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Digging beneath the surface behavioral and neural indices of lexical access during idiom comprehension in Aphasia : a multi-modal approach

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Digging Beneath the Surface
Behavioral and Neural Indices of lexical access during idiom comprehension in Aphasia:
A multi-modal approach

A dissertation submitted in partial satisfaction of the requirements for the degree Doctor of Philosophy in Language and Communicative Disorders by Kathleen Patricia Brumm

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2011
The Dissertation of Kathleen Patricia Brumm is approved, and is acceptable in quality and form for publication on microfilm and electronically:

Chair

University of California, San Diego
San Diego State University
2011
Dedication

To my Mom. You are the most awesome woman I know, and I deeply admire your spunkiness and determination. I can never thank you enough for teaching me to run after my dreams and supporting me with your love every step of the way.

To my dearest friends, who have become my family during my time in San Diego. You have been my cheerleaders and ensured that I grew at least as much emotionally and spiritually as I did intellectually during graduate school.
Epigraph

Why, anybody can have a brain.
That's a very mediocre commodity.
Every pusillanimous creature that crawls on
the earth or slinks through slimy seas has a brain!

~ The Wizard of Oz

So you see! There's no end to the things you
might know, depending how far beyond Zebra you go.

~Dr. Seuss
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List of Abbreviations

AFNI .............................................. Analysis of Functional NeuroImages
AMC .............................................. age-matched control
ANOVA .......................................... analysis of variance
ASL ............................................... arterial spin labeling
BA .................................................. Brodmann area
BDAE ........................................... Boston Diagnostic Aphasia Examination
BNT .............................................. Boston Naming Task
BOLD ............................................. blood oxygenation level-dependent
CASL ............................................... continuous arterial spin labeling
CBF ................................................ cerebral blood flow
CMLP ........................................... cross-modal lexical priming
CSF ................................................ cerebrospinal fluid
CT .................................................. Computerized Axial Tomography
CVA ............................................... cerebrovascular accident
DLPFC .......................................... dorsolateral prefrontal cortex
EC .................................................. elderly control
ERPs ............................................... event-related potentials
FAIR ............................................... flow-alternating inversion recovery
FMRI ............................................... functional magnetic resonance imaging
g .................................................... grams
HRF ............................................... hemodynamic response function
IFG ................................................ inferior frontal gyrus
Ips .................................................. idiomatic phrases
ITG ................................................ inferior temporal gyrus
LHD ............................................... left hemisphere damaged
MFG ............................................... middle frontal gyrus
mL .................................................. milliliter
MMSE ........................................... Mini Mental Status Examination
msec .............................................. millisecond
MTG ............................................... middle temporal gyrus
NP .................................................. noun phrase
PASL ........................................... pulsed arterial spin labeling
PET ............................................... positron emission tomography
PP .................................................. prepositional phrase
RTs ............................................... reaction times
SFG ............................................... superior frontal gyrus
SPGR……………………………………………………………………spooled gradient recalled
SVO……………………………………………………………………subject-verb-object
VP……………………………………………………………………verb phrase
WAB………………………………………………………………Western Aphasia Battery
WRIT………………………………………………………………Wide-Range Intelligence Test
YC……………………………………………………………………young control
YNC………………………………………………………………….young normal control
µL………………………………………………………………………microliter
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ABSTRACT OF THE DISSERTATION

Digging Beneath the Surface
Behavioral and Neural Indices of lexical access during idiom comprehension in Aphasia:
A multi-modal approach

by

Kathleen Patricia Brumm

Doctor of Philosophy in Language and Communicative Disorders

University of California, San Diego, 2011
San Diego State University, 2011

Professor Tracy Love, Chair

This project examines spoken language comprehension in Broca’s aphasia, a non-fluent language disorder acquired subsequent to stroke. Broca’s aphasics demonstrate impaired comprehension for complex sentence constructions. To account for this deficit, one current processing theory claims that Broca’s patients retain intrinsic linguistic knowledge, but that a delay in lexical access in these patients disrupts an intact syntactic system. The current work exploits the properties of long lexical items (idioms) that have multiple meanings (literal and figurative) represented in the lexicon to investigate this theory of lexical deficit in Broca’s aphasia. This work postulates that idioms allow for a temporally-extended investigation of lexical access in aphasia, as prior research demonstrates that healthy listeners access the figurative meaning of an idiom slightly prior to the literal meanings associated with the idiom’s
This temporal discontinuity will allow a close examination of the time course of lexical access in Broca’s aphasia. This dissertation investigates both the real-time psycholinguistic indices of lexical processing during auditory idiom comprehension in aphasia, as well as the neural manifestations of this processing.

Chapter 1 reviews hypotheses of lexical access deficits in Broca’s aphasia and motivates the use of idioms as a tool to investigate lexical processing in this population. Chapter 2 examines real-time lexical access for an idiom’s multiple meanings during sentence comprehension, in unimpaired and aphasic individuals. Chapters 3 and 4 examine the neural correlates of this lexical processing. Chapter 3 studies cerebral blood flow, an important variable in functional neuroimaging, among stroke survivors with aphasia, finding that special care must taken when analyzing functional neuroimaging data from this population in order to capture the full time course of the neural signal. Chapter 4 investigates lexical access during idiom comprehension via functional neuroimaging, localizing the neural indices of this processing.

This dissertation provides the first investigation of lexical access in Broca’s aphasia using idioms as a research tool. The results extend our understanding of lexical processing in this population, both behaviorally and neurally, during auditory sentence comprehension.
CHAPTER 1

Introduction
As listeners hear spoken language, they must make sense of the information contained in the message. To this end, the listener must perform numerous levels of analyses immediately. These include determining the meanings of individual constituent components of the message (such as identifying lexical items and attributing meaning to those items) and then figuring out (syntactically and at a broader discourse level) how these individual parts combine together to convey a meaning. As part of this process, when a listener hears a lexical item, that item must somehow be accessed in the mental lexicon, and information regarding that item (such as word category, role, meaning, tense, agreement etc.) must be integrated into the overarching meaning of a sentence. The process by which a lexical item is identified and its meaning retrieved from the lexicon becomes quite interesting when a single lexical form can possess multiple meanings, as in the case of lexical ambiguities (which are ubiquitous in English). This notion of lexical ambiguity can be extended beyond multiple meanings of a lexical item within or across word classes (e.g. /bank/: noun meanings: a piled up mass of snow; financial institution; slope of land adjoining a body of water; a cushion of a billiards table; and verb meanings: to tip laterally; conduct business; rely on). Especially interesting is the case of a lexical constituent that can denote either a literal or figurative, non-literal meaning (such as found with metaphors or idiomatic phrases). The current project specifically investigates the mechanisms and time course of lexical access for the literal and figurative meanings of idiomatic phrases (IPs) during on-going sentence processing with an aim to better understand how a purported unitary, automatic lexical access device deals with
ambiguous lexical phrases. This dissertation specifically employs IPs as a tool to explore lexical-level access in both language-unimpaired and language-impaired populations.

This dissertation seeks to investigate the behavioral and brain bases of lexical access for ambiguous IPs, and to uncover how brain damage impacts processing of these items. A multi-methodological behavioral, neurolinguistic, and neuroimaging approach will allow for the exploration of converging brain-behavioral patterns. In so doing, the current project draws upon contemporary work in brain-damaged individuals with the language disorder aphasia, which suggests that lexical access may be protracted (temporally delayed) in some individuals with this disorder. As will be described below, an investigation of lexical access during IP comprehension will provide a unique test to this hypothesis, as these temporally-long lexical items can be used as a tool to examine the time course of lexical access in this population. First, the literature of lexical access in aphasia will be reviewed, in order to provide a framework and motivation for the current set of studies. Then, the psycholinguistic literature of IP comprehension in healthy listeners will be reviewed, with a focus on understanding the lexical processes that may underlie IP comprehension. As little is yet known about the specific lexical means by which individuals with aphasia process IPs, the literature of unimpaired IP processing will be used to generate hypotheses of lexical processing of IPs in aphasia, with an eye towards generalizing these findings towards lexical access more generally in aphasia.
Comprehension deficits in Broca’s Aphasia

Aphasia is an acquired language disorder that occurs subsequent to neural trauma, namely, stroke. It has been proposed that this neural trauma damages regions of the brain that support language comprehension and/or production, most typically, in the left hemisphere of the brain (see original work by Broca, 1861; Wernicke, 1874), and more recent work (e.g. Goodglass & Kaplan, 1972). Aphasia is characterized by an impairment of receptive and/or expressive elements of language, with deficits evident across modalities (e.g. writing). Contrary to historical beliefs, impairments in sensation or perception are not underlying causes of aphasia, nor is aphasia a deficit in intellectual function (Goodglass & Kaplan, 1972). To further complicate matters, aphasia is not a unitary disorder, as many sub-types of the disorder have been classified (Kertesz, 1982; Goodglass & Kaplan, 1972), with these sub-classifications based on the constellation of symptoms and deficits that are present. The work presented here specific to this dissertation focuses on Broca’s aphasia, one of the most commonly studied typologies of aphasia. Individuals with Broca’s aphasia demonstrate an obvious expressive impairment, characterized by non-fluent speech (Goodglass & Kaplan, 1972) and certain types of comprehension deficits. Patients with Broca’s aphasia omit function words, such as “the” or “and,” as well as grammatical markers for tense, agreement, number, and gender. These omissions result in speech and written output that is described as “telegraphic” or “agrammatic.” For instance, an individual with Broca’s aphasia may say, “Boy kiss girl” to mean “The boy kissed the girl.” Although expressive deficits are most obvious in Broca’s
aphasia, individuals with this disorder have been demonstrated to have comprehension impairments as well (Caramazza & Zurif, 1976; Love et al., 2008; Grodzinsky, 2000, among others). As this dissertation aims to investigate a real-time language processing component of this comprehension impairment, the literature of comprehension deficits in Broca’s aphasia will be briefly reviewed, followed by a discussion of how this dissertation will contribute to our understanding of processing deficits in Broca’s aphasia and their connection to comprehension difficulties in these patients.

In the first study to highlight comprehension deficits in Broca’s aphasia, Caramazza and Zurif (1976) reported that this patient group demonstrated comprehension deficits for sentences that required an understanding of the underlying sentence structure. These authors compared patients’ comprehension patterns for semantically nonreversible and reversible sentences; the latter type of sentence being one in which multiple nouns in the sentence could viably perform the action of the sentence. Consider the following:

1) The pizza was eaten by the boy.

2) The girl was kicked by the boy.
Both of these sentences are passivized, in that the noun receiving the action of the verb actually precedes the verb. A semantically reversible sentence is shown in example 2, since the two nouns (“boy” and “girl”) are each capable of performing the action (the act of “kicking”), as they are both animate nouns. However, in example 1, the two nouns (“pizza” and “boy”) are not semantically reversible, because the boy is an animate noun, and is thus the only entity who can perform the action of eating. Pizza, as an inanimate object, cannot perform this action.

When Broca’s aphasic patients were presented with semantically reversible (e.g. example 2) and non-reversible (e.g. example 1) sentences in a sentence-to-picture matching task, they demonstrated above-chance performance non-reversible constructions and chance performance for reversible ones. Based on these results, the authors argued that patients used their real-world knowledge of the properties of animate and inanimate objects in order to determine who performed the action in non-reversible sentences. However, when both nouns in the sentence could possibly perform the action in reversible sentences, patients were unable to use any semantic cues to determine who performed the action of the sentence. Based on this set of findings, Caramazza and Zurif argued for a representational deficit for these individuals, arguing that Broca’s patients lack the syntactic knowledge needed to comprehend syntactically-complex sentence structures. They further argued that these patients would rely on heuristic strategies whenever possible to aid in understanding these types of sentences. Thus, in the same way that Broca’s patients lack grammar in

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1 English follows the strict canonical word order of Subject-Verb-Object (SVO). Thus in grammatical sentences where the object precedes the verb, it is considered a more complex, non-canonical structure.
their production, Caramazza and Zurif argued that these patients also lack the grammatical skills that are needed to properly comprehend sentences, and the authors described this collection of deficits under the new term “overarching agrammatism,” which refers to the purported grammatical deficit in Broca’s aphasia, across both receptive and expressive domains.

Beyond Caramazza and Zurif’s original study (1976), a great deal of work has been devoted to trying to more fully understand the nature of sentence comprehension deficits in Broca’s aphasia. It has been repeatedly demonstrated that Broca’s patients have comprehension deficits for non-canonical sentences (e.g. Grodzinsky, 2000; Hickok, 1992; Love et al., 2008; Sussman & Sedivy, 2003; M. K. Tanenhaus & Trueswell, 1995; Schwartz et al., 1980; Zurif et al., 1993, and many others). These are sentence structures that contain the movement or displacement of a sentence constituent from its original location in the structure to an earlier position in the sentence. Below is an example of a sentence with this type of displacement; here, the noun “wrestler” has been displaced in its surface form to a pre-verb position from its original base canonical position after the verb (from Love et al., 2008).

3) The audience liked the wrestler, \textit{object} that the parish priest \textit{subject} condemned(t)\textsubscript{i} \textit{verb} for foul language.

Some linguistic theories posit that when the object is fronted, it leaves a phonologically null marker (“trace”) allowing the noun to co-refer with its original
post-verb position (e.g. Frazier & D'Arcais, 1989; Garnsey et al., 1989; McElree & Griffith, 1995; Sussman & Sedivy, 2003; M. K. Tanenhaus & Trueswell, 1995, and others). It has been repeatedly demonstrated in the psycholinguistic literature that healthy listeners will lexically access the object of this sentence (“wrestler”), both at the offset of the object itself, and at the base-generated position of this object, here, at the offset of the verb (“condemned;” e.g. Hickok, 1992; Love et al., 2008; Swinney & Osterhout, 1990; Tanenhaus et al., 1989). By contrast, individuals with Broca’s aphasia do not show immediate lexical access of the object at either its initial offset or at its structurally-licensed location, at the offset of the verb\(^2\) (Love et al., 2008; Swinney et al., 1996).

**Lexical access and comprehension deficits in Broca’s Aphasia**

\(^2\) Individuals with Broca’s aphasia have been shown to have real-time (automatic) processing deficits for complex, non-canonical sentences, such as: “The audience liked the wrestler that the parish priest condemned for foul language” (from Love et al., 2008). This sentence has an object-subject-verb syntactic structure, and deviates from the canonical subject-verb-object order that is the default in English. Non-canonical sentence structures are linguistically more complex than canonical ones, making them harder for listeners to process (Grodzinsky & Friederici, 2006), although psycholinguistic work indicates that listeners reconstruct subject-verb-object order during comprehension (see Shapiro, 1997). Unimpaired participants have repeatedly demonstrated lexical access for an object (“wrestler”) both at its offset, and at the offset of the verb (“condemned”) (Shapiro, 1997; Shapiro et al., 1998). By contrast, patients with Broca’s aphasia showed lexical activation for the object 300ms after its offset and 500ms after the offset of the verb. As lexical access is delayed in Broca’s aphasics for the object at both positions, some researchers have argued that these results indicate *slowed lexical access* in this population. The authors assert a “*slow rise lexical hypothesis*” of comprehension deficits in Broca’s aphasia, claiming that lexical access mechanisms are protracted in the disorder. It has been argued that this delay disrupts many elements of higher-order automatic language processing, thus leading to both on-line and off-line processing and comprehension deficits (Love et al., 2008; Blumstein & Milberg, 2000).
In order to account for these abnormal patterns of lexical access in Broca’s aphasia, researchers have proposed representational and processing theories. Representational, linguistically-based, accounts have argued that Broca’s aphasics lack the ability to mentally represent closed-class words (Bradley et al., 1980); that Broca’s patients have lost the syntactic information needed to assign thematic roles (see Caplan & Futter, 1986); and perhaps most prominently, that Broca’s aphasics have lost the ability to represent traces (Grodzinsky, 1986; Grodzinsky, 1995; Grodzinsky, 2000; Hickok, 1992) and can no longer assign the appropriate thematic roles to the constituents in the sentence, which leads to a comprehension impairment with respect to who performs the action of the verb in a sentence and who receives it.

Processing based accounts argue that the linguistic knowledge is intact in this population, but instead, argue that Broca’s patients cannot use the information appropriately to successfully comprehend the sentence. Some processing theories argue that there are temporal delays at one or more processing levels in Broca’s aphasia (Avrutin, 2006; Burkhardt et al., 2008; Love et al., 2008; Pinango, 2000). One such processing theory argues that slowed syntax underlies the comprehension deficits of this population (Avrutin, 2006; Burkhardt et al., 2008; Piñango, 2000). Specifically, the Slowed Syntax theory asserts that individuals with Broca’s aphasia are able to access lexical content from the semantic system, but that these patients cannot build syntactic categories quickly enough to allow correct comprehension. This slowed sentence structure building leads to problems with assigning thematic roles to the constituents of the sentence (e.g. “who did what to whom”), which ultimately causes a
comprehension deficit in these patients. There exists some electrophysiological evidence in the literature to support this theory of delayed syntactic processing (see Friederici et al., 1998).

However, recent evidence suggests that syntactic linking is in fact intact in this population and the root cause of the delay is due to a problem at the lexical level of processing. In a recent study, individuals with Broca’s aphasia and their unimpaired age-matched counterparts listened to sentences such as example 3 (Love et al., 2008). The healthy, age-matched participants demonstrated immediate lexical access for the object of the sentence (“wrestler”), both at its offset and at the offset of the verb (“condemned”), where it is licensed and as has been reported previously (see above). By contrast, the individuals with Broca’s aphasia only showed lexical access for the object 300ms after its offset, and again 500ms after the offset of the verb. As lexical access is delayed for the object in both positions, the authors of this report asserted that lexical access is slowed in Broca’s aphasia (Love et al., 2008). The authors proposed the Delayed Lexical Activation Hypothesis, claiming that protracted lexical access in this population disrupts the fast-acting syntactic processes that must occur in order for comprehension to succeed. Thus, if lexical access is slowed, as it has been argued for Broca’s aphasics, sentence structure building breaks down and comprehension is ultimately impaired. In addition to psycholinguistic evidence that lexical access may be delayed in Broca’s aphasia, converging evidence from electrophysiological and eye-tracking work has also suggested that lexical processing is slowed during auditory comprehension in this population (e.g. Swaab et al., 1997;
Dickey & Thompson, 2009). Thus, there are two major processing theories of sentence comprehension deficits in Broca’s aphasia: the Slowed Syntax hypothesis and the Delayed Lexical Activation Hypothesis. By investigating the temporal indices of lexical access in Broca’s aphasia this dissertation will contribute new information to this field of inquiry.

As this dissertation closely investigates the time-course of lexical access during IP comprehension in Broca’s aphasia, the findings herein will add to the current discussion of lexical access mechanisms in this population. Specifically, IPs are argued to be ambiguous lexical items which are associated with multiple meanings represented in the lexicon: a figurative meaning for the IP as a whole, and literal meanings for each of the IP’s constituent words (Swinney & Cutler, 1979; Cacciari & Tabossi, 1988; Titone & Connine, 1994; Tabossi & Zardon, 1993; Tabossi & Zardon, 1995, and many others). To address real time IP processing, two theories have been proposed (Swinney & Cutler, 1979; Cacciari & Tabossi, 1988): the Lexical Representation Hypothesis and the Configuration Hypothesis. Prior research has indicated that unimpaired listeners begin to lexically access the figurative (non-literal) meaning of an IP slightly prior to the offset of the IP, whereas listeners access the literal meaning of the IP’s constituent words (verb at verb offset, noun at noun offset); this results in a slight temporal discontinuity of lexical access for these two meanings (e.g. Cacciari & Tabossi, 1988; Colombo, 1993; Titone & Connine, 1994). This temporal discontinuity will allow for a unique and novel examination of lexical access in Broca’s aphasia; examining lexical access during IP comprehension in this
population will indicate whether lexical access is indeed slowed in individuals with Broca’s aphasia, and if so, how. Specifically, the results of this study may show that: (a) lexical access for both the figurative and literal meanings is delayed to the same extent, resulting in the same pattern of lexical access that is observed with healthy listeners, but with a global temporal shift; (b) access is only delayed for one meaning of the IP; or (c) lexical access is not delayed in Broca’s aphasia and thus occurs in an identical manner as in healthy listeners. The present examination of lexical access during the comprehension of IPs within auditory sentences will therefore provide a detailed timeline of lexical access in this population, and will serve as a test of whether the Delayed Lexical Activation hypothesis holds true for ambiguous lexicalized IPs, and will thus more broadly inform what is currently understood about real-time lexical meaning retrieval in Broca’s aphasia.

Since this dissertation examines lexical access patterns in canonical sentence constructions, evidence for delayed lexical access would lend support to the already substantial body of literature that refutes the Slow Syntax Hypothesis’ claim of intact lexical access in Broca’s aphasia. In addition to the scientific and theoretical importance of this work, a focused investigation of lexical access in Broca’s aphasia also carries clinical significance. Should the current project find evidence of slowed lexical access in Broca’s aphasia, this will indicate that a lexically-based treatment may be an efficient form of therapy for individuals with this sub-type of aphasia (see e.g. Henry & Beeson, 2008; Kiran & Sandberg, 2009; Raymer et al., 2007). In sum, therefore, the psycholinguistic component of this dissertation will contribute new
evidence to the current theories of sentence comprehension and lexical processing in Broca’s aphasia. Before reviewing the literature of IP comprehension during sentence processing, some brief acknowledgement is needed of the scope of the current set of studies, and with regards to certain methodologies which are employed in this dissertation.

Real-time idiom processing during auditory sentence comprehension

The primary interest of the current work is a psycholinguistic and neurolinguistic study of IP processing during auditory sentence comprehension, in both unimpaired and aphasic individuals. Admittedly, IPs may be encountered in other contexts in natural language, such as in written text or in isolated contexts, and ultimately, a universal theory of lexical access during IP comprehension must account for how individuals understand IPs across modalities and in diverse contexts. However, given that processing differences occur at multiple levels (psycholinguistic, neurological, etc.) for comprehension of written vs. spoken linguistic material, it is beyond the scope of this current work to detail IP comprehension processes across these multiple modalities. The focus of this dissertation will be on comprehension of IPs during the processing of auditory sentences, as opposed to in isolation, because listeners likely encounter IPs most frequently when they are integrated into sentence contexts. As such, sentence-level studies may more closely reflect natural language processing than isolated phrase studies. The following sections will first review the methodologies that have been employed in detailing IP processing. Next, the
foundation for the use of IPs as lexical units is established through a review of the psycholinguistic evidence of IP processing.

Notes on Methodology

To set the stage for the current discussion, a review is needed of several approaches to investigating IP comprehension and lexical access during IP processing. One commonly used behavioral approach is to perform a detailed examination of the moment-by-moment operations that occur during ongoing sentence comprehension. One specific type of on-line methodology is cross-modal lexical priming, which measures real-time, automatic, and unconscious psycholinguistic processes that occur outside conscious reflection by the participant (e.g. Swinney et al., 1979; Swinney, 1979; Onifer & Swinney, 1981). This methodology allows for an examination of real-time lexical processing in sentences. In CMLP, participants hear a sentence and make a binary lexical decision for a visual letter string (probe) that appears on a computer screen during the uninterrupted sentence. Based on automatic semantic priming (Collins & Loftus, 1975; Neely, 1977), reaction times (RTs) are faster for probes (here, visual) that are semantically-related to material in the sentence (here, auditory), as compared to semantically-unrelated visual probes (Swinney et al., 1979; Onifer & Swinney, 1981). Consider the following (from Swinney, 1979):
4) Rumor had it that, for years, the government building had been plagued with problems. The man was not surprised when he found several bugs* in the corner of his room.

Here, participants’ lexical decision times will be faster when the visual probe word “insect” is presented immediately following the offset of “bugs” than when the unrelated word “sew” is presented at the same point during the sentence. These speeded RTs to the related word demonstrate priming, and are taken to be indicative of lexical access of information at the specific point in time that the probe is presented. For instance, in the above example, a faster RT to the probe word “insect” than to “sew” at the offset of the auditory word “bugs” in the sentence indicates that participants have lexically accessed the semantic meaning of the word “bugs.”

Importantly, in CMLP, participants do not make conscious, meta-linguistic judgments about the auditory sentences themselves while they are hearing them. They are instead instructed to make decisions about the visual probe that occurs while uninterruptedly listening to the sentences. This allows for the RTs to the visual probes to be influenced only by unconscious and automatic language processing. Importantly, speeded RTs indicate lexical access of items in the auditory sentence, not integration of the visual probes into ongoing sentence material (see Nicol et al., 2006 for a discussion). CMLP is a versatile technique because this task can be used to examine lexical access for more than one meaning of a lexical item. CMLP studies have indicated that participants’ lexical decision times are speeded for visual probe words
that are semantically related to multiple different meanings of lexical items in the auditory sentence. For instance, given example 4 above, participants will also show a speeded lexical decision to the visually-presented word “spy” when this visual probe word is presented immediately after participants hear “bugs”. This finding indicates that listeners access multiple semantic meanings of the word “bugs” (“insects” and “listening devices”) in this auditory sentence.

Another approach to studying language comprehension is via “off-line” methodologies, which examine the outcome of comprehension as revealed by conscious reflection by the participant. Examples of off-line studies include sentence- or phrase-to-picture matching tasks or phrase- or word-to-definition matching, to name a few. Importantly, in off-line tasks, participants are typically unconstrained with respect to the amount of time they can consider and reflect on a particular stimulus. Off-line studies are informative as to individuals’ final interpretation of what they hear, but these types of studies are limited in their ability to clarify the underlying real-time psycholinguistic mechanisms which contributed to the end result of the comprehension process, as they only measure language comprehension after the event of interest. However, both on-line and off-line studies are important in that they inform us as to different aspects of the comprehension process.

In addition to behavioral studies of IP comprehension, neuroimaging techniques have begun to play a role in the investigation of IP processing. Modern neuroimaging is a key tool in our quest to link behavioral processes with the neural regions that underlie and support these processes. This dissertation will employ one
type of neuroimaging, functional magnetic resonance imaging (FMRI), to examine the neural bases of IP comprehension during auditory sentence processing. In FMRI, researchers look for blood flow changes in different regions of the brain in order to infer neural activity in those brain regions in response to particular stimuli. Specifically, it has been most common to measure the blood oxygenation level-dependent signal (BOLD), a signal that represents the combination of the vascular and metabolic responses to neural activity (see Buxton, 2002). Fluctuations in BOLD signal within constrained neural regions are taken to indicate fluctuations in neural recruitment within that same region. While this technique has been used robustly in young, healthy individuals, there is mounting evidence that interpretations of the BOLD signal may need to be adjusted as a function of the population under study. Germane to the studies in this dissertation, several studies have found that the BOLD signal is altered in stroke survivors (e.g. Bonakdarpour et al., 2007; Carusone et al., 2002; Fridriksson et al., 2006; Roc et al., 2006; Krainik et al., 2005), possibly due to altered hemodynamic properties in this population. This dissertation will directly explore one element of the cerebrovascular system that underlies the BOLD signal, namely cerebral blood flow. Then, based on the findings regarding cerebral blood flow in stroke survivors, an FMRI study is designed to study IP processing across populations, while accounting for population-specific cerebrovascular issues. In the next section, the discussion focuses on prior research into the lexical properties of IPs, specifically with regard to the properties of IPs that make them well-suited as a tool to study lexical access in aphasia and unimpaired listeners.
Psycholinguistic Accounts of Auditory Idiom Comprehension

An IP is a multi-word phrase whose meaning cannot be understood simply as a function of its constituent words (Cacciari & Tabossi, 1988). Rather, IPs, such as “spill the beans,” may denote a figurative, or non-literal, interpretation (e.g. “tell a secret”). Listeners and speakers of a language must learn the meanings of IPs at some point during language acquisition, as there are generally no cues in the individual words themselves (spill+the+beans) to assist the listener in constructing a figurative interpretation (Cacciari & Tabossi, 1988). Because the figurative meaning of IPs must be learned and because the constituent words of an IP frequently co-occur with one another, several researchers have suggested that these phrases are lexicalized (e.g. Jackendoff, 2002; Swinney & Cutler, 1979). IPs occur frequently in spoken and written language, and healthy listeners typically understand them with ease.

Psycholinguistic researchers have examined how listeners understand IPs, particularly with respect to how lexical access proceeds during IP comprehension (Cacciari & Tabossi, 1988; Swinney & Cutler, 1979; Tabossi & Zardon, 1993, 1995; Colombo, 1993; Titone & Connine, 1994). In more recent work, neuroimaging researchers have begun to examine the neural substrates of IP comprehension (Zempleni et al. 2007; Romero Lauro et al., 2008; Hillert & Buracas, 2009; Mashal et al., 2008; Oliveri et al., 2004; Rizzo et al., 2007). These bodies of work have informed our understanding of IP comprehension and the neural processing of IPs, and this work has generated theories of how IP processing may occur in healthy listeners. In addition, although
some early work suggested non-literal language to be primarily subserved by the right hemisphere (e.g. Brownell et al., 1995; Winner & Gardner, 1977), more recent work has examined IP comprehension in individuals with left hemisphere damage and aphasia, demonstrating deficits in this population (Cacciari et al., 2006; Papagno & Caporali, 2007; Papagno et al., 2006; Papagno & Genoni, 2004; Papagno et al., 2004; Tompkins et al., 1992). However, there remains to date no investigation of the psycholinguistic bases of this deficit in aphasia, nor of the neural substrates of IP processing in this disorder.

IPs are one type of figurative, or non-literal language; other instances of non-literal language include metaphor, similes, and sarcasm, to name a few. IPs are unique among figurative language, however, in that they are often conventionalized (e.g. Cacciari & Tabossi, 1988; Yorio, 1980), meaning that these phrases occur in language as a functional unit that may be utilized in its same form by all speakers of a language. Consider the following:

5) The young boy **spilled the beans** about the secret.

Here, the IP “spilled the beans,” a verb phrase (VP) IP, is used to indicate that the boy revealed what he knew about the secret. The IP as an entity is associated with this figurative (non-literal) meaning, and a listener cannot derive this meaning simply by understanding the individual constituent words of the phrase. Thus, much like single words, which have arbitrary sound-meaning mappings, IPs may also be arbitrarily
linked to their figurative meanings. Listeners of a language must learn these linkages in order to correctly understand IPs, which suggests that IPs are lexicalized units (see e.g. Cacciari & Tabossi, 1988; Hillert & Swinney, 2001). At the same time, however, each constituent word in this VP IP also carries its own literal meaning (e.g. “spilled”: “dropped” and “beans”: “vegetables”). IPs have been a focus of numerous psycholinguistic studies because of this dual nature; that is, the fact that IPs are composed of individual words, each with their own literal meaning, while the phrase as a whole conveys an entirely different, figurative meaning. Psycholinguistic work to date that has investigated IP comprehension has suggested that listeners lexically access both the figurative and the literal meanings associated with an IP (see e.g. Cacciari & Tabossi, 1988; Hillert & Swinney, 2001). However, there remains some debate as to the time course of lexical access for these two meanings, and evidence that speaks to this issue is discussed below.

**Prior Psycholinguistic Studies of Idiom Comprehension**

One of the first psycholinguistic studies of IP processing found that individuals were able to process IPs more quickly than non-idiomatic phrases of the same length (Swinney & Cutler, 1979). In this study, participants performed a phrase classification task, in which they made a binary decision as to whether visually-presented word strings formed a meaningful, acceptable English phrase. Included in the stimuli were literal phrases, such as “lift the bucket” as well as IPs, such as “kick the bucket.” The authors report that participants demonstrated significantly faster reaction times when
to judging acceptability of IPs as compared to literal phrases. This result was significant, it was argued, because it suggested that individuals needed to retrieve each individual word of the non-idiomatic phrases from the lexicon, one-by-one, whereas IPs could be lexically accessed as a unitary chunk. Thus, IPs could be processed more quickly, because only a single lexical retrieval operation was required. This early study, while introducing the argument that common IPs are lexicalized, did not address the question of whether lexical access also proceeds for the literal meanings of an IP’s constituents. Rather, a later study examined just this question; that is, the question of whether lexical access occurs for both the literal and figurative meanings associated with an IP, and if so, the temporal nature of this access (Swinney, 1982). In this CMLP study, participants demonstrated lexical access for the figurative meaning of an IP at its offset, while they also demonstrated lexical access for the literal meanings of the IP’s constituent words, at the offset of each of those words. For example, consider the following example (Swinney, 1982):

6) It was hoped that the young man would see\(^1\) the light\(^2\) and come home safely.

Here, the author presented visual probe words that were related to either the literal or figurative meaning of the word “see” at the offset of the initial constituent of the IP (labeled with the superscript 1 above). At this point in the sentence, participants only demonstrated priming for the literal meaning of the IP’s first word. That is, it was
argued, participants only accessed the literal meaning of the word “see” from the lexicon, and did not lexically access the figurative meaning of the entire IP at this early point. Later in the ongoing auditory sentence, however, at the offset of the entire IP (labeled with superscript 2 above), participants demonstrated priming for both the literal meaning of the word “light” and the figurative meaning of the IP “see the light.” Several important points may be drawn from these effects. Importantly, this study suggests that lexical access for an IP’s meanings may be temporally discontinuous, with literal lexical access occurring at the offset of each constituent word. Meanwhile, figurative access for the IP as an entity occurs at some point after its initial components, but by the time a listener has heard the phrase’s offset. Also, it is important to note that the author reports the same pattern of lexical access regardless of the sentence’s biasing context prior to the IP; that is, lexical access was unaltered by whether this prior context biased a literal or a figurative interpretation of the IP. This is an interesting finding, as it suggests that lexical access for IPs may be form-driven and exhaustive, much in the same manner that lexical access proceeds for single words (e.g. Shapiro et al., 1998). A more recent study in German replicated the finding of exhaustive access for an IP’s literal and figurative meanings at the offset of the phrase (Hillert & Swinney, 2001). Interestingly in this study, this exhaustive access occurred even when the IPs had no plausible literal interpretation, further strengthening the argument that IPs are function as lexical items and undergo form-driven lexical access.
Additional psycholinguistic studies of IP processing during sentence comprehension have generally agreed with and extended these findings, and have at the same time raised new questions about lexical access for IPs. (e.g. Cacciari & Tabossi, 1988; see also Colombo, 1993; Tabossi & Zardon, 1993, 1995; Titone & Connine, 1994; Libben & Titone, 2008). Key in this work has been the concept of IP predictability, or how readily a listener may detect the presence of an IP based upon hearing the initial phonemes or constituents of the phrase (see Cacciari & Tabossi, 1988; Tabossi & Zardon, 1993, 1995). The more predictable an IP, the sooner lexical access for the figurative meaning of that IP would occur, according to these authors. Some work following this line of thinking, has argued that figurative lexical access for an IP may occur either prior to the offset of the phrase, at the offset of the phrase, or several hundred milliseconds post-offset (Cacciari & Tabossi, 1988; Colombo, 1993; Tabossi & Zardon, 1993, 1995; Titone & Connine, 1994; Libben & Titone, 2008).

With respect to the nature of lexical access for the literal meanings associated with an IP’s constituent words, however, very few studies have probed the time course of lexical access for these meanings. Thus far, studies have only reported lexical access for the literal meanings of the IP’s constituent words at their respective offsets (Colombo, 1993; Cacciari & Tabossi, 1988), but these studies have not probed more deeply into the time course of this literal lexical access throughout the course of the sentence. Likewise, no studies to date have titrated lexical access for an IP’s figurative meanings downstream from the phrase in an ongoing sentence. It thus remains an
empirical question as to the fate of lexical access for these multiple meanings past the point of IP offset.

Taken together, prior psycholinguistic work of IP processing strongly suggests that lexical access does indeed occur for both literal and figurative meanings that are associated with an IP (e.g. Swinney, 1982; Hillert & Swinney, 2001; Cacciari & Tabossi, 1988). However, the IP processing literature to date has not been able to clarify when precisely lexical access for these multiple meanings occurs. Some authors have suggested that lexical access for the figurative meaning of an IP begins before a listener has heard the entire phrase (see Tabossi & Zardon, 1993, 1995; Titone & Connine, 1994; Colombo, 1993); in example 6 above, this might mean that figurative lexical access commences by the point that a listener has heard the determiner (“the”) in the IP. Thus, it is possible that lexical access for the literal meanings of an IP’s constituent words occurs immediately upon hearing each of these words, while figurative lexical access occurs at some point after a listener hears the IP’s initial phonemes, but prior to the offset of the entire phrase. This dissertation thus aims to add to this body of psycholinguistic work and further clarify the time course of lexical access for these multiple meanings. In addition, as discussed above, no studies have yet followed the time course of lexical access for these multiple meanings of an IP to later points in an ongoing sentence. The current project seeks to determine the fate of lexical access for the literal and figurative meanings associated with an IP while auditory sentence comprehension continues downstream. This dissertation also
extends the investigation of lexical access during IP processing into the field of aphasia, for reasons discussed below.

Idiom Comprehension and Processing in Aphasia

Prior Studies of Idiom Comprehension in Aphasia

Although there have been no published reports of real-time IP processing in aphasia to date, there is a substantial literature of aphasic deficits for idiom comprehension (Papagno & Caporali, 2007; Papagno et al., 2004; Cacciari et al., 2006; Papagno & Genoni, 2004; Papagno et al., 2006; Tompkins et al., 1992). While early theories of lateralization of language function ascribed non-literal language processing to the right hemisphere (e.g. Brownell et al., 1995; Winner & Gardner, 1977), there is a robust relationship in the literature between left hemisphere damage and concomitant aphasia and IP comprehension deficits. One of the earliest studies to investigate IP processing among patients suggested that patients with either left or right hemisphere damage were spared in their automatic, fast-acting processing of these phrases (Tompkins et al., 1992). Here, the authors conducted a word-monitoring task, in which patients were shown a written word before each experimental trial and instructed to attend for that word as they listened to auditory sentences. When participants heard the target word, they were to press a button. For example, consider the following examples (from Tompkins et al., 1992):
7) My lawyer is studying my contracts. When he smelled a rat, he warned me.

8) My science class was studying rodents. When Jane saw a rat, she screamed.

Prior to hearing these sentences (which were not presented in close temporal proximity to each other), participants were shown the word “rat” and were told to attend to the sentences to be able to detect this word. Here, the authors argued that speeded RTs to target words within IPs was indicative of some level of automatic processing (at a lexical level, presumably) of IPs. Tompkins et al. enrolled unimpaired listeners, as well as a group of left-hemisphere-damaged patients and a group of right-hemisphere-damaged patients. Among the left-hemisphere-damaged individuals, about two-thirds (65%) of these participants had some form of aphasia, although these participants were heterogeneous with respect to their aphasic deficits and stroke etiologies. Interestingly, across these three participant groups, the significant majority of participants did indeed respond more quickly to target words that were a part of IPs in idiomatic contexts (example 7), as compared to when target words appeared in neutral contexts (example 8). The authors argued that listeners were able to verify target words that appeared within an IP because participants commenced lexical access for the IP upon hearing its initial components. For instance, the researchers suggest that listeners begin to lexically access the meaning of the IP “smell a rat” after hearing the beginning of this phrase (e.g. “smell a …”). Because
performance on the word-monitoring task did not differ significantly between the three participant groups, Tompkins et al. argued that some elements of lexical access for IPs proceed normally in individuals with brain damage to either hemisphere, including those individuals with aphasia. It is noteworthy, however, that Tompkins et al. (1992) included an off-line IP comprehension assessment in their study. Here, individuals with damage to either neural hemisphere evinced a comprehension impairment on an IP definition task, demonstrating chance performance. This indicated that although some levels of IP processing in individuals with brain damage proceeded in a similar fashion as in healthy participants, the individuals with neural damage did not show normal comprehension for IPs. Unfortunately, neither the word-monitoring task nor the IP definition task could lend information as to the real-time underpinnings of this IP deficit in participants with brain damage.

More recent studies with individuals with left hemisphere damage and aphasia have contributed further evidence that IP processing and comprehension are disordered in this population. In one study, left-hemisphere-damaged patients with aphasia completed a string-to-picture matching task, in which participants heard an isolated literal or idiomatic phrase (apart from sentence context) and were asked to select a picture that best represented the phrase from among several choices (Costanza Papagno et al., 2004). Importantly, IPs used in this study were unambiguously literal; that is, they had no plausible literal meaning (e.g. “far and away”). As compared to an age-matched control group of healthy participants, the aphasic participants in this study made significantly more errors in matching IPs to their corresponding pictorial
representations. Perhaps most interesting is that the patients tended to select pictures that depicted a literal interpretation of the phrase, even though this interpretation made no sense. Similarly, a slightly later study utilized a string-to-word matching task, in which participants again heard an IP and were instructed to select a word that best conveyed the figurative meaning of the phrase, from among several choice words (Cacciari et al., 2006). For example, a participant might hear the IP “kick the bucket” and see the word “death” among her word choices, which conveys the figurative interpretation of this phrase. At the same time, the experimenters included words that conveyed a different meaning of the IP, such as “pail,” which is a literal semantic associate of “bucket” in the IP “kick the bucket.” In comparison to age-matched healthy controls, the aphasic patients evinced worse performance overall on this task, and also tended to choose the literal semantic associate most frequently when they made errors. This findings concurs with the previously mentioned study of IP comprehension in aphasia (Papagno et al., 2004), in that the patients with aphasia interpreted IPs with a literal bias and evinced poor IP comprehension overall. Further studies of IP comprehension in aphasia have similarly employed string-to-picture matching (Papagno et al., 2006; Papagno & Genoni, 2004; Papagno & Caporali, 2007); string-to-word matching (Papagno & Caporali, 2007); and IP definition tasks (Papagno & Caporali, 2007).

These prior studies have all reported IP comprehension deficits among individuals with aphasia, and have consistently pointed out a literal interpretation bias for IPs within this population. Unfortunately, however, all prior work to date with IPs
in aphasia has solely consisted of off-line studies, which cannot illuminate the underlying processing bases of comprehension for IPs. It thus remains an open question as to the nature of real-time processing of IPs during auditory sentence comprehension in this population. The current work presented in this dissertation undertakes this task, in order to investigate the mechanisms of lexical access during IP comprehension in aphasia. In so doing, this dissertation aims to bridge the psycholinguistic literature of IP processing, which has heavily focused on lexical access for the multiple meanings of these phrases, with the patient literature, which has focused on the outcome of this processing. Additionally, it is important to note that all prior reported studies of IP comprehension in aphasia have enrolled very diverse patient populations, often including patients with varied symptoms, severity, sites of neural damage, and aphasic diagnoses. These patients are often grouped together and considered as a unitary population, when in fact, there exist observable differences in their symptomatology and patterns of deficit. Due to this heterogeneity, it is difficult to understand how IP processing and comprehension relate to specific aphasic deficits and how IPs fit into an individual’s pattern of aphasia. This dissertation therefore aims to examine IP comprehension and processing deficits, if any, in light of a patient’s particular symptoms and overall patterns of deficit. Rather than examining this population as a heterogeneous group, the current project will examine IP comprehension and processing within one particular sub-type of aphasia, Broca’s aphasia. This investigation will help to clarify the nature of IP deficits that are associated with this disorder. In addition, by examining the real-time markers of IP
processing in aphasic patients, this dissertation will explore the possible psycholinguistic foundations of the off-line comprehension deficits that are commonly reported in this population.

In addition to clarifying the psycholinguistic mechanisms that are specific to IP processing among patients with aphasia, the current work will contribute more broadly to a long-standing discussion in the aphasia literature. Specifically, as expanded upon later in this Chapter, the investigation of lexical access for IPs in this dissertation constitutes a novel approach to studying lexical access in aphasia; as discussed earlier, recent work has argued that lexical access is disordered in Broca’s aphasia, and that this disorder contributes to specific deficits that are observed in this population.

**Neuroimaging of Idiom Comprehension**

The latter portion of this dissertation is devoted to a neuroimaging investigation of IP comprehension. Via neuroimaging techniques, researchers have begun to localize the neural resources that support IP comprehension in healthy individuals. To date, a number of neuroimaging studies have looked specifically at IP processing (Zempleni et al., 2007; Romero Lauro et al., 2008; Hillert & Buracas, 2009; Mashal et al., 2008; Oliveri et al., 2004; Rizzo et al., 2007). One very recent study, which investigated the neural markers of IP comprehension enlisted healthy participants, who heard sentences one at a time, as in examples 9 and 10 (Hillert & Buracas, 2009).
9) She carried the torch.
10) He met her in the new mall.

Included with the idiomatic (9) and literal (10) stimuli were implausible sentences. After each sentence, participants made meaningfulness judgments, as to whether the sentence made sense. The authors reported that comprehension of the idiomatic sentences (such as 9), as compared to literal and implausible sentences, engaged the following left hemisphere regions: inferior frontal gyrus (BA44 & 45), middle frontal gyrus (BA11 & 47), superior frontal gyrus (BA8), and medial frontal gyrus (BA8 & 9). The authors argued that this left-lateralized network underlies comprehension of IPs within auditory sentences. As this is the only neuroimaging study to utilize full auditory sentences with embedded IPs, these results may be the best approximation to date of the neural regions that are engaged in this processing. It is important to note, however, that the stimuli in this study did not conclusively bias an IP toward a figurative interpretation. Consider again example 9, which contains the IP “carry the torch,” but does not definitively disambiguate this phrase toward a figurative interpretation. As this IP could plausibly be used in either a literal or figurative manner, the results from Hillert & Buracas are unable to address the neural mechanisms that support literal vs. figurative processing of IPs. Thus, it remains an empirical question as to which neural networks support the comprehension of the same IP, when that IP carries a literal or a figurative meaning. This is an important point, as IPs are certainly not restricted to one or the other meaning during natural
language, so it is imperative to have an understanding of how the brain processes these different meanings of ambiguous IPs. In addition, given the large amount of research that indicates that patients with aphasia have a tendency to interpret IPs literally in off-line tasks (see above), there is sound reason to hypothesize that distinct neural regions support literal and figurative interpretation of IPs.

In addition to the FMRI study of auditory IP processing by Hillert and Buracas (2009), several additional studies have investigated the neural indices of IP comprehension in the visual modality. As this dissertation is interested in a directed study of processing and comprehension of IPs within auditory sentences, some caution is needed when considering prior studies that present IPs apart from sentence context and in the visual modality. In addition, all prior neuroimaging studies of IPs have utilized meta-linguistic tasks, which may alter participants’ attention to the task or processing of the stimuli under consideration, as discussed earlier. Nonetheless, these studies will be broadly discussed with respect to how they might contribute to the hypotheses under investigation in this dissertation. To sum up prior neuroimaging studies of IP comprehension, these reports have implicated the following bilateral regions during IP processing: bilateral inferior frontal gyri (Brodmann areas [BA] 44, 45, and 47; Zempleni et al., 2007; Romero Lauro et al., 2008); bilateral middle temporal gyri (BA 21; Zempleni et al., 2007; Romero Lauro et al., 2008); and bilateral pre-frontal cortex (BA 9; Rizzo et al., 2007). In addition, FMRI studies have also detected left-lateralized regions of neural activation during idiom processing in areas such as left inferior frontal gyrus (BA 44&45; Hillert & Buracas, 2009; Mashal et al.,
2008; Oliveri et al., 2004); left superior frontal gyrus (BA 8; Hillert & Buracas, 2009), left medial frontal gyrus (BA 8 & 9); left inferior temporal gyrus (Romero Lauro et al., 2008); left middle temporal lobe (BA22; Oliveri et al., 2004); and left angular gyrus (BA 39; Romero Lauro et al., 2008). In one report, right-lateralized middle temporal gyrus/temporal pole (approximately BA21; Romero Lauro et al., 2008) was enlisted in IP processing.

Taken together, then, these prior neuroimaging studies indicate bilateral neural recruitment during IP comprehension, particularly among neural regions that are typically involved in literal language comprehension, including left hemisphere inferior frontal gyrus and middle temporal lobe areas. However, it is intriguing to note that the one FMRI study which presented all stimuli in the auditory modality (Hillert & Buracas, 2009) noted only left-lateralized activity in the frontal lobe during IP comprehension. It is therefore possible that different presentation modalities may in part underlie some of the variability in neural activity that is reported between these FMRI studies. In addition to differences in the modality of presentation, earlier research has demonstrated that task demands may modulate neural activity (Love, et al., 2006), thus the different tasks used in these prior neuroimaging studies of IP comprehension may have independently contributed to the results. In keeping with the goal of this dissertation, which is to investigate IP processing during auditory sentence comprehension, this project aims to provide a more complete understanding of the neural bases of auditory IP processing than is currently presented in the literature as based on visually-presented IPs. In addition, this dissertation seeks to observe the
neural indices of IP comprehension without drawing participants’ attention to the presence of idiomatic language, thereby attempting to mirror the conditions under which individuals typically experience IPs.

Importantly, too, all published neuroimaging studies of IP comprehension and processing of which we are aware have solely enrolled healthy participants. It remains uncertain which neural regions are patients with aphasia utilize while processing IPs. The current dissertation thus seeks to investigate patterns of neural recruitment during IP processing in patients with aphasia, and to relate this information to patients’ patterns of IP comprehension off-line. Also, by comparing patterns of neural recruitment during IP comprehension between patients with aphasia and their unimpaired peers, the present project seeks to determine whether patients rely on completely different neural regions for IP comprehension, or whether they utilize incomplete neural networks for this processing. For these reasons, this dissertation will thus undertake the first FMRI investigation of IP comprehension within patients with aphasia.

**Goals of the Dissertation**

This dissertation seeks to use IPs as a tool to investigate the psycholinguistic and neurolinguistic indices of lexical processing in Broca’s aphasia during auditory sentence comprehension. In so doing, this dissertation aims to build upon the literature of real-time lexical processing in aphasia, from both behavioral and neural perspectives. Chapter 2 undertakes a real-time psycholinguistic investigation of
lexical access during IP processing, across aphasic and unimpaired listeners. This study seeks to determine whether individuals with Broca’s aphasia show slowed lexical access for one or both meanings of an IP, as predicted by the slow rise lexical hypothesis of Broca’s aphasia. Chapters 3 and 4 investigate the neural resources that underlie lexical processing of IPs; Chapter 3 first addresses the issue of cerebral blood flow, a key variable in functional neuroimaging, among individuals with aphasia subsequent to stroke. Using the findings from Chapter 3, Chapter 4 comprises a functional neuroimaging study of IP comprehension, across both language-unimpaired and aphasic individuals. Following the original empirical evidence of these chapters, Chapter 5 discusses how the results contained therein thus extend our current understanding of IP comprehension across unimpaired and aphasic populations, as well as how the results of this dissertation extend our understanding of real-time lexical processing in aphasia more generally. This final chapter discusses directions for future work in this field.

**Contributions of the Dissertation**

This dissertation consists of three experimental chapters (Chapters 2-4), designed to investigate the psycholinguistic and neural indices of IP processing during auditory sentence comprehension. This work will examine IP comprehension in both healthy and aphasic individuals. The first study, detailed in Chapter 2, examines lexical access for the figurative and literal meanings associated with IPs that are embedded into auditory sentences. By examining lexical access for ambiguous IPs
that are embedded in auditory sentences, both at the offset of the IP and further downstream in the sentence, this work examines the time course of IP processing throughout a sentence, which is unique from all IP research to date. In addition, this experiment examines lexical access during IP comprehension in individuals with aphasia for the first time. In so doing, this work examines the relationship between on-line and off-line measures of IP comprehension in individuals with aphasia, to provide a more comprehensive description of their deficits. The results of Chapter 2 also speak to an ongoing discussion in the literature as to the core nature of sentence comprehension deficits in aphasia, by examining the time course of lexical access for IPs during auditory sentence processing.

Chapter 3 describes two neuroimaging experiments which examined cerebral blood flow in stroke survivors with aphasia; these studies are the first formal report in the literature that cerebral blood flow is both slowed and decreased in individuals with aphasia after stroke. The studies in Chapter 3 are foundational for the experiments in Chapter 4, which comprises an FMRI investigation of ambiguous IP processing across healthy and aphasic populations. The neuroimaging study examines the neural loci of comprehension for these phrases across unimpaired and aphasic participant groups, and provides the first FMRI study of IP processing in aphasia. In addition, this study contributed the first instance of auditory ambiguous IP comprehension in an FMRI report.

By drawing upon these psycholinguistic, neuroimaging, and neuropsychological observations, this dissertation bridges these different perspectives
into a holistic view of the behavioral and neural underpinnings of IP processing and comprehension across populations.
References


CHAPTER 2

Real-Time Psycholinguistic Indices of Lexical Access for Idiomatic Phrases During Auditory Sentence Comprehension
Abstract

Language processing is disrupted in distinct ways among individuals with the language disorder aphasia. This study aims to investigate the real-time indices of lexical access within one particular sub-type of this disorder, Broca’s aphasia. Previous work has argued that lexical access in Broca’s aphasia is temporally protracted, or delayed, and further, that this real-time processing abnormality in Broca’s aphasia plays a role in poor off-line comprehension for certain types of syntactically-complex sentences. However, there remains debate as to whether lexical access is indeed disordered in Broca’s aphasia, and the current study directly investigated the nature of lexical access in this population. In a novel investigation of the time-course of lexical access in Broca’s aphasia, this project assesses on-line processing of long lexical items that have multiple meanings: idiomatic phrases (IPs), since prior research demonstrates temporally-distinct patterns of lexical access in unimpaired populations for the multiple meanings that are associated with IPs. Because of this temporal discontinuity, IPs are particularly well-suited as a tool to investigate the time course of lexical access in Broca’s aphasia. Therefore, this study investigated lexical access for the multiple meanings associated with IPs in both patients with Broca’s aphasia and in an unimpaired control group. As expected, the control group demonstrated discontinuous lexical access for the meanings of IPs, showing immediate lexical access for the idiomatic meaning of the IP, followed by lexical access for IP’s literal constituent words. By contrast, the Broca’s aphasic patients showed temporally delayed lexical access for these multiple meanings,
consistent with the theory that lexical access is delayed in this population. Results are discussed with respect to how these findings inform our understanding of real-time lexical processing in Broca’s aphasia, with additional discussion of how the current study contributes to the literature of IP processing.
Listeners rarely find it difficult to understand spoken language; yet numerous complex, interactive cognitive and neurological processes must be coordinated to ensure successful language comprehension. The intricacy of the language processing system becomes all too evident when this system is impacted and becomes disordered due to language impairment. This chapter focuses specifically on the process by which a listener accesses an item from the lexicon during auditory sentence comprehension, and seeks to investigate how this process may be disrupted in the language disorder aphasia. Here, in a novel investigation of lexical access in this population, idiomatic phrases (IPs) are employed as tools to study both the quality and time course of lexical access in individuals with Broca’s aphasia. As discussed in Chapter 1 of this dissertation, prior research has suggested that lexical access is slowed in Broca’s aphasia, and that this slowing contributes to specific patterns of comprehension impairments for syntactically-complex sentence structures (see Chapter 1; see also (Grodzinsky, 2000; Hickok et al., 1992; Love et al., 2008; Sussman & Sedivy, 2003; Tanenhaus & Trueswell, 1995; Schwartz et al., 1980; Zurif et al., 1993)). Here, IPs are employed as a means by which to probe real-time lexical access in Broca’s aphasia, as was discussed in Chapter 1 and is elaborated on below.

However, before proceeding to motivate the hypotheses in the current study, special note should be made of the scope of this investigation. Here, the focus is on language processing at the sentence level, rather than, for instance, the word-level, for two reasons. First, this project takes the stance that the sentence is the basic unit of spoken language, in that we speak in sentences, as part of a larger discourse (see e.g.
Poirier & Shapiro, 2012). Second, ambiguous IPs, such as the ones under investigation in the current study, can only be disambiguated towards a literal or figurative interpretation when there is surrounding context that biases one interpretation over the other. Thus, although the current study is focused on investigating the indices of lexical access during auditory comprehension of IPs embedded in sentences, it is recognized that many other approaches may be employed to investigate different levels and aspects of the language processing system, such as written word comprehension or single-auditory-word comprehension.

**Idioms as Lexical Ambiguities: Tools for Investigating Lexical Access**

As discussed in Chapter 1, a fair bit of psycholinguistic research into the nature of lexical processing for IPs precedes the current work presented here. This body of prior research has suggested that lexical access occurs for both meanings of an IP, for the figurative meaning of the IP as a whole and for the literal meanings of the IP’s constituent words (Cacciari & Tabossi, 1988; Colombo, 1993; Titone & Connine, 1994; Tabossi & Zardon, 1995, and others). Some of this work suggests that lexical access for these multiple meanings is immediate and exhaustive (Hillert & Swinney, 2001), but a larger body of research suggests a temporal discontinuity of lexical access for these multiple meanings (Cacciari & Tabossi, 1988; Swinney, 1982; Tabossi & Zardon, 1993, 1995; Titone & Connine, 1994; Libben & Titone, 2008). That is, these studies suggest that literal and figurative meanings of IPs are lexically accessed on slightly offset time scales. Specifically, some of this work has suggested that
figurative lexical access occurs prior to the offset of the IP (e.g. Cacciari & Tabossi, 1988; Titone & Connine, 1994; Tabossi & Zardon, 1993, 1995). To illustrate this hypothesis, in example 1 below, figurative lexical access for the IP “spilled the beans” is predicted to commence before the offset of the phrase, likely at the offset of the IP’s first word, or when subjects hear the determiner (indicated by an asterisk).

1) The young boy spilled the* beans about the secret.

Thus, lexical access for an IP’s figurative meaning is argued to be exhaustive, with potentially distinct temporal signatures of lexical access for an IP’s two multiple associated meanings.

Importantly, prior research with IPs indicates that lexical access for an IP may depend on specific properties of the phrase. For instance, (Cacciari & Tabossi, 1988) argue that lexical access for an IP’s figurative meaning occurs prior to IP offset, but only for predictable IPs; the authors argue that lexical access for the figurative meaning of an unpredictable IP occurs several hundred milliseconds post-IP offset. Here, the authors define predictable IPs as those in which the IP’s first words and/or phonemes alert a listener to its presence. Other researchers have supported the assertion that figurative lexical access will occur prior to IP offset for predictable IPs (see Tabossi & Zardon, 1993, 1995; Titone & Connine, 1994). Similarly, predictability seems to be a key factor in lexical access for literal meanings associated with IPs. For instance, researchers have argued that when an IP is unpredictable, that
is, when a listener is uncertain that they are hearing an IP, literal lexical access may occur for the constituent components of the IP by the offset of the phrase (Titone & Connine, 1994). However, when an IP is predictable, and thus when a listener is highly likely to be hearing an IP, literal lexical access may not occur by IP offset (Titone & Connine, 1994; Cacciari & Tabossi, 1988). Thus, IP predictability may factor into lexical access patterns during IP comprehension; this issue is taken into consideration below (see Pre-Test 3).

In addition to varying in their predictability, IPs also vary in their familiarity, in the same manner as words (see Libben & Titone, 2008; Titone & Connine, 1994; Giora, 1997). Researchers have posited that IPs that are more familiar are retrieved from the lexicon more quickly than IPs that are less familiar (Schweigert, 1986; Libben & Titone, 2008). Here, we focus solely on lexical access during highly familiar IPs, in order to reduce any potential biases that different levels of familiarity might inject into our data (see Pre-Test 1).

Therefore, although there is a good deal of overlap in earlier studies of real-time processing during IP comprehension, prior work has yet to specifically titrate the time course of lexical access for the figurative and literal meanings associated with an IP, most likely due to differences in IPs across these previous studies. The current research seeks to account for these important characteristics of IPs, in order to hone in on lexical access for IPs with particular properties.

Important the purposes of the present study, all previously published reports of IP processing have solely enrolled young, unimpaired adults. Here, we aim to extend
this investigation by examining the indices of lexical access during IP processing in older, healthy adults. This is an important step towards ultimately better understanding the lexical system in both unimpaired and impaired populations. In the current study, as IPs will be utilized to investigate lexical access during auditory comprehension in aphasia, it is important to appropriately ascertain patterns of lexical access in a group of unimpaired individuals who are peers to the enrolled Broca’s patients. In addition, the current study will thus highlight whether there are any age-related differences in patterns of lexical access during IP processing in healthy, older adults and the patterns of lexical access that have been reported in the literature with young, healthy adults.

To summarize prior psycholinguistic research of IPs, this work has strongly suggested that lexical access is exhaustive for both figurative and literal meanings associated with an IP. However, this work has relied exclusively on data from young, unimpaired listeners, and as reviewed in Chapter 1, individuals with aphasia have demonstrated off-line comprehension impairments for IPs (e.g. Cacciari et al., 2006; Papagno et al., 2004; Papagno & Caporali, 2007; Papagno & Genoni, 2004). Crucially, though, and key to the current experiment, this literature of aphasia and IP comprehension remains underspecified for several reasons. First, all prior studies have enrolled very diverse aphasia patient samples. Frequently, descriptions of aphasia type, severity, and lesion location are brief or absent from these reports, which makes it difficult to ascertain how particular aphasic symptomology corresponds with patterns of IP comprehension impairment. Second and key to the current investigation,
studies of IP comprehension in aphasia have solely utilized off-line tasks to measure this process. Commonly these tasks required patients to complete meta-linguistic tasks, which likely enlisted higher order cognition. Thus, it is impossible to determine whether psycholinguistic processing problems are solely to blame for poor results on these tasks, or whether other, meta-linguistic or higher-level cognition problems contribute to this deficit. These off-line assessments are unable to pinpoint the psycholinguistic locus of these patients’ comprehension impairments. Numerous stages of processing occur between hearing a word, phrase or sentence and a listener’s final interpretation of that utterance (e.g. Friederici, 2002; Hickok & Poeppel, 2007), and thus, while these off-line studies suggest a disorder in the automatic language processes that underlie spoken language comprehension, the current study will specifically examine one aspect of the language processing system, that of automatic lexical access, in order to empirically test whether lexical access is disordered in Broca’s aphasia.

**Aims of the Current Study**

The current study aims to clarify the time course of lexical access during IP comprehension in auditory sentence contexts, in both unimpaired listeners and those diagnosed with the language disorder of Broca’s aphasia. As discussed above, there remains a good deal of debate between researchers as to the nature and time course of lexical access during IP processing (although so far this debate has been limited to healthy listeners), and our study seeks to further elucidate these mechanisms. In so
doing, this study also aims to examine lexical access in Broca’s aphasia, as a means to investigate whether lexical access is indeed slowed in this population. As discussed in Chapter 1, several outcomes are possible from this work. The present investigation of lexical access in Broca’s aphasia may reveal that lexical access is delayed for both meanings associated with an IP (figurative and literal), as compared to their peers, which would provide support for the Delayed Lexical Activation hypothesis. Lexical access may only be delayed for one meaning of an IP, which would also support the slow lexical rise hypothesis, but would require some qualification as to which meanings of a lexical item are affected by the slowed lexical rise time. Alternatively, lexical access in the Broca’s patients in this study may mirror that observed in the unimpaired listeners, in which case these results would not lend credence to the Delayed Lexical Activation hypothesis, and would argue that the lexical system remains intact in Broca’s aphasia. Therefore, any of these outcomes will be informative as to the current understanding of lexical processing in this language-impaired population.

Lastly, the current study seeks to bridge on-line and off-line indices of IP processing and comprehension. While all previous studies of IP comprehension in patient populations have solely relied on off-line measures, we have the benefit of comparing patterns of lexical access in Broca’s aphasia during IP processing to these patients’ eventual interpretations of those IPs. This comparison may help to reveal the underlying, processing-based reasons for patients’ frequently reported off-line IP comprehension deficits.
Methods

On-Line Experiment

Participants

Two groups of participants were enrolled in the current study: individuals with Broca’s aphasia subsequent to a single, unilateral cerebrovascular accident (CVA; N=7, mean age = 60.0, SD = 14.1, 6 male and 1 female) and a group of neurologically-unimpaired participants who were broadly age- and education-matched to the participants with aphasia (N=10, mean age = 66.0, SD = 13.4, 9 female and 1 male). All participants had normal-to-corrected hearing and visual acuity, and were recruited in accordance SDSU and UCSD IRB protocols. Participants were compensated financially ($15 per visit).

Participants with Broca’s Aphasia

Seven participants with Broca’s aphasia (LHD group) were recruited from the San Diego community, via distribution of information packets to local rehabilitation centers and classes, hospitals, and speech-language pathology clinics. Profiles of these aphasic patients are shown in Table 2-1. All LHD participants were pre-morbidly right-handed; native English speakers (with no foreign language acquisition prior to age 6); had no history of active or significant alcohol and/or drug abuse; had no active

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3 A total of 16 AMC participants were recruited and initially enrolled, but six of these participants were discovered to have not met the inclusion criteria, as detailed below, and were therefore excluded from further participation. Data from these participants were not included in our analyses.
psychiatric diagnoses; and had no history of other significant neurological disorders (e.g. Alzheimer’s Disease, dementia, Korsakoff’s Syndrome, Parkinson’s Disease, Huntington’s Disease). LHD participants were at least 6-months post-stroke and were neurologically and physically stable when enrolled. Individuals with aphasia were only enrolled if they were able to consent to participation, and this consent was obtained via a thorough review of an IRB-approved consent form with each participant. In addition, each participant was administered a post-consent checklist, to ensure that he/she understood his/her rights. Neurological records (CT or MRI scans) from each participant with aphasia were obtained to document the localization and extent of neural damage. The site and extend of each participant’s neural lesion is described in Table 2-1.

Assessment of each LHD participant was performed using the Boston Diagnostic Aphasia Examination (BDAE; (Goodglass & Kaplan, 1983), the Boston Naming Test (BNT; Goodglass & Kaplan, 1983), and the Western Aphasia Battery (WAB; Kertesz, 1982), among other assessments. Participant diagnosis was based on results from these standardized measures and clinical consensus. Based on the above criteria for inclusion, seven patients with Broca’s aphasia were enrolled in this study.

Neurologically-unimpaired participants
Ten age-matched neurologically intact participants (AMC group) were recruited from the local San Diego community, via public advertisements. All were right-handed (defined by 70% right-handed responses on the Edinburgh handedness inventory; Oldfield, 1971); native English speakers (with no foreign language acquisition prior to age 6); had no history of neural trauma or neurological disease; had no active psychiatric diagnoses; had no history of drug and/or alcohol abuse; and had no history of developmental speech, language, or learning disorders. AMC participants were administered the Mini-Mental State Exam (MMSE; Folstein et al., 1975) and the Wide-Range Intelligence Test (Glutting et al., 2000) assessment of neurocognitive functioning to screen for dementia or cognitive disorders. Age-matched participants received $15 per experimental session.

**Materials**

**Experimental Stimuli**

IPs for this study were drawn from a dictionary of idioms (Makkai et al., 1995) and all had the format VP NP⁴. Because of the current interest in examining the time course of literal and figurative processing of an IP, IPs with no plausible literal associations were excluded (such as “by and large”). This initial selection resulted in 60 IPs, which were then submitted to pre-testing prior to utilizing these items as stimuli.

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⁴ Verb phrase + Noun phrase
Stimuli Pre-Testing

**Pre-Test 1: Familiarity Rating**

In Pre-test 1, participants used a 5-point Likert scale to rate their familiarity with each IP (1 = unfamiliar, 5 = very familiar). IPs were embedded in sentences that took the form NP PP IP PP. Here, the first NP PP was a neutral context. After the IP, a figurative bias within the subsequent PP was presented (as in the example below, wherein the IP is shown in bold and the figurative bias is underlined).

2) The toddler in the dinosaur t-shirt **hit the sack** after a long day of playing outside.

Twelve UCSD undergraduates (mean age=20.1 yrs., SD=1.4) participated for Psychology or Cognitive Science course credit. Participants were monolingual, native English speakers with no exposure to a foreign language before the age of six, were right-handed, had no reported history of brain injury, emotional or learning disorders, and had normal-to-corrected vision and hearing. Forty IPs with a minimum average familiarity rating score of three (mean rating=4.4, SD=0.5) were selected for further use in the current study.

**Pre-Test 2: Probe Word Association**

Pre-Test 2 served to assess the suitability of experimental stimuli for use in a CMLP paradigm (see “Notes on Methodology” in Chapter 1 for details regarding this
methodology). The current CMLP study employed a *matched-sentence design* to control for *a priori* lexical decision reaction times (RTs) of the visual targets; probe words that are related to the figurative or literal meanings of the IP in one sentence served as the control words for another unrelated sentence. Consider examples 3 and 4, in which IPs (underlined) are embedded in *neutral* contexts:

3) The toddler in the dinosaur t-shirt **hit the sack** after a long day of playing outside with his best friend.

4) The burglar from Montana **spilled the beans** during dinner at his mother’s house.

For example 3, the related probe words “nap” and “bag” (figurative meaning of the IP and literal associate of “sack,” respectively) are also used as control (unrelated) probe words for example 4. Likewise, the related probe words for example 4 (“secret” and “coffee”) are used as control probe words for example 3 (see Figure 2-1 for a schematic diagram of this design). This matched design allows a comparison of lexical decision RTs to the *same word* in different conditions; for instance, RTs to “nap” when it appears during sentence 3 will be compared to RTs to “nap” when it appears during the unrelated sentence in 4. The *relative difference* in lexical decision RTs can thus be compared across all 40 experimental items, with a faster lexical decision time during related sentences indicating priming (and lexical access; see Figure 2-1 for a schematic representation of this design).
In Pre-Test 2, participants were asked to do two things. First, they were presented with an IP (such as “hit the sack”) in isolation and were instructed to consider the figurative or literal meaning of that IP. Next, they were presented with a word (e.g. noun, such as “bed”) and were asked to rate each probe word’s relatedness to the figurative or literal interpretation using a 5-point Likert scale (5 = Highly Related; 1 = Not Related at all). In order to ensure that the probe words used in the matched sentence design were in fact unrelated to the control IPs, this pre-test counterbalanced 4 conditions (2 Figurative or Literal lexical access [probe word for figurative or literal meaning] x 2 Probe word relatedness [related or control]). Thus, using the example (“hit the sack”) presented earlier, participants rated the association between “nap” and both the figurative and literal interpretation of “hit the sack” and “spilled the beans.” Probe words were all nouns, as prior work has suggested that listeners process nouns and verbs differently (Rayner, 1977; Damasio & Tranel, 1993; Caramazza & Hillis, 1991). Eight lists, counterbalanced for IPs and probe words, were administered to a new group of 88 UCSD undergraduates (mean age=19.7 yrs., SD=1.3) who participated for Psychology or Cognitive Science course credit. Participants met the same inclusion criteria as in Pre-Test 1.

The average association rating between figuratively-related probes and the figurative meaning of IPs was 4.3 (SD=0.6). The average association rating between
literally-related probes and the literal meanings of IPs was 4.2 (SD=0.7). These rating scores indicated that figurative and literal probe words were highly associated with figurative and literal meanings, respectively, of each IP. The average score for control probes across all conditions was 1.39 (SD=0.4), demonstrating very low association between control probe words and IPs. T-tests showed that association ratings were significantly different between figuratively-related and control probes (t (39) = 26.8, \( p < .001 \)) and between literally-related and control probes (t (39) = 21.6, \( p < .001 \)). Thus, Pre-Test 2 verified that probe words that were chosen were strongly related to the figurative and literal meanings of a related IP in sentence context, and were simultaneously weakly related to the figurative and literal meanings of an un-related IP. It was therefore determined that these probes would work in the on-line CMLP investigation.

Pre-Test 3: IP Predictability

As discussed in the Introduction, IP predictability, or the degree to which a listener may anticipate an IP based on its initial constituents, is hypothesized to be an important variable in IP processing (e.g. Cacciari & Tabossi, 1988; Tabossi & Zardon, 1993, 1995; Titone & Connine, 1994). Therefore, to determine whether predictability was a factor in our experiment, we gathered ratings of predictability for each IP used in the current study. To accomplish this, we designed a cloze task, in which participants would read the initial components of each experimental item, up to the determiner of each IP. Participants were then asked to continue the sentence from
that point with a word or short phrase. For example, participants read sentences such as the following:

5) The tattooed garbage man smelled a ____________.

Each of the 40 stimuli to be employed in the CMLP task was included in Pre-Test 3. In addition, 80 filler sentences of varying form and content were included to prevent participants from assuming the nature of the task. Eighteen college-aged participants completed this task (mean age = 20.2, SD = 1.2, 7 males and 11 females) for college course credit in Psychology or Cognitive Science. Participants met the same inclusion criteria as in Pre-Test 1 and 2.

Data from Pre-Test 3 were scored according to the proportion of participants who completed each IP with its actual final word. For example, for the IP “smelled a rat,” five of the 18 participants (28%) completed example 6, with “rat.” Results of this cloze-test were used as a factor in data analyses (see below). The average IP completion proportion was 0.18 (SD = 0.25), with a wide range of the proportion of idiomatic completions across all IPs (responses ranged from 0% idiomatic completions on some items to 94% idiomatic completion on one item). In order to incorporate this data into further analyses, IPs were coded as either high or low in their predictability. Here, a 6% cut-off was used, with IPs that were completed idiomatically by fewer than 6% of participants classified as being “low” in predictability, whereas IPs that were completed idiomatically by more than 6% of
participants were classified as being “high” in predictability. This threshold is similar to one used in a prior study that classified IPs according to predictability (Cacciari & Tabossi, 1988). This scoring metric resulted in 23 IPs that were classified as being low in predictability and 17 IPs that were classified as high in predictability.

**Stimuli preparation**

Following Pre-Test 3, the 40 pre-tested IPs were embedded into sentences, each of which provided no context for interpreting the IP prior to the occurrence of the phrase. A disambiguating phrase immediately followed each IP. This phrase always biased interpretation of the IP towards its figurative meaning:

6) The toddler in the dinosaur t-shirt hit the sack after a long day of playing outside with his best friend.

The decision to have neutral context prior to the IP and to begin testing lexical access at the IP’s offset was theoretically motivated; Swinney (1982) demonstrated that biasing contexts prior to IP onset did not affect patterns of lexical access. Furthermore, upon processing the initial verb in the IP, only the literal meaning for that verb was found to be lexically accessed. The figurative meaning for the entire IP was not detected until IP offset. Thus, given the predictions for both the AMC and LHD groups, it was believed that testing lexical access at IP offset and at several points
throughout the sentence would provide a strong test of the Delayed Lexical Activation Hypothesis. A full listing of experimental materials is provided in Appendix 2-1.

**Time course of IP processing during sentence comprehension**

In order to investigate the time course of figurative and/or literal processing of an IP during auditory sentence comprehension, three probe positions were tested in each sentence (probe positions indicated by superscript numerals and arrows in Figure 2-1). Probe position 1 occurred at the offset of the IP (termed the Idiom Offset probe position); probe position 2 at the offset of the disambiguating phrase (an average of 897ms post-IP offset; termed the Downstream 1 probe position); and probe position 3 was 500 ms after the offset of the disambiguating phrase (termed the Downstream 2 probe position). Examining lexical access for the figurative and literal meanings associated with IPs at the IP offset and these two downstream positions allowed for the comparison of lexical access patterns for IPs between unimpaired controls and LHD participants with Broca’s aphasia throughout the course of the sentence. Specifically, these latter two probe positions will allow us to test for delayed, or slowed, lexical access for IPs among our patients with Broca’s aphasia, as compared to the unimpaired participants in this study.

The 90 sentences, consisting of 40 experimental and 50 filler items, were pseudo-randomly organized into a single script, with the stipulation that no more than three sentences of a given type (experimental or filler) could occur together. Auditory sentence stimuli were recorded in Adobe Audition© by a female native English
speaker at a rate of 5.12 syllables/second (within the normal speech rate range of 4-6 syllables/second; see Love et al., 2008). The current experiment was conducted using the Tempo® software, in order to allow for millisecond-level precision in the timing of visual probe presentation and response recording.

In addition to these experimental items, 50 filler sentence stimuli were constructed; these were similar in length and structure to the experimental stimuli (at a similar rate of 5.00 syllables/second). Twelve of these filler stimuli sentences contained an IP, nine of which were embedded in sentences that biased interpretation toward the figurative meaning, and three of which were embedded in sentences that biased interpretation toward the literal meaning. Forty of these filler items were paired with a pronounceable non-word visual probe (such as “elote”), and ten filler items were paired with real words. Additionally, visual probes were presented at various times during each filler sentence; some visual probes were presented near the beginning of the sentence, some near the middle, and some near the end. This varied presentation was performed in order to avoid expectancy effects for visual probe words.

**Experimental Procedure**

In this CMLP paradigm, participants heard uninterrupted sentences like example 5 (above). While listening to these sentences, participants were seated in front of a computer at a comfortable distance from the screen. At a pre-specified point in each uninterrupted sentence (termed the *probe position*), a letter string appeared at
the center of the computer screen. Each letter string was either a word of English or a
pronounceable non-word. All experimental items were paired with either related or
control probes (as described above, Pre-test 2, see also Figure 2-1). Among the filler
items, 12 sentences were paired with English words, while the rest were paired with
non-words. The inclusion of filler items serves to distract participants from guessing
the purpose of the experiment and then adopting a strategy or consciously changing
the way in which they comprehend sentences. In addition, the inclusion of non-words
allows participants to make a binary choice during the lexical decision task, and thus
helps to encourage attention to the task.

Participants were instructed to listen carefully to each sentence and to
comprehend it to the best of their ability. They were also instructed to make a lexical
decision (word vs. non-word) about the letter string that appeared on the screen and to
indicate their decision via a button press on a button box that was placed directly in
front of them during the task.

Design

This study used a within-subjects design, such that each participant contributed
data to each condition and probe position. Visual probes and probe positions were
counterbalanced across multiple lists, with each list containing all conditions, but with
no one sentence or visual probe being repeated in any one visit. Experimental testing
for each of these lists occurred across separate experimental sessions. That is, an
individual was only given one list during each visit. In order to contribute data to all
condition and probe positions, participants returned for multiple experimental
sessions, always separated by at least one week, so as to minimize a potential exposure
effect. The same stimuli were administered in the same order to both AMC and LHD
participant groups, in order to best compare results between these groups. Among the
seven LHD participants, all participants completed testing at all probe positions.
Among the 10 AMC participants, eight contributed data to all three probe positions,
while the remaining two participants only contributed data to the IP offset probe
position (probe position 1).

Procedure

At the beginning of each testing session, an experimenter explained the task to
each participant, who was in turn given a chance to practice the cross-modal task prior
to starting the actual experiment. The experimenter instructed each participant that
s/he would hear sentences over the headphones, and that s/he should listen for
comprehension. In order to encourage careful listening, each experimental list paused
at pre-determined points during each testing session, during which the experimenter
asked the participant a multiple-choice question about the prior sentence. Questions
were focused on the general content of the prior sentence, and were not intended to be
difficult. Rather, they were only intended to encourage close attention to the auditory
materials. Thus, data from these questions were not formally analyzed.

The experimenter also informed each participant that while listening to the
auditory sentences for comprehension, s/he would perform a secondary task; the
experimenter explained that at some point during each sentence, a string of letters would briefly appear on the computer screen. Participants were told that they should decide as quickly and accurately as possible as to whether these words constituted a word in English. The experimenter instructed participants to indicate their response to each letter string via a button press on a button box that was placed in front of the computer\(^5\). That is, participants were told to press the right, “yes” button, if the letter string was indeed a word in English, and to press the left, “no” button, if it was not. Participants were also instructed that if they felt they had made an incorrect response, they should immediately refocus and prepare for the next sentence/letter string item.

For the unimpaired AMC group, the visual letter strings were presented for 300ms, and participants were given an additional 1000ms to make their response (for a total possible response window of 1300ms). For the LHD group, visual letter strings were presented for 1500ms, and participants were again given an additional 1000ms to respond (for a total response window of 2500ms). This more lengthy presentation time for visual letter strings for or patient group was in response to longer latencies in this population with this task in previous studies (e.g. Love et al., 2008); we wanted to ensure that patients had enough time to view the letter strings and execute a motor response as they judged whether the letter strings constituted a word of English.

The results for the on-line portion of this study are presented later in this Chapter.

\(^5\) Due to post-stroke motor deficits, LHD participants always used their non-dominant hand, ipsilateral to their lesion (left hand) while the AMCs used their dominant right hand.
Off-Line Experiment

In addition to the on-line study of real-time IP processing, we also conducted an off-line, post-sentence task to assess the result of IP comprehension in our participants. As discussed in the Introduction (see above), rather than employing frequently used idiom-to-picture matching designs, we take a different approach. Since a variety of pictorial representations for the figurative interpretation may exist, a picture representing the figurative interpretation of an IP may be more cognitively taxing to decipher than a picture depicting the literal interpretation (see Tompkins et al., 1992). Or, perhaps it is the case that the converse is true; that is, that a picture of the literal interpretation would be easier to decipher, as this picture might be more concrete than a picture of the figurative interpretation. In either case, there is no empirical evidence which speaks to the difficulty of understanding either type of pictorial representation, and we thus aim to use a different method to avoid any potential confounds of picture interpretability. Here, we employed an IP verification task, as described below.

Participants

We administered the IP verification off-line task to all participants who first completed all visits of the CMLP task; thus, this sample consisted of the same AMC and LHD participants as described above.

Materials
A subset of IPs from the CMLP study (20 of the original 40) were selected for this off-line task. IPs were embedded into auditory sentences that biased the IP toward either a figurative or a literal interpretation, as in 7 and 8, respectively.

7) The art critic **chewed the fat** with his friend for a very long time at the fancy dinner.

8) The art critic **chewed the fat** on his steak for a very long time at the fancy dinner.

Each auditory stimulus was paired with a verification question that probed the participants’ understanding of the IP in the sentence. For instance, sentence 7, might be paired with the question, “Does this sentence say that the art critic talked for a long time with his friend?” to which the correct response would be “yes.” Alternatively, sentence 8 might be paired with the question, “Does this sentence say that the art critic chomped on his food for a long time?” to which the correct response would be “yes.”

In addition to these correct choices, some stimulus items were paired with questions that were designed to elicit a “no” response. For instance, example 7, in which the IP is biased toward a figurative interpretation, might be paired with the question, “Does this sentence say that the art critic chomped his food for a long time?” Importantly, biasing conditions were balanced across two lists, so that an IP would be presented in both a figurative and a literal context, but on these separate experimental lists.
Experimental Design

This off-line task was a 2 x 2 design, with IP biasing context (figurative, literal) and question type (figurative, literal) fully-crossed. This study was a within-subjects (repeated-measures) task, in that all participants in both the AMC and LHD groups completed both lists, separated in time by at least one week to minimize repetition effects.

Procedure

Participants heard each stimulus, one at a time. Following each item, participants were asked a binary-choice question (yes or no) about the IP in each sentence. AMC and LHD participants spoke their responses to the experimenter, or in the case of aphasic individuals who had difficulty speaking, pointed to their answer on a response sheet. As described above, the off-line test was separated into two sessions, with stimuli counter-balanced across these sessions. For instance, if a participant heard a figuratively-biased IP during their first visit, that participant then heard the same IP in a literally-biasing condition during her second visit. Order of list presentation was counterbalanced across participants. There were no time limits imposed on this task; participants were allowed to work at their own pace. Off-line assessments were scored by calculating each participant’s correct proportion of IP verifications at each visit, in both literal- and figurative-biased conditions, and then combining these proportions across both visits to arrive at a total proportion correct for each participant and each condition.
Results

Analyses

On-Line Study

Data Screening

Prior to analysis, it was discovered that three of the sentence stimuli contained a potential semantic association between one of the sentence’s probe words and elements of the sentence that were unrelated to the IP under investigation. Data from these three sentences were excluded from further analyses, along with data from each sentence’s matched pair, as constituted by the matched sentence design (see Figure 2-1). In addition, it was also discovered that several of the 160 tested probe words (across all conditions) had low hit rates across participants (< 70%) for at least 3 of 4 conditions (e.g. figurative related, figurative control, literal related, or literal control) across more than one probe position. Listed in Appendix 2-1, for the LHD group, five words fell in to this category. It was decided that the words in those conditions, along with their matched pairs, should be removed from analysis, while sparing the data from the other conditions. Using the same criteria for the AMC group, three probe words fell below this screening metric (also listed in Appendix 2-1).

Before statistically investigating the data for evidence of priming effects, data from all participants were screened to remove incorrect responses and misses (in which a participant failed to make a button press response within the allotted time), which amounted to 5.2% of the LHD participants’ data and 7.1% of the AMC
participants’ data. Next, data were screened to remove outlying reaction times (RTs), defined \textit{a priori} as any RT less than 300ms and greater than 1200ms for the AMC participants or greater than 2000ms for the LHD participants. This longer response window was allotted for the LHD participants based on prior CMLP studies which have demonstrated long latencies in this population (e.g. Love et al., 2008; Poirier et al., 2010). This resulted in the minimal removal of a further 2.2% of the LHD data and 1.8% of the AMC data. Lastly, a two standard deviation screen was performed to reduce skewness prior to performing parametric analyses. Here, RTs that were less than or greater than two Z-scores from the group average for each condition (e.g. Figurative control) at each probe position were identified and replaced with the mean RT for the condition and probe position (e.g. mean of Figurative control RTs at IP Offset). This resulted in the replacement of 3.9% of the remaining LHD data and 4.9% of the remaining AMC data.

\textbf{Analysis Procedures}

Data from each group, AMC and LHD, were submitted to descriptive and inferential statistics, including an omnibus repeated-measures ANOVA, with probe position (IP Offset, Downstream 1, and Downstream 2), condition (Literal, Figurative), relatedness (Related, Control), and predictability (High, Low) as factors, with RT as the dependent measure. Most important to the question of interest in this study, \textit{a priori} planned paired t-tests were conducted between related and control mean RTs for each condition at each probe position. It is important to remember that
we are not interested in the absolute RTs of any participant, but instead the relative priming effect (faster RTs in the related condition as compared to the control) that will allow us to detect patterns of priming for figurative and literal meanings of IPs at these three positions during sentence processing.

**Unimpaired Control Participants – AMC group**

Means and standard deviations of the RTs from the AMC unimpaired participants are shown in Table 2-2. Again, here, a negative value resulting from the subtraction of “control” from “related” conditions suggests the existence of priming for the given condition. Here, there was a 46.5 msec priming effect observed for figurative meanings of highly predictable IPs at probe position 1 (IP offset); this priming effect decreased and was only 6.7 msec at probe position 2, but a strong priming effect for the figurative meaning of these highly predictable IPs was evident again at probe position 3, with a priming effect of 25.5 msec. There was only a very small priming effect of 6.7 msec for literal meanings of highly predictable IPs at probe position 2 for high predictable IPs, but not at the other two probe positions. There was no priming effect for the figurative meanings of low predictable IPs at probe position 1, but there was an 18.7 msec priming effect at probe position 2 and a very small 3.5 msec priming effect at probe position 2. For the literal meanings of these low predictable IPs, there was no priming observed at probe position 1, a 19.4 msec priming effect at probe position 2, and a 13.2 msec effect at probe position 3.

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Results from the ANOVA indicated a main effect of probe position ($F(2, 184) = 17.6, p < 0.001$); no other main effects or interactions reached statistical significance. *A priori* planned paired t-tests revealed statistically significant priming for the figurative meaning of IPs at IP Offset, only for high predictable IPs ($t(9) = 2.37, p = 0.021$, one-tailed). At the Downstream 1 position, t-tests revealed marginally significant priming for the literal condition, for low predictable stimuli at this Downstream 1 position ($t(7) = 1.60, p = 0.077$). There was also a trend toward priming for the figurative condition, also for low predictable stimuli, although this trend did not reach significance ($t(7) = 1.27, p = 0.12$). At Downstream 2, t-tests indicated significant priming for the figurative meaning of IPs, for high predictable items ($t(7) = 2.65, p = 0.017$), and significant priming for the literal meaning the tested noun of low predictable IPs ($t(7) = 2.03, p = 0.041$). T-tests did not reveal significant priming for any of the other conditions or probe positions that were tested. Means for each condition are illustrated in Figure 2-2. In sum, this set of results indicates contextually-specific priming for the figurative condition at the first probe position (IP Offset) for high predictable IPs, followed by priming for the literal condition at the Downstream 1 probe position for low predictable IPs. At the Downstream 2 probe position, there is then a re-emergence of priming for the figurative condition and high predictable IPs, along with strengthened priming for the literal condition and low predictable IPs. Importantly, when predictability was not
included as a factor in analyses, and t-tests were only conducted for each condition at each probe position, there were no significant priming effects for any condition.

Therefore, although it did not reach significance as a main effect in the omnibus repeated-measures ANOVA, predictability did turn out to be a factor in the present patterns of priming. The effects of predictability will be further addressed in the Discussion section below.

Of note in these data, there was a change in the pattern of priming for the literal meaning of the noun in the IP, from the IP offset probe position to the Downstream 1 probe position, wherein at the IP offset probe position, there is no evidence of priming in the literal condition for either high or low predictable IPs. By the Downstream 1 probe position, however, there is a weak effect of priming for low predictable IPs in the literal condition. In order to determine whether this change in priming patterns was significant between the two probe positions, a separate repeated-measures ANOVA was conducted, using only data from the literal condition at the IP Offset and Downstream 1 probe positions. The ANOVA revealed only a main effect of probe position, but there was not a significant interaction between probe position and relatedness. This pattern will be further explored in the discussion section of this paper below.
Broca’s aphasic patients – LHD group

Data from the LHD participants are shown in Table 2-2 and means by condition are illustrated in Figure 2-3. Results of the “related” minus “control” subtraction indicated a 38.6 msec priming effect for the figurative condition at IP offset (probe position 1) for high predictable IPs, followed by a 63 msec priming effect at probe position 2, and no priming effect at probe position 3. For the literal meanings of high predictable IPs, the Broca’s patients showed a small priming effect of 19.2 msec at IP offset (probe position 1), followed by no priming effect at probe position 2, and a 34.1 msec priming effect at probe position 3. Among low predictable IPs, for the figurative condition, the Broca’s patients showed no priming effect at probe position 1, a 15.2 msec effect at probe position 2, and a 18 msec effect at probe position 3. Within the literal condition for low predictable IPs, the Broca’s patients showed a very small 1.1 msec priming effect at probe position 1, followed by absent priming effects at the following two probe positions.

The omnibus repeated-measures ANOVA only indicated a significant main effect of probe position (F (2, 144) = 6.51, p = 0.0020). The results of *a priori* paired one-tailed t-tests revealed no significant priming at the IP offset probe position for either the literal or figurative condition, for low or high predictable IPs. At the Downstream 1 probe position there was significant priming for the figurative
condition meanings for high predictable items \( (t (6) = 3.36, p = 0.0076) \). At the Downstream 2 position, there was a marginally significant effect of priming for the literal condition for high predictable IPs \( (t (6) = 1.68, p = 0.072) \).

Similar to the data from the AMC group, there was a change in the pattern of priming for the literal meaning of the noun of IPs, between probe positions. Here, among the LHD participants, there is no evidence of priming at the Downstream 1 probe position for the literal condition, for either high or low predictable IPs, and across both levels of predictability, the related condition shows larger RTs than the control condition (suggestive of inhibition of the literal condition). However, by the Downstream 2 position, there is a marginally significant effect of priming for the literal condition, for high predictable IPs. As with the AMC participants, this pattern shift was tested for significance with a repeated-measures ANOVA between only the Downstream 1 and Downstream 2 probe positions, restricted only to the literal condition. The ANOVA did not indicate a significant interaction between probe position and relatedness, nor any other main effects or interactions. Yet, this pattern of priming effects among the LHD participants will be further expanded upon in the discussion section below, as the pattern mirrors that which was observed in the AMC group, but with a temporal shift.

*Off-Line Study*

*Analysis Procedures*
Responses from the off-line study were coded as correct or incorrect. An incorrect response was a trial in which the participant failed to verify the definition of the IP in that trial. Total proportion correct was calculated for IP verifications for the literal and figurative biasing conditions. In addition, as with the on-line study, IP predictability was taken into account in these analyses. IPs in this off-line study were classified using the same criteria that was used in the on-line study to categorize IPs as either high or low in their predictability (see above). This classification scheme resulted in 11 IPs that were highly predictable, and 9 IPs that were low in their predictability. Thus, in addition to examining overall proportion correct scores, analyses of the off-line data will also investigate the effect of predictability on off-line comprehension across our two participant groups.

**Unimpaired Control Participants – AMC group**

Off-line results from the AMC group are shown in Figure 2-4. As seen in this figure, overall accuracy was quite high for both literal and figurative biasing conditions in this off-line task, at 0.89 and 0.90 proportion correct, respectively. A paired t-test between these proportions indicated that they were not significantly different. In considering proportion correct for high vs. low predictable IPs, as seen in Figure 2-4, proportion correct for both literal and figurative biased IPs, across both high and low predictability, remains quite high. A paired t-test between high and low predictable IPs in the figurative biasing condition revealed no significant difference in proportion correct between these different levels of predictability. However, a paired t-
test between high and low predictable IPs in the literal biasing condition did reveal a significant difference in the proportion correct between these different levels of predictability \((t(7) = -3.28, p = 0.014)\). Here, AMC participants were significantly more accurate at verifying the meanings of low predictable literal IPs than they were at verifying the meanings of high predictable literal IPs. In sum, the AMC participants were highly correct in verifying the meanings of both high and low predictable ambiguous IPs off-line, regardless of whether the IP was biased toward a literal or figurative interpretation. Participants were slightly more accurate at identifying the correct definitions of low predictable, literal IPs. This pattern of results will be further elaborated upon in the Discussion below.

Broca’s aphasic patients – LHD group

Off-line results from the LHD group are shown in Figure 2-4. In comparison to the AMC group’s results, the LHD group evinces low accuracy across both the figurative and literal conditions. In fact, none of the means of proportion correct for either figurative or literal biased IPs, across or between levels predictability, differed significantly from chance. A paired t-test between literal and figurative biased IPs, for all items collapsed across predictability indicated no significant difference in accuracy between these two conditions. Likewise, there was no significant difference in
accuracy between high and low predictable figuratively-biased IPs, nor was there a significant difference in performance between high and low predictable literally-biased IPs. This pattern of results contrasts with that of the AMC group, in that the LHD patients showed no significant difference in accuracy for high vs. low predictable IPs, for either literal or figurative biasing conditions.

**Discussion**

The set of on-line and off-line experiments presented here aptly achieved the aims of this study. Namely, this study provided a comprehensive test of lexical access for IPs during auditory sentence comprehension, across unimpaired and language-impaired participants, throughout the course of an auditory sentence. In so doing, several important findings emerged, with regards to the extent of lexical access for an IP’s associated meanings, the difference in lexical access between our unimpaired and aphasic participants, and the temporal nature of lexical access during IP comprehension. Each of these findings will be discussed in turn.

**Patterns of Lexical Access – AMC group**

Within the AMC group, and consistent with prior reports, we observed immediate lexical access for the figurative meaning of IPs at their offset, but only for highly predictable IPs. Later in the sentence, we observed lexical access for the literal meaning of the IP’s final constituent word (the noun), at the offset of a phrase that disambiguated the IP’s meaning, only for low predictable IPs. Then, further
downstream in the course of the sentence at probe position 3, on average 500 milliseconds after AMC participants had heard the offset of the disambiguating phrase, we observed lexical access again for the figurative meanings of IPs for high predictable IPs only. In addition, there was continued and strengthened priming for the literal meanings associated with low predictable IPs at this late point in the sentence. These results support prior literature of on-line lexical processing during IP comprehension, although the current results extend what is current understood of this process by delineating lexical access throughout the course of an entire IP-containing sentence. As discussed in the Introduction, some prior on-line studies of IP comprehension have suggested that lexical access is immediate and exhaustive for all meanings associated with an IP at the phrase’s offset (Swinney, 1982; Hillert & Swinney, 2001). Other studies, however, have suggested a temporal offset in lexical access for the figurative and literal meanings associated with an IP, with figurative lexical access preceding literal lexical access (e.g. Cacciari & Tabossi, 1988; Tabossi & Zardon, 1993, 1995; Titone & Connine, 1994; Libben & Titone, 2008). In our data, we observed this latter pattern, with figurative lexical access preceding literal lexical access. However, this pattern of lexical access was only observable when IP predictability was taken into account. Here, the data indicate the lexical access only occurs for figurative meanings of IPs when they are highly predictable, suggesting that this figurative meaning may block lexical access for the literal meanings of the IP’s constituent components. Consistent with Cacciari & Tabossi (1988), literal meaning for the IP’s final noun was only evident in the low predictable items.
The data presented herein argue strongly that predictability is a key factor in on-line IP processing, such that differential patterns of lexical access are observed for high vs. low predictable IPs. Here, it appears that lexical access for an IP’s figurative meaning occurs by IP offset, only for highly predictable IPs, which suggests that the language processing system may be detecting the presence of an IP prior to hearing the entirety of the phrase. If an IP is detected prior to IP offset, only the figurative meaning of the IP is lexically accessed. However, if an IP is not predictable, the language processing system does not lexically access either the figurative or the literal meaning strongly until later in the ongoing auditory sentence. Recall that while priming was only marginally significant for the literal meanings associated with low probability IPs at the Downstream 1 probe position, there was an intriguing change in the pattern of priming between the Idiom Offset and Downstream 1 probe positions. While a repeated-measures ANOVA between just these two probe positions failed to find a significant main effect of probe position, the fact that RTs changed from showing no priming at IP offset, to showing a priming trend at the Downstream 1 probe position suggests the initiation of lexical access for this meaning between these two probe positions. Then, by Downstream 2, priming is significant for the literal meaning of the noun for low predictable IPs, which demonstrates a strengthening of this lexical access effect. In addition, at this latest probe position, there is also a re-emergence of significant priming for the figurative meaning of highly predictable IPs. Priming at this late point in the sentence for figurative meanings of high predictable IPs suggests integration with ongoing sentence context, as all sentences were biased
toward a figurative interpretation (see Friederici, Gunter et al., 2004; Friederici et al., 1999). However, the existence of priming for literal meanings of low predictable IPs at this same probe position is an unexpected finding. Taken together with the lack of significant priming at any probe position for high predictable IPs, this finding suggests that literal lexical access is maintained until a late point in the sentence, perhaps as the language processing system attempts to resolve the intended meaning of the ambiguous IP (e.g. Faust & Chiarello, 1998; Jung-Beeman, 2005).

Overall, the patterns of priming (and inferred lexical access) support the hypothesis that lexical access is temporally discontinuous for the literal and figurative meanings that are associated with IPs. This set of findings is in keeping with previous on-line studies of IP comprehension (Cacciari & Tabossi, 1988; Titone & Connine, 1999), yet the current study extends our knowledge of lexical access for an IP’s associated meanings throughout the course of the sentence. This study allowed for a more detailed examination of lexical access for these different meanings than has been observed previously in the literature. By testing for lexical access at the IP offset probe position and two later probe positions, we were able to observe not only the initial lexical access of figurative and literal meanings, but also the re-activation of the figurative meaning at the final probe position, as listeners work to integrate the IP’s meaning into ongoing sentence context. In addition, the concordance between the results presented here and earlier results of real-time IP processing suggest that indices of lexical access during IP comprehension remain relatively stable in healthy aging.
This is perhaps not surprising, as prior research has failed to demonstrate age-related changes in lexical access for single auditory words (e.g. Stern et al., 1991).

Patterns of Lexical Access – LHD group

Data from our AMC group provides a baseline pattern of priming for IPs across a sentence, against which patterns of priming from the LHD group may be compared. At probe position 1, the LHD group showed no priming for either the figurative or literal meanings associated with IPs. However, at probe position 2, we observed significant priming for figurative meanings, only for high predictable IPs. Later, at probe position 3, only priming for the literal meaning of the noun for high predictable IPs was evident. This pattern of priming is intriguing for several reasons. First, the absence of figurative priming at probe position 1 (IP offset) coupled with the appearance of priming for this condition at probe position 2 strongly suggests delayed lexical access for figurative meanings in this group. Interestingly, the LHD group showed a trend towards priming for the figurative meanings of IPs at idiom offset for high predictable IPs, although this priming does not reach significance until Probe Position 2. This suggests that lexical access starts to build by the offset of the idiom, but that this lexical access is not fully apparent until later in the sentence. Likewise, in comparison to the AMC group, the LHD participants show literal lexical access that was temporally-shifted by one probe position (Downstream 1 vs. Downstream 2), although this priming effect was only present for high predictable IPs, as discussed in the paragraph below. Thus, when contrasted with the pattern of priming that was
evident in the AMC group, the LHD participants show delayed lexical access for the multiple meanings associated with an IP, the implications of which are further discussed below.

Importantly, there is an additional divergence in the patterns of priming observed between our two participant groups. In the AMC group, we observed literal lexical access for low predictable IPs at the Downstream 1 probe position, but in the LHD group, there was never significant priming observed for low predictable IPs, for either the figurative or literal meaning. This may be a highly important finding for several reasons. For one, the lack of any significant priming for low predictable IPs suggests deficient or impaired on-line processing of these types of IPs among LHD participants. That is, these data indicate that Broca’s patients fail to lexically access any of the associated meanings for these types of IPs, at least not at the time points that were tested as probe positions in the current study. This is an intriguing finding because it parallels the literature of on-line single-word lexical ambiguity processing in this patient group. Specifically, work in the area of real-time lexical ambiguity processing in Broca’s aphasia has noted different lexical access patterns for highly frequent vs. less frequent meanings that are associated with a single-word lexical ambiguity (see Milberg et al., 1987; Swinney et al., 1989). Relevant to the current discussion, although our study did not include a direct measure of frequency for an IP’s associated meanings (that is, how frequently each IP is used in a context that biases a literal interpretation vs. a figurative one), the current data is not the first to report abnormal lexical access in Broca’s aphasia for one meaning of an ambiguous
item. Previous reports of lexical access in Broca’s aphasia for ambiguous words have suggested degraded or slowed lexical processing of low frequency meanings of single-word lexical ambiguities\(^6\). One study that examined this issue in Broca’s aphasia found that Broca’s patients only demonstrated lexical access for the most frequent meaning of an ambiguous word during on-going auditory sentence comprehension (Swinney et al., 1989), and these participants never showed priming for the low frequency meaning of the ambiguity. An additional study, using event-related potentials (ERPs), also supports the hypothesis that individuals with Broca’s aphasia exhibit delayed lexical processing of ambiguities (Swaab et al., 1995). Certainly, these prior reports concur with the observed results in this study, in that our patients with Broca’s aphasia failed to show any priming for the low predictable IPs. Of course, this comparison between lexical ambiguities and IPs is not one-to-one, as prior work with unimpaired individuals demonstrates exhaustive access for a lexical ambiguity at the word’s offset, while we found constrained lexical access to only the figurative meaning at IP offset. However, it is certainly noteworthy that our Broca’s patients have replicated a pattern of lexical access that was previously observed with single-word lexical ambiguities in this same population, but here with ambiguous lexicalized phrases.

\(^6\) For example, with the ambiguous word “bank,” a highly frequent meaning of this word is “a financial institution,” whereas a less frequent meaning is “the side of a river.”
In sum, the patterns of lexical access in Broca’s aphasia that were observed in this study indicate restricted lexical access for only highly predictable IPs. Priming was only observed for the figurative meaning at the offset of the disambiguating phrase (probe position 2), and weak priming was observed for the literal meaning at the probe position 3, later downstream in the course of the sentence. Below, a discussion aims to relate these findings to our understanding of real-time lexical access in Broca’s aphasia more generally.

**Lexical Access in Broca’s Aphasia**

The on-line data reported here present a temporally-shifted view of lexical access for IPs in our LHD group, as compared to lexical access in the unimpaired participants, a finding which supports the Delayed Lexical Activation hypothesis discussed earlier. The AMC group demonstrates figurative lexical access for high predictable IPs at the offset of the IP; the LHD group likewise demonstrates lexical access for the figurative meanings of these high predictable IPs, but the timing of this access is delayed and only appears at the offset of the disambiguating phrase. In addition, we observed lexical access for the literal meaning of the noun for low predictable IPs at probe position 2 in our AMCs, but observed literal lexical access for high predictable IPs at probe position 3 in our LHD participants. One possible explanation of this difference is that lexical access is again slowed in our LHD participants for the literal meanings of our IPs. However, because lexical access for these two groups differs with respect to predictability, it is possible that different
processing occurs within each of our groups for literal meanings of IPs. In the AMCs, as has been argued previously for unimpaired listeners, because literal lexical access only proceeds for low predictable IPs, it seems that the language processing system only retrieves the literal meaning of an the noun of the IP from the lexicon if a figurative meaning is unlikely or uncertain (see e.g. Titone & Connine, 1994; Cacciari & Tabossi, 1988). However, because the LHD group shows literal lexical activation for high predictable IPs, following figurative lexical access for these same IPs, it seems to be the case that the language processing system is insensitive to the factor of predictability. Instead, lexical access occurs sequentially, first for figurative meanings, and then for literal meanings, for the same IPs. That is, the language processing system in Broca’s aphasia is unable to make use of IP predictability to tailor lexical access for predictable vs. unpredictable IPs.

This differential effect of lexical access between our AMC and LHD groups may be due to imperviousness on the part of the LHD participants to ongoing sentence context. Recall that by the time participants reached probe position 2, they had heard enough information to determine that the IP should be understood figuratively, and not literally. Let us just consider high predictable IPs for the moment, as the most interesting comparison between our two participant groups can be made on the basis of these results. Among our AMC participants, we observed a re-access of figurative meanings for high predictable IPs at probe position 3, suggesting that context was driving this activation in order to integrate figurative meaning into the ongoing sentence. By contrast, the LHD participants show only figurative lexical access at
probe position 2, which alone could suggest that LHD participants are accessing the contextually-relevant meaning of the IP upon hearing the disambiguating phrase. However, taken together with results from probe position 3, at which LHD participants only demonstrate lexical access for literal meanings, these results appear to indicate automatic, sequential lexical access for an IP’s multiple meanings, with lexical access being driven by frequency of the associated meanings. That is, figurative meanings are accessed first, as they are most commonly associated with IPs, followed by literal meanings. As touched upon earlier, this pattern of results has been indicated and argued in the lexical ambiguity literature with Broca’s aphasia, where the most frequent meaning of the ambiguity is delayed from what is seen with unimpaired populations, but comes on-line first, followed by secondary meanings of the ambiguity (e.g. Shapiro, 1998; Swinney et al., 1989). Certainly, much further work must be done to more clearly map out the factors which underlie lexical access during IP processing in Broca’s aphasia, but the results presented here provide substantial evidence that lexical processing is disordered in this population during IP comprehension.

Off-Line Idiom Comprehension

As discussed in the Introduction, although off-line methodologies cannot speak to the real-time processes that underlie spoken language comprehension, off-line tasks are helpful for evaluating the outcome of comprehension. As anticipated, the AMC group achieved very accurate performance on all items in the task, across IPs that had
been biased toward either a figurative or literal interpretation, and across high and low predictability. It is perhaps a bit surprising that, given the on-line data from this group, in which we observed differential patterns of priming for high vs. low predictable IPs, the only observed significant difference in accuracy between high and low predictable IPs was in the literal biasing condition, and this difference indicated more accurate verification for low predictable IPs. This effect may be due to the fact that highly predictable IPs are presented in an unusual context in the off-line task; that is, while these highly predictable IPs are typically used in figurative contexts in speech, the off-line task employed here biased these IPs toward a literal interpretation. It is likely, therefore, that AMC participants faced some difficulty conceptualizing these highly predictable IPs in a literal manner, which may explain the lower accuracy for this condition. Overall, however, the AMC participants showed very high accuracy across all measures.

By comparison, the LHD participants evinced a great deal of difficulty with the off-line task, demonstrating chance-level performance for both literal and figurative biased IPs, across both high and low predictable items. Unlike their unimpaired peers, LHD participants were unaffected by predictability (a similar pattern to what was discovered in the on-line study). It is perhaps worthwhile to comment on the fact that the LHD participants did not show priming for low predictable IPs at any of the probe positions which were tested in this study, yet accuracy did not significantly differ between high and low predictability for either literal or figurative biased IPs in this off-line task. Of note is that, while not significant, the LHD group showed higher
accuracy for high predictable IPs biased towards a literal meaning than for low predictable IPs also biased towards a literal meaning. This is the opposite pattern of what we observed in the AMC participants, and this result suggests that LHD participants do not seem to face the same cognitive conflict as their unimpaired peers when comprehending the high predictable IPs with a literal bias. That is, LHD patients do not show a higher cost for comprehending IPs which are biased towards an unusual, or infrequent meaning, than they do for understanding IPs which are not readily predictable as being figurative phrases.

Although these off-line results do not cleanly correspond to patterns of priming from the on-line study, these off-line results are informative for several other reasons. In addition to the lack of differentiation between high and low predictable IPs with a literal bias in the LHD group, these results also replicate the comprehension difficulties for IPs that have been reported in the literature for individuals with aphasia. However, the current results provide a slightly different perspective than what has been previously reported in the literature. Specifically, the off-line task in this study failed to replicate reports in the literature of somewhat spared comprehension for the literal meanings of IPs (see Cacciari et al., 2006). There are two potential contributions to this divergence in these present results from previous reports. For one, the task used in the present study differs from the style of off-line task that many other researchers have used to investigate off-line IP comprehension in aphasia; as discussed earlier, many prior studies have employed picture-to-idiom matching tasks, but the current study instead used an IP verification task. As it has been argued previously
(Tompkins et al., 1992), these picture-matching tasks use very concrete images to represent the literal meanings of IPs and very abstract images to represent the figurative meanings of these phrases, which may therefore disproportionately bias results. This is so because a concrete picture of a literal meaning may be much easier for an aphasic patient to match to an IP than an abstract drawing is to match to a figurative meaning. Our task therefore calls into question whether aphasic patients have sparing for either off-line interpretation of IPs, literal or figurative, as the patients in our study demonstrated equivalently poor performance for both biasing conditions.

Additionally, the present off-line results may differ from other published reports due to the fact that the current study only enrolled patients who had one subset of aphasia. As the vast majority of prior studies have enrolled very heterogeneous patient samples (Papagno & Caporali, 2007; Papagno et al., 2004; Cacciari et al., 2006; Papagno & Genoni, 2004; Papagno et al., 2006; Tompkins et al., 1992), it is possible that this heterogeneity obscured off-line comprehension patterns that are specific to the different types of aphasia. Thus, the current study is better able to characterize the nature of off-line comprehension deficits in one sub-type of aphasia, Broca’s aphasia, finding that patients are equally impaired in their understanding of high and low predictable IPs, across ambiguous IPs that are biased towards either a figurative or literal interpretation.

**General Conclusions**
The data in the current studies establishes the time course of lexical access in Broca’s aphasia for the multiple meanings associated with IP. While these results are directly informative to the study of IP processing, and begin to help explain impaired comprehension of IPs in this population, these data also speak more broadly to the nature of lexical access in this population. This study was the first of its kind to utilize IPs as a tool to investigate the time course of lexical access for an IP’s multiple meanings during auditory sentence processing. By comparing patterns of lexical access between the AMC group and the Broca’s patients, evidence emerged in support of the Delayed Lexical Activation hypothesis of Broca’s aphasia, which claims that lexical access is protracted in this population. However, future research in this area must delve more deeply into the quality and temporal signatures of lexical access in this population, particularly with respect to the status of lexical access for IPs of different predictability, as patterns of priming diverged between the two groups with respect to this factor. In addition, the results presented here suggest that lexical access in Broca’s aphasia is unaffected by context, at least for the time points that were tested here. That is, these participants demonstrated weak lexical access for the literal meaning of the noun of the IPs at the final probe position that was tested, despite the fact that all sentence context by this point in the sentence was biased toward a figurative interpretation. Thus, the current study provides an intriguing look into some of the factors that may contribute to real-time patterns of slowed lexical access in Broca’s aphasia, but future work should attempt to further characterize the influence of each of these factors on real-time lexical processing.
Table 2-1. Demographic and diagnostic information for each of the LHD participants who were enrolled in the current study. The BDAE severity score ranges from 1-5, with lower numbers indicating a greater degree of impairment (e.g. 1 = most severely impaired). The WAB aphasia quotient ranges from 0-100, with lower numbers indicating more severe language impairment.

<table>
<thead>
<tr>
<th>Patients Enrolled in the Current Study</th>
<th>Subject</th>
<th>BDAE Severity Level</th>
<th>WAB Aphasia Quotient</th>
<th>Aphasia Diagnosis</th>
<th>Gender</th>
<th>Age at testing</th>
<th>Months post-stroke</th>
<th>Education</th>
<th>Lesion</th>
</tr>
</thead>
<tbody>
<tr>
<td>LHD09</td>
<td>2</td>
<td>72.7</td>
<td>Broca’s</td>
<td>M</td>
<td>49</td>
<td>107</td>
<td>17</td>
<td></td>
<td>L. posterior inferior frontal lobe, extending to middle and posterior temporal lobe, includes regions of the insula and subcortical regions</td>
</tr>
<tr>
<td>LHD019</td>
<td>1</td>
<td>54.1</td>
<td>Broca’s</td>
<td>F</td>
<td>50</td>
<td>181</td>
<td>12</td>
<td></td>
<td>L. middle and posterior frontal lobe; anterior and middle superior temporal lobe</td>
</tr>
<tr>
<td>LHD040</td>
<td>2</td>
<td>76.7</td>
<td>Broca’s</td>
<td>M</td>
<td>71</td>
<td>63</td>
<td>16</td>
<td></td>
<td>L. basal ganglia and subcortical areas, including left putamen, L. hippocampus</td>
</tr>
<tr>
<td>LHD043</td>
<td>3</td>
<td>79.6</td>
<td>Broca’s</td>
<td>M</td>
<td>86</td>
<td>69</td>
<td>18</td>
<td></td>
<td>L. frontal lobe (more precise localization unavailable)</td>
</tr>
<tr>
<td>LHD101</td>
<td>2</td>
<td>82.4</td>
<td>Broca’s</td>
<td>M</td>
<td>60</td>
<td>32</td>
<td>20</td>
<td></td>
<td>L. posterior inferior frontal lobe, extending to middle and posterior temporal lobe, includes regions of the insula and subcortical regions</td>
</tr>
<tr>
<td>LHD130</td>
<td>4</td>
<td>81.1</td>
<td>Broca’s</td>
<td>M</td>
<td>57</td>
<td>23</td>
<td>16</td>
<td></td>
<td>L. inferior occipital lobe, occipito-temporal junction, and posterior and middle temporal gyrus</td>
</tr>
<tr>
<td>LHD132</td>
<td>4</td>
<td>93</td>
<td>Anomia</td>
<td>M</td>
<td>47</td>
<td>68</td>
<td>18</td>
<td></td>
<td>L. anterior inferior and middle temporal lobe, L. insula, includes small portion of posterior inferior frontal gyrus</td>
</tr>
</tbody>
</table>
Table 2-2. Mean response times for each probe position and condition, across High predictable IPs (top) and Low predictable IPs (bottom), for each participant group (AMC and LHD). Mean response times are shown in milliseconds, along with the standard error in parentheses. Difference scores are indicated, and are calculated by subtracting the RT for “control” probe words from the RT for “related” probe words. A negative difference score indicates a faster RT for probe words that are related to either the figurative meaning of the IP or the literal meaning of IP’s noun in each sentence, and suggests priming for that meaning. Probe positions are numbered to correspond with the probe position numerals in Figure 2-1. Asterisks indicate significant priming.

| Example: The toddler in the dinosaur t-shirt hit the sack\(^1\) after a long\(^2\) day of playing\(^2\) outside ... |
|-------------------------------------------------|---------------------|---------------------|---------------------|
| Probe Position 1                                | Probe Position 2     | Probe Position 3     |
| Idiom Offset                                    | Downstream 1        | Downstream 2        |

**Unimpaired control participants – AMC Group**

<table>
<thead>
<tr>
<th>High Predictable IPs</th>
<th>Figurative Related probe</th>
<th>Figurative Control probe</th>
<th>Figurative Difference (Related – Control)</th>
<th>Literal Related probe</th>
<th>Literal Control probe</th>
<th>Literal Difference (Related – Control)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean RT (SD)</td>
<td>796.3 (78.0)</td>
<td>842.8 (78.1)</td>
<td>-46.5**</td>
<td>823.2 (86.3)</td>
<td>804.9 (87.3)</td>
<td>18.3</td>
</tr>
<tr>
<td>Mean RT (SD) downstream 1</td>
<td>762.8 (59.7)</td>
<td>764.3 (84.9)</td>
<td>-1.5</td>
<td>769.1 (95.8)</td>
<td>775.8 (39.7)</td>
<td>-6.7</td>
</tr>
<tr>
<td>Mean RT (SD) downstream 2</td>
<td>741.4 (38.9)</td>
<td>766.9 (46.9)</td>
<td>-25.5**</td>
<td>764.4 (37.0)</td>
<td>760.3 (36.9)</td>
<td>4.1</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Low Predictable IPs</th>
<th>Figurative Related probe</th>
<th>Figurative Control probe</th>
<th>Figurative Difference (Related – Control)</th>
<th>Literal Related probe</th>
<th>Literal Control probe</th>
<th>Literal Difference (Related – Control)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean RT (SD)</td>
<td>818.1 (65.2)</td>
<td>806.1 (71.5)</td>
<td>12.0</td>
<td>808.3 (69.1)</td>
<td>798.4 (77.4)</td>
<td>-19.4**</td>
</tr>
<tr>
<td>Mean RT (SD) downstream 1</td>
<td>738.3 (51.6)</td>
<td>756.8 (58.8)</td>
<td>-18.7</td>
<td>751.7 (59.2)</td>
<td>771.2 (60.4)</td>
<td>-3.5</td>
</tr>
<tr>
<td>Mean RT (SD) downstream 2</td>
<td>745.6 (48.6)</td>
<td>749.1 (48.0)</td>
<td>-3.5</td>
<td>747.1 (33.5)</td>
<td>730.6 (43.4)</td>
<td></td>
</tr>
</tbody>
</table>

**Broca’s patients- LHD Group**

<table>
<thead>
<tr>
<th>High Predictable IPs</th>
<th>Figurative Related probe</th>
<th>Figurative Control probe</th>
<th>Figurative Difference (Related – Control)</th>
<th>Literal Related probe</th>
<th>Literal Control probe</th>
<th>Literal Difference (Related – Control)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean RT (SD)</td>
<td>1105.0 (169.7)</td>
<td>1143.6 (153.9)</td>
<td>-38.6</td>
<td>1165.4 (168.4)</td>
<td>1184.6 (129.2)</td>
<td>-19.2</td>
</tr>
<tr>
<td>Mean RT (SD) downstream 1</td>
<td>1046.2 (139.4)</td>
<td>1109.2 (123.4)</td>
<td>-63.0**</td>
<td>1117.5 (142.6)</td>
<td>1074.0 (117.0)</td>
<td>43.5</td>
</tr>
<tr>
<td>Mean RT (SD) downstream 2</td>
<td>1089.2 (154.9)</td>
<td>1067.4 (139.2)</td>
<td>21.9</td>
<td>1034.0 (145.6)</td>
<td>1068.1 (135.2)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Low Predictable IPs</th>
<th>Figurative Related probe</th>
<th>Figurative Control probe</th>
<th>Figurative Difference (Related – Control)</th>
<th>Literal Related probe</th>
<th>Literal Control probe</th>
<th>Literal Difference (Related – Control)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean RT (SD)</td>
<td>1166.1 (155.9)</td>
<td>1145.0 (199.2)</td>
<td>21.1</td>
<td>1116.0 (164.2)</td>
<td>1117.1 (144.7)</td>
<td>-1.1</td>
</tr>
<tr>
<td>Mean RT (SD) downstream 1</td>
<td>1054.3 (145.8)</td>
<td>1069.5 (134.1)</td>
<td>-15.2</td>
<td>1087.9 (119.6)</td>
<td>1059.9 (123.7)</td>
<td>28.0</td>
</tr>
<tr>
<td>Mean RT (SD) downstream 2</td>
<td>1032.9 (142.2)</td>
<td>1051.0 (146.4)</td>
<td>-18.0</td>
<td>1021.8 (129.3)</td>
<td>1011.1 (123.8)</td>
<td></td>
</tr>
</tbody>
</table>
Figure 2-1. A schematic of the counterbalanced design used in this study. Two sample stimuli are shown here (IPs are italicized for reference). This study used a matched probe design, so that the related probe word for one sentence served as a control (unrelated) probe word for another sentence (FR = figurative related condition; FC = figurative control condition; LR = literal related condition; LC = literal control condition). Using this design, reaction times can be directly contrasted for the same probe word when it is used in a related vs. control condition. For instance, RTs were compared between the word “nap” when it was used as a related probe with the top sentence and RTs for the word “nap” when it was presented during the unrelated bottom sentence. The three probe positions are indicated by numeral superscripts, and were placed: 1) at the offset of each IP; 2) at the offset of a phrase that disambiguated the meaning of the IP towards a figurative interpretation; and 3) at another point downstream from the IP and disambiguating phrase. Conditions were counter-balanced across lists, so that participants did not hear the same sentence more than once or see the same probe word more than once in a list. Participants completed each list at a separate experimental session, and these sessions were separated by at least one week to reduce repetition effects.
Figure 2-2. Mean RTs by condition and by IP predictability in the AMC group. Significant priming is indicated where a paired t-test revealed a significant difference in the means of the related and control conditions. Error bars represent the standard error of the mean.
Figure 2-3. Mean RTs by condition and by IP predictability in the LHD group. Significant priming is indicated where a paired t-test revealed a significant difference in the means of the related and control conditions. Error bars represent the standard error of the mean.
Figure 2-4. Off-Line comprehension results for both AMC and LHD groups. Graphs indicate proportion of correct verifications in each group, across high and low predictable IPs for literal and figurative conditions, and collapsed across predictability.
Appendix 2-1
Listing of experimental stimuli

1. The teenager with curly blonde hair wore the pants in her family after the tragic accident that happened last September.
   LR-belt   LC-soil
   FR-duty   FC-gossip

2. The burglar from Montana spilled the beans about the money at his mother’s house after a long day of cooking with his family.
   LR-coffee LC-twine
   FR-secret FC-wedding

3. The world famous art critic chewed the fat with his friend for a very long time at the start of a pleasant evening.
   LR-meat   LC-wood
   FR-chat   FC-job

4. The middle-aged plumber saw the light about the argument before his young wife arrived in the expensive new SUV
   LR-blink   LC-catch
   FR-think   FC-enjoy

5. Yesterday afternoon Susan kicked the bucket without waking up after the children left to go play miniature golf
   LR-pail   LC-dollar
   FR-death   FC-blame

6. On her way to work, Jenny blew the whistle on the crook and then quickly ran away to hide in a safe place
   LR-alert   LC-hurt
   FR-tattle   FC-poor

7. The bored little boy pushed the envelope with bad behavior at the semiannual neighborhood street festival

---

Idiomatic phrases are bolded for ease of reference; disambiguating phrases are underlined. Abbreviations next to each probe word reference the following conditions: LR = literal related; LC = literal control; FR = figurative related; FC = figurative control (see Figure 2-1). Sentences are not listed which were excluded from analyses due to a relationship between a probe word and a portion of the sentence not under investigation in the current study. Probe words which showed low hit rates for each participant group, however, are included in this list, though data from these probe words were excluded from final analyses. The probe words excluded from the AMC analyses were: annoy, chime, outwit, poor, shoot, tattle. The probe words excluded from the LHD analyses were: advantage, annoy, begin, dare, outwit, poor, snitch, tattle.
8. The toddler in a dinosaur shirt **hit the sack** at eight o’clock after a long day of playing outside with his best friend

   LR-mail  
   LC-grow

   FR-dare  
   FC-begin

9. The tattooed garbage man **smelled a rat** at the secret meeting behind the row of abandoned houses near the old train tracks

   LR-bag  
   LC-scar

   FR-nap  
   FC-memory

10. At the reception the host **broke the ice** by seating everyone together before the band started to play well-known songs for the guests.

    LR-cold  
    LC-tall

    FR-smooth  
    FC-mad

11. The fireman from Chicago **got the picture** about the agreement between the two cities that solved the rush hour traffic problem

    LR-photo  
    LC-orchestra

    FR-concept  
    FC-punishment

12. The eager receptionist **ruffled some feathers** with an internet post before she sent it to her partner who lived in Chicago

    LR-brush  
    LC-pitch

    FR-annoy  
    FC-outwit

13. The celebrity contestant **jumped the gun** off the blocks at the charity event before the newspaper reporter arrived

    LR-shoot  
    LC-chime

    FR-rush  
    FC-remember

14. The Hollywood director **knocked them dead** with one show about the futuristic fly-swatter that the mad scientist made

    LR-murder  
    LC-dive

    FR-impress  
    FC-try

15. The older actor told Jane to **break a leg** on opening night before the crowd arrived on the evening of the performance

    LR-knee  
    LC-ruler

    FR-luck  
    FC-limit
16. The talented artist failed to **strike a chord** in his friend’s memory, even though they had been on the road together many times in the past.

<table>
<thead>
<tr>
<th>LR</th>
<th>LC</th>
<th>FR</th>
<th>FC</th>
</tr>
</thead>
<tbody>
<tr>
<td>music</td>
<td>captive</td>
<td>feeling</td>
<td>winner</td>
</tr>
</tbody>
</table>

17. The smart carpenter **sowed the seeds** of a **feud** with his wife's cousins when they came to visit last Spring.

<table>
<thead>
<tr>
<th>LR</th>
<th>LC</th>
<th>FR</th>
<th>FC</th>
</tr>
</thead>
<tbody>
<tr>
<td>grow</td>
<td>mail</td>
<td>begin</td>
<td>dare</td>
</tr>
</tbody>
</table>

18. On his drive home, Bobby **felt the pinch** in his wallet from a visit to the doctor for his monthly checkup.

<table>
<thead>
<tr>
<th>LR</th>
<th>LC</th>
<th>FR</th>
<th>FC</th>
</tr>
</thead>
<tbody>
<tr>
<td>hurt</td>
<td>alert</td>
<td>poor</td>
<td>tattle</td>
</tr>
</tbody>
</table>

19. The nurse told her boyfriend to **blow off steam** after the argument but he didn't listen to her and later regretted it.

<table>
<thead>
<tr>
<th>LR</th>
<th>LC</th>
<th>FR</th>
<th>FC</th>
</tr>
</thead>
<tbody>
<tr>
<td>boiling</td>
<td>deadly</td>
<td>frustrated</td>
<td>handsome</td>
</tr>
</tbody>
</table>

20. My uncle from Oregon **tied the knot** in the church on a sunny afternoon before he went to his sister’s house.

<table>
<thead>
<tr>
<th>LR</th>
<th>LC</th>
<th>FR</th>
<th>FC</th>
</tr>
</thead>
<tbody>
<tr>
<td>twine</td>
<td>coffee</td>
<td>wedding</td>
<td>secret</td>
</tr>
</tbody>
</table>

21. Every day the principal **passed the buck** to keep his schedule free before he had to meet with all of the teachers who were having trouble with difficult students.

<table>
<thead>
<tr>
<th>LR</th>
<th>LC</th>
<th>FR</th>
<th>FC</th>
</tr>
</thead>
<tbody>
<tr>
<td>dollar</td>
<td>pail</td>
<td>blame</td>
<td>death</td>
</tr>
</tbody>
</table>

22. My younger brother told Tom to **draw the line** at finishing his math **homework** after he got on the wrong bus for school last Tuesday.

<table>
<thead>
<tr>
<th>LR</th>
<th>LC</th>
<th>FR</th>
<th>FC</th>
</tr>
</thead>
<tbody>
<tr>
<td>ruler</td>
<td>knee</td>
<td>limit</td>
<td>luck</td>
</tr>
</tbody>
</table>

23. The young man from Australia **faced the music** for drinking too much in the United Kingdom's most famous historical village.

<table>
<thead>
<tr>
<th>LR</th>
<th>LC</th>
<th>FR</th>
<th>FC</th>
</tr>
</thead>
<tbody>
<tr>
<td>orchestra</td>
<td>photo</td>
<td>punishment</td>
<td>concept</td>
</tr>
</tbody>
</table>

24. The mysterious bank robber **got the axe** for stealing a truck just before the police arrived to investigate the report they received.
25. At 5 am, the old man **hit the ceiling** from the noise because his neighbors were still playing loud music after he asked them to stop.

26. The professor in a tweed jacket **opened old wounds** in the community when determining the cause of death for the local newscaster.

27. The little girl with lots of freckles **dished the dirt** about the test in front of all her friends and everyone was very surprised.

28. The goofy weatherman **took the plunge** into the investment to prove a point to his buddies so they would stop teasing him.

29. The clever manager **had a ball** watching TV on the long plane ride home from his trip to see the pyramids in Egypt.

30. The farmer told his nephew to **dress to kill** for the dance before the Thanksgiving feast that they had been planning for months.

31. The friendly librarian **didn't ring a bell** to the quiet students at the conservative college when they were studying for midterms.

32. The older man decided to **take no prisoners** in answering the quiz questions in the final round of the game show, and hoped the strategy would result in a quick victory.
33. The experienced sailor **threw a curve in the debate** on the forward deck of the ship on a dark and cloudy day
   LR-pitch LC-brush
   FR-outwit FC-annoy

34. The stylish designer **turned the tables on the client** before the contract was signed for over five million dollars
   LR-dinner LC-mouse
   FR-advantage FC-snitch
References


CHAPTER 3

An arterial spin labeling investigation of cerebral blood flow deficits in chronic stroke survivors
Preface

As established in Chapter 1, there remains a good deal of uncertainty as to the neural correlates of auditory IP processing. As the current dissertation seeks to undertake an investigation of this issue, via the FMRI methodology, in both unimpaired and aphasic individuals, it is first crucial to understand the neurophysiological underpinnings of the FMRI signal, and how the neurophysiological state may be disrupted in individuals with aphasia subsequent to stroke. Thus, to lay the groundwork for a neuroimaging investigation of IP comprehension in Chapter 4, Chapter 3 first examines cerebral blood flow, a neurophysiological variable, among stroke survivors with aphasia. An indication of disrupted or decreased cerebral blood flow in this population will require special accommodation in Chapter 4 for this aberration, in order to attempt to appropriately measure an FMRI signal in this patient population.
An arterial spin labeling investigation of cerebral blood flow deficits in chronic stroke survivors

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ABSTRACT
Although the acute stroke literature indicates that cerebral blood flow (CBF) may commonly be disordered in stroke survivors, limited research has investigated whether CBF remains aberrant in the chronic phase of stroke. A directed study of CBF in stroke is needed because reduced CBF (hypoperfusion) may occur in neural regions that appear anatomically intact and may impact cognitive functioning in stroke survivors. Hypoperfusion in neurologically-involved individuals may also affect BOLD signal in FMRI studies, complicating its interpretation with this population. The current study measured CBF in three chronic stroke survivors with ischemic infarcts (greater than 1 year post-stroke) to localize regions of hypoperfusion, and most critically, examine the CBF inflow curve using a methodology that has never, to our knowledge, been reported in the chronic stroke literature. CBF data acquired with a Pulsed Arterial Spin Labeling (PASL) flow-sensitive alternating inversion recovery (FAIR) technique indicated both delayed CBF inflow curve and hypoperfusion in the stroke survivors as compared to younger and elderly control participants. Among the stroke survivors, we observed regional hypoperfusion in apparently anatomically intact neural regions that are involved in cognitive functioning. These results may have profound implications for the study of behavioral deficits in chronic stroke, and particularly for studies using neuroimaging methods that rely on CBF to draw conclusions about underlying neural activity.

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Introduction
While a great deal of research has investigated disruptions of neurophysiological systems in acute stroke (hours to days post-onset), very little work has examined how these systems may continue to be disordered in patients who are in the chronic stage of stroke (months to years post-onset). Research from the acute ischemic infarction literature indicates that cerebral blood flow (CBF) is typically disrupted in the neural regions that are directly infarcted as well as in proximal neural regions (i.e. Chalela et al., 2000; Detre, 2001). However, there has been scarce literature to date directly assessing the state of CBF in chronic stroke survivors. A focused investigation of CBF in chronic stroke is needed for several reasons; decreased CBF in neuroanatomically intact regions may contribute to cognitive deficits (e.g. Hillis et al., 2005; Love et al., 2002) and abnormal CBF may have an effect on the hemodynamic response, thus leading to difficulty interpreting neuroimaging results with this population (e.g. Ronakdarpoor et al., 2007; Fridriksson et al., 2006). The following sections briefly review what is known regarding the nature of CBF in stroke survivors, and present evidence as to why a study of CBF in chronic stroke is of vital importance.

CBF refers to the amount of arterial blood arriving at, or perfusing, an area of neural tissue within a given time (Buxton, 2002). This concept differs from cerebral blood volume (CBV), which refers to all the blood that occupies a volume of neural tissue at any given time, including venous blood and arterial blood destined to arrive at a more distal neural region. There is an intricate relationship between CBF and neural activity, with increasing regional neurological demands closely followed by increasing blood flow to that region; however, the exact parameters of this relationship remain unclear (Buxton, 2002). Evidence from the extant stroke literature suggests that CBF in stroke survivors may be deficient in two ways: (1) baseline CBF levels (measured in a resting state, in the absence of a cognitive task) may be abnormally low (e.g. Love et al., 2002), and (2) transit delays

⁎⁎ Studies were conducted under the approval of local Institutional Review Boards (at San Diego State University and the University of California, San Diego), with full understanding and consent of each participant, in compliance with HIPAA mandates.
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(the amount of time needed for arterial blood to reach and perfuse neural tissue) may be abnormally long (Fridriksson et al., 2006; Hillis, 2007; Hillis et al., 2005). When either of these disruptions occurs, regional baseline CBF levels may be inadequate to sustain tissue viability, but may be inadequate to support efficient cognitive or neurological functioning (Astrup et al., 1977; Love et al., 2002; Ni et al., 1994; Sekhon et al., 1994). This condition of diminished but not abolished baseline CBF is termed hyperperfusion (see Hillis, 2007).

To date, research that has examined CBF in stroke survivors has primarily focused on acute and sub-acute stroke, studied within hours to weeks following stroke onset. This research strongly suggests that regionally specific hyperperfusion may impair cognitive and behavioral abilities supported by those regions. Hillis et al. (2001a) reported that sub-acute stroke survivors showed a correlation between reading impairments and hyperperfusion (measured as decreased regional baseline CBF and increased transit delay times) in the left angular gyrus and left posterior middle temporal gyrus; regions which are known to contribute reading performance (Price, 2004). An additional study by Hillis et al. (2001c) reported a strong correlation between hyperperfusion in the posterior superior temporal gyrus and impaired word comprehension abilities during acute stroke. With regards to the interplay between perfusion and visual attention, Hillis et al. (2005) demonstrated a correlation between hyperperfusion in the right superior temporal gyrus and right angular gyrus with the experience of visual-spatial neglect in acute stroke. A study by Okada et al. (1999) supported a relationship between frontal cortical hyperperfusion and the development of dysarthria in sub-acute stroke (see also Hillis, 2002; Hillis et al., 2000, 2004).

In addition to hyperperfusion in acute and sub-acute stroke, aberrant CBF may endure in chronic stroke patients and may contribute to cognitive deficits. Specifically, Love et al. (2002) correlated hyperperfusion in the region of the angular gyrus with slowed reading abilities in a chronic stroke survivor. Crucially, in each of the studies reported above, regardless of how much time had passed since stroke onset, hyperperfusion was found in regions that appeared anatomically intact, as measured by traditional neuroanatomical imaging (e.g., T1- or T2-weighted clinical MRI). That is, the affected regions retained structural integrity but did not receive adequate CBF to support optimal neural functioning. In the chronic stroke case, Love et al. (2002) termed the anomalous areas “functional lesions.”

As well as its importance for cognitive and behavioral function, CBF is also a crucial factor in neuroimaging studies. Many neuroimaging studies with stroke patients have utilized the blood oxygenation level dependent (BOLD) technique (Ogawa et al., 1990; Ogawa et al., 1992). BOLD is sensitive to changes in deoxygenated hemoglobin concentration following local changes in cerebral blood flow (CBF), cerebral blood volume (CBV), and cerebral metabolism, resulting from underlying changes in neural activity (see Buxton, 2002, for review). Interpretation of the BOLD signal is predicated upon a tight neurovascular coupling relationship, such that increasing regional neural activity is closely associated with increasing CBF in that region. Researchers using BOLD imaging typically assume consistent neurovascular coupling across patients and brain regions, and this assumption allows for conclusions to be drawn about underlying regional neural activity based on differences in BOLD signal amplitudes between subject populations or experimental conditions.

The assumption of tight neurovascular coupling may be appropriate for young and healthy individuals, but this assumption is questionable in other populations. For instance, reports indicate that neurovascular coupling may be altered with age, changing the amplitude and shape of the BOLD response, even in healthy aging (Brodtkmann et al., 2003; D’Esposito et al., 2003; Hueftel et al., 2001). Additionally, delayed or abnormal BOLD responses have been reported in cerebrovascular diseases such as stenosis (narrowing of blood vessels), gradual artery occlusion, and stroke (Ronaldspaur et al., 2007; Carusone et al., 2002; Fridriksson et al., 2000; Roc et al., 2006). Given this evidence, it is reasonable to suggest that assumptions about neurovascular coupling obtained from healthy populations may not be valid in stroke survivors, thus confounding the interpretation of BOLD imaging studies with stroke survivors. Indeed, it is possible that CBF disruptions in patients with cerebrovascular disease underlie an atypical BOLD signal in these participants. If CBF is disrupted in stroke patients, an increase in local neural activity may not be accompanied by a swift regional increase in CBF, thereby leading to the aberrant or delayed BOLD response that has been reported in previous patient studies (e.g., Ronaldspaur et al., 2007; Fridriksson et al., 2006). Thus, commonly held assumptions for BOLD imaging might lead to errant interpretations about the neural underpinnings of cognitive functions in stroke survivors.

In sum, the vital role of CBF in cognition/behavior and in functional neuroimaging studies demands that this neurophysiological factor be a target of study in both acute and chronic stroke survivors for several reasons. First, CBF must be quantified objectively, given evidence that it may be abnormally prolonged in stroke (e.g. Fridriksson et al., 2006; Hillis et al., 2001a). Second, baseline CBF levels must be calculated in standardized units, to both compare these values to healthy controls and to monitor hyperperfusion during stroke recovery (Hillis et al., 2001b). Third, qualitative and quantitative patterns of CBF in stroke survivors must be compared to those of healthy participants, so that neuroimaging studies which rely on CBF as an indirect indicator of neural activity may be mindful of potential confounds in studies of stroke survivors. The current study undertakes this essential investigation of the state of CBF in chronic stroke survivors.

**Measuring cerebral blood flow with perfusion MRI**

In order to investigate CBF in chronic stroke survivors, an appropriate methodology is needed. Early studies of CBF were conducted using Positron emission tomography (PET), but the use of radiolabeled tracers limits the repeatability of this method due to safety concerns and cost (Chen et al., 2008). CBF has also been studied via dynamic contrast magnetic resonance perfusion-weighted imaging, a technique which measures the arrival rate and clearance of an injected intravenous contrast bolus (see Hillis, 2007); however, like PET, this method is also invasive. More recently, researchers have developed new magnetic resonance imaging techniques that allow higher spatial resolution data acquisition and more widespread implementation than that available with previous imaging protocols. Arterial spin labeling (ASL) is an MR methodology for perfusion measurement, in which the blood flowing into the brain is magnetically labeled using a radiofrequency inversion pulse (for a more detailed discussion of ASL, the interested reader is referred to Liu and Brown, 2007). This “tagged” blood serves as a bolus, which is then allowed to flow normally via arterial pathways into brain tissue. At a specified time after the inversion pulse, termed the inversion time (TI), an image is acquired (Fig. 1A). A control image in which arterial blood is not “tagged,” or inverted is also acquired in the same spatial location (Fig. 1B). The tagged image is subtracted from the control image to remove signal from static tissue. This subtraction leaves an image of the tagged blood that has arrived during time TI, and is weighted both by the local CBF and transit delay values. The time taken by blood in the leading edge of the tagged bolus to reach the neuronal capillary bed is known as the transit delay. Thus transit delay is a crucial variable to consider in ASL imaging; transit delays should be long enough to allow the tagged arterial bolus to reach and perfuse the capillary bed of the imaging region in order to accurately assess CBF.

Given evidence that transit delays may be protracted in stroke (e.g., Hillis et al., 2001a), one of the aims of our study was to directly examine transit delays in chronic stroke. Transit delays can be measured by a variety of neuroimaging methods; in the current study, a pulsed ASL (PASL) technique called FAIR (flow-sensitive alternating
inversion recovery; Kim, 1995; Kwong et al., 1995) was used, with the QUIPSS II modification (Wong et al., 1998) to minimize the transit delay sensitivity of the subtraction image. In this modification, a saturation pulse is applied to the tagging region at time T11, effectively producing a well-defined bolus of tagged blood of temporal width T11. The image of the brain region of interest is then acquired at time T12, where T12-T11 should be sufficiently long so as to allow the delivery of the entire tagged bolus to the imaging slices, i.e. longer than the longest transit delay. CBF can then be quantified in neural regions of interest (for a discussion of quantifying CBF with ASL, see Liu and Brown, 2007; Wong, 2005; Wong et al., 1997, 1999).

As discussed above, long transit delays allow the tagged arterial bolus to perfuse the imaging region, yet transit delays should not be so long as to allow a significant loss of signal in the bolus. This can be challenging as typical transit delays in healthy participants (which have been measured to be on the order of 1000 milliseconds or less; Wong, 2005) vary in different parts of the brain, depending on both the distance from the tagging region as well as vascular anatomy. This challenge becomes even more daunting when implementing perfusion imaging in participants who might have compromised cerebrovascularature, such as stroke survivors. In these cases, it is vital to consider whether these participants’ transit delays might be longer than current standard perfusion protocols anticipate, due to altered vascular pathways and collateral perfusion pathways (Liebeskind, 2003). If the T11 and T12 values are set such that tagged blood is not allowed adequate time to reach its destination, perfusion imaging will underestimate the true CBF value.

In addition to affecting the accurate quantification of CBF, prolonged transit times may have strong implications for BOLD fMRI imaging, which assumes a tight temporal relationship between underlying neural activity and a rapid cerebrovascular response in a region. Prolonged transit times in chronic cerebrovascular disease may underlie aberrant hemodynamic responses to stimuli during neuroimaging studies if these long transit times lead to a slowed vascular response to neural activity. (e.g. Ronaldarpour et al., 2007; Carusone et al., 2002; Fridriksson et al., 2006; Prabhakaran et al., 2007). This means that neural regions that are recruited during a cognitive task may appear hypovactive in BOLD studies among individuals with cerebrovascular abnormalities, since the BOLD signal is heavily influenced by CBF. Given the influence of transit delay times in CBF quantification, and in BOLD imaging, it is therefore essential to assess transit delay times in chronic stroke survivors and to determine whether transit delays differ between stroke and unimpaired populations.

The aim of the current study was to employ non-invasive ASL-FAIR neuroimaging to determine CBF transit delays and to quantify CBF in chronic stroke survivors, as compared to healthy individuals. The experimental protocol used in this study is described below; Experiment A compared the transit time values in three chronic stroke survivors with varying lesion sizes to those of both young and older unimpaired controls. Experiment B quantified CBF in the same three stroke survivors from Experiment A and a separate group of unimpaired controls using information about transit delays from Experiment A.
Materials and methods

Experiment A: transit delay measurement in chronic stroke survivors

Participants
Participants in Experiment A included three stroke survivors (demographics shown in Table 1a), 10 elderly controls (8 female, mean age = 71.1 years, SD = 7.35), and 4 younger controls (2 female, mean age = 26.3 years, SD = 8.38) (control demographics shown in Table 1b). Both young and elderly control participants were recruited from San Diego State University (SDSU) and the University of California, San Diego (UCSD) under both universities’ IRB protocols. All participants were deemed qualified to take part in this study if they had no history of prior head injury, were right-handed (handiness defined by 70% right-handed responses to Edinburgh handedness inventory; Oldfield, 1971), had no reported history of neurological impairments (in the case of stroke survivors, prior to stroke) or significant drug/alcohol abuse and had normal or corrected-to-normal vision and hearing. Participants were compensated for their participation.

Stroke survivors were participants in the Cognitive Neuroscience Laboratory (CNL) at SDSU. Stroke survivors were native English speakers with normal or corrected-to-normal auditory and visual acuity for age, negative history of both drug or alcohol dependence and psychiatric disorders (based on self or family report), and were right-handed prior to stroke (according to self or family report). All had left hemisphere damage with a single lesion site, predominantly in frontal lobe regions with some extension into temporal lobe regions (see detailed descriptions of lesion locations below and Table 1a). Stroke survivors each had been diagnosed with aphasia and were enrolled as ongoing participants at the CNL at the time of the current study. Aphasia diagnosis was based on the convergence of clinical consensus and the results of standardized aphasia examinations—the Boston Diagnostic Aphasia Examination (BDAE-version 2; Goodglass and Kaplan, 1972) and the Western Aphasia Battery1 (WAAB; Kertesz, 1982). Diagnostic results were consistent with expressive aphasia in these three stroke survivors. LH1, LH2, and LH3 presented to the CNL with clinical symptoms common to left hemisphere frontal lobe stroke; problems included word-finding, articulation, and less obvious comprehension deficits (as measured by the SOAP; Love and Oster, 2002). In addition to aphasic symptomatology, each patient presented with right-lateralized hemiparesis in the hand, arm, and leg. LH1 and LH2 were able to walk unaided by assistive devices, and LH2 used a leg brace and cane for ambulation. LH1 had moderate oral apraxia and dysarthria; LH2 had moderate oral apraxia without dysarthria; LH1 had no signs of oral apraxia or dysarthria. Based on standard assessments, all three stroke survivors were negative for visual agnosia or visual neglect. Clinical symptoms are summarized in Table 1a. While these three participants were commonly enrolled in studies at the CNL due to their aphasia, the purpose of this study was to investigate CBF in chronic stroke survivors. Thus, from this point forward, we do not focus on their aphasic symptoms in particular, nor do we specifically detail the relationship between aphasia and CBF. Rather, the current study aims to present data that addresses the neurophysiological status of CBF in chronic stroke, and we present data from these stroke survivors as representative samples from the chronic stroke population.

Table 1a
Demographics of three chronic stroke survivors with aphasia who participated in Experiments A and B: LH1, LH2, and LH3, including clinical symptoms and description of each participant’s lesion.

<table>
<thead>
<tr>
<th>Subject</th>
<th>Experiments in which Ss participated</th>
<th>Gender</th>
<th>Age at testing (years)</th>
<th>Years post onset</th>
<th>Hemiparesis?</th>
<th>Clinical Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>LH1</td>
<td>A and B</td>
<td>F</td>
<td>56</td>
<td>11</td>
<td>R weakness</td>
<td>Reading, repetition, comprehension, naming deficits, moderate oral apraxia and dysarthria, absent neglect or visual agnosia</td>
</tr>
<tr>
<td>LH2</td>
<td>A and B</td>
<td>M</td>
<td>45</td>
<td>5</td>
<td>R weakness, leg brace and cane for walking</td>
<td>Word-finding difficulties, articulation and comprehension deficits, moderate oral apraxia without dysarthria, absent neglect or visual agnosia</td>
</tr>
<tr>
<td>LH3</td>
<td>A and B</td>
<td>M</td>
<td>68</td>
<td>2</td>
<td>R weakness</td>
<td>Word-finding difficulties, articulation deficit, absent oral apraxia and dysarthria, absent neglect or visual agnosia</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Lesion</th>
<th>Lesion Volume (cm³)</th>
</tr>
</thead>
<tbody>
<tr>
<td>LH1</td>
<td>l. middle and posterior frontal lobe; anterior and middle superior temporal lobe</td>
</tr>
<tr>
<td>LH2</td>
<td>l. posterior frontal lobe; anterior and medial superior temporal lobe</td>
</tr>
<tr>
<td>LH3</td>
<td>l. inferior frontal lobe</td>
</tr>
</tbody>
</table>

Table 1b
Demographics of elderly and young control participants who participated in Experiment A and Experiment B.

<table>
<thead>
<tr>
<th>Subject</th>
<th>Experiments in which Ss participated</th>
<th>Gender</th>
<th>Age at testing (years)</th>
<th>Education (years)</th>
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<td>F</td>
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<td>20</td>
</tr>
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<td>ECA2</td>
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<td>62</td>
<td>18</td>
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<td>ECA3</td>
<td>A</td>
<td>F</td>
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<td>A</td>
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<td>24</td>
<td>17</td>
</tr>
</tbody>
</table>

1 The WAAB aphasia quotients and BDAE severity scores, respectively, were as follows: LH1-56.1, 1; LH2-72.7, 2; LH3-75.3, 3.5. The WAAB aphasia quotient uses a scale from 0-100, with higher numbers indicating less aphasic impairment; a score above 91.8 is considered normal. The BDAE severity level is based on a scale from 1-5, with higher numbers indicating less aphasic impairment; for example, a score of 5 denotes “minimal discernable speech handicaps” and “subjective difficulties” of the patient.
Each participant completed a neuroradiological exam during the course of his or her evaluation at the CRL. Anatomical scans were segmented into gray matter, white matter, and CSF for further analyses using FSL (Smith et al., 2004). Structural MRI (Spoiled Gradient Recalled [SPGR]) images demonstrating the main site of lesion for each patient are shown in Fig. 2. LHD1’s MRI indicated damage to anterior and medial portions of the left hemisphere, including portions of the middle and posterior frontal lobe and superior and middle temporal lobe, with sparing of parts of the posterior superior temporal lobe and most of the inferior temporal gyrus and anterior frontal lobe. LHD2’s anatomical MRI indicated damage to the left anterior cortical hemisphere, extending throughout the posterior region of the frontal lobe and anterior and medial portions of the superior temporal lobe, with sparing of parts of the posterior superior temporal lobe and most of the inferior temporal gyrus and the majority of the anterior frontal lobe. LHD3’s MRI showed more restricted damage to the left inferior frontal lobe with no temporal involvement. A time-of-flight MR angiogram is also shown for each

![Fig. 2. Neuroradiological and cerebral blood flow (CBF) images for each stroke survivor: Column A shows images from participant LHD1. Column B shows images from LHD2, and Column C shows images from LHD3. The top row shows a time-of-flight angiogram for each participant, with occlusion of the middle cerebral artery territory indicated by the arrow in each participant’s scan. The second and third rows show high-resolution (1 mm isotropic voxels) Spoiled Gradient Recalled (SPGR) images from sagittal and axial viewpoints, respectively. Sagittal views show each participant’s left hemisphere as affected by stroke. The bottom row shows whole-brain CBF for each participant (scale shown at bottom).](image)
participant in Fig. 2. Each participant demonstrated occlusion in the left middle cerebral artery territory (indicated by arrow in top row). Lesion volume was calculated by defining the area of the lesion on each participant’s structural MRI scan, which was converted to cc by multiplying the number of voxels encompassed by the patient’s lesion by voxel size. As noted in Table 1a, the volume of these participants’ lesions varied, but included large (LHD1), medium (LHD2), and smaller (LHD3) volumes. These patients were therefore included in the study as representatives of stroke survivors with varying lesion volumes.

Procedures for perfusion transit delay data acquisition

Neuroimaging data were collected with a General Electric Signa EXCITE 3 T scanner (GE, Milwaukee, Wisconsin) fitted with an 8-channel receive-only head coil. A structural imaging scan (SPGR) was acquired with the following parameters: FOV = 25 × 25 cm, TE = 3.1 ms, TI = 450 ms, TR = 8.0 ms, flip angle = 12°, voxel size = 1 × 1 × 1 mm, slices = 172. Perfusion data were acquired using a pulsed ASL sequence, ASL-FAIR, with scan parameters: TR = 3700 ms, TE = 3.1 ms, 17 slices, each 6 mm thick (1 mm gap between slices), number of repetitions = 60, and FOV = 22 cm. Note that the QUIPSS II pulse was switched off for the transit delay data acquisition. For each subject, data were acquired at 8 different TI values: 300, 600, 1000, 1400, 1800, 2200, 2600, and 3000 ms, to allow fitting of the perfusion inflow curve on a voxel-wise basis. Data were fit to the following equations from (Buxton et al., 1998):

\[
\Delta M(T) = \begin{cases} 
0 & : T < T_D \\
2M_0\alpha_{CBF}(T - T_D)e^{-(T - T_D)/\tau} & : T_D < T < T_D + T_D \\
2M_0\alpha_{CBF}e^{-T/T_D} & : T > T_D + T_D \\
T_D > T_D + T_D & : T > T_D + T_D
\end{cases}
\]

Where \(\Delta M(T)\) is the measured perfusion signal (i.e. surround subtraction of the tag/control image series; Liu and Wong, 2005). \(M_0\) is the equilibrium magnetization of blood, \(\alpha\) is the inversion efficiency (assumed to be 1), \(\tau\) is the temporal width of the bolus, and \(T_D\) is the TI of arterial blood, assumed to be 1.064 s (Lu et al., 2004). Data were fit for transit delay (TD) and bolus width (\(\tau\)). Data processing was performed in MATLAB® using software written in-house.

Results: Experiment A

Healthy control participants. Results from transit delay imaging are shown in Table 2. Mean transit delay values for gray matter are significantly higher in the elderly (mean 809 ms) as compared to young control group (mean 567 ms) (F(12) = 2.85, p = 0.01). Importantly, there is no significant difference in variance between elderly (SD = 138 ms) and young controls (SD = 156 ms) (F(9, 3) = 0.77, p > 0.05). These mean transit delay values are used to set appropriate QUIPSS II parameters for quantitative CBF measurement in Experiment B.

Stroke survivors. Results from transit delay imaging are shown in Table 2. LHD1’s data indicated a mean transit delay of 749 ms with a standard deviation of 422 ms in gray matter throughout the brain. A Crawford t-test (Crawford and Garthwaite, 2005) was used to compare data between each aphasic participant and each group of unimpaired control participants. The Crawford t-test of mean transit delays in gray matter demonstrated no significant differences between LHD1 and young controls (t(3) = 1.03, p = 0.05) or between LHD1 and elderly controls (t(9) = -0.41, p = 0.05). Additionally, a t-test of the standard deviations of transit delays showed no differences between LHD1 and young controls (t(3) = 1.35, p = 0.05) or between LHD1 and elderly controls (t(9) = 0.46, p = 0.05). This second comparison of standard deviations was performed due to the markedly greater standard deviation in all our stroke survivors, as compared to both young and elderly controls.

By contrast, LHD2’s data revealed that his transit delay mean was 1177 ms with a standard deviation of 508 ms in gray matter throughout the brain. A Crawford t-test of mean transit delays in gray matter revealed a significant difference between LHD2 and young controls (t(3) = 3.14, p = 0.05) and between LHD2 and elderly controls (t(9) = 2.13, p = 0.05). Additionally, a t-test of the standard deviations of transit delays showed differences between LHD2 and both young controls (t(3) = 2.33, p = 0.05) and between LHD2 and elderly controls (t(9) = 2.01, p = 0.05).

The mean transit delay of LHD3 was 890 ms with a standard deviation of 525 ms throughout gray matter. While a Crawford t-test of mean transit delays in gray matter revealed no significant difference between LHD3 and young controls (t(3) = 1.84, p = 0.05) or between LHD3 and elderly controls (t(9) = 0.53, p = 0.05), a t-test of the transit delay standard deviations did reveal significant differences between LHD3 and young controls (t(3) = 2.53, p = 0.05) and between LHD3 and elderly controls (t(9) = 2.32, p = 0.05). These findings crucially indicate that although LHD3’s mean transit delays are comparable to both control groups, this stroke survivor shows a much greater amount of variability than his healthy peers, a result that is not particularly surprising in a chronic stroke survivor.

Experiment B uses the transit delay results to set appropriate scanning parameters for the acquisition of quantitative whole-brain perfusion data from healthy controls as well as the three stroke survivors, allowing the investigation of CBF levels globally and within regions of interest.

Experiment B: perfusion measurement

Given prior research suggesting that CBF levels may be related to cognitive and behavioral deficits in acute and chronic stroke survivors (Hillis et al., 2001c; Love et al., 2002), Experiment B sought to quantify CBF levels throughout the brains of chronic stroke survivors in comparison to a set of healthy control subjects. As discussed earlier, for reliable perfusion imaging using a PASE sequence with the QUIPSS II modification, it is vital that the imaging parameters T1I and T2I are chosen appropriately such that the entire tagged bolus of blood is given time to arrive in the imaging slices before image acquisition (Wong, 2005). In our chronic stroke patients, the explicit measurement of transit delays in Experiment A ensures appropriate setting of T1I and T2I acquisition parameters for each subject.

Participants

Experiment B enrolled the same three stroke survivor participants as Experiment A, as well as seven different young unimpaired controls (5 female, mean age = 22, SD = 1.5, and 13 elderly unimpaired controls (4 female, mean age = 64.9, SD = 8.03) (demographics shown in Table 1b).

Perfusion data acquisition with optimal scanning parameters

In line with previous studies, T1I was set to 600 ms for all subjects (Wong et al., 1998), and T2I values were then selected based on the transit delay measurements of Experiment A, with the aim of satisfying the criteria that [T1I-TI1] should ideally be longer than the longest transit delay. However, the selection of a T1I value involves a
compromise between ensuring sufficient time for inflow of the tagged blood into the imaging slices (favoring a long T2), and avoiding excessive loss of the “tag” by T1 decay (favoring a short T2).

For the young and elderly control subjects, T2 was set to 1600 ms, since the transit delay results indicated that 1000 ms is sufficient for the delivery of the entire bolus of tagged blood to the majority of voxels. This is in good agreement with earlier research (Wong et al., 1998).

Each of the three stroke survivor groups was considered individually. Given that LH1’s transit delays were not significantly different from those of either control group, the same T2 was used with this participant as with the controls. By contrast, LH2 demonstrated significantly longer transit delays and larger standard deviation than either control group, and LH3 demonstrated transit delay means that did not differ significantly from either control group, but did show a significantly larger amount of variability in transit delay times than either control group. Thus, to select T2 times for LH2 and LH3 that were long enough to appropriately accommodate their transit delay results, while still trying to keep T2 as short as possible to avoid loss of the “tag” due to T1 decay, T2 times were set by adding the T11 value (600 ms) to the sum of each participant’s mean transit delay and standard deviation. This allowed us to incorporate information about how much transit delay means deviated from healthy populations, while also attempting to keep T2 reasonably short. Bearing these issues in mind, the following T2 values were selected for the FAIR-QUIPSS II experiment: for LH1, T2 = 1600 ms, for LH2, T2 = 2300 ms, and for LH3, T2 = 2000 ms.

Data were acquired with the same scanner used to collect the transit delay data. A FAIR-QUIPSS II sequence was employed with the following parameters: TR = 3000 ms, TE = 3.1 ms, T11 (i.e. QUIPSS II saturation pulse) = 600 ms (following Wong et al., 1998), 18 slices, each 6 mm thick (1 mm gap between slices), and FOV = 22 cm. There were 40 repetitions for T2 values of 1600 ms, and 100 repetitions for T2 values of 2000 ms (due to lower SNR for these higher T2 values).

Each participant also underwent a high-resolution anatomical scan with the same SPGR parameters as Experiment A. Anatomical scans were segmented into gray matter, white matter, and CSF using FSL (Smith et al., 2004). Perfusion data were analyzed within gray matter using MATLAB® and were overlaid onto each participant’s anatomical scan using AFNI software (Cox, 1996). In addition, a cerebral spinal fluid (CSF) scan and a minimum contrast scan were acquired for use in CBF quantification (see below). The CSF scan consisted of a single scan acquired at full relaxation (no inversion or saturation pulses), using the same slice prescription as the ASL scan and TE = 3.1 ms. The minimum contrast scan was acquired with TR = 2 s, TE = 11 ms to achieve little contrast between gray matter, white matter, and CSF. Two 8-interleave scans were acquired using the same slice prescription as the CSF scan.

Quantification of CBF
The FAIR-QUIPSS II data were used to compute a perfusion map by first taking the surround subtraction of the tag/control image series (Liu and Wong, 2005) and then averaging these data over all time points (repetitions) for each voxel. These maps were then corrected for inhomogeneities in the coil sensitivity profiles using the smoothed minimum contrast images (Wang et al., 2005) and subsequently converted to absolute units (ml/100 ml/min) using the signal from the lateral ventricles on the CSF image as a reference signal (Chaela et al., 2000).

During the quantification of CBF for the stroke survivors, data from any neural tissue deemed within the lesion boundaries was excluded from the whole brain analysis. CBF levels were quantified for each participant at the whole-brain level, and within left and right cortical hemispheres (again, not including lesion site among stroke survivors). We also were interested in exploring the cortical tissue bordering the lesion site, as numerous studies have implicated this region in (a) spontaneous recovery post stroke (Furlan et al., 1996), (b) the site with the potential for recovery via treatment thus rendering it the target for interventional therapy (Baron, 2001; Heiss, 2000) and (c) in some cases, spreading depression negatively affecting recovery (Selman et al., 2004). Given that studies from the acute stroke literature have noted that this region, referred to as the penumbra (see Fisher and Ginsberg, 2004; Hillis, et al., 2005), may be particularly susceptible to variations in blood flow, we present calculated CBF within each survivor’s penumbra in addition to other regional measurements.

Definition of the penumbra in stroke survivors
To systematically define the penumbra, lesion borders were outlined for each patient using his or her anatomical MRI. Next, a 2-voxel mask was delineated around the borders of the lesion, to define a penumbra region. Voxel size was dictated by the CBF data from the ASL-scan parameters, and measured 3.44 mm in the right–left direction, 3.44 mm in the anterior–posterior direction, and 6.94 mm in the inferior–superior direction. Thus each 2 voxel mask extended outwards from lesion boundaries by 6.88 mm in the right–left direction, 6.88 mm in the anterior posterior direction, and 13.88 mm in the inferior–superior direction (Fig. 3A). Each patient’s penumbra mask was copied and transposed to the right hemisphere (Fig. 3B) to examine within-brain CBF relationships in these regions of interest.

Results: Experiment B
Healthy control participants. Results from CBF quantification in young and elderly controls are shown in Table 3, including CBF means and standard deviations of each group. Mean CBF values for gray matter are significantly higher in the young vs. elderly control group across whole-brain (t(16) = 3.97, p = 0.005), left hemisphere (t(16) = 3.76, p = 0.01), and right hemisphere (t(16) = 4.02, p = 0.005). The literature indeed concurs with these findings: gray matter atrophy even in healthy aging has been associated with longer transit delays and lower levels of CBF (Afdhal et al., 2009; Parkes et al., 2004).

Stroke survivors. CBF quantification results from stroke survivors are illustrated in Fig. 2 (bottom row), which shows representative axial images of each patient’s CBF maps, calculated from the FAIR-QUIPSS II data. Regions of relative hypoperfusion are visually evident throughout the left hemisphere, particularly within peri-lesional penumbra regions, as compared to each participant’s CBF in the right hemisphere. Table 3
Table 3

CBF values (ml blood/100 g tissue/minute) for gray matter at whole-brain, hemispheric, and penumbra levels are shown for each stroke survivor participant. Data for young controls consist of mean CBF rates for whole-brain and hemispheric measurements. CBF ratios between left and right hemispheres (hemispheric CBF ratios) are shown for stroke survivors and young controls, and ratios between penumbra regions in the left hemisphere and a comparable region in the right hemisphere (penumbra CBF ratios) are shown for stroke survivors only. Paired t-test results for both young and elderly controls are shown for CBF comparisons between left vs. right hemispheres. Paired t-tests are shown for within-brain comparisons of all stroke survivors between: left vs. right hemisphere, and the 2 voxel perilesional region vs. the homologous region in the right hemisphere.

<table>
<thead>
<tr>
<th></th>
<th>LH1D</th>
<th>LH2D</th>
<th>LH3D</th>
<th>Young controls</th>
<th>Elderly controls</th>
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<tr>
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<td>28.4</td>
<td>71.1</td>
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</tr>
<tr>
<td>(ml/100 ml/min)</td>
<td>(32.1)</td>
<td>(44.1)</td>
<td>(41.4)</td>
<td>(18.3)</td>
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<td>(44.4)</td>
<td>(43.1)</td>
<td>(17.4)</td>
<td>(5.7)</td>
</tr>
<tr>
<td>Right hemisphere CBF</td>
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<td>30.9</td>
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<tr>
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<td>(39.4)</td>
<td>(14.6)</td>
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<td>t-test results: Left hemisphere vs. right hemisphere CBF</td>
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<td>p=0.0001</td>
<td>p&gt;0.0001</td>
<td>p&gt;0.0001</td>
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<td>0.82</td>
<td>1.08</td>
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<td>26.8</td>
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<td>Right hemisphere</td>
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<td>43.2</td>
<td>33.9</td>
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<td>–</td>
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<tr>
<td>penumbra CBF mean (SD)</td>
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<td>(45.5)</td>
<td>(35.7)</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>t-test results: Left hemisphere vs. right hemisphere penumbra CBF</td>
<td>p=0.0001</td>
<td>p&gt;0.0001</td>
<td>p&gt;0.0001</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td>CBF ratio</td>
<td>0.57</td>
<td>0.61</td>
<td>0.67</td>
<td>–</td>
<td>–</td>
</tr>
</tbody>
</table>

shows mean global (whole-brain), left hemisphere, and right hemispheric gray matter CBF values for all participants (inclusive of penumbra regions in stroke survivors), as well as CBF values within each stroke survivor’s left hemisphere penumbra and right hemisphere homologous regions. Data for young controls consists of mean gray matter CBF rates for whole-brain and hemispheric measurements.

To examine trends of CBF levels in stroke survivors and unimpaired controls, CBF ratios were calculated and are shown in Table 3. As is commonly used in the acute stroke literature (similar to Fridriksson et al., 2002), perfusion ratios may be employed to compare CBF at an inter-hemispheric level in acute stroke. These levels can help characterize the severity of hypoperfusion in the affected hemisphere, using the patient’s undamaged cortical hemisphere as a within-participant control. CBF ratios clearly indicate that both young and elderly control participants show comparable levels of CBF in both hemispheres, with a slight left hemisphere bias (young controls’ average ratio = 1.08, elderly controls’ average ratio = 1.06), whereas the stroke survivors show moderate degrees of right hemisphere CBF bias: LH1D’s ratio = 0.80, LH2D’s ratio = 0.76, LH3D’s ratio = 0.82. (Note, all hemispheric CBF values for stroke survivors include data from the penumbra region). These data indicate chronic left hemisphere hypoperfusion in each of these three participants, an expected finding given their cerebrovascular disorders.

Ratios of each stroke survivor’s CBF levels within the 2-voxel lesion penumbra and within the homologous region in the contralateral hemisphere are also shown in Table 3. (LH1D’s ratio = 0.57, LH2D’s ratio = 0.61, LH3D’s ratio = 0.67). It is noteworthy that the discrepancy in CBF between left and right hemisphere penumbra regions is more exaggerated than inter-hemispheric CBF differences in these stroke survivors. The fact that these ratios are lower than those of whole-hemisphere CBF levels indicates more pronounced hypoperfusion within the penumbra region of each stroke survivor.

- Tests were performed on each stroke survivor’s data, examining differences in CBF between the left and right hemispheres, and be-

tween the left hemisphere peri-lesional region and the right hemisphere homologous region. Results for participant LH1D indicated significantly greater right hemisphere CBF than left hemisphere CBF (t (4756) = 4.86, p=0.0001) and significantly greater CBF within the right hemisphere peri-lesional homologous area as compared to the left hemisphere peri-lesional area (t (1784) = 0.95, p=0.0001).

Results for participant LH2D indicated significantly greater right hemisphere CBF than left hemisphere CBF (t (6921) = 9.95, p=0.0001) and significantly greater CBF within the right hemisphere peri-lesional homologous area as compared to the left hemisphere peri-lesional area (t (1813) = 16.44, p=0.0001). Results for participant LH3D indicated significantly greater right hemisphere CBF than left hemisphere CBF (t (8506) = 5.31, p=0.0001) and significantly greater CBF within the right hemisphere peri-lesional homologous area as compared to the left hemisphere peri-lesional area (t (1558) = 11.18, p=0.0001). Implications of this hypoperfusion will be discussed below.

Discussion

The application of arterial spin labeling methods in this experiment demonstrated several important and previously unreported findings in chronic stroke survivors. In Experiment A, we used ASL to investigate CBF transit delay times in three chronic stroke survivors and compared their results with two groups of unimpaired control participants—young and elderly. In examining the control groups, we note that elderly controls exhibited significantly longer transit delay times in gray matter than their younger counterparts, although variability between these control groups was not significantly different. The longer transit delays are likely related to the significantly lower mean gray matter CBF in the elderly vs. the young controls, a finding which probably reflects some level of gray matter atrophy in the elderly control group (Aslanli et al., 2009; Vernooy et al., 2008). However most prior reports of arterial spin labeling perfusion MRI use T11 and T12 values that would minimize transit delay sensitivity for all control participants (Brown et al., 2007; Hendriks et al., 2004; Wong, 2005).

When we compared our three chronic stroke survivors to each control group, the data revealed protracted transit delays in one of our stroke survivors and significantly greater transit delay variability in another stroke survivor. LH2D and LH3D showed transit delay patterns that were significantly different from the patterns of both control groups, likely related to these patients’ compromised cerebrovascular systems. The differences we observed in transit delays between LH2D and LH3D as compared to older control participants demonstrated that longer transit delays and larger amounts of variability in transit delays among these stroke survivors are due to factors other than just increased age. Results from Experiment A therefore demonstrate the importance of determining individual transit delay times for participants with compromised cerebrovascular function prior to collecting CBF data for quantification or other purposes.

To our knowledge, the findings from Experiment A contribute the first quantitative report of baseline CBF transit delays using ASL-FAIR techniques with chronic stroke survivors. The general findings from Experiment A offer converging evidence with previous reports of slowed hemodynamic responses in patients with cerebrovascular diseases (Bonakdarpour et al., 2007; Carusone et al., 2002; Fridriksson et al., 2000; Roc et al., 2006). Bonakdarpour et al., Carusone et al., and Roc et al. present evidence of delayed BOLD responses in participants

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1 All t-test results for stroke survivors remained statistically significant (p<0.05, uncorrected) when only voxels were considered which fulfilled the following criteria: T11-T12 = transit delay. For example, for participant LH1D, this calculation resulted in a CBF map of voxels whose transit delay values were equal to or less than 1000 ms (calculated by subtracting the T11 of 600 ms from the T12 of 1600 ms).
with compromised cerebrovascular systems; our results which indicate prolonged CBF transit delays suggest that baseline hemodynamic irregularities may at least partially account for these aberrant BOLD results.

Experiment B used the transit delay data from Experiment A to select appropriate, personalized scan parameters for quantitative CBF scans in our stroke survivor participants. Given data from Experiment A that indicated abnormally long mean transit delays and/or an abnormally large amount of transit delay variability for stroke survivors LDL2 and LDL3, we selected T22 values of 2000 ms and 2300 ms, respectively, for acquisition of whole-brain FAIR-QUIPSS II data for CBF quantification. LDL1’s data from the first experiment suggested an optimal T22 of 1600 ms for CBF data collection in this participant, which was the value used for the unpaired control participants.

Such personalization of transit delay times during CBF data acquisition was necessary to ensure that the bolus of tagged blood had adequate time to reach neural tissue, thereby allowing us to collect cerebral perfusion data while controlling for the potentially confounding factor of extended transit delays. Had whole-brain perfusion imaging been performed with LDL2 and LDL3 with a more typical (and shorter) 1600 ms T22 that is typically used for unpaired participants, the data would have underestimated CBF. An underestimated CBF in some neural regions might have led us to conclude that these participants exhibited hypoperfusion in neural areas that in fact had extended transit delays.

Crucially, despite the use of carefully chosen ASL scan parameters in Experiment B, quantified CBF levels in each stroke survivor still indicated hypoperfusion in structurally intact portions of the left hemisphere. We note that hypoperfusion was observed in areas throughout the left cerebral hemisphere of each stroke survivor, yet this hypoperfusion was most dramatic in peri-lesional regions. CBF ratios of the entire left hemisphere to the entire right hemisphere (“hemispheric CBF ratios”) demonstrated lower CBF within the intact portions of the insularted left hemisphere as compared to the intact right hemisphere. These results sharply contrast with hemispheric CBF ratios from a group of unpaired young controls, who showed an average CBF ratio of approximately 1, with comparable CBF values in left and right hemispheres. This discrepancy in hemispheric CBF ratios between stroke survivors and young controls indicates chronic hypoperfusion throughout the structurally intact portions of the left hemisphere in each of the stroke survivors.

A particularly interesting finding in Experiment B concerns perfusion patterns in our chronic stroke participants within the peri-lesional region, known as the penumbra. The acute/sub-acute stroke literature frequently relies on CBF data from the penumbra region to assess whether this neural tissue will remain viable or progress to infarct in the hours following stroke onset (Fishier and Ginsberg, 2004; Schafer et al., 2003). As a reminder, this area has been linked to the acute stroke population to spontaneous recovery, has been the site of targeted intervention therapies, and has also been cited as a source of spreading depression which has been linked to a failure in recovery (Baron, 2001; Furlan et al., 1996; Heiss, 2000; Selman et al., 2004). Here, we find that pronounced hypoperfusion remains in the penumbra, even in the chronic stage of stroke, in the years post-onset. The finding of chronic penumbra hypoperfusion leads to the conclusion that this region of neural tissue need not be re-perfused to healthy levels (i.e. levels found in the intact right hemisphere) to remain neuroanatomically intact. Indeed, CBF ratios between the left hemisphere penumbra and a homologous region in the unaffected right hemisphere (“penumbra CBF ratios”) showed more profound levels of hypoperfusion than whole-hemisphere level CBF ratios. Thus, chronic hypoperfusion may occur to variable degrees within the damaged hemisphere of stroke survivors, and hypoperfusion may be more pronounced within the neural regions directly surrounding chronic infarct territory.

We note that hypoperfusion in our stroke survivors may be related to chronic occlusion of arterial pathways in the MCA territory and perfusion via collateral arterial channels (Derdyn et al., 1999; Hendrikse et al., 2004; Liebeskind, 2003; Wityk et al., 2002). It is possible that stroke survivors who experience greater levels of recanalization of arterial occlusion may not demonstrate hypoperfusion to the same extent as was observed in the current study (Schellingen et al., 2000; Soares et al., 2009). The relationship between degree of arterial occlusion and recanalization and hypoperfusion should be further investigated in chronic stroke.

Hypoperfusion and lesion size

The relationship between a participant’s lesion size and penumbra CBF ratio is particularly noteworthy. Participant LDL1 had the largest lesion among stroke survivors in this study and also showed the lowest penumbra CBF ratio, while participant LDL3 had the smallest lesion and showed the highest penumbra CBF ratio. We reiterate our analysis methods, which examined average CBF in the penumbra area and within-participant ratios of CBF between the lesion penumbra and each participant’s intact hemisphere. None of our analyses depended on the absolute amount of intact cortical tissue in any participants. We therefore strongly feel that evidence for reduced perfusion in LDL1 as compared to LDL3 is not solely due to a smaller volume of intact left hemisphere cortical tissue in LDL1. We contend that data from these two participants appear to support an inverse relationship between lesion size and penumbra CBF ratio. Further research with a larger sample size is required to more thoroughly explore the nature of any relationship between lesion size and cerebral perfusion.

Hypoperfusion and aphasia severity

While the main purpose of the current study was not to examine brain–behavior relationships between CBF and cognitive deficits, we do wish to note a relationship between CBF and cognitive symptomatology in our chronic stroke survivors. All three of our stroke survivors were diagnosed with varying severity levels of expressive aphasia. The results from Experiment B indicated that all three stroke survivors, despite their varying language deficits, exhibited comparable hemispheric CBF ratios. By contrast, we see a trend towards an inverse relationship between penumbra CBF ratio and aphasia severity: LDL1, who showed the most severe aphasic profile also showed the lowest penumbra CBF ratio, while LDL3, who showed the least severe aphasic profile showed the highest penumbra CBF ratio. LDL2, who showed an aphasic profile with a severity level that fell between those of LDL1 and LDL3, also showed a penumbra CBF ratio that fell between these two participants. While we acknowledge that the use of global measurements of perfusion like hemispheric or penumbra CBF ratios cannot fully detail the neurophysiological markers that contribute to a focal disorder like aphasia, this finding is intriguing and the relationship between regional CBF and cognitive deficits in stroke should be explored further in future research. Greater detail about the nature of CBF in chronic stroke survivors may be greatly beneficial to understanding the behavioral consequences of regional hypoperfusion, and such an investigation may elucidate some of the variability in this population.

Implications for neuroimaging

Chronic hypoperfusion as demonstrated in Experiment B has strong implications for the ways in which contemporary neuroimaging protocols are structured. While the precise mechanisms underlying the BOLD signal are still under investigation (Buxton, 2002), the signal represents the combination of the vascular and metabolic responses to activation. It is therefore likely that both hypoperfusion and extended transit delays in intact neural tissue will affect the BOLD
signal during FMRI studies with chronic stroke survivors. Despite this, relatively little research has investigated the neurophysiological consequences of chronic stroke on the BOLD signal. A study by Krawinkl et al. (2005), however, found decreased BOLD signal amplitude in sensorimotor and supplementary motor cortices of the stroke-damaged hemisphere, as compared to the undamaged hemisphere, of chronic stroke survivors (approximately 1–7 years post-onset) during a manual task. Importantly, the authors note that these neural regions were structurally intact among stroke survivors. From the results presented in the current study, it can be postulated that hypoperfusion of the structurally intact sensorimotor and supplementary motor cortices of the stroke survivors in Krawinkl et al.’s paper might explain their findings of reduced BOLD signal in these areas relative to the contralateral hemisphere. Similarly, a study by Prabhakaran et al. (2007) demonstrated reduced BOLD signal in hypoperfused cortical regions of chronic stroke survivors during a verbal fluency task. Chronic hypoperfusion may therefore account for or contribute to variability in the functional neuroimaging literature of stroke survivors (Caltzoni and Baron, 2003; Cheney and Smerer 2006; Heiss et al., 1999; Ward et al., 2003) given the reliance on the BOLD signal as an indicator of underlying neural activity. The present findings of hypoperfusion and prolonged transit delays in stroke survivors suggest that baseline CBF is compromised in these participants, thus potentially confounding BOLD studies that do not simultaneously measure CBF in this population.

While a good deal of research has investigated perfusion in acute and sub-acute stroke patients (e.g. Hillis et al., 2001a,c), the current study is one of very few studies to extend the study of CBF and hypoperfusion to chronic stroke. Our findings indicate that hypoperfusion may be an enduring, not naturally resolving feature of chronic stroke, the implications of which must be further studied. Future research with chronic stroke survivors should examine the correlations between behavioral/cognitive deficits and hypoperfusion, as has been done in the sub-acute and acute stroke literature. This is vital because we cannot assume that the relationship between hypoperfusion and cognition is the same in chronic vs. acute/sub-acute stroke survivors. It is well known that neural reorganization may occur following damage to neural tissue during stroke; therefore, a thorough investigation of the interplay between behavior/cognition, hypoperfusion, and neural reorganization in chronic stroke is needed. The present findings also extend the results from Love et al. (2002) who reported chronic hypoperfusion in a stroke survivor 16 years post-onset. However, the present study uses novel paradigms to measure transit delays and then incorporates these results to the parameters used for CBF data acquisition. These two components allow more precise and localized quantification of hypoperfusion in chronic stroke than previously employed methods.

Results from the current study call for additional investigation into the nature of the neurovascular system in populations with compromised cerebrovascularature. Increased CBF transit delays and hypoperfusion in chronic stroke survivors may have consequences for both behavioral and neuroimaging research within this population. Researchers using neuroimaging protocols with participants who have cerebrovascular diseases may draw misleading conclusions about underlying neural activity unless the altered vascular dynamics are taken into account. As demonstrated in the current study, significant adjustment of scanning parameters can be required when patient stroke survivors are scanned. Further research into the nature of CBF and cognitive functioning in stroke survivors is therefore needed to elucidate the complex interplay between neural activity, cerebrovascular status, and cognition in this population. Future studies should also investigate how CBF contributes to variability in both behavioral and neuroimaging studies in order to better understand and conduct such studies across multiple populations.

Acknowledgments

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References

CHAPTER 4

Neural indices of lexical access during idiom comprehension
Abstract

Prior research has consistently indicated that patients with aphasia demonstrate impaired off-line comprehension for idiomatic phrases, and Chapter 2 of this dissertation found real-time lexical access abnormalities in Broca’s aphasia during processing of these phrases. The current chapter further advances this discussion by examining the neural indices of lexical processing during idiom comprehension in individuals with Broca’s aphasia and their language-unimpaired peers. Prior neuroimaging studies of idiom comprehension with young, healthy listeners have reported bilateral neural recruitment during processing of these phrases, and neuropsychological studies have consistently found idiom comprehension impairments among individuals with left hemisphere damage. Therefore, the current study aimed to clarify the neural mechanisms which underlie processing of idiomatic phrases in auditory sentences, in both unimpaired listeners and in individuals with aphasia. Results indicated that unimpaired listeners recruit distinct neural regions for the processing of an idiom’s literal and figurative meanings, and evidence indicated that figurative meanings were neurally processed in advance of literal meanings. In the patient sample, neural markers of processing for both meanings associated with idioms were delayed as compared to the unimpaired control participants. In addition, patients demonstrated unique loci of neural recruitment during idiom processing, with recruitment occurring in peri-lesional areas and right hemisphere homologues of language processing regions of the brain. These results provide detail about the neural idiom processing in aphasia and suggest that patients with aphasia recruit non-ideal
brain regions to process these phrases. In addition, this work extends the findings from Chapter 2 in establishing delayed lexical processing of idiomatic meanings in aphasic patients, here at the neural level.
Early neurolinguistic research established the essential role of the left hemisphere in language comprehension and production\(^8\) (e.g. Broca, 1861; Wernicke, 1874). However, more contemporary neurolinguistic work has suggested that other, non-syntactic, aspects of language may be preferentially served by the right hemisphere, such as figurative, or non-literal, language (e.g. Brownell et al., 1995; Winner & Gardner, 1977). Figurative language refers to phrases or expressions whose meanings are unrelated to the literal interpretation of the phrase’s constituent words (see e.g. Cacciari & Tabossi, 1988; Zempleni et al., 2007a). For example, the metaphor “have a heavy heart” means that someone is sad, although this meaning could not be deduced from the individual constituent words of the phrase. Within the class of figurative phrases are idioms, metaphors, and similes. In a seminal study, Winner and Gardner (1977) demonstrated a comprehension impairment for metaphors among patients with right hemisphere damage. Since this study, other researchers have reported impaired comprehension among right-hemisphere-damaged patients for other types of non-literal language (see Giora et al., 2000; Brownell et al., 1995) However, upon closer investigation of the neural bases of figurative language processing, there emerges a unique dissociation of neural laterality for different types of figurative expressions. While the right hemisphere has been linked to processing of indirect requests, metaphors, and sarcastic language, a good deal of evidence from both neuroimaging and patient studies strongly suggests that the left hemisphere subsumes idiomatic phrase (IP) processing (e.g. Hillert & Buracas, 2009; Papagno et

\(^8\) This is true for approximately 98% of the population. The remainder have language represented bilaterally or, even more rarely, in the right hemisphere.
Neural Bases of Idiomatic Processing

While a full review of the IP literature beyond the psycholinguistic evidence presented in Chapter 1 is beyond the scope of the current write-up, the important characteristics of IPs as they relate to the current study is presented below. The interested reader is referred to (Glucksberg, 2001; Titone & Connine, 1994); and (Cacciari & Tabossi, 1993), among others for more detailed information. As discussed in Chapters 1 and 2, many IPs are ambiguous as they can potentially denote either a literal or a figurative meaning. The present study investigates the neural underpinnings of lexical processing for each of these meanings. As discussed earlier, patients with aphasia due to left hemisphere damage have been demonstrated to have comprehension impairments for IPs (Tompkins et al., 1992; Papagno et al., 2004; Cacciari et al., 2006; Papagno et al., 2006; Papagno & Caporali, 2007). In fact, several of these studies found that while damage to either the left or right hemisphere resulted in impaired IP comprehension as compared to healthy individuals, left hemisphere damaged individuals were more impaired than their right hemisphere damaged peers (Tompkins et al., 1992; Papagno et al., 2006). These patient reports strongly suggest a role of the left hemisphere in IP comprehension.
In addition to the patient literature, there is yet further reason to suspect left hemisphere involvement during idiom comprehension. As discussed earlier and in Chapters 1 and 2, IPs are argued to be represented in the lexicon and are associated with multiple meanings: a figurative meaning of the IP as an entire phrase and literal meanings that are associated with each constituent word in the IP. Because they are associated with more than one meaning, IPs may be similar to single-word lexical ambiguities (see Swinney, 1979; Onifer & Swinney, 1981) for a discussion of the properties of lexical ambiguities). If indeed IPs are comparable to lexical ambiguities, then left hemisphere mechanisms are predicted to underlie their processing. Prior literature indicates that the left hemisphere helps to select the contextually-appropriate meaning of a lexical ambiguity, and then works to maintain that meaning for integration into ongoing context (see Swinney & Love, 2002; Jung-Beeman, 2005). Further, it appears that left hemisphere damage in the frontal lobe will impair processing of lexical ambiguities (e.g. Swinney et al., 1989; Swaab et al., 1998), which suggests that the left hemisphere plays an important role in resolving lexical ambiguities during comprehension. The current study will investigate whether left frontal neural regions are similarly implicated in comprehension of ambiguous IPs.

**Neuroimaging Studies of Idiom Comprehension**

Along with prior patient studies and the literature of single-word lexical ambiguities, several neuroimaging studies provide more detail regarding the neural mechanisms of IP comprehension. Here, the review of these studies is limited to those
which have embedded IPs within sentence contexts, as this most closely mirrors the experimental paradigm in the current study. Researchers who have studied IP comprehension via neuroimaging methodologies have utilized a variety of experimental tasks to test idiom understanding throughout an experiment, including sentence-picture matching (Romero Lauro et al., 2008; Oliveri et al., 2004; Rizzo et al., 2007), sentence meaningfulness decisions (Hillert & Buracas, 2009), and probe word-sentence relatedness judgments (Zempleni et al., 2007a). A summary of these different neuroimaging studies, the methodology used in each, and the main findings are shown in Table 4-1. To briefly summarize and concatenate these results, researchers report recruitment of these bilateral neural regions for the comprehension of IPs: inferior frontal gyri (BA 45 and 47), middle temporal gyri (BA 21), and dorsolateral prefrontal cortex (Brodmann area [BA] 9). FMRI studies also indicate activation of these left hemisphere regions during IP comprehension: inferior frontal gyrus (BA 44, 45, and 47), superior frontal gyrus (BA 8), middle frontal gyrus (BA 11 and 47), medial frontal gyrus (BA 8 and 9), middle temporal lobe (BA 22), and angular gyrus. Lastly, the following right hemisphere regions have been reported to be involved in IP comprehension: middle temporal gyrus (no BA listed) and temporal pole. Overall, prior neuroimaging studies of IP comprehension implicate many regions of left hemisphere language networks in this process (Hickok & Poeppel, 2007; Poeppel & Hickok, 2004).

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Insert Table 4-1 about here.
**Issues in prior FMRI investigations**

While previous neuroimaging studies help outline the neural regions involved in figurative processing of IPs, it is important to qualify these results with the understanding that prior studies have been quite heterogeneous with respect to the types of stimuli, methods, and approaches utilized to studying IP comprehension.

**Stimuli**

Differences in the classes of stimuli included in a study (e.g. ambiguous or unambiguous IPs, varying strengths of context to disambiguate an IP’s intended meaning) may certainly account for some of the differences in neural recruitment patterns across studies. In addition, of the neuroimaging studies cited above, only (Hillert & Buracas, 2009) utilized auditory presentation of idiomatic sentences, while the remainder of the studies employed visual stimuli presentation. The modality of presentation may affect the ways that participants process stimulus input (Holcomb & Neville, 1990; Carpentier et al., 2001) and the time course of processing (e.g. Friederici, 2002). Additionally, in several of the aforementioned neuroimaging studies of IP comprehension, the authors did not solely employ ambiguous IPs (Hillert & Buracas, 2009; Romero Lauro et al., 2008; Oliveri et al., 2004; Rizzo et al., 2007), and
thus did not investigate neural differences between processing for the figurative versus the literal interpretation of an IP.

Methods

In addition to potential limitations with respect to their stimuli, all of the above-listed neuroimaging studies of IP comprehension have utilized meta-linguistic tasks, which may affect the neural signature of processing for these stimuli (Love et al., 2006). For instance, a meta-linguistic task may lead participants to devote more attention to a particular aspect of a stimulus, which may in turn alter the way in which that stimulus is processed (e.g. participants may consciously reflect on particular aspects of the stimuli, which could affect neural processing demands and resources; see Shapiro et al., 1998).

Approach

It is important to note also that alongside the aforementioned limitations of contemporary neuroimaging studies of IP comprehension, studies to date have primarily enrolled young, healthy participants, with the mean age of participants being 25 yrs (see Table 4-1). As the current study seeks to investigate the neural indices of lexical access during IP comprehension across language-impaired and language-unimpaired populations, it is imperative to investigate this question across ages. This is because a good deal of research indicates changes in the BOLD signal and/or neural recruitment with age (e.g. D’Esposito et al., 1999; Fridriksson et al., 2006). Thus, in
order to ascertain abnormalities in neural recruitment among patients with aphasia, these patients must be compared to their peers. At the same time, however, this study will generate novel information about the neural bases of IP processing in aging, as this process will be examined in unimpaired young and older adults.

**Aims of the Current Study**

The current study has three specific aims. First, this study seeks to augment the existing literature regarding the neural bases of IP processing in healthy individuals. Here, the focus is exclusively on comprehension of ambiguous IP, which may potentially be interpreted either figuratively or literally, based on the context into which they are embedded. For instance, an ambiguous IP such as “hit the sack” (underlined below) can be interpreted either figuratively (as in example 1) or literally (as in example 2).

1. The toddler in a dinosaur shirt \textit{hit the sack} at 8 o’clock.
2. The toddler in a dinosaur shirt \textit{hit the sack} with a fist.

This study will investigate whether there are distinct patterns of neural recruitment for IPs that are biased towards a figurative interpretation, as compared to IPs that are biased towards a literal interpretation. The stimuli in this experiment are designed in such a way as to elicit differential neural activation based on the intended meaning of an IP (see below). In this way, this study will hone in on the neural regions
which are responsible for the processing of IPs in figurative versus literal contexts. However, as discussed earlier, evidence from the psycholinguistic literature suggests that figurative and literal meanings associated with IPs may be processed on slightly offset time scales. Thus, the current neuroimaging experiment is designed to examine the neural signatures of this temporal discontinuity. That is, this study concentrates not just on elucidating which brain regions serve literal and/or figurative processing of ambiguous IPs, but also when certain neural areas are engaged in IP processing.

The second aim of the present study is to directly compare the neural indices of IP comprehension in three populations: young and older healthy control participants, and stroke survivors with left hemisphere damage and aphasia. As discussed earlier, FMRI studies of IP comprehension of which we are aware have enrolled young individuals, and it is unclear if the neural signatures of IP comprehension remain stable throughout the lifespan. Additionally, by enrolling a control group comprised of older, healthy adults, age-related differences in neural activity during IP comprehension may be controlled.

This study’s third aim stems from numerous patient reports of impaired IP comprehension among individuals with aphasia. Although these studies demonstrate that IP comprehension is impacted in aphasia, the specific neural networks that are enlisted during IP comprehension in these individuals remain underspecified. Additionally, by comparing patterns of neural activity during IP processing in each patient with respect to his or her IP comprehension performance, we may be able to discern how patterns of neural recruitment in these patients ultimately impact IP
comprehension outcomes. At the same time, this neuroimaging study will investigate whether the *temporal signatures* of IP processing differ between patients and controls. As Chapter 2 of this dissertation indicated that patients with chronic neural damage (greater than 6 months post-onset) and Broca’s aphasia show *delayed* processing of lexical items, we may see evidence of this delay in the neural correlates of IP processing among our patients with this sub-type of aphasia. As was described in Chapter 3, some aphasic individuals show slowed cerebral blood flow, which may in turn delay the BOLD signal. Therefore, this study will investigate the two potential sources of slowed neuronal signal in the aphasic participants.

Lastly, although not a specific aim of the current study, it is worth noting a particular methodological approach that will be utilized here. As discussed above, the majority of prior neuroimaging studies of IP comprehension have presented these phrases in isolation, apart from sentence context. The current study, by contrast, utilizes ambiguous IPs that are embedded into natural sentence contexts, with the goal of elucidating the time course of neural processing that underlies automatic IP comprehension in this more naturalistic setting.

**Methods**

**Participants**

*Unimpaired participants*

Twenty healthy individuals participated in this study. Participants were enrolled if they were had no contraindications for participating in neuroimaging
research, were native English speakers (no exposure to a foreign language prior to age 6), had normal-to-corrected vision and hearing, and had no history of neurological or psychiatric diagnoses, learning disorders, head injury, or substance abuse. Data from three individuals were excluded from the analyses reported here; one was excluded due to uncorrectable motion artifacts and two were excluded due to failure to meet the inclusionary criteria. The remaining 17 participants ranged in age from 22-62 years old. In order to examine possible differences in IP processing as a factor of aging, participants were categorized into two groups according to age. The younger group (YNC) contained 8 participants, ranging in age from 22-30 (mean age = 25.8, SD = 3.4; 3 female, 5 male). The older group (AMC) contained 9 participants, and ranged in age from 40-62 years old (mean age = 52.1 years, SD = 7.9; 4 female, 5 male). All participants were right-handed, indicated by self-report and scores of at least 70% right-handedness on the Edinburgh handedness inventory (Oldfield, 1971). Participants received $40 or college course extra credit for participation. Participants provided informed consent.

**Aphasic Patients**

Eight individuals with chronic aphasia participated in the current study. Each individual had sustained neural trauma subsequent to a cerebrovascular accident (CVA, commonly known as stroke) minimally 6 months prior to participation. Diagnostic testing confirmed that five of these participants were classified as having non-fluent Broca’s aphasia (details of test results are in Table 4-2), and three were
classified as having Anomic aphasia. All participants met the criteria for participation in neuroimaging studies. Two participants were excluded from the final analyses as one participant was unable to complete the study due to fatigue. Data from one other patient were removed due to uncorrectable motion artifact. The remaining 6 participants ranged in age from 35-60 years old (mean age = 53.2, SD = 9.8; 1 female, 5 male), and the time since stroke ranged from 23-107 months (mean time post-onset = 79.5 months, SD = 50.1; see Table 4-2 for patient demographics). Participants provided informed consent and completed a post-consent checklist to ensure understanding of their experimental rights and received $40 for their participation. High-resolution (spoiled gradient echo [SPGR]) MRI images from each aphasic patient, showing location and extent of neural damage, are shown in Figure 4-1. This study was approved by Institutional Review Boards of the University of California, San Diego and San Diego State University.

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Insert Table 4-2 about here.

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Insert Figure 4-1 about here.

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Materials
Stimuli in this experiment were auditory sentences that contained ambiguous IPs. Forty ambiguous IPs were chosen, each with a plausible literal or figurative interpretation. IPs were three words long, with a V + NP form (e.g. *hit the sack*). We constructed minimal pair sentences for each IP (80 items total): one sentence disambiguated the phrase towards its figurative meaning (3), and one disambiguated the phrase towards its literal meaning (4). These matched sentences were identical except for the disambiguating phrase (immediately following the IP, underlined in 3 and 4). Sentence length and syntactic complexity were controlled across items.

3. The toddler in a dinosaur shirt hit the sack at 8 o’clock after a long day of playing outside

4. The toddler in a dinosaur shirt hit the sack with a fist after a long day of playing outside

Also included in the stimuli were 40 “filler” auditory sentence stimuli. These sentences varied in length and complexity from the experimental idiom stimuli, in order to avoid participant expectancy effects (See Appendix 4-1 for a full list of stimuli). Ten of these filler sentences contained an IP, but idioms were varied in structure and did not all have the form V + NP. All auditory sentence stimuli were recorded by a female, native English speaker at a normal speech rate (5.19)

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9 Verb + Noun Phrase
syllables/second for both literally- and figuratively-biased sentences). In total, there were 120 stimuli: 80 experimental items and 40 filler items.

*Design:* In this event-related FMRI experiment, four lists were created, each lasting 6 minutes 40 seconds. Within each list, 30 stimuli were pseudo-randomized, with the stipulation that no more than three occurrences of the same type (e.g. literally-biased sentences) could be presented sequentially. This study used a within-subjects design, so that each participant received all conditions in the same scanning session. As described below, although participants heard IPs in both figurative and literal biasing conditions in the same experimental session, exposure to these two conditions was separated by an intervening task.

**Task Design and Procedure**

*FMRI Task*

Participants lay supine in the MRI scanner during the study, and motion was limited and discouraged by fitting foam padding snugly around each individual’s head inside the head coil. A screen was placed at the foot of the scanner bed, and a mirror was attached to the head coil to allow participants to view visual materials. We presented all stimuli via Presentation software (Version 13.0, neurobs.com).

Participants in this study completed auditory listening and probe word verification tasks. Individuals heard each auditory sentence stimuli, one at a time, in an event-related FMRI paradigm. Following each sentence, a visual word appeared on the screen at the foot of the scanner bed, and the participant indicated via a binary
button response whether that word had been present in the immediately preceding auditory sentence. For instance, after hearing example 3 above, the participant might see the word “TODDLER,” to which a participant should indicate that, yes, this word was contained within the preceding sentence.

This simple probe verification task was selected for two main reasons. First, research has demonstrated modulations in the BOLD signal as a function of task demands for sentence processing FMRI tasks (Love et al., 2006). Specifically, this earlier study found greater recruitment of neural regions that are typically associated with language processing (BA 44 and 45) as task demands increased. In order to reduce potential contributions to the FMRI signal from difficult task demands, we selected this straightforward probe verification task. Second, this task was used to investigate neural processing of IPs in stroke survivors with aphasia, and we thus chose a task that would work with this special population without excessively taxing working memory or processing resources (see, e.g. Caplan et al., 2007). In addition, to reduce any potential differences in cognitive processing for “yes” vs. “no” responses, all visual probe words for idiomatic stimuli were designed to elicit a “yes” response. By contrast, all probe words that were paired with filler stimuli were designed to elicit a “no” response. As several filler items contained IPs, the decision to make all experimental stimuli verifications affirmative should not draw participants’ attention to the experimental manipulation in this task. To balance task complexity across experimental items, half of the affirmative verification probe words were drawn from the initial components of the sentence, prior to the IP, and the other
half of the affirmative probe words were taken from the latter portion of the sentence, following both the IP and the disambiguating phrase.

All participants received all conditions during this experiment. Participants heard half of the stimuli (two of the four experimental lists), performed an unrelated task and scan, and then heard the remainder of the stimuli (the remaining two lists). Importantly, to decrease exposure effects, as participants heard each IP twice during this study (once in a figurative context and once in a literal context), participants only encountered each IP once during the first half of the experiment, and then again in the second half of the experiment, after performing the unrelated task. During debriefing following the experiment, none of the participants remarked on the repetition of IPs in literal and figurative contexts.

**Image Acquisition Parameters**

MRI images were acquired at the University of California, San Diego’s Keck Neuroimaging Center which has a 3T GE Signa HDx MR scanner (Milwaukee, Wisconsin) and an 8-gradient head coil. A high resolution anatomical scan (FSPGR; TR = 7.772 msec; TE = 2.976 msec; flip angle = 12°; FOV = 256 mm; matrix 256 x 192; 172 sagittal slices, resolution = 1mm³ voxels) was obtained for each participant for anatomical localization. Two 2D FLASH sequences were collected to estimate magnetic field maps and were collected to be used in post-processing to correct for geometric distortions. For functional imaging scans, whole-brain T2*-weighted axial images were acquired with a gradient echo planar imaging pulse sequence (TR = 2000
msec; TE = 30 msec; 32 interleaved slices; slice thickness = 4mm; flip angle = 90°; FOV = 240mm; matrix = 64 x 64, in-plane resolution = 3.75mm²). Each sentence of the comprehension task was time-locked to the onset of a TR. Each of the four experimental runs included 200 acquisitions and was 6:40 in length.

**FMRI Pre-Processing Analysis**

FMRI data were preprocessed and analyzed using Analysis of Functional NeuroImages (AFNI; http://afni.nimh.nih.gov/afni) and FSL (http://www.fmrib.ox.ac.uk/fsl). An in-house script corrected for geometric distortions prior to further analyses, using the 2D FLASH sequences and the FSL FUGUE program. Automated motion correction and slice-timing correction were performed, with each volume in a time series co-registered to the middle four volumes of the task run. Data were smoothed at FWHM = 8, and all datasets were transformed to standardized space (N27 atlas, http://afni.nimh.nih.gov/afni).

**Off-Line Task of Idiom Comprehension**

In order to assess each participant’s understanding of IPs in sentence contexts, patients completed an off-line comprehension task outside of the scanner, after completing the FMRI task. While many off-line IP comprehension studies use idiom-picture matching designs (e.g. Papagno et al., 2004; Cacciari et al., 2006), the current study utilized a different form of off-line IP assessment. As discussed earlier, a pictorial representation of a literal interpretation of an idiomatic item may be very
specific (e.g. a boy striking a bag, as in example 4 above), while a much wider possible range may exist for pictorial situations to represent the figurative interpretation. Thus, the figurative picture may be more cognitively taxing to decipher than the literal picture (Tompkins et al., 1992), and this extra cognitive load may confound results that indicate differential figurative or literal processing of IPs.

Here, participants completed an aural IP verification task, which was described in Chapter 2. Briefly, participants heard a sentence with an embedded IP that was biased either towards a figurative or literal interpretation, were given a possible definition for the IP, and were asked whether that definition was correct for the present sentence. This task included 20 IP stimuli, separated into lists that were counterbalanced for condition. That is, an IP was embedded in a figuratively biasing context in one list and a literally biasing context in the other list. Participants were administered the two lists with at least one week in between sessions.

In addition to administering the task to the aphasic participants in this study, recall that a group of older, unimpaired participants likewise completed the IP verification task, as described in Chapter 2. These data will be discussed with respect to the present study, as the off-line task in Chapter 2 is the same one administered here and data from these older control participants can provide a baseline for normal performance on this task. For comparison purposes, this off-line task was also administered to a separate group of young, language-unimpaired individuals who met the above inclusion criteria (N = 83, mean age = 21.5, SD = 2.7). Results from this
young participant group will be employed to determine any age-related differences in performance on the task.

FMRI Analyses of Individual Participant Data

Unimpaired Participant Analysis

Individual-level data from the unimpaired control groups were analyzed in AFNI, using a deconvolution analysis in the 3dDeconvolve program. Seven piecewise linear splines (“tent functions”) were used to estimate the hemodynamic response function (HRF) following the offset of the disambiguating phrase in each sentence. Upon hearing this phrase, participants had received enough information to determine whether each IP should be interpreted literally or figuratively, and it was hypothesized that modeling the HRF at this point would reveal neural processing differences between the two interpretations of an IP. Here, the piecewise linear spline functions modeled the HRF from 0-12 seconds following the offset of the disambiguating phrase (the 6 TRs immediately following this offset; see Figure 4-2).

Data were then submitted to multiple regression analyses, which included stimulus HRF parameters, six motion parameters (three rotation and three displacement variables), and linear, cubic, and quadratic trends of no interest. Results from these regression analyses were converted into percent BOLD signal change values by dividing each regression weight by the voxel-wise global mean activation estimates. The resulting datasets represented percent BOLD signal change for each participant, during each HRF time segment (as prescribed during the tent function
deconvolution). These datasets were transformed to standard space and were used in all further analyses.

Insert Figure 4-2 about here.

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**Aphasic Patients**

Analysis procedures for the aphasic participants were nearly identical to the data processing procedures used for the unimpaired participants. With the patients, however, 10 piecewise linear splines (“tent functions”) were employed to estimate the HRF at the offset of the disambiguating phrase. Here, the time span over which the HRF was modeled was expanded for this population, due to a body of recent work which has implicated slowed cerebral blood flow in chronic stroke survivors (Chapter 3; see also (Bonakdarpour et al., 2007; Fridriksson et al., 2006). This work suggests that the BOLD signal in chronic stroke may be delayed as compared to healthy individuals, so by extending the “time window” of analyses for the aphasic stroke survivors in this study, we aimed to accommodate any potential delays in BOLD signal peak in this population.

Patient data from the deconvolution analysis were likewise submitted to multiple regression analyses, which included HRF parameters, the six motion parameters, and the trends of no interest. Results from the regression analyses were converted to percent signal change for each HRF time segment. All patient datasets
were analyzed and are reported in native space, and were not registered to standard anatomical templates. The decision to analyze data in native space was motivated by the large lesion sizes of many of our patients, which often results in distortion of intact neural tissue during typical algorithm-based registration procedures.

**Whole-brain analyses**

*Unimpaired Participants*

**Inter-group Analysis**

Whole-brain analyses of data were conducted in two stages. First, data from all unimpaired participants were analyzed to detect differences in BOLD signal between the two groups (AMC vs. YNC), collapsed across HRF time segments. A t-test (3dttest) was performed and a cluster threshold was applied to the results to control for multiple comparisons and correct against Type I error. A cluster threshold of $p<0.00001$ was applied with an effective alpha $= 0.01$ and a minimum cluster size of $135 \, \mu$L. This inter-group analysis was performed because we anticipated differences in neural recruitment during IP processing between these two groups, based on earlier research which suggests changes in neural and/or cognitive processing with age (see above; (D’Esposito et al., 1999; Fridriksson et al., 2006). To preface the results, the groups did indeed show significantly different patterns of neural activation, and so further analyses were restricted to within-group comparisons.

**Intra-Group Analysis**
Data were analyzed within each unimpaired group to determine the effects of biasing condition (literal vs. figurative) on neural activation. Here, data from each group (AMC and YNC) were submitted to a separate repeated-measures ANOVA, with condition (literal vs. figurative; fixed effect), HRF time segment (tent number; fixed effect), and subject (random effect) as factors. A cluster threshold was applied to the results from each ANOVA to guard against Type I error. A cluster threshold of \( p < 0.005 \) was applied, resulting in a minimum cluster size of 1161 \( \mu \text{L} \), with the exception of the cluster threshold for the main effect of time. Because a typical hemodynamic response in healthy individuals fluctuates dramatically over a 6-8 second period following stimulus presentation (e.g. Logothetis et al., 2001) a cluster threshold of \( p < 0.005 \) would be too weak to delineate separate clusters. For the main effect of time, we instead applied a cluster threshold of \( p < 0.00001 \), resulting in a minimum cluster size of 135 \( \mu \text{L} \).

**Aphasic Participants**

Data from the aphasic participants were analyzed at the individual level only, in order to detect effects within each subject of condition (literal vs. figurative) and HRF time segment. Here, several analyses were conducted to ascertain the loci and time course of literal and figurative processing for IPs in auditory sentences. First, a t-test was performed between conditions, collapsed across all 10 HRF time segments. This first analysis was planned to detect HRF differences between the two conditions (literal and figurative biasing context), over a generous amount of time after the...
sentence segment of interest. Then, these 10 time segments were divided equally, and a t-test was performed between conditions within the first 5 HRF time segments, and likewise another t-test was performed between conditions within the second 5 HRF time segments. These analyses were performed in order to provide temporal localization for any differences between conditions, while still preserving some power by examining a reasonably long time period.

Analyses were limited to the 3 t-tests delineated above in order to lower the risk of Type I error. However, the current data faced several limitations on power. First, within-subjects FMRI analyses are typically limited in power, by the nature of the very minute fluctuations of the BOLD signal in response to any stimuli, typically on the order of one to two percent change in signal from baseline, at best. Second, the contrast here between literal and figurative biased IPs is a very tight one. Therefore, an uncorrected threshold of \( p < 0.005 \) was applied, along with a reporting criteria of 405 \( \mu L \) (15 contiguous voxels) minimum of to define neural activation\(^{10}\). This is consistent with statistical thresholds that have been used in previous FMRI studies of IP comprehension, in which neural activation is contrasted between literal and figurative biased IPs (e.g. Hillert & Buracas, 2009; Zempleni et al., 2007a; Romero Lauro et al., 2008; Mashal et al., 2008).

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\(^{10}\) When the patient data were analyzed using the same cluster threshold criteria as was used for the AMC and YNC analyses, very few significant clusters were detected among patients, with some patients showing no significant activation at all. The reduced threshold for significance at \( p < 0.005 \) (uncorrected) among patients yielded a comparable number of clusters and volume of clusters as in the YNC and AMC analyses. We acknowledge, however, that the risk of Type I error is increased due to this more liberal statistical analysis.
Off-Line Task Analyses

Results from the off-line task of IP comprehension were scored, and proportions of correct responses were calculated for participants. These scores reflected the proportion of responses for which a participant correctly identified an ambiguous IP’s definition, in both figurative and literal biasing conditions.

Results

Unimpaired Participants

FMRI Task - Behavioral Performance

An analysis of participant responses to the probe verification task indicated that all participants performed this task exceptionally well (> 90% accuracy). From this, it was concluded that the task was sufficiently straightforward and encouraged attention to the stimuli.

Inter-Group Analyses

Results from the t-test between AMC and YNC groups indicated significant differences in BOLD signal change between these two groups. Despite a stringent cluster threshold, there were numerous statistically significant clusters between the two groups that survived the stringent threshold. The largest 5 clusters are indicated in Table 4-3 and in Figure 4-3; all of these 5 largest clusters indicated significantly stronger BOLD signal for the AMC group, as compared to the YNC group. From this inter-group comparison, it is noted that the AMC group demonstrates significantly
stronger regions of BOLD signal increase during IP processing, as compared to the YNC group. Having established significant differences between the YNC and AMC groups in neural recruitment during IP processing (in partial satisfaction of the second aim of this study), each group was henceforth analyzed individually.

Intra-Group Analyses

YNC Group

ANOVA results from the YNC group revealed significant clusters for the main effects of condition (literal vs. figurative) and HRF time segment (tent number). There was also a significant interaction between condition and time segment. Significant clusters for the main effect of condition and interaction between condition and time are detailed in Table 4-4. While these main effects localize the neural resources that are recruited for processing literal vs. figurative IPs, as well as the neural regions that are significantly modulated as listeners process IPs over time, these main effects cannot delineate the temporal signatures of literal and figurative processing of IPs.
Therefore, contrasts from the ANOVA were considered between these two conditions at each time point (“tent”).\textsuperscript{11}

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Insert Table 4-4 about here.

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In the YNC group, there were no significant clusters for the contrast of literally- vs. figuratively-biased IPs at either the second, fifth or sixth time points that were modeled. At the first time point, one cluster (1188 \( \mu \)L) was significant in left inferior frontal gyrus (orbitalis portion), extending into subcortical regions (lentiform nucleus and nucleus accumbens; peak signal at \( xyz = -16, 14, -16 \); center of cluster mass at \( xyz = -14, 14, -7 \)). This cluster indicated significantly stronger activity in this region for figuratively-biased IPs than for literally-biased IPs (see Figure 4-4).

At the third time point, one cluster (1458 \( \mu \)L) was significant in bilateral posterior cingulate (peak signal at \( xyz = 3, -54, 25 \); center of cluster mass at \( xyz = 3, -54, 25 \)). This cluster was also significant for figuratively-biased IPs versus literally-biased ones (see Figure 4-4).

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Insert Figure 4-4 about here.

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At the fourth time point, two clusters were significant. The first significant cluster was centered in the posterior left middle temporal gyrus (1539 \( \mu \)L, peak signal

\textsuperscript{11} Each contrast had 7 degrees of freedom.
at xyz = --43, -79, 23; center of cluster mass at xyz = -40, -75, 19). This cluster was
the only cluster among the YNC results to indicate significantly stronger BOLD
response for literally-biased IPs, as compared to figuratively-biased ones. The second
significant cluster at this time point was centered in the left middle frontal gyrus (1566
µL, peak signal at xyz = -25, 38, 29; center of cluster mass at xyz = -29, 28, 30), and
extended into the left superior frontal gyrus. This second cluster indicated greater
BOLD signal for figuratively-biased IPs, as compared to literally-biased IPs (see
Figure 4-4).

**AMC Group**

ANOVA results among the AMC group indicated no significant clusters for
the main effect of condition, but did reveal several significant clusters for the main
effect of time. There were also several significant clusters for the interaction of
condition and time. These clusters are described in Table 4-5. Again, however, the
main focus of investigation was in the contrasts from the ANOVA between these
literal and figurative sentences conditions at each time point (“tent”)^12.

| Insert Table 4-5 about here. |

Among the AMC participants, there were no significant clusters for the
contrast of literally- vs. figuratively-biased IPs at the second, third, or fourth time

^12 Each contrast had 8 degrees of freedom.
points that were modeled. At the first time point, three significant clusters were evident. The first cluster (2727 µL) was significant in the left middle frontal gyrus (peak signal at xyz = -52, 14, 32; center of cluster mass at xyz = -39, 17, 32). The second cluster (1512 µL) was present in the left middle occipital gyrus and left lingual gyrus (peak signal at xyz = -28, -58, 5; center of cluster mass at xyz = -27, -64, 9). The third cluster (1269 µL) was present in the left inferior and superior parietal lobules (peak signal at xyz = -34, -64, 44; center of cluster mass at xyz = -31, -60, 44). All three of these clusters indicated significantly stronger BOLD signal for literally-biased sentences, as compare to figuratively-biased stimuli (see Figure 4-5).

At the fifth time point, one cluster was significant (1431 µL) in right inferior frontal gyrus, extending into the right insula (peak signal at xyz = 38, 14, 13; center of cluster mass at xyz = 43, 7, 5). This cluster was significant for increased BOLD signal for figuratively-biased IPs over literally-biased IPs. At the sixth time point, two clusters were significant. The first cluster (2619 µL) was located in left middle occipital gyrus and left cuneus (peak signal at xyz = -28, -88, 17; center of cluster mass at xyz = -22, -84, 19). The second cluster (1377 µL) was located in the right cuneus (peak signal at xyz = 26, -85, 29; center of cluster mass at xyz = 20, -78, 29). Both clusters that were significant at this sixth time segment showed greater BOLD signal for literally-biased IPs than for figuratively-biased phrases.
Patient Analyses

Results from the within-subjects analyses for each patient are indicated in Table 4-6. Results across all time segments will be discussed first, followed by a consideration of results for the first and last five time segments of analyses.

Patient results across all 10 time segments\(^{13}\)

Across the entirety of the time span modeled following stimulus presentation (disambiguating phrase offset), within-subjects t-test results revealed significant differences in neural activation between figurative and literal biased IPs among 4 of the 6 patients studied here (LHD017, LHD051, LHD130, LHD140; full results for this analysis are indicated in Table 4-6). Within these patients, regions of activation were noted for both figuratively- and literally- biased IPs. Among these areas, two patients showed recruitment of right inferior temporal gyrus for figuratively biased IPs, three patients showed recruitment of occipital regions for literally biased IPs, and two patients showed recruitment of bilateral medial frontal gyri for literally biased IPs. In addition, frontal lobe regions were recruited in two patients, for both literal and figurative biased IPs.

\[\text{Insert Table 4-6 about here.}\]

\(^{13}\) Within-subjects t-tests across 10 time segments each had 18 degrees of freedom
Patient results across the first five time segments

Results from the first five time segments that were modeled revealed significant differences between literal and figurative conditions in only 2 of 6 patients: LHD 130 and LHD140 (see Table 4-6 for full details of these data). Among these patients, LHD130 demonstrated limited activation, with activation only noted within left superior frontal gyrus for figuratively biased IPs. By comparison, LHD140 showed much broader patterns of neural recruitment for both figurative and literal biased IPs. This participant recruited bilateral occipital regions for literally biased IPs, and recruited right frontal and parietal regions for figuratively biased IPs (see Figure 4-6, which shows activation results from patient LHD140). She also engaged the left cuneus for figuratively biased IPs. No other significant (nor even nearly significant) regions of activation were indicated among the current patient sample.

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Insert Figure 4-6 about here.

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Patient results across the final five time segments

Results from the final five modeled time segments indicated significant differences between literal and figurative conditions in 5 of 6 patients: LHD 017, LHD051, LHD101, LHD130, and LHD140 (see Table 4-6). Regions of activation

\[14\] Within-subjects t-tests across 5 time segments each had 8 degrees of freedom
again varied widely between patients, but some overlap was observed. Left and/or bilateral occipital regions were found activated for literally biased IPs among 2 patients (LHD017 and LHD130). Middle and medial frontal gyri were activated in 2 patients during the literal condition (LHD051 and LHD140). In addition to these common areas of activation, unique activation patterns included the left anterior inferior temporal gyrus for literal biased IPs (LHD017); the right inferior temporal gyrus for figuratively biased IPs (LHD051); the right parahippocampal gyrus, right insula, and right superior frontal gyrus for figuratively biased IPs (LHD101); and right middle temporal gyrus for literally biased IPs (LHD130; see Figure 4-6 for activation of a representative patient [LHD017] during this modeled time window).

It is noteworthy that one patient in this study, LHD09, did not show significant effects for either condition at any of the time segments that were analyzed. This participant showed the most severe impairment of language function, and the possible reasons for the lack of a significant effect in this patient are considered below.

**Off-Line Study**

Results from the IP definition behavioral task are shown in Table 4-7. While there was a good deal of variability between patients for this task, we note that all patients showed better comprehension for figuratively biased idioms than for their literally biased counterparts. LHD 130 and LHD101 showed the greatest magnitude of difference between these two conditions. Three patients, LHD09, LHD 101, and LHD130 were at or below chance levels of performance (50% correct) on the literal
condition. By contrast, our control groups demonstrated highly accurate comprehension performance for both figuratively- and literally- biased IPs, although there was higher variability for the literally-biased IPs.

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Insert Table 4-7 about here.

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Discussion

In the present study, we investigated the neural architecture underlying comprehension of ambiguous IPs. The main aims of the current study were threefold. First, we aimed to determine whether different neural mechanisms were engaged for idiom comprehension when ambiguous IPs were biased toward either a figurative or literal interpretation. Along with this aim, we sought to determine whether the time signatures of idiom processing differed between IPs biased toward a literal interpretation, as compared to those biased toward a figurative interpretation. Secondly, we sought to investigate potential differences in the neural markers of IP comprehension between young and older healthy individuals. As all prior FMRI studies of IP comprehension have relied on relatively young participant groups, we sought to determine whether functional differences in idiom processing occurred as a result of age. Lastly, we investigated the neural mechanisms that underlie IP comprehension in aphasia using FMRI, in what we believe is the first reported measurement of this process in this population.
We will discuss the differences in FMRI signal between the YNC and AMC group first, as all subsequent analyses were performed at a within-group level. The between groups t-test revealed a number of significantly different clusters between the groups, with the 5 largest clusters (by volume) indicating significantly stronger BOLD signal change for the AMC group, as compared to the YNC group, collapsed across conditions and time points. This finding is in line with prior reports that indicate increased BOLD signal for language-related FMRI tasks concurrent with aging. Researchers have proposed that this increase in BOLD signal in older adults is related to increased processing demands for lexical access as we age (Fridriksson et al., 2006). As prior work has likened IPs to large lexical items (e.g. Swinney & Cutler, 1979; Hillert & Swinney, 2001), lexical retrieval of idioms could indeed demand greater neural resources in older, healthy adults than in their younger counterparts.

With respect to the neural regions in which the AMC group showed increased BOLD signal over the YNC group, several of these significant clusters have previously been implicated in IP comprehension; specifically, bilateral middle temporal gyrus, left inferior frontal gyrus, and bilateral medial frontal gyrus (Hillert & Buracas, 2009; Zempleni et al., 2007a; Romero Lauro et al., 2008). In addition, we found significant clusters of BOLD response for the AMC group in several regions which have not been reported in previous FMRI reports of IP comprehension, such as bilateral superior temporal gyrus and left insula. Taken together, these findings suggest that older, unimpaired more strongly recruit portions of language neural
networks (see Price, 2010) during IP comprehension than do their younger counterparts.

In addition, the AMC group showed a highly significant cluster in anterior cingulate cortex. This region has been purported to be a primary component of attention networks and to play a role in evaluating incoming information to prepare for an attentional response (e.g. Carter et al., 2000; MacDonald et al., 2000; Milham et al., 2002). Given that half the stimuli in this experiment were idiomatic phrases embedded in literal contexts, an uncommon scenario in which to encounter an IP, participants may have been monitoring sentence context to assign appropriate meanings. Increased activity among the AMC participants in the anterior cingulate cortex suggests that this process was more effortful for this group than for the YNC participants (e.g. Milham et al., 2002).

Importantly, as this is the first FMRI study of IP comprehension to enroll unimpaired older participants, we find that the neural markers of IP processing change with age. Specifically, it appears that, when YNC and AMC participants are directly contrasted, the AMC group shows evidence of extensive, bilateral, strong recruitment of brain regions that are linked to language and attention during IP comprehension. Next we turn our discussion to within-group results.

**YNC Discussion**

In the YNC group, there is a main effect of condition (literal or figurative bias) as well as a main effect of time (e.g. tent number; see Table 4-4). There is also a
significant interaction between condition and time, which extended throughout bilateral and left frontal regions, bilateral posterior cingulate, and left parahippocampal gyrus. However, the most informative results come from the contrast between literal and figurative conditions at each time point. Here, there emerge differences in neural recruitment between conditions at the first, third, and fourth time points, modeled from the offset of the disambiguating phrase, which biased the sentence toward a literal or figurative interpretation.

At the first time point, which corresponds to 0-2 seconds following the offset of the disambiguating phrase, significant activation emerges for the figurative condition in orbital inferior frontal gyrus and subcortical regions. However, a typical hemodynamic response peaks approximately 4-8 seconds after a stimulus (Logothetis et al., 2001). Since only 2 seconds have elapsed after the disambiguating phrase, these results are likely related to cognitive processing of earlier portions of the sentence. However, there is a strong literature linking the orbital inferior frontal gyrus to semantic processing, particularly with respect to semantic retrieval in sentence contexts when meaning is particularly hard to extract from context (e.g. Roskies et al., 2001; Noppeney & Price, 2001; Snijders et al., 2009). This result suggests, therefore, that YNC participants are already processing the semantic meanings of ambiguous IPs prior to receiving enough information to definitively determine the IP’s meaning.

At the third time point, bilateral posterior cingulate cortex was significantly recruited for figuratively biased sentences. Interestingly, this same pattern of activation was reported in the only other FMRI study of auditory IP comprehension (in
sentence contexts), with posterior cingulate becoming engaged for the comprehension of ambiguous IPs (Hillert & Buracas, 2009). The authors argue that posterior cingulate is one component of a network of brain regions that contributes to processing of the figurative meaning of IPs, which is consistent with the findings here. Several possibilities exist for the engagement of the posterior cingulate for figurative processing of idioms. One theory is related to this brain area’s connection to emotional processing (see Diaz et al., 2011; Kensinger & Schacter, 2006). Specifically, some researchers have argued that the figurative meanings associated with IPs carry greater emotional connotation than literal meanings associated with the same phrases (Proverbio et al., 2009). In addition, the posterior cingulate has been argued to be engaged in semantic processing, particularly with respect to meaningful versus non-meaningful stimuli (see Price, 2010, and references therein). With respect to the current study, this could indicate that participants hold meaningful semantic representations of IPs in their figurative state, but do not maintain similar representations for literal meanings of these phrases.

At the fourth time point, the YNC group showed significant activity for literally biased IPs in the posterior left middle temporal gyrus. Prior research in which ambiguous IPs were biased toward a literal interpretation did not find this same pattern of results (Zempleni et al., 2007a). However, research of the neural correlates of semantic ambiguity processing has implicated this region during the resolution of ambiguous lexical items in sentence contexts (Rodd et al., 2005; Zempleni et al., 2007b). Important for the current discussion, the latter study reports stronger
engagement of posterior middle temporal gyrus for the less frequent meaning of a word, as compared to its more frequent interpretation (Zempleni et al., 2007b). A similar situation may have occurred with our stimuli, where a literal interpretation of our IPs was plausible but less frequent than a figurative interpretation.

Also during the fourth time segment, we observed a BOLD response for figuratively biased IPs in left middle frontal and superior frontal gyri. Previous studies of IP comprehension and processing have likewise implicated these regions (Hillert & Buracas, 2009; Romero Lauro et al., 2008; Boulenger et al., 2009). Outside of the IP literature, other FMRI studies have suggested a role for the left middle frontal gyrus in the lexical retrieval for single words (Binder et al., 2009) and for comprehension of ambiguous words (Bilenko et al., 2009). This is certainly in keeping with hypotheses of IPs as lexical items (see Introduction). Likewise, the superior frontal gyrus has been implicated in semantic processing (Binder et al., 2009) and processing of ambiguous words (Bilenko et al., 2009).

In sum, results from the YNC group across conditions and time segments suggest that literal or figurative processing of IPs enlists neural regions that are associated with lexical and semantic processes. However, the localization of activation in posterior middle temporal gyrus for literally biased IPs suggests overlap in the neural systems that are recruited for single-word lexical ambiguities and ambiguous IPs.

AMC Discussion
In the AMC results, there emerges a different pattern of neural recruitment for both literal and figurative processing of idioms, and on a different time scale, as compared to the YNC group. Interestingly, many of the neural regions that are activated for the AMC group have been reported in prior FMRI studies of IP comprehension. At the first time segment, the AMC group activated left middle frontal gyrus, left middle occipital gyrus, left lingual gyrus, and left inferior and superior parietal lobules. Recall that activation at this time segment is actually related to portions of the sentence that occur prior to the idiom’s disambiguating phrase. This activation thus reflects processing differences between the two conditions at a very early stage of the sentence, while a participant is still receiving information that definitively delineates figurative from literal bias for idioms. At this point, however, is interesting to observe activation for literal sentences in the left middle frontal gyrus, which has been posited to play a role in semantic retrieval and analysis (Davis & Gaskell, 2009; Binder et al., 2009).

Likewise, it is notable that the left inferior and superior parietal lobules showed activation for literal sentences at this first time segment, as these regions have been linked to literal sentence processing in earlier studies of IPs (Romero Lauro et al., 2008) and figurative language (Bottini et al., 1994). Additionally, these parietal regions have been shown to engage during listening of sentences that contain action (Tettamanti et al., 2005). As our literally-biased IPs were all verb phrases that conveyed a physical action, recruitment of these regions concurs with these earlier findings. Lastly, recruitment of visual areas (left middle occipital gyrus and left
lingual gyrus) directly replicates an observation in a previous FMRI study of IP comprehension (Zempleni et al., 2007a). In this study, the authors attributed recruitment of these visual areas to the concrete, imageable nature of literal stimuli, and this factor could likewise account for the results here.

In contrast to the YNC group who demonstrated significant activation at the first time segment and then again at the third, the AMC group only shows significant activation again at the fifth time segment. At this point, the AMC group demonstrates recruitment of the right inferior frontal gyrus and right insula, areas which have previously been noted in the literature for figurative IP processing (Proverbio et al., 2009; Zempleni et al., 2007a; Oliveri et al., 2004). Previous work has suggested that recruitment of these right-lateralized regions occurs when language processing is difficult or demanding (Poldrack et al., 2001; Meyer et al., 2000). Other research has implicated the right inferior frontal gyrus in resolution of semantic ambiguity when surrounding context contains conflicting information (Snijders et al., 2009; Peelle et al., 2004). It is notable that only right, and not left, inferior frontal recruitment was observed in this group, as nearly all neuroimaging studies of IP comprehension to date have implicated left inferior frontal regions (e.g. Zempleni et al., 2007a; Hillert & Buracas, 2009; Romero Lauro et al., 2008). However, as we are examining a very specific set of time windows which span only a portion of each sentence, it is possible that left inferior frontal gyrus activity would be found during another time segment during IP processing.
Lastly, during the sixth time point, the AMC group again shows activation of visual regions, here the left middle occipital gyrus and bilateral cuneus, for literal comprehension of IPs. Recall the argument above for why these visual regions may be engaged during this task, and it is possible that AMC participants were visualizing the literal scenarios that were portrayed in these stimuli, particularly after hearing enough information to determine that IPs were intended in a literal manner.

**YNC and AMC summary**

In sum, between the YNC and AMC groups, we see some overlapping neural regions and associated functions associated with IP processing, but we also see a good deal of divergence between the two groups. Most especially, the finding that the AMC group recruits visual brain regions at two time segments during idiom processing suggests that this group may rely on a different strategy for literal comprehension of idioms than does the YNC group. Both groups, however, show evidence of neural activation in regions that contribute to semantic retrieval and semantic processing, particularly for ambiguous lexical items and in complex contexts. From these results, it appears that both participant groups rely on slightly differing networks for literal and figurative comprehension of idioms.

In addition to their different localization profiles for idiom processing, the AMC and YNC groups diverge quite dramatically in their time signatures of idiom processing. Among the YNC group, figurative activation is detected at the offset of the disambiguating phrase, which suggests that this group is already processing literal and
figurative biased idioms differently. Then, at the third time point, we see additional evidence of figurative idiom processing, followed closely by literal processing at the fourth time point. By contrast, although the AMC group also shows activation at the first time point, in this group this activation is significant for literal processing, and it suggests a visual imagery strategy of for understanding IPs that are biased towards a literal interpretation. It is not until the fifth time point that we see neural recruitment differences for figurative and literal biased idioms, when we observe figurative activation in this AMC group.

Interestingly, although the AMC group shows delayed activation of figurative and literal biased idioms as compared to the YNC group, the AMC group demonstrates the same temporal signature of activation, with figurative activation preceding literal activation. While it is difficult to directly link FMRI results, where timescales are on the order of seconds, with psycholinguistic timescales on the order of milliseconds, it is fascinating to note that the psycholinguistic literature suggests that figurative lexical processing of idioms occurs prior to literal processing of the idiom’s constituent words (see Chapter 2). Thus, the results presented here mirror these psycholinguistic patterns and suggest a temporal discontinuity for processing the multiple meanings associated with an IP.

**Patient Discussion**

While we fully acknowledge the limitations of our patient study (e.g. small sample size, variability of aphasia type and severity, variability of lesion size and
location), we feel that some strong inferences can be drawn from the patient results in this study. First, as a broad statement, we were able to find evidence at a neural level of differing neural recruitment between the two idiom biasing conditions, suggesting that stroke survivors with aphasia do indeed process these ambiguous IPs differently depending on their intended meaning. We also found differences in processing as a function of time segment, with a striking finding that half of our patients (3 of 6 patients in this sample) failed to show any signs of neural recruitment for either condition until at least 10 seconds after disambiguating phrase offset. This finding confirms the suspicion of delayed BOLD response in these patients, which will be discussed further below.

Several interesting findings emerge when we examine the patient data more closely. First, there was some overlap between neural regions that the patients recruited during IP processing and the regions that both the YNC and AMC groups recruited during the same task. For example, LHD140 showed activation of bilateral lingual gyrus and left cuneus for literally-biased IPs, which closely parallels a finding in the AMC group during literal IP processing. Likewise, LHD130 recruits the left middle occipital gyrus for literal IP processing, which overlaps with the AMC findings.

However, there was also observed recruitment of regions that are homologous to those recruited by the AMC and YNC groups. For instance, LHD130 showed recruitment of right middle temporal gyrus for literally biased IPs, whereas the YNC group had showed left-lateralized activation in this region for the literal condition.
Admittedly, however, there is limited overlap in patterns of neural activity between the patients and both control groups.

Another interesting observation in the patient data relates to the temporal signature of literal and figurative processing. First, we see that in the two patients who showed neural activation during the first five time segments that were modeled (LHD130 and LHD140), both show exclusively or predominantly figurative activation during this time window. However, during the last five time segments, these patients show only literal activation. This temporal offset mirrors that seen in both the YNC and AMC groups, with figurative activation preceding literal.

Importantly, one participant failed to show any patterns of neural activation for either figurative or literal biased idioms (LHD09). Given prior research with this population, we can hypothesize why this patient failed to show significant BOLD signal for either condition. The BOLD signal arises from a complex interplay of several neurophysiological measures, including cerebral blood flow (CBF), neural metabolism rate for oxygen in blood, and the amount of oxygen that is extracted from inflowing arterial blood. Prior research has indicated abnormal, slowed CBF in chronic stroke survivors, such as the patients involved in this study (see Chapter 3). That is, patients in this population may have decreased CBF to regions of the brain that remain anatomically intact, and this decreased CBF can be associated with language and behavioral impairments (see Chapter 3).

Additional research has suggested a link between decreased CBF in chronic stroke and a lack of BOLD signal in neural regions that are known to be involved in
particular language tasks (Prabhakaran et al., 2007). Other work has shown a vastly delayed or absent BOLD signal in this population during cognitive and linguistic tasks (Bonakdarpour et al., 2007; Fridriksson et al., 2006). Thus, it is posited that participant LHD09 may have compromised CBF, leading to the absence of a detectable task-related BOLD signal in this individual. Decreased and/or slowed CBF may also help to account for remarkable temporal delays that we observed in BOLD signal for idiom processing in our other patients. As three patients only showed significant BOLD response during the latter half of the time segments that were modeled, it is hypothesized that these patients also likely have a limiting neurophysiological factor, such as slowed CBF, that accounts for this delayed BOLD response.

Sub-Types of Aphasia

As one of the primary purposes of this dissertation is to delve into language processing in Broca’s aphasia, special comment must be made with respect to the relationship between classification of aphasic symptomatology in the patients who were enrolled in this study with the patterns of neural activity that each patient demonstrated during IP comprehension. Here, four patients with Broca’s aphasia participated in the current study, in addition to two patients with anomic aphasia. In Chapter 2, it was discovered that lexical access is protracted during IP processing in Broca’s aphasia, and a similar pattern of results emerged here. With respect to overall slowing of processing of IPs, two Broca’s patients in this sample failed to show statistically significant neural activation for IPs during the first time segment that was
modeled. Among the two Broca’s patients who did show neural recruitment for IPs during the first time window that was modeled, the majority of this activation was for IPs that were biased towards a figurative meaning; only one significant cluster of activation was detected in patient LHD140 for IPs biased towards a literal meaning. Note that although these patients did demonstrate significant activation during this first time segment, this does not imply immediate activation. Due to the temporal width of this time segment and the long latency of the HRF, it is possible that significant activation during this first time segment is still delayed when compared to activation in the unimpaired groups.

Additionally, during the second time segment that was modeled, there is further evidence at the neural level that lexical processing is delayed in Broca’s aphasics. As already discussed, there is significant activation for literally-biased IPs during this second time window, in Broca’s patients LHD130 and LHD140, following their figurative activation earlier. This pattern of results parallels that which was observed for real-time lexical access in this population during IP comprehension in Chapter 2. In addition, during the second time window, there is finally evidence of significant activation for figuratively biased IPs in Broca’s patient LHD101. Given this result, it appears that this patient demonstrates an even more delayed time course of neural processing for figuratively biased IPs than either LHD130 or LHD140. At the same time, LHD101’s neural processing of IPs is incomplete, as he never shows significant neural activation for literally biased IPs, at least during the time points that were observed here. It is possible that this individual might show neural processing for
literally biased IPs further downstream, but this would be difficult to measure with the current experimental paradigm due to power issues. However, this remains a question for further research.

Lastly, as has already been discussed above, LHD09 failed to show a statistically reliable neural signal for either condition during either of the time segments modeled here. This does not, of course, indicate that this patient never processed the stimuli in this experiment at a psycholinguistic level, and he does evince relatively high accuracy for comprehension of figuratively biased IPs in the off-line task. However, LHD09’s underlying neurophysiological state may contribute to the lack of signal that was observed in this study. That is, if this individual has decreased levels of CBF or slowed CBF reactivity to increasing neural demands, it is possible that this individual does not manifest a significant BOLD signal increase in response to actual neural activity. Recall that the BOLD signal is an indirect measure of neural function that assumes rapid CBF changes in regions where neural activity occurs, and such reduced cerebrovascular reactivity in LHD09 may explain the lack of a significantly detectable BOLD signal in this individual during task performance.

**Conclusion**

Several major findings emerged from this study. First, it was established that older and younger unimpaired adults recruit different, but somewhat overlapping networks during comprehension of ambiguous IPs. It was also demonstrated that differing neural regions were engaged for figurative and literal comprehension of
idioms; figuratively biased IPs engaged brain regions that are associated with lexical ambiguity resolution, semantic selection, and semantic retrieval. Literally biased IPs engaged several brain regions in our older adults that are associated with concrete, actionable stimuli, including visual cortices and parietal lobules. Literal IPs also engaged neural regions that are important for semantic processing and word retrieval in both unimpaired groups.

Second, with respect to the time signatures of processing literal and figurative IPs at a neural level, we found evidence in both groups of figurative processing occurring in advance of literal processing, which corresponds with the literature of online IP processing and with the results presented in Chapter 2 of this dissertation (see also e.g. Titone & Connine, 1994; Cacciari & Tabossi, 1988).

Third, it was shown that patients with chronic stroke and aphasia recruited some of the same neural regions for IP processing as did our unimpaired participants, along with some homologous regions to those activated by control participants. Interestingly, however, patients largely activated unique brain regions during this task. Importantly, most patients showed a temporal delay in BOLD signal for IP processing, with figurative and literal activation occurring at least 10 seconds after the offset of the disambiguating phrase in each sentence. Lastly, in patients who showed early and late BOLD signal for IP processing, figurative activation preceded literal activation, as in our control participants.

There are several implications of these findings. First, as the YNC and AMC groups showed differential recruitment of neural regions during figurative and literal
idiom processing, it is suggested that these differing patterns reflect divergent patterns of lexical access for these two meanings that are associated with IPs. Additionally, as figurative and literal biased IPs engaged different neural networks in our unimpaired participants, it is possible that these differing patterns reflect divergent patterns of lexical access for these two meanings that are associated with IPs. These diverging processing streams may also be reflected in psycholinguistic and behavioral studies of IP comprehension.

With respect to the patient findings, the current study implicates slowed neural processing of literal and figurative idioms in chronic aphasia patients. While we observed neural activity in our control groups for idioms within 6-10 seconds after disambiguation offset, in some patients, the neural response was not detected until later. We argue that this delay in the BOLD response is likely driven by neurophysiological factors, but there may also be a cognitive component involved. It may be the case that these patients have slowed lexical processing of idioms for figurative and/or literal meanings of these phrases (Love et al., 2008), and that this slowing is reflected in the MRI response observed here. It is also possible that our observations reflect a combination of slowed lexical processing and decreased neurophysiological reactivity to cognitive stimuli. Current and future research is aimed at untangling these factors in chronic stroke survivors.
<table>
<thead>
<tr>
<th>Source</th>
<th>Experimental Design</th>
<th>Stimuli</th>
<th>Findings Reported</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hillert &amp; Buracas (2009)</td>
<td>Event-related FMRI</td>
<td>Auditory English sentences; 1/3 of which contained idiomatic phrases; 1/3 of which were literal; 1/3 of which were implausible; meaningfulness judgment</td>
<td>Greater engagement of the following regions for comprehension of idiomatic sentences vs. literal and implausible sentences: Left IFG (BA 44&amp;45); Left MFG (BA 11&amp;47); Left SFG (BA 8); Left Medial Frontal Gyrus (BA 8&amp;9)</td>
</tr>
<tr>
<td>Zempleni et al. (2007a)</td>
<td>Event-related FMRI</td>
<td>Written Dutch sentences, half of which contained idiomatic phrases; sentence-final word for relatedness judgment</td>
<td>Greater engagement of the following regions for reading/comprehension of sentences containing an idiomatic phrase vs. literal sentences: Bilateral IFG (BA 45&amp;47); Bilateral MTG (BA21)</td>
</tr>
<tr>
<td>Romero Lauro et al. (2008)</td>
<td>Event-related FMRI</td>
<td>Written Italian sentences, half of which contained idiomatic phrases; picture matching task</td>
<td>Greater engagement of the following regions for reading/comprehension of sentences containing an idiomatic phrase vs. literal sentences: Bilateral IFG (BA44&amp;45); Bilateral Anterior MTG (BA21); Left SFG; Left ITG; Left angular gyrus (BA39); Right MTG; Right temporal pole</td>
</tr>
<tr>
<td>Oliveri et al. (2004)</td>
<td>rTMS</td>
<td>Written Italian phrases, half of which were idiomatic, half of which were literal; picture matching task</td>
<td>Increased error rates and slower responses for matching task when rTMS applied to Left temporal lobe (BA22); Bilateral IFG (BA44&amp;45)</td>
</tr>
<tr>
<td>Rizzo et al. (2007)</td>
<td>rTMS</td>
<td>Written Italian phrases, half of which were idiomatic, half of which were literal; picture matching task</td>
<td>Increased error rates for matching task when rTMS applied to Bilateral DLPFC (BA 9)</td>
</tr>
</tbody>
</table>
Table 4-2. Demographics of patients who participated in the current study.

<table>
<thead>
<tr>
<th>Subject</th>
<th>BDAE Severity Level</th>
<th>WAB Aphasia Quotient</th>
<th>Aphasia Diagnosis</th>
<th>Gender</th>
<th>Age at testing</th>
<th>Months post-stroke</th>
<th>Education</th>
<th>Lesion</th>
</tr>
</thead>
<tbody>
<tr>
<td>LHD09</td>
<td>2</td>
<td>72.7</td>
<td>Broca’s</td>
<td>M</td>
<td>49</td>
<td>107</td>
<td>17</td>
<td>L posterior inferior frontal lobe, extending to middle and posterior temporal lobe, includes regions of the insula and subcortical regions</td>
</tr>
<tr>
<td>LHD017</td>
<td>4</td>
<td>91.2</td>
<td>Anomia</td>
<td>M</td>
<td>60</td>
<td>141</td>
<td>14</td>
<td>L anterior frontal, including superior, middle, and inferior frontal lobe; includes regions of superior temporal lobe, insula, and subcortical regions</td>
</tr>
<tr>
<td>LHD051</td>
<td>5</td>
<td>96.6</td>
<td>Anomia</td>
<td>M</td>
<td>58</td>
<td>52</td>
<td>15</td>
<td>L inferior frontal gyrus, insula, putamen, nucleus accumbens</td>
</tr>
<tr>
<td>LHD101</td>
<td>2</td>
<td>82.4</td>
<td>Broca’s</td>
<td>M</td>
<td>60</td>
<td>32</td>
<td>20</td>
<td>L posterior inferior frontal lobe, extending to middle and posterior temporal lobe, includes regions of the insula and subcortical regions</td>
</tr>
<tr>
<td>LHD130</td>
<td>4</td>
<td>81.1</td>
<td>Broca’s</td>
<td>M</td>
<td>57</td>
<td>23</td>
<td>16</td>
<td>L inferior occipital lobe, occipito-temporal junction, and posterior and middle temporal gyrus</td>
</tr>
<tr>
<td>LHD140</td>
<td>2</td>
<td>72.9</td>
<td>Broca’s</td>
<td>F</td>
<td>35</td>
<td>122</td>
<td>16</td>
<td>L posterior inferior frontal lobe, extending to middle and posterior temporal lobe and inferior parietal lobe, includes regions of the insula and subcortical regions</td>
</tr>
</tbody>
</table>
Table 4-3. T-Test results of a between-groups comparison (AMC vs. YNC) across conditions. The five largest clusters from this analysis are reported here (n=17 [n = 8 YNC, n = 9 AMC], 202 degrees of freedom). Talairach atlas coordinates are listed in the following order: Left-Right, Posterior-Anterior, Inferior-Superior.

<table>
<thead>
<tr>
<th>Cluster location</th>
<th>Cluster size (µL)</th>
<th>Coordinates of cluster’s center of mass</th>
<th>Coordinates of cluster’s peak signal value</th>
<th>Brodmann area(s)</th>
<th>Significant for which group?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left middle temporal gyrus, extending to the superior temporal gyrus and inferior to the fusiform gyrus</td>
<td>9558</td>
<td>-45, -52, 0</td>
<td>-55, -43, -22</td>
<td>37/39</td>
<td>AMC</td>
</tr>
<tr>
<td>Bilateral medial frontal gyrus, anterior cingulate</td>
<td>4347</td>
<td>5, 47, -12</td>
<td>2, 59, -10</td>
<td>10/11</td>
<td>AMC</td>
</tr>
<tr>
<td>Left precuneus and left cingulate</td>
<td>4185</td>
<td>4, -53, 38</td>
<td>-1, -46, 32</td>
<td>7</td>
<td>AMC</td>
</tr>
<tr>
<td>Right middle temporal gyrus and right superior temporal gyrus</td>
<td>2835</td>
<td>57, 5, -9</td>
<td>59, 8, 2</td>
<td>22</td>
<td>AMC</td>
</tr>
<tr>
<td>Left superior temporal gyrus, left inferior frontal gyrus, left insula, left precentral gyrus</td>
<td>1404</td>
<td>-50, 11, 6</td>
<td>-52, 11, 5</td>
<td>22</td>
<td>AMC</td>
</tr>
</tbody>
</table>
Table 4-4. Repeated measures Analysis of variance (ANOVA) results from the YNC group (n = 8). Main effects and interactions are listed. Only the largest five clusters for the main effect of time are shown.

<table>
<thead>
<tr>
<th>Effect</th>
<th>Degrees of Freedom</th>
<th>Cluster location</th>
<th>Cluster size (µL)</th>
<th>Brodmann area(s)</th>
<th>Coordinates of cluster’s center of mass</th>
<th>Coordinates of cluster’s peak value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Main Effect of Condition</td>
<td>1, 7</td>
<td>1. Right Caudate</td>
<td>3834</td>
<td>25</td>
<td>6, 12, 4</td>
<td>2, 14, -1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2. Bilateral posterior cingulate</td>
<td>3024</td>
<td>23/30/31</td>
<td>-1, -50, 22</td>
<td>2, -49, 17</td>
</tr>
<tr>
<td>Main Effect of Time</td>
<td>5, 35</td>
<td>1. Bilateral cingulate gyrus, Left medial frontal gyrus</td>
<td>15012</td>
<td>9/10/32</td>
<td>2, 21, 35</td>
<td>-1, 62, 17</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2. Left superior temporal gyrus and transverse temporal gyrus</td>
<td>14364</td>
<td>22/41</td>
<td>-51, -17, 7</td>
<td>-64, -22, 8</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3. Right superior temporal gyrus</td>
<td>13905</td>
<td>22</td>
<td>57, -15, 3</td>
<td>65, -7, 2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4. Left Inferior Parietal Lobule and Supramarginal gyrus</td>
<td>13500</td>
<td>44</td>
<td>-39, -46, 43</td>
<td>-43, -55, 50</td>
</tr>
<tr>
<td></td>
<td></td>
<td>5. Left Insula, claustrum, putamen</td>
<td>8505</td>
<td>13/47</td>
<td>-31, 9, 5</td>
<td>-31, 23, 8</td>
</tr>
<tr>
<td>Interaction of Condition X Time</td>
<td>5, 35</td>
<td>1. Bilateral medial frontal gyrus, Bilateral anterior cingulate, Left superior frontal gyrus</td>
<td>3969</td>
<td>20/21/37</td>
<td>-4, 54, 14</td>
<td>-13, 68, 14</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2. Left middle temporal gyrus and inferior temporal gyrus</td>
<td>3591</td>
<td>23/31</td>
<td>-57, -45, -9</td>
<td>-61, -40, -13</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3. Bilateral posterior cingulate, Bilateral cuneus</td>
<td>1755</td>
<td>10/32</td>
<td>-9, -64, 21</td>
<td>-1, -49, 17</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4. Left parahippocampal gyrus</td>
<td>1566</td>
<td>36</td>
<td>-35, -30, -10</td>
<td>-46, -25, -16</td>
</tr>
</tbody>
</table>
Table 4-5. Repeated measures Analysis of variance (ANOVA) results from the AMC group (n = 9). Main effects and interactions are listed. Only the largest five clusters for the main effect of time are shown.

<table>
<thead>
<tr>
<th>Effect</th>
<th>Degrees of Freedom</th>
<th>Cluster location</th>
<th>Cluster size (mm&lt;sup&gt;3&lt;/sup&gt;)</th>
<th>Brodmann area(s)</th>
<th>Coordinates of cluster’s center of mass</th>
<th>Coordinates of cluster’s peak value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Main Effect of Condition</strong></td>
<td>5, 40</td>
<td>No significant clusters</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Main Effect of Time</strong></td>
<td>5, 40</td>
<td>1. Left Inferior Parietal Lobule, Left Superior parietal lobule, Left precuneus, Left supramarginal gyrus</td>
<td>19143</td>
<td>40</td>
<td>-38, -38, 47</td>
<td>-34, -67, 50</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2. Left superior temporal gyrus and left insula</td>
<td>15930</td>
<td>13, 22, 41</td>
<td>-52, -18, 8</td>
<td>-64, -13, 8</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3. Right superior temporal gyrus and Right insula</td>
<td>14985</td>
<td>13, 22</td>
<td>56, -15, 5</td>
<td>65, -13, 5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>5. Left fusiform gyrus</td>
<td>5238</td>
<td>20, 37</td>
<td>-36, -52, 13</td>
<td>-40, -64, -19</td>
</tr>
<tr>
<td><strong>Interaction of Condition x Time</strong></td>
<td>5, 40</td>
<td>1. Left Lingual gyrus and left middle occipital gyrus</td>
<td>2457</td>
<td>30</td>
<td>-26, -64, 6</td>
<td>-13, -73, 5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2. Left inferior parietal lobule</td>
<td>1701</td>
<td>40</td>
<td>-36, -36, -39</td>
<td>-46, -34, 53</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3. Left medial frontal gyrus and left anterior cingulate</td>
<td>1593</td>
<td>10, 32</td>
<td>-7, 36, -6</td>
<td>-1, 44, -10</td>
</tr>
</tbody>
</table>
Table 4-6. Results from individual patient analyses, indicated by patient. Results are collapsed across all time segments (top) and then indicated by the first half of the modeled time segments (middle) and the latter half of the modeled time segments (bottom).

<table>
<thead>
<tr>
<th>Participant</th>
<th>Neural Regions Activated (Number of Voxels Activated; Condition)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Activation Across all 10 Time Segments</strong></td>
<td></td>
</tr>
<tr>
<td>LHD09</td>
<td>No statistically significant regions detected</td>
</tr>
<tr>
<td>LHD017</td>
<td>1) Right inferior temporal lobe (30 voxels; Figurative)</td>
</tr>
<tr>
<td></td>
<td>2) Left superior occipital gyrus (28 voxels; Literal)</td>
</tr>
<tr>
<td></td>
<td>3) Left anterior inferior temporal gyrus (18 voxels; Literal)</td>
</tr>
<tr>
<td>LHD051</td>
<td>1) Right inferior temporal lobe (57 voxels; Figurative)</td>
</tr>
<tr>
<td></td>
<td>2) Bilateral medial frontal gyri (43 voxels; Literal)</td>
</tr>
<tr>
<td></td>
<td>3) Left inferior frontal gyrus (17 voxels; Figurative)</td>
</tr>
<tr>
<td></td>
<td>4) Right inferior temporal gyrus (17 voxels; Figurative)</td>
</tr>
<tr>
<td>LHD101</td>
<td>No statistically significant regions detected</td>
</tr>
<tr>
<td>LHD130</td>
<td>1) Bilateral medial frontal gyri (59 voxels; Literal)</td>
</tr>
<tr>
<td></td>
<td>2) Left superior frontal gyrus (33 voxels; Figurative)</td>
</tr>
<tr>
<td></td>
<td>3) Left middle occipital gyrus (27 voxels; Literal)</td>
</tr>
<tr>
<td></td>
<td>4) Right inferior occipital gyrus (15 voxels; Figurative)</td>
</tr>
<tr>
<td>LHD140</td>
<td>1) Left inferior occipital gyrus (47 voxels; Literal)</td>
</tr>
<tr>
<td><strong>Activation During the first 5 Time Segments</strong></td>
<td></td>
</tr>
<tr>
<td>LHD09</td>
<td>No statistically significant regions detected</td>
</tr>
<tr>
<td>LHD017</td>
<td>No statistically significant regions detected</td>
</tr>
<tr>
<td>LHD051</td>
<td>No statistically significant regions detected</td>
</tr>
<tr>
<td>LHD101</td>
<td>No statistically significant regions detected</td>
</tr>
<tr>
<td>LHD130</td>
<td>1) Left superior frontal gyrus (21 voxels; Figurative)</td>
</tr>
<tr>
<td>LHD140</td>
<td>1) Bilateral lingual gyrus (36 voxels; Literal)</td>
</tr>
<tr>
<td></td>
<td>2) Right superior frontal gyrus (20 voxels; Figurative)</td>
</tr>
<tr>
<td></td>
<td>3) Left cuneus (15 voxels; Figurative)</td>
</tr>
<tr>
<td></td>
<td>4) Left inferior parietal lobule and left supramarginal gyrus (15 voxels; Figurative)</td>
</tr>
<tr>
<td><strong>Activation During the last 5 Time Segments</strong></td>
<td></td>
</tr>
<tr>
<td>LHD09</td>
<td>No statistically significant regions detected</td>
</tr>
<tr>
<td>LHD017</td>
<td>1) Left superior occipital gyrus (19 voxels; Literal)</td>
</tr>
<tr>
<td></td>
<td>2) Left anterior inferior temporal gyrus (18 voxels; Literal)</td>
</tr>
<tr>
<td>LHD051</td>
<td>1) Right inferior temporal gyrus (25 voxels; Figurative)</td>
</tr>
<tr>
<td></td>
<td>2) Bilateral medial frontal gyri (22 voxels; Literal)</td>
</tr>
<tr>
<td>LHD101</td>
<td>1) Right parahippocampal gyrus (59 voxels; Figurative)</td>
</tr>
<tr>
<td></td>
<td>2) Right insula and superior frontal gyrus (18 voxels; Figurative)</td>
</tr>
<tr>
<td>LHD130</td>
<td>1) Left middle occipital gyrus (22 voxels; Literal)</td>
</tr>
<tr>
<td></td>
<td>2) Right middle temporal gyrus (15 voxels; Literal)</td>
</tr>
<tr>
<td>LHD140</td>
<td>1) Right middle frontal gyrus (15 voxels; Literal)</td>
</tr>
</tbody>
</table>
Table 4-7. Summary of off-line results, indicated for each individual patient, as well as by group for the unimpaired control groups. Data represent proportion of correct IP verifications in the off-line task.

<table>
<thead>
<tr>
<th>Subject</th>
<th>Figuratively biased Idioms: Proportion Correct</th>
<th>Literally biased Idioms: Proportion Correct</th>
</tr>
</thead>
<tbody>
<tr>
<td>LHD09</td>
<td>0.80</td>
<td>0.50</td>
</tr>
<tr>
<td>LHD017</td>
<td>0.65</td>
<td>0.60</td>
</tr>
<tr>
<td>LHD051</td>
<td>0.90</td>
<td>0.85</td>
</tr>
<tr>
<td>LHD101</td>
<td>0.75</td>
<td>0.25</td>
</tr>
<tr>
<td>LHD130</td>
<td>1.00</td>
<td>0.50</td>
</tr>
<tr>
<td>LHD140</td>
<td>0.70</td>
<td>0.55</td>
</tr>
<tr>
<td>YNC Control Group (SD)</td>
<td>0.91 (0.01)</td>
<td>0.84 (0.02)</td>
</tr>
<tr>
<td>AMC Control group (SD)</td>
<td>0.90 (0.065)</td>
<td>0.89 (0.094)</td>
</tr>
</tbody>
</table>
Figure 4-1. Magnetic resonance images (MRIs) indicating neuroanatomy and site and extent of neural trauma in each LHD participant. Patient labels are indicated below the corresponding images. Left and right are reversed in this neuroradiological space.
Figure 4–2. Illustration of FMRI modeling using piecewise linear splines, or “tents,” fit to the offset of the disambiguating phrase (underlined) following each IP (italicized).

The toddler in a dinosaur shirt hits the sack at eight o’clock...
Figure 4-3. Results of the t-test contrast between YNC and AMC participants. Significant clusters (yellow) indicate neural regions that were recruited significantly more strongly by the AMC group than by the younger controls.
Figure 4-4. Significant clusters among the YNC group for the repeated-measures ANOVA, contrast between literal and figurative biasing conditions. Clusters which denote a negative value for this contrast (shown in blue) indicate neural regions that were significantly more engaged in literal processing of IPs than in figurative processing. Clusters which denote a positive value for the contrast (shown in yellow) indicate neural regions that were significantly more engaged in figurative processing of IPs than in literal processing. These images represent significant difference between the two conditions at the first (left), third (right), and fourth (bottom) time segments that were modeled.
Figure 4-5. Significant clusters among the AMC group for the repeated-measures ANOVA, contrast between literal and figurative biasing conditions. Clusters which denote a negative value for this contrast (shown in blue) indicate neural regions that were significantly more engaged in literal processing of IPs than in figurative processing. Clusters which denote a positive value for the contrast (shown in yellow) indicate neural regions that were significantly more engaged in figurative processing of IPs than in literal processing. These images represent significant difference between the two conditions at the first (left), third (right), and fourth (bottom) time segments that were modeled.
Figure 4-6. Patients LHD140 and LHD017, exemplifying the current analysis method. Here, LHD140 (left) shows significant BOLD signal response within the first 5 time segments (10 seconds) modeled, and Patient 017 (right) demonstrates BOLD signal from the final 5 time segments (10 seconds) modeled.
Appendix 4-1

FMRI Stimuli

Below are the stimuli within each list that participants heard in this FMRI study. For ease of reference here only, IPs are in bold, and disambiguating phrases are underlined. (F) indicates a figurative bias, and (L) indicates a literal bias. The visual probe word that was paired with each sentence is presented in bold letters after the sentence.

List 1

1. (F) The burglar from Montana spilled the beans about the money at his mother’s house after a long day of cooking with his family.

   HOUSE

2. (F) The world famous art critic chewed the fat with his friend for a very long time at the start of a pleasant evening.

   FAMOUS

3. (L) The teenager with curly blonde hair wore the pants to her interview after the tragic accident that happened last September.

   TEENAGER

4. (L) Jim’s twin brothers buried the hatchet under their porch yesterday afternoon before their mother called them for dinner.

   AFTERNOON

5. (L) The middle-aged plumber saw the light through the window before his young wife arrived in the expensive new SUV.

   WIFE

6. (L) On her way to work, Jenny blew the whistle in the crowd and then quickly ran away to hide in a safe place.

   SAFE

7. (L) The toddler in a dinosaur shirt hit the sack with a fist after a long day of playing outside with his best friend.

   TODDLER

---

15 Only experimental materials are reprinted here; filler stimuli are not listed as data from these items were not analyzed in the current study. Fillers were included in the counterbalancing of stimuli for this task, so that no more than three occurrences of a given condition (e.g. figuratively-biased IPs, literally-biased IPs, or fillers) were presented in a row.
8. (F) Yesterday afternoon Susan **kicked the bucket** without waking up after the children left to go play miniature golf.

   **GOLF**

9. (F) The tattooed garbage man **smelled a rat** at the secret meeting behind the row of abandoned houses near the old train tracks.

   **TATTOOED**

10. (L) At the reception, the host **broke the ice** by hitting it with a hammer before the band started to play well-known songs for the guests.

    **RECEPTION**

11. (F) The older man decided to **take no prisoners** in answering the quiz questions in the final round of the game show, and hoped the strategy would result in a quick victory.

    **SHOW**

12. (L) Catherine the Great **went belly up** into the swimming pool in my favorite short story from the creative writing course I took.

    **STORY**

13. (L) The eager receptionist **ruffled some feathers** on a homing pigeon before she sent it to her partner who lived in Chicago.

    **PARTNER**

14. (F) After the fancy dinner, Peter **cut a rug** with his wife at the opening ceremony for his new office building.

    **DINNER**

15. (F) The fireman from Chicago **got the picture** about the agreement between the two cities that solved the rush hour traffic problem.

    **CITIES**

16. (L) The Hollywood director **knocked them dead** with one blow from the futuristic fly-swat ter that the mad scientist made.

    **DIRECTOR**

17. (F) The celebrity contestant **jumped the gun** off the blocks at the charity event before the newspaper reporter arrived.

    **EVENT**

18. (L) The talented artist failed to **strike a chord** before his friend’s entrance, even though they had been on the road together many times in the past.

    **TALENTED**
19. (F) The older actor told Jane to break a leg on opening night before the crowd arrived on the evening of the performance.
   ACTOR

20. (F) At the breakfast buffet, Brian had the guts to eat snails but couldn't finish before his sister started eating her dessert
   SISTER

List 2

1. (L) The smart carpenter sowed the seeds in the field with his wife's cousins when they came to visit last Spring.
   COUSINS

2. (F) On his drive home, Bobby felt the pinch in his wallet from a visit to the doctor for his monthly checkup.
   HOME

3. (F) My uncle from Oregon tied the knot in the church on a sunny afternoon before he went to his sister's house.
   SUNNY

4. (L) The nurse told her boyfriend to blow off steam from the chicken soup but he didn't listen to her and later regretted it.
   NURSE

5. (L) Matt's best friend connected the dots to make a picture of the famous ancient city that she was interested in.
   FRIEND

6. (F) Every day the principal passed the buck to keep his schedule free before he had to meet with all of the teachers who were having trouble with difficult students.
   TEACHERS

7. (L) My younger brother told Tom to draw the line to finish his math homework after he got on the wrong bus for school last Tuesday.
   YOUNGER

8. (F) The repairman Frank shook a leg to catch the fly ball during the softball game at the brand new and very expensive ballpark.
   EXPENSIVE

9. (L) The young man from Australia faced the music in his favorite pub in the United Kingdom's most famous historical village.
   HISTORICAL
10. (F) The mysterious bank robber got the axe for stealing a truck just before the police arrived to investigate the report they received.
   REPORT

11. (L) At 5 am, the old man hit the ceiling with a broom because his neighbors were still playing loud music after he asked them to stop.
   OLD

12. (L) The little girl with lots of freckles dished the dirt into the hole in front of all her friends and everyone was very surprised.
   FRECKLES

13. (F) The professor in a tweed jacket opened old wounds in the community when determining the cause of death for the local newscaster.
   TWEED

14. (F) The goofy weatherman took the plunge into the investment to prove a point to his buddies so they would stop teasing him.
   BUDDIES

15. (F) The farmer told his nephew to dress to kill for the dance before the Thanksgiving feast that they had been planning for months.
   FARMER

16. (L) The clever manager had a ball in his suitcase on the long plane ride home from his trip to see the pyramids in Egypt.
   TRIP

17. (F) The stylish designer turned the tables on the client before the contract was signed for over five million dollars.
   STYLISH

18. (L) The friendly librarian didn't ring a bell to quiet the students at the conservative college when they were studying for midterms.
   COLLEGE

19. (L) The experienced sailor threw a curve to his teammate on the forward deck of the ship on a dark and cloudy day.
   DECK

20. (F) The bored little boy pushed the envelope with bad behavior at the semi-annual neighborhood street festival.
   LITTLE
List 3

1. (L) The fireman from Chicago **got the picture** of the highway between the two cities that solved the rush hour traffic problem.
   **FIREMAN**

2. (L) The older actor told Jane to **break a leg** off the dinner table before the crowd arrived on the evening of the performance.
   **CROWD**

3. (F) The Hollywood director **knocked them dead** with one show about the futuristic fly-swatter that the mad scientist made.
   **MAD**

4. (F) The toddler in a dinosaur shirt **hit the sack** at eight o’clock after a long day of playing outside with his best friend.
   **OUTSIDE**

5. (F) Catherine the Great **went belly up** in the stock market in my favorite short story from the creative writing course I took.
   **WRITING**

6. (F) At the reception the host **broke the ice** by seating everyone together before the band started to play well-known songs for the guests.
   **SONGS**

7. (F) Jim’s twin brothers **buried the hatchet** after their fight yesterday afternoon before their mother called them for dinner
   **TWIN**

8. (L) The older man decided to **take no prisoners** back to the central base camp in the final round of the game show, and hoped the strategy would result in a quick victory.
   **OLDER**

9. (L) Yesterday afternoon Susan **kicked the bucket** around the large yard after the children left to go play miniature golf
   **AFTERNOON**

10. (F) On her way to work, Jenny **blew the whistle** on the crook and then quickly ran away to hide in a safe place.
    **WORK**

11. (L) After the fancy dinner, Peter **cut a rug** with his knife at the opening ceremony for his new office building.
    **OFFICE**
12. (F) The teenager with curly blonde hair **wore the pants** in her family after the tragic accident that happened last September.
   **TRAGIC**

13. (F) The middle-aged plumber **saw the light** about the argument before his young wife arrived in the expensive new SUV.
   **PLUMBER**

14. (L) The tattooed garbage man **smelled a rat** in the glue trap behind the row of abandoned houses near the old train tracks.
   **HOUSES**

15. (L) The world famous art critic **chewed the fat** on his steak for a very long time at the start of a pleasant evening.
   **LONG**

16. (F) The talented artist failed to **strike a chord** in his friend’s memory, even though they had been on the road together many times in the past.
   **ROAD**

17. (L) At the breakfast buffet, Brian **had the guts** on his plate but couldn't finish before his sister started eating her dessert.
   **BUFFET**

18. (F) The eager receptionist **ruffled some feathers** with an Internet post before she sent it to her partner who lived in Chicago.
   **EAGER**

19. (L) The burglar from Montana **spilled the beans** on the table at his mother’s house after a long day of cooking with his family.
   **BURGLAR**

20. (L) The celebrity contestant **jumped the gun** on the floor at the charity event before the newspaper reporter arrived.
   **CELEBRITY**

**List 4**

1. (F) The young man from Australia **faced the music** for drinking too much in the United Kingdom's most famous historical village.
   **YOUNG**

2. (L) The bored little boy **pushed the envelope** across the table at the semi-annual neighborhood street festival.
   **NEIGHBORHOOD**
3. (L) The stylish designer **turned the tables** against the wall before the contract was signed for over five million dollars.

   **CONTRACT**

4. (F) The friendly librarian **didn't ring a bell** to the quiet students at the conservative college when they were studying for midterms.

   **FRIENDLY**

5. (F) My younger brother told Tom to **draw the line** at finishing his math **homework** after he got on the wrong bus for school last Tuesday.

   **WRONG**

6. (L) The mysterious bank robber **got the axe** from the stolen truck just before the police arrived to investigate the report they received.

   **BANK**

7. (F) At 5 am, the old man **hit the ceiling** from the noise because his neighbors were still playing loud music after he asked them to stop.

   **LOUD**

8. (L) The goofy weatherman **took the plunge** into the soft snow to prove a point to his buddies so they would stop teasing him.

   **GOOFY**

9. (F) The experienced sailor **threw a curve** in the debate on the forward deck of the ship on a dark and cloudy day.

   **SAILOR**

10. (L) The farmer told his nephew to **dress to kill** the chickens before the Thanksgiving feast that they had been planning for months.

    **FEAST**

11. (F) The clever manager **had a ball** watching TV on the long plane ride home from his trip to see the pyramids in Egypt.

    **MANAGER**

12. (F) The smart carpenter **sowed the seeds** of a feud with his wife's cousins when they came to visit last spring.

    **SMART**

13. (L) My uncle from Oregon **tied the knot** on the boat on a sunny afternoon before he went to his sister’s house.

    **UNCLE**
14. (L) The repairman Frank **shook a leg** to **scare away a fly** during the softball game at the brand new and very expensive ballpark.

   REPAIRMAN

15. (L) Every day the principal **passed the buck** into his desk drawer before he had to meet with all of the teachers who were having trouble with difficult students.

   PRINCIPAL

16. (F) Matt’s best friend **connected the dots** to solve the mystery of the famous ancient city that she was interested in.

   ANCIENT

17. (L) The professor in a tweed jacket **opened old wounds** during the **examination** when determining the cause of death for the local newscaster.

   LOCAL

18. (F) The little girl with lots of freckles **dished the dirt** about the test in front of all her friends and everyone was very surprised.

   EVERYONE

19. (F) The nurse told her boyfriend to **blow off steam** after the argument but he didn't listen to her and later regretted it.

   BOYFRIEND

20. (L) On his drive home, Bobby **felt the pinch** in his arm from a visit to the doctor for his monthly checkup.

   DOCTOR
References


CHAPTER 5

Conclusion
The studies in this dissertation sought to investigate the nature of lexical processing, specifically lexical access, in individuals with the language disorder Broca’s aphasia. Using a multi-methodological approach, this work examined lexical processing in real time, via on-line behavioral measures and neuroimaging paradigms. The value of this approach was that, by combining these approaches, the current set of experiments was able to shed light on lexical access deficits in Broca’s aphasia in a new way. In addition, data from these different studies informed the design and interpretation of one another. Chapter 2 confirmed the hypothesis that lexical access is delayed in Broca’s aphasia, but that lexical access is also incomplete in this population for an IP’s associated meanings, as compared to lexical access patterns in unimpaired listeners. In order to then investigate the neural bases of this disordered lexical system in Broca’s aphasia, Chapter 3 provided crucial information about the protracted time course of cerebral blood flow in chronic stroke survivors with aphasia, and this information informed the design and analysis of the neuroimaging studies in Chapter 4. Taking this delay into consideration, Chapter 4 then examined the neural bases of IP comprehension in aphasia, both with the goal of localizing this processing in individuals with this disorder, but also with an eye towards understanding the temporal signatures of IP processing at a neural level. These three studies met the goals of the dissertation to investigate lexical access in Broca’s aphasia via a novel approach, and provided information that addresses issues in the idiom literature, as well as issues within the broader literature of lexical processing in Broca’s aphasia. Both of these issues are discussed in turn.
While the current set of studies aimed to speak to the nature of lexical deficits in Broca’s aphasia, by utilizing IPs as a tool to investigate automatic lexical processing across language-impaired and unimpaired populations, the results herein contribute to current understanding of the psycholinguistics of IP comprehension. First, Chapter 2 comprises the first known report to study on-line IP processing in both individuals with aphasia and in older unimpaired listeners. Results from this study indicated that healthy older listeners lexically accessed both the figurative meaning of an IP and the literal meaning of the IP’s final component word, but that these healthy listeners accessed the figurative meaning in advance of the literal one. This finding is significant because it indicates that lexical access for IPs is exhaustive, meaning that all meanings associated with an IP are accessed, but that this access is not immediate for the literal meaning associated with an IP.

Along with this, data from Chapter 2 revealed that this pattern of lexical access depends on IP predictability, such that the figurative meaning of an IP is accessed immediately, but only if that IP is highly predictable. Then, later during on-going sentence comprehension, healthy listeners lexically access the literal meaning associated with an IP’s final word, but only for IPs that are not highly predictable. As was discussed in Chapter 2, this set of findings suggests that healthy, older listeners rely to some extent on predictability with respect to lexical access for multiple meanings of an ambiguous IP, which both concurs with some earlier work in the IP literature (Cacciari & Tabossi, 1988; Titone & Connine, 1994), as well as with reports that hypothesize lexical predictability to interact with real-time lexical access (e.g.
Titone & Connine, 1994). Thus, the current findings speak to the influence of predictability on real-time lexical processing patterns during IP comprehension, and argue that this factor must be considered when examining real-time IP processing (Titone & Connine, 1994; Libben & Titone, 2008). Future research should extend this investigation into which properties of IPs influence patterns of lexical access.

Furthermore, the current dissertation uniquely demonstrated the time course of lexical access for IPs throughout the course of a sentence in which the IP was embedded, and in so doing, this work demonstrated re-access of the figurative meanings of highly predictable IPs at a late time point in the sentence. By titrating the temporal dynamics of lexical access in these unimpaired listeners, Chapter 2 was able to map the ebb and flow of lexical access for an IP’s figurative meaning.

In addition to the pattern of results that was observed for lexical access during IP comprehension in healthy listeners, the current dissertation comprises the first report of on-line IP processing indices in aphasia, specifically, in Broca’s aphasia. This is an important step in the study of IPs for several reasons. First, many prior reports have indicated that aphasic patients evince off-line comprehension impairments for IPs, yet, there has been little to no conjecture in the literature as to the real-time underpinnings of this deficit. Here, evidence has demonstrated for the first time that delayed access of an IP’s meanings occurs in individuals with Broca’s aphasia. In addition, Chapter 2 presented evidence of restricted lexical access in this patient population, as a factor of IP predictability, such that individuals with Broca’s aphasia failed to show significant evidence of lexical access for low predictable IPs.
This finding should serve as an impetus for future studies of on-line lexical processing of IPs in aphasia, so that we may better understand the characteristics of IPs which elicit particular patterns of lexical access in this population. Another benefit of the current study is that this is the first report of IP comprehension and processing within a well-defined typology of aphasia. As all prior reports of aphasic IP deficits have relied on heterogeneous samples (e.g. Cacciari et al., 2006; Papagno & Caporali, 2007; Papagno et al., 2006; Papagno et al., 2004), the current step of examining IP processing solely in Broca’s aphasia specifically links patterns of lexical access with a well-described set of symptoms. Future studies should extend this investigation of lexical access during IP comprehension into work with other aphasic typologies, in order to uncover the real-time signatures of IP processing that correspond with particular typologies.

Also in Chapter 2, this dissertation included a new study of off-line IP comprehension across aphasic and unimpaired participants. Similar to what has been reported previously, the unimpaired participants evinced very high accuracy for IPs that were biased towards either a literal or figurative interpretation (Cacciari et al., 2006; Papagno et al., 2004). By contrast, patients with Broca’s aphasia demonstrated chance-level performance for comprehension of IPs that were biased towards either a literal or figurative interpretation. This result diverges with some previous reports of off-line IP comprehension in aphasia, as some authors have reported that aphasic patients may be biased to interpret IPs literally (Cacciari et al., 2006), which would suggest that patients had some sparing for comprehension of literally-biased IPs.
However, in the results of the off-line study in Chapter 2, patients showed no significant difference in performance between figurative and literal IPs, and generally showed poor performance overall. This difference in the present results from prior reports of a literal IP bias in aphasia may stem from either the task that was used or from the relatively homogeneous patient population that was enrolled in the current study. The majority of prior off-line studies of IP comprehension have utilized tasks that may bias patients to select a literal interpretation of an IP when the patient is administered an IP-to-picture or IP-to-word matching task. The off-line task in Chapter 2 was designed to minimize this potential confound, and so it is possible that the results observed in this chapter reflect the true state of equally impaired comprehension for both the literal and figurative meanings of ambiguous IPs. In addition, the present off-line results may diverge from earlier reports due to the patient population that was enrolled in the current study. Here, only patients with Broca’s aphasia were enrolled, whereas prior studies have used patients with a wide range of aphasic symptomatologies. Thus, the off-line results presented in Chapter 2 indicate that individuals with Broca’s aphasia are impaired in comprehension of IPs, and that this impairment extends equally over IPs biased towards a literal or figurative interpretation.

In addition to contributing the first report of on-line lexical access for IPs in aphasia, this dissertation reports the first investigation of the neural correlates of IP processing in this population. Before proceeding to a neuroimaging study of IP comprehension, however, it was necessary to investigate the underlying
neurophysiology of aphasic stroke survivors. Chapter 3 revealed that this neurophysiological baseline state can differ dramatically between patients, and that some chronic stroke survivors with aphasia demonstrate markedly slowed cerebral blood flow. This was a very important finding because it indicated a need to consider this slowed cerebral blood flow when analyzing neuroimaging data from chronic stroke survivors. Just so, in Chapter 4, this dissertation implemented an analysis methodology that allowed observation and detection of a neural signal at long time intervals in this patient population. By extending the temporal window over which neuroimaging data were observed, Chapter 4 was able to detect markedly delayed neural signal in the majority of patients in the sample; standard neuroimaging analysis parameters might have missed this neural signal by constraining analysis to a very short time period after the stimulus of interest.

Chapter 4 then examined the neural correlates of IP processing among individuals with aphasia, as well as in healthy individuals. This chapter found that the neural correlates of an IP’s associated meanings were largely variable between patients, but included intact neural regions that have been shown to subserve IP processing in healthy individuals, but also included regions of the right hemisphere that are homologous to neural regions that were recruited by the unimpaired listeners in this study, as well as in prior reports of IP comprehension (Hillert & Buracas, 2009; Zempleni et al., 2007). Importantly, despite the fact that the majority of patients, except for one, did eventually show evidence of neural recruitment for either the figurative or literal processing of IPs, a similar temporal pattern was observed as in
Chapter 2; chiefly, figurative processing tended to occur neurally prior to literal processing. This same pattern was also mirrored in the FMRI data from the young and older unimpaired participants, and in this manner, the results from Chapter 4 suggested a neural bases for the results that were observed in the on-line study in Chapter 2.

In addition to the implications of the current results for our specific understanding of IP processing during auditory sentence comprehension, the findings in this dissertation speak more broadly to issues of lexical access and real-time processing in Broca’s aphasia. To tie these results back to the discussion of lexical processing in Chapter 1, the results presented in this dissertation both support the Delayed Lexical access hypothesis in Broca’s aphasics, and also suggest additional avenues for research into this hypothesis. As discussed in Chapter 2, delayed lexical access for an IP’s associated meanings was indeed observed in the Broca’s patients in this study, consistent with the delayed lexical access model. However, this study indicated that lexical access was also restricted to highly predictable IPs, and that individuals with Broca’s aphasia failed to demonstrate lexical access for IPs that had low predictability. If this finding is extrapolated to the study of lexical processing more generally, it suggests that characteristics of a lexical item play a significant role in on-line lexical processing in this population. This result argues that future work in the area of lexical processing in Broca’s aphasia should further investigate this and other lexical properties, such as frequency of the lexical item, in order to clarify the impact that these different properties exert on lexical access in this population.
Importantly, the results in Chapter 2 speak against the slowed syntax hypothesis of Broca’s aphasia, which asserts that lexical access is unimpaired in this population. Clearly, as Chapter 2 found aberrant patterns of lexical access in Broca’s patients, as compared to their unimpaired peers, it cannot be the case that the lexical system remains wholly unaffected in this disorder. Additionally, as the sentence stimuli that were utilized in Chapter 2 contained no syntactic transformations and were all standard canonical sentences, it cannot be argued that this delayed lexical access was related to increased syntactic demands. Alongside the results from Chapter 2, Chapter 4 allowed an investigation into the neural correlates of this slowed lexical access in Broca’s aphasia. While the neuroimaging signal that was observed in Chapter 4 is more temporally-course than the real-time measures of lexical access that were used in Chapter 2, it is significant that the same pattern of lexical processing for an IP’s multiple meanings was observed across these two studies. It is an exciting finding in Chapter 4 that all three participant groups showed temporally-offset neural signal for the multiple meanings of an IP. In addition, the patterns of neural activity that were observed in patients with Broca’s aphasia in Chapter 4 suggest that individuals with this disorder may recruit non-optimal neural regions during comprehension of ambiguous lexical items, which may ultimately play a large role in slowed lexical access.

While this dissertation contributed significantly to our understanding of lexical processing in Broca’s aphasia, this set of studies also raised a number of significant questions that should be investigated in future research. As already mentioned above,
intriguing patterns of lexical access were noted in Broca’s aphasics during IP comprehension, such that future work should investigate more closely the lexical properties that influence these patterns of lexical access. For instance, future work may wish to examine the frequency of an IP’s figurative meaning as compared to its literal constituent meanings, and use this frequency information in an analysis of lexical access, as some prior work indicates that frequency is an important factor in lexical access (Beretta et al., 2005; Simpson, 1981; Tabossi, 1988; Tabossi et al., 1987). However, other work has indicated no effect of meaning frequency on immediate lexical access, which contrasts with what was observed here (Onifer & Swinney, 1981). Further research with IPs should attempt to clarify how the frequency of an IP’s associated meanings corresponds with patterns of real-time lexical access.

In addition, the current research found intriguing differences in lexical access between the three probe positions that were tested, but these probe positions were temporally rather distant from one another. Future studies may wish to utilize probe positions at closer intervals to more fully track the time course of lexical access across populations. In addition, future work with larger sample sizes may be able to perform more analysis of the relationship between off-line patterns of IP comprehension and on-line indices of lexical access for these phrases. Such a comparison may allow us to better understand why and how a lexical deficit may in-turn cause poor comprehension of these lexical items.

With respect to the neural underpinnings of lexical access in aphasia, the current study revealed a great deal of variability in neural activity during the
comprehension of IPs, which is not an uncommon finding in neuroimaging studies of aphasia (see e.g. Bonakdarpour et al., 2007; Thompson & den Ouden, 2008; Fridriksson et al., 2007) However, future studies, perhaps with larger sample sizes, may be better able to characterize the relationship between patterns of lexical access in Broca’s aphasia and neural recruitment for those same lexical meanings. Also, additional methodologies to study the neural bases of language processing, such as ERPs or voxel-lesion symptom mapping (Bates et al., 2003) may be particularly helpful in understanding this complex relationship.

In sum, this dissertation demonstrated lexical processing deficits, at both behavioral and neural levels, in Broca’s aphasia, via a novel approach. This work served to expand what is currently understood about lexical access in this population, and will hopefully serve as an impetus for further much-needed work in this arena, so that we may better understand the real-time processing impairments that ultimately contribute to comprehension impairments in Broca’s aphasia.
References


