious.

Last, but not least, I would like to thank my family members, Sina, mom, dad and my brother for their love, support, and faith in me.

I am grateful for the financial support of this research from William Orr Dingwall Dissertation Fellowship, UCSD Friend of International, Dr. David Swinney Fellowship, and ASH Foundation Scholarship.

Chapter 2, in full, is a reprint of material as it appears in Akhavan, N., Sen, C., Baker, C., Abbott, N., Gravier, M., & Love, T. (2022). Effect of Lexical-Semantic Cues during Real-Time Sentence Processing in Aphasia. Brain Sciences, 12(3), 312. The dissertation author was the primary investigator and author of this paper.

Chapter 3, in full, is a reprint of material that is currently under review for publication in the Journal of Neurolinguistics. This chapter is coauthored with Dr. Henrike K. Blumenfeld, Dr. Lewis P. Shapiro, and Dr. Tracy Love. The dissertation author was the primary investigator and author of this paper.

Chapter 4 is being prepared for submission for publication of the material. This chapter is coauthored with Yusheng Wang, Dr. Stephanie Riès, and Dr. Tracy Love. The dissertation author was the primary investigator and the primary author of this paper.

.

VITA

2013 Bachelor of Science in Psychology, Middle East Technical University, Turkey

2016 Master of Arts in Psychology, Koç University, Turkey

2022 Doctor of Philosophy in Language and Communicative Disorder, San Diego State University/University of California San Diego

GRANTS

William Orr Dingwall Foundation Dissertation Fellowship in the Cognitive, Clinical, and Neural Foundations of Language (2021-2022)

UCSD Friend of International (2021)

Dr. David Swinney Fellowship (2021)

PUBLICATIONS

Akhavan, N., Blumenfeld, H., Shapiro, L., & Love, T. (under review). Using Lexical Semantics Cue to Mitigate Interference Effects during Real-Time Sentence Processing in Aphasia.

Akhavan, N., Sen, C., Baker, C., Abbott, N., Gravier, M., & Love, T. (2022). Effect of Lexical-Semantic Cues during Real-Time Sentence Processing in Aphasia. *Brain Sciences*, *12*(3).

Akhavan, N., Blumenfeld, H. K., & Love, T. (2020). Auditory sentence processing in bilinguals: The role of cognitive control. *Frontiers in psychology*, *11*, 898.

Akhavan, N., Göksun, T., & Nozari, N. (2018). Integrity and function of gestures in aphasia. *Aphasiology*, *32*(11), 1310-1335.

Akhavan, N., Nozari, N., & Göksun, T. (2017). Expression of motion events in Farsi. *Language, Cognition and Neuroscience*, *32*(6), 792-804.

Akhavan, N., Göksun, T., & Nozari, N. (2016). Disfluency production in speech and gesture. In *CogSci*.

Akhavan, N., Nozari, N., & Göksun, T. (2015). Motion event expressions in language and gesture: Evidence from Persian. In *CogSci*.

Göksun, T., Karaduman, A., Çatak, E., & **Akhavan, N**. (2016). Language and Thought: A Neuropsychological Approach. In M. Irak (Ed.), *Information Processing in Psychopathology: From Theory to Application.*

ABSTRACT OF THE DISSERTATION

Mitigating Sentence Comprehension Difficulty in Individuals with Aphasia

by

Niloofar Akhavan

Doctor of Philosophy in Language and Communicative Disorders

University of California San Diego, 2022
San Diego State University 2022

Professor Tracy Love, Chair
Professor Henrike K. Blumenfeld, Co-Chair

Aphasia is a condition resulting from stroke that impairs individual's communicative abilities. There are currently one million individuals living with aphasia in the US and within this population many have sentence comprehension impairments. This dissertation aims to investigate (1) approaches with which sentence comprehension impairment can be mitigated in individuals with aphasia, and (2) whether the integrity of connectivity between frontal and temporo-parietal regions is predictive of individuals' sensitivity to the proposed mitigation approaches. Overall, the data in the current dissertation revealed that reducing the interference level via semantic cues can benefit the real-time sentence processing in individuals with aphasia. Moreover, there is an emerging pattern for the functional role of the anterior segment of the arcuate fasciculus and frontal aslant tract in the left hemisphere regarding real-time sensitivity to semantic cues during sentence comprehension.

CHAPTER 1

General Introduction

The rapid auditory comprehension of sentences is a remarkable but poorly understood human skill. Listeners must convert incoming acoustic information into a meaningful message. Central to this process is accessing the meaning of each word as it is heard and integrating them into a syntactic structure to form an interpretation of the sentence. Listeners are not typically aware of the processes that lead to final comprehension, but the intricate complexity of sentence processing becomes obvious after an individual suffers neural trauma (e.g., stroke) that results in a language disorder known as aphasia. Aphasia affects nearly one million people in the U.S. (1 in 250) and there are approximately 180,000 new cases per year (Disorders, 2015). Within this population, many suffer from sentence comprehension impairments due to neural lesions in portions of the frontal, temporal, and parietal lobes. This dissertation has two purposes: (1) understanding the nature of sentence impairment in aphasia and proposing approaches for its mitigation; (2) understanding the neural substrates that results in variability among individuals with aphasia (IWA) in benefiting from mitigation approaches.

Sentence-level integration processes

One property of natural language is the ability to integrate sentential constituents and establish linguistic relations between the auditorily incoming sentence components; in other words, creating dependencies as the sentence unfolds in real-time. According to the cue-based retrieval approach, for this process information needs to be encoded, stored in memory, and retrieved at subsequent points for efficient processing (Gibson et al., 2000; Just & Carpenter, 1992; Lewis & Vasishth, 2005). For instance, in object-extracted constructions [1a, 1b], successful parsing requires the retrieval of the direct object of the verb /the general/ to be integrated with the verb when the verb is encountered (known in some linguistic approaches as the 'gap'(Kluender & Kutas, 1993).

[1a] It was the general$_i$ that the lawyer chased$_i$ <~~the general~~> from the office yesterday.

[1b] It was the general$_i$ that Christopher chased$_i$ <~~the general~~> from the office yesterday.

The cue-based parsing approach describes the integration mechanism by indicating that words and phrases in a sentence are stored in memory as a bundle of feature-value pairs (Lewis & Vasishth, 2005; Van Dyke & Lewis, 2003). These features are used as retrieval cues to carry out the search and retrieve a co-dependent item from memory in the integration process. Therefore, successful sentence parsing is accomplished through a series of efficient cue-based memory retrievals. Although using features makes the retrieval mechanism efficient, it makes the process sensitive to interference from elements in memory whose featural specification also matches with the retrieval cues (e.g., interference induced by /the lawyer/ in [1a]) once the verb is encountered (Jäger et al., 2017). The feature competition amongst similar elements of sentence elements in memory decreases the distinctiveness and the quality of those memory representations, ultimately reducing the retrieval probability of the syntactically licensed dependent element at the verb (Hofmeister & Vasishth, 2014; Oberauer & Lange, 2008), thus hindering integration and comprehension accuracy (Gordon et al., 2006). Previous reading studies with unimpaired individuals have demonstrated that a mismatch in the features of encoded referents of the sentence, such as /the general/ and /Christopher/ in [1b] can minimize what is termed similarity-based interference effects and therefore increase the probability of on-time target retrieval of /the general/ after the verb /chased/ and result in successful integration (Gordon et al., 2004; Gordon et al., 2006; Gordon et al., 2002). In addition, other studies have shown that adding a modifier increases the syntactic and semantic representational complexity of the to-be-retrieved item (e.g., “It was the *victorious four-star* general$_i$ that the lawyer…”) and facilitate its representational activation and increase its chances of retrieval when the verb is encountered (Hofmeister, 2011; Hofmeister & Vasishth, 2014). The effect of these manipulations on integration processes have been primarily documented via reading paradigms. This dissertation investigated the integration mechanism moment-by-moment during auditory processing using visual-world eye-tracking paradigm.

Sentence comprehension in aphasia

Individuals with aphasia (IWA) often experience difficulty comprehending sentences, especially when they involve long-distance dependencies, as described above (Caramazza & Zurif, 1976). It is argued that the architecture of the syntactic system is intact, but processing deficiencies lead to pathological computations, which lead to failed comprehension. There are multiple accounts of the nature of sentence processing deficits in IWA. Several researchers have found that sentence processing speed is slowed in aphasia. Some researchers attribute the slowed sentence processing to slowed syntactic computations (Burkhardt et al., 2008) while others suggest that delayed lexical activation in aphasia, compared to neurotypical individuals, crucially affects sentence processing abilities (Ferrill et al., 2012; Love et al., 2008). An alternative account indicates that aberrant lexical integration, rather than slowed processing, may underlie IWA comprehension failure (Dickey et al., 2007). In Event Related Potential studies of N400 effects (a component that reflects semantic processing), IWA showed intact access to multiple meanings of polysemous words, but significant impairments in the selection of appropriate meanings when these words were encountered in sentence contexts (Swaab et al., 1997; Swaab et al., 1998). Similarly, in an eye-tracking-while-listening study, it was argued that IWA demonstrated interference effects in trials where the overall comprehension of sentences was incorrect (Choy & Thompson, 2010; Dickey et al., 2007; Thompson & Choy, 2009). This interference effect was manifested by looks to a competitor rather than target items at the end of the sentence end. These results failed to explain the source of the interference effect during ongoing integration but rather revealed the presence of interference effect during the wrap-up stage for final comprehension. Yet, these findings indicate the susceptibility of IWA to interference in the integration of appropriate lexical information into the syntactic structure to correctly comprehend sentences. Another eye-tracking study also attested to the susceptibility of IWA to interference elicited from similarly structured noun phrases during the integration of non-adjacent sentential elements (Sheppard et al., 2015). From these accounts, it can be inferred that IWA evince sentence integration and comprehension deficits resulting from the disruption in the timely activation of compatible representations and/or experiencing interference when competing representations are available. This dissertation investigates whether interference is the source of auditory sentence comprehension difficulty in aphasia by conducting highly controlled experiments in which the level of interference was modulated using different lexical-semantic cues.

Neural basis of integration in sentence comprehension

Neuroimaging research has suggested that a sentence-level integration mechanism involves cortical activation in widespread regions of the left hemisphere including L-IFG (left-inferior-frontal-gyrus), and L-temporo-parietal regions. However, there is ongoing debate as to the functional role of L-IFG in this process. Existing findings suggest that syntactic and semantic integration can occur with the contribution of left posterior-superior temporal gyrus (pSTG) and left posterior-middle temporal gyrus (pMTG) (Friederici et al., 2003; Yi G. Glaser et al., 2013; Hagoort, 2005), without the involvement of L-IFG when sources of interference are not present (Y. G. Glaser et al., 2013; Matchin & Hickok, 2020; Matchin & Rogalsky, 2017). Moreover, individuals with L-IFG damage can show good comprehension of sentences with low conflict

(Novick et al., 2009). Yet, alternative accounts indicate that L-IFG lesions modulate integration regardless of conflict resolution demands when sentence processing is measured using online approaches (Fedorenko & Blank, 2020; Friederici & Gierhan, 2013; Hagoort, 2005; Love et al., 2008; Nozari et al., 2016; Vuong & Martin, 2015). More specifically, it is reported that specific subregions within L-IFG are involved with distinct processes; Brodmann area[1] (BA) 47 and BA45 of L-IFG are involved in semantic integration, while BA45 and BA44 are purportedly involved in syntactic processing (Hagoort, 2005, 2013). For instance, in an eye-tracking study, individuals with L-IFG (BA44, 45, 47) damage but intact temporo-parietal regions showed less sensitivity to contextual information (e.g., sentences with the restrictive verb /*eat*/ compared to the non-restrictive verb /*see*/ in "*She will eat/see the apple*.") to locate the target (/*apple*/) when conflict resolution demands were minimal (Nozari et al., 2016). The results of this study, which was interpreted under the framework of the Drift Diffusion Model (Ratcliff et al., 2004; Ratcliff & Rouder, 2000), indicated that when the L-IFG is intact, it can affect the drift rate or activation gain parameter by boosting the associations between the bottom-up cues of (/*eat*/) and the target (/*apple*/). Drift rate is defined as the rate of accumulation of information, and it is determined by the quality of the information extracted from the stimulus. Therefore, the L-IFG can play a role in the integration of sentential elements by facilitating the processing of associations when no overt conflict resolution demands are posed. This is in line with other studies that have investigated the role of L-IFG in sentence comprehension using cross-modal priming. Researchers have shown that individuals with damage to the L-IFG evince delayed lexical

[1] The Brodmann areas are a way of mapping the cortex and its distinguished functions, pioneered by Korbinian Brodmann.

activation patterns which can disrupt fast-acting integration processes in both syntactically complex (Love et al., 2008) and simple structures (Ferrill et al., 2012). This processing role of L-IFG is difficult to capture with overt measures of performance such as comprehension accuracy and reaction times, but it can be captured with more sensitive processing measures such as tracking subtle differences in gaze movements and priming effects. According to these accounts, L-IFG damage can lead to disruptions in the timely access of relevant lexical representations as well as the inhibition of irrelevant ones during sentence-level integration (Love et al., 2008; Nozari & Thompson-Schill, 2016).

In addition to the controversies on L-IFG's contribution to sentence processing, less is known about the involvement of white-matter pathways that connect the prefrontal cortex to temoporo-parietal regions, namely the subsections of arcuate fasciculus (AF), frontal aslant tract (FAT), uncinate fasciculus (UF), and inferior fronto-occipital fasciculus (IFOF) (Jung et al., 2017). Currently, there is only evidence of the relationship between the integrity of AF and IFOF and sentence comprehension using offline paradigms which measure final reflective understanding (Wright et al., 2012; Xing et al., 2017) and do not capture the incremental processes involved in sentence comprehension. The functional role of AF-subsections, FAT, UF and IFOF for specific capacities in sentence processing can be captured by combining eye-tracking gaze data with structural lesion analysis and Diffusion Tensor Imaging (DTI) tractography. This dissertation, using a multimodal approach, investigates the neural substrates of the online integration mechanism in sentence comprehension by linking lesion features and real-time sentence processing in a group of individuals with aphasia. Moreover, this dissertation evaluated the integrity of the abovementioned white matter tracts in the right hemisphere (contralateral to the lesioned hemisphere) to examine their functional role in sentence processing.

Dissertation goals and overview

The overarching goal of this dissertation is to investigate (1) the behavioral approaches with which sentence comprehension impairment can be mitigated in individuals with aphasia, and (2) whether the connective integrity between the prefrontal cortex and temporo-parietal regions is predictive of individuals' sensitivity to the proposed mitigation approaches. In this dissertation, we examined the effect of mitigation approaches to the online processing of individuals with aphasia (and unimpaired controls to establish normal patterns of processing) via an eye-tracking-while-listening paradigm and combined it with information about the structural integrity of specific neural regions Diffusion Tensor Imaging (DTI) techniques.

The **behavioral** component of this dissertation includes manipulating the semantic properties of specific lexical items embedded in a sentence to reduce the interference effect during sentence comprehension. These lexical-semantic cues were designed to facilitate processing by a) boosting access of lexical representations (Chapter2), and b) reducing similarity-based interference effects (Chapter 3). Moreover, the **neuroimaging** component of this dissertation included measuring the performance variability within IWA and relating their individual level outcome measures with the DTI data.

The central hypothesis was that manipulating the level of interference level using lexical-semantic cues improve real-time sentence processing of individuals with aphasia. Moreover, if tracts that connect prefrontal cortex to temporo-parietal regions in the left hemispheres are related to online integration, then lack of structural integrity in these connections should manifest as lower sensitivity to the lexical-semantic cues, thus revealing less change in the listener's real-time processing pattern. The structure of this dissertation from this point on is as follows:

Chapter 2 presents an experiment with non-canonical sentences that required long-distance dependency linking. In these sentences, the target noun was manipulated by adding a semantically biasing adjective to boost its representational access (Hofmeister, 2011). To examine the effect of this manipulation, two experimental conditions were designed in which the target noun was either presented with a semantically biased adjective (e.g., /the venomous snake/) or an unbiased adjective (e.g., /the voracious snake/). It was hypothesized that the semantically biasing adjective would facilitate initial encoding of the target noun-phrase and subsequently its retrieval during the dependency linking process. To measure the behavioral differences between the conditions, this experiment utilized a visual-world-eye-tracking-while-listening paradigm to measure the real-time processing patterns and comprehension questions to measure individuals overall understanding of the sentences.

Chapter 3 presents an experiment with canonical sentences that required long-distance dependency linking (via unaccusative verbs). In these sentences that included two noun-phrases, the animacy feature of the noun-phrases were manipulated to create a mismatch condition in order to reduce similarity-based interference effects (Gordon et al., 2006). To examine the effect of this manipulation, two experimental conditions were designed in which the target noun-phrase (/the pirate/- which has a semantically animate feature) was included together with either an inanimate noun-phrase (e.g., /the pirate that observed *the pumpkin*/, mismatch condition) or an animate noun-phrase (e.g., /the pirate that observed *the wizard*/, match condition). It was hypothesized that the mismatch condition would result in a reduced level of the interference effect which would subsequently facilitate retrieval of the target noun-phrase during the dependency-linking process. To capture the change in behavior as a result of this manipulation, this experimental setup included a visual-world-eye-tracking-while-listening paradigm to measure the real-time processing patterns and comprehension questions to measure individuals overall understanding of the sentences.

Chapter 4 presents a study that examined whether damage to AF, FAT, UF and IFOF in the left hemisphere affects sensitivity to lexical-semantic cues. The relationship between the behavioral performances of each IWA and their lesion features were analyzed. To establish lesion profiles, structural lesion mapping and DTI were used to specify lesion size and the integrity of white matter pathways in both the left and right hemispheres. This study investigated the relationship between eye-tracking performance in chapters 2 and 3, and the integrity (i.e., fractional anisotropy) of abovementioned tracts at the individual level in IWA in both the ipsilateral and contralateral lesion hemispheres.

Chapter 5 presents a general conclusion of these studies. This dissertation presented experimental approaches to study sentence processing in aphasia as well as data analysis approaches to examine the relationship between structural integrity and functional outcomes of real-time sentence processing. The findings from this dissertation have the potential to expand on the current models of cognitive engagement, and neural networks underlying language processing in aphasia.

References

Burkhardt, P., Avrutin, S., Piñango, M. M., & Ruigendijk, E. (2008). Slower-than-normal syntactic processing in agrammatic Broca's aphasia: Evidence from Dutch. *Journal of Neurolinguistics, 21*(2), 120-137.

Caramazza, A., & Zurif, E. B. (1976). Dissociation of algorithmic and heuristic processes in language comprehension: Evidence from aphasia. *Brain and Language, 3*(4), 572-582.

Choy, J. J., & Thompson, C. K. (2010). Binding in agrammatic aphasia: Processing to comprehension. *Aphasiology, 24*(5), 551-579.

Dickey, M. W., Choy, J. J., & Thompson, C. K. (2007, 2007/01). Real-time comprehension of wh- movement in aphasia: Evidence from eyetracking while listening. *Brain and Language, 100*(1), 1-22. https://doi.org/10.1016/j.bandl.2006.06.004

Disorders, N. I. o. D. a. O. C. (2015). *NIDCD fact sheet: Aphasia*. NIH Pub. No. 97-4257. https://www.nidcd.nih.gov/sites/default/files/Documents/health/voice/Aphasia6-1-16.pdf

Fedorenko, E., & Blank, I. A. (2020). Broca's area is not a natural kind. *Trends in Cognitive Sciences, 24*(4), 270-284.

Ferrill, M., Love, T., Walenski, M., & Shapiro, L. P. (2012). The time-course of lexical activation during sentence comprehension in people with aphasia. *American Journal of Speech-Language Pathology*.

Friederici, A. D., & Gierhan, S. M. (2013). The language network. *Current opinion in neurobiology, 23*(2), 250-254. https://www.sciencedirect.com/science/article/abs/pii/S0959438812001614?via%3Dihub

Friederici, A. D., Rüschemeyer, S.-A., Hahne, A., & Fiebach, C. J. (2003). The role of left inferior frontal and superior temporal cortex in sentence comprehension: localizing syntactic and semantic processes. *Cerebral Cortex, 13*(2), 170-177.

Gibson, E., Marantz, A., Miyashita, Y., & O'Neil, W. (2000). Image, language, brain: Papers from the first Mind Articulation Project symposium.

Glaser, Y. G., Martin, R. C., Van Dyke, J. A., Hamilton, A. C., & Tan, Y. (2013, Sep). Neural basis of semantic and syntactic interference in sentence comprehension. *Brain Lang, 126*(3), 314-326. https://doi.org/10.1016/j.bandl.2013.06.006

Glaser, Y. G., Martin, R. C., Van Dyke, J. A., Hamilton, A. C., & Tan, Y. (2013, 2013/09). Neural basis of semantic and syntactic interference in sentence comprehension. *Brain and Language, 126*(3), 314-326. https://doi.org/10.1016/j.bandl.2013.06.006

Gordon, P. C., Hendrick, R., & Johnson, M. (2004, 2004/07). Effects of noun phrase type on sentence complexity. *Journal of Memory and Language, 51*(1), 97-114. https://doi.org/10.1016/j.jml.2004.02.003

Gordon, P. C., Hendrick, R., Johnson, M., & Lee, Y. (2006). Similarity-based interference during language comprehension: Evidence from eye tracking during reading. *Journal of experimental psychology: Learning, Memory, and Cognition, 32*(6), 1304. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1766329/pdf/nihms-14274.pdf

Gordon, P. C., Hendrick, R., & Levine, W. H. (2002, 2002/09). Memory-Load Interference in Syntactic Processing. *Psychological Science, 13*(5), 425-430. https://doi.org/10.1111/1467-9280.00475

Hagoort, P. (2005, 2005/09). On Broca, brain, and binding: a new framework. *Trends in Cognitive Sciences, 9*(9), 416-423. https://doi.org/10.1016/j.tics.2005.07.004

Hagoort, P. (2013). MUC (Memory, Unification, Control) and beyond. *Frontiers in psychology, 4*. https://doi.org/10.3389/fpsyg.2013.00416

Hofmeister, P. (2011). Representational Complexity and Memory Retrieval in Language Comprehension. *Lang Cogn Process, 26*(3), 376-405. https://doi.org/10.1080/01690965.2010.492642

Hofmeister, P., & Vasishth, S. (2014). Distinctiveness and encoding effects in online sentence comprehension. *Frontiers in psychology, 5*, 1237.

Jäger, L. A., Engelmann, F., & Vasishth, S. (2017). Similarity-based interference in sentence comprehension: Literature review and Bayesian meta-analysis. *Journal of Memory and Language, 94*, 316-339.

Jung, J., Cloutman, L. L., Binney, R. J., & Ralph, M. A. L. (2017). The structural connectivity of higher order association cortices reflects human functional brain networks. *Cortex, 97*, 221-239.

Just, M. A., & Carpenter, P. A. (1992). A capacity theory of comprehension: individual differences in working memory. *Psychological Review, 99*(1), 122.

Kluender, R., & Kutas, M. (1993). Bridging the gap: Evidence from ERPs on the processing of unbounded dependencies. *Journal of cognitive neuroscience, 5*(2), 196-214.

Lewis, R. L., & Vasishth, S. (2005). An activation□based model of sentence processing as skilled memory retrieval. *Cognitive science, 29*(3), 375-419. https://onlinelibrary.wiley.com/doi/pdfdirect/10.1207/s15516709cog0000_25?download=true

Love, T., Swinney, D., Walenski, M., & Zurif, E. (2008). How left inferior frontal cortex participates in syntactic processing: Evidence from aphasia. *Brain and Language, 107*(3), 203-219. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2650827/pdf/nihms-79787.pdf

Matchin, W., & Hickok, G. (2020). The cortical organization of syntax. *Cerebral Cortex, 30*(3), 1481-1498. https://academic.oup.com/cercor/article-abstract/30/3/1481/5588467?redirectedFrom=fulltext

Matchin, W., & Rogalsky, C. (2017). Aphasia & syntax.

Novick, J. M., Kan, I. P., Trueswell, J. C., & Thompson-Schill, S. L. (2009). A case for conflict across multiple domains: Memory and language impairments following damage to ventrolateral prefrontal cortex. *Cognitive Neuropsychology, 26*(6), 527-567.

Nozari, N., Mirman, D., & Thompson-Schill, S. L. (2016, Jun-Jul). The ventrolateral prefrontal cortex facilitates processing of sentential context to locate referents. *Brain Lang, 157-158*, 1-13. https://doi.org/10.1016/j.bandl.2016.04.006

Nozari, N., & Thompson-Schill, S. L. (2016). Left Ventrolateral Prefrontal Cortex in Processing of Words and Sentences. In *Neurobiology of Language* (pp. 569-584). https://doi.org/10.1016/b978-0-12-407794-2.00046-8

Oberauer, K., & Lange, E. B. (2008). Interference in verbal working memory: Distinguishing similarity-based confusion, feature overwriting, and feature migration. *Journal of Memory and Language, 58*(3), 730-745.

Ratcliff, R., Gomez, P., & McKoon, G. (2004). A diffusion model account of the lexical decision task. *Psychological Review, 111*(1), 159.

Ratcliff, R., & Rouder, J. N. (2000). A diffusion model account of masking in two-choice letter identification. *Journal of Experimental Psychology: Human perception and performance, 26*(1), 127.

Sheppard, S. M., Walenski, M., Love, T., & Shapiro, L. P. (2015). The auditory comprehension of wh-questions in aphasia: Support for the intervener hypothesis. *Journal of Speech, Language, and Hearing Research, 58*(3), 781-797. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4490095/pdf/JSLHR-58-3-781.pdf

Swaab, T., Brown, C., & Hagoort, P. (1997). Spoken sentence comprehension in aphasia: Event-related potential evidence for a lexical integration deficit. *Journal of cognitive neuroscience, 9*(1), 39-66.

Swaab, T. Y., Brown, C., & Hagoort, P. (1998, 1998/08). Understanding ambiguous words in sentence contexts: electrophysiological evidence for delayed contextual selection in Broca's aphasia. *Neuropsychologia, 36*(8), 737-761. https://doi.org/10.1016/s0028-3932(97)00174-7

Thompson, C. K., & Choy, J. J. (2009). Pronominal resolution and gap filling in agrammatic aphasia: Evidence from eye movements. *Journal of psycholinguistic research, 38*(3), 255-283. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2823636/pdf/nihms176438.pdf

Van Dyke, J. A., & Lewis, R. L. (2003). Distinguishing effects of structure and decay on attachment and repair: A cue-based parsing account of recovery from misanalyzed ambiguities. *Journal of Memory and Language, 49*(3), 285-316.

Vuong, L., & Martin, R. (2015). The role of LIFG-based executive control in sentence comprehension. *Cognitive Neuropsychology, 32*(5), 243-265. https://www.tandfonline.com/doi/full/10.1080/02643294.2015.1057558

Wright, P., Stamatakis, E. A., & Tyler, L. K. (2012). Differentiating hemispheric contributions to syntax and semantics in patients with left-hemisphere lesions. *Journal of Neuroscience, 32*(24), 8149-8157.

Xing, S., Lacey, E. H., Skipper-Kallal, L. M., Zeng, J., & Turkeltaub, P. E. (2017). White Matter Correlates of Auditory Comprehension Outcomes in Chronic Post-Stroke Aphasia. *Front Neurol, 8*, 54. https://doi.org/10.3389/fneur.2017.00054

CHAPTER 2

Effect of Lexical-Semantic Cues during Real-Time Sentence Processing in Aphasia

brain sciences

MDPI

Article

Effect of Lexical-Semantic Cues during Real-Time Sentence Processing in Aphasia

Niloofar Akhavan [1,2,3,*], Christina Sen [1,2,3], Carolyn Baker [1,2,3], Noelle Abbott [1,2,3], Michelle Gravier [4] and Tracy Love [1,2,3]

1 School of Speech, Language, and Hearing Sciences, San Diego State University, San Diego, CA 92182, USA; csen7960@sdsu.edu (C.S.); cjbaker@ucsd.edu (C.B.); ntodd6857@sdsu.edu (N.A.); tlove@sdsu.edu (T.L.)
2 Department of Cognitive Science, University of California San Diego, San Diego, CA 92122, USA
3 Joint Doctoral Program in Language and Communicative Disorders, San Diego State University/ University of California San Diego, San Diego, CA 92182, USA
4 Department of Speech, Language and Hearing Sciences, California State University East Bay, Hayward, CA 94542, USA; michelle.gravier@csueastbay.edu
* Correspondence: nakhavan@ucsd.edu

Abstract: Using a visual world eye-tracking paradigm, we investigated the real-time auditory sentence processing of neurologically unimpaired listeners and individuals with aphasia. We examined whether lexical-semantic cues provided as adjectives of a target noun modulate the encoding and retrieval dynamics of a noun phrase during the processing of complex, non-canonical sentences. We hypothesized that the real-time processing pattern of sentences containing a semantically biased lexical cue (e.g., the venomous snake) would be different than sentences containing unbiased adjectives (e.g., the voracious snake). More specifically, we predicted that the presence of a biased lexical cue would facilitate (1) lexical encoding (i.e., boosted lexical access) of the target noun, snake, and (2) on-time syntactic retrieval or dependency linking (i.e., increasing the probability of on-time lexical retrieval at post-verb gap site) for both groups. For unimpaired listeners, results revealed a difference in the time course of gaze trajectories to the target noun (snake) during lexical encoding and syntactic retrieval in the biased compared to the unbiased condition. In contrast, for the aphasia group, the presence of biased adjectives did not affect the time course of processing the target noun. Yet, at the post-verb gap site, the presence of a semantically biased adjective influenced syntactic re-activation. Our results extend the cue-based parsing model by offering new and valuable insights into the processes underlying sentence comprehension of individuals with aphasia.

Keywords: semantic cue; eye tracking; real-time sentence processing; syntax; aphasia

Citation: Akhavan, N.; Sen, C.; Baker, C.; Abbott, N.; Gravier, M.; Love, T. Effect of Lexical-Semantic Cues during Real-Time Sentence Processing in Aphasia. *Brain Sci.* **2022**, *12*, 312. https://doi.org/10.3390/brainsci12030312

Academic Editors: Jason Rothman, Vincent DeLuca, Alicia Luque, Yanina Prystauka and Toms Voits

Received: 14 December 2021
Accepted: 22 February 2022
Published: 25 February 2022

1. Introduction

One property of language processing is the ability to integrate sentential constituents and establish linguistic relationships between non-adjacent pieces of information. This latter process creates syntactic dependencies and is critical for the determination of the underlying meaning of the sentence. To successfully understand an utterance, the listener must assign appropriate roles of the nouns to the linked verbs in the sentence. This is accomplished automatically (i.e., it is an automatic process which is a reflexive, unconscious, moment by moment operations that unfolds in real-time during sentence processing) through thematic role assignment (for example, determining which noun is the agent or actor and which noun is the theme or object of the verb). In English (which has a strict subject–verb–object word order), this process aligns quite nicely with the order of input of a simple active sentence (1a); that is, the first noun encountered is the actor or agent, and the noun after the verb is the object. This process is also simple for more complex sentence constructions that maintain canonical word order, such as those found in subject-relative constructions (1b):

(1a) The girl *hits* the boy.

(1b) The girl that *hits* the boy is angry.

(1c) The boy$_i$ that the girl *hit*$_i$ <~~the boy~~> was angry.

This automatic process of assigning thematic roles becomes more challenging for listeners when the sentence structure deviates from the canonical word order. Sentence (1c), above, is an example of a non-canonical sentence (object-relative construction). In this example, the object of the verb 'hit' (/the boy/) is fronted or displaced to the beginning of the sentence, causing it to be structurally separated from its underlying (post-verb) position. When processing this sentence, the listener, upon hearing the verb, must link the verb to its object (noted by the subscript 'i'). This retrieval process allows for its integration with the syntactic and semantic properties of the verb to facilitate interpretation.

Numerous studies have found evidence of re-activation of the direct object at the gap site (the position from where the noun phrase has been displaced is known as a gap; the 'i' indexation represents a link between the verb and its structurally licensed direct object) using various online methodological approaches including probe recognition tasks [1], cross-modal priming tasks [2], and eye-tracking [3,4]. Although dependency linking occurs rapidly and relatively automatically in neurologically healthy individuals, the associated processing cost is higher in non-canonical sentences compared to canonically ordered constructions due to the need of forming long-distance dependencies [5–9]. Theoretical models of sentence processing, namely cue-based parsing, make specific predictions regarding the processing costs associated with long-distance dependencies. According to these models, the success (as measured by reaction time methods) of retrieving the displaced constituent (i.e., syntactic dependency linking) is a function of the degree of interference from similar items in memory that compete with the retrieval of the target item [9–11]. The higher the interference, the more likely the wrong target will be retrieved. Although these models are based on data from neurotypical adults, interference has also been found to contribute to comprehension impairments in post-stroke aphasia [3,12,13]. For individuals with aphasia, the presence of interference can overwhelm the impaired system and lead to breakdowns in comprehension [14–17], thus the focus of the current study (see Section 1.3 below).

It is generally accepted that comprehension deficits in aphasia are not the result of an irrevocable loss of stored linguistic representations [15,18], but rather stem from disruptions to the automatic operations involved in sentence processing. According to some researchers, these deficits stem from processing impairments at the lexical level [16,19–23] which includes disruptions to the processes of lexical access and integration. These are fundamental mechanisms that provide the system with timely lexical information and allow for the incorporation of that information into a syntactic frame. Lexical-level deficits can emerge from impairments of representational encoding and retrieval which can amplify the effects of interference. As described below, the current paper investigates whether semantic-level manipulations during encoding can reduce interference effects and alleviate retrieval difficulties during sentence processing [24,25]. We expect the semantic-level manipulations during encoding to facilitate (1) lexical processing (i.e., boost representational access) and (2) online syntactic dependency linking (i.e., reduce interference effect) in neurologically unimpaired adults as well as in individuals with aphasia.

1.1. *Interference Effect during Sentence Processing*

As discussed previously, under many theoretical accounts, the successful linking processing of the verb "chased" in object-relative sentences such as (2) depends on the retrieval of its syntactic direct object *bear* upon encountering the verb *chased* [26–28].

(2) It was the bear$_i$ that the hunters chased$_i$ in the cold forest yesterday.

According to the cue-based parsing retrieval theory, a memory representation of the noun *bear*, is formed (encoded) as a bundle or vector of certain syntactic and semantic features such as [+nominative; +animate; +singular] that are activated when the noun is first encountered in the sentence. These features remain active in some form of memory—but outside the focus of attention—as the sentence constituents unfold. When the comprehender reaches a retrieval point (e.g., the verb), the representation of the noun phrase (NP; "the bear") must be integrated into the structural frame to be assigned its thematic role. Cue-based parsing theory assumes that dependencies are resolved via a direct-access operation based on their representational content (i.e., content addressability) [29–31]. For example, at the verb 'chased' in sentence (2), a retrieval mechanism based on linguistic and contextual features is assumed to be immediately triggered, which seeks out a representation with the [+nominative; +animate] features (i.e., something that can be chased). During this content-addressable search, these features or retrieval cues are matched against all possible candidates (i.e., recently activated items) in memory. The likelihood of retrieving a given item is determined by the strength of the match between the features encoded with a given item and the features contained in the retrieval cue.

Although the cue-based parsing approach does not make specific predictions regarding the quality of encoding having an impact on retrieval probability and latency, recent studies have shown that enriching a word, via the addition of modifiers, facilitates its subsequent retrieval compared to conditions in which the same word is left unmodified [24,25,32–34]. In a self-paced reading study, Hofmeister (2011) investigated reading times in neurologically unimpaired participants for sentences which contained a critical noun that was either modified by zero, one, or two adjectives (low, mid, and high complexity conditions, respectively); see (3) below for an example of the high complexity condition. Note that the brackets, parentheses, and indexation have been added to highlight the manipulation but were not used in the study itself.

(3) It was [the injured and dangerous bear]$_i$ that the hunters chased$_i$ in the cold forest yesterday.

This study reported decreased reading times for the main verb for items in the highest complexity condition (i.e., where the direct object noun was preceded by two adjectives) compared to the other conditions. In a similar experiment, such findings were also observed for nouns that were semantically richer/more specific (e.g., "soldier") compared to less semantically rich/less specific (e.g., "person"). Hofmeister (2011) interpreted these results as evidence that, for unimpaired comprehenders, the addition of semantic and syntactic features increased the uniqueness of the target representation compared to other lexical items in the sentence and facilitated retrieval of information and subsequent integration later in the sentence. This finding is in accordance with the predictions of encoding interference, which is assumed to arise from competition associated with the encoding of items with similar features [35]. By increasing the distinctness of the target item, a higher-quality representation was created, reducing encoding interference. An additional finding was increased encoding times for the more complex NP, which may have indexed additional cognitive effort required to perform combinatorial processing (i.e., incorporating the adjectives into the NP). Increased cognitive effort and the extended time dedicated to the NP within the auditory signal may have both served to raise the salience or activation level of the representational network [11,36].

1.2. Evidence from Aphasia of the Effect of Lexical Processing Deficits on Syntactic Processing

As previously mentioned, lexical processing accounts suggest that auditory comprehension deficits in individuals with aphasia (IWA) are mainly due to lexical processing impairments. One such account is the delayed lexical activation hypothesis [16,19], which claims that slowed lexical activation precludes the timely formation of syntactic structure building as the parser is not provided with the necessary lexical information when needed. Delayed lexical activation occurs in both canonical and non-canonical sentences; however, when a delay occurs in non-canonical constructions, it feeds the syntactic processor too slowly, throwing off retrieval, which results in comprehension breakdowns. Evidence for this hypothesis comes from studies with IWA that have found delayed activation of NPs when they were first encountered in an auditory object-relative sentence as well as at the gap site following a verb [16]. The delayed re-activation of the displaced direct object NP was taken as evidence that IWA are able to perform syntactic computations;

reaches a retrieval point (e.g., the verb), the representation of the noun phrase (NP; "the bear") must be integrated into the structural frame to be assigned its thematic role. Cue-based parsing theory assumes that dependencies are resolved via a direct-access operation based on their representational content (i.e., content addressability) [29–31]. For example, at the verb 'chased' in sentence (2), a retrieval mechanism based on linguistic and contextual features is assumed to be immediately triggered, which seeks out a representation with the [+nominative; +animate] features (i.e., something that can be chased). During this content-addressable search, these features or retrieval cues are matched against all possible candidates (i.e., recently activated items) in memory. The likelihood of retrieving a given item is determined by the strength of the match between the features encoded with a given item and the features contained in the retrieval cue.

Although the cue-based parsing approach does not make specific predictions regarding the quality of encoding having an impact on retrieval probability and latency, recent studies have shown that enriching a word, via the addition of modifiers, facilitates its subsequent retrieval compared to conditions in which the same word is left unmodified [24,25,32–34]. In a self-paced reading study, Hofmeister (2011) investigated reading times in neurologically unimpaired participants for sentences which contained a critical noun that was either modified by zero, one, or two adjectives (low, mid, and high complexity conditions, respectively); see (3) below for an example of the high complexity condition. Note that the brackets, parentheses, and indexation have been added to highlight the manipulation but were not used in the study itself.

(3) It was [the injured and dangerous bear]$_i$ that the hunters chased$_i$ in the cold forest yesterday.

This study reported decreased reading times for the main verb for items in the highest complexity condition (i.e., where the direct object noun was preceded by two adjectives) compared to the other conditions. In a similar experiment, such findings were also observed for nouns that were semantically richer/more specific (e.g., "soldier") compared to less semantically rich/less specific (e.g., "person"). Hofmeister (2011) interpreted these results as evidence that, for unimpaired comprehenders, the addition of semantic and syntactic features increased the uniqueness of the target representation compared to other lexical items in the sentence and facilitated retrieval of information and subsequent integration later in the sentence. This finding is in accordance with the predictions of encoding interference, which is assumed to arise from competition associated with the encoding of items with similar features [35]. By increasing the distinctness of the target item, a higher-quality representation was created, reducing encoding interference. An additional finding was increased encoding times for the more complex NP, which may have indexed additional cognitive effort required to perform combinatorial processing (i.e., incorporating the adjectives into the NP). Increased cognitive effort and the extended time dedicated to the NP within the auditory signal may have both served to raise the salience or activation level of the representational network [11,36].

1.2. Evidence from Aphasia of the Effect of Lexical Processing Deficits on Syntactic Processing

As previously mentioned, lexical processing accounts suggest that auditory comprehension deficits in individuals with aphasia (IWA) are mainly due to lexical processing impairments. One such account is the delayed lexical activation hypothesis [16,19], which claims that slowed lexical activation precludes the timely formation of syntactic structure building as the parser is not provided with the necessary lexical information when needed. Delayed lexical activation occurs in both canonical and non-canonical sentences; however, when a delay occurs in non-canonical constructions, it feeds the syntactic processor too slowly, throwing off retrieval, which results in comprehension breakdowns. Evidence for this hypothesis comes from studies with IWA that have found delayed activation of NPs when they were first encountered in an auditory object-relative sentence as well as at the gap site following a verb [16]. The delayed re-activation of the displaced direct object NP was taken as evidence that IWA are able to perform syntactic computations;

however, this process is slowed compared to neurologically unimpaired comprehenders. In this same study, Love and colleagues (2008) found that when the rate of speech input was slowed, IWA showed both on-time initial lexical activation and re-activation at the post-verb gap site, and critically, improved final sentence comprehension. Several other studies with IWA using various methods have also found either delayed lexical activation and/or delayed integration of lexical information into the sentence context [21,37]. For example, Swaab and colleagues (1997), in an event-related potential study, reported that IWA had an N400 component (a neurophysiological index of semantic integration processing) upon hearing a sentence-final word that violated the sentential-semantic constraints (e.g., "The girl dropped the candy on the sky") that were either reduced in amplitude or delayed compared to neurologically unimpaired individuals [20,21]. Other studies using the eye-tracking-while-listening paradigm (ETL) have also indicated processing deficits in IWA. In an ETL visual world paradigm, participants are asked to listen to sentences over headphones while viewing a visual array displaying four items (characters mentioned in the sentence as well as item(s) unrelated to the sentence). The timing of eye gazes to the characters on the screen while listening to the unfolding sentences is argued to index underlying linguistic processing in real-time [38–41]. Many studies using ETL consistently indicated a late-emerging influence of competitor interpretations during sentence processing for IWA (i.e., interference effects) in incorrectly comprehended trials, providing further evidence for delayed integration [12,13,23]. In these ETL studies, the delay in lexical activation is proposed to result in interference effects when subsequent sentence constituents are activated during auditory processing. Altogether, these studies support the idea that encoding deficits at the lexical level plays a significant role in sentence processing, and consequently comprehension deficits for IWA. These findings are also in line with theoretical models of sentence processing such as the cue-based parsing theory which proposes that representational encoding at the word level is the core component of the sentence processing mechanism.

1.3. The Current Study

Using the eye-tracking-while-listening method, we investigate whether local contextual information at the semantic level (provided by an adjective preceding a target lexical item) can be used to facilitate the representational encoding of the nouns for listeners with and without aphasia during sentence processing. We further investigate whether the encoding pattern has any downstream effects on the retrieval of the target representations during dependency linking for both groups. Previous studies on this topic have primarily used self-paced reading paradigms to explore these effects during real-time sentence processing [24,25]. To tap into real-time auditory sentence processing, we employed the ETL method with a visual world paradigm (VWP). This method allows us to explore the time course of the proposed manipulation and its effect on processing throughout the sentence. As mentioned above, the way in which a word is encoded during sentence processing will impact the processing of subsequent constituents in the sentence. Therefore, to distill the encoding process of nouns, we examined their activation and de-activation patterns during an ongoing stream of the sentence (see Figure 1). The activation pattern is an indication of processing phonological and semantic features to access the target item (manifested as an increasing pattern of gaze movement toward an item). The de-activation pattern is an indication of a change in the level of representation at that time. Here, we operationalized de-activation as representing a shift **from** integrating the previously processed constituent into the sentence structure **to** accessing the new input. This is manifested as a decreasing pattern of gaze movement away from an item. Moreover, to distill the retrieval process that is involved in the verb-frame window, we examined the re-activation of the displaced object and its interference with distractor nouns in the sentence. The interference pattern is an indication of the competitive processing between the nouns that are lingering to be linked to the verb for the means of thematic role assignment.

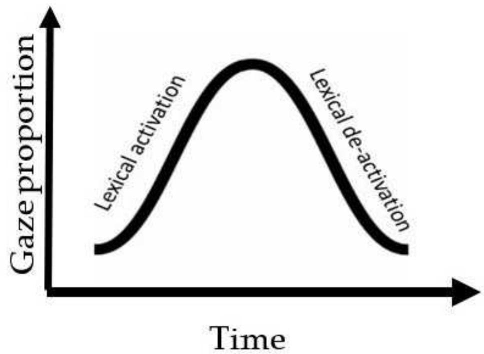


Figure 1. An illustration of the overall pattern of lexical processing in an ongoing sentence that involves an activation and de-activation phase. Activation is represented by increase in gaze proportion toward the heard item in the sentence while de-activation is represented by reduction in gaze proportion over time.

Table 1 demonstrates the different types of gaze movements that can be used as a metric to reflect varying stages of sentence processing including lexical and structural processing.

Table 1. Gaze movement metrics of specific sentence-level processes.

Processing Level	Gaze Movement Pattern
Lexical access	Gaze movement toward a visual representation of a target noun upon hearing it in the sentence
Lexical integration	After lexical access, gaze divergence from a previously accessed target noun indicates its integration into the syntactic structure
Dependency linking	Gaze movement that returns to a noun representation that was previously activated (re-activation) when it is syntactically licensed
Interference effects	An equivalent proportion of gazes toward related as well as non-target nouns (i.e., that are not relevant at a given point in a sentence) indicates an individual's susceptibility to the interference effect

Here, we hypothesized that the lexical-semantic cues (in form of adjectives, see examples 4a and 4b) would facilitate (1) lexical encoding (i.e., boost representational access) and in turn (2) on-time syntactic retrieval or dependency linking (i.e., increasing the probability of on-time lexical retrieval at the gap site) during auditory sentence processing for both groups. Based on prior research, we anticipate that the overall pattern of online processing in individuals with aphasia to be delayed across conditions compared to the pattern in neurologically unimpaired individuals [13,16,23].

(4a) Unbiased adjective: The eagle saw the voracious snake$_i$ that the bear cautiously encountered$_i$ <~~the snake~~> underneath the narrow bridge.
(4b) Biased adjective: The eagle saw the venomous snake$_i$ that the bear cautiously encountered$_i$ <~~the snake~~> underneath the narrow bridge.

2. Methods

2.1. Participants

Eleven individuals with chronic aphasia (IWA: female = 5, M_{age} = 54.2 years, SD_{age} = 8.2) and 11 age-matched controls (AMC: female = 7, M_{age} = 61.9, SD_{age} = 2.3) were recruited for this study. The inclusion criteria for both groups were as follows: participants were monolingual native English speakers with no exposure to a foreign language before the age of six; right handed (premorbidly for IWA); had no self-reported history of emotional or learning disorders or drug abuse and had normal to corrected self-reported vision and hearing. IWA had to have experienced a single left-hemisphere stroke at least 6 months prior to participation to control for the effect of spontaneous recovery. The diagnosis and severity of aphasia were assessed using standardized aphasia examinations, the Boston Diagnostic Aphasia Examination (BDAE-version 3; [42]) and the Western Aphasia Battery-Revised (WAB-R; [43]), and were confirmed by clinical consensus. Sentence comprehension ability was assessed using the S.O.A.P. Test of Sentence Comprehension [44] (see Table 2); IWA participants in this study demonstrated comprehension deficits, which we defined as at- or below-chance performance on the comprehension of sentences with non-canonical word order (object relatives and passives). The neurologically unimpaired age-matched participants additionally had no self-reported history of brain injury. Participants were excluded from this study if they did not meet the above criteria or were unable to understand directions and complete this study.

Table 2. IWA Participants' characteristics ($n = 11$).

IWA	Sex	Years Post-Stroke	Age at Testing	Years of Education	Aphasia Subtype	Lesion Location	BDAE-v3	WAB-R AQ	SOAP-SR (%)	SOAP-OR (%)
009	M	15	55	17	Mixed non-fluent	Large L lesion, IFG (BA 44/BA45) w/posterior	4	67.7	60%	40
017	M	18	66	15	Anomic	L anterior cerebral and middle cerebral infarct	4	95.4	100	90
101	M	9	67	20	Broca	Large L lesion posterior IFG (BA 44) w/posterior	2	82.6	100	30
130	M	8	63	16	Broca /Anomia	L IPL with posterior ext. sparing STG	4	90.5	75	55
140	F	16	42	-	-	L MCA infarct	2	75.7	80	30
151	F	7	65	16	Anomic	L MCA infarct with subcortical extension	4	95.8	100	100
159	F	6	64	16	Broca	L MCA infarct	3	92.4	100	70
165	F	4	64	12	Broca	L MCA infarct	3	ND	80	60
169	M	4	59	12	Broca	L MCA infarct	2	28.2	80	40
190	F	6	76	12	Broca	Left superior temporal lobe	3	88.2	90	40
191	M	1	57	16	Broca	L MCA infarct	4.5	98.4	100	60
AMC Group	Ages 57–66 years (mean = ~61.9); 7 females, 4 males; education 14–18 years (mean = 15.7) *									

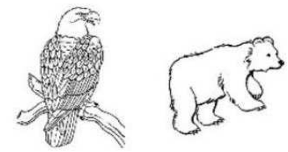
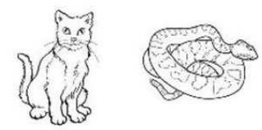
M = male, F = female; L = left; LH = left hemisphere; BA = Brodmann area; IPL = inferior parietal lobule; STG = superior temporal gyrus; MCA = middle cerebral artery. BDAE = Boston Diagnostic Aphasia Examination (0 = no usable speech or auditory comprehension; 5 = minimal discernable speech handicap). SOAP SR = average percent correct on subject-relative items from the SOAP Test of Auditory Sentence Comprehension. SOAP OR = average percent correct of object relative items from the SOAP Test of Auditory Sentence Comprehension. * Missing education data for four AMC individuals.

All participants were tested at the Language and Neuroscience Group Laboratory at San Diego State University and were paid $15 per session. A review of treatment history reveals that six of our seven participants had received prior treatment for sentence-level deficits, though the extent of treatment (number of sessions, type of treatment, and treatment response) was not available.

2.2. Materials

This study utilized eye-tracking-while-listening with a visual world paradigm (ETL-VWP) to measure auditory sentence processing in real time. In this paradigm, participants listen to sentences over headphones while viewing a 2×2 visual array displaying four items (three characters mentioned in the sentence and one item unrelated to the sentence). The timing of eye gazes to the characters on the screen while listening to the unfolding sentences, such as those shown in Table 3, is argued to index underlying linguistic processing in real time [45,46].

Table 3. Example of experimental sentence and visual stimuli.

Condition	Sample Sentence	Visual Array
Unbiased Adjective	"The eagle saw the voracious snake that the bear cautiously encountered underneath the narrow bridge."	
Biased Adjective	"The eagle saw the venomous snake that the bear cautiously encountered underneath the narrow bridge."	

2.2.1. Visual Stimuli

Visual stimuli consisted of freely available black-and-white line drawings of animals obtained from the internet and clip art resources that were resized to 450 $\times$ 450 pixels. During each trial, 4 images were displayed on the screen. Three of the images corresponded to each of the nouns in the experimental sentence. The fourth image was an unrelated control (e.g., "cat" in Table 3, above). The location of the images was counterbalanced across trials such that pictures corresponding to each noun in the sentence appeared equally as often in the 4 quadrants.

Visual stimuli pretesting: All images used in the experiment had 90% or greater name agreement on a naming pretest conducted with college-aged students naive to the goals of the present experiment (n = 34, M_{age} = 20.1 years, SD = 1.4).

2.2.2. Sentence Stimuli

The experimental sentences consisted of 30 sentence pairs (60 sentences total) containing non-canonical object-relative constructions that involved a long-distance dependency linking the displaced object (e.g., /snake/) and the relative clause verb (e.g., /encountered/; see Appendix A for the full list of sentences). These sentences were presented in two conditions: with a semantically neutral adjective preceding the displaced NP (i.e., the unbiased adjective condition), or with a semantically related adjective preceding the displaced NP (i.e., the biased adjective condition; see Table 3). The unbiased condition was included to control for the potential effect of the presence of a modifier increasing the salience of the NP (i.e., cognitive effort related to combinatorial processing) and to allow for isolation of the unique effect of the semantic information provided by the adjective (i.e., feature enrichment). In addition to these experimental sentences, 60 canonical sentence structures were included as non-experimental filler sentences. All sentences were recorded by a native English-speaking female at an average rate of 4.47 syllables per second. Each sentence trial was followed by a yes/no question to ensure that participants attended to the sentences.

Sentence stimuli pretesting: Two pretests were conducted to ensure the selection of strong semantically related experimental adjective–noun pairs in the biased condition. In the first pretest, neurologically unimpaired college-aged participants (n = 34, M_{age} = 20.1 years, SD = 1.4) were shown a series of 120 black and white line drawings one at a time and were instructed to generate a descriptive word (an adjective) that corresponded with the image pictured. Sixty adjective–noun pairs were chosen for which a minimum agreement criterion (i.e., the concurrence of adjective choice (exact or semantically related) across participants) of 50% was met (M = 61%, SD = 10%). As a follow-up, a second pretest assessing semantic relatedness was conducted on the sixty adjective–noun pairs that were generated from the first pretest (e.g., "venomous snake"). A separate group of neurologically unimpaired college-aged participants (n = 23, M_{age} = 23.3 years, SD = 3.7) rated the semantic relatedness of each adjective–noun pair using a 5-point Likert scale (1 = Not Related; 5 = Highly Related). The thirty adjective–noun pairs with the highest ratings were selected for the ETL-VWP experiment (M = 4.59, SD = 0.41). To create an unbiased match for each of the experimental sentences, unbiased or neutral adjectives were chosen that were matched for syllable length, lexical frequency, and phonemic onset ($t(59) = 0.08$, $p = 0.94$).

2.3. Procedure

This was a within-subjects experiment in which the trials were distributed and counterbalanced across 4 visits. Visits were spaced a minimum of one week apart. At the beginning of each visit, 10 practice trials were conducted to ensure understanding of the task. During the practice trials, the experimenter provided feedback as necessary. During each visit, participants were seated 60 cm from a computer screen with an attached Tobii X-120 eye-tracker and wore over-the-ear headphones for auditory stimulus presentation. The eye-tracker was calibrated at the beginning of each experimental session. Across each trial, gaze location was sampled at a rate of 60 Hz (every 17 ms) from both eyes. Stimuli were presented using E-Prime 2.0 software (Psychology Software Tools, Pittsburgh, PA, USA). Each trial began with a fixation cross presented for 500 ms, followed by a blank screen for 250 ms. Next, the four-picture display was presented for 1500 ms before the auditory sentence began and remained on screen for 500 ms after the sentence ended (see Figure 2). To ensure that all participants were attending to the sentences, following each trial, an offline measure was administered during which participants heard a question related to the sentence (e.g., was the bear under the narrow bridge?). Participants were instructed to respond as quickly as possible with a binary decision via a button box (YES/NO) using their left, non-dominant hand. The questions were either related to the action of the first or the third noun phrase of each sentence so as not to bring specific attention to the target displaced object NP. Half of the questions were designed to elicit a YES response.

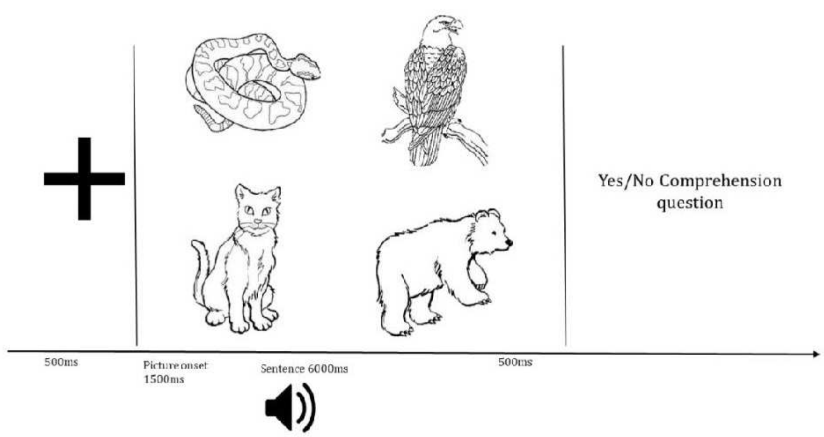


Figure 2. Example of a visual world eye-tracking paradigm. The speaker represents the auditory sentence.

2.4. Analysis Approach

Preprocessing and analyses of eye-tracking data were performed using the eyetrackingR package [47] in R (R Core Team, 2019). In this study, gaze data from 60 trials across 22 individuals (11 in each AMC and IWA group) were sampled. All data across both groups and conditions were inspected to ensure that gaze patterns for the initial NP were evident. Furthermore, visual inspection revealed that for two sentences (in the biased condition) there were no discernable gazes to the first noun in the sentence (N1) after the auditory presentation of N1. Based on the rationale that lack of gazes to NP1 reflected either technical errors in gaze sampling during data collection or listeners' difficulty distinguishing the visual items on the screen, data from these two sentences were removed from further analysis. Moreover, data from one sentence (from the unbiased condition) was excluded from analysis as the gaze patterns reflected semantic biasing towards a distractor noun in the sentence. In total, data from the 57 remaining experimental sentences were subjected to further analyses.

2.4.1. Preprocessing

Preprocessing of the eye-tracking data was conducted to check for trackloss, aggregate the data points across trials, and group them into temporal bins. Trackloss occurs when the gaze data are unavailable for both of the participant's eyes (e.g., when they turn away or blink), which results in the validity of recorded gaze location being low (Tobii's acceptable validity range is 0–2 on the scale of up to 4). Trials in which the trackloss proportion was greater than 25% were excluded from further analyses resulting in the removal of data from 19% of the trials. After reviewing the number of remaining trials available for analysis, it was determined that any participant who had more than 50% of their trials excluded due to the criteria listed above was to be removed from further analysis. This resulted in the exclusion of three participants (2 in the AMC and 1 in the IWA group) from the dataset. Data from the remaining 9 AMC and 10 IWA participants were aggregated across trials and aggregated into 100 ms time-bins. This approach is used as a strategy to account for the inherent dependency in time-series eye-tracking data which can inflate type I error rates. For each bin, the proportion of gaze within each AOI from the binary response variable (within or outside of an AOI) were estimated [48]. Gaze proportions were then subjected to statistical analysis (described below).

2.4.2. Statistical Analysis Approaches

Growth curve analysis (GCA) was used to explore the dynamic patterns of gaze movement over time in a preselected window of interest within the sentence. The GCA approach has been widely used in the analysis of gaze data in the visual world paradigm [49–54]. GCA is a multi-level modeling technique specifically designed to capture change over time using orthogonal polynomials [50]. The effects of the variables of interest on the polynomial terms provide a way to quantify and evaluate those effects on statistically independent (i.e., orthogonal) aspects of the gaze proportion trajectory. In the GCA approach, the level 1 model captures the overall gaze time course, with the intercept term reflecting the average overall gaze proportion. The linear term reflects a monotonic change in gaze proportion (similar to a linear regression of gaze proportion as a function of time) while the quadratic term reflects the symmetric rise and fall rate around a central inflection point [50]. The level 2 submodels capture the fixed effects of experimental conditions or group effects (categorical variables) on the level 1 time terms. The models in the current study included random effects of participants and items on intercept, linear, and quadratic time terms. Moreover, random slopes for condition were added per subject to achieve a maximal random effects structure [55]. Using the GCA approach, the fixed effects of variables of interest were added individually and their effects on the model were evaluated using model comparisons in order to examine whether a particular effect made a statistically significant contribution to model fit. Improvements in model fit were evaluated using -2 times the change in log-likelihood, which is distributed as x^2 with degrees of freedom equal to the number of parameters added [48]. In this study, all analyses were conducted with the statistical software R-3.2.1, using the package LmerTest [56].

Cluster analysis was used to determine whether there were any time windows in which the looking patterns significantly differed between conditions (e.g., biased versus unbiased) within groups. The rationale of this method is to identify whether there is a series of consecutive time bins that show a significant effect of conditions. If the number of the consecutive time bins is larger than the observed null distribution, we can be confident that that the gaze pattern is different for the two conditions during the specified time window. Cluster analysis has been used in EEG studies [57] and in the visual world paradigm [52,58,59]. In this method, a separate test for the critical interaction at each individual time-bin was conducted (see below). If the time bins (20 ms) pass a determined threshold (p-value smaller than 0.05), then the adjacent time bins are clustered together. Finally, to correct for multiple comparisons, a non-parametric permutation test was conducted to determine the p-value for given cluster size. For this analysis, we used the eyetrackingR divergence analysis package [47].

3. Results

Offline processing: Recall that participants were asked a yes/no question after each trial to ensure that they paid attention to the sentences. While these data were not used to inform the online analysis, we conducted a mixed-effects logistic regression model to explore group and condition differences. The results revealed an effect of group (AMC and IWA); specifically, the IWA group performed worse than the AMC group (estimate = -1.12, SE = 0.23, $p < 0.05$). No effect of condition was found for accuracy within the AMC or IWA group (AMC: biased = 77.8%, unbiased = 79.3%; IWA: biased = 60.6%, unbiased = 61.4%).

Online processing: The subsequent analyses are focused on the condition differences between each group at specified windows of interest that are discussed in Figure 3.

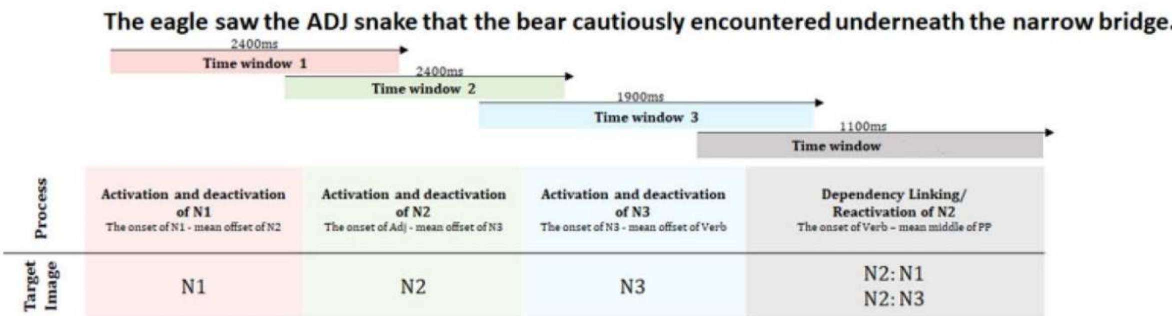


Figure 3. Specified windows of interest. The arrows represent when in the sentence a prespecified window starts and ends. The windows of analysis were overlapping as we wanted to capture the full morphology of the gaze pattern toward a targeted image. In these windows, we capture the activation (gazes toward) and deactivation (gazes away) parts of lexical processing. Here, we divided our sentence into four analysis windows to capture processing patterns via the gaze dynamics to the three images of the nouns that were mentioned in the sentence (here N1 represents the illustration of eagle, N2 the snake, N3 the bear).

Figure 4 represents the time course of gazes during sentence processing for the two groups (AMC and IWA) across the two conditions (biased and unbiased). As shown in Figure 4 using colored dashed lines, there are critical parts of the sentences that were the focus of the analysis as described below.

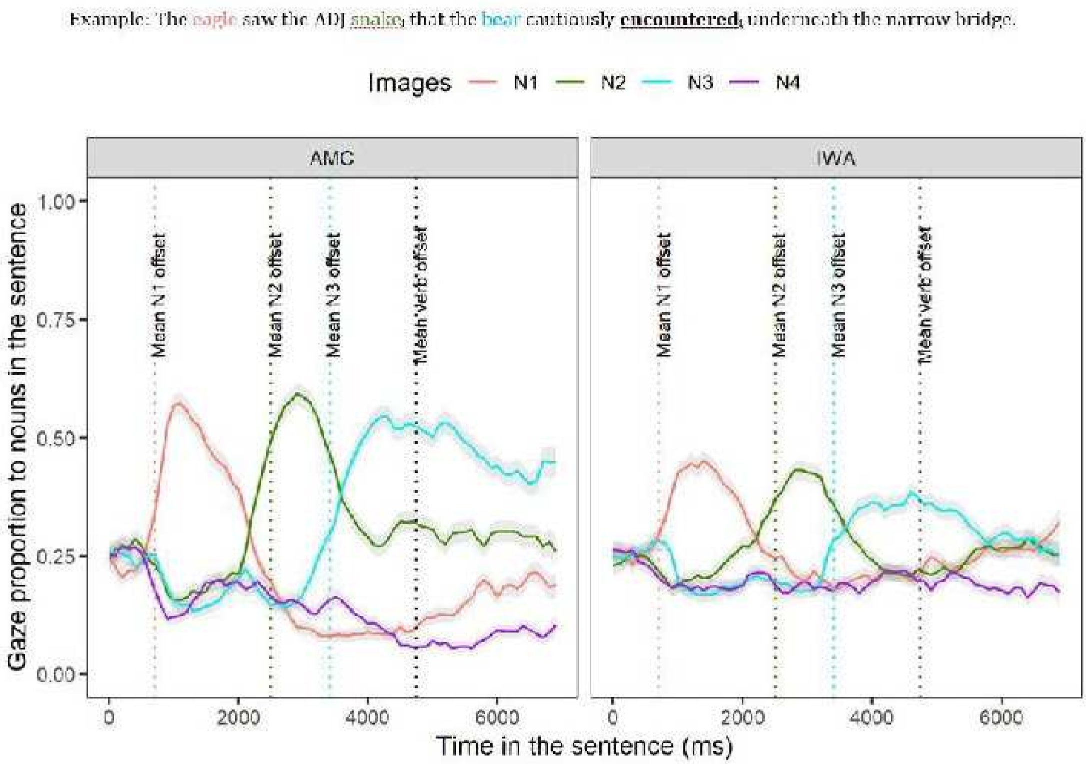


Figure 4. Mean gaze over time toward N1 (first noun, solid salmon line), N2 (second noun, solid green line), N3 (third noun, solid blue line), and a distractor image (solid purple line) averaged across conditions for each group which begins at the auditory onset of the sentence (N1), N4 (unrelated noun, purple line). Shaded areas represent 95% confidence intervals within subject. The dotted salmon line represents mean offset N1; the dotted green line represents mean offset N2; the dotted blue line represents mean offset N3; the dotted black line represents mean offset of the verb.

3.1. *Experimental Condition Effect on Lexical Processing*

In an ongoing sentence, the way in which a word is processed will impact the processing of subsequent words in the sentence. Below, we present the processing patterns of nouns starting from the beginning of the sentence and moving forward in time in a linear fashion. In the following section, we examine the processing of each noun by analyzing their activation as well as de-activation patterns.

3.1.1. Effect of Condition on Encoding the Noun Preceding the Manipulation (N1)

Here, we examined if the adjective manipulation affected the processing of the preceding noun (e.g., deactivation of N1 upon hearing the adjective). We specified the window of analysis to occur 100 ms after the onset (this parameter allows time for planning and execution of an eye movement) of the first noun phrase until 2500 ms afterward (corresponding to the average offset of N2—"the eagle saw the/adjective/snake", see Figure 3). Gaze data and curve fits for the interaction effects of group (AMC, IWA) and condition (biased and unbiased) for processing N1 are plotted in Figure 5 (see Appendix B for GCA modeling details). Upon visual inspection, unlike the IWA, the AMC show a stronger de-activation pattern in the biased condition compared to the unbiased condition.

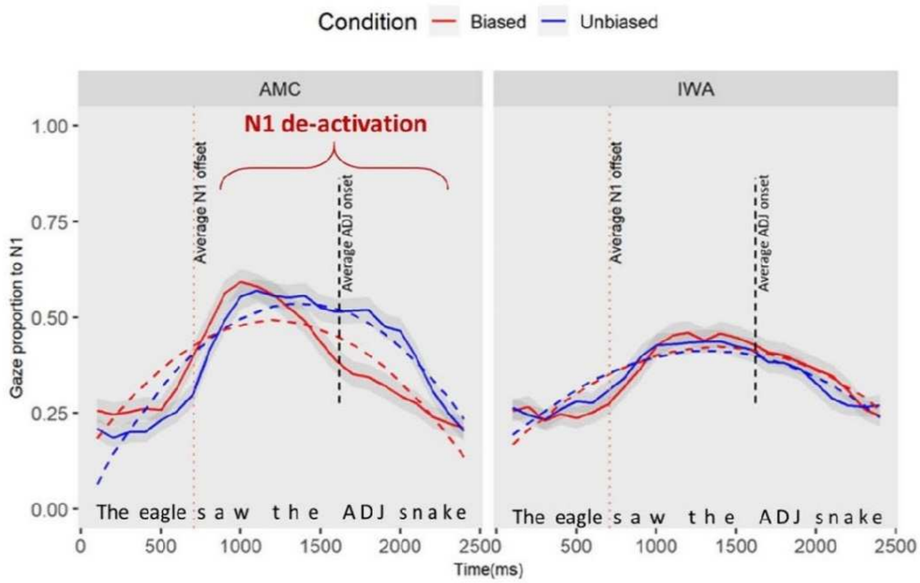


Figure 5. The plot captures the part of the sentence as "the eagle saw the/adjective/snake". This plot demonstrates the gaze proportion differences to N1 between conditions and groups. Solid lines represent observed data and dashed lines represent the GCA model fit. The graphic representation of the model is showing the quadratic fit, yet the significant results for the condition effect were observed at the linear term.

The results of the individual parameter estimates revealed a simple effect of condition at the linear term which indicates that the average rate of change in gazes to and away from N1 for the AMC group changed in the biased condition compared to the unbiased condition (estimate = 0.31, SE = 0.13, $t = 2.50$, $p = 0.02$). The positive estimate indicated that the average rate of N1 processing (i.e., activation and deactivation over time) was lower in the unbiased condition compared to the biased condition. Moreover, there was an interaction effect of group and condition at the linear term (estimate = −0.37, SE = 0.14, $t = -2.67$, $p = 0.01$): the negative estimates on the linear terms indicated that the difference in the processing of N1 between conditions in the IWA group is smaller than the difference between the two conditions for the AMC group. Table 4 shows the full results of this analysis.

Table 4. Results of GCA analysis for time window 1 (processing N1).

Predictors	Estimates	CI	P (Two Tailed)
(Intercept)	0.37	0.31–0.42	<0.001
Linear	−0.08	−0.31–0.15	0.506
Quadratic	−0.53	−0.72–−0.34	<0.001
Condition [Unbiased]	0.02	−0.03–0.07	0.497
Group [IWA]	−0.02	−0.09–0.05	0.512
Linear × Condition [Unbiased]	**0.31**	**0.07–0.56**	**0.012**
Quadratic × Condition [Unbiased]	−0.05	−0.24–0.14	0.589
Linear × Group [IWA]	0.19	−0.09–0.47	0.178
Quadratic × Group [IWA]	0.20	−0.03–0.43	0.093
Condition [Unbiased] × Group [IWA]	−0.02	−0.06 0.02	0.367
(Linear × Condition [Unbiased]) × Group [IWA]	**−0.37**	**−0.64–−0.10**	**0.008**
(Quadratic × Condition [Unbiased]) × Group [IWA]	0.07	−0.14–0.27	0.523

Note: The table provides the test of the full model including the interaction of group and condition on the intercept, linear, and quadratic time terms. The AMC group and the biased condition are set as the reference estimates. Results in **boldface** are presented in the text.

In summary, the GCA analysis suggests that there is a main effect of condition for the AMC group. To understand when in the time course the difference between conditions occurred, we conducted a permutation cluster analysis. In 2000 permuted samples, with an alpha of 0.05, the analyses revealed one significant cluster within 1640–2280 (cluster sum statistic = 97.03, $p = 0.01$) which corresponded with the onset of the adjective. Therefore, the difference between conditions for AMC individuals occurred at the point where the biased adjective was heard in the sentence. Moreover, when the adjective was semantically biased toward the next upcoming item (N2), AMC listeners showed an earlier disengagement from N1.

3.1.2. Effect of Condition on Encoding the Noun following the Manipulation (N2)

Recall that time window 2 begins at the onset of the adjective until the average offset of noun 3 ("the/adjective/snake that the bear", see Figure 3). Here, we seek to capture the effect of adjective bias on the processing patterns of the upcoming noun (N2). We employed the same analysis approach as described above in time window 1 (see Appendix C for GCA modeling details). Table 5 shows the full results of this analysis and Figure 6 shows the trajectory of effects.

Table 5. Results of GCA analysis for time window 2 (processing N2).

Predictors	Estimates	CI	P (Two Tailed)
(Intercept)	0.38	0.33–0.43	<0.001
Linear	0.35	0.07–0.62	0.014
Quadratic	−0.51	−0.71–−0.31	<0.001
Condition [Unbiased]	0.01	−0.05–0.07	0.763
Group [IWA]	**−0.05**	**−0.11–0.00**	**0.066**
Linear × Condition [Unbiased]	**0.20**	**−0.02–0.41**	**0.078**
Quadratic × Condition [Unbiased]	0.11	−0.07–0.30	0.237
Linear × Group [IWA]	−0.12	−0.48–0.23	0.497
Quadratic × Group [IWA]	0.18	−0.06–0.43	0.149
Condition [Unbiased] × Group [IWA]	−0.00	−0.06–0.06	0.971
(Linear × Condition [Unbiased]) × Group [IWA]	**−0.22**	**−0.46–0.02**	**0.075**
(Quadratic × Condition [Unbiased]) × Group [IWA]	−0.08	−0.27–0.10	0.362

Note: The table provides the test of the full model including the interaction of group and condition on the intercept, linear, and quadratic time terms. The AMC group and the biased condition are set as the reference estimates. Results in **boldface** are presented in the text.

The result of the individual parameter estimates revealed a marginal effect of the group at the intercept term (estimate = −0.05, SE = 0.02, $t = -1.84$, $p = 0.066$): this negative estimate, while not statistically significant at the 0.05 level, suggests that the average proportion of gazes toward N2 in the IWA is less than the AMC group. In addition, there was a marginal effect of condition for the AMC group at the linear term (estimate = 0.20, SE = 0.11, $t = 1.76$, $p = 0.08$): the positive estimate indicates that that the average rate of N2 processing (i.e., activation and deactivation over time) was lower in the unbiased condition compared to the biased condition. While not statistically significant at the 0.05 level, this result suggests that the average rate of change in looking at the N2 for the AMC is different between the conditions. Furthermore, the results revealed a marginal interaction effect of group and condition at the linear term (estimate = −0.22, SE = 0.12, $t = -1.78$, $p = 0.07$): the negative estimates on the linear terms indicated that the difference in the processing of N2 between conditions in the IWA group is smaller than the difference between the two conditions in the AMC. Overall, the GCA analysis indicated no effect of the biased conditions for the IWA group.

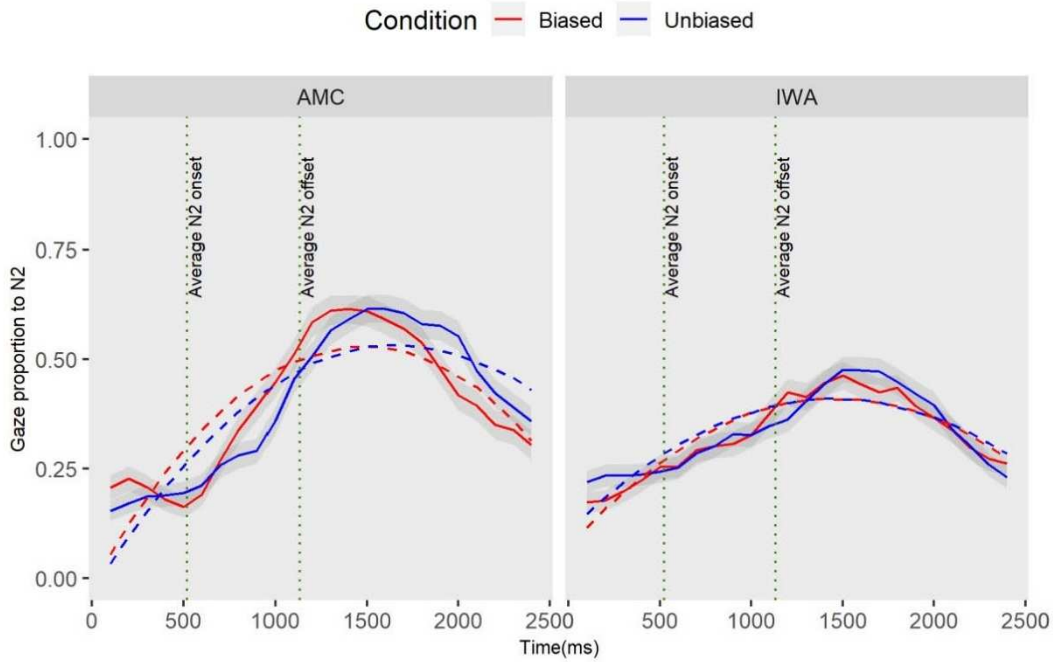


Figure 6. The plot captures the following part of the sentence "/adjective/snake that the bear". This plot demonstrates the gaze proportion differences to N2 between conditions and groups. Solid lines represent observed data and dashed lines represent the GCA model fit. The graphic representation of the model is showing the quadratic fit, yet the marginal results for the group effect were observed at the intercept level, in addition to the interaction effect which was significant at the linear term.

The GCA analysis revealed a marginal difference between the groups on the proportion of gazes toward N2. Moreover, the results revealed a marginal effect of condition in the AMC group. To determine when in the time course the difference between conditions occurred for the AMC group, we conducted a permutation cluster analysis. In the 2000 permuted samples, with an alpha of 0.05, the analyses revealed one significant cluster within 1920–2160 (cluster sum statistic = −40.56, $p = 0.06$) which corresponds with the offset of the N2. The marginal difference between conditions for AMC individuals occurred later when N3 was heard in the sentence. The biased condition resulted in an earlier disengagement from the N2 compared to the unbiased condition. Therefore, the condition difference is mainly reflected in the earliness of disengaging from the already activated item. The analysis of the downstream effect of adjectives on encoding the third noun (N3) is discussed in Appendix D.

In summary, the results of encoding the noun phrases (N1, N2, and N3) revealed that the presence of the adjective had a local effect during processing the first and second nouns in the sentence for the AMC group. In the biased condition, the AMC group revealed earlier disengagement from N1 and N2 upon hearing the next upcoming target nouns which means that the addition of adjective had facilitated the semantic integration processes as the speech stream unfold. However, IWA revealed impaired lexical processing patterns when compared with AMC. This was demonstrated by the lower rate of the magnitude of gaze proportions toward the targeted nouns upon hearing them in the sentence among IWA.

3.2. Experimental Condition Effect on Syntactic Retrieval

Recall that in the post-verb window, successful dependency linking is evidenced as a re-activation of the direct-object noun (N2). The post-verb window is specified to begin at the onset of the verb until 1200 ms afterward (corresponding to "encountered$_i$ underneath the narrow", see Figure 3) to allow time for re-activation at the verb site as well as the spillover region. In this window, we explored whether re-activation occurred and inspected the presence of an interference effect during dependency linking by analyzing the gaze proportion of N2 (to-be-retrieved noun, henceforth "target") relative to N1 and N3 (interfering nouns, henceforth "competitors"). Based on the cue-based parsing approach, upon encountering the verb, retrieval cues are triggered to search for a direct-object noun (N2); however, there are additional noun phrases whose features overlap with the target creating competition between the target (N2) and the non-target nouns (N1 and N3). Of importance is how the biased adjective is modulating the interference effects of non-target items across the groups. The evidence for the re-activation of N2 in the gap site (verb-frame) across the AMC and IWA groups is discussed in Appendix E. In the sections that follow, we examined each group separately and explored the effect of condition on the interference effects of N1 (3.2.1) and N3 (3.2.2) during re-activation of N2.

3.2.1. Effect of Condition on Re-Activation of N2 Relative to N1 at the Verb-Frame (Time Window 4b)

After establishing the presence of re-activation, the next question is whether the adjectives led to facilitation in retrieval. To understand the effect of condition on the proportion of N2 retrieval at the gap site, we built separate models for each group by including the interaction of fixed effect of images (N2 and N1) and condition. This interaction term reflects the extent to which the difference between N2 and N1 fixation time courses differed between conditions.

The individual parameter estimates for the AMC group (Table 6) revealed that the activation of N2 was lower in the unbiased condition compared to the biased condition (estimate = −0.031, SE = 0.02, $t = -1.97$, $p < 0.05$).

Table 6. Results of GCA analysis of AMC data for time window 4 (processing N2 relative to N1).

Predictors	Estimates	CI	P (Two Tailed)
(Intercept)	0.12	0.04–0.19	0.002
Linear	0.01	−0.12–0.14	0.857
Quadratic	0.03	−0.04–0.10	0.413
Images [N2]	0.19	0.11–0.27	<0.001
Condition [Unbiased]	0.00	−0.04–0.05	0.924
Linear × Images [N2]	0.05	−0.11–0.20	0.547
Quadratic × Images [N2]	−0.02	−0.12–0.08	0.725
Linear × Condition [Unbiased]	−0.06	−0.17–0.06	0.333
Quadratic × Condition [Unbiased]	−0.07	−0.15–0.00	0.059
Images [N2] × Condition [Unbiased]	**−0.03**	**−0.06–−0.00**	**0.049**
(Linear × Images [N2]) × Condition [Unbiased]	−0.04	−0.14–0.07	0.473
(Quadratic × Images [N2]) × Condition [Unbiased]	0.05	−0.05–0.16	0.323

Note: The table provides the test of the full model including the interaction of condition and images of interest (N1 and N2) on the intercept, linear, and quadratic time terms. The biased condition and the N1 are set as the reference estimate. Results in **boldface** are presented in the text.

The individual parameter estimates for IWA (Table 7) revealed that the activation level of the N1 competitor was higher in the unbiased condition compared to the biased one (estimate = 0.05, SE = 0.02, $t = 2.15$, $p < 0.05$). Moreover, the activation of target N2 at the intercept level was lower in the unbiased condition (estimate = −0.10, SE = 0.01, $t = -6.26$, $p < 0.05$) compared to the biased condition. There was a significant interaction effect at the linear term that revealed a later emerging increase in activation of N2 in the unbiased condition (estimate = 0.24, SE = 0.05, $t = 4.79$, $p < 0.05$).

Overall, these results indicate a larger interference effect of N1 in the unbiased condition. Nevertheless, the lexical-semantic cues in the biased condition did not seem to benefit the IWA listeners enough to robustly reactivate N2 compared to N1.

Table 7. Results of GCA analysis of IWA data for time window 4 (processing N2 relative to N1).

Predictors	Estimates	CI	P (Two Tailed)
(Intercept)	0.20	0.14–0.25	<0.001
Linear	0.06	−0.01–0.12	0.081
Quadratic	−0.03	−0.08–0.02	0.255
Images [N2]	0.03	−0.02–0.09	0.217
Condition [Unbiased]	**0.05**	**0.00–0.10**	**0.031**
Linear × Images [N2]	−0.12	−0.21–−0.04	0.003
Linear × Images [N2]	0.03	−0.04–0.10	0.362
Linear × Condition [Unbiased]	**−0.11**	**−0.19–−0.04**	**0.004**
Quadratic × Condition [Unbiased]	0.07	0.00–0.15	0.044
Images [N2] × Condition [Unbiased]	**−0.10**	**−0.13–−0.07**	**<0.001**
(Linear × Images [N2] × Condition [Unbiased]	**0.24**	**0.14–0.34**	**<0.001**
(Quadratic × Images [N2] × Condition [Unbiased]	−0.05	−0.15–0.05	0.359

Note: The table provides the test of the full model including the interaction of condition and images of interest (N1 and N2) on the intercept, linear, and quadratic time terms. The biased condition and the N1 are set as the reference estimate. Results in boldface are presented in the text.

Altogether, these sets of results from AMC and IWA indicated that the adjective type affected the dynamics of target re-activation at the gap site. In the biased condition, for the AMC group, the level of N2 re-activation was higher. Moreover, for the IWA group, the level of target N2 activation was higher while N1 interference was reduced (see Figure 7, red boxes).

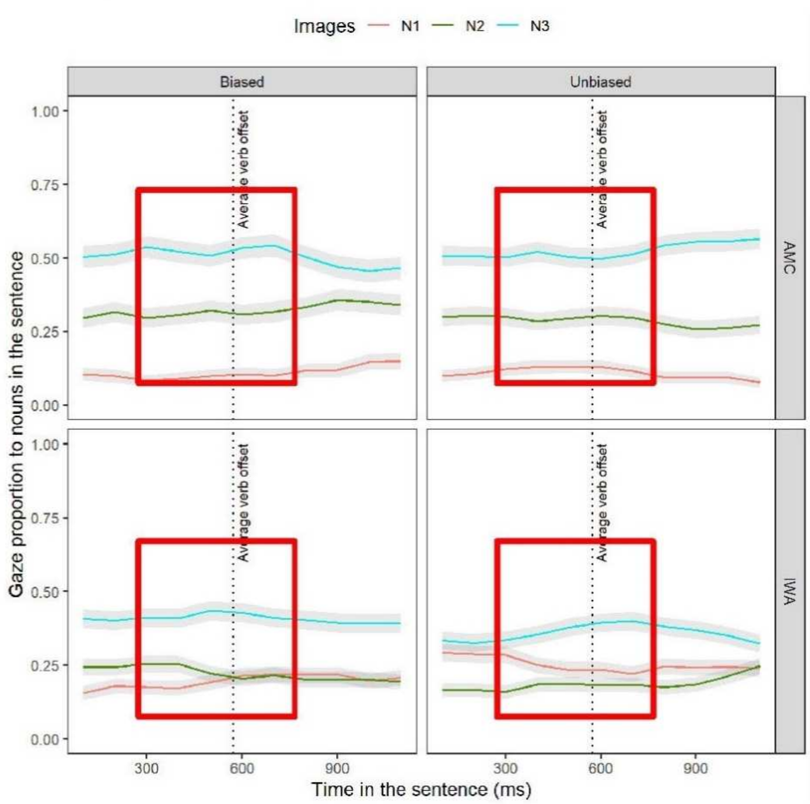


Figure 7. Averaged gaze proportions to N1, N2, and N3 between groups and conditions. This is the raw data observation of gaze toward N1, N2, and N3 in the verb-frame window. The gray shaded ribbons around the lines represent standard errors. The red boxes indicate the window in which the effect is expected.

3.2.2. Effect of Condition on Re-Activation of N2 Relative to N3 at the Verb-Frame (Time Window 4b)

After establishing the interference effect of N1, we conducted another analysis to observe the interference effect of N3 (subject of the relative-clause verb) during the re-activation of N2. Previously, we discussed that the recently activated representation of N3 can induce an interference effect during N2 re-activation. To investigate the effect of condition on the interference effect of N3, we repeated the same models for each group that was constructed before and looked at the interaction of condition with images N2 and N3.

The results of the AMC group (Table 8) revealed that the re-activation of N2 was lower in the unbiased condition when compared to the biased one (linear term estimate = −0.10, SE = 0.05, $t = -2.22$, $p < 0.05$). Moreover, the activation of N3 was higher in the unbiased condition (intercept term estimate = 0.04, SE = 0.02, $t = 2.02$, $p < 0.05$) and its rate was increasing (linear term estimate = 0.21, SE = 0.06, $t = 3.19$, $p < 0.05$) when compared to the biased condition. These results revealed that the biased adjective affected the dynamics of target re-activation at the gap site and reduced the interference effect of N3.

Table 8. Results of GCA analysis of AMC data for time window 4 (processing N2 relative to N3).

Predictors	Estimates	CI	P (Two Tailed)
(Intercept)	0.31	0.21–0.41	<0.001
Linear	0.07	−0.08–0.21	0.368
Quadratic	0.01	−0.06–0.08	0.777
Images [N3]	0.21	0.07–0.35	0.003
Condition [Unbiased]	−0.03	−0.07–0.00	0.080
Linear × Images [N3]	−0.10	−0.31–0.11	0.347
Quadratic × Images [N3]	−0.07	−0.17–0.03	0.168
Linear × Condition [Unbiased]	**−0.10**	**−0.19–−0.01**	**0.026**
Quadratic × Condition [Unbiased]	−0.02	−0.11–0.07	0.654
Images [N3] × Condition [Unbiased]	**0.04**	**0.00–0.08**	**0.044**
(Linear × Images [N3]) × Condition [Unbiased]	**0.21**	**0.08–0.33**	**0.001**
(Quadratic × Images [N3]) × Condition [Unbiased]	0.11	−0.02–0.23	0.089

Note: The table provides the test of the full model including the interaction of condition and images of interest (N2 and N3) on the intercept, linear, and quadratic time terms. The biased condition and the N2 are set as the reference estimate. Results in **boldface** are presented in the text.

The results of the IWA group (Table 9) revealed an earlier increase in the rate of N2 activation overtime in the biased compared to the unbiased condition (linear term estimate 0.13, SE = 0.04, $t = 3.09$, $p < 0.05$). Yet, the activation dynamics of N3 did not change between the conditions.

Table 9. Results of GCA analysis of IWA data for time window 4 (processing N2 relative to N3).

Predictors	Estimates	CI	P (Two Tailed)
(Intercept)	0.23	0.15–0.31	<0.001
Linear	−0.07	−0.14–0.01	0.073
Quadratic	0.00	−0.07–0.07	0.986
Images [N3]	0.18	0.07–0.28	0.001
Condition [Unbiased]	−0.04	−0.09–0.01	0.118
Linear × Images [N3]	0.04	−0.05–0.14	0.368
Quadratic × Images [N3]	−0.02	−0.12–0.07	0.638
Linear × Condition [Unbiased]	**0.13**	**0.05–0.21**	**0.002**
Quadratic × Condition [Unbiased]	0.03	−0.05–0.10	0.474
Images [N3] × Condition [Unbiased]	0.01	−0.03–0.04	0.687
(Linear × Images [N3]) × Condition [Unbiased]	−0.09	−0.19–0.02	0.101
(Quadratic × Images [N3]) × Condition Unbiased]	−0.08	−0.19–0.02	0.128

Note: The table provides the test of the full model including the interaction of condition and images of interest (N2 and N3) on the intercept, linear, and quadratic time terms. The biased condition and the N2 are set as the reference estimate. Results in **boldface** are presented in the text.

Altogether, these sets of results indicated that the biased adjective modulated the re-activation of N2 in both groups and reduced the interference effect of N3 in the AMC group (see Figure 7, red boxes). See Appendix F for the full summary of the results section.

4. Discussion

In this study, we examined whether lexical-semantic cues as premodifiers of a target noun (N2) modulated the encoding (activation and deactivation gaze patterns) and retrieval (re-activation) dynamics of a noun phrase during the auditory processing of non-canonical sentences in both age-matched neurologically unimpaired listeners (AMC) and individuals with aphasia (IWA). We hypothesized that the lexical-semantic cues (in the form of adjectives) would facilitate (1) lexical encoding (i.e., boost representational access) and (2) downstream syntactic retrieval or dependency linking (i.e., increasing the probability of lexical retrieval at the gap site) during auditory sentence processing for both groups. The results revealed that the AMC group had a higher rate of activation and deactivation of nouns in the biased compared to the unbiased/neutral condition. Moreover, at the gap site, the accessibility of the target item (the displaced object noun, N2) was higher in the biased condition, which resulted in facilitated retrieval at the gap site. Our results from the AMC group are consistent with previous studies showing that semantically richer noun phrases that are encoded more 'deeply' are more accessible in memory at critical syntactic positions during sentence processing [24,25,32–34]. In contrast to the results found for the AMC group, the presence of biased adjectives did not affect the rate of lexical access of the target noun in the IWA group upon hearing the adjective in the sentence. Yet, in the post-verb-frame window, there was higher activation of target N2 and reduction in interference from the first noun competitor (N1). In the following sections, we discuss the results of the AMC group and then turn our discussion toward the IWA group to interpret the mechanism underlying the effect of the lexical-semantic cues (premodifier, adjective) during auditory sentence processing.

4.1. Real-Time Dynamics of Lexical Encoding and Retrieval during Sentence Processing in Unimpaired Individuals

In a self-paced reading paradigm, Hofmeister (2011) found that in neurotypical individuals, semantic complexity of the displaced object noun phrase or to-be-retrieved noun (e.g., "the injured and dangerous bear" versus "the bear") resulted in longer reading times (i.e., longer encoding, or deeper processing) but then later yielded faster reading times at sentence-internal retrieval or re-activation sites [25]. The author suggested that richer representations containing typical or highly predictable feature combinations yielded retrieval facilitation at the retrieval site during sentence processing. In this study, using an eye-tracking-while-listening visual world paradigm, regarding the initial processing of the target noun, we found that the semantically biasing adjectives boosted the activation of representational features. We suggest that the presence of a biased adjective led to a greater spreading of activation such that accessing the set of features associated with the adjective primed the activation of semantic features of the target noun [60–62]. In other words, the semantically biased adjective increased the function of associative strengths and representational complexity during the processing of the target lexical item. Specifically, the presence of an adjectival cue as a premodifier provides a contextually unique feature for the target item that no other competitor shares. This can reduce the interference effect arising from the simultaneous presence of representations with overlapping features in memory (i.e., similarity-based interference) and improve the chances of its recoverability. As suggested by Nairne [35,63,64], the probability of retrieving a memory representation increases with the similarity or feature-overlap of the retrieval cues and target and decreases with the similarity of the cues to other memory candidates (see [65] for the full description of feature-based retrieval model of Nairne). Based on Nairne's conceptual formulation, the probability of retrieving a representation E_1, given a retrieval cue set X_1, depends on the similarity or relatedness in features of X_1 and E_1, as well as the similarity or relatedness of X_1 to other memory candidates (E_2, E_3, E_4, ..., E_n). This ratio model is designed to describe the distinctiveness property of a cue (e.g., "venomous snake" versus "voracious snake" when both "bear" and "eagle" can be also voracious) during the retrieval.

$$P_r(E_1|X_1) = \frac{S_1(X_1, E_1)}{\sum S_1(X_1, E_n)} \quad (1)$$

The numerator of this formulation refers to the similarity of X_1 and E_1, which varies as a function of the number of matching and mismatching features between the two terms which can be illustrated as the formulation below using the relating distance (d). This means that similar items (items containing few mismatching features) will be nearby items and produce the largest effects.

$$s(X_1,\ E_1) = e^{-d(E_1, X_1)} \quad (2)$$

If the goal is to recover the representation E_1 in the presence of a particular cue X_1, the probability of retrieving E_1 is highest when its features are similar to the cue X_1 (the numerator of the equation), and dissimilar to other possible retrieval candidates (denominator). Therefore, the target retrieval is proportional to the cue-target match and inversely proportional to the amount of cue overload. Ultimately, the greater number of contextually unique features in E_1, the greater it possesses a feature that no other competitor shares and, the greater the probability for compatibility with X_1, and thus better chances for successful retrieval. In our case, the biasing adjectives make the target noun (snake: E_1) distinct from the other competitor items (Eagle: E_2 and bear: E_3), thus reducing the level of cue overload, which can result in a higher probability of target item E_1 retrieval. Moreover, using this feature-based model of retrieval, Hoffmeister et al. (2013) suggested that increasing representational complexity increases the probability that some features will be unique and therefore helps distinguish a representation from other competitors in memory [65]. With respect to the cue-based retrieval theories, such uniqueness may create a better match with the set of retrieval cues at the gap site [9]. Therefore, adding unique information can be quite helpful for memory retrieval. In the present study, regarding the downstream effects, the additional lexical-semantic information provided by the biasing adjective increases the representational complexity of the target noun and increases the distinctiveness of the target at the time of retrieval for neurotypical individuals. The results revealed that the AMC group disengaged from the first noun phrase earlier upon hearing the biasing adjective noun phrase when compared to the neutral adjective in the unbiased condition. Moreover, they retrieved (reactivated) the target N2 earlier in the retrieval site (post-verb-frame window) and manifested an increase in its rate of re-activation in the biased condition compared to the unbiased condition. Therefore, the results from AMC are consistent with previous studies showing that semantically richer nouns are more accessible in memory [24,25,32,34].

4.2. Real-Time Dynamics of Lexical Encoding and Retrieval during Sentence Processing in Individuals with Aphasia

Unlike the AMC group, IWA did not demonstrate sensitivity to the lexical-semantic cues (biased adjectives) in their rate of initial lexical access. However, their re-activation processes of the displaced item changed in the post-verb-frame window. IWA demonstrated a reduction in interference-effect arising from the competitor item in the sentence. The lack of sensitivity of IWA to the lexical-semantic cue during real-time processing could be attributed to their inefficiency in accessing or maintaining the representational features in real time. Research exploring real-time processing in aphasia has suggested that these individuals have a delay in lexical access causing the critical semantic features to be unavailable for fast-acting syntactic processes [13,16,37]. Yet, the deficits could be overcome when the rate of auditory input is slowed down and the time constraints for retrieval are relaxed [16]. This is in line with studies with neurotypical individuals that have suggested that the addition of time at specific points during processing allows for a deeper encoding of sentential constituents, leading to a strengthened representation [52,66]. In the current study, we aimed to strengthen the representations via biasing adjectives, though the approach was unsuccessful. One explanation for the lack of sensitivity of IWA to the contextual cue could be attributed to the interference of active representations that are outside of the scope of other sentential element constraints such as phonological form [67–69]. Although we do not have direct evidence to support this, it has been suggested that impairments in cognitive control processes (such as cognitive flexibility and inhibitory control) can increase the interference from context-independent distractors during sentence processing [70]. Investigations into the effect of these impaired processes in IWA should be considered in future endeavors.

4.3. The Underlying Nature of Lexical-Semantic Processing Deficit in Aphasia

Nozari (2019) introduced a theoretical framework that explains all the empirical findings surrounding lexical-access deficits in aphasia [71]. The framework, which is based on language production, can be generalized to comprehension processes as it pertains to shared mechanisms (namely representational semantic storage and cognitive control processes) that are involved in both production and comprehension. Nozari (2019) demonstrated that lexical access deficits in aphasia can have two distinct etiologies by presenting a case of a double dissociation between two IWA. One case showed a profile of impaired activation of semantic features of the target lexical items (activation deficit), while the other case showed a profile compatible with impaired inhibition of competing for lexical items (inhibition deficit). Those IWA with activation deficits suffer from lower-than-normal activation of representational features (semantic or phonological) which can lead to smaller differences between items during the spread of activation and ultimately impede the absolute selection of an item [72]. Those IWA with inhibition deficits suffer from increased activation of semantic competitors which hinges on the malfunction of the inhibitory process that suppresses the activation of unrelated representations. Deficits in any of these mechanisms can explain why IWA, upon first hearing a target noun, demonstrated a lack of sensitivity to the distinctiveness in the biased condition. This framework is related to the feature-based retrieval formulation of Nairne (2006 and references therein) which expresses that the probability that a target representation will be selected depends on cue-target features match and distinctiveness of the target from competitor items which dictate the level of interference within the potential representations. Our results demonstrate that IWA do not appear to be initially sensitive to the distinctiveness property of a cue during the fast-acting real-time processing of sentences as they have impairments in the timely processing of these functions. However, since they evinced a later emerging reduced interference effect between the target noun and the competitor noun (N1) during the post-verb-frame window, this suggests that distinctiveness is processed, just delayed.

Altogether, if the intention is to mitigate initial delay in lexical access, then the addition of biasing adjectives as premodifiers may not be an ideal approach for IWA to boost representational access in the memory as they have a delay in timely access to representational features. Future investigations may explore adding modifiers after the noun (post-modifiers, e.g., "It was the bear with large claws that the hunter chased into the evening", as compared to a matched sentence with a neutral preposition phrase after the target noun) as those may offer a better route for enriching the semantic features of a representation. Post-modifiers may be more efficiently encoded by IWA during online sentence processing. It is suggested from neurotypical studies that in the case of postmodifiers, the memory representation (semantic and syntactic features) of the head noun becomes reactivated as the modifying information is being encoded [11]. Since the full lexical semantics of the head noun is available in the case of postmodifiers, an immediate re-activation of both syntactic and semantic information can lead to more robust representational access and allows time for lexical processing to be fully executed. Future studies need to look at the effect of pre and postmodifiers in sentence processing patterns of individuals with aphasia. Another viable approach to modulate sentence processing and reduce the interference effect for IWA is to directly manipulate the representational features of the target item and make them inherently mismatching from other competitor items in the sentence. In a similar vein, previous reading studies with neurotypical individuals have shown that a mismatch in the properties of encoded referents of the sentence, such as "the general" and "Christopher" in (5b) can minimize the similarity-based interference effects when compared to (5a) and therefore increase the probability of on-time target retrieval [5,6,73]. This approach could be more useful for IWA rather than increasing the syntactic and semantic representational complexity of the to-be-retrieved item by adding modifiers.

(5a) It was *the general*$_i$ that the lawyer chased$_i$ <~~the general~~> in the office yesterday.

(5b) It was *the general*$_i$ that Christopher chased$_i$ <~~the general~~> in the office yesterday.

(5c) It was the *victorious four-star general*$_i$ that the lawyer chased$_i$ <~~the general~~> in the office yesterday.

One limitation in this study is the small sample size of the aphasia group. The sample size limited the ability to conduct individual-level analyses. Moving forward, it would be useful to relate features of stroke-induced lesions, such as size, location, and white-matter damage, to variability in language outcomes across individuals with aphasia.

5. Conclusions

Altogether, the current study improves our understanding of how words are encoded, processed against competitor items, and retrieved during language comprehension in neurologically unimpaired as well as impaired populations. Here, we demonstrate that a boost in representational access via premodifiers (biasing adjectives) can facilitate the syntactic processing of unimpaired populations. However, disruption in the timely activation of compatible representations can reduce the sensitivity to premodifying lexical-semantic cues among IWA.

Author Contributions: Conceptualization, N.A. (Niloofar Akhavan), M.G. and T.L.; methodology, N.A. (Niloofar Akhavan), C.B. and T.L.; formal analysis, N.A. (Niloofar Akhavan), C.S. and C.B., writing—original draft preparation, N.A. (Niloofar Akhavan); writing—review and editing, N.A. (Niloofar Akhavan), C.S., C.B., N.A. (Noelle Abbott), M.G. and T.L.; supervision, T.L.; visualization, N.A. (Niloofar Akhavan) and T.L.; funding acquisition, N.A. (Niloofar Akhavan), C.S., C.B. and T.L. All authors have read and agreed to the published version of the manuscript.

Funding: This research was funded by the William Orr Dingwall Foundation (N.A.); UCSD Friends of the International Center (N.A.); The David A. Swinney Fellowship (N.A. and C.J.B.); the UCSD Tribal Membership Initiative (C.M.S); NIH NIDCD award numbers T32 DC007361 (trainees: M.G., C.J.B., N.T.A, C.M.S.; PI: T.E.L.); R21 DC015263 (PI: T.E.L.); R01 DC009272 (PI: T.E.L.).

Institutional Review Board Statement: This study was conducted according to the guidelines of the Declaration of Helsinki and approved by the Institutional Review Board of the University of California, San Diego and San Diego State University (IRB number: 171023, continuous approval since 06-03-2015).

Informed Consent Statement: Informed consent was obtained from all subjects involved in this study.

Data Availability Statement: The data used to support the findings of this publication can be requested from the corresponding author upon request.

Acknowledgments: We thank Natalie Sullivan and Lewis Shapiro for their assistance during various stages of data collection and processing, and all of our participants, their families, and our funding agencies for supporting this work.

Conflicts of Interest: The authors declare no conflict of interest. The funders had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript, or in the decision to publish the results.

Appendix A

Table A1. The list of sentence stimuli used in this study is shown in the table below.

Unbiased Adjective	Biased Adjective
The duck followed the perfect kitten that the cow deliberately nudged across the grassy meadow.	The duck followed the playful kitten that the cow deliberately nudged across the grassy meadow.
The veterinarian greeted the popular king that the criminal mistakenly expected at the stunningly lavish gala.	The veterinarian greeted the powerful king that the criminal mistakenly expected at the stunningly lavish gala.
The scorpion annoyed the anxious bull that the bee constantly pestered in the abandoned railroad yard.	The scorpion annoyed the angry bull that the bee constantly pestered in the abandoned railroad yard.
The crocodile spied the weird owl that the chameleon momentarily faced in the exotic animal show.	The crocodile spied the wise owl that the chameleon momentarily faced during the exotic animal show.
The crab helped the coy puppy that the rabbit relentlessly teased before playful tussle.	The crab helped the cute puppy that the rabbit relentlessly teased before the playful tussle.
The lawyer visited the forgetful gymnast that the butler allegedly helped with the illegal cover-up.	The lawyer visited the flexible gymnast that the butler allegedly helped with the illegal cover-up.
The magician passed the redheaded nun that the mailman compassionately soothed after the traumatic event.	The magician passed the religious nun that the mailman compassionately soothed after the traumatic event.
The ladybug observed the smelly bat that the opossum deliberately avoided near the historic monument.	The ladybug observed the scary bat that the opossum deliberately avoided near the historic monument.
The astronaut approached the sad jockey that the salesman incorrectly judged throughout the dinner party.	The astronaut approached the short jockey that the salesman incorrectly judged throughout the dinner party.
The otter spotted the shiny octopus that seagull unsurprisingly smelled after the hot and sunny day.	The otter spotted the slimy octopus that seagull unsurprisingly smelled after the hot and sunny day.
The deer noticed the male gorilla that the hummingbird thoroughly amused with the acrobatic display.	The deer noticed the mean gorilla that the hummingbird thoroughly amused with the acrobatic display.
The ostrich recognized the delightful toucan that the baboon hesitantly touched during the bizarre encounter.	The ostrich recognized the colorful toucan that the baboon hesitantly touched during the bizarre encounter.
The spider scared the live rooster that the porcupine accidentally bumped on the side of the country road.	The spider scared the loud rooster that the porcupine accidentally bumped on the side of the country road.
The dentist helped the tired maid that the plumber heartlessly cheated in spite of the cautious investment.	The dentist helped the tidy maid that the plumber heartlessly cheated in spite of the cautious investment.
The orangutan examined the defenseless cockroach that the parrot quickly located near the bottom of the staircase.	The orangutan examined the disgusting cockroach that the parrot quickly located near the bottom of the staircase.

Appendix B. Model Details for Analyzing the Noun Preceding Adjective

The data for this analysis was composed of gaze proportions to N1 across the window for the 9 AMC and 10 IWA. This window captures the full dynamics of N1 processing, which includes its activation and deactivation pattern over time as the speech unfolds.

We began the GCA analysis using a base model that included only the time terms (linear and quadratic) without any modulation of group and condition. The addition of group (AMC vs. IWA) and condition (biased vs. unbiased) parameters to the model significantly improved the model fit ($\chi^2(12) = 154.91$, $p < 0.001$). Of interest was the interaction term between the condition and group reflects the extent to which the difference in N1 gaze proportion between biased and unbiased conditions differed between participant groups. The AMC group served as the comparison group and coefficients were estimated for the IWA relative to the AMC group.

Appendix C. Model Details for Analyzing the Noun following Adjective

To capture the full pattern of N2 processing (i.e., its activation and deactivation over time) and examine the effect of the biased adjective, we specified the window of analyses to include the onset of adjective until 2500 ms afterward (corresponding to the average offset of N3—"the/adjective/snake that the bear"). The data for this analysis was composed of N2 gaze proportion over time for the 9 AMC and 10 IWA participants. Here, we built a baseline model including only the time terms (linear and quadratic). The addition of group (AMC vs. IWA) and condition (biased vs. unbiased) improved the model fit ($\chi^2(12) = 161.43$, $p < 0.001$). This interaction term reflects the extent to which N2 gaze proportion differences between biased and unbiased conditions differed between participant groups.

Appendix D. Downstream Effect of Condition on Encoding the Noun after the Manipulation (N3)

For this analysis, the window was specified at the onset of N3 until 2000 ms afterward (corresponding to the average offset of the verb—"the bear cautiously encountered"). We began the GCA analysis using the base model that includes time without any modulation of group and condition. The addition of group (AMC vs. IWA) and condition (biased vs. unbiased) improved the model fit ($\chi^2(12) = 150.41$, $p < 0.001$). See Figure A1 for the gaze data and curve fits for this interaction model.

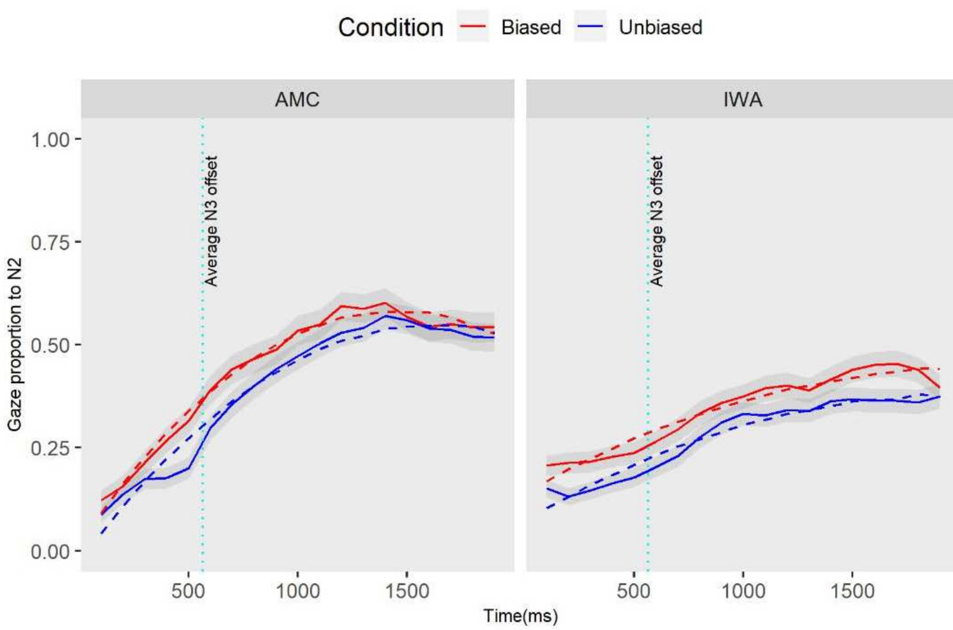


Figure A1. Gaze proportion differences toward N3 between conditions and groups. Solid lines represent observed data and dashed lines represent the GCA model fit.

The result of the individual parameter estimates (Table A2) revealed a marginal effect of condition for N3 processing in the AMC group at the intercept term (estimate = −0.06, SE = 0.03, $t = -1.09$, $p = 0.06$): this negative estimate indicated that the average proportion of gazes toward N3 in the unbiased condition was less than the biased condition. Furthermore, there was an effect of the group at the intercept term (estimate = −0.11, SE = 0.05, $t = -2.09$, $p = 0.04$), which indicated that the average proportion of gazes toward N3 for IWA was less than the AMC group (this result corresponds to the biased condition which is the reference estimate). Additionally, the main effect of the group was also significant at the quadratic term (estimate = 0.23, SE = 0.10, $t = 2.22$, $p = 0.03$), which is indicative of a steeper rise and fall (curvature inflection point) for the AMC compared to IWA in the biased condition.

Table A2. Results of GCA analysis for time window 3.

Predictors	Estimates	CI	P (Two Tailed)
(Intercept)	0.44	0.36–0.53	<0.001
Linear	0.53	0.26–0.81	<0.001
Quadratic	−0.31	−0.47–−0.15	<0.001
Condition [Unbiased]	**−0.06**	**−0.12–0.00**	**0.056**
Group [IWA]	**−0.11**	**−0.22–−0.01**	**0.036**
Linear × Condition [Unbiased]	0.09	−0.14–0.32	0.458
Quadratic × Condition [Unbiased]	0.07	−0.09–0.22	0.387
Linear × Group [IWA]	−0.20	−0.56–0.16	0.275
Quadratic × Group [IWA]	**0.23**	**0.03–0.43**	**0.027**
Condition [Unbiased] × Group [IWA]	0.01	−0.06–0.07	0.853
(Linear × Condition [Unbiased]) × Group [IWA]	−0.04	−0.32–0.24	0.774
(Quadratic × Condition [Unbiased]) × Group [IWA]	−0.08	−0.26–0.10	0.397

Note: The table provides the test of the full model including the interaction of group and condition on the intercept, linear, and quadratic time terms. The AMC group and the biased condition are set as the reference estimates. Results in **boldface** are presented in the text.

The marginal effect of the condition which was found in the AMC group was reevaluated using the permutation cluster analysis (2000 permuted samples, with an alpha of 0.05). The analysis did not result in any significant clusters that would indicate differences between conditions. The cluster analysis did not validate the GCA finding, and therefore we cannot report any consistent effect of group or condition difference for N3 processing.

Appendix E. Evidence of N2 Re-Activation at the Verb-Frame (Time Window 4)

We inspected the re-activation of N2 relative to N1 as an index of syntactic re-activation at the gap site window, for two reasons: first, if gaze proportions to N2 and N1 were similar, then it means that the listeners must have maintained activation for items on the screen regardless of their syntactic roles. In other words, at this verb-frame position, individuals' gazes must be away from N1 as the syntactic role of these items should have been already assigned. The activation of N1 at this verb-frame position would only indicate the presence of an interference effect. However, at this point in the sentence, there are two NPs that have not yet been fully integrated into the syntactic structure; that is N2 and N3. It is to be expected that the most recently encountered N3 would have high gazes as its traces of representation can remain active after hearing the verb. Therefore, if syntactic linking is triggered at the verb offset, then we would be expecting higher gazes toward N2 and not N1. To indicate if individuals in each group have shown evidence of re-activation at the verb-frame, we formed a second-order orthogonal polynomial and added the fixed effect of group (IWA vs. AMC) and gazes toward the images of interest (N2 vs. N1) to the model. See Figure A2 for the gaze data and curve fits for this interaction model.

Adding the group and images and their interaction with the higher-order time terms improved the baseline model fit ($\chi^2(12) = 697.09$, $p < 0.001$). This interaction term reflects the extent to which the difference between N2 (target) and N1 (competitor) gaze time courses differed between participant groups. In Table A3 we report the results of individual parameter estimates of the full quadratic model. The analysis revealed an effect of the group such that the average gaze of IWA toward the competitor image (N1) was higher than the AMC group (estimate = 0.10, $p < 0.05$). There was also an interaction effect showing that the IWA group had a significantly lower intercept term (estimate = −0.19, SE = 0.05, $t = -3.88$, $p < 0.001$) relative to the AMC group. The effect on the intercept term indicates that the difference in overall fixation of N1 vs. N2 was smaller for the IWA group than for the AMC group. As shown in the plots, the AMC group did not maintain activation of N1 and had a higher proportion of gazes toward N2, which is indicative of reduced interference effect in this group.

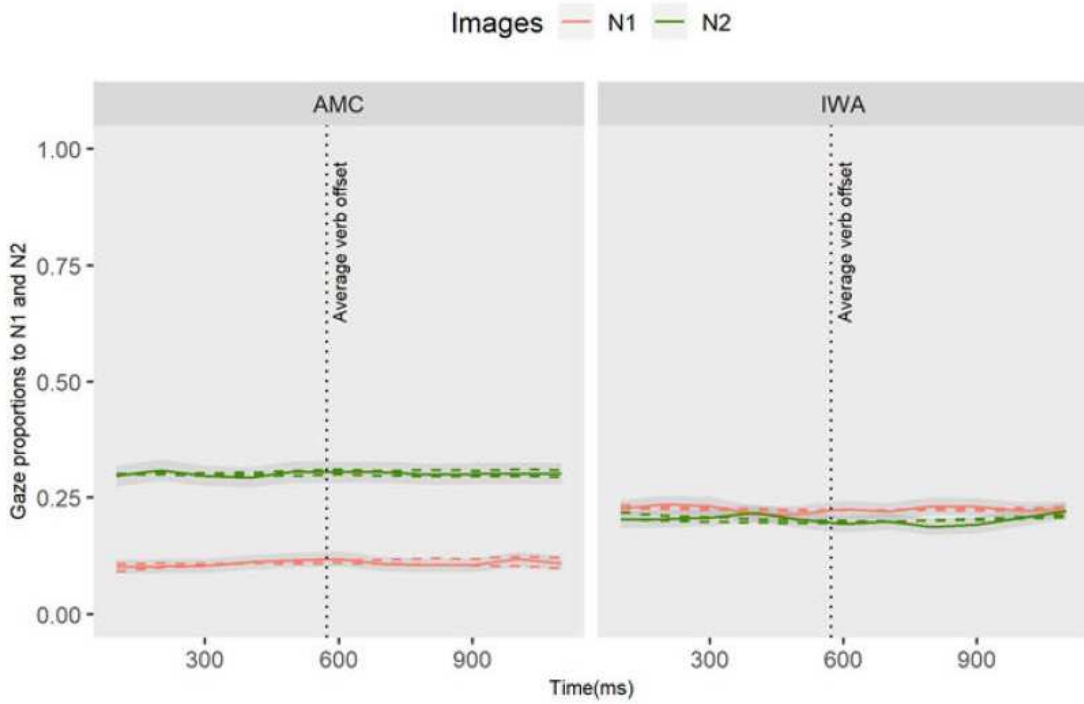


Figure A2. Gaze proportion differences to N1 and N2 between groups. Solid lines represent observed data and dashed lines represent the GCA model fit.

Altogether, we can summarize that IWA were experiencing interference effects during the verb-frame window (i.e., gap site where syntactic dependency linking must occur). The next analysis investigates whether the condition modulated the pattern of gazes toward N2 at the verb-frame position.

Table A3. Results of GCA analysis for time window 4.

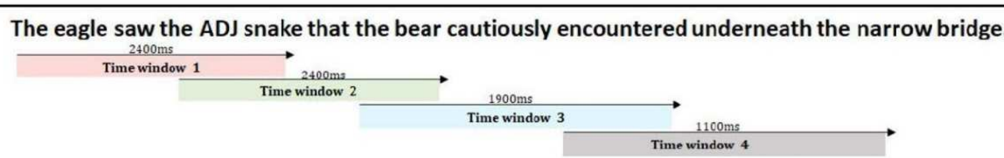
Predictors	Estimates	CI	P (Two Tailed)
(Intercept)	0.12	0.06–0.18	<0.001
Linear	−0.01	−0.10–0.07	0.793
Quadratic	−0.01	−0.05–0.03	0.654
Images [N2]	0.17	0.10–0.24	<0.001
Group [IWA]	**0.10**	**0.02–0.18**	**0.016**
Linear × Images [N2]	0.02	−0.09–0.14	0.696
Quadratic × Images [N2]	0.01	−0.05–0.07	0.764
Linear × Group [IWA]	0.01	−0.10–0.13	0.832
Quadratic × Group [IWA]	0.02	−0.04–0.08	0.532
Images [N2] × Group [IWA]	**−0.19**	**−0.29–−0.09**	**<0.001**
(Linear × Images [N2]) × Group [IWA]	−0.02	−0.18–0.14	0.803
(Quadratic × Images [N2]) × Group [IWA]	−0.00	−0.08–0.08	0.982

Note: The table provides the test of the full model including the interaction of group and images of interest (N1 and N2) on the intercept, linear, and quadratic time terms. The AMC group and the N1 are set as reference estimates. Results in boldface are presented in the text.

Appendix F. Summary of Results

Table A4. Summary of the results for the online sentence processing of AMC and IWA based on GCA and Cluster analyses.

Process



	Activation and Deactivation of N1	Activation and Deactivation of N2	Activation and Deactivation of N3	Dependency Linking/Re-Activation of N2
Results-AMC	Across the entire time course of processing N1, there was an effect of condition. The effect emerges upon hearing the adjective. In the biased condition, deactivation (looking away from N1 when processing the adjective occurred earlier than in the unbiased condition.	Across the entire time course of processing N2, there was a marginal effect of condition. The difference emerges at the offset of N2. In the biased condition, N2 was deactivated earlier as compared to the unbiased condition.	AMC did not show a significant effect of condition for activation and deactivation of N3.	There was a condition effect for the AMC group such that they revealed a higher rate of activation of N2 in the biased compared to the unbiased condition. Moreover, the level and rate of activation of N3 were lower in the biased condition.
Results-IWA	IWA did not show an effect of condition for N1 processing.	IWA did not show an effect of condition for N2.	IWA did not show an effect of condition for N3.	IWA showed an earlier rise in the re-activation of N2 in the biased condition They revealed a reduced interference effect in the biased condition as manifested by reduced looks to N1. They revealed no different gaze patterns toward N3 between the conditions.

References

1. McElree, B.; Foraker, S.; Dyer, L. Memory structures that subserve sentence comprehension. *J. Mem. Lang.* **2003**, *48*, 67–91. [CrossRef]
2. Nicol, J.; Swinney, D. The role of structure in coreference assignment during sentence comprehension. *J. Psycholinguist. Res.* **1989**, *18*, 5–19. [CrossRef] [PubMed]
3. Sheppard, S.M.; Walenski, M.; Love, T.; Shapiro, L.P. The auditory comprehension of wh-questions in aphasia: Support for the intervener hypothesis. *J. Speech Lang. Hear. Res.* **2015**, *58*, 781–797. [CrossRef] [PubMed]
4. Koring, L.; Mak, P.; Reuland, E. The time course of argument reactivation revealed: Using the visual world paradigm. *Cognition* **2012**, *123*, 361–379. [CrossRef] [PubMed]
5. Gordon, P.C.; Hendrick, R.; Johnson, M.; Lee, Y. Similarity-based interference during language comprehension: Evidence from eye tracking during reading. *J. Exp. Psychol. Learn. Mem. Cogn.* **2006**, *32*, 1304. [CrossRef] [PubMed]
6. Gordon, P.C.; Hendrick, R.; Levine, W.H. Memory-Load Interference in Syntactic Processing. *Psychol. Sci.* **2002**, *13*, 425–430. [CrossRef]
7. Gordon, P.C.; Hendrick, R.; Johnson, M. Memory interference during language processing. *J. Exp. Psychol. Learn. Mem. Cogn.* **2001**, *27*, 1411–1423. [CrossRef]
8. Van Dyke, J.A. Interference effects from grammatically unavailable constituents during sentence processing. *J. Exp. Psychol. Learn. Mem. Cogn.* **2007**, *33*, 407. [CrossRef]
9. Van Dyke, J.A.; McElree, B. Retrieval interference in sentence comprehension. *J. Mem. Lang.* **2006**, *55*, 157–166. [CrossRef]
10. Lewis, R.L.; Vasishth, S.; Van Dyke, J.A. Computational principles of working memory in sentence comprehension. *Trends Cogn. Sci.* **2006**, *10*, 447–454. [CrossRef]
11. Lewis, R.L.; Vasishth, S. An activation-based model of sentence processing as skilled memory retrieval. *Cogn. Sci.* **2005**, *29*, 375–419. [CrossRef] [PubMed]
12. Thompson, C.K.; Choy, J.J. Pronominal resolution and gap filling in agrammatic aphasia: Evidence from eye movements. *J. Psycholinguist. Res.* **2009**, *38*, 255–283. [CrossRef]
13. Dickey, M.W.; Choy, J.J.; Thompson, C.K. Real-time comprehension of wh- movement in aphasia: Evidence from eyetracking while listening. *Brain Lang.* **2007**, *100*, 1–22. [CrossRef] [PubMed]
14. Caramazza, A.; Zurif, E.B. Dissociation of algorithmic and heuristic processes in language comprehension: Evidence from aphasia. *Brain Lang.* **1976**, *3*, 572–582. [CrossRef]
15. Grodzinsky, Y. The neurology of syntax: Language use without Broca's area. *Behav. Brain Sci.* **2000**, *23*, 1–21. [CrossRef]
16. Love, T.; Swinney, D.; Walenski, M.; Zurif, E. How left inferior frontal cortex participates in syntactic processing: Evidence from aphasia. *Brain Lang.* **2008**, *107*, 203–219. [CrossRef]
17. Murphy, E. *The Oscillatory Nature of Language*; Cambridge University Press: Cambridge, UK, 2020.
18. Grodzinsky, Y. A restrictive theory of agrammatic comprehension. *Brain Lang.* **1995**, *50*, 27–51. [CrossRef]
19. Ferrill, M.; Love, T.; Walenski, M.; Shapiro, L.P. The time-course of lexical activation during sentence comprehension in people with aphasia. *Am. J. Speech-Lang. Pathol.* **2012**, *21*, S179–S189. [CrossRef]
20. Swaab, T.Y.; Brown, C.; Hagoort, P. Understanding ambiguous words in sentence contexts: Electrophysiological evidence for delayed contextual selection in Broca's aphasia. *Neuropsychologia* **1998**, *36*, 737–761. [CrossRef]
21. Swaab, T.; Brown, C.; Hagoort, P. Spoken Sentence Comprehension in Aphasia: Event-related Potential Evidence for a Lexical Integration Deficit. *J. Cogn. Neurosci.* **1997**, *9*, 39–66. [CrossRef]
22. Hagoort, P.; Brown, C.M.; Swaab, T.Y. Lexical—Semantic event–related potential effects in patients with left hemisphere lesions and aphasia, and patients with right hemisphere lesions without aphasia. *Brain* **1996**, *119*, 627–649. [CrossRef] [PubMed]
23. Choy, J.J.; Thompson, C.K. Binding in agrammatic aphasia: Processing to comprehension. *Aphasiology* **2010**, *24*, 551–579. [CrossRef] [PubMed]
24. Hofmeister, P.; Vasishth, S. Distinctiveness and encoding effects in online sentence comprehension. *Front. Psychol.* **2014**, *5*, 1237. [CrossRef]
25. Hofmeister, P. Representational Complexity and Memory Retrieval in Language Comprehension. *Lang. Cogn. Process.* **2011**, *26*, 376–405. [CrossRef]
26. Kluender, R.; Kutas, M. Bridging the gap: Evidence from ERPs on the processing of unbounded dependencies. *J. Cogn. Neurosci.* **1993**, *5*, 196–214. [CrossRef]
27. McElree, B. Sentence Comprehension Is Mediated by Content-Addressable Memory Structures. *J. Psycholinguist. Res.* **2000**, *29*, 111–123. [CrossRef]
28. Trueswell, J.C.; Tanenhaus, M.K.; Garnsey, S.M. Semantic influences on parsing: Use of thematic role information in syntactic ambiguity resolution. *J. Mem. Lang.* **1994**, *33*, 285–318. [CrossRef]
29. Martin, A.E.; McElree, B. Retrieval cues and syntactic ambiguity resolution: Speed-accuracy tradeoff evidence. *Lang. Cogn. Neurosci.* **2018**, *33*, 769–783. [CrossRef]
30. McElree, B.; Dosher, B.A. Serial position and set size in short-term memory: The time course of recognition. *J. Exp. Psychol. Gen.* **1989**, *118*, 346–373. [CrossRef]
31. Parker, D.; Shvartsman, M.; Van Dyke, J.A. The cue-based retrieval theory of sentence comprehension: New findings and new challenges. In *Language Processing and Disorders*; Cambridge Scholars Publishing: Newcastle upon Tyne, UK, 2017; pp. 121–144.

32. Karimi, H.; Diaz, M.; Ferreira, F. "A cruel king" is not the same as "a king who is cruel": Modifier position affects how words are encoded and retrieved from memory. *J. Exp. Psychol. Learn. Mem. Cogn.* **2019**, *45*, 2010. [CrossRef]
33. Karimi, H.; Brothers, T.; Ferreira, F. Phonological versus semantic prediction in focus and repair constructions: No evidence for differential predictions. *Cogn. Psychol.* **2019**, *112*, 25–47. [CrossRef] [PubMed]
34. Troyer, M.; Hofmeister, P.; Kutas, M. Elaboration over a discourse facilitates retrieval in sentence processing. *Front. Psychol.* **2016**, *7*, 374. [CrossRef]
35. Nairne, J.S. A feature model of immediate memory. *Mem. Cogn.* **1990**, *18*, 251–269. [CrossRef] [PubMed]
36. Vasishth, S.; Lewis, R.L. Argument-head distance and processing complexity: Explaining both locality and antilocality effects. *Language* **2006**, *82*, 767–794. [CrossRef]
37. Choy, J.J. *Effects of Lexical Processing Deficits on Sentence Comprehension in Agrammatic Broca's Aphasia*; Northwestern University: Evanston, IL, USA, 2011.
38. Cooper, R.M. The control of eye fixation by the meaning of spoken language: A new methodology for the real-time investigation of speech perception, memory, and language processing. *Cogn. Psychol.* **1974**, *6*, 84–107. [CrossRef]
39. Huettig, F.; Rommers, J.; Meyer, A.S. Using the visual world paradigm to study language processing: A review and critical evaluation. *Acta Psychol.* **2011**, *137*, 151–171. [CrossRef] [PubMed]
40. Tanenhaus, M.K.; Trueswell, J.C. Sentence Comprehension. In *Speech, Language, and Communication*; Academic Press: San Diego, CA, USA, 1995.
41. Wendt, D.; Brand, T.; Kollmeier, B. An eye-tracking paradigm for analyzing the processing time of sentences with different linguistic complexities. *PLoS ONE* **2014**, *9*, e100186. [CrossRef] [PubMed]
42. Goodglass, H.; Kaplan, E.; Barresi, B. *BDAE-3: Boston Diagnostic Aphasia Examination*, 3rd ed.; Lippincott Williams & Wilkins: Philadelphia, PA, USA, 2001.
43. Kertesz, A. *WAB-R: Western Aphasia Battery-Revised*; PsychCorp: San Antonio, TX, USA, 2007.
44. Love, T.; Oster, E. On the categorization of aphasic typologies: The SOAP (a test of syntactic complexity). *J. Psycholinguist. Res.* **2002**, *31*, 503–529. [CrossRef]
45. Altmann, G.T.; Kamide, Y. Incremental interpretation at verbs: Restricting the domain of subsequent reference. *Cognition* **1999**, *73*, 247–264. [CrossRef]
46. Eberhard, K.M.; Spivey-Knowlton, M.J.; Sedivy, J.C.; Tanenhaus, M.K. Eye movements as a window into real-time spoken language comprehension in natural contexts. *J. Psycholinguist. Res.* **1995**, *24*, 409–436. [CrossRef]
47. Dink, J.W.; Ferguson, B. *eyetrackingR: An R Library for Eye-Tracking Data Analysis*; 2015; Volume 6, p. 2017. Available online: www.eyetracking-r.com (accessed on 20 November 2021).
48. Mirman, D. *Growth Curve Analysis and Visualization Using R*; Chapman and Hall/CRC: Boca Raton, FL, USA, 2017.
49. Mirman, D.; Yee, E.; Blumstein, S.E.; Magnuson, J.S. Theories of spoken word recognition deficits in aphasia: Evidence from eye-tracking and computational modeling. *Brain Lang* **2011**, *117*, 53–68. [CrossRef] [PubMed]
50. Mirman, D.; Dixon, J.A.; Magnuson, J.S. Statistical and computational models of the visual world paradigm: Growth curves and individual differences. *J. Mem. Lang.* **2008**, *59*, 475–494. [CrossRef] [PubMed]
51. Brown, M.; Salverda, A.P.; Dilley, L.C.; Tanenhaus, M.K. Expectations from preceding prosody influence segmentation in online sentence processing. *Psychon. Bull. Rev.* **2011**, *18*, 1189–1196. [CrossRef] [PubMed]
52. Baker, C.; Love, T. It's about time! Time as a parameter for lexical and syntactic processing: An eye-tracking-while-listening investigation. *Lang. Cogn. Neurosci.* **2021**, *37*, 1–21. [CrossRef]
53. Akhavan, N.; Blumenfeld, H.K.; Love, T. Auditory Sentence Processing in Bilinguals: The Role of Cognitive Control. *Front. Psychol.* **2020**, *11*, 898. (In English) [CrossRef]
54. Hadar, B.; Skrzypek, J.E.; Wingfield, A.; Ben-David, B.M. Working memory load affects processing time in spoken word recognition: Evidence from eye-movements. *Front. Neurosci.* **2016**, *10*, 221. [CrossRef]
55. Barr, D.J.; Levy, R.; Scheepers, C.; Tily, H.J. Random effects structure for confirmatory hypothesis testing: Keep it maximal. *J. Mem. Lang.* **2013**, *68*, 255–278. [CrossRef]
56. Bates, D.; Mächler, M.; Bolker, B.; Walker, S. Fitting linear mixed-effects models using lme4. *arXiv* **2014**, arXiv:1406.5823.
57. Maris, E.; Oostenveld, R. Nonparametric statistical testing of EEG-and MEG-data. *J. Neurosci. Methods* **2007**, *164*, 177–190. [CrossRef]
58. Hahn, N.; Snedeker, J.; Rabagliati, H. Rapid linguistic ambiguity resolution in young children with autism spectrum disorder: Eye tracking evidence for the limits of weak central coherence. *Autism Res.* **2015**, *8*, 717–726. [CrossRef]
59. Huang, Y.; Snedeker, J. Evidence from the visual world paradigm raises questions about unaccusativity and growth curve analyses. *Cognition* **2020**, *200*, 104251. [CrossRef] [PubMed]
60. Anderson, J.R.; Budiu, R.; Reder, L.M. Theory of sentence memory as part of a general theory of memory. *J. Mem. Lang.* **2001**, *45*, 337–367. [CrossRef]
61. Bradshaw, G.L.; Anderson, J.R. Elaborative encoding as an explanation of levels of processing. *J. Verbal Learn. Verbal Behav.* **1982**, *21*, 165–174. [CrossRef]
62. Waddill, P.J.; McDaniel, M.A. Distinctiveness effects in recall. *Mem. Cogn.* **1998**, *26*, 108–120. [CrossRef]
63. Nairne, J.S. Modeling distinctiveness: Implications for general memory theory. In *Distinctiveness and Memory*; Oxford University Press: Oxford, UK, 2006; pp. 27–46.

64. Nairne, J.S. A Functional Analysis of Primary Memory. 2001. Available online: https://psycnet.apa.org/record/2001-00138-015 (accessed on 20 November 2021).
65. Hofmeister, P.; Jaeger, T.F.; Arnon, I.; Sag, I.A.; Snider, N. The source ambiguity problem: Distinguishing the effects of grammar and processing on acceptability judgments. *Lang. Cogn. Processes* **2013**, *28*, 48–87. [CrossRef]
66. Karimi, H.; Ferreira, F. Good-enough linguistic representations and online cognitive equilibrium in language processing. *Q. J. Exp. Psychol.* **2016**, *69*, 1013–1040. [CrossRef]
67. Huettig, F.; Altmann, G.T. Word meaning and the control of eye fixation: Semantic competitor effects and the visual world paradigm. *Cognition* **2005**, *96*, B23–B32. [CrossRef]
68. Yee, E.; Blumstein, S.E.; Sedivy, J.C. Lexical-Semantic Activation in Broca's and Wernicke's Aphasia: Evidence from Eye Movements. *J. Cogn. Neurosci.* **2008**, *20*, 592–612. [CrossRef]
69. Kukona, A.; Cho, P.W.; Magnuson, J.S.; Tabor, W. Lexical interference effects in sentence processing: Evidence from the visual world paradigm and self-organizing models. *J. Exp. Psychol. Learn. Mem. Cogn.* **2014**, *40*, 326. [CrossRef]
70. Nozari, N.; Trueswell, J.C.; Thompson-Schill, S.L. The interplay of local attraction, context and domain-general cognitive control in activation and suppression of semantic distractors during sentence comprehension. *Psychon. Bull. Rev.* **2016**, *23*, 1942–1953. [CrossRef]
71. Nozari, N. The dual origin of semantic errors in access deficit: Activation vs. inhibition deficit. *Cogn. Neuropsychol.* **2019**, *36*, 31–53. [CrossRef] [PubMed]
72. Nozari, N.; Dell, G.S.; Schwartz, M.F. Is comprehension necessary for error detection? A conflict-based account of monitoring in speech production. *Cogn. Psychol.* **2011**, *63*, 1–33. [CrossRef] [PubMed]
73. Gordon, P.C.; Hendrick, R.; Johnson, M. Effects of noun phrase type on sentence complexity. *J. Mem. Lang.* **2004**, *51*, 97–114. [CrossRef]

Chapter 2, in full, is a reprint of material as it appears in Akhavan, N., Sen, C., Baker, C., Abbott, N., Gravier, M., & Love, T. (2022). Effect of Lexical-Semantic Cues during Real-Time Sentence Processing in Aphasia. *Brain Sciences, 12(3)*, 312. The dissertation author was the primary investigator and author of this paper

CHAPTER 3

Using Lexical Semantics Cue to Mitigate Interference Effects during Real-Time Sentence Processing in Aphasia

Abstract

Using a visual-world eye-tracking paradigm, we investigated the real-time auditory sentence processing of neurologically unimpaired listeners and individuals with aphasia on canonical sentence constructions that contained multiple noun phrases and an unaccusative verb, the latter of which formed a long-distance dependency link between the verb and its direct object. To explore the likelihood of similarity-based interference during the real time linking of the verb and its direct object noun, we manipulated the animacy feature of the noun phrases (matched or mismatched). The goals of the study were to examine whether (a) reducing the similarity-based interference by mismatching animacy features would modulate the encoding and retrieval dynamics of noun phrases in real-time; and (b) whether individuals with aphasia would demonstrate on time sensitivity to this lexical-semantic cue. Results revealed a significant effect of this manipulation in individuals both with and without aphasia. In other words, the mismatch in the representational features of the noun phrases increased the distinctiveness of the direct-object target at the time of retrieval (verb offset) for individuals in both groups. Moreover, individuals with aphasia were shown to be sensitive to the lexical-semantic cue, even though they appeared to process it slower than unimpaired listeners. Our results extend the cue-based retrieval model by offering new and insights into the processes underlying sentence comprehension of individuals with aphasia.

Keywords: Aphasia; Sentence Processing; lexical property manipulation; Eye-Tracking

Introduction

In this paper we describe an experiment that investigates whether semantic cuing (in the form of animacy) can mitigate sentence processing impairments in individuals with aphasia. Before discussing the study, we describe the relevant sentence processing literature based on neurologically unimpaired adults to set the stage for a subsequent description of the relevant literature on aphasia.

Sentence processing in unimpaired adults

One property of natural language is the ability to integrate sentential constituents and establish linguistic relations between the auditorily incoming sentence components. In other words, as the sentence unfolds in real-time, the listener creates links between the sentence constituents (e.g., nouns and verb). As part of this 'dependency linking', information needs to be encoded when it is first perceived and then retrieved at subsequent points for efficient processing (Gibson et al., 2000; Lewis & Vasishth, 2005). For instance, in object-extracted constructions (e.g., [a] and [b] below], successful comprehension requires the retrieval of the direct object of the verb (/the general/) to be integrated and linked with the verb when it is encountered (Kluender & Kutas, 1993). Note that, this is just an example sentence to demonstrate the processes involved in dependency linking.

[a] It was *the general*$_i$ that the lawyer chased$_i$ <~~the general~~> from the office yesterday.

[b] It was *the general*$_i$ that Christopher chased$_i$ <the general> from the office yesterday.

A model that describes this dependency linking process is the cue-based parsing approach (Lewis & Vasishth, 2005; Van Dyke & Lewis, 2003). According to this model, the linguistic representations of words and phrases in a sentence are encoded as bundles of feature-value pairs. These features are then used as retrieval cues to carry out the cue-based search and retrieve a co-dependent item (i.e., N1 = /*the general*/) during the integration process once the verb is reached. This series of efficient cue-based retrievals can shape the integration mechanism of sentence processing.

It is important to note that although retrieval using the features of sentence constituents makes the integration mechanism efficient, it makes the process sensitive to interference from elements whose featural specification also matches with the retrieval cues. For instance, take sentence [a] versus [b] above. In sentence [a], the direct-object noun[2] /the general/ has a similar syntactic and semantic (feature) representation to the subject of the embedded clause, /the lawyer/; both have the same structural configuration /det N/ and share semantic features (i.e., are animate). However, in sentence [b], the features of the direct object differ from the subject of the embedded clause (the personal pronoun /Christopher/) both structurally and semantically. The feature similarity amongst elements of the sentence can decrease the distinctiveness of encoded representations which ultimately may reduce the probability of efficient retrieval at the syntactically dependent gap site (Hofmeister & Vasishth, 2014; Oberauer & Lange, 2008). This similarity-based interference between sentence components with featural overlap can hinder semantic integration in real-time and can impact sentence comprehension accuracy in the context of an inefficient monitoring system (Gordon et al., 2006). Previous studies that investigated reading skills in unimpaired individuals (Gordon et al., 2004; Gordon et al., 2006; Gordon et al., 2002) have demonstrated that a dissimilarity in the features of encoded referents of the sentence (such as /the general/ and /Christopher/ in [b]) can minimize the similarity-based interference

---

[2] In this manuscript we also use [N] as an abbreviation for noun. In this study, the first encountered noun in the sentence is referred to as N1 and the second noun as N2.

effects and therefore increase the probability of on-time target retrieval (i.e., /the general/ after the verb /chased/). Therefore, comprehension has been found to be more successful for sentences such as [b] compared to sentences such as [a]. In addition, other studies (Akhavan et al., 2022; Hofmeister, 2011; Hofmeister & Vasishth, 2014) have shown that adding a modifier increases the syntactic and semantic representational complexity of the to-be-retrieved item (e.g., "It was /the *victorious four-star* general/$_i$ that the lawyer chased $_i$…") and facilitates its representational activation and increase its chances of retrieval when the verb is encountered.

According to studies investigating the cue-based model and similarity-based interference effect, unimpaired individuals can use lexical representational information (e.g., semantic) in real-time to aid their sentence processing as these cues determine the bundles of features that are used for successful dependency linking (Lewis & Vasishth, 2005; Van Dyke & Lewis, 2003). Given the evidence that lexical cues (such as animacy) play an important role in unimpaired sentence processing, one useful avenue in understanding sentence comprehension deficits in individuals with aphasia is to investigate whether and when individuals with aphasia use these types of cues during their integration process in real-time to resolve interference effects. Below, we review the literature examining sentence processing in aphasia and how lexical-semantic cues are processed during sentence comprehension.

Sentence processing in aphasia

Several studies have provided evidence indicating that Individuals with Aphasia (IWA) experience sentence comprehension problems. The nature of these problem that can be classified as *processing* accounts state that there is no loss of knowledge in IWA, but that the ability to apply the knowledge is impaired (Choy & Thompson, 2010; Ferrill et al., 2012; Hagoort et al., 1996; Love et al., 2008; Swaab et al., 1997; Swaab et al., 1998). According to this class of theory, IWA are aware of the cue, but they are not able to process it accurately and/or efficiently. The specific nature of the processing deficit remains controversial.

Within the processing accounts, some argue that sentence comprehension impairments are caused by deficits in real-time lexical processes which is assumed to serve as the interface between sound input and the construction of a grammatical and interpretative representation of an utterance. Specifically, some suggest that IWA have delayed lexical access (Love et al., 2008) and/or lexical integration (Thompson & Choy, 2009), which results in disruption of the on-time availability of lexical representations for syntactic processing and can ultimately bring about comprehension failure. A number of factors may be at the root of these lexical processing impairments. First, limitations of working memory capacity have been identified post-stroke, such that IWA may have difficulty maintaining the activation of lexical representations which can impede sentence processing (Martin & Gupta, 2004; Martin et al., 1999). Others suggest that IWA may have trouble selecting among competing activated representations during the lexical access and integration stages of sentence processing due to executive function deficits because of damage to a specific language network (e.g., the left inferior frontal gyrus which is an area commonly implicated in IWA impairments) (Gotts & Plaut, 2002; Jefferies & Lambon Ralph, 2006; Jefferies et al., 2008; Novick et al., 2005; Sheppard et al., 2015). Therefore, given challenges in lexical processing and sentence comprehension, once similarity of features between noun phrases is high, IWA are likely to be susceptible to experiencing an interference effect. While unimpaired listeners also show an interference effect, it does not hamper real time processing or final interpretation. Further, in unimpaired individuals, providing semantic cues has been shown to reduce similarity-based interference and aid comprehension (Akhavan et al., 2022; Hofmeister, 2011; Hofmeister & Vasishth, 2014). Yet, while semantic cueing is wellestablished as a productive offline strategy in clinical intervention with IWA (Python et al., 2021), it is still unknown whether IWA can use a salient lexical-semantic cue in real-time to mitigate any interference effects during sentence comprehension.

Processing lexical cues during sentence comprehension in aphasia

Previous research suggests that, in the context of sentence comprehension impairment, IWA may rely on semantic information in their processing of sentences that require dependency linking. A seminal study examining the sensitivity of individuals with aphasia to semantic information during sentence comprehension was conducted by Caramazza and Zurif (Caramazza & Zurif, 1976). In this study, individuals with Broca's aphasia were presented with sentences like the following in a sentence-picture matching task:

[c] The book that the girl is reading is yellow.

[d] The cat that the dog is biting is black.

To understand non-canonical sentences like [c] and [d], the listener must integrate the lexical items as they are heard based on structural rules to determine who is doing what to whom. However, research has shown that listeners can enlist other strategies to help make the processing of these non-canonical sentence constructions easier (Bhandari et al., 2021). The Caramazza and Zurif [28] study revealed that IWA had little difficulty understanding non-canonical sentences when the information provided from the nouns allowed for an easy determination of who was performing the action and who was receiving the action. For example, in [c], the listener can take advantage of the fact that in this non-reversible sentence, only the animate noun (/the girl/) can perform the action of reading. However, in semantically reversible (non-canonical) sentences like [d], where both noun phrases (/the cat/ and /the dog/) can perform the action of biting, individuals with Broca's aphasia demonstrated comprehension difficulty. As discussed earlier, both noun phrases (/the dog/ and /the cat/) have similar lexical features that prevent reliance on featural cues such as animacy, as shown in [c]. This work demonstrated that IWA, in some linguistic contexts, could rely on semantic cues to compensate for difficulty in syntactic dependency linking.

In another sentence comprehension study, Gibson and colleagues (Gibson et al., 2016) examined the sensitivity of individuals with aphasia to semantic plausibility by using an act-out task (where comprehension is measured by asking participants to act out sentences with dolls) using active/passive[3] sentences as well as Double-Object (DO)/Prepositional-phrase Object (PO)[4] sentence structures (see the footnote for examples of each sentence structures). They found that compared to the control group, individuals with aphasia relied more heavily on plausibility information across all different sentence types. Specifically, IWA were more likely to use plausibility information in non-canonical passive relative to canonical active constructions.

Altogether, these studies showed that IWA ultimately relied on semantic information in their processing of sentences that require dependency linking. However, these studies did not capture the processing patterns moment by moment and we still do not know the immediate effect of these cues for IWA. Here, we examine whether and when IWA can use lexical-semantic cues to resolve any potential interference effects stemming from syntactic properties of the sentence.

[3] Active: The tiger chased the lion.
Passive: The lion was chased by the tiger.

[4] Double-Object: The sister mailed the brother the letter.
Prepositional-phrase Object: The sister mailed the letter to the brother.

Current study

In the current study, we employed an eye-tracking while listening visual world paradigm (ETL) to study how lexical-semantic cues (in the form of animacy) impact sentence processing in individuals with aphasia. Eye-tracking while listening is a method that allows us to investigate online sentence processing with millisecond-level temporal resolution. Additionally, this experiment used a natural speech paradigm without any behavioral response required during sentence processing. Being able to index participant responses without requiring overt participant decisions is a significant advantage of employing eye-tracking methods in IWA.

We seek to understand how IWA process lexical-semantic cues (animacy features) during the processing of canonical sentences that require dependency linking by comparing their performance in conditions with [see sentence e, below] and without [see sentence f, below] lexical-semantic cues. We use sentences containing unaccusative verbs as they can provide a case of long syntactic dependency in a canonical order structure (Bever & Sanz, 1997; Burkhardt et al., 2003; Friedmann et al., 2008; Koring et al., 2012; Poirier et al., 2012; Sullivan et al., 2017a, 2017b). The subject and the direct-object of the first verb (/noticed/), also known in linguistic terminology as arguments are /the model/ as the agent and /the designer/ as the theme respectively. Critically, the argument structure of the second verb (the unaccusative verb /fell/) is different, as it can be considered as something that happened to the subject (/the model/), rather than being initiated by it. In other words, the canonically assigned subject position also has the properties of the argument that are syntactically associated with the object (Burzio, 1981, 1986; Perlmutter, 1978).

Condition	Example sentences
[e] Inanimate	This evening at the fashion show, the model$_i$ $^{\text{animate, subject}}$ that noticed the dress $^{\text{inanimate, object}}$ surprisingly **fell**$_i$ $^{\text{[animate, subject]}}$ during the evening gown showcase.
[f] Animate	This evening at the fashion show, the model$_i$ $^{\text{animate, subject}}$ that noticed the designer $^{\text{animate, object}}$ surprisingly **fell**$_i$ $^{\text{[animate, subject]}}$ during the evening gown showcase.

A group of age-matched unimpaired individuals (AMC) were also included in the study to establish a baseline processing performance, in comparison to IWA, on these sentences using eye-tracking while listening. In this mixed-subject design study, we examine not only the potential differences between the two participant groups but also assess individual differences across the members of each group in each condition.

Questions and predictions of the current study

We asked the following three questions:

Question 1: Are listeners of each group sensitive to lexical-semantic cues (animacy) that resolve semantic interference during sentence comprehension? For this question, we compared the performance of each group across the two experimental conditions (animate, inanimate). We predicted that listeners in both groups would be sensitive to lexical semantic stimulus properties during sentence comprehension. In the inanimate condition, upon encountering the inanimate noun (N2), both groups (IWA and AMC) were predicted to show a reduced similarity-based interference effect. In this eye-tracking while listening paradigm, the susceptibility to the interference effect was operationalized as an equivalent proportion of gazes toward target noun (N1) and non-target or intervening noun (N2) (Akhavan et al., 2020).

Question 2: Do IWA demonstrate their sensitivity to lexical-semantic cues in real-time or is there a delay? For this question we compared the performance of IWA versus AMC in the inanimate condition to examine whether IWA process the lexical-semantic cue at the same time as AMC. Based on previous studies that revealed the temporal delay of IWA in processing lexical-semantic representations (Engel et al., 2018; Ferrill et al., 2012; Love et al., 2008; Prather et al., 1997), we expected IWA to show a delay compared to AMC individuals in using the lexical-semantic cue (animacy) in real-time.

Question 3: Does the lexical-semantic cue have a downstream effect on syntactic dependency linking at the gap-site? Recall that the sentences in this experiment include a gap-site when the unaccusative verb is encountered. For this question, we examined the effect of condition for each group. We predict that the lexical-semantic cue will have a downstream effect for both groups as the inanimate N2 ('the dress' versus 'the designer') will induce a smaller interference effect during the syntactic dependency linking process. In other words, the inanimate noun will improve the real-time processing as well as final comprehension for listeners.

Method

Participants

Age-Matched Control Participants (AMC): Eleven AMC participants were included in this study (mean age at the time of testing: 62 years old [range: 57-66 years], with an average 15.2 years of education [range: 12-20]). All the AMC participants were monolingual native English speakers with normal or corrected-to-normal visual and auditory acuity. None of the participants reported a history of active or significant alcohol and/or drug abuse, active psychiatric illness or intellectual disability, and/or other significant brain disorder or dysfunction (e.g., Alzheimer's/dementia, Parkinson's, Huntington's, Korsakoff's).

Individuals with Aphasia (IWA): Eleven individuals diagnosed with Aphasia participated in this study (mean age at the time of testing: 64 years old [range: 56-77 years], with an average 15.7 years of education [range: 14-18 years]). IWA did not significantly differ from AMC participants in terms of age ($p > 0.05$). The demographic information for these participants is presented in Table 3-1. All IWA experienced a single, unilateral left-hemisphere stroke, were native English speakers with normal or corrected-to-normal visual and auditory acuity and were right-handed before their stroke. The clinical diagnosis of aphasia was made based on the administration of standardized language testing to determine the extent and severity of each participant's language impairment, specifically, in the areas of fluency and auditory comprehension ability. Testing included the Boston Diagnostic Aphasia Examination—Third Edition [BDAE– 3] (Goodglass et al., 2001), the Western Aphasia Battery-Revised [WAB-R] (Kertesz, 2007), and a test of auditory sentence comprehension [SOAP: Subject-relative Object-relative Active and Passive] (Love & Oster, 2002). All participants were neurologically and physically stable (i.e., at least 6 months post-stroke), with no reported history of active or significant alcohol and/or drug abuse, active psychiatric illness or intellectual disability, and/or other significant brain disorder or dysfunction (e.g., Alzheimer's/dementia, Parkinson's, Huntington's, Korsakoff's).

All participants underwent protocols approved by IRB from both San Diego State University and University of California San Diego. The protocols were conducted at the Language and Neuroscience Group Laboratory at San Diego State University (SDSU). Each participant received $15 per session.

Table 3-1. Characteristics of IWA (n =11) and neurotypical control participants (n = 11).

IWA	Sex	Years Post-Stroke	Age at Testing	Years of Education	Aphasia Subtype	Lesion Location	BDAE-v3	WAB-R AQ	SOAP-SR (%)	SOAP-OR (%)
009	M	15	55	17	Mixed non-fluent	L lesion, IFG (BA 44/BA45) w/ posterior ext.	4	67.7	60%	40
017	M	18	66	15	Anomic	L anterior cerebral and middle cerebral infarct	4	95.4	100	90
101	M	9	67	20	Broca	L lesion posterior IFG (BA 44) w/ posterior ext.	2	82.6	100	30
130	M	8	63	16	Broca /Anomic	L IPL w/ posterior ext. sparing STG	4	90.5	75	55
140	F	16	42	NA	NA	L MCA infarct	2	75.7	80	30
151	F	7	65	16	Anomic	L MCA infarct w/ subcortical ext.	4	95.8	100	100
159	F	6	64	16	Broca	L MCA infarct	3	92.4	100	70
165	F	4	64	12	Broca	L MCA infarct	3	NA	80	60
169	M	4	59	12	Broca	L MCA infarct	2	28.2	80	40
190	F	6	76	12	Broca	L superior temporal lesion	3	88.2	90	40
191	M	1	57	16	Broca	L MCA infarct	4.5	98.4	100	60
AMC Group	Ages 57-66 years (mean = ~61.9); 7 females, 4 males; Education 14-18 years (mean = 15.7)									

L = left; LH=left hemisphere; BA = Brodmann area; IPL = inferior parietal lobule; STG = superior temporal gyrus; MCA = middle cerebral artery; BDAE = Boston Diagnostic Aphasia Examination (0 = no usable speech or auditory comprehension, 5 = minimal discernable speech handicap); SOAP SR = Average percent correct on subject relative items from the SOAP Test of Auditory Sentence Comprehension; SOAP OR = Average percent correct of object relative items from the SOAP Test of Auditory Sentence Comprehension; NA = Data is not available

Materials and Design

Fifteen intransitive (unaccusative) verbs were selected to be embedded in the canonical subject-relative sentences used in the inanimate (with inanimate theme) and animate (with animate theme) conditions. The selected verbs were used twice, once in each of the two conditions as indicated below [e, f], resulting in 60 sets of sentences.

> [e] Inanimate condition: This evening at the fashion show, the model [animate, subject] that noticed the dress [inanimate, object] surprisingly **fell** [animate, subject] during the evening gown showcase
>
> [f] Animate condition: This evening at the fashion show, the model [animate, subject] that noticed the designer [animate, object] surprisingly **fell** [animate, subject] during the evening gown showcase

An additional 120 filler sentences were included that were not further analyzed in the current study and that differed from the experimental and control condition sentences in terms of grammatical structure. Thus, participants completed a total of 180 sentences. For each sentence trial, line drawings depicting each of the Ns of interest were constructed (Figures 3-1a and 3-1b). All images were sized at 450 x 450 pixels.

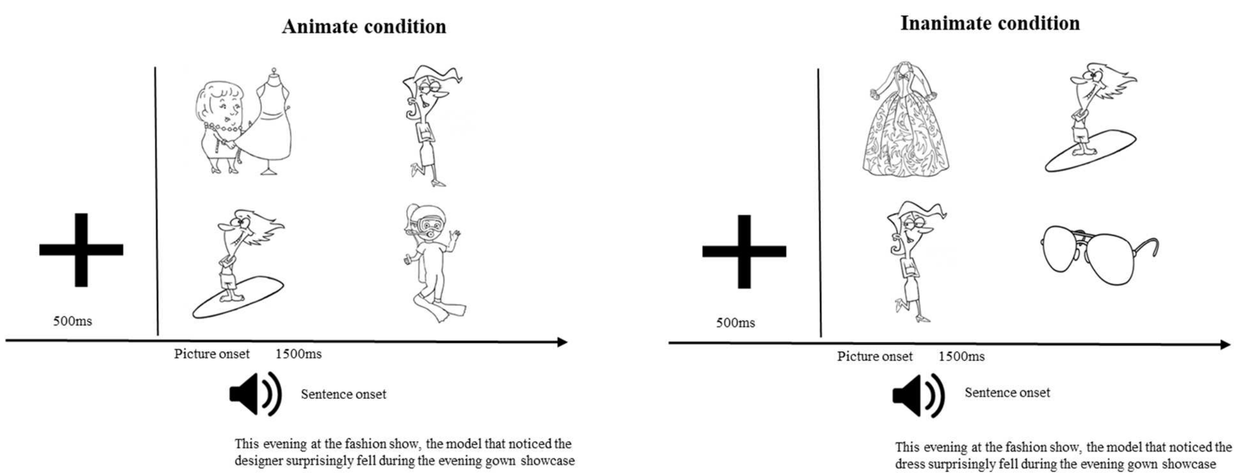


Figure 3-1. Example of the animate (left column) and inanimate conditions (right column) in the visual world paradigm where participants view four images, hear a sentence, and identify the corresponding target noun from the visual display. Sample stimuli are presented along the trial timeline, with corresponding auditorily presented sentences listed below.

In the current experiment, we used a switch target design such that the nouns [Ns] of interest from one experimental set serves as distractor items for another experimental set and vice versa. For example, for the animate condition, the display contained the two animate Ns mentioned in the sentence (e.g., model and designer), and the two animate referents from another experimental sentence (e.g., surfer and scuba diver). This design ensures that gazes to Ns were indicative of lexical processing, and not due to a preference for a particular image. The sentence trials were counterbalanced across four presentation lists and the location of the images presented was counterbalanced across items. The order of presentation across participants was also counterbalanced, with participants returning for four visits to complete this within-subjects experiment. There was at least a week between visits. A native English-speaking female recorded all sentences at an average rate of 4.47 syllables per second.

Stimulus pre-testing

Two pre-tests were conducted to ensure the stimuli were appropriate for use. In the first pre-test, images of the noun phrases were presented to college-age unimpaired participants (N=20) during a naming task to ensure that they clearly depicted the N of interest (i.e., that the image of the model was easily and readily named as intended). In this picture naming task, all pictures included in the study had a minimum of 75% agreement (exact naming and semantically related naming matches). In the second pre-test, in order to reduce plausibility effects, all of the Ns were pretested with another group of college-age students (N = 27) to confirm that they were all equally likely to be at the place mentioned in the initial PP of each sentence. For example, /the model/ and /the designer/ were matched to be equally likely to appear after /This evening at the fashion show/.). Participants were presented with two words (Person - Place) and asked to rate on a 1-5 Likert scale how likely (1-not very likely, 5-extremely likely) it was that the person (e.g., designer) would be at the place (e.g., fashion show). All items included in the study received ratings of 4s and 5s regarding the likelihood of being at the place tested (N1 *M*=4.8, *SD* = .6); (N2 *M* = 4.7, *SD* = .8).

Procedure

Participants listened to uninterrupted auditory sentences over headphones while viewing a four-picture display of black-and-white line drawings. Participants were seated in front of a computer screen and a Tobii X-120 eye-tracker with their eyes a distance of 60 cm from the eye-tracker and stimulus presentation screen. Each experimental session began with the calibration of the eye-tracker. Stimuli were presented with E-prime 2.0 software (Psychology Software Tools, Pittsburgh, PA).

Each trial began with a 500ms fixation cross, followed by a 250ms blank screen. As shown in Figure 3-2, each four-picture display was presented for 1500ms before participants began hearing the corresponding sentence and remained on the screen for 500ms after the sentence ended. For all trials, gaze location was sampled at a rate of 60 Hz, resulting in gaze location being recorded every 17ms across each trial. To keep participants on task, they were instructed that they would be asked Yes/No questions after each sentence (for example: Did the model fall during the evening gown showcase?). These questions were intended to reinforce the need for the participants to attend to the sentences. Participants responded to the questions via a button box (with Yes/No keys) using their left hand (non-dominant). To familiarize each participant with the task, 10 practice trials were conducted prior to each experimental session. This allowed the experimenter to provide feedback or redirection as necessary prior to beginning the task. See Figure 3-2 for schematic illustration of the eye-tracking paradigm.

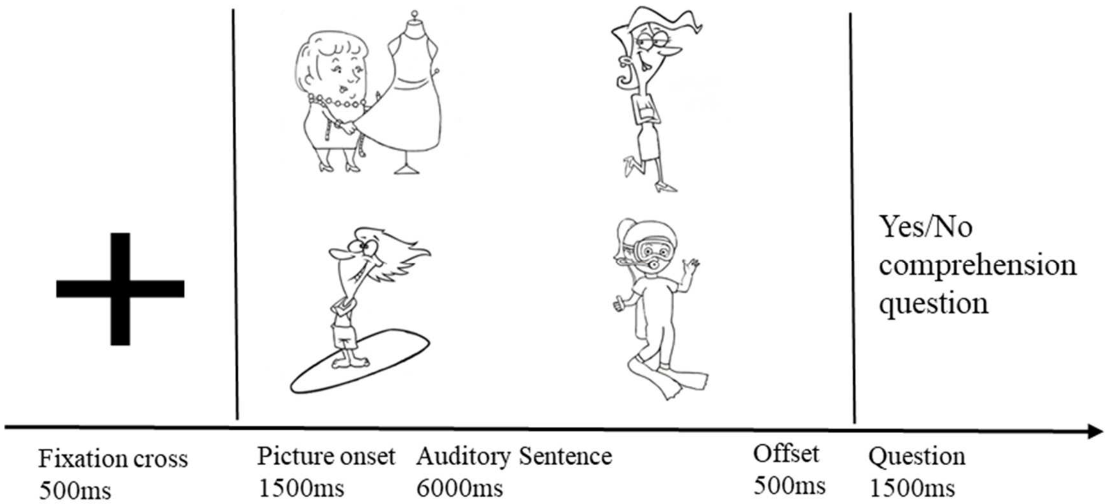


Figure 3-2. Schematic illustration of a trial including the online and offline sections in a visual world eye-tracking paradigm.

Data analysis approach

In this section we

describe the approach taken to post-process and analyze both the eye-tracking (gaze position captured every 17 ms) and end of sentence comprehension question (Yes/No) data.

Comprehension question data preparation. After listening to each sentence, participants were asked a Yes/No comprehension question. Both button press (Yes or No) and time to respond (in ms) were captured. Responses that had less than 100ms response latencies were excluded from the analysis as this is not a feasible voluntary response.

Eye-tracking gaze data preparation. Processing of the eye-tracking data was conducted to (1) check for trackloss and (2) aggregate the gaze data points across temporal bins.

(1) Trackloss occurs when the gaze data are not accessible from both participant's eyes (e.g., when they turn away or blink). The Tobii system provides a metric for validity of each datapoint which can be used to account for trackloss in the analysis. Trials in which the proportion of trackloss was greater than 25% were excluded from further analyses. The total percent of trackloss was calculated for each participant across all trials. AMC participants

had an average trackloss of 10% while IWA had an average trackloss of 7% which was no statistically different ($p > 0.05$).

(2) Gaze proportions toward each image on the screen for each trial were aggregated into time bins of 100ms. This method is employed as a tactic to take into account the underlying dependency between datapoints (i.e., autocorrelation) in time-series eye-tracking data which can inflate Type I error rates. For each bin, the proportion of gazes was estimated within each area of interest on the display (AOI) (Mirman, 2017). Gaze data were then subjected to statistical analysis (described below).

Time windows of analysis

Although sentences had similar lengths and syllable numbers, to account for slight timing differences, we coded the timing onset for each of the sentence constituents (initial prepositional phrase, noun phrase 1 [NP1], relativizer, noun phrase 2 [NP2], adverb, verb and final prepositional phrase; see Table 2) across all experimental items. This allowed us to normalize the onset as we identified the windows of interest across sentences. We identified two main windows of analysis. The first window captured the average onset of NP1 until the average offset of NP2. The second window captured the average onset of the adverb until the average offset of the final PP to ensure the inclusion of the gap-site. See Table 3-2 for the average timings at which these windows happen across sentences of each condition.

Table 3-2. The pre-identified windows of interest across the sentences

This evening at the fashion show,	the model	that noticed	the designer	surprisingly	fell	during the evening gown showcase
This evening at the fashion show,	the model	that noticed	the dress	surprisingly	fell	during the evening gown showcase
INITIAL PP	**NP1**	**REL**	**NP2**	**ADV**	**VERB**	**FINAL PP**

	Time window 1 Embedded clause	**Time window 2** Dependency processing
Mean onset time	1800-4800	4400-7200

Growth Curve Analysis

We used Growth Curve Analysis (GCA) to explore the dynamic patterns of gaze fixations over time in two pre-selected time windows of interest within the sentence (see Table 3-2, gray and yellow boxes). The GCA is a widely used method in the analysis of gaze fixation time- course data in the visual world paradigm (Akhavan et al., 2020; Baker & Love, 2021; Brown et al., 2011; Hadar et al., 2016; Mirman et al., 2008; Mirman et al., 2011). GCA is a multi-level modeling technique which employs fitting time-course data on orthogonal polynomials to capture change over time (Mirman et al., 2008). By adding the effects of the variables of interest on the polynomial terms, we can quantify the magnitude of their effects on statistically independent (i.e., orthogonal) aspects of the gaze proportion trajectory. In the GCA approach, the Level-1 model captures the overall gaze time course. Each of time terms reflect a specific aspect of gaze behavior. For this case, the intercept term reflects the average overall gaze proportion; the linear term reflects a monotonic change in gaze proportion (similar to a linear regression of gaze proportion as a function of time); the quadratic term reflects the symmetric rise and fall rate around a central inflection point (Mirman et al., 2008). The Level-2 submodels capture the fixed effects of experimental conditions or group effects on the Level-1 time terms. In the current study, we included the random effects of participants and items on intercept, linear, and quadratic time terms. Moreover, we added the random slopes for condition per subject to achieve a maximal random effects structure (Barr et al., 2013). Using the GCA approach, we added the fixed effects of variables of interest individually and we evaluated their effects on the model using model comparisons to see whether a particular variable imporved the model fit significantly. Improvements in model fit were evaluated using -2 times the change in log-likelihood, which is distributed as x^2 with degrees of freedom equal to the number of parameters added (Mirman, 2017). We conducted all analyses on the statistical software R-3.2.1, using the package LmerTest (Bates et al., 2014).

Results and Discussion

Offline comprehension performance

Recall that after each trial, participants were asked a Yes/No question. For the question accuracy, the mixed-effects logistic regression model revealed an effect of condition in the AMC group showing, as expected, that they had significantly better performance in the inanimate (98% accuracy) than the animate (94% accuracy) condition (Estimate = 1.02, SE = 0.45, $p < 0.05$). However, while IWA's means across conditions followed the same pattern of better performance in the inanimate (75% accuracy) condition (as compared to 69% accuracy for the animate condition), the same statistical model remained insignificant when tested for the IWA group (Estimate = 0.26, SE = 0.26, p = .32, see Table 3-3). This is likely due to the increased variability in performance for IWA across both conditions.

Table 3-3. The mean proportion accuracy of comprehension questions across groups and conditions

	Animate	**Inanimate**
AMC (n =11)	0.94 (0.28)	0.98 (0.14)
IWA (n =11)	0.69 (0.46)	0.75 (0.43)

Real-time gaze analysis

The subsequent analyses were completed on all trials, including those with correct and incorrect responses for offline comprehension questions; for a similar approach, see (Akhavan et al., 2022; Baker & Love, 2021). Analyses were focused on the condition differences between each group at specified windows of interest that were illustrated in Table 3-2. We first present a birds-eye view of the full time-course of the sentence in Figure 3-3; that is, gazes to each of the four AOIs throughout the time-course of each sentence in the animate and inanimate conditions. This time-course includes the initial activation of N1 in real-time (blue line, e.g., “the model”), followed by the deactivation of N1 and activation of N2 (red line, “the dress”/”the designer”), and finally the deactivation of N2 and expected re-activation of N1 at the gap site once the unaccusative verb was encountered (“fell").

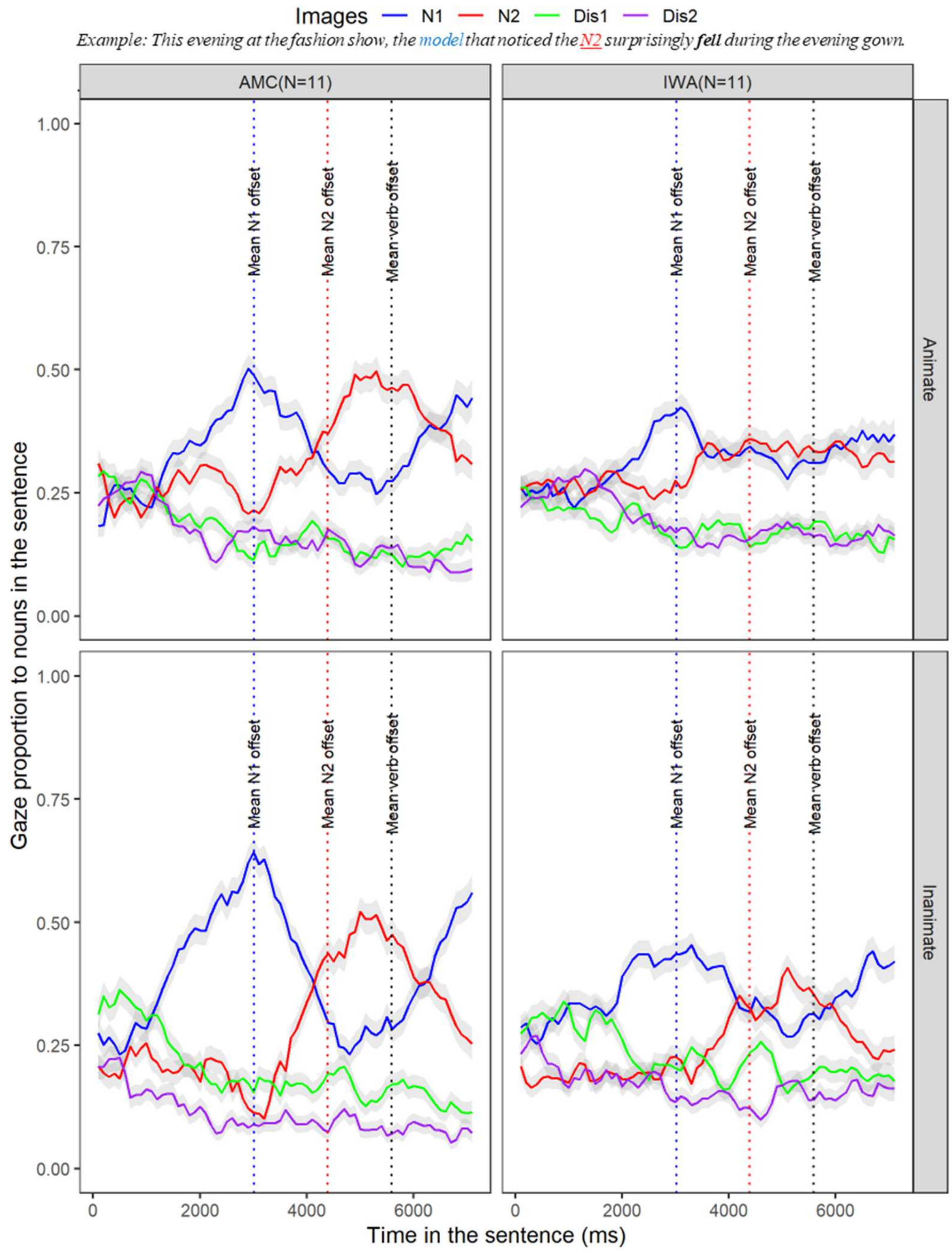


Figure 3-3. Time course of gaze patterns for all four AOIs across the whole sentence for AMC (n=11) and IWA (n=11) in the animate condition (top) and inanimate condition (bottom). Both groups show gaze proportions to the distractor items at the chance level 0.25.

To begin, we want to note that neither AMC nor IWA participants showed gaze proportions to the two distractor items more than at chance level, which is 0.25 in this case (Figure 3-3, green line [Dis1] and purple line [Dis2]). Thus, statistical analyses were focused on investigating the group differences (IWA versus AMC) on the proportion of gazes toward N1 and N2. To investigate the group difference on proportion of gazes to N1 and N2, we ran a linear mixed effects model that included the group factor as the fixed effect and subjects and items as the random effects. The model confirmed a significant difference between the IWA and AMC such that the overall proportion of gazes to both N1 and N2 in IWA was revealed to be lower than AMC (Estimate = -.03, $p < .05$). This finding reveals expected group differences in lexical activation for IWA relative to AMC. Given the identified differences between the IWA and AMC in online and offline processing, we built separate multilevel models for each group to examine the sensitivity of listeners to semantic cues upon initial encounter (question 1) and downstream in the sentence (question 3). Further, given the overall lexical activation differences in IWA compared to AMC group, to confirm that individuals with aphasia were experiencing a delay in processing the semantic cue (question 2), we compared their processing to the unimpaired group which served as the baseline. The findings for each question are presented below:

Result of Question 1: Sensitivity to lexical-semantic cues

We examined whether participants in each group demonstrated sensitivity to the lexical-semantic cue of animacy. We proposed that sensitivity to the lexical-semantic cue would yield a smaller interference effect in the inanimate condition where the noun-phrases are mismatching in animacy. In the eye-tracking paradigm, the interference effect is defined as an equivalent proportion of gazes toward related (N1) as well as intervening items (N2). We specified the window of analysis to occur at 200ms before the mean onset of the first N until 3000ms afterward (corresponding to the average offset of N2 –see Table 3-2). Gaze data by group (AMC, IWA) and condition (animate, inanimate) for processing N1 (target noun) and N2 (intervening noun) are plotted in Figure 3-4. Of interest for this analysis is the average proportion of looks to N2 relative to N1 between conditions. A significant interaction of images (N1, N2) and condition (animate, inanimate) at the intercept level with a negative estimate would correspond to a smaller proportion of gazes toward N2 (i.e., a smaller interference effect) in the inanimate condition. Moreover, a significant interaction of the same parameters at the linear level with a positive estimate would correspond to a slower rate of N2 activation in the inanimate condition.

AMC group. We first modeled gaze patterns for the AMC group. The linear mixed effect analysis revealed a significant effect of condition on gaze differences between the N1 and N2 for this group. These results (see Table 3-4) revealed that, as expected, the inanimate (mismatch) condition yielded reduced interference between N1 and N2 (Intercept: Estimate = -.16, $p < .001$; Linear: Estimate = .25, $p < .001$). This effect is apparent in Figure 3-4 in the steeper slopes of N1 deactivation and N2 activation as well as the greater separation between N1 and N2 curves for the inanimate condition than the animate condition.

Table 3-4. Results of GCA analysis for time window 1 (interference in embedded clause) within the AMC group.

Predictors	***Estimates***	***CI***	***p***
Intercept	0.38	0.34 – 0.42	<0.001
Linear	-0.20	-0.38 – -0.02	0.031
Image[N2]	-0.08	-0.13 – -0.02	0.004
Condition[Inanimate]	0.10	0.06 – 0.13	<0.001
Linear*Image[N2]	0.45	0.21 – 0.69	<0.001
Linear*Condition[Inanimate]	-0.11	-0.24 – 0.02	0.095
Image[N2]*Condition[Inanimate]	-0.16	-0.18 – -0.14	**<0.001**
Linear*Image[N2]*Condition[Inanimate]	0.25	0.13 – 0.37	**<0.001**

Note: The table provides the test of the full model including the interaction of images and condition on the intercept and linear time terms within the AMC group. Results in **boldface** are presented in the text.

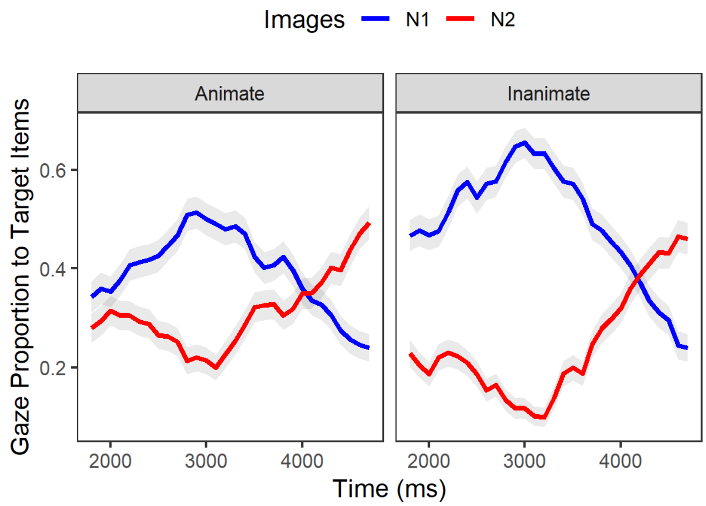


Figure 3-4. Gaze proportion differences between the animate and inanimate conditions within the AMC group [**…**the model that noticed the designer…].

IWA group. The same analysis approach was used for the IWA group, revealing highly similar results (see Table 3-5). Individuals with aphasia experienced a smaller interference effect in the inanimate condition, which is apparent in the significant interaction between condition (animate, inanimate) and the sentence constituent (N1, N2; Intercept: Estimate = -.12, $p < .001$; Linear: Estimate = .22, $p < .001$). As apparent in Figure 3-5, IWA also showed greater separation between the N1 and N2 curves in the inanimate than the animate condition. The results from both groups demonstrate the sensitivity of participants to the lexical-semantic manipulation.

Table 3-5. Results of GCA analysis for time window 1 (interference in embedded clause) within the IWA group**.**

Predictors	***Estimates***	***CI***	***p***
Intercept	0.34	0.30 – 0.38	<0.001
Linear	-0.00	-0.14 – 0.14	0.998
Image[N2]	-0.04	-0.09 – 0.00	0.062
Condition[Inanimate]	0.05	0.02 – 0.08	<0.001
Linear*Image[N2]	0.18	0.01 – 0.35	0.040
Linear*Condition[Inanimate]	-0.13	-0.24 – -0.02	0.025
Image[N2]*Condition[Inanimate]	-0.12	-0.14 – -0.10	**<0.001**
Linear*Image[N2]*Condition[Inanimate]	0.22	0.11 – 0.32	**<0.001**

Note: The table provides the test of the full model including the interaction of images and condition on the intercept and linear time terms within the IWA group. Results in **boldface** are presented in the text.

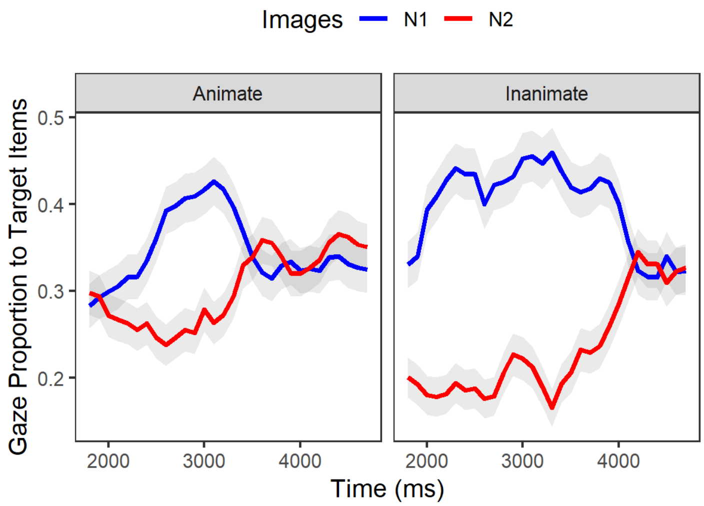


Figure 3-5. Gaze proportion differences between the animate and inanimate conditions within the IWA […the model that noticed the designer/dress…].

Result of Question 2 – Time-course of sensitivity to the lexical-semantic cue

Having shown that both groups are sensitive to the lexical-semantic cue presented in the inanimate condition, we more closely examined the time-course of sensitivity to it. Specifically, we asked whether IWA evince a temporal delay in their lexical processing as compared to AMCs. Within the same window of analysis that was examined for Research Question 1 (time window 1, see Table 3-2), we analyzed the deactivation pattern of N1. Faster deactivation of N1 indicates faster disengagement from N1 upon hearing the N2 in the sentence. This disengagement shows that listeners are switching focus to the next item (N2) without experiencing competition between the two Ns. We used growth curve analysis to see if there was a time-course difference between IWA and AMC in disengagement from N1 in the inanimate condition. Results (see Table 3-6) reveal a significant difference of group on the rate of N1 disengagement (Intercept: Estimate = -0.09, 9 $p < .05$; Quadratic: Estimate = 0.27, $p < .05$). As seen in Figure 3-6, the IWA group had a lower intercept of overall gaze proportion and a shallower curvature of N1 deactivation compared to AMC who had a steep rise and fall of gaze pattern to N1.

Table 3-6. Results of GCA analysis for time window 1. Group differences in the time-course of sensitivity to the cue.

Predictors	***Estimates***	***CI***	***p***
Intercept	0.49	0.42 – 0.56	<0.001
Linear	-0.37	-0.64 – -0.11	0.006
Quadratic	-0.49	-0.69 – -0.28	<0.001
Group[IWA]	-0.09	-0.17 – -0.01	**0.022**
Linear*Group[IWA]	0.24	-0.06 – 0.55	0.110
Quadratic*Group[IWA]	0.27	0.03 – 0.50	**0.026**

Note: The table provides the test of the full model including the effect of group on the intercept, linear and quadratic time terms. Results in **boldface** are presented in the text.

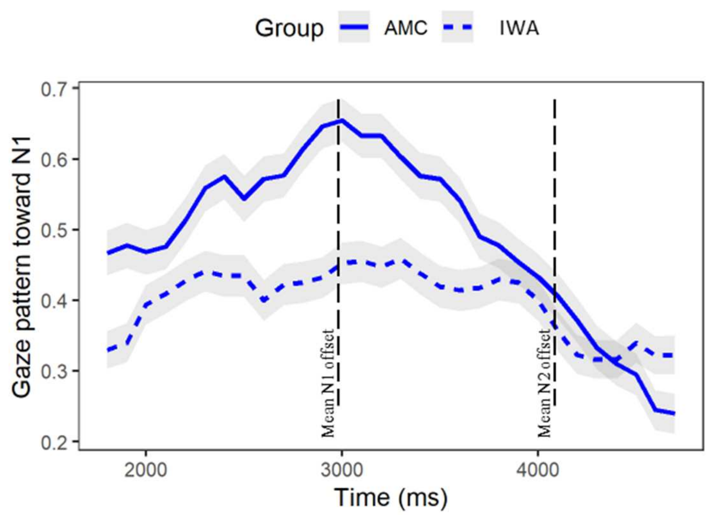


Figure 3-6. Comparing IWA with AMC on the timecourse of disengagement from N1 upon hearing N2 […the model that noticed the dress…].

Result of Question 3 – Downstream effect of the lexical-semantic cue on the dependency linking process

Recall that at the gap-site once the unaccusative verb is reached (e.g., "fell"), successful dependency linking is evidenced as a re-activation of the N1. The gap-site window is specified to begin at the onset of the adverb that immediately precedes the verb (e.g., "surprisingly") until 2800ms afterward (time window 2, see Table 3-2). This allowed time for re-activation at the verb site as well as during the spillover region. In this window, we inspected the presence of an interference effect during dependency linking by analyzing the gaze proportion of N1 (target or to-be-retrieved noun) relative to N2 (intervening noun). According to the cue-based parsing approach, upon encountering the verb, retrieval cues are triggered to search for a direct-object noun (N1), however, there is an additional N whose features overlap with the target creating competition between the target (N1) and the non-target noun (N2). Of importance is how the animacy of N2 is modulating the reactivation pattern of N1 and the interference effect of the intervening noun item in each group. To understand the downstream effect of the animacy manipulation at the gap site, for each group we built separate models and included the interaction of fixed effects of images (N1, N2) and condition. Of interest for the analysis here was the deactivation pattern of N2 as N1 was reactivated. We expected a steeper fall of N2 relative to N1 in the inanimate compared to the animate condition.

AMC group. The individual parameter estimates for the AMC group (Figure 3-7, Table 3-7) revealed a significant effect of condition on the difference between N1 and N2 at the linear level (Estimate = -.4, $p < .05$). This suggested a faster rate of deactivation for N2 relative to N1 in the inanimate condition compared to the animate condition. This faster deactivation is evident in Figure 3-7 in terms of steeper N2 deactivation and N1 activation slopes after the verb offset in the inanimate condition, as well as a greater difference in fixations to N1 versus N2 towards the end of the time window. This finding shows a clear influence of the pre-verbal lexical-semantic animacy cue on post-verbal dependency linking.

Table 3-7. Results of GCA analysis for time window 2 (dependency processing) within the AMC group.

Predictors	***Estimates***	***CI***	***p***
Intercept	0.33	0.28 – 0.39	<0.001
Linear	0.23	0.04 – 0.43	0.018
Quadratic	0.13	0.01 – 0.26	0.038
Image[N2]	0.10	0.02 – 0.17	0.017
Condition[Inanimate]	0.02	-0.01 – 0.04	0.274
Linear*Image[N2]	-0.33	-0.61 – -0.06	0.016
Quadratic*Image[N2]	-0.32	-0.50 – -0.15	<0.001
Linear*Condition[Inanimate]	0.20	0.10 – 0.31	<0.001
Quadratic*Condition[Inanimate]	0.07	-0.03 – 0.17	0.187
Image[N2]*Condition[Inanimate]	-0.04	-0.07 – -0.02	0.001
Linear*Image[N2]*Condition[Inanimate]	**-0.37**	**-0.51 – -0.24**	**<0.001**
Quadratic*Image[N2]*Condition[Inanimate]	-0.06	-0.20 – 0.07	0.347

Note: The table provides the test of the full model including the interaction of images and condition on the intercept, linear, and quadratic time terms within the AMC group. Results in **boldface** are presented in the text.

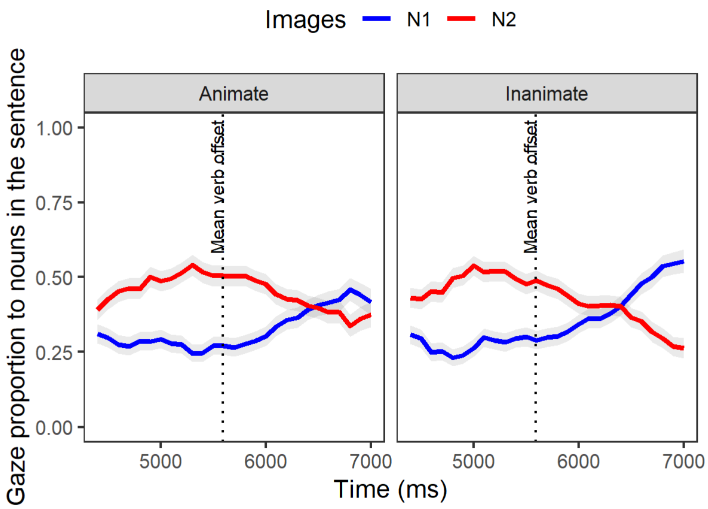


Figure 3-7. Gaze proportions of AMC individuals to the target (N1) and intervening (N2) items at the gap-site […surprisingly fell during the evening gown…].

IWA group. The individual parameter estimates for IWA (Figure 3-8, Table 3-8) also revealed a significant effect of condition on the difference between N1 and N2 deactivation (Estimate = -.3, $p < .05$). In IWA, while Figure 3-8 reveals no clear differentiation between looks to N1 and N2 during post-verbal dependency linking, reflecting the expected similarity-based interference, the N1 is clearly reactivated while the N2 is deactivated in the inanimate condition. Thus overall, these results indicate a reduced interference effect of N2 in the inanimate condition for both groups.

Table 3-8. Results of GCA analysis for time window 2 (dependency processing) for the IWA group.

Predictors	***Estimates***	***CI***	***p***
Intercept	0.33	0.28 – 0.38	<0.001
Linear	0.08	-0.07 – 0.23	0.279
Quadratic	0.05	-0.04 – 0.14	0.241
Image[N2]	0.01	-0.05 – 0.08	0.693
Condition[Inanimate]	0.01	-0.02 – 0.04	0.570
Linear*Image[N2]	-0.12	-0.33 – 0.08	0.241
Quadratic*Image[N2]	-0.05	-0.17 – 0.08	0.475
Linear*Condition[Inanimate]	0.10	-0.00 – 0.20	0.060
Quadratic*Condition[Inanimate]	0.10	0.02 – 0.19	0.015
Image[N2]*Condition[Inanimate]	-0.04	-0.06 – -0.02	<0.001
Linear*Image[N2]*Condition[Inanimate]	**-0.27**	**-0.39 – -0.16**	**<0.001**
Quadratic*Image[N2]*Condition[Inanimate]	-0.28	-0.39 – -0.17	<0.001

Note: The table provides the test of the full model including the interaction of images and condition on the intercept, linear, and quadratic time terms within the IWA group. Results in **boldface** are presented in the text.

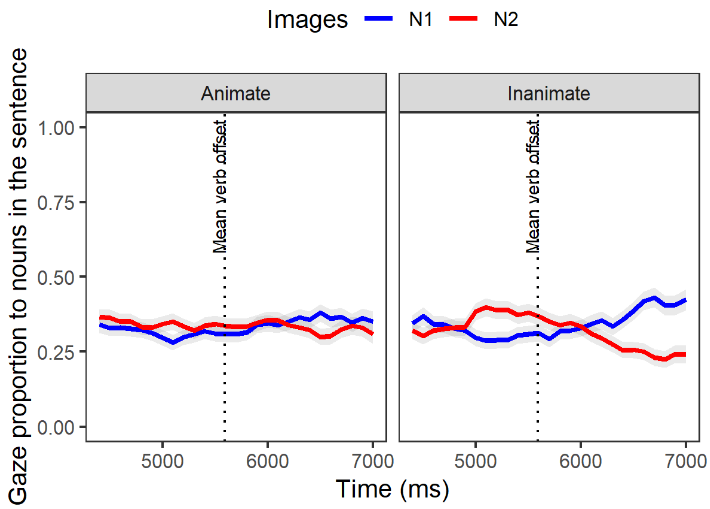


Figure 3-8. Gaze proportions of IWA individuals to the target (N1) and intervening (N2) items at the gap-site […surprisingly fell during the evening gown…].

Discussion

In the current study, we examined whether unimpaired listeners and individuals with aphasia can use lexical-semantic cuing in real-time during comprehension of canonical unaccusative sentences that require long-distance dependency linking. First, we examined the sensitivity of listeners in both groups to a lexical-sematic animacy cue. Second, we examined the time course of processing the lexical-semantic cue and its effects on N1 activation and deactivation in individuals with aphasia compared to the age-matched unimpaired control individuals. Third, we assessed whether the lexical-semantic cue has a downstream effect on dependency linking at the gap-site for both groups. We used animacy as the semantic cue to reduce the similarity-based interference effect. We employed an eye-tracking visual world paradigm to capture the real-time processing stream during auditory comprehension. We confirmed our predicted hypothesis that listeners in both groups would be sensitive to the semantic-lexical cue in the inanimate condition. We also confirmed our predicted hypothesis for individuals with aphasia that they would show sensitivity to the lexical-semantic cue, but with a delay in processing. Finally, we confirmed in both groups that the lexical-semantic cue resulted in significant reduction in a similarity-based interference effect throughout the sentence processing stream, with markedly changed gaze patterns during dependency linking at the gap-site.

Sensitivities to lexical-semantic cues across the sentence processing timeline (research questions 1 and 3)

Our results from both AMC and IWA confirmed the predictions of the similarity-based interference approach. We found that IWA were experiencing an interference effect during real-time dependency linking and integration. Specifically, in windows where the argument verbs had to be specified (time window 1 and 2, see Table 3-2), IWA showed a lack of ability in distinguishing each noun phrase (See Figures 3-6 and 3-8). However, when the level of competition was reduced (via a semantic-animacy manipulation), IWA showed a facilitation effect, as they were able to distinguish between the two noun phrases and reactivate the antecedent (N1) at the gap-site. These results revealed that IWA were able to access the lexical-semantic representation of the words and used it during their auditory processing in real-time. However, vulnerability in the processing system of IWA was apparent when there was a potential case of interference in the animate condition. This is in line with predictions of the Relativized Minimality approach (Friedmann et al., 2009) and the Intervener hypothesis (Engel et al., 2018; Sheppard et al., 2015), which emphasize that computing the dependency relationship for IWA between two elements becomes more difficult because the structurally similar intervener can pose competition for the to-be-retrieved target item during the dependency linking.

Timecourse of sensitivity to the lexical-semantic cues (research question 2)

Individuals with aphasia were shown to be sensitive to the animacy information, even though they appeared to process it slower than neurologically unimpaired participants, as was apparent in delayed deactivation of N1 in IWA when N2 was encountered. The delay in processing of IWA has also been shown using other methodologies. For instance, using a self-paced listening task, DeDe (2012) found that IWA (individuals with anomia) have delayed processing of lexical-semantic and prosodic information (DeDe, 2012). Moreover, in a study using Event-related potentials (ERP), Sheppard and colleagues found that IWA (individuals with agrammatism) showed a delayed N400 effect (Sheppard et al., 2017). In this ERP study, the individuals with agrammatism were unable to integrate semantic and prosodic cues to predict upcoming syntactic structure and prevent garden path effects in sentences with incongruent prosody. These findings converge with the current findings of overall lower offline comprehension accuracy in IWA, particularly in the animate condition; further, they confirm that a delay in lexical processing can negatively impact sentence processing success (Choy & Thompson, 2009; Dickey et al., 2007; Love et al., 2008; Thompson & Choy, 2009). The nature of this delay in processing lexical-semantic representations can have a multifactorial etiology. Jefferies and Lambon Ralph (Jefferies & Lambon Ralph, 2006) have proposed that deficits in processing can reflect impairments of "semantic control processes". Such semantic control processes allow task- and context-relevant aspects of knowledge to be brought to the fore, while irrelevant information is suppressed (Jefferies, 2013; Jefferies & Lambon Ralph, 2006; Jefferies et al., 2008; Mirman & Britt, 2014). In case of left-hemisphere stroke, damage to networks comprising inferior prefrontal cortex, posterior middle temporal gyrus and the intraparietal sulcus (Noonan et al., 2013; Rodd et al., 2005; Thompson-Schill et al., 1997) results in an impaired ability to inhibit irrelevant semantic information, to retrieve weak or less automatic semantic associations and to resolve competition between multiple competing representations (Paul Hoffman et al., 2011; Jefferies & Lambon Ralph, 2006; Noonan et al., 2010). For a full discussion of these control processes, see (Hoffman, 2018; Hoffman et al., 2009; Hoffman et al., 2013; P. Hoffman et al., 2011).

Limitations and implications

There are limitations to the current study that can be addressed in future research. First, there were a relatively small number of participants within the aphasia group. This is particularly important because inter-participant variability is inherent in individuals with aphasia, thus it is essential that the questions in the current study be addressed with a larger number of participants in future studies. Second, our study did not specifically investigate the nature of the underlying memory and cognitive control system supporting individual differences in sensitivity to the semantic cue and in the response timecourse during sentence comprehension. Finally, our study did not specifically examine which lesion characteristics impacted the extent of benefiting from the lexical-semantic cueing in real-time. We believe that the current study makes an important initial contribution in suggesting that a semantic cue at the sentence level, specifically an animacy-mismatch between a target and intervening noun, can considerably and reliably support sentence processing in an initial group of individuals with aphasia. This finding will provide a useful basis for new research and has clear implications for intervention in IWA. Specifically, in interventions targeting complex sentence processing in IWA, an initial step to increase comprehensibility of a sentence may be an animacy mismatch between nouns as was undertaken here. Instead, if the clinician desires that the client focus solely on syntactic processes, an animacy match between noun constituents may be a valuable strategy.

Conclusions

The current study improves our understanding of how lexical-semantic representations are encoded and processed during language comprehension in neurologically unimpaired as well as impaired populations. Here we demonstrate that reduction in representational interference via a semantic manipulation can facilitate the syntactic processing of unimpaired populations and those with aphasia. However, disruption in the timely activation of lexical representations can slow down the IWA's sensitivity to cues in real-time processing.

References

Akhavan, N., Blumenfeld, H. K., & Love, T. (2020, 2020-May-27). Auditory Sentence Processing in Bilinguals: The Role of Cognitive Control [Original Research]. *Frontiers in psychology, 11*(898). https://doi.org/10.3389/fpsyg.2020.00898

Akhavan, N., Sen, C., Baker, C., Abbott, N., Gravier, M., & Love, T. (2022). Effect of Lexical-Semantic Cues during Real-Time Sentence Processing in Aphasia. *Brain Sciences, 12*(3), 312.

Baker, C., & Love, T. (2021). It's about time! Time as a parameter for lexical and syntactic processing: an eye-tracking-while-listening investigation. *Language, Cognition and Neuroscience*, 1-21.

Barr, D. J., Levy, R., Scheepers, C., & Tily, H. J. (2013). Random effects structure for confirmatory hypothesis testing: Keep it maximal. *Journal of Memory and Language, 68*(3), 255-278.

Bates, D., Mächler, M., Bolker, B., & Walker, S. (2014). Fitting linear mixed-effects models using lme4. *arXiv preprint arXiv:1406.5823*.

Bever, T. G., & Sanz, M. (1997). Empty categories access their antecedents during comprehension: Unaccusatives in Spanish. *Linguistic Inquiry*, 69-91.

Bhandari, P., Demberg, V., & Kray, J. (2021). Semantic Predictability Facilitates Comprehension of Degraded Speech in a Graded Manner. *Frontiers in psychology*, 3769.

Brown, M., Salverda, A. P., Dilley, L. C., & Tanenhaus, M. K. (2011). Expectations from preceding prosody influence segmentation in online sentence processing. *Psychonomic Bulletin & Review, 18*(6), 1189-1196.

Burkhardt, P., Piñango, M. M., & Wong, K. (2003). The role of the anterior left hemisphere in real-time sentence comprehension: Evidence from split intransitivity. *Brain and Language, 86*(1), 9-22.

Burzio, L. (1981). *Intransitive verbs and Italian auxiliaries* Massachusetts Institute of Technology].

Burzio, L. (1986). *Italian syntax: A government-binding approach* (Vol. 1). Springer Science & Business Media.

Caramazza, A., & Zurif, E. B. (1976). Dissociation of algorithmic and heuristic processes in language comprehension: Evidence from aphasia. *Brain and Language, 3*(4), 572-582. https://www.sciencedirect.com/science/article/abs/pii/0093934X76900481?via%3Dihub

Choy, J. J., & Thompson, C. K. (2009, 2009/05/25). Binding in agrammatic aphasia: Processing to comprehension. *Aphasiology, 24*(5), 551-579. https://doi.org/10.1080/02687030802634025

Choy, J. J., & Thompson, C. K. (2010). Binding in agrammatic aphasia: Processing to comprehension. *Aphasiology, 24*(5), 551-579.

DeDe, G. (2012). Lexical and prosodic effects on syntactic ambiguity resolution in aphasia. *Journal of psycholinguistic research, 41*(5), 387-408.

Dickey, M. W., Choy, J. J., & Thompson, C. K. (2007, 2007/01). Real-time comprehension of wh- movement in aphasia: Evidence from eyetracking while listening. *Brain and Language, 100*(1), 1-22. https://doi.org/10.1016/j.bandl.2006.06.004

Engel, S., Shapiro, L. P., & Love, T. (2018, 2018/02). Proform-Antecedent linking in individuals with agrammatic aphasia: A test of the Intervener Hypothesis. *Journal of Neurolinguistics, 45*, 79-94. https://doi.org/10.1016/j.jneuroling.2017.10.001

Ferrill, M., Love, T., Walenski, M., & Shapiro, L. P. (2012). The time-course of lexical activation during sentence comprehension in people with aphasia. *American Journal of Speech-Language Pathology*.

Friedmann, N., Belletti, A., & Rizzi, L. (2009). Relativized relatives: Types of intervention in the acquisition of A-bar dependencies. *Lingua, 119*(1), 67-88.

Friedmann, N., Taranto, G., Shapiro, L. P., & Swinney, D. (2008). The leaf fell (the leaf): The online processing of unaccusatives. *Linguistic Inquiry, 39*(3), 355-377.

Gibson, E., Marantz, A., Miyashita, Y., & O'Neil, W. (2000). Image, language, brain: Papers from the first Mind Articulation Project symposium.

Gibson, E., Sandberg, C., Fedorenko, E., Bergen, L., & Kiran, S. (2016). A rational inference approach to aphasic language comprehension. *Aphasiology, 30*(11), 1341-1360.

Goodglass, H., Kaplan, E., & Barresi, B. (2001). *BDAE-3: Boston Diagnostic Aphasia Examination–Third Edition*. Lippincott Williams & Wilkins Philadelphia, PA.

Gordon, P. C., Hendrick, R., & Johnson, M. (2004, 2004/07). Effects of noun phrase type on sentence complexity. *Journal of Memory and Language, 51*(1), 97-114. https://doi.org/10.1016/j.jml.2004.02.003

Gordon, P. C., Hendrick, R., Johnson, M., & Lee, Y. (2006). Similarity-based interference during language comprehension: Evidence from eye tracking during reading. *Journal of experimental psychology: Learning, Memory, and Cognition, 32*(6), 1304. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1766329/pdf/nihms-14274.pdf

Gordon, P. C., Hendrick, R., & Levine, W. H. (2002, 2002/09). Memory-Load Interference in Syntactic Processing. *Psychological Science, 13*(5), 425-430. https://doi.org/10.1111/1467-9280.00475

Gotts, S. J., & Plaut, D. C. (2002, 2002/09/01). The impact of synaptic depression following brain damage: A connectionist account of "access/refractory" and "degraded-store" semantic impairments. *Cognitive, Affective, & Behavioral Neuroscience, 2*(3), 187-213. https://doi.org/10.3758/cabn.2.3.187

Hadar, B., Skrzypek, J. E., Wingfield, A., & Ben-David, B. M. (2016). Working memory load affects processing time in spoken word recognition: Evidence from eye-movements. *Frontiers in neuroscience, 10*, 221.

Hagoort, P., Brown, C. M., & Swaab, T. Y. (1996). Lexical—semantic event–related potential effects in patients with left hemisphere lesions and aphasia, and patients with right hemisphere lesions without aphasia. *Brain, 119*(2), 627-649. https://doi.org/10.1093/brain/119.2.627

Hoffman, P. (2018, May 25). An individual differences approach to semantic cognition: Divergent effects of age on representation, retrieval and selection. *Sci Rep, 8*(1), 8145. https://doi.org/10.1038/s41598-018-26569-0

Hoffman, P., Jefferies, E., Ehsan, S., Hopper, S., & Ralph, M. A. L. (2009). Selective short-term memory deficits arise from impaired domain-general semantic control mechanisms. *Journal of experimental psychology: Learning, Memory, and Cognition, 35*(1), 137.

Hoffman, P., Jefferies, E., Haffey, A., Littlejohns, T., & Lambon Ralph, M. A. (2013). Domain-specific control of semantic cognition: A dissociation within patients with semantic working memory deficits. *Aphasiology, 27*(6), 740-764. https://doi.org/10.1080/02687038.2012.751578

Hoffman, P., Jefferies, E., & Ralph, M. A. (2011, Feb). Explaining semantic short-term memory deficits: evidence for the critical role of semantic control. *Neuropsychologia, 49*(3), 368-381. https://doi.org/10.1016/j.neuropsychologia.2010.12.034

Hoffman, P., Rogers, T. T., & Ralph, M. A. L. (2011). Semantic diversity accounts for the “missing” word frequency effect in stroke aphasia: Insights using a novel method to quantify contextual variability in meaning. *Journal of cognitive neuroscience, 23*(9), 2432-2446.

Hofmeister, P. (2011). Representational Complexity and Memory Retrieval in Language Comprehension. *Lang Cogn Process, 26*(3), 376-405. https://doi.org/10.1080/01690965.2010.492642

Hofmeister, P., & Vasishth, S. (2014). Distinctiveness and encoding effects in online sentence comprehension. *Frontiers in psychology, 5*, 1237.

Jefferies, E. (2013). The neural basis of semantic cognition: converging evidence from neuropsychology, neuroimaging and TMS. *Cortex, 49*(3), 611-625. https://www.sciencedirect.com/science/article/abs/pii/S0010945212003103?via%3Dihub

Jefferies, E., & Lambon Ralph, M. A. (2006, 2006/06/30). Semantic impairment in stroke aphasia versus semantic dementia: a case-series comparison. *Brain, 129*(8), 2132-2147. https://doi.org/10.1093/brain/awl153

Jefferies, E., Patterson, K., & Ralph, M. A. L. (2008). Deficits of knowledge versus executive control in semantic cognition: Insights from cued naming. *Neuropsychologia, 46*(2), 649-658. https://doi.org/10.1016/j.neuropsychologia.2007.09.007

Kertesz, A. (2007). *WAB-R: Western aphasia battery-revised*. PsychCorp.

Kluender, R., & Kutas, M. (1993). Bridging the gap: Evidence from ERPs on the processing of unbounded dependencies. *Journal of cognitive neuroscience, 5*(2), 196-214.

Koring, L., Mak, P., & Reuland, E. (2012). The time course of argument reactivation revealed: Using the visual world paradigm. *Cognition, 123*(3), 361-379.

Lewis, R. L., & Vasishth, S. (2005). An activation□based model of sentence processing as skilled memory retrieval. *Cognitive science, 29*(3), 375-419. https://onlinelibrary.wiley.com/doi/pdfdirect/10.1207/s15516709cog0000_25?download=true

Love, T., & Oster, E. (2002). On the categorization of aphasic typologies: The SOAP (a test of syntactic complexity). *Journal of psycholinguistic research, 31*(5), 503-529.

Love, T., Swinney, D., Walenski, M., & Zurif, E. (2008). How left inferior frontal cortex participates in syntactic processing: Evidence from aphasia. *Brain and Language, 107*(3), 203-219. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2650827/pdf/nihms-79787.pdf

Martin, N., & Gupta, P. (2004). Exploring the relationship between word processing and verbal short-term memory: Evidence from associations and dissociations. *Cognitive Neuropsychology, 21*(2-4), 213-228.

Martin, R. C., Breedin, S. D., & Damian, M. F. (1999, 1999/12). The Relation of Phoneme Discrimination, Lexical Access, and Short-Term Memory: A Case Study and Interactive Activation Account. *Brain and Language, 70*(3), 437-482. https://doi.org/10.1006/brln.1999.2184

Mirman, D. (2017). *Growth curve analysis and visualization using R*. Chapman and Hall/CRC.

Mirman, D., & Britt, A. E. (2014). What we talk about when we talk about access deficits. *Philos Trans R Soc Lond B Biol Sci, 369*(1634), 20120388. https://doi.org/10.1098/rstb.2012.0388

Mirman, D., Dixon, J. A., & Magnuson, J. S. (2008). Statistical and computational models of the visual world paradigm: Growth curves and individual differences. *Journal of Memory and Language, 59*(4), 475-494.

Mirman, D., Yee, E., Blumstein, S. E., & Magnuson, J. S. (2011, May). Theories of spoken word recognition deficits in aphasia: evidence from eye-tracking and computational modeling. *Brain Lang, 117*(2), 53-68. https://doi.org/10.1016/j.bandl.2011.01.004

Noonan, K. A., Jefferies, E., Corbett, F., & Ralph, M. A. L. (2010). Elucidating the nature of deregulated semantic cognition in semantic aphasia: evidence for the roles of prefrontal and temporo-parietal cortices. *Journal of cognitive neuroscience, 22*(7), 1597-1613.

Noonan, K. A., Jefferies, E., Visser, M., & Lambon Ralph, M. A. (2013, 2013/11). Going beyond Inferior Prefrontal Involvement in Semantic Control: Evidence for the Additional Contribution of Dorsal Angular Gyrus and Posterior Middle Temporal Cortex. *Journal of cognitive neuroscience, 25*(11), 1824-1850. https://doi.org/10.1162/jocn_a_00442

Novick, J. M., Trueswell, J. C., & Thompson-Schill, S. L. (2005, 2005/09). Cognitive control and parsing: Reexamining the role of Broca's area in sentence comprehension. *Cognitive, Affective, & Behavioral Neuroscience, 5*(3), 263-281. https://doi.org/10.3758/cabn.5.3.263

Oberauer, K., & Lange, E. B. (2008). Interference in verbal working memory: Distinguishing similarity-based confusion, feature overwriting, and feature migration. *Journal of Memory and Language, 58*(3), 730-745.

Perlmutter, D. M. (1978). Impersonal passives and the unaccusative hypothesis. annual meeting of the Berkeley Linguistics Society,

Poirier, J., Walenski, M., & Shapiro, L. P. (2012). The role of parallelism in the real-time processing of anaphora. *Language and cognitive processes, 27*(6), 868-886.

Prather, P., Zurif, E., Love, T., & Brownell, H. (1997). Speed of lexical activation in nonfluent Broca's aphasia and fluent Wernicke's aphasia. *Brain and Language, 59*(3), 391-411. https://www.sciencedirect.com/science/article/abs/pii/S0093934X9791751X?via%3Dihub

Python, G., Pellet Cheneval, P., Bonnans, C., & Laganaro, M. (2021). Facilitating word retrieval in aphasia: which type of cues for which aphasic speakers? *Frontiers in human neuroscience*, 722.

Rodd, J. M., Davis, M. H., & Johnsrude, I. S. (2005). The neural mechanisms of speech comprehension: fMRI studies of semantic ambiguity. *Cerebral Cortex, 15*(8), 1261-1269.

Sheppard, S. M., Love, T., Midgley, K. J., Holcomb, P. J., & Shapiro, L. P. (2017). Electrophysiology of prosodic and lexical-semantic processing during sentence comprehension in aphasia. *Neuropsychologia, 107*, 9-24.

Sheppard, S. M., Walenski, M., Love, T., & Shapiro, L. P. (2015). The auditory comprehension of wh-questions in aphasia: Support for the intervener hypothesis. *Journal of Speech, Language, and Hearing Research, 58*(3), 781-797.

Sullivan, N., Walenski, M., Love, T., & Shapiro, L. P. (2017a). The comprehension of sentences with unaccusative verbs in aphasia: a test of the intervener hypothesis. *Aphasiology, 31*(1), 67-81.

Sullivan, N., Walenski, M., Love, T., & Shapiro, L. P. (2017b). The curious case of processing unaccusative verbs in aphasia. *Aphasiology, 31*(10), 1205-1225.

Swaab, T., Brown, C., & Hagoort, P. (1997, 1997/01). Spoken Sentence Comprehension in Aphasia: Event-related Potential Evidence for a Lexical Integration Deficit. *Journal of cognitive neuroscience, 9*(1), 39-66. https://doi.org/10.1162/jocn.1997.9.1.39

Swaab, T. Y., Brown, C., & Hagoort, P. (1998, 1998/08). Understanding ambiguous words in sentence contexts: electrophysiological evidence for delayed contextual selection in Broca's aphasia. *Neuropsychologia, 36*(8), 737-761. https://doi.org/10.1016/s0028-3932(97)00174-7

Thompson-Schill, S. L., D'Esposito, M., Aguirre, G. K., & Farah, M. J. (1997). Role of left inferior prefrontal cortex in retrieval of semantic knowledge: a reevaluation. *Proceedings of the National Academy of Sciences, 94*(26), 14792-14797.

Thompson, C. K., & Choy, J. J. (2009, 2009/04/16). Pronominal Resolution and Gap Filling in Agrammatic Aphasia: Evidence from Eye Movements. *Journal of psycholinguistic research, 38*(3), 255-283. https://doi.org/10.1007/s10936-009-9105-7

Van Dyke, J. A., & Lewis, R. L. (2003). Distinguishing effects of structure and decay on attachment and repair: A cue-based parsing account of recovery from misanalyzed ambiguities. *Journal of Memory and Language, 49*(3), 285-316.

Chapter 3, in full, is a reprint of material that is currently under review for publication in the Journal of Neurolinguistics. The dissertation author was the primary investigator and author of this paper.

CHAPTER 4

Functional Contributions of the Prefrontal Cortex Tracts to Real Time Sentence Processing

Introduction

The left inferior frontal region has been implicated in numerous processes, such as semantic processing, phonological segmentation, phoneme-to-grapheme conversional processes, and conflict-resolution processes among others; see (Nozari & Thompson-Schill, 2016) for citations therein. Yet, there is an ongoing debate as to the functional role of the left inferior frontal region in sentence processing. Existing findings suggest that syntactic and semantic processes can occur with the contribution of left posterior-superior temporal gyrus, posterior-middle temporal gyrus (Friederici et al., 2003; Yi G. Glaser et al., 2013; Hagoort, 2005), and without the involvement of the left inferior frontal gyrus when sources of interference are not present (Y. G. Glaser et al., 2013; Matchin & Hickok, 2020; Matchin & Rogalsky, 2017). Moreover, individuals with frontal damage in the left hemisphere can show good comprehension of sentences with low conflict (Novick et al., 2009). Yet, alternative accounts indicate that lesion in the inferior frontal gyrus in the left hemisphere can modulate sentence processing regardless of conflict resolution demands when the process is measured using online approaches (Fedorenko & Blank, 2020; Friederici & Gierhan, 2013; Hagoort, 2005; Love et al., 2008; Nozari et al., 2016; Vuong & Martin, 2015). For instance, in an eye-tracking study, individuals with damage in the inferior frontal regions but intact temporo-parietal regions showed less sensitivity to contextual information (e.g., sentences with the restrictive verb /*eat*/ compared to the non-restrictive verb /*see*/ in "*She will eat/see the apple*.") to locate the target (/*apple*/) when conflict resolution demands were minimal (Nozari et al., 2016). The results of this study, which was interpreted under the framework of the Drift Diffusion Model (Ratcliff et al., 2004; Ratcliff & Rouder, 2000), indicated that when the frontal region, in particular in left hemisphere, is intact, it can affect the drift rate or activation gain parameter by boosting the associations between the bottom-up cues (/*eat*/) and the target (/*apple*/). Drift rate is defined as the rate of accumulation of information, and it is determined by the quality of the information extracted from the stimulus. Therefore, left frontal regions can play a role in sentence comprehension by facilitating the processing of association when no overt conflict resolution demands are posed. The present study addresses this debate by taking a multi-modal approach and focusing on the white matter tracts that pass through the frontal region. Here, we examined the online processing of individuals with aphasia via an eye-tracking-while-listening paradigm and combined it with information about the structural integrity of specific tracts via Diffusion Tensor Imaging (DTI) techniques. The overarching goal of the current study is to investigate whether the integrity of four tracts that pass through the prefrontal cortex, namely the arcuate fasciculus (AF), frontal aslant tract (FAT), uncinate fasciculus (UF), and inferior fronto-occipital fasciculus (IFOF) in left hemispheres is predictive of real-time sentence processing performance in individuals with aphasia. Moreover, the integrity of these homologous (right hemisphere) tracts are also evaluated to examine their role in sentence processing.

Arcuate Fasciculus

The arcuate fasciculus (AF) is a white matter fiber bundle that connects the IFG to temporo-parietal regions. The AF is currently known as the most crucial tract for language processing (Catani et al., 2005; Dronkers et al., 2007; Dronkers et al., 2000). Most studies still consider the AF as one indivisible entity following classical language models (Geschwind, 1970; Wernicke, 1874). Recent research has highlighted the multifactorial role of different segments of the AF in language processing (see Figure 4-1). According to previous studies, the anterior part of the AF which extends from Broca's area to inferior parietal areas is crucial for expressive language abilities, such as fluency and naming (Bates et al., 2003; Fridriksson et al., 2013; Gajardo-Vidal et al., 2021; Wang et al., 2013) as cited in (Ivanova et al., 2021). The posterior part which connects the inferior parietal areas with Wernicke's area is associated with lexical-semantic processing (Ivanova et al., 2016) as well as comprehension (Wilson et al., 2011). Moreover, Friederici and Gierhan (2013) indicated that the long segment of the AF that connects the superior temporal gyrus (STG) to Broca's area (BA 44, pars opercularis) is involved in complex syntactic processing (Friederici & Gierhan, 2013). Recently, Ivanova et al. (2021) revisited the function of the segments of the AF for language processing using a more advanced tractography algorithm relying on High Angular Resolution Diffusion Imaging. The authors demonstrated that the microstructural integrity of the anterior segment related to fluency and naming; the posterior segment linked to comprehension; and the long segment of the AF contributed to naming abilities (Ivanova et al., 2021). In addition to characterizing the role of the AF in the left hemisphere, few studies have indicated that AF in the right hemisphere may play a compensatory role in language processing. Schlaug and colleagues (2009) found an increase in the volume of the right AF in individuals with chronic aphasia following Melodic Intonation Therapy, which indicates the importance of contralesional hemisphere for long-term recovery (Schlaug et al., 2009). In another study, using a general assessment of aphasia severity, researchers showed that the volume of the long part of the AF in the right hemisphere when evaluated at 2 weeks post-onset was aossociated with the language outcome at 6 months (Forkel et al., 2014). Other research, however, were unable to show a similar relationship between right hemisphere tracts and residual linguistic abilities (Geva et al., 2015; Ivanova et al., 2016). Future studies are needed to elucidate further the contribution of the AF segments in the contralesional hemisphere to sensitivity to language interventions and, ultimately language outcome in aphasia.

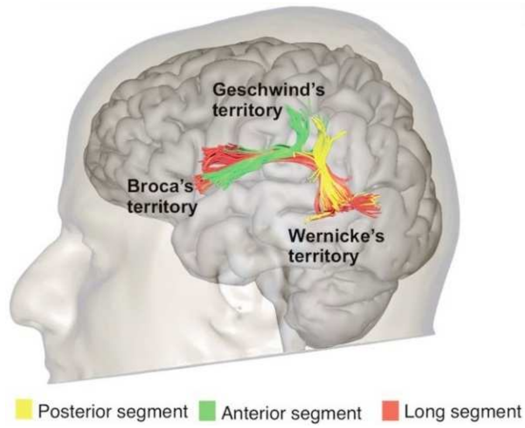


Figure 4-1. Tractography dissections of the three segments of the arcuate fasciculus. Image taken from (Catani et al., 2016).

Frontal Aslant Tract

One recently discovered tract within the network models of speech and language processing is the frontal aslant tract (FAT). This tract runs from the supplementary motor area to the pars opercularis of the IFG (Catani & De Schotten, 2012; Catani et al., 2016) (see Figure 4-2). Within the domain of speech and language processing, the FAT has been commonly associated with verbal fluency, initiation and inhibition of speech, sentence production, and lexical decision, working memory and attention. Several studies showed that the FAT is related to performance on verbal fluency tasks (Kinoshita et al., 2015; Li et al., 2017). The lesion load of the FAT was negatively correlated with both semantic and phonological fluency task performance in stroke patients (Li et al., 2017). Moreover, tumor resection in proximity to the FAT has similarly been shown to be associated with transient deficits on semantic and phonological fluency tasks (Kinoshita et al., 2015). It has been hypothesized that the FAT is also critical for lexical selection and retrieval because of the roles of the two cortical areas it connects (Robinson et al., 1998; Satoer et al., 2014). In addition, it is suggested that FAT has functional implication for working memory. Varriano and colleagues evaluated the function of FAT in the right and left hemisphere by selecting four groups of participants from a total of 900 subjects according to their performance in language and working memory tasks. The authors reported statistically significant differences in the volume of the left FAT between the groups of best performers versus worst performers in the language task and of the right FAT between top performers and bottom performers for 2-back[5] working memory task, but not for the 0-back working memory task(Varriano et al., 2020). In terms of language comprehension abilities, researchers did not find an association between the FAT and measures of overall language impairment, grammar deficit, repetition or single word comprehension as measured respectively by Western Aphasia Battery Aphasia Quotient, Northwestern Anagram Test Western Aphasia Battery Repetition and Peabody Picture Vocabulary Test. This calls for further research as sentence processing relies on lexical retrieval and working memory capacities that FAT has previously been associated with. Given the methodology used here to capture sentence processing in real-time, it is important to examine whether integrity of the FAT is indicative of an individual's sensitivity to lexical-semantic cues during sentence comprehension.

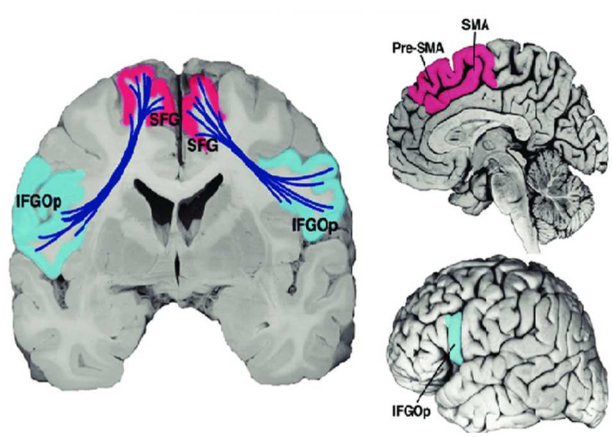


Figure 4-2. Tractography dissections of the frontal aslant tract. Image taken from (Dick et al., 2014).

---

[5] The n-back tasks entail presentation of a series of visual stimuli in which the subjects are asked to determine whether it corresponds a stimulus n trials ahead (20).

Uncinate Fasciculus

The uncinate fasciculus (UF) is a long-range fiber tract that connects the frontal and temporal lobes. The UF is traditionally considered to be part of the limbic system (see Figure 4-3). The shape of the UF is similar to a hook that arcs around the Sylvian fissure (Schmahmann et al., 2007). The left UF has been associated with language function by numerous researchers because it connects regions of the brain that are implicated in language processing, namely: the anterior temporal lobes and portions of the inferior frontal lobes. Both structures are known to be involved in encoding, storing, and retrieving semantic knowledge (Catani & Mesulam, 2008). Based on this anatomy, it was proposed that the UF, particularly on the left, was part of the ventral language pathway and that it relays sensory information about objects from ventral temporal cortex to language supporting regions in the lateral frontal lobe (Parker et al., 2005). In a similar vein, Harvey and colleagues (2013) reported that the UF mediates semantic control during word comprehension by connecting regions specialized for cognitive control with those storing word meanings (Harvey et al., 2013). However, other researchers disagree with this geographical indication of the functional role of the UF in language processing (Duffau et al., 2009). It is argued that the UF does not connect the specific region of the frontal lobe known to be critical for language processing, namely the inferior frontal gyrus, to the anterior temporal lobe. Instead, the UF connects regions in the ventral and medial frontal lobe to the anterior temporal lobe and surrounding structures that are not commonly associated with linguistic function. Therefore, there is still a need for further research to clarify the specific role that the UF may play in language processing. Yet, there is some evidence that UF plays a minor supporting role, particularly in lexical retrieval of semantic knowledge. For instance, Yang et al. (2015) examined the relationship between different tracts and language outcomes (auditory word and sentence comprehension) in 40 individuals with chronic post-stroke aphasia(Shihui Xing et al., 2017). The authors reported that the integrity loss in the UF was significantly related to word-level comprehension deficits. Therefore, damage to the connectivity between the prefrontal and temporal regions can lead to severe deficits of semantic control. Given that the real-time lexical-semantic processing is the targeted language outcome in the present study, it is important to examine whether the integrity of UF can indicate individual's variability in benefiting from the lexical-semantic cues during sentence comprehension.

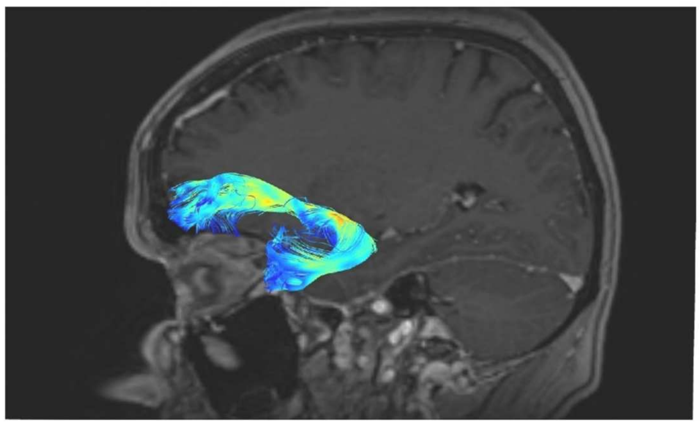


Figure 4-3. Tractography dissections of the uncinate fasciculus. Image taken from (Kierońska et al., 2020)

Inferior Fronto-Occipital Fasciculus

The Inferior Fronto-Occipital Fasciculus (IFOF) is commonly described as the longest associative bundle that connects various parts of the occipital cortex, temporo-basal area and the superior parietal lobule to the frontal lobe through the external/extreme capsule complex (see Figure 4-4). The functional role of the IFOF in language is suggested to be serving as the principal pathway for a ventral semantic system. This finding is proposed by Duffau and colleagues (Duffau, 2008; Duffau et al., 2005) by showing that semantic paraphasias can be induced by electrical stimulation of the IFOF. The evidence for this finding came from patients performing a picture naming task while undergoing neurosurgery. Moreover, Turken and Dronkers (2011) extended this idea by proposing the possibility that semantic selection processes, relying on top-down signals from the inferior frontal gyrus to temporal lobe, are in fact disrupted during IFOF stimulation, causing the semantic misnaming errors observed by Duffau and colleagues (Turken & N. F. Dronkers, 2011). Furthermore, Yang and colleagues (2017) who examined the functional role of the IFOF in stroke survivors found that reduced IFOF integrity was significantly associated with both word- and sentence-level comprehension deficits(S. Xing et al., 2017). These researchers also found that the IFOF related not only to word-level comprehension but also to sentence-level comprehension after regressing out word-level deficits. As a result, they proposed that the IFOF, with its long course from the inferior frontal lobe through the temporal lobe, could be involved in linking control areas of the frontal lobe to multiple levels of semantic representations in the temporal lobe (Binder et al., 2009; A. Turken & N. Dronkers, 2011). Altogether, previous research suggests that the IFOF plays a role either in multi-level semantic processing or in domain general processes such as cognitive control that subserve language comprehension. Yet, it is important to examine whether the integrity of IFOF is indicative of individual's responses to lexical-semantic interference processes during sentence comprehension.

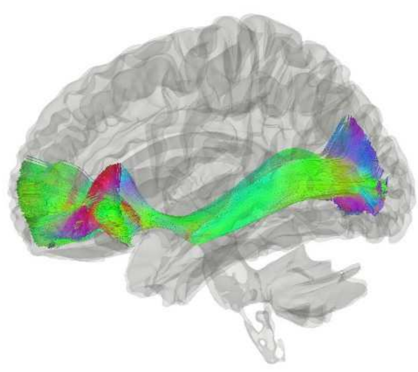


Figure 4-4. Tractography dissections of the inferior fronto-occipital fasciculus. Image taken from (Yeh et al., 2018).

Current study

The overarching goal of the current study is to provide a functional evaluation of the AF, FAT, UF and IFOF in both left and right hemispheres for sentence processing in a series of cases with chronic post-stroke aphasia. Specifically, the aims of the study are to:

(1) Explore whether damage to the either of left hemisphere tracks namely AF, FAT, UF, IFOF contributes to real-time sensitivity to lexical-semantic processing in individuals with chronic post-stroke aphasia.

(2) Explore whether variations in the integrity of any of the right hemisphere tracts namely AF, FAT, UF, IFOF contribute to real-time sentence processing deficits in aphasia.

To explore these questions, we ran a qualitative case series study with 5 individuals with aphasia who took part in the eye tracking paradigms (chapters 2 and 3) and Diffusion Tensor Imaging. This study utilized data from individuals' performance on two eye-tracking experiments, lesion volume in IFG and the temporo-parietal regions, and the integrity (i.e., fractional anisotropy) of the FAT, UF, IFOF and anterior segments of the AF, in both hemispheres at the individual level. In the eye-tracking paradigms in each study, we were interested in capturing each individual's sensitivity to the semantic cue. This sensitivity is operationalized as the magnitude of reduction of interference in the experimental condition (upon encountering the semantic cues) as compared to the control condition. Given that there is evidence for the role of posterior and long segments of the AF in lexical-semantic and sentence level processing, the first hypothesis here is regarding the anterior segment of the AF. It is hypothesized that greater damage or reduction in the integrity of the anterior segment of the AF in the left hemisphere will result in less sensitivity and ability to benefit from the lexical-semantic cues during sentence comprehension, similar to individuals that have temporo-parietal deficits. Thus, there should not be differences between experimental and control conditions. The

FAT's role has not yet been investigated in sentence processing alone but given the data demonstrating its role in working memory and lexical retrieval, it is hypothesized that its functionality in the left hemisphere will be related to the magnitude of the benefit from the semantic manipulations that were used in the experiments presented here. Moreover, given that there is evidence for the role of UF on semantic control, it is hypothesized that the extent to which participants benefit from the lexical-semantic cues will be associated with the degree of integrity of this tract in the left hemisphere. Given the evidence for the role of the IFOF in sentence comprehension, we hypothesize that the integrity of the left IFOF will be indicative of the extent of individual's benefit from the lexical-semantic cues. Based on findings in the literature, right hemisphere tracts are not hypothesized to reveal an effect between their integrity and real-time sensitivity to the lexical-semantic cue during sentence comprehension.

Methods

Participants

For years, the Language and Neuroscience Group and Laboratory for the Brain Dynamics of Language at San Diego State University have been working with stroke survivors who have post-stroke speech and language deficits. Those with left hemisphere lesions who participate in research at these laboratories undergo neuroimaging and comprehensive language testing with their IRB-approved consent in accordance with the San Diego State University ethical board. In the last three years, a diffusion-tensor imaging sequence was added to their scanning protocol, yielding a group of fifteen successively scanned participants with aphasia (PWA) following a left hemisphere stroke. Of these 15 patients, 5 have also participated in two eye-tracking tasks (see chapters 2 and 3). These participants were proficient monolingual English speakers prior to their stroke. All participants had a single stroke. Patients in this sample presented with a wide range of speech and language deficits. The neurological evaluations included the standardized aphasia examinations: the Boston Diagnostic Aphasia Examination [BDAE-version 3] ((Goodglass et al., 2001), the Western Aphasia Battery-Revised [WAB-R] (Kertesz, 2007), S.O.A.P. Test of Sentence Comprehension (Love & Oster, 2002). The BDAE-version 3 is scored on a scale of 0-5, where the score of 0 indicates no usable speech or auditory comprehension and the score of 5 indicates minimal discernable speech handicap. The WAB-R is measured based on aphasia quotient which is a weighted average of all subtest scores relating to spoken language, the score within the range of 0-25 indicate very severe aphasia, 26-50 indicate severe aphasia, 51-75 is moderate aphasia, and 76+ is indication of mild aphasia. The S.O.A.P test includes examination of individual's performance on four different sentence types (Subject relative, Object relative, Active, and Passive). The score is measured by average percent correct on all items or per sentence group. Results of these assessments measures are described in detail with each case in the results and it can also be seen in Table 4-1. Moreover, the estimated lesion load to three cortical language areas: frontal, temporal, and parietal cortex are reported in Table 4-2 based on the Automated Anatomical Labeling Atlas.

Table 4-1. Characteristics of individuals with aphasia (n =5).

Cases	Sex	Years Post-Stroke	Age at Testing	Years of Education	Aphasia Subtype	Lesion Location	BDAE-v3	WAB-R AQ	SOAP-SR (%)	SOAP-OR (%)
009	M	15	55	17	Mixed non-fluent	Large L lesion, IFG (BA 44/BA45) w/ posterior	4	67.7	60%	40
017	M	18	66	15	Anomic	L anterior cerebral and middle cerebral infarct	4	95.4	100	90
101	M	9	67	20	Broca	Large L lesion posterior IFG (BA 44) w/ posterior	2	82.6	100	30
130	M	8	63	16	Broca /Anomia	L IPL with posterior ext. sparing STG	4	90.5	75	55
151	F	7	65	16	Anomic	L MCA infarct with subcortical extension	4	95.8	100	100

Note: L = left; LH=left hemisphere; BA= Brodmann area; IPL= inferior parietal lobule; STG= superior temporal gyrus; MCA= middle cerebral artery; BDAE= Boston Diagnostic Aphasia Examination (0 = no usable speech or auditory comprehension, 5 = minimal discernable speech handicap); SOAP-SR= Average percent correct on subject relative items from the SOAP Test of Auditory Sentence Comprehension; SOAP-OR= Average percent correct of object relative items from the SOAP Test of Auditory Sentence Comprehension.

Table 4-2. Percentage of lesion in the critical language regions.

	009	017	101	130	151
Frontal	15.55	10.20	11.08	0.00	2.74
Temporal	58.88	49.01	49.83	9.18	4.09
Parietal	39.82	28.77	35.29	4.58	2.65

Note: The frontal language area was defined as the inferior frontal gyrus, including both pars opercularis and pars triangularis. The temporal language area was based on the superior temporal gyrus posterior division and the middle temporal gyrus posterior division. The parietal language area included the angular gyrus and the supramarginal gyrus (both the anterior and the posterior divisions). For each participant, lesion load for each area (i.e., the percentage of the area covered by the lesion) was calculated.

Real-time Sentence Processing task

This multimodal study included behavioral (Visual-world eye tracking while listening paradigm) and structural neuroimaging (Diffusion Tensor Imaging). The behavioral portion of the study is extensively described in chapters 2 and 3 but is briefly reviewed below.

In study 2, the experiment included non-canonical sentences in which the target noun-phrase were manipulated by adding a semantically biasing adjective to boost representational access (see Figure 4-5). In this experimental setup, two different sets of adjectives were chosen that were matched for syllable length, lexical frequency and phonemic onset. In the Biased condition, the adjective was uniquely associated with the target (/snake/), not the distractor images. These sentences were compared to the control condition which contained a Neutral semantic adjective that did not uniquely link to the target. For this within-subject design experiment, 60 non-canonical sentences were used.

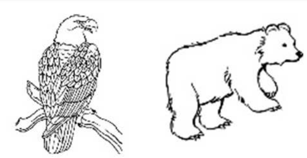
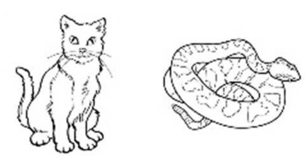
Conditions	Sample sentences	Visual array
Neutral Adjective	**“The eagle saw the <u>voracious snake</u>$_i$ that the bear cautiously encountered$_i$ <~~the snake~~> underneath the narrow bridge.”**	
Biased Adjective	**“The eagle saw the <u>venomous snake</u>$_i$ that the bear cautiously encountered$_i$ <~~the snake~~> underneath the narrow bridge.”**	

Figure 4-5. Example of experimental sentence and visual stimuli of study 2.

In study 3, this experiment included canonical sentences with long-distance dependencies that manipulated the animacy of the noun-phrases to mismatch and to reduce the similarity-based interference effects (see Figure 4-6). In this experimental setup, the sentences were manipulated to differ in the similarity between the semantic features of the two noun-phrases embedded in the sentence, resulting in two experimental conditions. In the Animate condition, both noun-phrases (e.g., /the model/ and /the designer/) were animate entities while in the Inanimate condition there was a mismatch in animacy between the two noun phrases (e.g., /the model/ and /the dress/). Each sentence was followed by a yes/no comprehension question (e.g., Did the model fall?). For this within-subject design experiment, 60 subject-relative sentences were used.

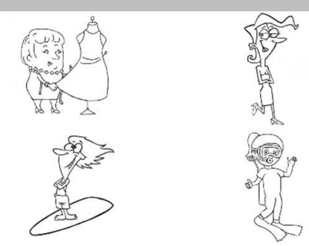
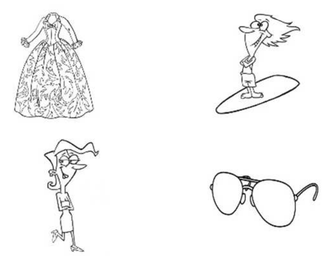
Conditions	Sample sentences	Visual array
Animate	"This evening at the fashion show, **the model that noticed <u>the designer</u> surprisingly fell** <~~the model~~> during the evening gown showcase."	
Inanimate	"This evening at the fashion show, **the model that noticed <u>the dress</u> surprisingly fell** <~~the model~~> during the evening gown showcase."	

Figure 4-6. Example of experimental sentence and visual stimuli of study 3.

Structural Neural Imaging

Diffusion tensor imaging (DTI) is a magnetic resonance imaging (MRI) technique that captures the macrostructure of the white matter in vivo and provides unprecedented insight into the existence and nature of white matter abnormalities. By using existing MRI technology, DTI provides image contrast through measurement of the diffusion properties of water within tissues (Charles-Edwards & Nandita, 2006). Moreover, DTI is it can provide data on the orientation and quantitative anisotropy of water molecules that diffuse differently along the tissues determined by the type, integrity, architecture, and presence of barriers in that tissue (Chenevert et al., 1990; Moseley et al., 2002) as cited in (Soares et al., 2013). More specifically, diffusion in white matter is anisotropic (directionally dependent) whereas in gray matter is usually less anisotropic and in the Cerebrospinal fluid is isotropic which means its flow is unrestricted in all directions(Hagmann et al., 2006; Song et al., 2002). The section that follows provide more information regarding the protocol used for DTI implementation.

Data Acquisition

T1 and T2-weighted scans, as well as diffusion imaging (DTI), were acquired with SDSU's 3T Siemens Prisma scanner with a 32-channel head coil. For T1 scans, 3D T1 weighted-images were acquired using an MP-RAGE (magnetization-prepared rapid gradient echo) protocol with 1 mm3 isotropic resolution (TR= 2300, TE = 2.98 ms, flip angle = 9°; FOV = 256 mm; 176 sagittal slices imaging matrix = 256 x 256). The T2 weighted images were acquired with the same imaging resolution, with the TR = 3000, TE = 409 ms. Diffusion-tensor imaging sequences were collected with the following parameters: TR = 3100 ms, TE = 55 ms, flip angle = 90°, b = 1000 s/mm2, 64 directions, 10 b0, FOV = 256 mm, voxel size 2 × 2 × 2 mm, 70 slices, bandwidth = 2053 Hz/voxel, and GRAPPA factor = 2.

Lesion Reconstruction

The participants' lesions were traced directly onto the patient's native T1-weighted images using ITK-snap software (Yushkevich et al., 2006). During this procedure, the T2-weighted was co-registered to the T1 images to verify lesion boundaries. The lesion masks were used to ensure that reconstructed tracts did not cross the lesion boundaries.

DTI Data Processing

Before the DTI data can be analyzed, several denoising steps needs to be taken. In the current study, diffusion-tensor imaging data were first preprocessed using (1) a fieldmap correction to resolve geometric distortion and loss of signal (FSL ver. 5.09, Jenkinson et al., 2012); (2) movement and eddy current corrections (FSL ver. 5.09, Jenkinson et al., 2012); (3) DIPY: Self-Supervised Denoising via Statistical Independence to separate structure from noise; (4) DIPY: Suppress Gibbs oscillations to remove truncation artifact or ringing artifact that is a common type of MRI artifact. Next, using ExploreDTI (Leemans et al., 2009) deterministic streamline tractography was done using these parameters: ALFA – 1.8, iterations – 300, n – 0.002, r – 15, ABS threshold – 0.003, step size (mm) – 0.5, angle threshold – 35, minimal length (mm) – 50. This enables reconstructing of fiber direction within a voxel.

Manual Tract Segmentation

To ensure each of the segmentations were done in a way that respected the individuality of each individual's brain structure, in vivo manual tract dissections of the AF, FAT, UF and IFOF from whole brain tractograms in native space were completed using TrackVis ver. 0.6.1 (Wang et al., 2007). In collaboration with Yusheng Wang, we performed the reconstructions for the abovementioned tracts in the left and right hemispheres according to the criteria outlined in (Ivanova et al., 2021; Zhong et al., 2022). The reconstructions were then reviewed and revised together with supervisors Dr. Stephanie Ries and Dr. Maria Ivanova.

Segmentation of Arcuate Fasciculus (AF)

The AF in both hemispheres were manually reconstructed in native space using 3-segment Catani model (Catani et al., 2005) as described in (Ivanova et al., 2021). We used this model to be able to reconstruct a modified version of the AF complex. This process entailed using 3 ROIs that best highlight the connection between different lobes to segment the three branches of the AF (see Figure 4-7 for ROI placement and an example of AF segmentation in the right hemisphere). Here is the description of the three ROIs that we used: (1) Frontal ROI – we placed a 2D disk on the coronal slice at the front of the frontal lobe (anterior to the central sulcus), (2) Temporal ROI – on the axial slice, we placed a 2D disk at the entrance to the temporal lobe below the Sylvian fissure, (3) Parietal ROI – we placed a 3D sphere tangent to the inferior parietal cortex. The dimentions of the disks and spheres was determined slightly different between participants depending on their brain size. See Figure 4-6 for ROI placement and an example of AF segmentation in the right hemisphere. Using this approach, the three segments of the AF in both hemispheres were extracted to construct the long segments of AF, the segments of AF, and the posterior segments of the AF. Below is the description of the criteria of each segment:

AF long. This tract which is defined by the Frontal and Temporal ROIs captures the connection between the temporal and the frontal areas dorsally. During the reconstruction, the ROIs were modulated to ensure the inclusion of all the fibers. We used 'NOT' ROIs (in the shape of rectangles which exclude fibers) to remove the looping fibers and the fibers that were going between the temporal and the frontal lobe ventrally through the external capsule.

AF anterior. This tract which is defined by the Frontal and Parietal ROIs captures the connection between frontal regions and inferior parietal areas. The localization of the ROIs ensured that the anterior segment passed directly adjacent and laterally to the long segment of the AF. Moreover, the fibers passing more superiorly to the AF long tract, as well as those separated from it by a gap were excluded. Moreover, the Temporal ROI was used as a NOT region. This ensured that only fibers extending dorsally from the frontal to the inferior parietal areas were captured and not any fibers continuing to the temporal lobe.

AF posterior. This tract which is defined by the Parietal and Temporal ROIs captures the connection between the inferior parietal regions and the temporal lobes. Moreover, the Frontal

ROI was used as a NOT region. This ensured that only fibers extending laterally from the inferior parietal areas to the temporal cortex were captured and any fibers continuing to the frontal lobe were excluded. Additionally, we verified that this posterior short section connected laterally to the AF's long segment.

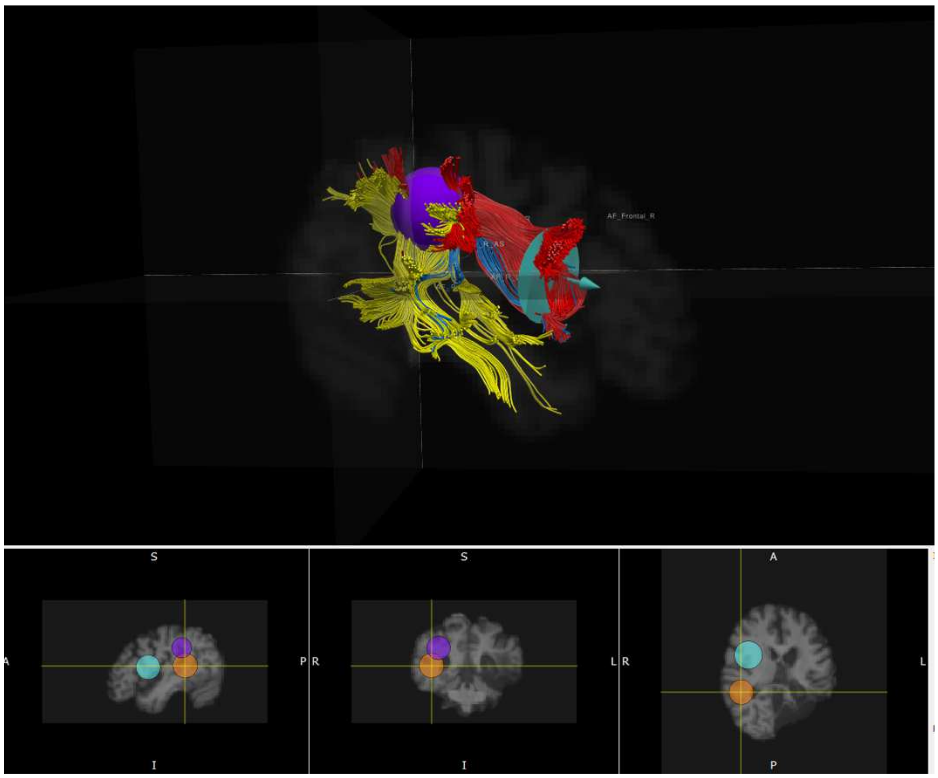


Figure 4-7. Placement of ROIs and segmentation of the AF (the right hemisphere is shown) according to the modified Catani model: AF long – blue, AF anterior – red, and AF posterior – yellow.

<u>*Segmentation of Frontal Aslant Tract (FAT)*</u>

The FAT in both hemispheres was manually reconstructed in native space using a two-ROI stem-based approach based on placements suggested by Catani and colleagues (Catani & De Schotten, 2012) as described in (Zhong et al., 2022). This process entailed using 2 ROI disks which enabled us to trace all the fibers going through the area of the disk in a specific direction. Here is the description of the two ROIs: (1) <u>Inferior Frontal ROI</u> – a 2D disk placed in the white matter underneath the pars opercularis of the inferior frontal gyrus. In cases where the FAT was particularly large, the boundary for the ROI was within the white matter underneath the border between pars triangularis/pars opercularis anteriorly and the inferior frontal sulcus superiorly, (2) Superior Frontal ROI – a 2D disk placed in the white matter underneath the supplementary motor and pre-supplementary motor area anterior to the pre-central sulcus. In cases where the FAT was particularly large, the posterior boundary was placed at the pre-central sulcus. The Angle threshold of these ROI disks were kept at the default 90 degrees. In each individual case, ROI disk size was determined based on brain and tract size to capture all streamlines of interest while avoiding inclusion of other aberrant or looping fibers. In cases where aberrant and/or looping fibers that appeared, we placed sphere-shaped 'NOT' ROIs as needed to remove them from the tract segmentations. See Figure 4-8 for ROI placement and an example of FAT segmentation in the right hemisphere.

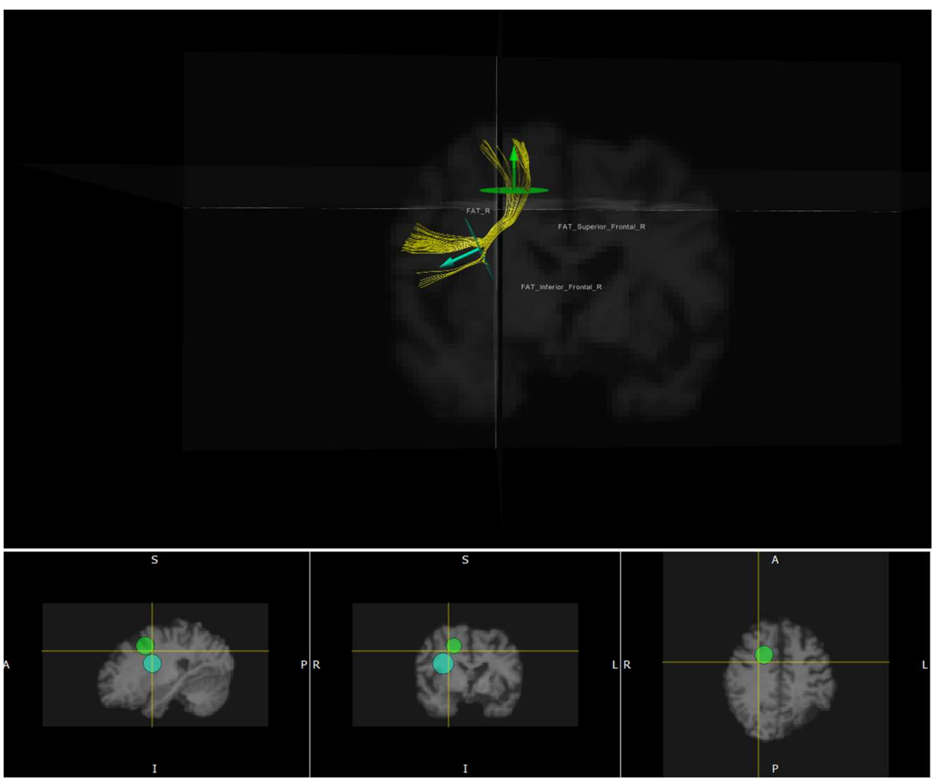


Figure 4-8. Placement of ROIs and segmentation of the FAT (the right hemisphere is shown).

Segmentation of Uncinate Fasciculus (UF)

The UF in both hemispheres was manually reconstructed in native space using a two-ROI stem-based approach based on placements suggested by (Catani et al., 2005). This process entailed using two disk ROIs which enabled us to trace all the fibers going through the area of the disk in a specific direction. Here is the description of the two ROIs: (1) Temporal ROI – a 2D disk placed in the anterior temporal lobe (according to the MNI anatomical reference -15 to -19), (2) external/extreme capsule ROI – a 2D disk which is places on the anterior floor of the external/extreme capsule, usually on five axial slices (according to the MNI anatomical reference 1 to -7). See Figure 4-9 for ROI placement and an example of UF segmentation in the right hemisphere.

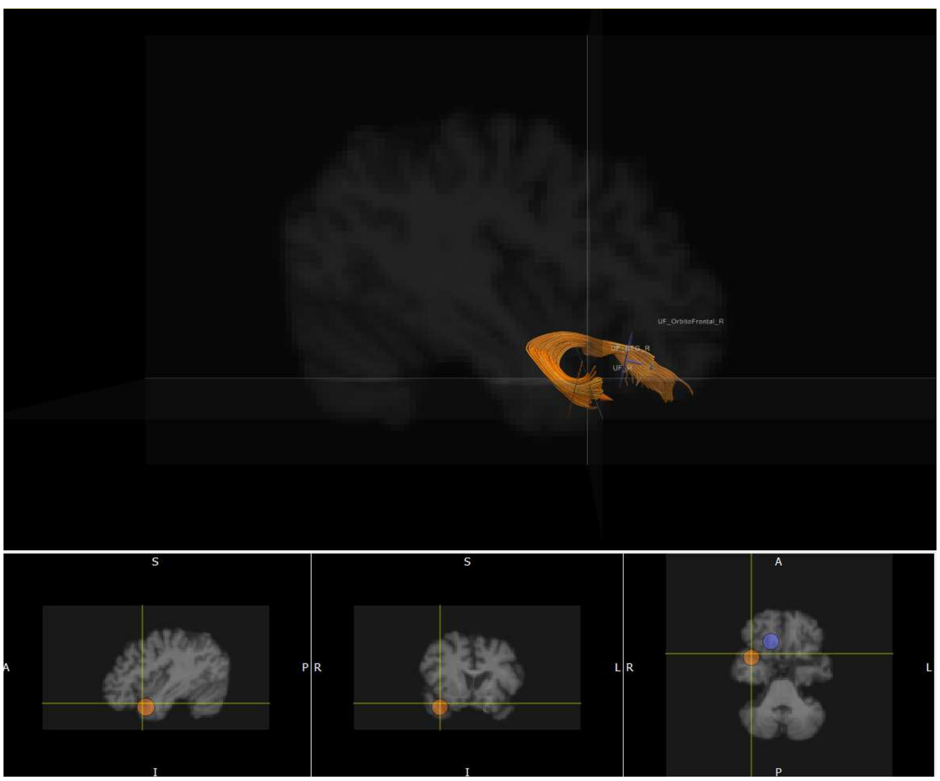


Figure 4-9. Placement of ROIs and segmentation of the UF (the right hemisphere is shown).

Segmentation of Inferior Fronto-Occipital Fasciculus (IFOF)

The IFOF in both hemispheres was manually reconstructed in native space using a two-ROI stem-based approach based on placements suggested by (Catani & Mesulam, 2008). This process entailed using two disk ROIs which enabled us to trace all the fibers going through the area of the disk in a specific direction. Here is the description of the two ROIs: (1) Occipital ROI – we placed a 2D disk in the white matter region between the genu of corpus callosum and the anterior part of the head of caudate nucleus; (2) external/extreme capsule ROI – we placed a 2D disk in the white matter region of the middle temporal gyrus, anterior to the radiation of corpus callosum. We used 'NOT' ROIs to exclude corpus callosum tracts. In each individual case, ROI disk size was determined based on brain and tract size to capture all streamlines of interest while avoiding inclusion of other aberrant or looping fibers. In cases where aberrant and/or looping fibers that appeared, we placed sphere-shaped 'NOT' ROIs as needed to remove them from the tract segmentations. See Figure 4-10 for ROI placement and an example of UF segmentation in the right hemisphere.

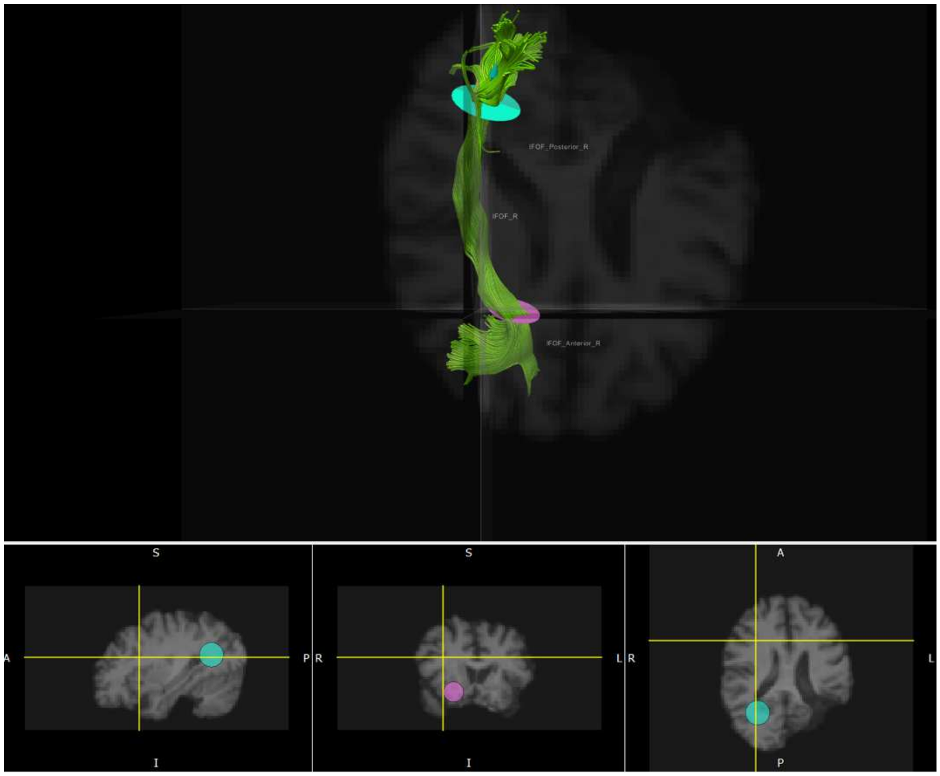


Figure 4-10. Placement of ROIs and segmentation of the IFOF (the right hemisphere is shown).

Measurements of tracts and their sub-components

For each segmented tract (three branches of AF, FAT, UF and IFOF for both left and right hemispheres), the fractional anisotropy (FA) value was extracted. The fractional anisotropy, or FA (Soares et al., 2013), is the most widely used DTI measure. Broadly speaking, in DTI protocols water molecules and their direction of diffusion are captured. This can be used to reveal the integrity of the white matter tracts. If the water molecules are flowing in a particular direction together, the FA (diffusivity) value is high. If the FA value is low, it means that there is a lack of tissue integrity. In mathematical terms, the FA is an expression that characterizes the directional preference of diffusion or the extent to which the diffusivity deviates from being isotropic. FA is a normalized variance of the eigenvalues, corresponding to the degree of anisotropic diffusion or directionality and ranges from 0 (isotropic diffusion) to 1 (anisotropic diffusion):

$$FA = \frac{1}{\sqrt{2}} \frac{\sqrt{(\lambda_1 - \hat{\lambda})^2 + (\lambda_2 - \hat{\lambda})^2 + (\lambda_3 - \hat{\lambda})^2}}{\sqrt{\lambda_1^2 + \lambda_2^2 + \lambda_3^2}} \tag{4-1}$$

λ_1, λ_2 and λ_3 are eigenvalues of the diffusivity tensor and $\hat{\lambda}$ is the mean diffusivity. The denominator of the equation is the magnitude of the eigenvalues vector while the nominator indicates the diffusivity from the mean diffusivity. When FA is equal to zero, the diffusivity is isotropic. Meaning that the water molecules diffuse with the same rate at all directions, in other words, there is no tissue to channel the molecules in a specific direction. When the FA is larger than zero, the diffusivity is anisotropic. Meaning that there is a tract structure to channel the molecules in a certain direction. Therefore, FA is usually related with alterations in structure (possibly due to particular conditions/disease) pointing to specific myelination levels and axonal injury (Budde et al., 2009; Song et al., 2002). In other words, FA is often used to describe a measure of 'white matter integrity'. Yet, it is important to note that the changes in FA may be caused by many factors. For the purpose of this study, we used the FA value for each tract segmentation. In those instances when segments of the AF had been destroyed by the stroke and could not be reconstructed, zeroes were imputed for respective tract FA value (Ivanova et al., 2021).

Results

First, the effect sizes of each individual's responsiveness to the experimental condition in each eye-tracking experiment is measured. Then, the correlation between FA value of all tract segments for each hemisphere with extracted effect sizes is computed. The analyses were run in R Core Team (Dink & Ferguson, 2015).

Individual level analysis of performance on the eye-tracking experiments

In chapter 2 (the adjective experiment), it was found that the addition of adjective did not have any effect for the group of individuals with aphasia. Moreover, in chapter 3 (the animacy experiment), it was found that the manipulation of animacy reduced the interference effect for the group of individuals with aphasia. However, because group-level analyses conceal the variability in the performances of each IWA, individual-level analyses using random (i.e., residual) effect structures were conducted to investigate which IWA show sensitivity to the cues. The effect sizes show the magnitude of the sensitivity to the lexical-semantic cues presented in auditory stream of sentences. In the current chapter, for each individual, the magnitude of benefit from the lexical-semantic cue in each design was calculated as average gaze proportions on the target item in the experimental minus control conditions where the cues were neutral. Moreover, a positive effect size indicates a bigger effect in the experimental condition thus sensitivity to the lexical semantic cue. More specifically for the adjective experiment (chapter 2), the individual-level effects were calculated by measuring the difference in the rate of activation (i.e., slope) of N2 in the Biased (experimental) condition relative to the Neutral (control) condition for each of the five IWA. Descriptive analysis revealed that participants varied in their gaze proportion in the experimental versus control conditions, with a standard deviation of 0.053. For the animacy experiment (chapter 3), the individual-level effects were calculated by measuring the difference in the rate of activation of N2 and deactivation of N1 over time (i.e., slope) in the Inanimate (experimental) relative to Animate (control) condition for each of the five IWA. This contrast allows us to capture the degree that lexical-semantic cues are used by each IWA in the experimental versus control condition in both experiments. Descriptive analysis revealed that participants varied in their gaze proportion in the experimental versus control conditions, with a standard deviation of 0.051. Table 4-3 summarizes the effect sizes of each individual case in each study.

Table 4-3. The individual effect sizes in both eye-tracking experiments. Effect size is calculated as the average of looks to the target item in the experimental conditions – control conditions in the time-window of the analysis, thus capturing the degree that lexical-semantic cue were used.

Cases	Fixed effects Adjective study	Fixed effects Animacy study
9	0.02	0.02
17	-0.01	0.06
101	-0.02	-0.08
130	0.11	0.01
151	0.01	-0.01

FA value of AF, FAT and UF in both hemispheres

Based on the DTI analysis, the FA values of specific tracts were measured. As mentioned earlier, in those instances when segments of the AF had been destroyed by the stroke and could not be reconstructed, zeroes were imputed for respective tract FA value (Ivanova et al., 2021). To further probe the status of the FA values in the remaining tracts in the ipsilesional hemisphere, we compared these indices for each case to the average FA value of that tract in the controlesional hemisphere of the group using the corrected t-test proposed by (Crawford & Garthwaite, 2007):

$$t = \frac{X_i - X}{s\sqrt{\frac{n+1}{n}}} \tag{4-2}$$

In this formula the X_i is the FA value of tract in left hemisphere, X is the mean score of the FA values for that tract in the right hemisphere of the group, s is the SD of the FA value of that tract in the right hemisphere of the group, and n is the size of the group which their right hemisphere values is used. The advantage of this method over the traditional t-test is that it treats the mean and SD of the control sample as sample statistics instead of population parameters, which is more appropriate for small control sample sizes, and avoids Type I error. An additional advantage of this test is that the p value provides a point estimate for where the FA value falls compared to the population (See Table 4-4). The FA values that are highlighted in red were significantly lower than the average FA value in the right hemisphere. Therefore, the integrity of these tracts cannot be interpreted as intact. Based on this individual level analysis, the tracts with lower than within-group normal FA values in the right hemisphere were coded as impaired tracts.

Table 4-4. Single-case statistics for individualized inspection of tract integrity.

Cases	L-AF-ant	*t*	*p*	L-AF-pst	*t*	*p*	L-AF-L	*t*	*p*	L-FAT	*t*	*p*	L-UF	*t*	*p*	L-IFOF
9	0	-		0	-	-	0	-	-	0	-	-	0	-	-	0
17	0	-		0.41	-0.59	0.56	0	-	-	0	-	-	0	-	-	0
101	0	-		0	-		0	-	-	0	-	-	0.38	-2.38	0.03	0
130	0.41	-1.37	0.19	0	-	-	0	-	-	0.39	-0.10	0.92	0.34	-4.6	0.00	0
151	0.34	-4.29	0.00	0.39	-1.23	0.24	0.34	-3.21	0.01	0	-	-	0.39	-1.56	0.14	0
RH-Mean	0.44			0.42			0.44			0.39			0.42			0.46
RH-SD	0.02			0.02			0.03			0.02			0.02			0.01
N=13																

Note: The highlighted red boxes indicate that the FA value is significantly below the normal range when compared to the corresponding FA value in the contralesional hemisphere; thus, the integrity is lost. The highlighted green boxes indicate that the FA value of ipsilesional tract is not statistically lower than a typical FA value in the contralesional hemisphere; thus, the integrity of the tract is maintained. RH = Right Hemisphere; L = left; AF-ant: anterior segment of arcuate fasciculus; AF-pst: posterior segment of arcuate fasciculus; FAT: frontal aslant tract; UF: uncinate fasciculus; IFOF: inferior fronto-occipital fasciculus.

Role of left AF, FAT, UF and IFOF in lexical-semantic processing

Here are the exploratory analyses (due to the small sample size) that looked at correlations between integrity of tracts (defined individually) in the left hemisphere and the real-time language processing skills. To do this, we performed point-biserial correlations between effect sizes in each experiment and the integrity of the left hemisphere tracts. In these analyses, we included the effect sizes of individuals in each experiment as a continuous variable and the integrity of the left hemisphere tracts (AF, FAT, UF, IFOF) as a binary variable (0 = impaired, 1 = intact). The results revealed that the anterior segments of the AF and the FAT in left hemisphere are associated with the extent of benefit from the adjective cue. Individuals with higher integrity in these tracts were able to show a bigger effect from the lexical-semantic cue in the adjective experiment. However, these tracts were not related to performance in the animacy study.

Table 4-5. Correlations between tracts in the ipsilesional hemisphere and language measures extracted from eye-tracking experiments. L: left hemisphere; EF: effect size; AF-ant: anterior segment of arcuate fasciculus; AF-pst: posterior segment of arcuate fasciculus; FAT: frontal aslant tract; UF: uncinate fasciculus. We were not able to extract any correlation coefficients for AF-long and IFOF as the standard deviation was zero. Therefore, they are not included in the table.

	Adjective-EF	**Animacy-EF**
L-AF-ant	0.96*	0.12
L-AF-pst	-0.48	0.448
L-AF-long	NA	NA
L-FAT	0.968*	0.11
L-UF	-0.298	-0.11
L-IFOF	NA	NA

Note: Asterisk (*) indicates significant p-value.

Role of right AF, FAT, UF, IFOF in lexical-semantic processing

Here are the exploratory analyses (due to the small sample size) that looked at correlations between integrity of tracts in the contralesional hemisphere and the real-time language processing skills. Here we conducted Pearson correlations by using both the effect sizes in each experiment and the FA values in the right hemisphere as continuous variables. The analysis revealed no significant correlation between the tracts and individual level performances on any of the experiments.

Table 4-6. Correlations between tracts in the contralesional hemisphere and language measures extracted from eye-tracking experiments. R: Right hemisphere; EF: effect size; AF-ant: anterior segment of arcuate fasciculus; AF-ant: posterior segment of arcuate fasciculus; AF-long: long segment of arcuate fasciculus; FAT: frontal aslant tract; UF: uncinate fasciculus; IFOF: inferior fronto-occipital fasciculus.

	Adjective-EF	**Animacy-EF**
R-AF-ant	0.05	0.37
R-AF-pst	0.52	0.48
R-AF-long	-0.17	0.27
R-FAT	0.29	0.05
R-UF	-0.53	0.17
R-IFOF	-0.33	-0.13

Discussion

The aim of this study was to investigate the functional role of the tracts that pass through the frontal region, namely the AF, FAT, UF and IFOF in both ipsilesional and contralesional hemispheres, in real-time sentence processing. Given that the sample size was a challenge for this study as it required recruiting individuals with aphasia to participate in studies with multiple sessions during the pandemic, the analysis for the study remains exploratory and requires further investigation for clear interpretations. Nevertheless, below is the discussion of the patterns of the findings for each of the research question proposed in this study, as well as the proposed approaches that can be taken in the future studies with a larger sample size.

The first question in this study was whether damage to either of left tracts namely, AF, FAT, UF, and IFOF contributes to real-time sensitivity to lexical-semantic processing in individuals with chronic post-stroke aphasia. The AF, FAT, UF and IFOF in the left hemisphere have been proposed to have multifactorial roles for language processing. However, there is less evidence regarding their role in sentence comprehension. The results revealed a positive association between the integrity of both anterior-AF and FAT in the left hemisphere and sensitivity to lexical-semantic cue in real-time. According to previous findings (Bates et al., 2003; Fridriksson et al., 2013; Gajardo-Vidal et al., 2021) these tracts are crucial for lexical-retrieval abilities during production. However, the neural architecture which underlies language production can be generalized to some extent to comprehension processes as the processes pertains to shared mechanisms (namely representational semantic activation and cognitive control processes) to modulate lexical-semantic processing in general. In a similar vein, in another large study of stroke survivors, it is suggested that components of language comprehension and production cannot be so readily separated, by showing that component of speech fluency ability are mutually loaded onto both levels of comprehension and production (Fridriksson et al., 2018).

The current study did not find any relationship between sentence processing and the integrity of posterior-AF, IFOF and UF. While initially surprising, upon further observation of lesion sizes and lesion locations (see Table 4-2), it was recognized that three of the five participants had significant involvement of these posterior areas. Despite our lack of findings, numerous publications have supported the role of posterior-AF and IFOF in sentence comprehension. In a study with large cohort of individuals with aphasia, Ivanova and colleagues (2016) demonstrated that the posterior-AF is significantly associated with sentence-level processing. In addition, in another large-scale study on individuals with aphasia, it was shown that the IFOF relate not only to word-level comprehension but also to sentence-level comprehension after regressing out word-level deficits (S. Xing et al., 2017). Moreover, other studies in healthy subjects have also found that auditory sentence comprehension is mediated in part by the IFOF. Therefore, additional studies with larger sample sizes are needed to elucidate the functional role of these tracts for the real-time mechanism in sentence processing. These larger sample sizes should include a variety of lesion sizes and lesion locations such that these posterior tracts can be investigated.

The second question in this study was whether the integrity of AF, FAT, UF and IFOF in the right hemisphere is associated with real-time sentence processing patterns in aphasia. The results in this study did not indicate any association between the integrity of contralesional tracts and sensitivity to lexical-semantic cue. As noted earlier, given the current sample size, this finding is not conclusive, but it lends support to previous studies that did not find any clear contribution of the right hemisphere tracts to language performance in individuals with aphasia (Geva et al., 2015; Ivanova et al., 2016; Meier et al., 2019). In other clinical populations however, such as individuals with left hemisphere tumor (Jehna et al., 2017) and children with developmental disorders (Paldino et al., 2016), it has been demonstrated that a structurally smaller volume of AF in the right hemisphere leads to worse language outcomes. To determine the right tracts' function in language outcomes and its development or rehabilitation over time, more research is required (Ivanova et al., 2021).

In future studies with a larger sample size, more advanced statistical analysis approaches can be used. This study implemented correlational analysis without the chance to account for the effect of lesion size in critical language regions and other potential covariates. Future studies can run a series of multiple regression analyses to determine whether residual tracts' integrity in the left hemisphere (or right) is related to the language metric of interest beyond damage to specific frontal and temporal cortical language areas (Ries et al., 2021). In doing so, researchers can conduct hierarchical regression analysis, by entering lesion load to frontal, temporal, and parietal language areas as covariates. Additionally, other demographic information such as age, stroke time onset, and years of education which can all have impact on aphasia outcome (Aftonomos et al., 1999; Fabian et al., 2020) can be added to the model as covariates. Using such regression analyses, the significant role of tracts beyond cortical damage and demographic variabilities can be extracted.

Limitation of the current study, beside the small sample size, is the tractography protocol. This study relied on tensor-based DTI tractography to determine the structure of the tracts which has been widely used (Catani et al., 2013; Mandelli et al., 2014; Misaghi et al., 2018). However, traditional tensor-based DTI tractography has demonstrated problems with properly reconstructing crossing fibers (because it can model only one primary fiber direction per voxel), leading to incomplete tract reconstructions and posing limitation to determining tract functionality. Future work can rely on advanced tractography algorithms that are tensor-free such as High Angular Resolution Diffusion Imaging (HARDI). The tensor-free modeling techniques have been proposed to have more sensitivity to account for complex intra-voxel fiber architectures and to detect multiple fiber tract orientations in regions with heterogeneous fiber populations (Auriat et al., 2015; Farquharson et al., 2013; Tournier et al., 2011). There are currently limited number of studies that have used this technique to investigate the neural basis of language deficit in stroke survivors (Ivanova et al., 2021).

In conclusion, this study revealed the importance of individual level analysis in relating features of stroke-induced lesions, namely white-matter damage, to variability in language-deficit outcomes across individuals with aphasia. Given the small sample size, we were not able to decisively elucidate neural substrates of real-time mechanisms involved in auditory sentence comprehension. Nevertheless, we demonstrated the importance of connectivity within the frontal region for real-time sensitivity to lexical-semantic cue which is a central mechanism for successful sentence comprehension.

References

Aftonomos, L. B., Appelbaum, J. S., & Steele, R. D. (1999). Improving outcomes for persons with aphasia in advanced community-based treatment programs. *Stroke, 30*(7), 1370-1379.

Auriat, A. M., Neva, J. L., Peters, S., Ferris, J. K., & Boyd, L. A. (2015). A review of transcranial magnetic stimulation and multimodal neuroimaging to characterize post-stroke neuroplasticity. *Frontiers in Neurology, 6*, 226.

Bates, E., Wilson, S. M., Saygin, A. P., Dick, F., Sereno, M. I., Knight, R. T., & Dronkers, N. F. (2003). Voxel-based lesion–symptom mapping. *Nature neuroscience, 6*(5), 448-450.

Binder, J. R., Desai, R. H., Graves, W. W., & Conant, L. L. (2009). Where is the semantic system? A critical review and meta-analysis of 120 functional neuroimaging studies. *Cerebral Cortex, 19*(12), 2767-2796.

Budde, M. D., Xie, M., Cross, A. H., & Song, S.-K. (2009). Axial diffusivity is the primary correlate of axonal injury in the experimental autoimmune encephalomyelitis spinal cord: a quantitative pixelwise analysis. *Journal of Neuroscience, 29*(9), 2805-2813.

Catani, M., & De Schotten, M. T. (2012). *Atlas of human brain connections*. Oxford University Press.

Catani, M., Dell'Acqua, F., Budisavljevic, S., Howells, H., Thiebaut de Schotten, M., Froudist-Walsh, S., D'anna, L., Thompson, A., Sandrone, S., & Bullmore, E. T. (2016). Frontal networks in adults with autism spectrum disorder. *Brain, 139*(2), 616-630.

Catani, M., Jones, D. K., & Ffytche, D. H. (2005). Perisylvian language networks of the human brain. *Annals of Neurology: Official Journal of the American Neurological Association and the Child Neurology Society, 57*(1), 8-16. https://onlinelibrary.wiley.com/doi/pdfdirect/10.1002/ana.20319?download=true

Catani, M., & Mesulam, M. (2008). The arcuate fasciculus and the disconnection theme in language and aphasia: history and current state. *Cortex, 44*(8), 953-961.

Catani, M., Mesulam, M. M., Jakobsen, E., Malik, F., Martersteck, A., Wieneke, C., Thompson, C. K., Thiebaut de Schotten, M., Dell'Acqua, F., & Weintraub, S. (2013). A novel frontal pathway underlies verbal fluency in primary progressive aphasia. *Brain, 136*(8), 2619-2628.

Charles-Edwards, E. M., & Nandita, M. d. (2006). Diffusion-weighted magnetic resonance imaging and its application to cancer. *Cancer imaging, 6*(1), 135.

Chenevert, T. L., Brunberg, J. A., & Pipe, J. G. (1990). Anisotropic diffusion in human white matter: demonstration with MR techniques in vivo. *Radiology, 177*(2), 401-405.

Crawford, J. R., & Garthwaite, P. H. (2007). Using regression equations built from summary data in the neuropsychological assessment of the individual case. *Neuropsychology, 21*(5), 611.

Dick, A. S., Bernal, B., & Tremblay, P. (2014). The language connectome: new pathways, new concepts. *The Neuroscientist, 20*(5), 453-467.

[Record #457 is using a reference type undefined in this output style.]

Dronkers, N. F., Plaisant, O., Iba-Zizen, M. T., & Cabanis, E. A. (2007). Paul Broca's historic cases: high resolution MR imaging of the brains of Leborgne and Lelong. *Brain, 130*(5), 1432-1441.

Dronkers, N. F., Redfern, B. B., & Knight, R. T. (2000). The neural architecture of language disorders. *The new cognitive neurosciences, 2*, 949-960.

Duffau, H. (2008). The anatomo-functional connectivity of language revisited: new insights provided by electrostimulation and tractography. *Neuropsychologia, 46*(4), 927-934.

Duffau, H., Gatignol, P., Mandonnet, E., Peruzzi, P., Tzourio-Mazoyer, N., & Capelle, L. (2005). New insights into the anatomo-functional connectivity of the semantic system: a study using cortico-subcortical electrostimulations. *Brain, 128*(4), 797-810.

Duffau, H., Gatignol, P., Moritz-Gasser, S., & Mandonnet, E. (2009). Is the left uncinate fasciculus essential for language? *Journal of neurology, 256*(3), 382-389.

Fabian, R., Bunker, L., & Hillis, A. E. (2020). Is Aphasia Treatment Beneficial for the Elderly? A Review of Recent Evidence. *Current physical medicine and rehabilitation reports, 8*(4), 478-492.

Farquharson, S., Tournier, J.-D., Calamante, F., Fabinyi, G., Schneider-Kolsky, M., Jackson, G. D., & Connelly, A. (2013). White matter fiber tractography: why we need to move beyond DTI. *Journal of Neurosurgery, 118*(6), 1367-1377.

Fedorenko, E., & Blank, I. A. (2020). Broca's area is not a natural kind. *Trends in Cognitive Sciences, 24*(4), 270-284.

Forkel, S. J., Thiebaut de Schotten, M., Dell'Acqua, F., Kalra, L., Murphy, D. G., Williams, S. C., & Catani, M. (2014). Anatomical predictors of aphasia recovery: a tractography study of bilateral perisylvian language networks. *Brain, 137*(7), 2027-2039.

Fridriksson, J., den Ouden, D.-B., Hillis, A. E., Hickok, G., Rorden, C., Basilakos, A., Yourganov, G., & Bonilha, L. (2018). Anatomy of aphasia revisited. *Brain, 141*(3), 848-862.

Fridriksson, J., Guo, D., Fillmore, P., Holland, A., & Rorden, C. (2013). Damage to the anterior arcuate fasciculus predicts non-fluent speech production in aphasia. *Brain, 136*(11), 3451-3460.

Friederici, A. D., & Gierhan, S. M. (2013). The language network. *Current opinion in neurobiology, 23*(2), 250-254. https://www.sciencedirect.com/science/article/abs/pii/S0959438812001614?via%3Dihub

Friederici, A. D., Rüschemeyer, S.-A., Hahne, A., & Fiebach, C. J. (2003). The role of left inferior frontal and superior temporal cortex in sentence comprehension: localizing syntactic and semantic processes. *Cerebral Cortex, 13*(2), 170-177.

Gajardo-Vidal, A., Lorca-Puls, D. L., Team, P., Warner, H., Pshdary, B., Crinion, J. T., Leff, A. P., Hope, T. M., Geva, S., & Seghier, M. L. (2021). Damage to Broca's area does not contribute to long-term speech production outcome after stroke. *Brain, 144*(3), 817-832.

Geschwind, N. (1970). The Organization of Language and the Brain: Language disorders after brain damage help in elucidating the neural basis of verbal behavior. *Science, 170*(3961), 940-944.

Geva, S., Correia, M. M., & Warburton, E. A. (2015). Contributions of bilateral white matter to chronic aphasia symptoms as assessed by diffusion tensor MRI. *Brain and Language, 150*, 117-128.

Glaser, Y. G., Martin, R. C., Van Dyke, J. A., Hamilton, A. C., & Tan, Y. (2013, Sep). Neural basis of semantic and syntactic interference in sentence comprehension. *Brain Lang, 126*(3), 314-326. https://doi.org/10.1016/j.bandl.2013.06.006

Glaser, Y. G., Martin, R. C., Van Dyke, J. A., Hamilton, A. C., & Tan, Y. (2013, 2013/09). Neural basis of semantic and syntactic interference in sentence comprehension. *Brain and Language, 126*(3), 314-326. https://doi.org/10.1016/j.bandl.2013.06.006

Goodglass, H., Kaplan, E., & Barresi, B. (2001). *BDAE-3: Boston Diagnostic Aphasia Examination–Third Edition*. Lippincott Williams & Wilkins Philadelphia, PA.

Hagmann, P., Jonasson, L., Maeder, P., Thiran, J.-P., Wedeen, V. J., & Meuli, R. (2006). Understanding diffusion MR imaging techniques: from scalar diffusion-weighted imaging to diffusion tensor imaging and beyond. *Radiographics, 26*(suppl_1), S205-S223.

Hagoort, P. (2005, 2005/09). On Broca, brain, and binding: a new framework. *Trends in Cognitive Sciences, 9*(9), 416-423. https://doi.org/10.1016/j.tics.2005.07.004

Harvey, D. Y., Wei, T., Ellmore, T. M., Hamilton, A. C., & Schnur, T. T. (2013). Neuropsychological evidence for the functional role of the uncinate fasciculus in semantic control. *Neuropsychologia, 51*(5), 789-801.

Ivanova, M. V., Isaev, D. Y., Dragoy, O. V., Akinina, Y. S., Petrushevskiy, A. G., Fedina, O. N., Shklovsky, V. M., & Dronkers, N. F. (2016). Diffusion-tensor imaging of major white matter tracts and their role in language processing in aphasia. *Cortex, 85*, 165-181.

Ivanova, M. V., Zhong, A., Turken, A., Baldo, J. V., & Dronkers, N. F. (2021). Functional contributions of the arcuate fasciculus to language processing. *Frontiers in human neuroscience, 15*, 672665.

Jehna, M., Becker, J., Zaar, K., von Campe, G., Ali, K. M., Reishofer, G., Payer, F., Synowitz, M., Fazekas, F., & Enzinger, C. (2017). Symmetry of the arcuate fasciculus and its impact on language performance of patients with brain tumors in the language-dominant hemisphere. *Journal of Neurosurgery, 127*(6), 1407-1416.

Kertesz, A. (2007). *WAB-R: Western aphasia battery-revised*. PsychCorp.

Kierońska, S., Sokal, P., Dura, M., Jabłońska, M., Rudaś, M., & Jabłońska, R. (2020). Tractography-Based Analysis of Morphological and Anatomical Characteristics of the Uncinate Fasciculus in Human Brains. *Brain Sciences, 10*(10), 709. https://www.mdpi.com/2076-3425/10/10/709

Kinoshita, M., de Champfleur, N. M., Deverdun, J., Moritz-Gasser, S., Herbet, G., & Duffau, H. (2015). Role of fronto-striatal tract and frontal aslant tract in movement and speech: an axonal mapping study. *Brain Structure and Function, 220*(6), 3399-3412.

Leemans, A., Jeurissen, B., Sijbers, J., & Jones, D. K. (2009). ExploreDTI: a graphical toolbox for processing, analyzing, and visualizing diffusion MR data. Proc Intl Soc Mag Reson Med,

Li, M., Zhang, Y., Song, L., Huang, R., Ding, J., Fang, Y., Xu, Y., & Han, Z. (2017). Structural connectivity subserving verbal fluency revealed by lesion-behavior mapping in stroke patients. *Neuropsychologia, 101*, 85-96.

Love, T., & Oster, E. (2002). *Journal of psycholinguistic research, 31*(5), 503-529. https://doi.org/10.1023/a:1021208903394

Love, T., Swinney, D., Walenski, M., & Zurif, E. (2008). How left inferior frontal cortex participates in syntactic processing: Evidence from aphasia. *Brain and Language, 107*(3), 203-219. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2650827/pdf/nihms-79787.pdf

Mandelli, M. L., Caverzasi, E., Binney, R. J., Henry, M. L., Lobach, I., Block, N., Amirbekian, B., Dronkers, N., Miller, B. L., & Henry, R. G. (2014). Frontal white matter tracts sustaining speech production in primary progressive aphasia. *Journal of Neuroscience, 34*(29), 9754-9767.

Matchin, W., & Hickok, G. (2020). The cortical organization of syntax. *Cerebral Cortex, 30*(3), 1481-1498. https://academic.oup.com/cercor/article-abstract/30/3/1481/5588467?redirectedFrom=fulltext

Matchin, W., & Rogalsky, C. (2017). Aphasia & syntax.

Meier, E. L., Johnson, J. P., Pan, Y., & Kiran, S. (2019). The utility of lesion classification in predicting language and treatment outcomes in chronic stroke-induced aphasia. *Brain imaging and behavior, 13*(6), 1510-1525.

Misaghi, E., Zhang, Z., Gracco, V. L., Luc, F., & Beal, D. S. (2018). White matter tractography of the neural network for speech-motor control in children who stutter. *Neuroscience letters, 668*, 37-42.

Moseley, M., Bammer, R., & Illes, J. (2002). Diffusion-tensor imaging of cognitive performance. *Brain and cognition, 50*(3), 396-413.

Novick, J. M., Kan, I. P., Trueswell, J. C., & Thompson-Schill, S. L. (2009). A case for conflict across multiple domains: Memory and language impairments following damage to ventrolateral prefrontal cortex. *Cognitive Neuropsychology, 26*(6), 527-567.

Nozari, N., Mirman, D., & Thompson-Schill, S. L. (2016, Jun-Jul). The ventrolateral prefrontal cortex facilitates processing of sentential context to locate referents. *Brain Lang, 157-158*, 1-13. https://doi.org/10.1016/j.bandl.2016.04.006

Nozari, N., & Thompson-Schill, S. L. (2016). Left Ventrolateral Prefrontal Cortex in Processing of Words and Sentences. In *Neurobiology of Language* (pp. 569-584). https://doi.org/10.1016/b978-0-12-407794-2.00046-8

Paldino, M., Hedges, K., & Golriz, F. (2016). The arcuate fasciculus and language development in a cohort of pediatric patients with malformations of cortical development. *American Journal of Neuroradiology, 37*(1), 169-175.

Parker, G. J., Luzzi, S., Alexander, D. C., Wheeler-Kingshott, C. A., Ciccarelli, O., & Ralph, M. A. L. (2005). Lateralization of ventral and dorsal auditory-language pathways in the human brain. *NeuroImage, 24*(3), 656-666.

Ratcliff, R., Gomez, P., & McKoon, G. (2004). A diffusion model account of the lexical decision task. *Psychological Review, 111*(1), 159.

Ratcliff, R., & Rouder, J. N. (2000). A diffusion model account of masking in two-choice letter identification. *Journal of Experimental Psychology: Human perception and performance, 26*(1), 127.

Ries, S. K., Schendel, K. L., Herron, T. J., Dronkers, N. F., Baldo, J. V., & Turken, A. U. (2021, 2021-February-10). Neural Underpinnings of Proactive Interference in Working Memory: Evidence From Patients With Unilateral Lesions [Original Research]. *Frontiers in Neurology, 12*(75). https://doi.org/10.3389/fneur.2021.607273

Robinson, G., Blair, J., & Cipolotti, L. (1998). Dynamic aphasia: an inability to select between competing verbal responses? *Brain: a journal of neurology, 121*(1), 77-89.

Satoer, D., Kloet, A., Vincent, A., Dirven, C., & Visch-Brink, E. (2014). Dynamic aphasia following low-grade glioma surgery near the supplementary motor area: a selective spontaneous speech deficit. *Neurocase, 20*(6), 704-716.

Schlaug, G., Marchina, S., & Norton, A. (2009). Evidence for plasticity in white□matter tracts of patients with chronic Broca's aphasia undergoing intense intonation□based speech therapy. *Annals of the New York Academy of Sciences, 1169*(1), 385-394.

Schmahmann, J. D., Pandya, D. N., Wang, R., Dai, G., D'Arceuil, H. E., De Crespigny, A. J., & Wedeen, V. J. (2007). Association fibre pathways of the brain: parallel observations from diffusion spectrum imaging and autoradiography. *Brain, 130*(3), 630-653.

Soares, J. M., Marques, P., Alves, V., & Sousa, N. (2013). A hitchhiker's guide to diffusion tensor imaging. *Frontiers in neuroscience, 7*, 31.

Song, S.-K., Sun, S.-W., Ramsbottom, M. J., Chang, C., Russell, J., & Cross, A. H. (2002). Dysmyelination revealed through MRI as increased radial (but unchanged axial) diffusion of water. *NeuroImage, 17*(3), 1429-1436.

Tournier, J.-D., Mori, S., & Leemans, A. (2011). Diffusion tensor imaging and beyond. *Magnetic resonance in medicine, 65*(6), 1532.

Turken, & Dronkers, N. F. (2011). The neural architecture of the language comprehension network: converging evidence from lesion and connectivity analyses. *Frontiers in System Neuroscience, 5*, 1.

Turken, A., & Dronkers, N. (2011). The neural architecture of the language comprehension network: converging evidence from lesion and connectivity analyses. Front Syst Neurosci. 2011; 5: 1.

Varriano, F., Pascual-Diaz, S., & Prats-Galino, A. (2020). Distinct components in the right extended frontal aslant tract mediate language and working memory performance: A tractography-informed VBM Study. *Frontiers in neuroanatomy, 14*, 21.

Vuong, L., & Martin, R. (2015). The role of LIFG-based executive control in sentence comprehension. *Cognitive Neuropsychology, 32*(5), 243-265. https://www.tandfonline.com/doi/full/10.1080/02643294.2015.1057558

Wang, J., Marchina, S., Norton, A. C., Wan, C. Y., & Schlaug, G. (2013). Predicting speech fluency and naming abilities in aphasic patients. *Frontiers in human neuroscience, 7*, 831.

Wang, R., Benner, T., Sorensen, A. G., & Wedeen, V. J. (2007). Diffusion toolkit: a software package for diffusion imaging data processing and tractography. Proc Intl Soc Mag Reson Med,

Wernicke, C. (1874). Der aphasische symptomencomplex.

Wilson, S. M., Galantucci, S., Tartaglia, M. C., Rising, K., Patterson, D. K., Henry, M. L., Ogar, J. M., DeLeon, J., Miller, B. L., & Gorno-Tempini, M. L. (2011). Syntactic processing depends on dorsal language tracts. *Neuron, 72*(2), 397-403.

Xing, S., Lacey, E. H., Skipper-Kallal, L. M., Zeng, J., & Turkeltaub, P. E. (2017). White matter correlates of auditory comprehension outcomes in chronic post-stroke aphasia. *Frontiers in Neurology, 8*, 54.

Xing, S., Lacey, E. H., Skipper-Kallal, L. M., Zeng, J., & Turkeltaub, P. E. (2017). White Matter Correlates of Auditory Comprehension Outcomes in Chronic Post-Stroke Aphasia. *Front Neurol, 8*, 54. https://doi.org/10.3389/fneur.2017.00054

Yeh, F.-C., Panesar, S., Fernandes, D., Meola, A., Yoshino, M., Fernandez-Miranda, J. C., Vettel, J. M., & Verstynen, T. (2018). Population-averaged atlas of the macroscale human structural connectome and its network topology. *NeuroImage, 178*, 57-68.

Yushkevich, P. A., Piven, J., Hazlett, H. C., Smith, R. G., Ho, S., Gee, J. C., & Gerig, G. (2006). User-guided 3D active contour segmentation of anatomical structures: significantly improved efficiency and reliability. *NeuroImage, 31*(3), 1116-1128.

Zhong, A. J., Baldo, J. V., Dronkers, N. F., & Ivanova, M. V. (2022). The unique role of the frontal aslant tract in speech and language processing. *NeuroImage: Clinical, 34*, 103020.

Chapter 4 is being prepared for submission for publication of the material. The dissertation author was the primary investigator and the primary author of this paper.

CHAPTER 5

General Discussion

The overarching goal of this dissertation was to investigate (1) approaches with which sentence comprehension impairment can be mitigated in individuals with aphasia, and (2) whether integrity of connectivity between prefrontal cortex and temporo-parietal regions are predictive of individuals' sensitivity to the proposed mitigation approaches. In this dissertation, we examined the online processing of individuals with aphasia (and unimpaired controls to establish normal patterns of processing) via an eye-tracking-while-listening paradigm and combined it with information about the structural integrity of specific neural regions via Diffusion Tensor Imaging (DTI) techniques.

With respect to the first goal of this dissertation, chapter 2 and chapter 3 presented two experimental behavioral studies that examined the real-time processes involved in the comprehension of sentences requiring long distance dependency-linking. These studies proposed and evaluated mitigation approaches that aimed to reduce sentence processing difficulty in individuals with aphasia (and unimpaired population which served as the baseline group) by reducing the interference level via lexical level manipulation. In each of these studies, the sentence structures included a target noun that was syntactically licensed for retrieval at the verb offset (gap-site) despite the presence of an intervening noun. The first mitigation approach involved adding semantically biasing modifiers to the target item. The second mitigation approach involved reducing the similarities between the target and intervening noun by only differentiating a single lexical property feature; animacy. The mechanism with which these manipulations could be effective can be explained by the feature-based retrieval formulation of Nairne (2006) that has been adapted by the cue-based retrieval approach (Lewis et al., 2006). This framework expresses that the probability that a target representation will be selected depends on two main parameters: cue-target features match (also postulated by cue-based retrieval model of sentence processing) and distinctiveness of the target from competitor items. Focusing on the latter to manipulate the distinctiveness of the target, we used two different types of semantic manipulations. In chapter 2, by adding pre-modifiers, we aimed to increase the distinctiveness parameter of the target item during the encoding process to see if this would facilitate its downstream retrieval at the gap-site. For the unimpaired group, the premodifiers resulted in enhanced encoding and retrieval at the gap-site. However, for the aphasia group, the premodifiers did not result in a statistically differentiated real-time sentence processing patterns at either the encoding or the retrieval points. In chapter 3, by changing the animacy features between the target and intervening item, we aimed to increase the uniqueness of encoded constituents to reduce similarity-based interference. The results of this study revealed a significant effect of this manipulation for the unimpaired individuals as well as individuals with aphasia. However, in line with reports in the literature, individuals with aphasia demonstrated a delay in showing a benefit from this manipulation.

The findings for the aphasia group in both studies can be explained under two etiologies of access deficit or inhibition deficit at the lexical-representational level. IWA may demonstrate access deficits and suffer from lower-than-normal activation of representational features (semantic in this case). This can lead to smaller differences between encoded items during the spread of activation and ultimately impede the retrieval of an item. Moreover, IWA can have inhibition deficits and suffer from increased activation of semantic competitors. When there is impairment of the inhibitory process that are designed to suppress the activation of unrelated representations, there is an increase in interference. Deficits in any of these mechanisms can explain why IWA demonstrated a lack or delay in sensitivity to the manipulations that provided distinctiveness for the target noun and led to impaired comprehension

With respect to the second goal of this dissertation, chapter 4 presented a study that focused on the individual variability that exists among the IWA in their level of sensitivity or magnitude of benefit from the lexical-semantic cues that were used in chapters 2 and 3. Here we examined whether damage to specific left hemisphere white matter tracts (AF, FAT, UF and IFOF) are predictive of the magnitude of benefit in processing from the lexical-semantic cues. To this end, the relationship between the behavioral performances of each IWA and their lesion features were analyzed. To establish lesion features, Diffusion Tenor Imaging and Tractography approaches were used to specify the integrity of white matter pathways. This experiment investigated the relationship between eye-tracking performance in chapters 2 and 3, and the integrity (i.e., fractional anisotropy) of abovementioned tracts at the individual level in IWA in both the ipsilateral and contralateral lesion hemispheres. Overall, the results revealed an emerging pattern between reduction in integrity of FAT, and the anterior sections of AF in left hemisphere and less sensitivity to the lexical-semantic cues. However, given the small sample size in this study, the results are exploratory and requires further investigation. Yet, this set of preliminary finding are in accordance with the previous findings in the literature that indicated the functional role of anterior-AF and FAT in lexical-semantic processes. Unlike the current approach in the field, future studies must utilize time-sensitive paradigms (such as eye-tracking) to measure patterns of IWA's impairment at the level of sub-processes involved in sentence comprehension and then map associations with the lesion patterns. This will allow researchers to identify the brain regions necessary for the specific processes involved in sentence comprehension.

In conclusion, understanding and identifying the underlying processes of sentence comprehension using online paradigms, as well as their neuroanatomical substrates, is an important undertaking. It does not only have the potential to inform typical models of language comprehension but is highly relevant for understanding how the system might be affected post-stroke. Discerning such impairments can affect how clinical treatment protocols are developed and enacted thus having a direct impact on treatment and rehabilitation approaches in aphasia.