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Neural Stages of Word Encoding Across Languages, Proficiency Levels, and Modalities

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Neural Stages of Word Encoding Across Languages, Proficiency Levels, and Modalities

A dissertation submitted in partial satisfaction of the
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in

Cognitive Science

by

Matthew Kanter Leonard

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Professor Rachel Mayberry

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The Dissertation of Matthew Kanter Leonard is approved, and it is acceptable in quality and form for publication on microfilm and electronically:

Co-Chair

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2011

DEDICATION

For my parents, David and Susan, and my brother, Adam

TABLE OF CONTENTS

LIST OF FIGURES

NOTE: Supplementary figures, tables, and text can be found online using DOI numbers for study 1 (doi:10.1016/j.neuroimage.2009.12.009) and study 2 (doi:10.1371/journal.pone.0018240).

LIST OF TABLES

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PUBLICATIONS

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ABSTRACT OF THE DISSERTATION

Neural Stages of Word Encoding Across Languages, Proficiency Levels, and Modalities

by

Matthew Kanter Leonard

Doctor of Philosophy in Cognitive Science

University of California, San Diego, 2011

Professor Jeffrey L. Elman, Chair
Professor Eric Halgren, Co-Chair

A growing majority of the world's population is able to speak and understand more than one language, yet most of our knowledge of how the brain processes words comes from monolingual speakers of a small number of languages. Furthermore, most studies of both monolingual and bilingual individuals have utilized brain imaging methods that provide either excellent spatial or temporal resolution, but not both. In aggregate, these studies have demonstrated that information is encoded in both local and regional brain networks across time, so it is therefore necessary to understand the specific spatiotemporal dynamics of these processes.

This dissertation seeks to advance our knowledge of the various stages of word processing across languages in bilinguals and across the various modalities in which language occurs. Using a multimodal imaging approach that combines the temporal resolution of magnetoencephalography (MEG) with the spatial resolution of magnetic resonance imaging (MRI), we focus on an early word form encoding stage and a later lexico-semantic stage in both the visual and auditory modalities.

In two studies with bilingual participants, we show that the less proficient language (regardless of whether it was learned first or second) recruits an extended network of brain regions beginning during the earliest stages of word encoding (~150 ms for written words and ~100 ms for auditory words) and continuing through lexico-semantic processing (~400 ms).

In a third study, we investigate the properties of a newly discovered neural response that occurs at ~100 ms to auditory words. This response represents the encoding of acoustic information into a phonemic code, which can then be passed onto the classical lexico-semantic brain areas (and the extended network in less proficient languages) for integrating the word into the surrounding semantic context.

These studies help clarify the importance of proficiency and experience in evaluating how bilinguals process each of their languages, which provides a unique perspective on the general process of language acquisition. Furthermore, understanding the spatiotemporal dynamics of word encoding in both the visual and auditory modalities allows us to identify fundamental neural mechanisms that are modality- and stimulus-independent.

INTRODUCTION

One of the most significant traits that sets humans apart from all other animals is our use of highly complex linguistic systems. Language allows us to communicate to each other and to ourselves an infinite palette of thoughts, emotions, observations, and predictions, which take advantage of a rich, interconnected network of concepts and representations.

These representations are instantiated in neural systems through dynamic networks of brain regions, which interact over time to form and access information (Indefrey and Levelt, 2004). Generally speaking, it takes ~100 ms for a written word to be encoded in visual cortex, and by ~150 ms, the information is encoded as a word form that is invariant to low-level stimulus properties by a network of regions including left ventral occipitotemporal cortex (Cohen et al., 2000; McCandliss et al., 2003). This information is then sent to the classical left hemisphere fronto-temporal language network where lexico-semantic processing is thought to occur by ~400 ms (Marinkovic et al., 2003; Halgren et al., 1994a; Patterson et al., 2007; Kutas and Federmeier, 2011). For auditory words, the sensory encoding stage occurs by ~60 ms and the lexico-semantic stage is similar to that for written words (Marinkovic et al., 2003). The word form encoding stage, however, has not been well characterized.

Within the monolingual adult population, these stages are remarkably consistent across individuals (though there still exists a significant amount of variability in their timing and locations, particularly for later processing stages). However, the vast majority of the world's population is not monolingual. Anyone who has interacted with a bilingual speaker has likely observed cross-language intrusions and rapid code switching, which suggest that having two languages in one head means that both languages are constantly active, and that they interact with and intrude upon each other (Costa and Santesteban, 2004; Gollan et al., 2002; Potter et al., 1984; Silverberg and Samuel, 2004; Thierry and Wu, 2007; Martin *et al*., 2009).

Furthermore, it is often the case that bilinguals are more proficient in one language, which may alter the way in which words in each language are represented in the brain (Perani and Abutalebi, 2005; Chee et al., 2001; Xue et al., 2004). However, the existing literature does not present a clear picture of how first and second language representations differ, both in terms of the neural substrates and the nature of the representations themselves (Indefrey, 2006).

Part of the reason for these discrepancies may be that most studies have used methods that obscure important aspects of the processing dynamics. The majority of studies with both monolingual and bilingual populations use hemodynamic methods such as functional magnetic resonance imaging (fMRI) and positron emission tomography (PET), which provide excellent spatial resolution, and allow us to see which areas of the brain are active when subjects are presented with or produce words. On the other hand, it is well understood that language processing occurs across time on a millisecond scale, so studies using electro- and magneto- encephalography (E/MEG) have provided crucial information about the timing of neural activity. Each of these methods excels in one dimension of measurement but leaves out the other, and it is difficult to interpret the processing dynamics across studies and methodologies.

This dissertation seeks to provide a better understanding of the spatiotemporal dynamics of the various stages of word processing, and to use bilingual populations to identify the influences of variables such as proficiency and order of language acquisition. We utilize a multimodal imaging approach that combines the millisecond temporal resolution of MEG with the spatial resolution of MRI to examine how dynamic activity in both local and long-distance networks allows us to encode written and auditory words as meaningful stimuli in multiple languages. This method, known as dynamic statistical parametric mapping (dSPM; (Dale et al., 2000)) has been used extensively to study language processing (Dale and Halgren, 2001; Marinkovic, 2004; Dhond et al., 2001; Travis et al., 2011; Leonard et al., 2010; Leonard et al., 2011), and has been validated with direct intracranial recordings (Halgren et al., 1994a; Halgren et al., 1994b; McDonald et al., 2010). Mapping the millisecond-by-millisecond changes in brain activity allows us to create "brain movies", which visualize the dynamic processes that characterize complex cognitive behaviors.

Spatiotemporal dynamics of bilingual word processing

There are three studies that make up this dissertation. The first two examine word processing in Spanish-English bilinguals to understand when specific brain regions become active in the two languages. The first study (Leonard et al., 2010) examines a group of individuals who are native Spanish speakers who began learning English when they started school, around age 5. College age adults at the time of testing, these subjects are more proficient in their native language. We recorded MEG while these subjects read words on a screen and made a semantic decision about them, and we identified a network of brain regions that is more active in the less proficient language, English. While both languages show significant activity in the classical left hemisphere fronto-temporal language network, English additionally recruits bilateral posterior visual cortex. These differences between languages begin during the earliest word encoding stage (~140 ms) and continue through the later lexico-semantic stage, which is indexed by the N400m. The N400m (and its EEG counterpart, the N400) is a neural response that peaks approximately 400 ms after the onset of a meaningful stimulus, and is thought to reflect higher level semantic integration processes (Kutas and Federmeier, 2011). It is modulated by the degree of difficulty of contextual integration, stimulus frequency, and most relevant to the present studies, stimulus repetition. The between language differences occurred mostly for words that were only presented once in the experiment (as opposed to those that were repeated several times), suggesting that the extended network of brain regions is recruited only for less familiar words in the less familiar language.

However, it may be the case that because English was acquired after Spanish in these subjects, it is not proficiency that drives the recruitment of these extra regions, but rather order of acquisition. Even though these subjects are classified as "early learners" because they began acquiring English at age 5, their Spanish-only experience should not be discounted. Age of acquisition is known to have profound effects on language processing and representations (Mayberry, 2007; Hernandez and Li, 2007), and the native language may gain special access to the classical language networks that then become less directly available to later learned languages. Models of bilingual lexical representation take into account differential access to a higher level conceptual store, which may be modulated by proficiency or age of acquisition, depending on the specific linguistic domain (Kroll and Stewart, 1994).

Language proficiency modulates the recruitment of non-classical language areas in bilinguals

To test whether proficiency or order of acquisition modulates the recruitment of non-classical language areas, the second study (Leonard et al., 2011), investigated a second group of bilinguals who were similar to those in the first study except that they had become more proficient in their second language (English). Using the same task and methods, we found that Spanish, the less proficient language, recruited the extended bilateral posterior network to a greater extent than English. Again, this difference started during the earliest word encoding stage and continued through the time period of the N400m. Because both groups of subjects began acquiring English at the same age, language proficiency at the time of testing appears to be the main factor in determining the amount of activity in the extended network during word reading.

We additionally wanted to know whether these areas exhibited the same functional properties as the left fronto-temporal network, and specifically whether their response is invariant to stimulus modality (and thus reflect higher level lexico-semantic processes), so we also presented subjects with auditory words in both languages. Again, Spanish words evoked greater responses in the extended network, beginning during what is assumed to be the auditory word form encoding stage (~100 ms) and continuing through lexico-semantic processing.

Taken together, the results of the first two studies support the notion that language proficiency is an important factor in the networks that are recruited to process words (Moreno and Kutas, 2005; Perani and Abutalebi, 2005; Chee et al., 2001; Xue et al., 2004). We propose that the recruitment of these additional regions reflects the difficulty of encoding and integrating the stimulus, both in the global language context and in the context of specific words during the task (i.e., new versus repeated stimuli). These findings are important because they present evidence of a systematic difference between expert and non-expert processing in the domain of language. Many of the regions we have identified as being active during word processing in the less proficient language are also more active in children than adults (Brown et al., 2005), and may reflect a different underlying representational structure for concepts (Gentner, 1988; Storck and Looft, 1973). Understanding these differences will have profound implications for how second languages are taught in schools, and also for the treatment of language disorders in bilingual adults and children.

Neural Separation of Acousto-phonemic from Lexico-semantic Word Encoding

Finally, the third study (Travis & Leonard *et al.*, In Preparation) addresses an issue that arose in the second bilingual study: The earliest differences in the auditory modality occurred at ~100 ms, suggesting that by that time, the brain is capable of distinguishing the language it is hearing. The time course and anatomy of auditory processing are fairly well established, with a progression from the dorso-medial and lateral portions of Heschl's gyrus in the superior temporal plane at ~10-60 ms, to a large auditory evoked potential at ~100 ms centered in the planum temporale (Liégeois-Chauvel et al., 1994). This later component has been observed in EEG as the N100 (or the M100 in MEG), and is sensitive to acoustic properties, but is not thought to be sensitive to higher level linguistic differences such as phoneme contrasts (Hari, 1991).

However, our finding that a large peak at ~100 ms in planum temporale is sensitive to Spanish versus English contrasts is consistent with findings that the M100 is modulated by attention, with inter-hemispheric differences being the most prominent (Poeppel et al., 1996). This suggests that there may be multiple processes occurring during the time window of the N/M100, some of which could be sensitive to linguistic features.

To investigate this question, we recorded a set of 250 single syllable English concrete nouns, and then constructed time- and frequency- matched control stimuli from the words using a noise vocoding procedure (Shannon et al., 1995). The contrast between words and their noise counterparts was designed to activate the early sensory components in an identical manner, while the later components (including those during the time of the M100) should be different due to the unintelligible nature of the noise. Furthermore, we wanted to know whether any word-selective processes at ~100 ms were also sensitive to higher level and top-down features like lexico-semantics. Therefore, we paired the word/noise stimuli with a picture of an object that was either matched or mismatched to the sound (i.e., a picture of a dog followed by the word or noise for "dog", versus a picture of a dog followed by the word or noise for "scarf"). We predicted that this would evoke N400-like activity for congruous versus incongruous words that began after the early word-noise effect.

Indeed, we found a dissociation between word-selective and lexico-semantic activity. Due to the timing and location of the early component, which we term the M100w (word-selective), we suggest that this process represents the encoding of the word stimuli from their acoustic features to the phonemic code, which can then be passed along to the lexico-semantic areas to determine if the sound that was heard matched the picture context. The M100w is invariant to task (active versus passive listening), speaker, and stimulus characteristics, and it is also spatially distinct from the classical M100 component, which we evoked using binaurally presented tones.

All of these findings suggest that the auditory modality has a process that is similar to the visual word encoding process that has been found for written words (Cohen et al., 2000; McCandliss et al., 2003), and which we found is affected by language proficiency (Leonard et al., 2010; Leonard et al., 2011). This opens up a set of interesting questions regarding the availability of higher level knowledge during the initial stages of word encoding in both modalities. Are between language differences at ~100-150 ms due to phonemic differences between Spanish and English, or are there top-down influences that tag information as being in one specific language? Our data on the M100w suggest that this encoding process does not have access to higher level information about the language, though there may be other factors that can influence activity at this time, especially when words are placed in richer contexts like sentences.

Conclusions

Bilingualism provides a unique opportunity to examine questions ranging from how experience and maturation interact in neural development to how networks in the brain communicate to influence both early and late stages of processing. This dissertation addresses these questions at a certain level, but most importantly, the results of these studies have introduced a new set of questions. It is of great interest why a bilateral posterior network of mostly visual regions is recruited to a greater extent in the less proficient language (and in a less developed language in the case of school-age children). Are the representations themselves different? Is it simply a matter of greater resources necessary to process more difficult stimuli? These are questions I am currently pursuing in collaboration with Tim Brown and Lara Polse, who are investigating the neural underpinnings of conceptual development and representation in children. Regarding the M100w, how specifically does this response differ for highly and essentially non-proficient languages in bilinguals? How early does this process develop in infants, who have similar lexico-semantic networks as adults (Travis et al., 2011)? Is this process affected in language disorders such as dyslexia and specific language impairment, and if so, is it affected differentially in bilinguals' two languages? Katie Travis and I plan to examine these questions directly using both the dSPM approach with MEG and with direct intracranial recordings to dissociate specific cortical areas involved in these processes.

Finally, I have been working with Rachel Mayberry and Naja Ferjan Ramirez, using the dSPM method to understand the spatiotemporal dynamics of sign language processing. American Sign Language (ASL) is a language that occurs in another modality, most commonly among individuals who are deaf or hard of hearing. One question we hope to address is whether the existence of visual and auditory word form encoding processes implies that there is a sign form encoding process. What are the earliest stages of sign-specific activity? Additionally, many signers are bilingual in ASL and English since most learn to read and in some cases speak English. How do multimodal bilinguals differ from bilinguals who learn two auditory languages? Are proficiency effects similar? Finally, since many congenitally deaf individuals acquire ASL as a first language later than people who are born hearing, how does age of acquisition affect both early and late stages of sign encoding?

I am excited by the prospect of so many new questions, and I look forward to pursuing their answers throughout my career. I am fortunate to have so many complementary methods at my disposal, some invasive and others harmless, which allow us to see inside the live, functioning, and communicating human brain. We are just beginning to understand the fundamental properties of how the brain works. The next revolution in cognitive neuroscience should consider applying these methods to non-monolingual and non-English speaking populations as often and with as much interest as they are applied to university undergraduates because without doing so, any understanding of the brain is incomplete.

A note about the studies

The first two studies in this dissertation are published papers, which can be found online at the journals' websites or on PubMed. It is recommended that readers access these articles by searching online for the following DOI information, as the formatting and quality of the manuscripts stapled her are different and represent pre-production proof stages of the text and figures. In addition, all supplementary figures, tables, movies, and text are available online. The third study is not yet published, and therefore it appears here in its ideal form.

Study 1: doi:10.1016/j.neuroimage.2009.12.009
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CHAPTER 1:

Spatiotemporal Dynamics of Bilingual Word Processing

1.1: Abstract

Studies with monolingual adults have identified successive stages occurring in different brain regions for processing single written words. We combined magnetoencephalography and magnetic resonance imaging to compare these stages between the first (L1) and second (L2) languages in bilingual adults. L1 words in a size judgment task evoked a typical left-lateralized sequence of activity first in ventral occipitotemporal cortex (VOT: previously associated with visual word-form encoding), and then ventral frontotemporal regions (associated with lexico-semantic processing). Compared to L1, words in L2 activated right VOT more strongly from ~135 ms; this activation was attenuated when words became highly familiar with repetition. At ~400ms, L2 responses were generally later than L1, more bilateral, and included the same lateral occipitotemporal areas as were activated by pictures. We propose that acquiring a language involves the recruitment of right hemisphere and posterior visual areas that are not necessary once fluency is achieved.

1.2: Introduction

More than two-thirds of the global population is proficient in more than one language, yet we do not understand how the brain organizes and processes multiple lexicons. Language processing has been studied extensively in monolingual populations, and it has been shown that for written words, over the course of ~1000 ms, there are multiple stages subserved by different cortical regions and networks that are strongly lateralized to the left hemisphere. For single words out of context, early sensory processing occurs in bilateral primary visual cortex ~100 ms after the word is shown. Before ~200 ms, the information is encoded as words in a particular language in an extended network of regions that receive modulated input from an area of left ventral occipitotemporal cortex (VOT) centered on the fusiform gyrus (McCandliss et al., 2003). While VOT's exact functions in word reading are unknown (Price and Devlin, 2003), the region appears to be a crucial early-stage area for successful visual word encoding, which is influenced by both orthographic and lexical manipulations (Pugh et al., 2001; Miozzo and Caramazza, 1998). Finally, lexico-semantic processing is thought to occur at ~400 ms in a network of left fronto-temporal regions including anterior temporal and inferior prefrontal cortex (Halgren et al., 1994b; Marinkovic et al., 2003; Patterson et al., 2007).

Do bilinguals recruit the same left lateralized network for visual word processing? How early does the brain distinguish the language of word presentation? Does the information maintain the posterior-to-anterior flow from early to late processing stages in both languages? During the early visual word encoding stage (~130-200 ms), it has been suggested that the two languages rely on at least partially distinct neural systems, however it is unclear whether areas such as VOT are recruited in both the first (L1, or the language that was first acquired) and second (L2) languages to the same extent (Ohno et al., 2002; Proverbio et al., 2002). Furthermore, the conditions under which L2 recruits additional regions during this early time period are not well characterized.

Later lexico-semantic processing stages have been studied more extensively in bilingual populations. It has been demonstrated behaviorally using lexical decision and other priming paradigms that L1 and L2 are not completely isolated from one another, with both interfering and reinforcing effects having been observed (Gollan et al., 2002; Silverberg and Samuel, 2004; Thierry and Wu, 2007; Potter et al., 1984; Costa and Santesteban, 2004). Yet the existing neuroimaging literature on bilingual lexico-semantic representation is inconclusive and contradictory with respect to how the brain represents the two languages (Simos et al., 2005; Indefrey, 2006). Some studies using functional magnetic resonance imaging (fMRI) and positron emission tomography (PET) have found distinct neural representations for L1 and L2 within the classical left hemisphere language regions (Kim et al., 1997; Marian et al., 2007b; Perani et al., 1998). In studies that specifically examined lexico-semantic processes in bilinguals, in the less proficient language, the left posterior middle frontal gyrus, left inferior frontal gyrus, left anterior cingulate gyrus, and left posterior inferior parietal lobule all show greater activity that is modulated by L2 proficiency (Chee et al., 2001; Xue et al., 2004). In contrast, other studies have found that cortical activation for L1 and L2 is located in identical regions of the left hemisphere (Nakada et al., 2001; Tan et al., 2003; Chee et al., 1999; Klein et al., 1995; Illes et al., 1999).

Though such inconsistencies are likely due in part to different methodologies, subject populations, and tasks being used among studies, it is also the case that the hemodynamic signals (blood flow and oxygenation) that are measured by fMRI and PET indirectly reflect neuronal activity. Because the hemodynamic response is slow (on the order of several seconds), these studies neglect significant information about the temporal dynamics of language processing, which may be critical for isolating brain regions that subserve specific processing stages, including early sensory, visual word encoding, and late lexico-semantic responses.

Other studies have used electroencephalography (EEG) to investigate the temporal dynamics of bilingual lexico-semantic processing, and have found that a negative-going event-related potential (ERP, which is derived from the stimulus-locked EEG signal) known as the N400 is delayed in the less proficient L2 compared to L1 (Alvarez et al., 2003; Hahne, 2001; Ardal et al., 1990; Phillips et al., 2006; Moreno and Kutas, 2005). The N400 (and its magnetic counterpart, N400m) has been used as a measure of linguistic processing, since it has been shown to vary its amplitude and latency in relation to the degree of difficulty of contextual integration, stimulus frequency, and stimulus repetition (Kutas and Federmeier, 2000). The differences in N400 latency that have been found in bilingual populations suggest that at the very least, L1 and L2 are processed on different time scales in the brain. However, the poor spatial resolution inherent to EEG makes it difficult to determine whether these temporal differences are localized within common brain areas or whether longer latency N400 responses are related to the recruitment of additional regions in the less dominant language.

In addition to identifying distinct stages in bilingual language processing, we sought to expand the focus of the late lexico-semantic stage beyond the classical left hemisphere frontal and prefrontal regions. There is reason to suspect that when a speaker is not as proficient in L2 compared to the native language, the locations of all or some of the representations may be different (Silverberg and Samuel, 2004; Perani et al., 1998). In the present study, we hypothesized that in addition to a shared left fronto-temporal substrate, L2 learners would show significant activity in right hemisphere (Dehaene *et al.*, 1997) and other areas in the less proficient second language. It has been suggested previously that the right hemisphere's specialized functions may aid both first and second language learners by providing an additional level of analysis when processing stimuli is more difficult (Goldberg and Costa, 1981; Goldberg et al., 1978; Seliger, 1982). Furthermore, studies of child L1 acquisition have shown that bilateral posterior visual processing areas including lateral and ventral occipitotemporal cortex are more active in children than in adults (Brown *et al.*, 2005; Schlaggar *et al.*, 2002). We sought to examine whether these regions are more active in the non-dominant L2, even though the bilingual individuals in this study had already attained fluency in one language.

The primary aim of this study was to provide a novel perspective on bilingual word processing by examining both early (~150 ms) and late (~400 ms) stages in L1 and L2 with high spatiotemporal accuracy. We used a multimodal imaging approach, which combines magnetoencephalography (MEG) and high-resolution structural MRI to obtain a detailed spatiotemporal picture of dynamic brain activity. MEG is generated principally by the current flows within the apical dendrites of cortical pyramidal cells that result from synaptic and other active transmembrane currents (Cohen and Halgren, 2009). To localize the sources in the cortex, we applied a noise-normalized cortically-constrained minimum norm inverse solution known as dynamic statistical parametric mapping (dSPM) (Dale et al., 2000; Dale and Sereno, 1993). Although source estimation from MEG or EEG is always uncertain, this method has been shown to produce results that are consistent with intracranial recordings of local field potentials during language tasks (Halgren et al., 1994a; Halgren et al., 1994b; Marinkovic, 2004). dSPM provides maps of event-related cortical activity with millisecond temporal resolution and spatial resolution of about a centimeter.

Eleven adult Spanish-English bilingual participants who began acquiring English around age six, but who consider themselves more proficient in their native Spanish, viewed single visually presented concrete nouns in each language and simple line drawings and made size judgments about the stimuli while whole-head high-density MEG signals were recorded. N400m-like responses were evoked using a repetition priming paradigm, in which some of the stimuli were repeated throughout the experiment, and were interspersed with novel stimuli that were seen only once. This classical N400 manipulation allowed us to vary the ease with which subjects processed words in both languages (specifically during lexico-semantic processing), thereby permitting us to examine whether hypothesized differences in right hemisphere and bilateral visual areas related to proficiency in the non-native language.

1.3: Materials and Methods

1.3.1: Subjects

Eleven healthy right-handed adults (3 males, age range 18-29 years, mean 21.42 ± 3.00 years) participated in this study. Participants reported no history of psychological or neurological impairment, and all had completed at least some college. All were native Spanish speakers and were sequential L2 English learners, although they began acquiring English early in life when they entered school (mean age of acquisition = 5.83 years, SD = 2.17 years). We selected this group because these subjects are likely to be homogeneous in terms of proficiency, and they have had significant experience with both languages. Therefore, any neural differences are likely to be chronic and fundamental, rather than passing or nonspecific effects of incomplete learning. Language history and proficiency in both languages were assessed by a detailed questionnaire that asked subjects to rate learning sources and degrees of exposure to each language, and their reading, writing, and speaking abilities in each language (adapted from (Marian et al., 2007a; see **Supplementary Materials**). L1 is defined as the language that was acquired first, however these subjects also considered L1 to be the dominant language.

On a scale from 1-10, all subjects rated their abilities in both languages between 7 and 10, so they can be considered proficient speakers in both languages. With one exception, all participants rated their L2 abilities lower than their L1 abilities, which was also confirmed by ten subjects reporting that they would always choose to speak in their native language (Spanish) if given a choice. All but one participant indicated that they began reading in L1 prior to L2, and five subjects rated their L1 reading abilities (mean = 9.0) higher than their L2 reading abilities (mean = 8.6), while two subjects rated L1 and L2 reading skills at the same level, and three subjects rated L2 better than L1 (one subject's self assessment scores were lost). Seven subjects responded that they would choose to read in L2 at least as often as in L1. All but two subjects reported using L2 more on a daily basis as adults, and every subject indicated that he or she spoke L1 more as a child. In general, these types of self-assessments of language proficiency have been shown to be accurate measures that correspond with more objective assessments (Marian et al., 2007a; Ross, 1998). Participants gave informed, written consent and were paid for their time. This study was approved by the Institutional Review Board at the University of California, San Diego.

1.3.2: Task

Subjects performed a semantic size judgment task for visually presented words and line drawings while MEG was recorded. The task is similar to a previous MEG lexico-semantic language study (Marinkovic *et al.*, 2003) and a concurrent study of monolingual adults and children. All stimuli were concrete, highly imageable objects, and were both high frequency and early-learned words in each language of presentation. Approximately 85% of the stimuli were not cognates in Spanish and English, which helps to control for the overlap between representations across languages at initial levels of processing. The base set of stimuli was taken from a standardized dataset (Snodgrass and Vanderwart, 1980), and was complemented by stimuli from another database that has been standardized across multiple languages (Szekely *et al.*, 2004). The participants were told that they would not see definite or indefinite articles in front of the words, since one potential flaw in studies of Spanish-English bilinguals is that Spanish words presented without an article are unnatural to native speakers and highly proficient L2 learners (Peña, 2007). By setting up an expectation that the nouns would be presented in isolation, we hoped to reduce these effects.

Participants were instructed to lift one finger from a response paddle if the object “fits into a shoebox,” and to lift the other finger if the object was too large to fit into a shoebox. The response hand mappings were counterbalanced across subjects. In addition, subjects were asked to remain still during data acquisition (they were told that they would be given breaks between each 3 minute block), and to respond as quickly as possible. The stimuli were mixed in terms of difficulty for the size judgment task (see

Supplementary Table 1 for examples of word and picture stimuli).

Each participant completed four blocks of stimuli in each of L1, L2, and picture conditions (12 blocks total). The first block of each condition was a practice block that was used to set up the repetition priming effect, where subjects were presented with ten stimuli that repeated six times each in a random order. Throughout the next three blocks of that condition, those same 10 stimuli appeared six more times as repeated presentations, interspersed with 60 stimuli that were shown only once ('novel' stimuli). Within each participant, different stimuli were presented in each language to ensure that the novel stimuli were truly novel within the task. Stimulus presentation order within each block was randomized, with the only constraint being that there must be at least one intervening novel stimulus between presentations of a particular repeated stimulus. For each trial, a word was presented for 300 ms, followed by a masking fixation cross for 2000-2200 ms, during which subjects made their responses.

To ensure that subjects were processing words in L1 and L2 as if they were in an environment where only one language was being used (i.e., not code switching), all blocks in one language were presented in succession, followed by four blocks with non-verbal pictures, and then four blocks in the other language. The order of the languages was counterbalanced across subjects. All interactions with the subjects and instructions for each block were presented verbally in the language of the subsequent stimuli. Once subjects had completed all blocks of the first language of presentation, the experimenter switched to the other language and informed the subjects that the rest of the experiment would be carried out in that language. This was done to allow us to focus on the organizations of the two lexicons, rather than interactions between languages or mechanisms for language switching (despite the fact that these highly proficient subjects were adept at code switching).

1.3.3: MEG recording

Subjects sat in a magnetically shielded room (IMEDCO-AG, Switzerland) with the head in a Neuromag Vectorview helmet-shaped dewar containing 102 magnetometers and 204 gradiometers (Elekta AB, Helsinki, Finland). Data were collected at a continuous sampling rate of 2000 Hz with minimal filtering (0.1 to 200 Hz). The positions of four non-magnetic coils affixed to the subjects' heads were digitized along with the main fiduciary points such as the nose, nasion, and preauricular points for subsequent coregistration with high-resolution MRI images. The average 3-dimensional Euclidian distance for head movement from the beginning of the session to the end of the session was 7.97 mm (SD = 4.19 mm). Most of this movement was in the up-down direction, due to the subjects slowly sinking into the cushions. The mean distances (and standard deviations) in each direction were: X = 1.43 mm (1.64), Y = 1.62 mm (2.34), Z = 7.08 mm (4.37).

1.3.4: Anatomically Constrained MEG Analysis

The data were analyzed using a multimodal imaging approach that constrains the activity to the cortical surface as determined by high-resolution structural MRI (Dale et al., 2000; Dale and Halgren, 2001). This noise-normalized linear inverse technique, known as dynamic statistical parametric mapping (dSPM) provides a solution to the inverse problem that also allows the data to be visualized across time on the cortical surface as movies. Note that EEG and MEG are not sufficient for unambiguous current source localization, because any given extracranial electromagnetic field is consistent with an infinite number of possible equivalent current dipole (ECD) configurations in the brain. The dSPM method reduces this ambiguity with the reasonable assumption that sources are located in the cortex, and the solutions in language tasks have been validated by comparison with direct intracranial recordings (Halgren et al., 1994a; Halgren et al., 1994b; Marinkovic, 2004).

The cortical surface was reconstructed in each individual from high-resolution 3D T1-weighted structural MRI (TE = 4.87 ms, TR = 10.7 ms, TI = 1 sec, flip angle = 8 deg, bandwidth = 16.13 KHz, FOV = 25.6 cm, matrix = 256 x 192, slice thickness = 1.0 mm). Proton density- (PD) weighted MRI (TE = 4 ms, TR = 17 ms, TI = 0 sec, flip angle = 5 deg, bandwidth = 31.25 KHz, FOV = 25.6 cm, matrix = 256 x 192, slice thickness = 1.0 mm) was collected for defining the inner skull surface on each subject for a Boundary Element Model forward solution (the expected MEG sensor values based on known activity in the cortex) (Oostendorp and Van Oosterom, 1992).

The cortical surface was then downsampled to ~2500 dipole locations per hemisphere (Dale *et al.*, 1999; Fischl *et al.*, 1999), and the activity of each of these dipoles was estimated at each latency (however, the dipoles at each location were not constrained by their orientations). The noise sensitivity at each dipole location was estimated from the average baseline across all conditions. Significance levels reported on the mean dSPM images were derived by taking the square root of the F-distributed mean activity with 33 degrees of freedom in the numerator (3 dipoles at each location X 11 subjects). The denominator degrees of freedom were 50, derived from the number of time points used to calculate the average noise covariance matrix for each condition. For each individual condition, significance thresholds were set at $p < 10^{-11}$, with a full yellow response indicating $p < 10^{-21}$. The *p*-values in these maps, which do not compare activity between conditions or directly take into account between-subject variance, should be viewed as measures of signal to noise at each point on the cortical surface.

The data were inspected for bad channels (channels with excessive noise, no signal, or unexplained artifacts), which were excluded from all further analyses. Additionally, trials with large (>3000 fT for gradiometers) transients were rejected. Blink artifacts were removed using independent components analysis (ICA; (Delorme and Makeig, 2004) by pairing each MEG channel with the electrooculogram (EOG) channel, and rejecting the independent component that contained the blink. This allowed us to include approximately 55-60 trials per condition for each subject. The data were epoched from -200 ms to 1000 ms relative to stimulus onset, and all valid trials were included in the analysis, regardless of task performance. See **Supplementary Figure 4** for a single representative subject's data in sensor space. Individual subject dSPMs were constructed from the averaged data in the 1200 ms epoch for each condition using only data from the gradiometers, and then these data were combined across subjects by taking the mean activity at each vertex on the cortical surface and plotting it on an average brain. Vertices were matched across subjects by morphing the reconstructed cortical surfaces into a common sphere, optimally matching gyral-sulcal patterns and minimizing shear (Sereno et al., 1996; Fischl et al., 1999). All statistical comparisons and ROI analyses were made on these group data, as described in the results.

1.4: Results

1.4.1: Reaction Time

Reaction time data was obtained in 10 subjects. One participant's behavioral responses were lost due to an equipment malfunction. Reaction times were entered into a repeated-measures ANOVA, with stimulus type (L1 vs. L2 vs. pictures) and repetition (novel vs. repeated) as factors. Subjects responded significantly faster to repeated than novel stimuli, F(1,9) = 181.65, $p < 0.0001$ (**Table 1**). There was also a main effect of stimulus type [F(2,18) = 13.00, $p < 0.0001$], however post-hoc *t*-tests determined that the difference between L1 words and L2 words was not significant. There were significant differences between novel L1 words and pictures [t(9) = 2.99, $p < 0.02$], repeated L1 words and pictures [t(9) = 3.02, $p < 0.02$], novel L2 words and pictures [t(9) = 4.03, $p < 0.004$], and repeated L2 words and pictures [t(9) = 4.05, $p < 0.004$]. The interaction between stimulus type and repetition was not significant.

Table 1.1: Mean reaction times with standard deviations for ten subjects. Subjects responded faster to repeated words in both languages (and for pictures), and did not differ significantly between L1 and L2. The responses to pictures were significantly faster than for both languages.

Condition	**Mean (SD)** **reaction time in ms**
L1 Novel	972 (151)
L1 Repeat	760 (131)
L2 Novel	915 (116)
L2 Repeat	753 (142)
Pics Novel	844 (112)
Pics Repeat	642 (67)

1.4.2: MEG Estimates

Noise normalized dSPMs were calculated for each subject, and then averaged onto a common space as a group mean of the estimates (**see Supplementary Movies 1 and 2** for the dynamic activity over the full time course). From the group mean time courses of the activity, temporal windows were selected for statistical analysis in various regions of interest (ROIs). 17 ROIs were selected based on *a priori* hypotheses about the data, combined with information from a grand average of the activity across all subjects and all conditions. In most cases, each ROI was anatomically constrained to part of a single sulcus or gyrus (**Supplementary Figure 1**). The group average F-values from the time course of the mean activity within each ROI were entered into a repeated-measures ANOVA with language (L1 vs. L2) and repetition (novel vs. repeated) as within-subject factors (pictures were added as a level in the language factor for additional analyses). All reported *p*-values are uncorrected for multiple comparisons.

1.4.3: Early Sensory Processing (~90-110 ms)

To ensure that there were no early perceptual processing differences at ~100 ms post-stimulus onset that could affect downstream cognitive responses, we examined the activity in the primary visual cortex ROI during this time period (**Supplementary Figure 2**). The only effect during this time window was a marginally significant language by repetition interaction in the right occipital pole [F(1,10) = 4.66, $p = 0.056$], however no post-hoc paired samples *t*-tests were significant.

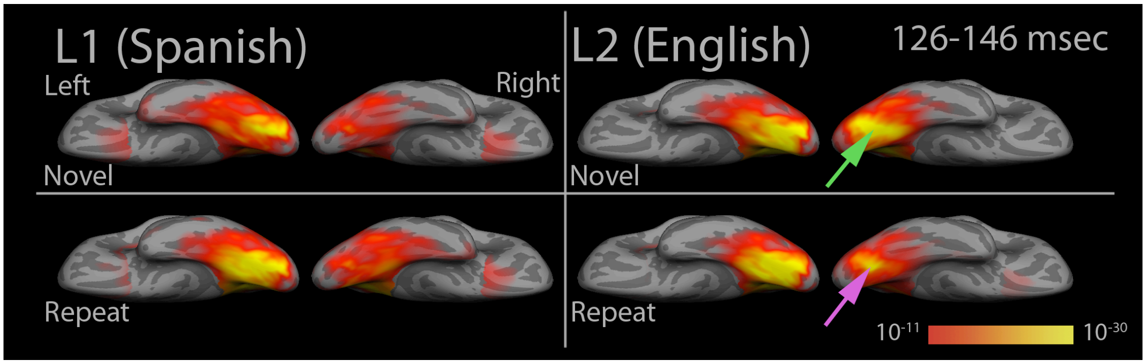


Figure 1.1: Group dSPM images of the mean activity during early visual word encoding (~136 ms post-stimulus onset) for 11 subjects. Spanish (L1) showed strongly left lateralized activity in VOT. In contrast, English (L2) showed activity in bilateral VOT (green arrow). In addition, right VOT in L2 showed an effect of stimulus repetition (purple arrow). Significance levels (a measure of signal-to-noise) are indicated by the color bar.

1.4.4: Early Visual Word Encoding Responses (~126-146 ms)

The group mean dSPM revealed an activity peak in VOT at ~136 ms post-stimulus onset, which lasted until approximately 180 ms. The data were averaged over a

20 ms time window surrounding 136 ms (126-146 ms), and we compared the activity in left and right VOT across conditions. In the left hemisphere, the posterior fusiform ROI did not show any significant effects of either language or repetition (**Figure 1**). However, the right posterior fusiform demonstrated a significant language by repetition interaction [F(1,10) = 7.09, $p = 0.02$], with novel L2 words > novel L1 words, t(10) = -2.55, $p = 0.03$ (**Figure 1** and **Figure 2**). In L2, repeated words were suppressed relative to novel words, t(10) = 2.59, $p = 0.03$.

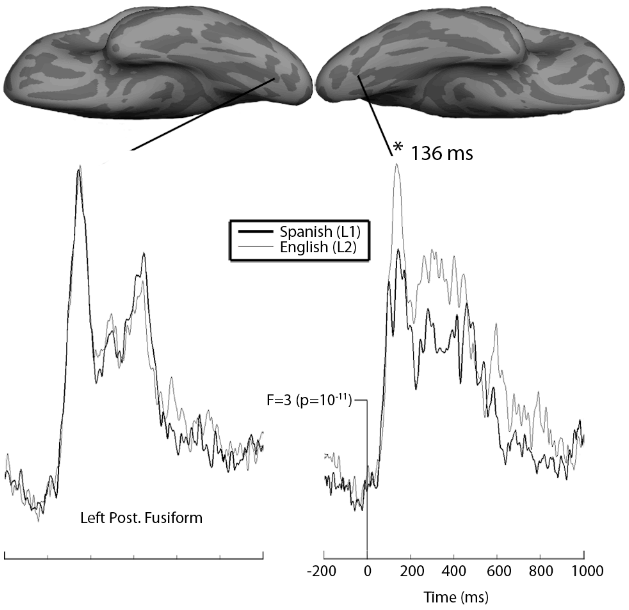


Figure 1.2: Average time courses for the estimated noise-normalized dipole strength to initial presentation words in Spanish (L1) (thick lines) and English (L2) (thin lines) in posterior fusiform cortex. Although there was no difference between languages in left posterior fusiform gyrus, right posterior fusiform showed a L2 > L1 response during an early peak at ~136 ms.

1.4.5: Lexico-semantic Responses (~380-420 ms)

Numerous areas in both hemispheres were found to generate significant activity to words in L1 and in L2 during a 40 ms window around 400 ms chosen *a priori* as during the construction of lexico-semantic representations (**Figure 3** and **Figure 4**; see **Supplementary Materials** and **Supplementary Figure 3** for analyses of a slightly earlier peak response time window). During this time window, two regions showed significant main effects of language. The posterior superior temporal sulcus (STS) in the left hemisphere showed a significantly greater response to L2 words than to L1 words, $F(1,10) = 6.07, p < 0.05$. The posterior STS also showed a main effect of repetition, with novel > repeated words, $F(1,10) = 5.38, p < 0.05$. The only other region to show a significant main effect of language at this time was the right hemisphere inferior precentral sulcus, where L2 words elicited a greater response than L1 words, $F(1,10) = 6.54, p < 0.05$. This region also showed a trend toward an interaction between language and repetition, with novel L2 words showing a greater response than novel words in L1, [$F(1,10) = 3.90, p = 0.076$], which was confirmed by a post-hoc paired samples *t*-test, $t(10) = -2.84, p < 0.02$.

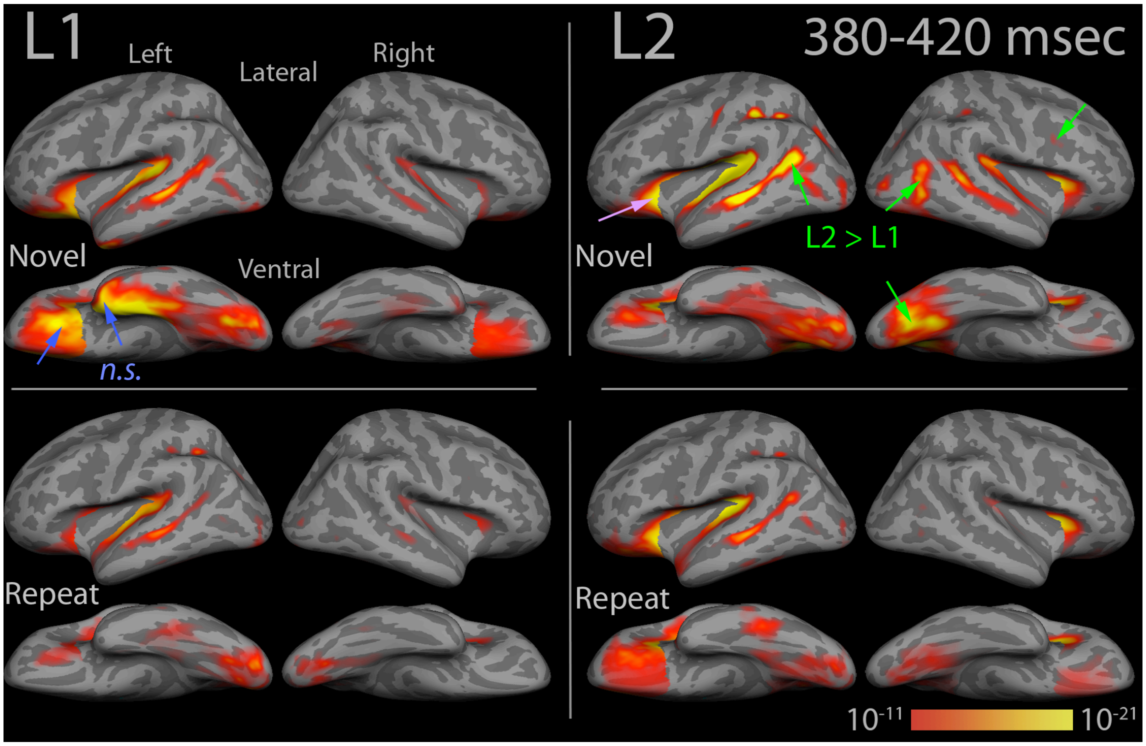


Figure 1.3: Group dSPM images of the mean activity during the *a priori* lexico-semantic time window (~400 ms) for 11 subjects. L2 showed greater activity than L1 in posterior regions including right LOT, left posterior STS, and right lateral VOT, and in right inferior precentral sulcus (green arrows). Despite differences in the mean maps in left inferior frontal and anterior temporal regions (blue arrows), the between-subject variability was too high for such language differences to reach significance. Stimulus repetition effects were significant for many regions in both hemispheres. The light purple arrow indicates left anterior insula, which showed significant L2 > L1 language effects during the peak time window around ~372 ms. Significance levels (a measure of SNR) are indicated by the color bar.

Additionally, in a lateral region of ventral occipitotemporal cortex (VOT) in the right hemisphere, at ~400 ms, responses to repeated words were suppressed relative to novel words [$F(1,10) = 5.50$, $p < 0.05$], and there was a trend toward a significant language by repetition interaction, $F(1,10) = 4.03$, $p = 0.07$. Post-hoc paired samples *t*-tests confirmed that this interaction was driven by differences between novel words in each language [$t(10) = -3.20$, $p = 0.01$], and also by a strong repetition effect in L2, $t(10) = 3.42$, $p < 0.01$.

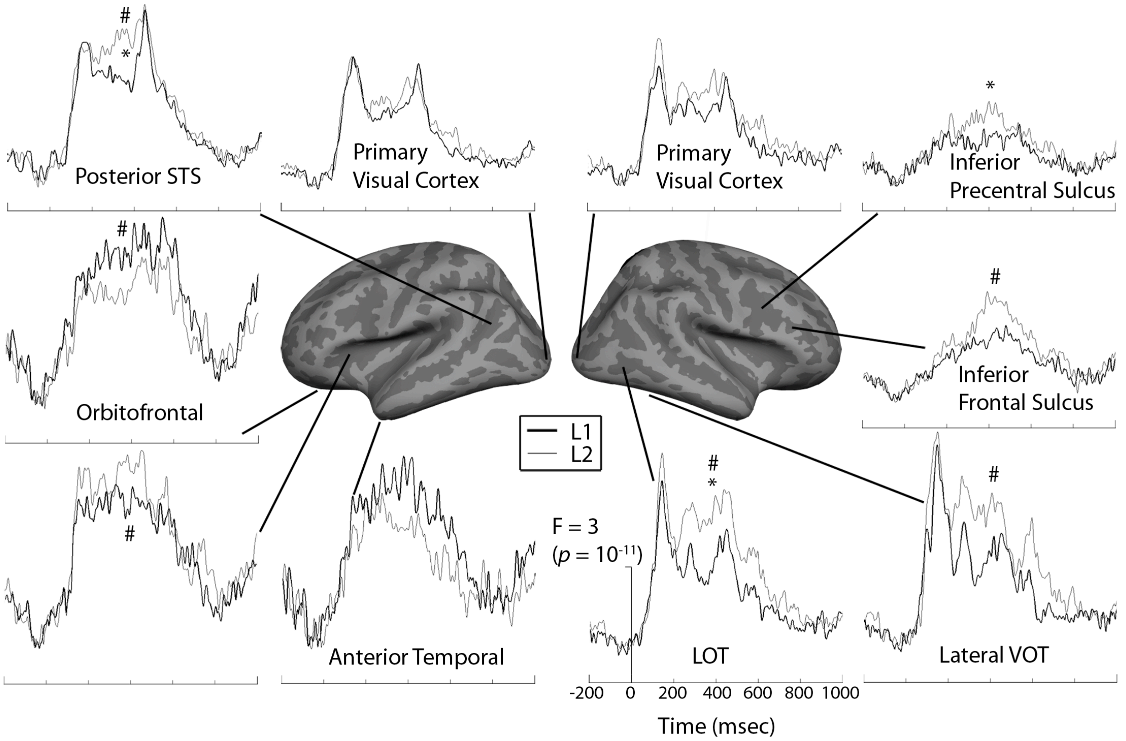


Figure 1.4: Average time courses for the estimated noise-normalized dipole strength to novel words in L1 (thick lines) and L2 (thin lines). Shown for both hemispheres are a selection of the 17 ROIs that were chosen for statistical analysis. Time courses with a * denote regions with a significant language difference at ~400 ms, while time courses with a # denote additional regions that were significant during the peak window at ~372 ms.

Several other regions showed significant main effects of repetition at ~400 ms, all with novel > repeated words. In the left hemisphere, these regions included an area of posterior fusiform cortex [F(1,10) = 7.77, $p < 0.05$], and a nearby area of medial VOT, F(1,10) = 5.76, $p < 0.05$. In the right hemisphere, intraparietal sulcus [F(1,10) = 5.50, $p < 0.05$], anterior STS [F(1,10) = 6.95, $p < 0.05$], and posterior STS [F(1,10) = 16.90, $p < 0.005$] all showed novel > repeated effects.

Also in the right hemisphere, a region of lateral occipitotemporal (LOT) cortex showed a similar main effect of repetition, F(1,10) = 11.82, $p < 0.007$. This region also demonstrated a significant interaction [F(1,10) = 6.26, $p < 0.05$], which was driven by an L2 > L1 difference for novel words [t(10) = -3.90, $p < 0.005$] and by a strong repetition effect in L2, t(10) = 3.53, $p = 0.005$.

In left anterior temporal cortex, the mean dSPM images appeared to show strong effects of both language and repetition. While the repetition effect was significant [F(1,10) = 8.59, $p < 0.02$], the apparent language-related effects were not, due to relatively high variability between subjects in these regions.

1.4.6: Words vs. Pictures

Since we hypothesized that L2 would show activity in posterior visual processing regions during lexico-semantic encoding, we compared the activity between words and line drawings of objects. Overall, pictures produced a more bilateral response than words, as we anticipated. At ~400 ms, we found similarities in the mean dSPM images between L2 words and pictures, both of which differed from L1 words (**Figure 5**). A repeated-measures ANOVA with stimulus type (L1 vs. L2 vs. pictures) and repetition (novel vs. repeated) revealed statistically significant main effects of stimulus type in left posterior STS [F(2,20) = 4.77, $p = 0.02$], right posterior fusiform [F(2,20) = 3.52, $p < 0.05$], right inferior precentral sulcus [F(2,20) = 4.32, $p < 0.03$], right inferior temporal cortex [F(2,20) = 3.47, $p = 0.05$], right lateral VOT [F(2,20) = 4.26, $p < 0.03$], and right anterior temporal cortex, F(2,20) = 3.89, $p < 0.04$. The following left hemisphere regions showed significant main effects of repetition: posterior STS, posterior fusiform, and anterior temporal cortex. Repetition effects were also found in these right hemisphere regions: intraparietal sulcus, anterior STS, posterior STS, and LOT.

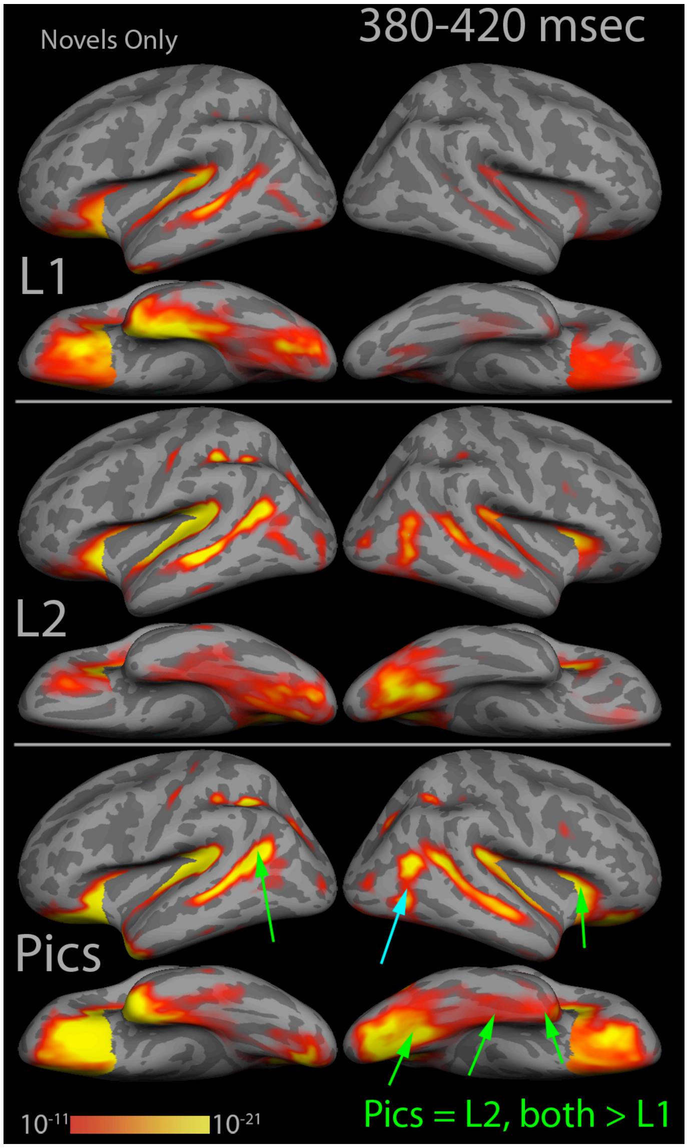


Figure 1.5: Group dSPM images of the mean activity for novel stimuli ~400 ms for 11 subjects. In several areas, main effects of stimulus type (L1 vs. L2 vs. pictures) were significant such that L2 words and pictures showed similar responses that differed significantly from L1 words (green arrows). One region of particular interest, right LOT, showed an interaction where this pattern emerged only for novel stimuli (cyan arrows), suggesting that LOT processes novel pictures and L2 words similarly, but shows less of a response for L1 words. Significance levels (a measure of SNR) are indicated by the color bar.

Several regions also showed stimulus type by repetition interactions. The only region on the left with such an effect was lateral VOT [F(1,10) = 5.04, $p < 0.02$], although no post-hoc tests were significant. In the right hemisphere, LOT showed a trend toward an interaction [F(1,10) = 2.96, p = 0.075], where novel L1 words differed significantly from novel L2 words [t(10) = 3.90, p < 0.005] and from novel pictures [t(10) = 2.50, p = 0.03] (**Figure 6**). Lateral VOT and inferior precentral sulcus showed the same pattern of L2 and pictures having similar responses, and both differing from L1.

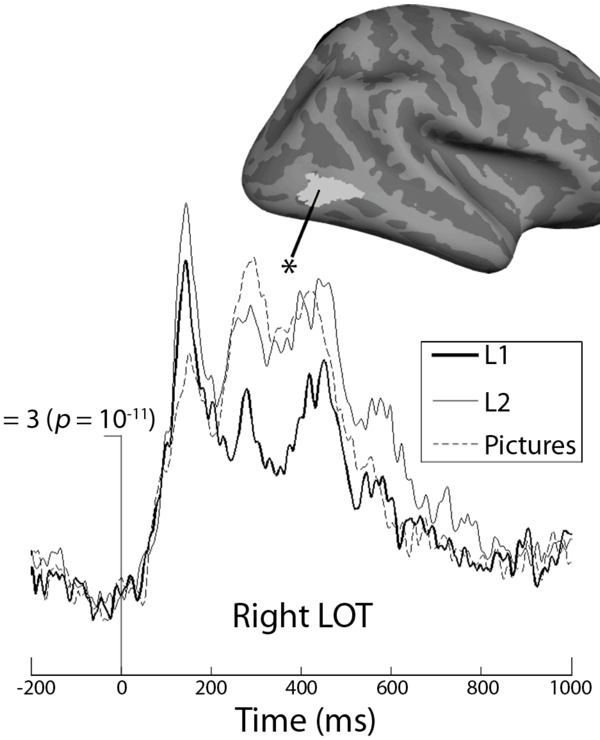


Figure 1.6: Average time course for the estimated noise-normalized dipole strength to novel stimuli in right LOT for words in L1 (thick line), L2 (thin line), and pictures (dashed line). At ~400 ms, pictures and L2 words show a similar response that differs significantly from L1 words.

1.4.7: Peak Latency Effects

An additional hypothesis relates to the timing of peak N400m activity in L1 versus L2. Previous electrophysiological studies have demonstrated a delay in the peak of the N400 response in L2 compared to L1 (or the non-dominant compared to the dominant language). Therefore, we obtained peak response latencies for 9 of the 17 ROIs that appeared to be involved in generating the lexico-semantic responses that we observed in this study (denoted by ** in **Supplementary Figure 1**). Full 1200 ms epochs (with a 200 ms baseline period) for each of these 9 ROIs were extracted, and then lowpass filtered at 5 Hz (width = 1), so that broad peak latencies could be measured.

In the left hemisphere, the only significant effect was in the posterior STS, which had an earlier peak response to repeated words (repeated: 310 ms, novel: 354 ms), F(1,10) = 16.95, $p < 0.005$. Although this region reached its peak amplitude before the time windows used in other analyses, it remained near this peak until ~450-500 ms.

In the right hemisphere at ~400 ms, the pars opercularis of the inferior frontal gyrus demonstrated a delayed peak for L2 compared to L1 words (L1: 386 ms, L2: 426 ms), F(1,10) = 5.03, $p < 0.05$. Similarly, the right posterior STS showed the same effect of language (L1: 300 ms, L2: 332 ms), F(1,10) = 4.79, $p = 0.05$. Like its left hemisphere counterpart the posterior STS reached its peak magnitude at ~300 ms, however this response was sustained until well after the 400 ms time window that was used in the analyses above.

Additionally, there was a marginally significant effect of language in right LOT at ~300 ms post-stimulus onset, with L2 words peaking later than L1 words (L1: 292 ms, L2: 332 ms), F(1,10) = 4.28, $p = 0.065$. This region was selected for peak latency analysis because it demonstrated a significant effect during the late lexico-semantic time window, with L2 novel words > L1 novel words. Like the effects in posterior STS, the peak response was largely sustained during the 400 ms time window, despite the fact that the region initially reached its peak earlier.

1.5: Discussion

In this study, we sought to investigate the neural representations of first and second language word processing using a multimodal imaging approach that affords high spatiotemporal accuracy. We wanted to compare between languages specific processes involved in the language stream that are expected to occur sequentially, such as sensory processing, early visual word encoding, and late lexico-semantic processing. Responses to Spanish (L1) and English (L2) words differentiated as early as ~135 ms after word onset, when word selective activity first occurs. While both languages recruited left posterior fusiform cortex, only L2 novel words additionally evoked strong early activity in the right fusiform. This early bilateral distribution for novel stimuli continued through the language stream to ~400 ms, when L2 showed greater activity than L1 in bilateral posterior and right frontal regions. Strikingly, the responses to simple line drawings and L2 words were similar in these regions, and both differed significantly from L1 words. Additionally, consistent with previous electrophysiological studies, we found that an equally activated frontal region, as well as a posterior temporal area that was more strongly active in L2, showed delays in the timing of the peak lexico-semantic activity for L2 compared to L1. In general, we have shown that the brain distinguishes the language of word presentation early in the language stream, and that throughout the course of processing, L2 recruits a more extended network of regions in posterior visual and right hemisphere areas when the stimuli are less familiar.

It is striking that the brain distinguishes language identity so early, especially since English and Spanish share an orthographic system and the word stimuli used here were high frequency concrete nouns. While left fusiform activity reflecting both orthographic and lexical features is consistently observed during word reading (Fiez and Petersen, 1998; McCandliss et al., 2003), activity in the right fusiform has been observed in a number of studies, especially when encoding is more difficult. Developmental studies of word reading find right VOT activity, which declines as children grow up and become proficient readers (Turkeltaub et al., 2003; Maurer et al., 2005). In monolingual adults, this region may be recruited in a sustained attentionally-based top-down manner when it is initially uncertain if the stimulus is a word, and its activity decreases as lexical certainty increases (Tagamets et al., 2000). Furthermore, when words are embedded in progressively greater amounts of visual noise, right VOT activity as early as ~130 ms increases compared to words without noise (Tarkiainen et al., 1999). Thus, early recruitment of the right hemisphere by English words in native Spanish speakers may reflect a more general propensity for bilateral engagement of VOT when the visual word encoding system is not entirely tuned to the stimuli. The current study provides strong support for this interpretation in that right but not left posterior fusiform activation decreased for L2 words when they were presented repeatedly.

Besides boosting the visual encoding of unfamiliar words, right VOT engagement may route such information to the right hemisphere homologues of anterior language areas that are involved in later lexico-semantic processing. We found that at ~400 ms, the non-native (and non-dominant, though highly proficient) language recruits both the classical left hemisphere language network (Halgren et al., 1994b; Marinkovic et al., 2003; Dhond et al., 2001; Cabeza and Nyberg, 2000) and an additional set of posterior and right hemisphere regions. It has been suggested previously that non-native languages may recruit more right hemisphere regions (Dehaene et al., 1997; Perani et al., 1998;

Abutalebi et al., 2001), however this effect tends to appear only in studies that show differential L1/L2 left hemisphere responses (Chee *et al.*, 1999; Klein *et al.*, 1995). It is important to note that although there is a general focus in the literature on left-lateralized N400 generators, intracranial recordings with monolingual subjects have demonstrated right hemisphere generators as well (Halgren et al., 1994a; Halgren et al., 1994b; Smith et al., 1986).

Greater right hemisphere activity in the non-dominant language could be related to a processing strategy wherein the brain recruits regions that may be able to provide supplementary information regarding the nature of the stimuli (Goldberg and Costa, 1981; Goldberg et al., 1978). It is difficult to determine from our data whether such supplementary information (such as coarser analyses of both linguistic and meta-linguistic features) is required due to greater difficulty associated with encoding the stimuli, however the bilateral VOT activity during early visual word encoding could support this hypothesis. Additionally, since many of the areas that show strong activity in L2 are areas that are known to be useful for language processing when the analogous left hemisphere regions are damaged (Hertz-Pannier *et al.*, 2002), it is possible that they are recruited when the language system encounters stimuli that do not fit the mold of the entrenched native language. Although the subjects in the present study considered themselves less proficient in L2, their equal behavioral performance in both languages suggests that this is only achieved by engaging additional cortical areas. Further studies with bilinguals who have highly variable L2 proficiency will be required to determine whether these effects are more strongly influenced by language proficiency, order of acquisition, or other factors.

Additional support for the hypothesis that the right hemisphere is recruited when the brain is presented with stimuli in a less familiar language comes from our analysis of peak latency effects. We have replicated the finding that lexico-semantic responses in L2 are delayed by approximately 40-50 ms compared to L1 (Hahne, 2001). Since the direction of this effect can be reversed if L1 is the non-dominant language (Moreno and Kutas, 2005), it may be a reasonable interpretation to suggest that difficulty and familiarity are factors in right hemisphere recruitment. Although the peak responses in the present study are approximately 80-100 ms earlier than those that have been found with ERP, the similarities between the tasks and processes that are being probed between studies suggests that the delay in our results may be similar to the N400-like effects in other studies. A possible explanation for this timing discrepancy may relate to differences between the N400 as measured by EEG and similar, but not identical MEG responses that have been termed the N400m (Halgren *et al.*, 2002).

In addition to hemispheric and timing differences between L1 and L2 lexico-semantic representations, an anterior-posterior difference emerged in our results. These results are consistent with evidence from object naming deficits due to direct cortical stimulation suggesting that L1/L2 differences are greater in posterior visual areas including LOT, despite the general focus in the literature on left frontal cortex. In one study, posterior sites including posterior STS and occipito-temporo-parietal cortex showed a greater proportion of L2-specific regions than L1-specific regions in some subjects, while left frontal areas had a higher number of L1-specific and shared regions (Lucas *et al.*, 2004). Although the stimulation sites were limited compared to whole-brain techniques such as fMRI and MEG (and the task involved language production rather than comprehension), there is a striking concordance between the L2-specific regions and the areas that we have shown in the present study to have greater activity in L2, providing support for the hypothesis that there are greater posterior differences between L1 and L2 for lexico-semantic representations in some bilinguals. The more extreme posterior differences between languages found in the present study simply may reflect a difference among the various imaging and recording modalities, however in general, the relatively high spatiotemporal resolution of the distributed-source MEG method used here provides a useful link between previous intracranial, EEG, and fMRI results.

The nature of this posterior secondary visual cortex activity during lexico-semantic processing is unclear based solely on the present results. One possibility is that regions such as LOT become active for high-level visualization of lexico-semantic content (Grill-Spector *et al.*, 2001; Malach *et al.*, 1995). Such an interpretation is consistent with the similarities that we observed between pictures and L2 words in these regions. This may be related to a more perceptually-grounded set of representations in the non-dominant L2, similar to what has been observed in children who are in the process of acquiring their native language (Brown et al., 2005; Schlaggar et al., 2002; Mandler, 2000; Nelson, 1974; Saltz et al., 1972; Ojemann et al., 2003). Furthermore, similarities in posterior visual brain activity between children and adult L2 learners could support the hypothesis that sequential L2 learning is similar to native language acquisition during childhood, and that successful L2 acquisition relies on adequate L1 development (Mayberry, 1993, 2007). Alternatively, it may simply be the case that L2 relies more on visual analysis in the size judgment task used in the present study. Future studies will probe the nature of these representations in the second language to determine whether L2 learners do indeed rely more on perceptual features in the second language relative to the high level abstract concepts that form the basis of the L1 lexico-semantic system.

1.6: Supplementary Materials

1.6.1: Supplementary Text

Previous results in the literature regarding the time-course of lexico-semantic processing led to the *a priori* choice of 380-420 ms as the primary analysis interval. However, an examination of the source waveforms demonstrated that in many areas, the peak activity to words was evoked at a latency of ~372 ms. During the 372 ms peak window, many regions showed effects that were similar to those that occurred during the 400 ms window, with several important differences (**Figure 1.3**; see also **Figure S1.2**). In the left hemisphere, a language by repetition interaction appeared in orbitofrontal cortex [F(1,10) = 5.19, $p < 0.05$], with L1 words > L2 words (however, all post-hoc tests were non-significant). Additionally, a region of the anterior insula demonstrated a marginally significant main effect of language, where L2 words > L1 words, F(1,10) = 4.72, $p = 0.055$.

In the right hemisphere, the inferior frontal sulcus (IFS) showed a main effect of language, with L2 words > L1 words, F(1,10) = 4.81, $p = 0.05$. In addition, lateral VOT demonstrated a significant L2 > L1 language effect [F(1,10) = 4.89, $p = 0.05$], and a trend toward a main effect of repetition, F(1,10) = 4.28, $p = 0.07$. The effects in right LOT were identical to those during the 400 ms time window, except that a trend toward a significant main effect of language emerged, with L2 words eliciting larger responses, F(1,10) = 3.98, $p = 0.07$.

Thus, the overall pattern of results was similar in the windows around 372 vs 400 ms, with language and/or repetition effects in three broad regions: left anteroventral temporal and posteroventral prefrontal cortices (classical language areas), the right hemisphere homologues of these areas, and bilateral occipitotemporal cortex. However, there were several effects that were statistically significant at ~400 ms, but not at ~372 ms, or vice versa. In the left hemisphere, a repetition effect in posterior fusiform cortex at ~400 ms was not significant during the earlier peak time window. In right anterior STS, the repetition effect was common between the two time windows, while a marginally significant interaction emerged at ~372 ms [F(1,10) = 4.50, $p = 0.06$], which was driven largely by repetition in L2 [t(10) = 3.60, $p = 0.005$] and greater activity for repeated words with L1 > L2 [t(10) = 2.55, $p < 0.05$]. Finally, the language difference in right inferior precentral sulcus was not significant during this earlier time window.

1.6.2: Supplementary Figures and Tables

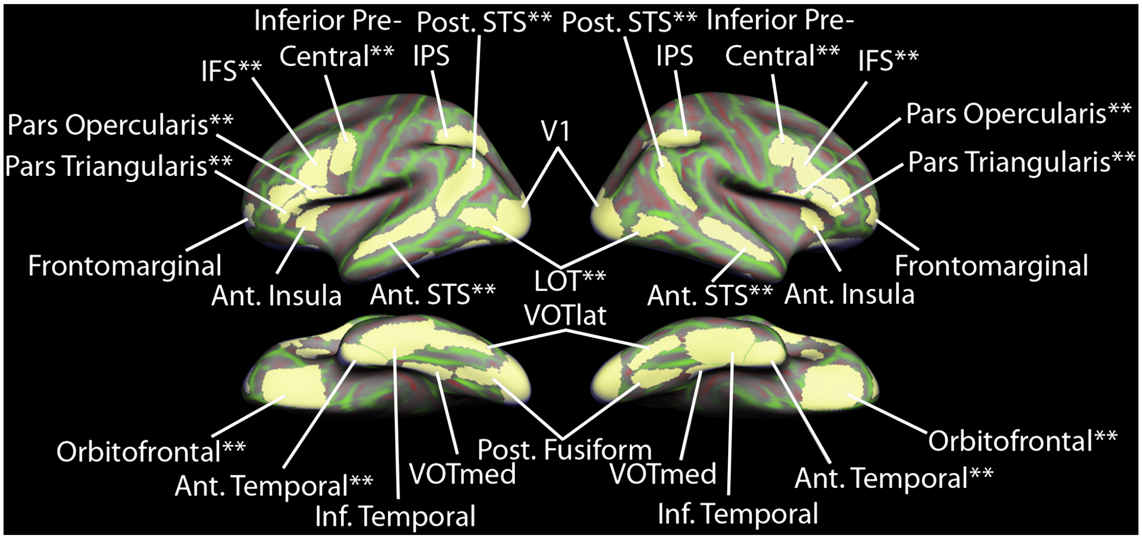


Figure S1.1: Regions of interest selected for statistical analysis. All 17 ROIs were tested in the ANOVA for between-condition signal magnitude differences. ROIs marked by ** were used in the peak latency analysis. Abbreviations: V1: primary visual cortex; LOT: lateral occipitotemporal; Post. STS: posterior superior temporal sulcus; IPS: intraparietal sulcus; VOTmed: medial ventral occipitotemporal; VOTlat: lateral ventral occipitotemporal; Ant. STS: anterior superior temporal sulcus; IFS: inferior frontal sulcus.

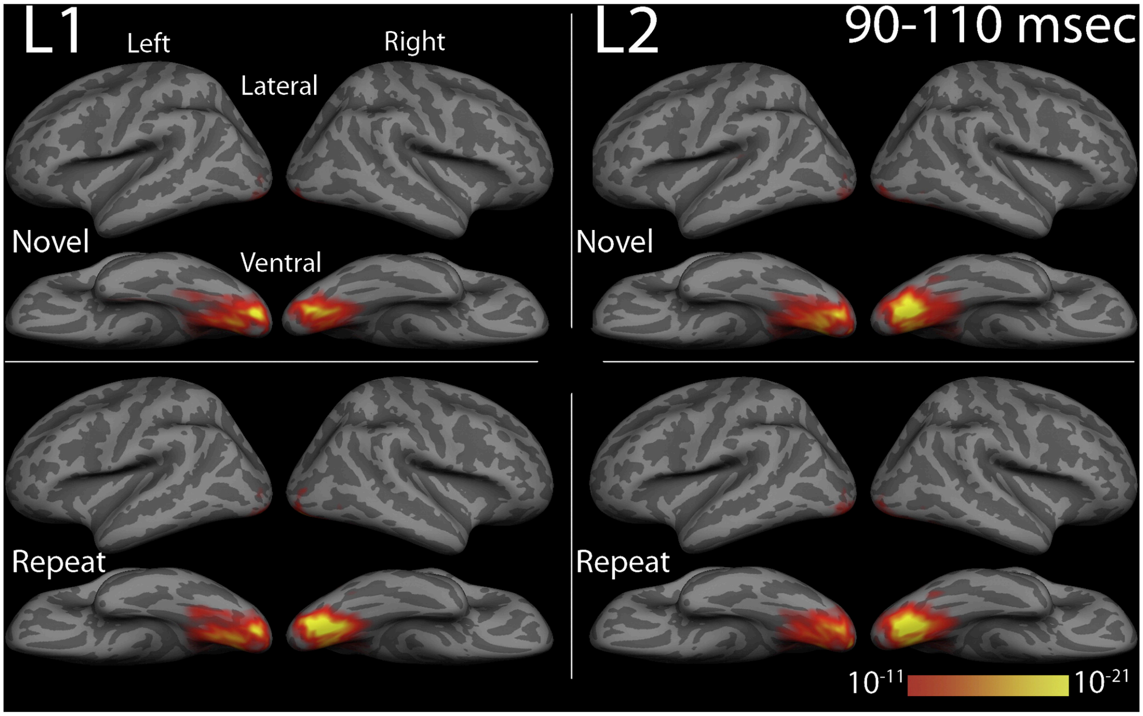


Figure S1.2: Group dSPM images of the mean activity during the early visual processing time window for 11 subjects. There were no significant differences between languages or novel (top row)/repeat (bottom row) conditions, suggesting that early visual processing was the same in all conditions. Significance levels (a measure of SNR) are indicated by the color bar.

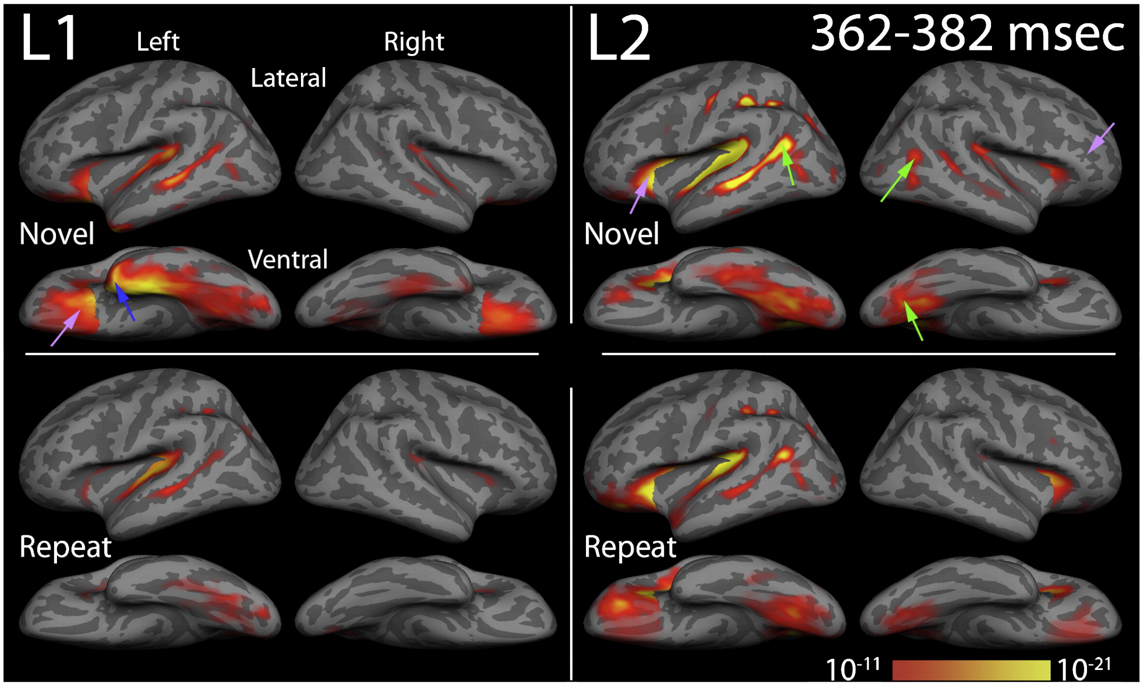


Figure S1.3: Group dSPM images of the mean activity during the peak lexico-semantic time window (~372 ms) for 11 subjects. Between-condition differences were similar to the 400-ms time window (green arrows indicate no changes between time windows), except for L2 > L1 differences in anterior insula, IFS, and right posterior fusiform cortex, and a significant interaction in left orbitofrontal cortex (light purple arrows). Similar to the ~400 ms time window, the apparent difference in left anterior temporal cortex was not significant (blue arrow). Significance levels (a measure of SNR) are indicated by the color bar.

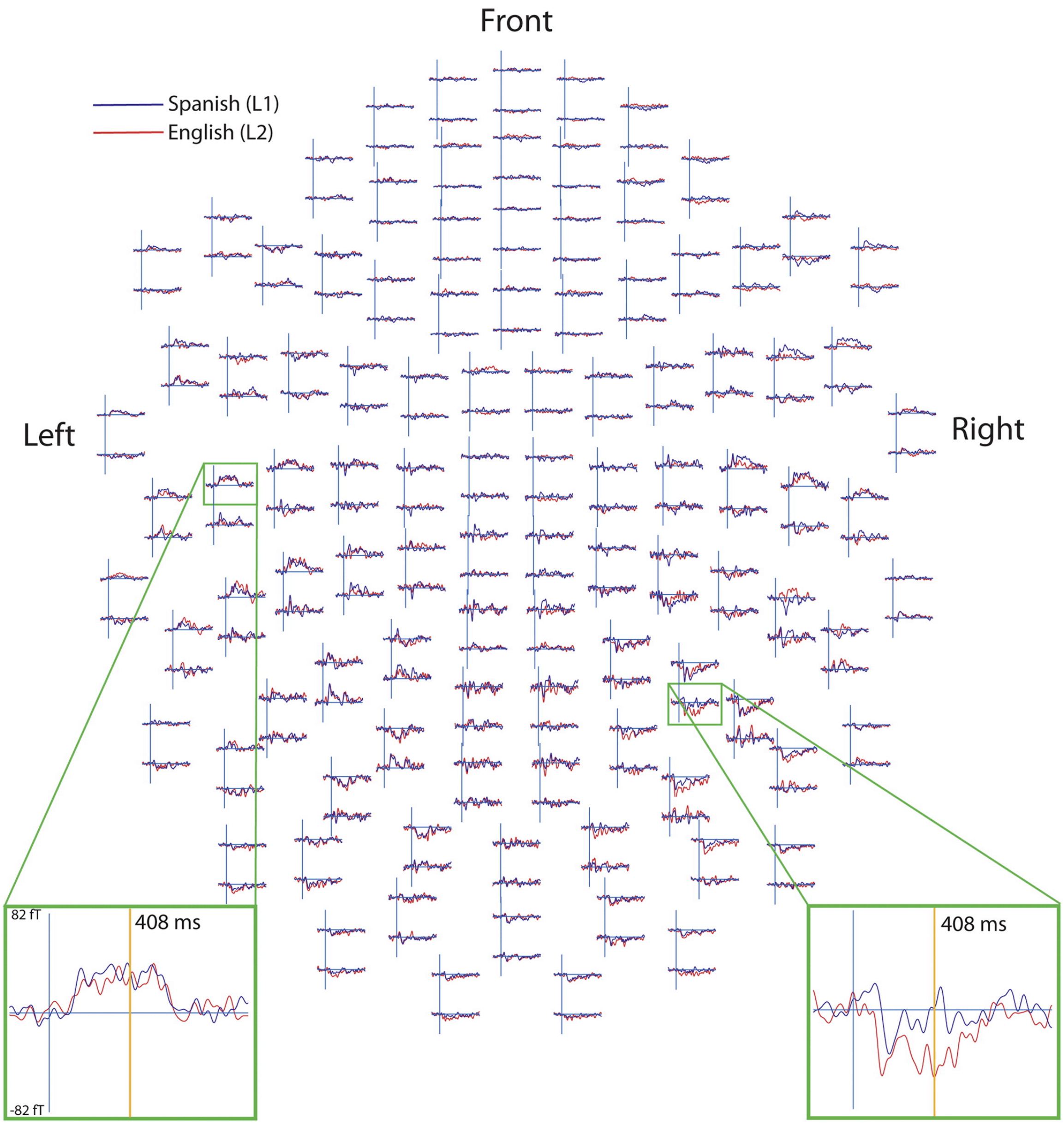


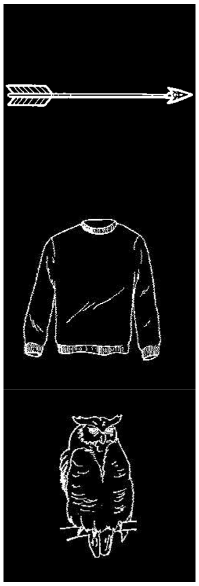
Figure S1.4: Single subject MEG data in source space with one left temporal channel and one right occipitotemporal channel highlighted. The average data for novel words in L1 (blue lines) and L2 (red lines) show that at ~400 ms, there are no differences in left fronto-temporal channels, but L2 words show a larger response in the right hemisphere, particularly in occipitotemporal channels (positive and negative are not meaningful; differences are measured relative to zero fT). The *y*-axis scale ranges from − 82 to 82 fT.

Table S1.1: Example Stimuli

ENGLISH
fork
desk
shirt
snowman
toaster
watermelon

SPANISH
hormiga
formón
cabra
falda
cisne
árbol

PICTURE



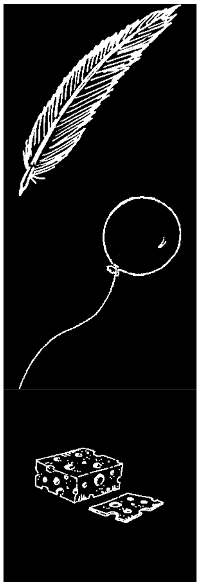
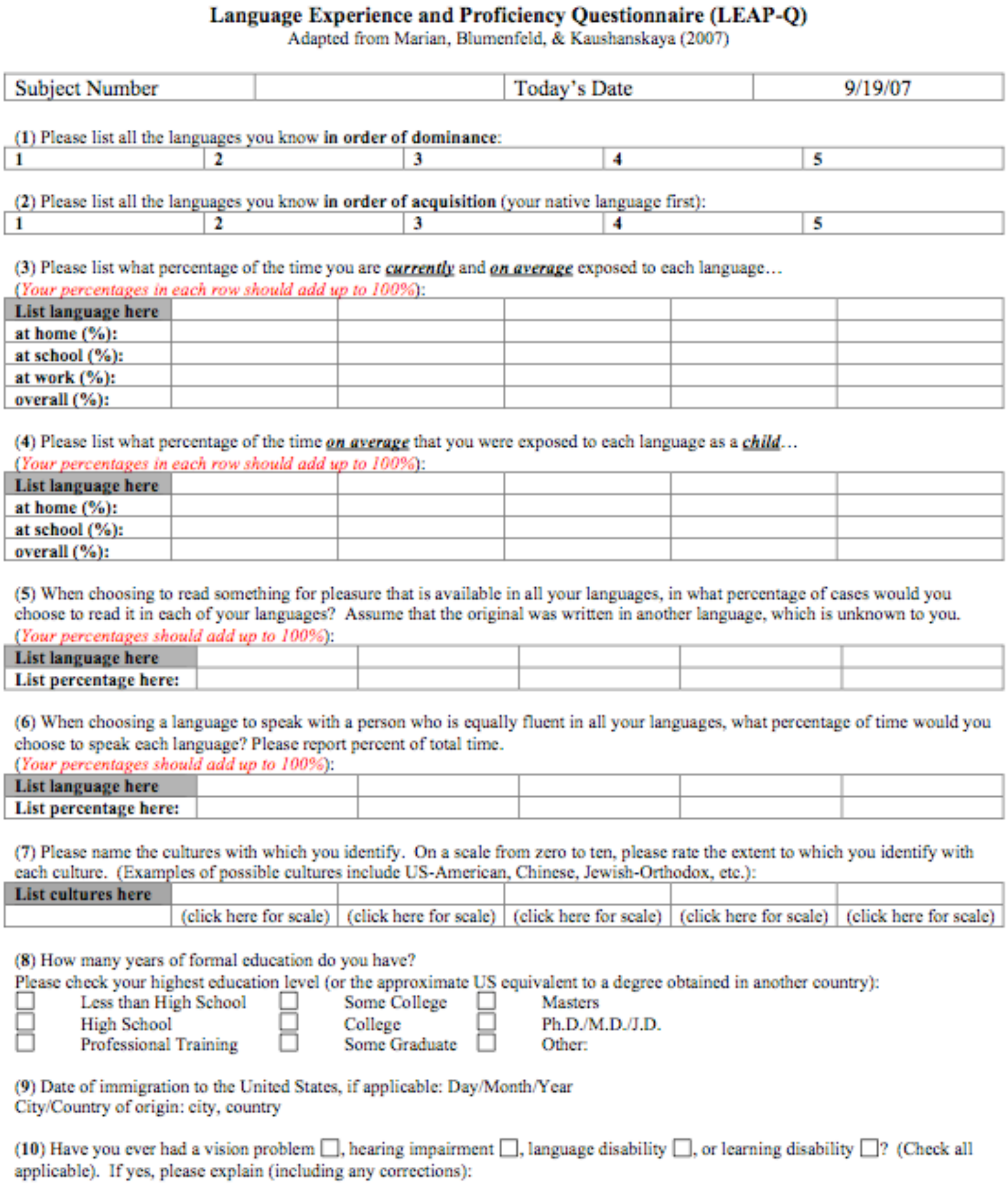


Table S1.2: Summary of findings in early (126-146 ms) and late (380-420 ms) time windows for selected ROIs.

	X	Y	Z	Language	Repetition	Interaction
126-146 ms						
L Post. Fusiform	-23	-75	0	--	--	--
R Post. Fusiform	-25	-70	0	L2 > L1	--	L2 Nov > L2 Rep
380-420 ms						
R VOT lat	41	-60	-9	--	Nov > Rep	L2 Nov > L1 Nov, L2 Nov > L2 Rep, Pics = L2, both > L1
R LOT	42	-61	3	--	Nov > Rep	L2 Nov > L1 Nov, L2 Nov > L2 Rep, Pics = L2, both > L1
R Inf. Precentral Sulcus	41	2	35	L2 > L1	--	L2 Nov > L1 Nov, Pics = L2, both > L1
L Post. STS	-38	-53	22	L2 > L1	Nov > Rep	--
L Ant. Temporal	-48	-25	-6	--	Nov > Rep	--
L Post. Fusiform	-18	-75	-2	--	Nov > Rep	--
L VOT med	-35	-41	-7	--	Nov > Rep	--
R IPS	34	-49	38	--	Nov > Rep	--
R Ant. STS	47	-22	-8	--	Nov > Rep	--
R Post. STS	45	-50	22	--	Nov > Rep	--

X,Y, and Z coordinates for ROIs represent the center of the ROI. See **Figure S1.1** for ROI locations.

1.6.3: Language Questionnaire



Language Experience and Proficiency Questionnaire (LEAP-Q)
Adapted from Marian, Blumenfeld, & Kaushanskaya (2007)

Subject Number		Today's Date	9/19/07

(1) Please list all the languages you know **in order of dominance**:

1	**2**	**3**	**4**	**5**

(2) Please list all the languages you know **in order of acquisition** (your native language first):

1	**2**	**3**	**4**	**5**

(3) Please list what percentage of the time you are ***currently*** and ***on average*** exposed to each language…
(*Your percentages in each row should add up to 100%*):

List language here					
at home (%):					
at school (%):					
at work (%):					
overall (%):					

(4) Please list what percentage of the time ***on average*** that you were exposed to each language as a ***child***…
(*Your percentages in each row should add up to 100%*):

List language here					
at home (%):					
at school (%):					
overall (%):					

(5) When choosing to read something for pleasure that is available in all your languages, in what percentage of cases would you choose to read it in each of your languages? Assume that the original was written in another language, which is unknown to you.
(*Your percentages should add up to 100%*):

List language here					
List percentage here:					

(6) When choosing a language to speak with a person who is equally fluent in all your languages, what percentage of time would you choose to speak each language? Please report percent of total time.
(*Your percentages should add up to 100%*):

List language here					
List percentage here:					

(7) Please name the cultures with which you identify. On a scale from zero to ten, please rate the extent to which you identify with each culture. (Examples of possible cultures include US-American, Chinese, Jewish-Orthodox, etc.):

List cultures here					
	(click here for scale)	(click here for scale)	(click here for scale)	(click here for scale)	(click here for scale)

(8) How many years of formal education do you have?
Please check your highest education level (or the approximate US equivalent to a degree obtained in another country):

☐ Less than High School
☐ High School
☐ Professional Training
☐ Some College
☐ College
☐ Some Graduate
☐ Masters
☐ Ph.D./M.D./J.D.
☐ Other:

(9) Date of immigration to the United States, if applicable: Day/Month/Year
City/Country of origin: city, country

(10) Have you ever had a vision problem ☐, hearing impairment ☐, language disability ☐, or learning disability ☐? (Check all applicable). If yes, please explain (including any corrections):

Language:

This is my (please select from scoll-down menu) language.

All questions below refer to your knowledge of .

(**1**) Age when you…:

began acquiring :	*became fluent* in :	*began reading* in :	*became fluent reading* in :

(**2**) Please list the number of years and months you spent in each language environment:

	Years	Months
A country where is spoken		
A family where is spoken		
A school and/or working environment where is spoken		

(**3**) On a scale from zero to ten, please select your *level of* ***proficiency*** in speaking, understanding, and reading in the following contexts from the scroll-down menus:

	With friends	With family	With teachers	Academic books	Magazines
Speaking:	(click here for pull	(click here for pull	(click here for pull	N/A	N/A
Understanding spoken language:	(click here for pull	(click here for pull	(click here for pull	N/A	N/A
Reading:	N/A	N/A	N/A	(click here for pull	(click here for pull

(**4**) On a scale from zero to ten, please select how much the following factors contributed to you learning :

Interacting with friends	(click here for pull-down menus)	Language tapes/self instruction	(click here for pull-down menus)
Interacting with family	(click here for pull-down menus)	Watching TV	(click here for pull-down menus)
Reading	(click here for pull-down menus)	Listening to the radio	(click here for pull-down menus)
Formal language courses	(click here for pull-down menus)	Other	Please list

(**5**) Please rate to what extent you are currently exposed to in the following contexts:

Interacting with friends	(click here for pull-down menus)	Listening to radio/music	(click here for pull-down menus)
Interacting with family	(click here for pull-down menus)	Reading	(click here for pull-down menus)
Watching TV	(click here for pull-down menus)	Language-lab/self instruction	(click here for pull-down menus)
Formal language courses	(click here for pull-down menus)	Other	Please list

(**6**) How many years of ***formal language classes*** have you attended in ?

(click here for pull-down scale)

Where did you attend these classes?

☐ No classes
☐ Elementary School
☐ Junior High School
☐ High School
☐ College
☐ Community College
☐ Adult Education Program
☐ Other (please list):

(**7**) In your perception, how much of a foreign accent do you have in ?

(click here for pull-down scale)

(**7**) Please rate how frequently others identify you as a non-native speaker based on your ***accent*** in :

(click here for pull-down scale)

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CHAPTER 2:

Language Proficiency Modulates the Recruitment of Non-classical Language Areas in Bilinguals

2.1: Abstract

Bilingualism provides a unique opportunity for understanding the relative roles of proficiency and order of acquisition in determining how the brain represents language. In a previous study, we combined magnetoencephalography (MEG) and magnetic resonance imaging (MRI) to examine the spatiotemporal dynamics of word processing in a group of Spanish-English bilinguals who were more proficient in their native language. We found that from the earliest stages of lexical processing, words in the second language evoke greater activity in bilateral posterior visual regions, while activity to the native language is largely confined to classical left hemisphere fronto-temporal areas. In the present study, we sought to examine whether these effects relate to language proficiency or order of language acquisition by testing Spanish-English bilingual subjects who had become dominant in their second language. Additionally, we wanted to determine whether activity in bilateral visual regions was related to the presentation of written words in our previous study, so we presented subjects with both written and auditory words. We found greater activity for the less proficient native language in bilateral posterior visual regions for both the visual and auditory modalities, which started during the earliest word encoding stages and continued through lexico-semantic processing. In classical left

fronto-temporal regions, the two languages evoked similar activity. Therefore, it is the lack of proficiency rather than secondary acquisition order that determines the recruitment of non-classical areas for word processing.

2.2: Introduction

Bilingualism is a fascinating and complex phenomenon of culture, identity, and skill that deserves attention for its prominence among modern societies and also for what it can tell us about language and cognitive ability more broadly. Previous studies have shown that proficiency modulates lexico-semantic processing in both languages in bilinguals, as indexed by reaction time priming tasks (Dimitropoulou et al.; Duñabeitia et al., 2010; Gollan et al., 2002; Costa and Santesteban, 2004), electroencephalographic methods (Moreno and Kutas, 2005; Ardal et al., 1990), and brain imaging studies (Perani and Abutalebi, 2005; Chee et al., 2001; Xue et al., 2004; Meschyan and Hernandez, 2006; Chee et al., 2004). The Revised Hierarchical Model (RHM) for bilingual language representation predicts these findings as arising from proficiency-modulated links between the first (L1) and second (L2) languages and a supramodal conceptual store (Kroll and Stewart, 1994).

It is unclear how these links are mediated in the neural systems that underlie word processing in the two languages and how they change when one becomes more proficient in the second-learned language. In a previous study, we combined magnetoencephalography (MEG) and structural MRI to show that when reading words in Spanish and English, native Spanish speakers who are still dominant in Spanish have overlapping activity for both languages in classical left fronto-temporal regions during lexico-semantic processing (Leonard et al., 2010). In contrast, activity to words in the less proficient English additionally involves right hemisphere and bilateral secondary visual regions such as lateral and ventral occipitotemporal cortex (LOT and VOT) as early as ~135 ms, and continuing through long latency time windows (~400 ms after a word was shown). Furthermore, only less familiar words in the less familiar language showed this pattern, suggesting that these regions may become active when the initial task of identifying words is more difficult (Tagamets et al., 2000; Tarkiainen et al., 1999). Several imaging studies have found more distributed activity for the less proficient language (Dehaene et al., 1997; Albert and Obler, 1978; Abutalebi et al., 2001; Perani et al., 1996; Perani et al., 1998; Chee et al., 2001; Leonard et al., 2010), however this is a controversial interpretation (Perani and Abutalebi, 2005).

In the present study, we tested native Spanish speakers who had become dominant in English to examine whether greater activity in non-classical language areas is associated with lower proficiency (where Spanish would evoke greater activity in LOT and VOT) or order of acquisition (where English would evoke greater activity in these areas, identical to our previous study). We also sought to examine whether bilateral visual activity that occurs after sensory-perceptual processing is related to the visual paradigm we used in our previous study. Therefore, we presented subjects with words in both the visual and auditory modalities to confirm that bilateral visual activity in object processing regions like LOT is lexico-semantic in nature, and not tied to the stimulus modality. We found that although the pattern was weaker than in our previous study, a lack of proficiency rather than secondary acquisition order was clearly associated with activity outside of classical language areas, and that this effect occurred for words in both the visual and auditory modalities.

2.3: Materials And Methods

2.3.1: Ethics Statement

This study was approved by the Institutional Review Board at the University of California, San Diego. All subjects gave informed, written consent prior to enrolling in the study, and were paid for their time.

2.3.2: Subjects

Sixteen healthy right-handed adults (nine females; age range = 20-28 years; mean = 22.31 years) participated in this study. Participants reported no history of psychological or neurological impairment, and all had completed at least some college. All were native Spanish speakers who began acquiring English as a second language early when they entered school (mean age of acquisition = 5.27 years, SD = 1.44 years). Language history and proficiency in both languages were assessed by a detailed questionnaire that asked subjects to rate on a scale from 1-10 their language abilities for speaking, understanding, and reading, and to indicate the sources/methods that contributed to learning each language (adapted from (Marian et al., 2007)). One subject's questionnaire was excluded due to improper data collection. No subjects indicated higher proficiency in Spanish for any of these domains, although three indicated equal abilities for speaking (Spanish mean = 7.73, English mean = 8.87), and two subjects were equally proficient in reading (Spanish mean = 6.93, English mean = 8.73). For understanding, seven subjects noted that they comprehended both languages equally (Spanish mean = 8.27, English mean = 8.93). Furthermore, subjects indicated a strong preference for how often they would choose to read in English (89.33% of the time), which was also the case for speaking (59.6% vs. 37.4% Spanish; three subjects knew a third language). Subjects also responded that they currently receive more English exposure in general (72.6% English vs. 29.4% Spanish), although their relative exposures during childhood were more balanced (55% English vs. 45% Spanish). From these self assessments, we concluded that all subjects in this study were more proficient and comfortable in their second learned language, English.

2.3.3: Task

The task presented here is nearly identical to that in our previous study (Leonard et al., 2010). Subjects performed a semantic size judgment task to words ("Does this object fit into a shoebox?") while MEG was recorded. The difference between this study and the previous one is that words were presented in both the visual and auditory modalities in separate blocks. The first block was visual words followed by a block of auditory words, each of which consisted of ten stimuli that repeated six times each in random order. These blocks were meant to provide practice and training, and to set up a repetition priming effect. They were not included in the analyses described below. The order of the next blocks (visual vs. auditory) was counterbalanced across subjects, and each block contained a mix of repeated stimuli ('old') from the practice blocks, and words that were presented one time only ('new'). In the following two visual and two auditory blocks, subjects saw and heard 60 new words and six more repetitions of each of the 10 old words in each modality (**Figure S1**). No new or old words repeated across modalities or languages, and the order of the stimuli in each block was randomized with the constraint that there must be an average of 19 words (10 new and 9 old, or ~45 seconds) between presentations of a given old word.

This task was designed to allow for comparisons between activity in the two languages. Of specific interest were earlier components related to modality-specific lexical encoding (at ~170 ms to peak in the visual modality and ~100 ms for auditory), as well as later components indexing lexico-semantic associations (peaking at ~400ms in both modalities). The later component, the N400, has been intensely studied with EEG where it is found to be modulated by the degree of difficulty of contextual integration, stimulus frequency, and stimulus repetition (Kutas and Federmeier, 2000). The N400m is the magnetic counterpart of the N400, with similar cognitive correlates, but is easier to localize. Both early and late components are generated by current flows within the apical dendrites of cortical pyramidal cells, with the earlier peak due to feedforward synaptic excitation, and later components due to more associative synaptic inputs (Halgren et al., 2006). We predicted that some areas would show N400 repetition suppression effects ~400 ms after stimulus presentation in both modalities, and that the locations of some of these effects would differ between languages.

For each visual trial a written word was presented centrally for 300 ms, followed by a masking fixation cross for 2000-2200 ms, during which subjects made their size judgment responses by lifting their index fingers from a fiber optic response paddle (the response hand mappings were counterbalanced across subjects). The fixation cross was on the screen during the entire trial for auditory blocks. All words were concrete, highly imageable objects, and were both high frequency (Spanish mean occurrences per million = 39.71, English occurrences per million = 35.23, $p > 0.6$) and early-learned words in each language of presentation. Some objects were easier to judge than others; while "bug" and "elephant" clearly do and do not fit into a shoebox, "apron" and "shirt" are less obvious. As the task was designed to activate word meanings implicitly, these differences do not affect our current analyses, however future studies may examine these variables parametrically. Visual words were equated for word length (Spanish mean = 5.46 letters; English mean = 5.61 letters). Auditory words were recorded in a soundproof booth with a condenser microphone by a fluent Spanish-English bilingual speaker who did not have a strong accent in either language. The stimuli were edited to be the shortest possible length while maintaining intelligibility (mean length Spanish = 470 ms, SD = 84 ms; mean length English = 528 ms, SD = 99 ms) and all stimuli were equated for mean intensity at 65 dB. Due to the semantic constraints and inherent phonemic differences between Spanish and English, it was not possible to equate the words in the frequency domain. No auditory stimuli were homophones either within or across languages.

All blocks in one language (both visual and auditory) were presented sequentially, followed by three blocks of non-verbal line drawings of objects, and then the six blocks of stimuli in the other language. Due to persistent differences in activity evoked by each modality, visual and auditory words were analyzed separately. The order of the languages was counterbalanced across participants. Although these subjects were highly proficient at code switching, we wanted to examine the relative organizations of the two languages, so it was necessary to minimize the effects of attentional and language switching mechanisms. Therefore, all interactions with the subjects and instructions for each block were presented in the language of the subsequent block by a fluently bilingual research assistant.

2.3.4: MEG Recording

Subjects sat in a magnetically shielded room (IMEDCO-AG, Switzerland) with their heads in a Neuromag Vectorview helmet-shaped dewar containing 102 magnetometers and 204 planar gradiometers (Elekta AB, Helsinki, Finland). Data were collected at a continuous sampling rate of 2000 Hz with minimal filtering (0.1 to 200 Hz). The locations of four non-magnetic coils affixed to the subjects' heads were digitized along with the main fiduciary points (nasion and preauricular points) for subsequent coregistration with high-resolution structural MR images. Subjects were instructed to remain as still as possible during the ~45 minute recording session, and head position indicator (HPI) measurements at the beginning of each stimulus block (approximately every 3-4 minutes) confirmed that the subjects moved minimally (average 8.82 mm Euclidean distance from the beginning to the end of the session). With the exception of one subject, movement in all directions was less than 1.7 cm. One subject moved 2.7 cm in the front-to-back direction, however the average head locations between runs for the two languages were less than 2.1 cm apart.

2.3.5: Anatomically-constrained MEG analysis

The data were analyzed according to the same procedures described in our previous study (Leonard et al., 2010). Briefly, we used a multimodal imaging approach that constrains the MEG activity to the cortical surface as determined by high-resolution structural MRI (Dale and Halgren, 2001; Dale et al., 2000). This noise-normalized linear inverse technique, known as dynamic statistical parametric mapping (dSPM) provides source estimates that can be visualized across time on the cortical surface as movies. EEG and MEG are not sufficient for unambiguous current source localization because any given extracranial electromagnetic field is consistent with an infinite number of possible equivalent current dipole (ECD) configurations in the brain. The dSPM method reduces this ambiguity with the reasonable assumption that sources are located in the cortex, and the source estimates in language tasks have been validated by comparison with direct intracranial recordings (Halgren et al., 1994a; Halgren et al., 1994b; Marinkovic, 2004; McDonald et al., 2010).

Noise normalized dSPMs were calculated for each subject and then averaged onto a common space as a group mean of the estimates. From the group mean time courses of the activity, temporal windows were selected for statistical analysis in various regions of interest (ROIs). Twelve ROIs were selected based on *a priori* hypotheses. These ROIs overlapped with the regions that were used in our previous study, however they were drawn based on a grand average across all subjects and all conditions in the new dataset, so they differed slightly in location and extent (**Figure S2**). The group average F-values (represented by the color bars in the figures below) from the time course of the mean activity within each ROI were entered into a repeated-measures analysis of variance (ANOVA) with language (Spanish vs. English) and repetition (new vs. old) as within-subject factors. All reported *p*-values are uncorrected for multiple comparisons.

2.4: Results

2.4.1: Reaction Time

Reaction times were measured from the onset of the stimulus to the time the subject lifted his or her finger from the response paddle. Reaction times for visual and auditory words were entered into separate repeated-measures ANOVAs, with language (Spanish vs. English) and repetition (new vs. old) as factors.

For visual words, subjects responded significantly faster to old words [$F(1,15) = 143.66$, $p < 0.0001$], and also showed an effect of words in English being faster than words in Spanish [$F(1,15) = 7.66$, $p = 0.014$] (**Figure 1**). Additionally, there was a marginally significant interaction [$F(1,15) = 4.35$, $p = 0.055$] with new English words faster than new Spanish words [$t(15) = 3.12$, $p = 0.007$]. There was a marginal effect of English old words being faster than Spanish old words [$t(15) = 1.97$, $p = 0.067$].

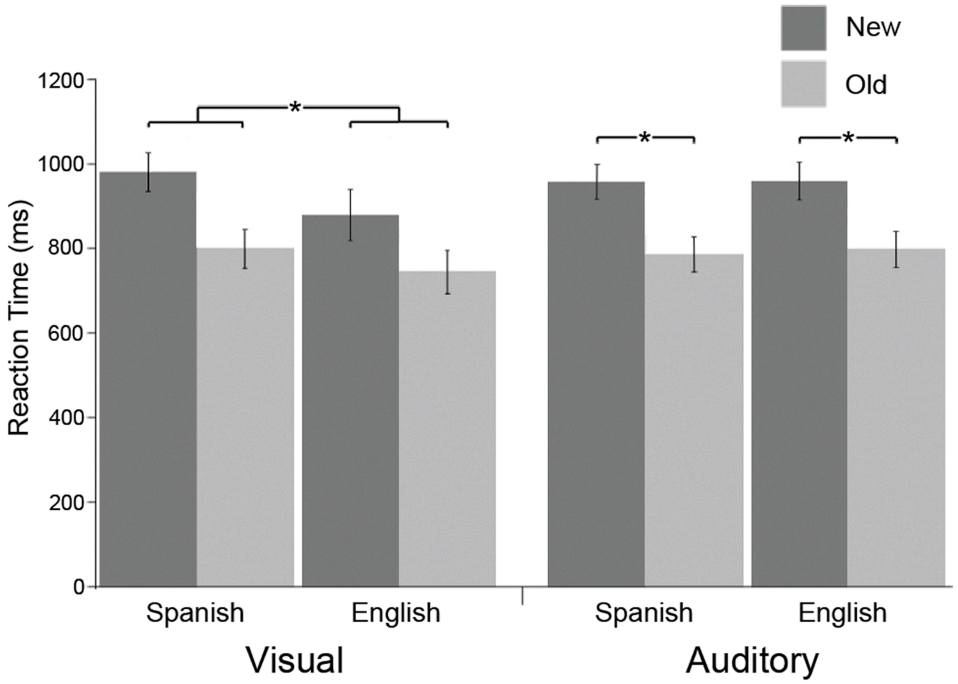

Figure 2.1: Mean reaction times for 16 subjects. Subjects responded faster to old words in both languages and modalities, and responded faster to English words in the visual modality. Error bars represent the standard error of the mean.

In the auditory modality, there was only a main effect of repetition, with old words being faster than new words [F(1,15) = 185.70, p < 0.0001] (**Figure 1**). There were no effects of language and the interaction was not significant.

2.4.2: Early Visual Word Encoding (~170 ms)

For visual words, the first peak in ventral occipitotemporal regions occurred ~170 ms post-stimulus onset. The group mean dSPM from the posterior fusiform ROI was averaged across a 40 ms time window from 150-190 ms, and we compared the activity in the left and right regions across conditions (**Figure 2 top and Figure 3**). In the left hemisphere, there was only a marginal effect of repetition with new>old, [F(1,15) = 4.17, p = 0.059]. In the right hemisphere, there was a trend toward a main effect of language, with Spanish>English [F(1,15) = 3.09, *p* = 0.099]. None of the interactions were significant.

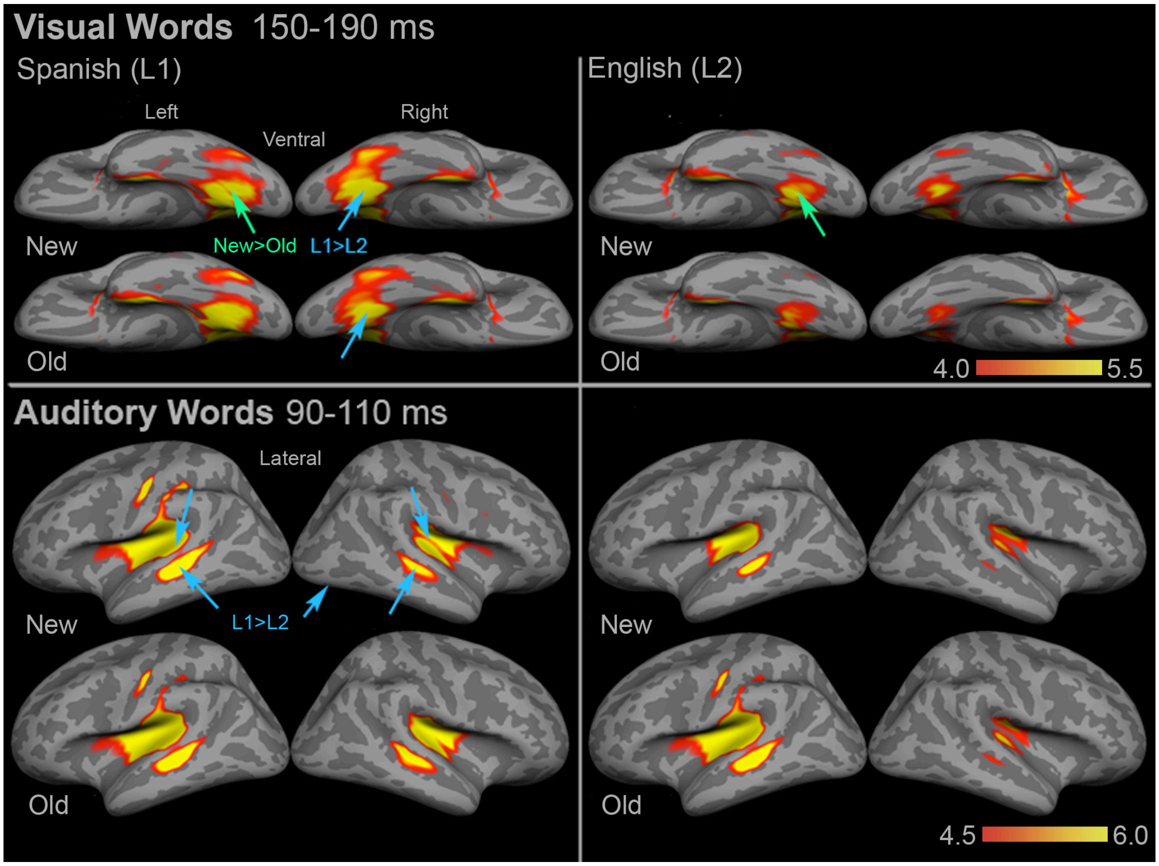

Figure 2.2: Group dSPM of the mean activity during early visual (top) and auditory (bottom) word encoding. In both modalities, activity appears to be strongly lateralized for English but largely bilateral for Spanish. For visual words, left VOT showed a marginal repetition effect (green arrows), and right VOT showed a trending Spanish>English language effect (blue arrows). For auditory words, right planum temporale, bilateral anterior STS, and right posterior fusiform showed Spanish>English effects (blue arrows). Left planum temporale showed a trending Spanish>English effect. See **Supplementary Figure 2** for ROI locations and names. Color bars represent square root of F values, which are a measure of signal-to-noise.

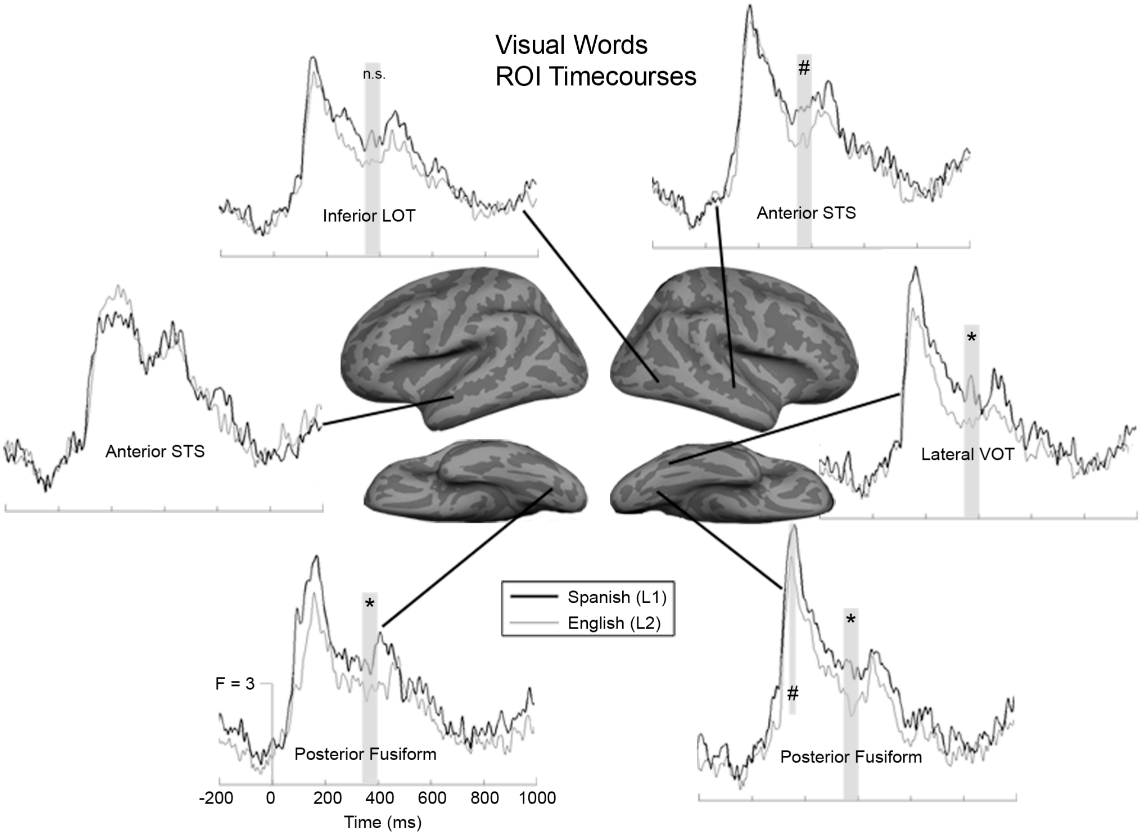

Figure 2.3: Average time courses for selected ROIs to new visual words. Several regions show significant (denoted by *) or marginal (denoted by #) Spanish (thick lines) > English (thin lines) effects during the early (150-190 ms) and late (350-400 ms) time windows (gray bars). Responses appear generally greater over an extended time period for Spanish than for English, especially in right hemisphere and posterior areas.

2.4.3: Early Auditory Word Encoding (~100 ms)

For auditory words, the first major peak in bilateral superior temporal regions occurred ~100 ms post-stimulus onset. The group mean dSPMs were averaged across a 20 ms time window from 90-110 ms, and we compared the activity across conditions in the bilateral temporal regions where the peak was maximal (**Figure 2 bottom and Figure 4**). In left planum temporale, there was a trend toward a main effect of language, with Spanish>English [F(1,15) = 3.47, p = 0.082]. In the right hemisphere homologue, there was a significant main effect of language in the same direction, [F(1,15) = 4.72, p = 0.046]. Anterior superior temporal sulcus (STS) also showed a strong peak at ~100 ms, and both left ([F(1,15) = 11.55, p = 0.004]) and right ([F(1,15) = 14.78, p = 0.002]) regions showed significant main effects of language in the Spanish>English direction. Finally, right posterior fusiform showed a main effect of language with Spanish>English, [F(1,15) = 4.47, p = 0.052].

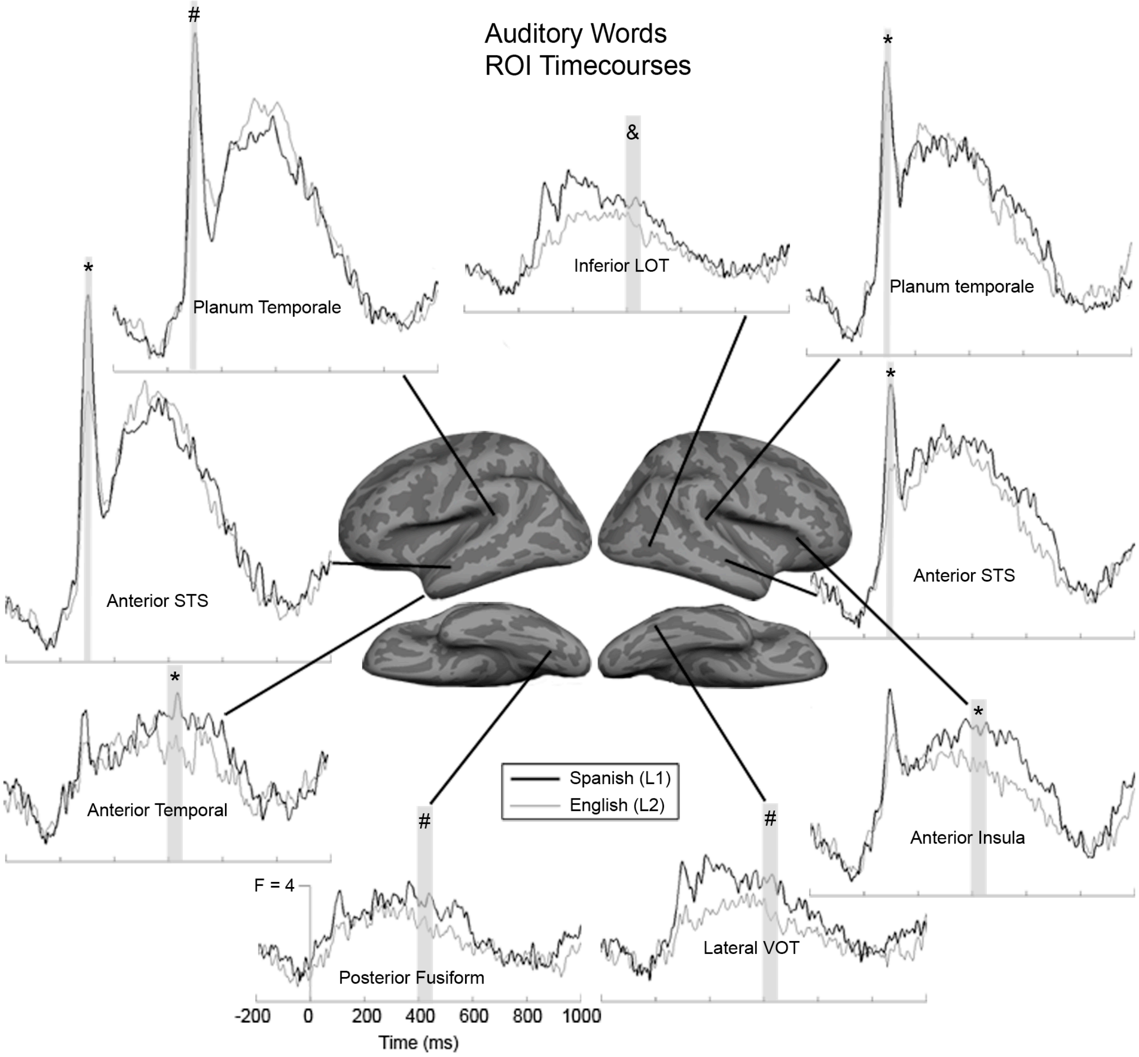

Figure 2.4: Average time courses for selected ROIs to new auditory words. Overall responses appear greater over an extended time period for Spanish (thick lines) than for English (thin lines), especially in right hemisphere and posterior areas. Planum temporale and anterior STS show significant (denoted by *) or marginal (denoted by #) Spanish>English effects during the early encoding stage (90-110 ms), while other areas show language effects during the late lexico-semantic stage (400-450 ms). Of particular interest is the activity evoked by auditory words in right inferior LOT and lateral VOT, which are typically associated with visual object processing. The right inferior LOT area also has a significant new>old effect in Spanish, but not in English (denoted by &).

2.4.4: Lexico-semantic Responses to Visual Words (~400 ms)

As in our previous study, there were several regions in both hemispheres that showed significant activity to words in both languages, which peaked around 400 ms. During a 50 ms time window from 350-400 ms, multiple regions showed significant new>old repetition effects that are characteristic of N400 modulation. In the left hemisphere, inferior temporal cortex ([F(1,15) = 6.92, *p* = 0.019]), inferior LOT ([F(1,15) = 8.21, *p* = 0.012]), superior LOT ([F(1,15) = 5.10, *p* = 0.039]), and posterior STS ([F(1,15) = 15.48, *p* = 0.001]) had significantly greater responses to new words (**Figure 5**). Lateral VOT also showed a trend toward a significant main effect of repetition, [F(1,15) = 3.27, *p* = 0.091]. In the right hemisphere, anterior insula ([F(1,15) = 6.39, *p* = 0.023]) and the inferior pre-central sulcus ([F(1,15) = 6.49, *p* = 0.022]) showed significant repetition effects, however they were both old>new.

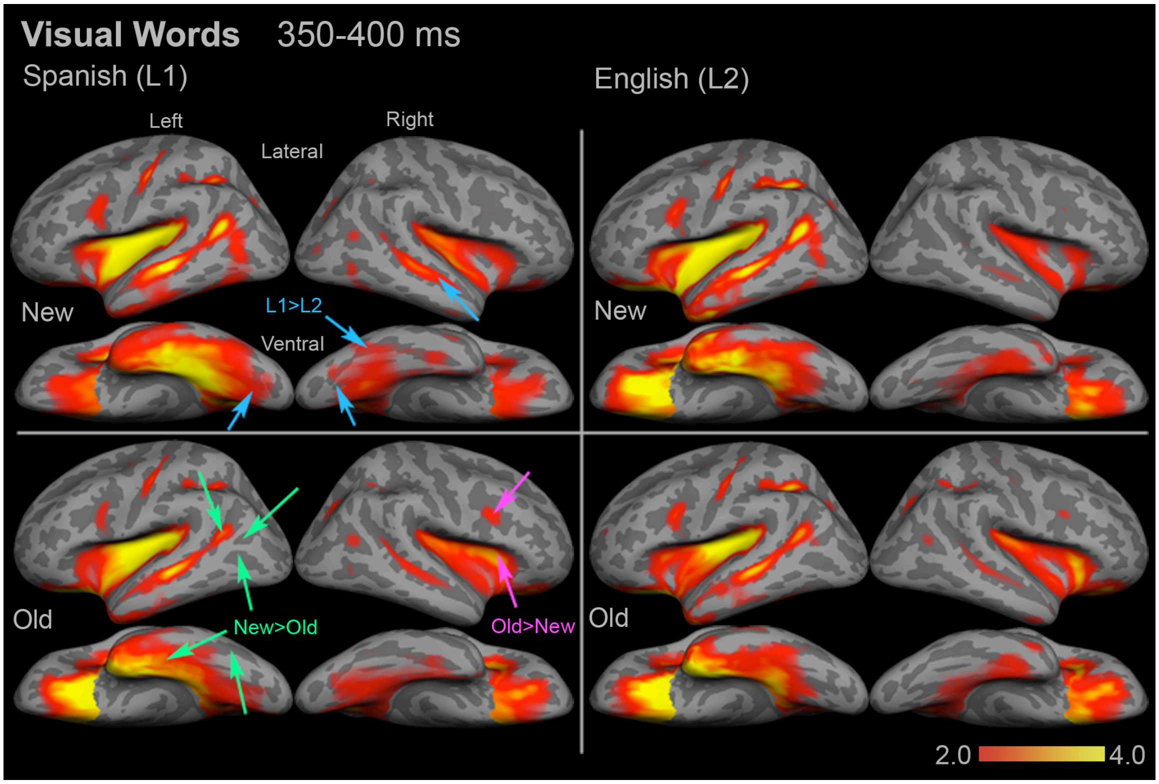

Figure 2.5: Group dSPM images of the mean activity evoked by visual words from 350-400 ms. Several regions in bilateral posterior and right anterior temporal cortex showed significant Spanish>English effects (blue arrows). The activity associated with the N400m in classical left temporal and frontal language areas was not significantly different between Spanish and English. Stimulus repetition effects (green arrows) were also significant in many regions, including two regions with old>new effects (magenta arrows). See **Supplementary Figure 2** for ROI locations and names. Color bars represent square root of F values, which are a measure of signal-to-noise.

There were several areas that showed significant Spanish>English language effects (**Figure 3 and Figure 5**). In the left hemisphere, only posterior fusiform cortex showed this pattern, [F(1,15) = 4.54, *p* = 0.05]. Left orbitofrontal cortex demonstrated a marginal interaction ([F(1,15) = 4.11, *p* = 0.061]), however this was driven by an old>new effect in Spanish ([t(15) = -2.05, *p* = 0.059]). In the right hemisphere, there was a significant Spanish>English effect in posterior fusiform cortex [F(1,15) = 5.24, *p* = 0.037]. There was also a non-significant trend toward a language effect in lateral VOT

([F(1,15) = 2.85, p = 0.112]), which was driven by a Spanish>English effect for new words, [t(15) = 2.21, p = 0.043]. A non-significant trend toward an interaction was also found in anterior STS ([F(1,15) = 2.82, p = 0.114]), which was driven primarily by a difference between new words, [t(15) = 2.04, p = 0.059].

2.4.5: Lexico-semantic Responses to Auditory Words (~400 ms)

We selected a 50 ms time window from 400-450 ms that encompassed the largest between-condition differences for auditory words. During this time window, multiple regions showed significant repetition effects. In the left hemisphere, the inferior pre-central sulcus ([F(1,15) = 6.43, p = 0.023]), superior LOT ([F(1,15) = 12.65, p = 0.003]), anterior STS ([F(1,15) = 30.21, p < 0.0001]), and posterior STS ([F(1,15) = 16.36, p = 0.001]) all showed significant new>old effects (**Figure 6**). Inferior LOT showed a marginal effect in the same direction, [F(1,15) = 3.90, p = 0.067]. In the right hemisphere, the following regions showed significant or trending new>old effects: anterior insula ([F(1,15) = 3.98, p = 0.065]), anterior temporal ([F(1,15) = 3.76, p = 0.071]), inferior LOT ([F(1,15) = 15.57, p = 0.001]), superior LOT ([F(1,15) = 11.50, p = 0.004]), and anterior STS ([F(1,15) = 6.21, p = 0.025]).

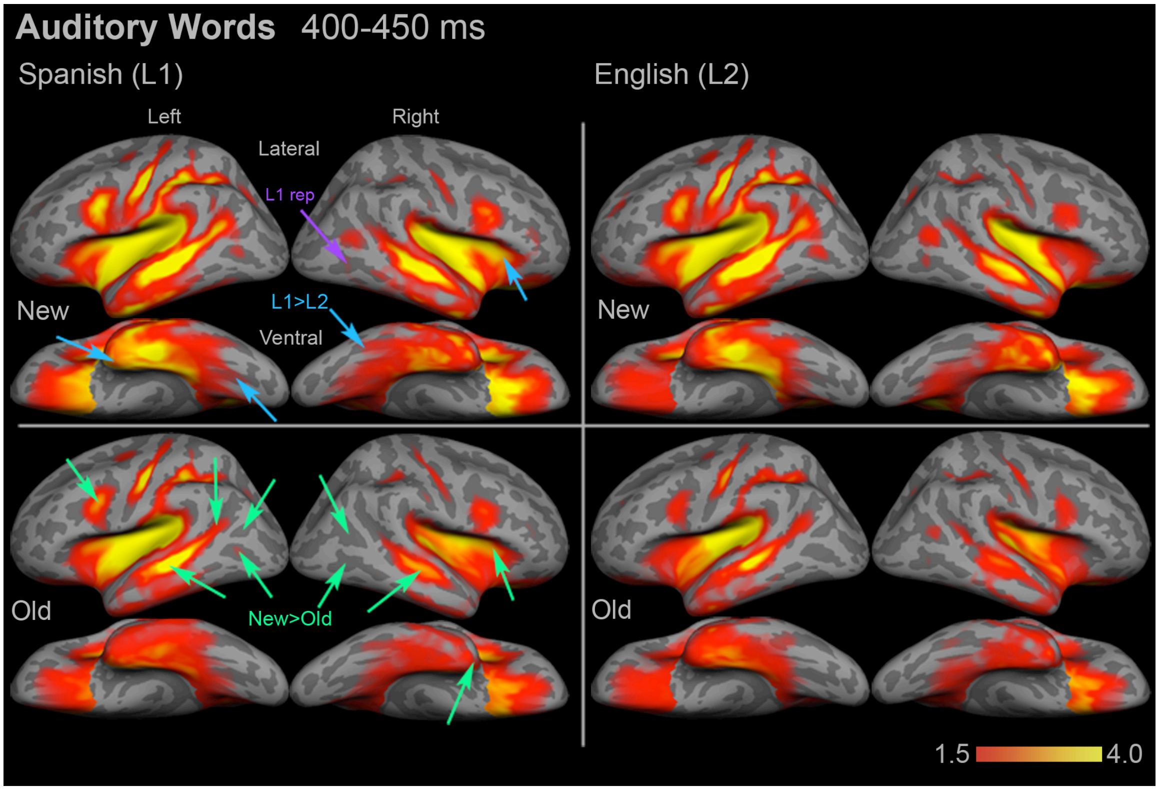

Figure 2.6: Group dSPM images of the mean activity evoked by auditory words from 400-450 ms. Several regions in both hemispheres showed Spanish>English effects (blue arrows). Note that the activity associated with the N400m in the regions of Wernicke's and Broca's areas was not significantly different between Spanish and English. Stimulus repetition effects (green arrows) were significant in many regions. One area, right inferior LOT, showed a new>old N400 effect in Spanish but not in English (purple arrow). See **Supplementary Figure 2** for ROI locations and names. Color bars represent square root of F values, which are a measure of signal-to-noise.

Several regions showed significant or marginal Spanish>English effects, including left anterior temporal ([F(1,15) = 5.08, *p* = 0.04]) and left posterior fusiform, [F(1,15) = 3.92, *p* = 0.066] (**Figure 4 and Figure 6**). Also on the left, anterior STS showed a trend toward an interaction ([F(1,15) = 3.08, *p* = 0.10]), which was driven primarily by a strong repetition effect in English ([t(15) = 5.29, *p* < 0.0001]).

In the right hemisphere, anterior insula showed a strong Spanish>English effect [F(1,15) = 14.61, *p* = 0.002]. Lateral VOT showed a trend toward an interaction between language and repetition ([F(1,15) = 3.37, *p* = 0.087]), which was driven by a trending difference between new words in each language, [t(15) = 1.89, *p* = 0.079]. Finally, inferior LOT showed a trend toward a significant interaction, [F(1,15) = 3.23, *p* = 0.092]. This was driven by a strong repetition effect in Spanish ([t(15) = 3.46, *p* = 0.003]) that was not present for English words.

2.5: Discussion

We examined how language proficiency affects the recruitment of classical and other language areas during various stages of word processing in both the visual and auditory modalities. We used a multimodal imaging technique that combines the temporal resolution of MEG with the spatial resolution of MRI to distinguish activity in different brain regions during both early encoding (~170 ms for visual words and ~100 ms for auditory words) and late lexico-semantic (~400 ms) processing stages. In this group of native Spanish speakers who began acquiring English around age six, and who have since become more proficient in English, responses to the less proficient Spanish were greater in multiple brain regions across both hemispheres beginning at the earliest stages of word encoding, and regardless of modality. This effect, though weak in some regions, persisted through ~400 ms in both modalities, when lexico-semantic processing is thought to occur. During this time period bilateral occipito-temporal areas including posterior fusiform, lateral VOT, and LOT showed Spanish>English effects (or they showed new>old N400 effects in Spanish but not in English). Other right hemisphere regions including anterior STS and anterior insula showed similar effects, while no areas showed significant English>Spanish patterns. As in other studies using the same tasks with monolinguals, the most prominent activity during the N400 time window was estimated to lie in or near the classical language areas of the left hemisphere (Marinkovic et al., 2003). However, with the exception of the left temporal pole for auditory words, activity in these fronto-temporal areas did not differ significantly between English and Spanish.

Previously, we showed that in a group of Spanish-English bilinguals who were still dominant in their native language, the less proficient English recruited many of these same areas when subjects performed the visual task presented here (Leonard et al., 2010). However, it was unclear from that study whether proficiency or order of acquisition determined the extent of bilateral activity in English, and whether such activity is specific to the rather unnatural act of reading (Gough and Hillinger, 1980). In the context of these findings, the present results suggest that regardless of modality, proficiency is the main factor in the recruitment of areas such as VOT and LOT during early encoding and late lexico-semantic processing stages, although other factors may contribute as well.

As one gains greater control over a language, both performance and the underlying neural substrates change to reflect increased proficiency, and presumably, more automatic processing (Costa and Santesteban, 2004; Silverberg and Samuel, 2004; Potter et al., 1984; Duñabeitia et al., 2010; Basnight-Brown and Altarriba, 2007; Meschyan and Hernandez, 2006; Chee et al., 2001). We manipulated automaticity by inducing a repetition priming effect, in which some stimuli occurred once while others repeated multiple times over a delayed period. Particularly during the N400 time window, most of the between-language differences occurred between 'new' words, suggesting that the subjects' relative familiarity with words in each language influence the regions that are recruited to process them. Furthermore, the fact that regions such as right LOT showed significant new>old effects in the less proficient Spanish, but not in English, indicates that this region is performing a process that is modulated by language proficiency.

Our finding that order of acquisition is less relevant than proficiency in determining the amount of right hemisphere and posterior activity during early encoding and especially late semantic processing stages is important because it shows that models such as Kroll and colleagues' RHM (Kroll and Stewart, 1994) must include mechanisms to account for changes in language dominance. Behaviorally, when the second-learned language is the dominant language, it shows a pattern of cross-language priming effects that is similar to when the native language is dominant (Basnight-Brown and Altarriba, 2007). Neurophysiological and neuroimaging data support the idea that proficiency is crucial for determining the neural mechanisms recruited for each language, regardless of order of acquisition (Moreno and Kutas, 2005; Chee et al., 2001). Therefore, the notion of L1 and L2 as first and second languages must be qualified in relation to proficiency, which is a common issue for bilinguals in the United States, particularly those who are second or third generation Americans going to school in English, and who eventually become dominant in their second-learned language.

Our interpretation relies on previous work to conclude that proficiency drives the recruitment of non-classical language areas, yet there are some interesting differences between the English-dominant subjects and the Spanish-dominant group from our previous study. The magnitude of the between-language differences is smaller in the present study, and some regions did not show effects that appeared in our earlier work.

We also did not replicate exactly the early visual word encoding effect, in which the right hemisphere fusiform region was only active for new words in English. There are several possible reasons for these discrepancies. It is possible that although proficiency is the main factor, order of acquisition interacts such that the native language retains much of its representational structure in the brain despite being used less frequently than the second-learned language (and it may even influence second-language representations (Meschyan and Hernandez, 2002b)). Furthermore, proficiency is a somewhat poorly defined construct that is not independent of other factors such as daily use and age of acquisition. Age of acquisition is known to have strong effects on representations (Mayberry and Lock, 2003; Hernandez and Li, 2007), though it appears to affect different linguistic constructs than proficiency, including phonology, morphology, and syntax (Wartenburger et al., 2003; Perani et al., 1998; Hernandez and Li, 2007). In contrast, proficiency has more profound effects on lexical and semantic processing, which are the focus of the present study. However, age and context of acquisition of individual words also play a role in how proficient one is at processing those particular words (Hernandez and Li, 2007; Meschyan and Hernandez, 2002a). For example, many of the concrete nouns in the present study were more likely to have been learned in a Spanish home context (“table”, “strawberry”, etc), compared to words that were learned in a school or work context (“giraffe”, “magnet”, etc) where English is the predominant language. Some of these words may also have been learned slightly earlier in one language or another. Future studies will examine the effects of acquisition context on neural representations to further refine the concept of proficiency.

It is also possible that the relative language proficiencies were different between the two groups. If subjects in the present study were more balanced, the magnitude of between-language effects should be weaker as both languages rely more exclusively on the classical language networks. Because we used self assessments (which are mostly designed to measure global dominance rather than precise levels of proficiency), it is difficult to determine whether this is the case. Future studies will employ objective measures of vocabulary knowledge to be able to correlate proficiency scores in each language with brain activity.

It is of great interest what differential recruitment of brain regions means in terms of the underlying processing mechanisms. It may be the case that even when there is greater involvement of right hemisphere resources, the mechanisms are the same as those in the classical left hemisphere language areas (Hull and Vaid, 2007). Our results may be consistent with this theory, and in fact help refine it. Since we have found significant overlap in the areas associated with word processing in both languages, it is clear that the neural substrate is at least partially shared. Any areas that differ (showing a less proficient>more proficient or a new>old pattern in one language but not the other) may be performing the same functions as the shared regions, which is supported by the presence of N400-like repetition effects in bilateral secondary visual areas. This would suggest that lower proficiency is a matter of recruiting more resources to process words.

An alternative hypothesis is that these supplementary regions are functionally distinct from the shared left fronto-temporal network. We suggested previously that the lexico-semantic repetition effects seen in secondary visual regions during bilingual language processing may be related to a more perceptual semantic system, compared to the abstract system that is mediated by classical language regions (Leonard et al., 2010). Presently, there is only indirect evidence from child language acquisition studies that supports this hypothesis (Pierce and Gholson, 1994; Gentner, 1988; Namy and Gentner, 2002; Storck and Looft, 1973; Saltz et al., 1972; Brown et al., 2005), and further work is necessary to elucidate the functions of these regions during language processing. Whether these regions are performing similar or different functions as the classical left fronto-temporal network, their involvement in word processing in the less proficient language suggests that they could be neural markers of inexperience. Studies examining the neural substrates of learning and skill acquisition should take note of these regions and how their activity changes as skill increases.

While there are some differences between responses to visual and auditory stimuli that are likely due to inherent properties of the stimulus signal (visual being more ephemeral than auditory), we have also shown that especially during high-level language processing, modality does not greatly affect the pattern of representations in each language. In monolinguals, written and auditory words evoke activity in the same left fronto-temporal network during lexico-semantic processing (Marinkovic et al., 2003), however it was previously unknown whether this was also true across languages in bilinguals. In addition to left fronto-temporal regions that show this supramodal response, supplementary regions that become active in the less proficient language such as LOT and VOT show a similar response across modalities. This suggests that the activity is not sensory or perceptual, but rather higher level and perhaps reflects similar lexico-semantic functions as the fronto-temporal networks.

Finally, our previous work suggested the existence of a right hemisphere analogue to the so-called "visual word form area" (McCandliss et al., 2003) that is selectively active in the less proficient language, or in any task in which reading words is more difficult (Tagamets et al., 2000; Tarkiainen et al., 1999; Maurer et al., 2005; Turkeltaub et al., 2003). Although right posterior fusiform did not show the same repetition modulation in the English-dominant group (perhaps due to an interaction between proficiency and order of acquisition for reading), the trending Spanish>English effect in that region suggests a similar function. Furthermore, the analogous effect for auditory words in superior temporal regions suggests that this early encoding stage is affected by language proficiency in a similar manner as lexico-semantic processing. Given the early latency and location of this activity, it is possible that superior temporal regions function as an "auditory word form area", which extracts lexical information from auditory stimuli and passes that information on to lexico-semantic regions, similar to the visual analogue. The existence of an auditory word form area has been a controversial topic (Price et al., 2003), however this may be due to a lack of appropriate control stimuli that match the sensory characteristics of words across the spectrum over time. Our data support the notion of an area that provides a first-pass identification for words in the auditory modality, much like the posterior fusiform does for visual words.

The average person speaks or hears thousands of words per day. Our subjects had experienced tens of millions of words in each language, and for an average of 17 years, those languages were intermingled. Thus, bilingualism provides a powerful tool for studying how rich and complicated symbolic-semantic systems can be represented in the brain after extended, intense learning. Proficiency seems to drive many of the neural differences that occur between languages for single words, but it remains unknown whether non-classical language areas are recruited to a greater extent for later learned languages (or even later learned words), or for sentence and discourse level processing in the less proficient language. These questions provide a fascinating and fruitful platform for future study, which can help inform how experience and familiarity modulate neural representations.

2.6: Supplementary Figures

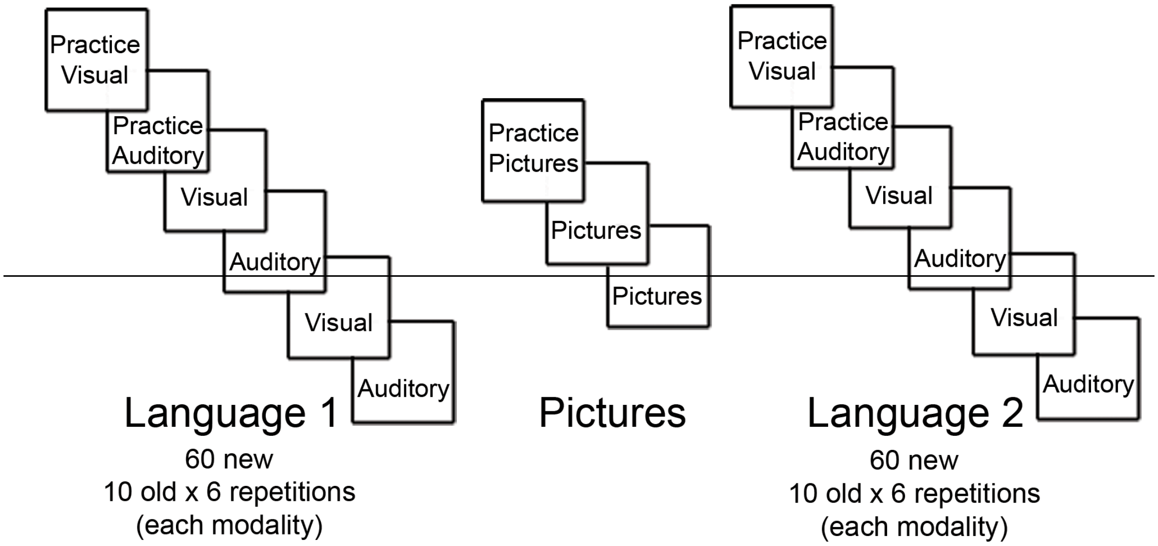

Figure S2.1: Task diagram. Language order and modality order within language were counterbalanced across subjects.

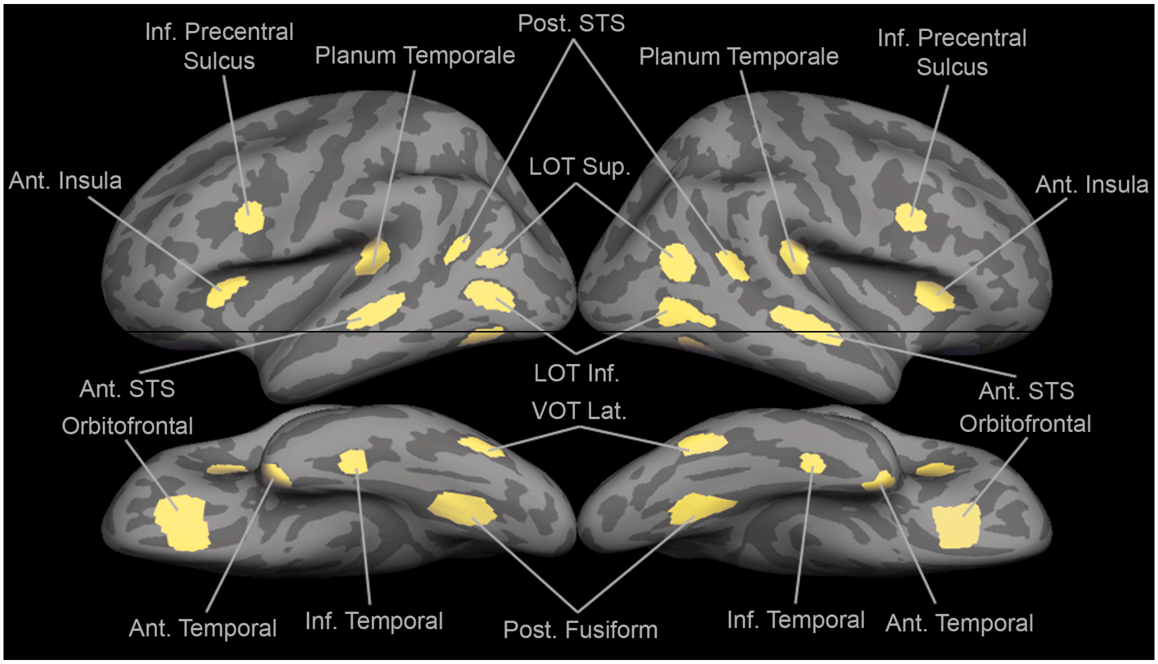

Figure S2.2: Regions of interest (ROIs) selected for statistical analysis. Abbreviations: STS: superior temporal sulcus; LOT: lateral occipitotemporal; VOT: ventral occipitotemporal.

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2.8: Acknowledgements

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Chapter 2, in full, is a reprint of the material as it appears in PLoS ONE 2011. Leonard, M.K., Torres, C., Travis, K.E., Brown, T.T., Hagler, D.J., Dale, A.M., Elman, J.L., & Halgren, E. (2011). Language proficiency modulates the recruitment of non-classical language areas in bilinguals. *PLoS ONE*, 6(3): e18240. doi:10.1371/journal.pone.0018240. The dissertation author was the primary investigator and author of this paper.

CHAPTER 3:

Neural Separation of Acousto-phonemic from Lexico-semantic Word Encoding

Speech perception can logically be divided into successive stages that convert the acoustic input into a meaningful word. Traditional accounts distinguish several stages: initial acoustic (nonlinguistic), phonetic (linguistic featural), phonemic (language specific segments), and finally, word recognition (Frauenfelder and Tyler, 1987; Samuel, 2011). In addition, some theories posit a flow of information that is exclusively bottom-up (Norris *et al*., 2000; Marslen-Wilson, 1987), whereas others hypothesize feedback to at least the phonemic stage (McClelland and Elman, 1986; Morton, 1969) based on behavioral evidence showing that lexico-semantic context can influence phoneme identification (Ganong, 1980; Warren, 1970). However, the neurobiological evidence for these processes remains virtually nonexistent. It is not known whether there is any stage in processing where a signal is recognized as "word-like", but prior to its actual recognition as a word. Nor is there any neural evidence either for or against top-down processes in speech recognition. This is in part because hemodynamic measures such as PET and fMRI find that all these processes activate overlapping cortical locations (Price, 2010) and do not have the resolution to separate them temporally. Since word sounds last several hundred milliseconds, later processing stages triggered by the word's beginning proceed in parallel with earlier sensory processing of the word's ending. Temporal resolution is thus essential for untangling the dynamic interaction of the different processes contributing to speech understanding. Such spatiotemporal resolution is possible by combining magnetoencephalography (MEG) with MRI (Dale *et al*., 2000). Here, we demonstrate neural currents generated within superior temporal regions that distinguish words from control stimuli individually-matched on acoustic properties beginning ~60ms after stimulus onset. Within the same task, we show that semantic priming of the same words by a related picture modulates brain processing in a broader network, beginning at ~180ms. The present findings provide the first direct isolation in time and space of the neural processes underlying acousto-phonemic versus lexico-semantic encoding. The ability to measure these components non-invasively invites research into their respective roles in speech perception, their normal development, as well as their integrity in common language impairments.

In the visual modality, words preferentially activate the left posterior fusiform gyrus, peaking at ~170ms (McCandliss *et al*., 2003). This activity reflects how closely a letter string resembles words (Binder *et al*., 2006), and is followed by distributed activation underlying lexico-semantic associations peaking at ~400ms termed the N400 (Kutas and Federmeier, 2000), or N400m when recorded with MEG (Halgren *et al*., 2002). Intracranial recordings find N400 generators in the left temporal and posteroventral prefrontal cortices (Smith *et al*., 1986; Halgren *et al*., 1994a; Halgren *et al*., 1994b; Nobre and McCarthy, 1995). These classical language areas also exhibit hemodynamic activation during lexico-semantic tasks (Hickok and Poeppel, 2007; Price, 2010). While the N400m is also evoked by auditory words (Marinkovic *et al*., 2003), until now there has been no clear evidence for a preceding acousto-phonemic process wherein lexically relevant word-form information is extracted and encoded.

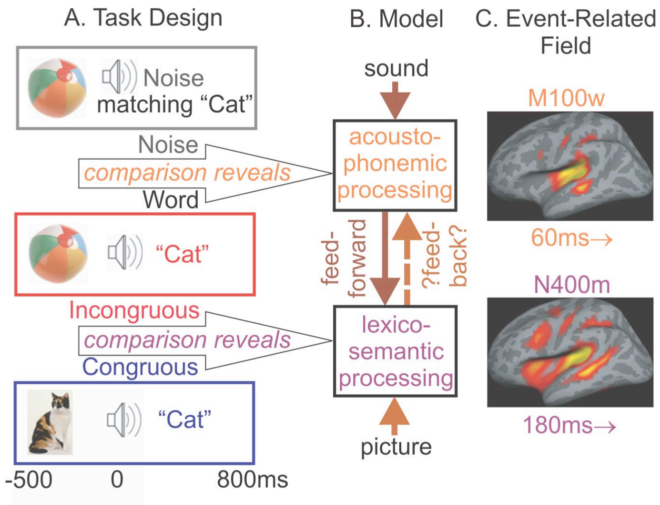

Figure 3.1: Experimental Design. **A**. Trials present words (preceded by a congruous or incongruous picture), or matched noise. **B**. Comparison of noise and word trials reveals acousto-phonemic processing; comparison of congruous and incongruous trials reveals modulation of lexico-semantic processing. Feedforward communication of the identified phonemes is required for speech comprehension; feedback influences are debated. **C**. Cortical currents estimated to the posterior superior temporal plane and sulcus distinguish words from noise beginning at ~60ms; the congruity of the preceding picture to the word does not influence the evoked currents until ~180ms, and involve a broader region.

While recording MEG, eight adult subjects listened to single-syllable auditory words randomly intermixed with unintelligible matched noise control sounds (**Figure 1a**). Each word was noise vocoded (Shannon *et al*., 1995) to produce a control stimulus with identical time-varying spectral acoustics. The word-selective MEG response peaked in a left posterosuperior temporal sensor at ~100ms (**Figure 2a**). When examined in each subject separately, this sensor showed a similar significant early difference between individual word and noise trials using a nonparametric randomization test with temporal clustering to correct for multiple comparisons (Maris and Oostenveld, 2007) (**Supplementary Figure 1**). These effects were replicated in an additional experiment in which nine subjects listened passively to a separate set of single syllable words, recorded by a different speaker, and noise control stimuli constructed in the same manner

(**Supplementary Figure 2**). We refer to this response as the M100w, a word-selective member of the family of auditory processing components occuring in this latency range (Näätänen and Picton, 1987). A direct comparison of the M100w to the M100 evoked by tones shows that they are lateralized to opposite hemispheres in both individual-subject sensors (**Figure 3a**) and group-based estimated localization (**Figure 3b**). The M100w occurs at about the same time as MEG responses in the left posterosuperior temporal lobe that vary with phonemic characteristics of sublexical stimuli such as voice onset time (Frye *et al*., 2007) or presence of the first fundamental (Parviainen *et al*., 2005).

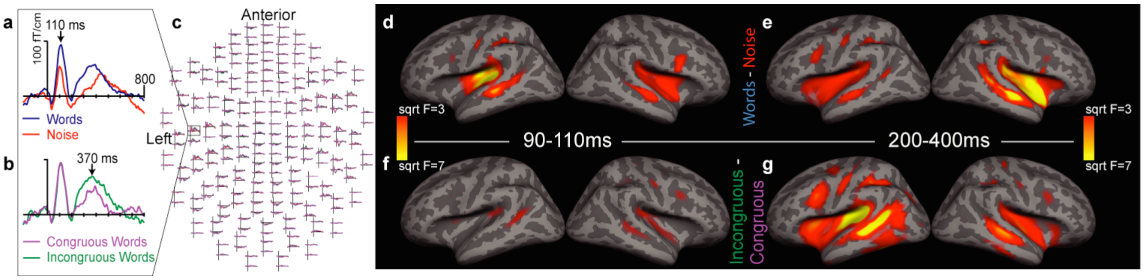

Figure 3.2: Acousto-phonemic processing indexed by M100w is distinct from later lexico-semantic processing indexed by N400m. **a**. Single subject left temporal gradiometer shows early word>noise response at 110ms. **b.** The same left temporal gradiometer channel shows an incongruous>congruous word difference at 370ms. No semantic difference is observed during M100w response. **c.** Plot of all 204 gradiometers indicating the location of the left temporal channel shown in **a** and **b**. **d-g.** Estimated cortical localization of group average activity using dSPM (8 subjects). The earliest significant words>noise response occurs in superior temporal regions between 90-110 ms (**d**) and becomes more distributed by later time windows (**e**). Significant incongruous>congruous semantic effects are absent at ~100ms (**f**), occurring later in both hemispheres, especially left (**g**). Color bars represent square-root of F values, which are a measure of signal-to-noise.

The lexico-semantic response in the same MEG sensor to the same words was compared between trials when its meaning had been preactivated with a congruous picture versus control incongruous pictures, but no difference was observed until ~120ms after the word>noise difference began (**Figure 2b**). One subject had poor behavioral performance and did not show a significant difference between incongruous and congruous trials. Considering the remaining 7 subjects, word>noise differences occurred significantly earlier (average onset 61±22ms) than incongruous>congruous semantic priming effects (average onset 183±93ms; $t(6)=-3.69$ $p<0.02$; **Supplemental Materials**).

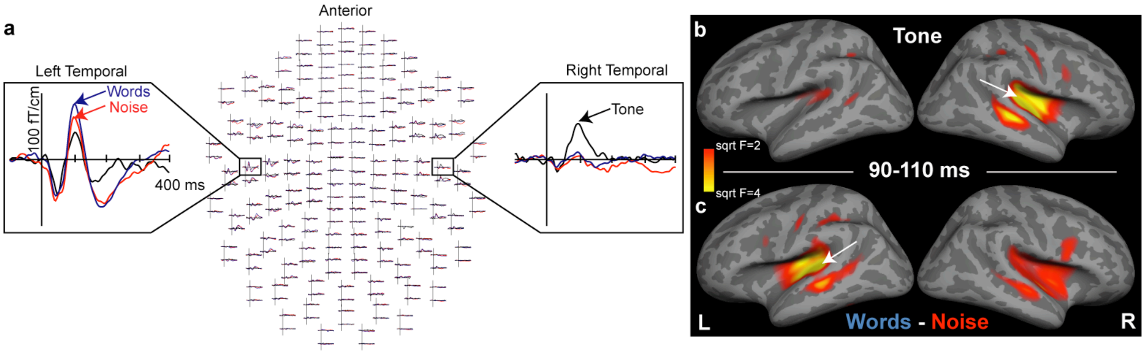

Figure 3.3: The word-selective M100w has different spatiotemporal characteristics than the M100 to tones. **a.** Single subject left and right posterior superior temporal gradiometer channels show a right-lateralized M100 response to tones, in contrast to the left-lateralized words>noise response at the same latency. **b.** Significant group (n=7) dSPM M100 to tones estimated mainly to right superior temporal areas (arrow). **c.** Significant group (n=8) dSPM M100w to words estimated mainly to left superior temporal areas (arrow; this panel is reproduced from panel 2d for convenience).

Although the 61ms latency of acousto-phonemic effects observed here occurs early in the word, they are >48ms after the arrival of acoustic information in primary auditory cortex, providing ample time for surrounding association areas to become engaged in higher processing (Liégeois-Chauvel *et al.*, 1994). It has been difficult to precisely time the component stages of speech perception using purely behavioral measures. However, the ability of some subjects to rapidly shadow a recorded passage (Marslen-Wilson, 1975), and the priming effects on visual words when presented at different points in an auditory passage (Zwitserlood, 1989), both suggest that some lexico-semantic information is available ~150ms after word onset, in reasonably good agreement with the 183ms latency of the lexico-semantic effects reported here. This latency is also consistent with previous N400 recordings to auditory words primed by congruous sentences (Van Petten *et al*., 1999).

The cortical sources of these responses were estimated with dynamic statistical parametric mapping (dSPM) in each subject, and then averaged across subjects on the cortical surface (Dale *et al*., 2000). The cortical distribution for words versus matched noise during the time of the M100w (90-110ms) concentrated mainly to superior temporal regions, especially on the left (**Figure 2d-e**). No significant differences to incongruous versus congruous word were observed at this time, but were present during later windows (200-400ms; **Figure 2f-g**) in the left inferior frontal, insular, ventral temporal and posterior superior temporal regions. Right hemispheric activity was concentrated mainly within insular and superior temporal regions (**Figure 2g**). Such differences are consistent in their task correlates, timing and left temporal distribution with previous dSPM estimates of N400m activity using similar (Marinkovic *et al*., 2003; Marinkovic, 2004) or identical (Travis *et al*., 2011) paradigms. Random effects tests of dSPM values in cortical regions of interest generally confirmed these maps for both the early acousto-phonemic response in superior temporal regions (**Figure 4a**) and the lexico-semantic effect in more widespread areas (**Figure 4b**).

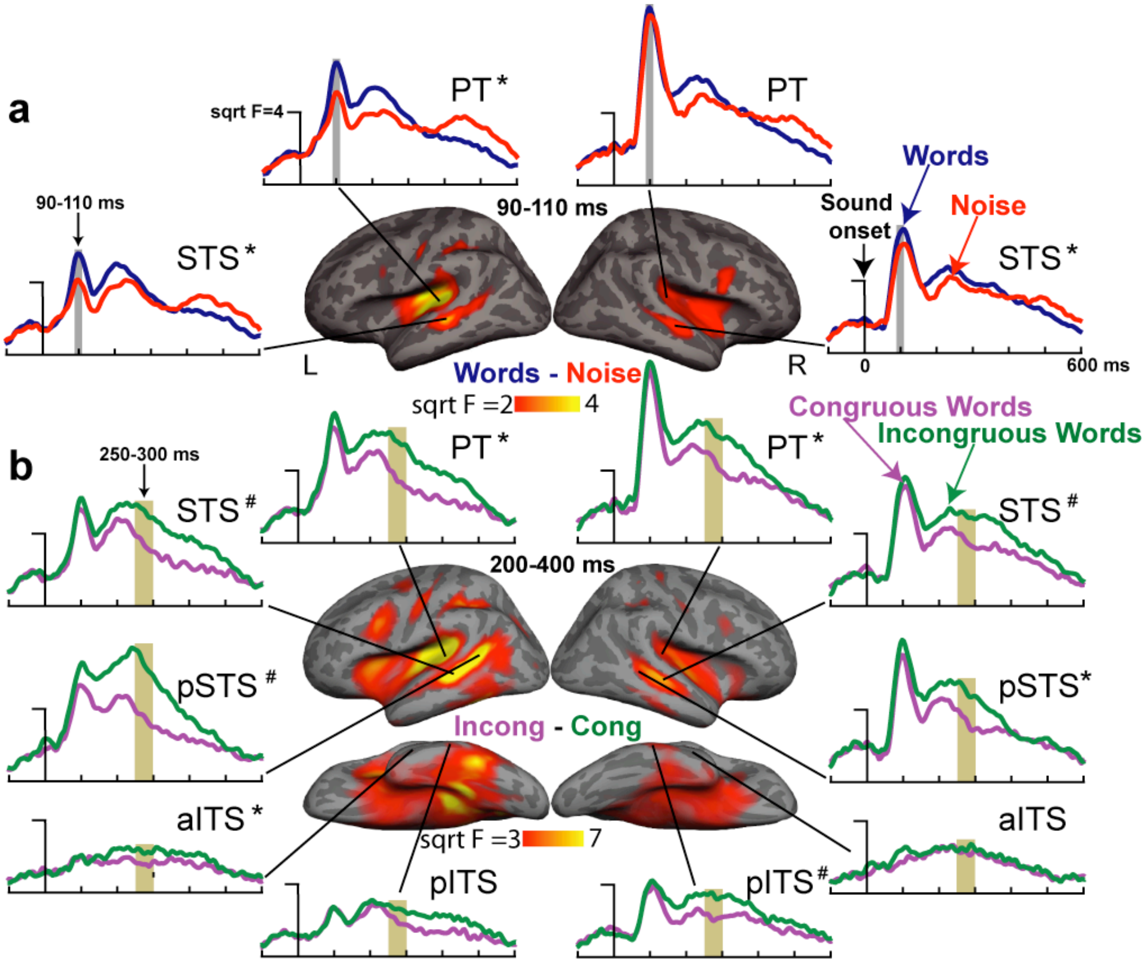

Figure 3.4: Estimated localizations and time-courses of early acousto-phonemic and late lexico-semantic processes. a. Group (n=8) dSPM estimates from 90-110ms (gray bar) are greater to words than noise in bilateral STS (left $(1,7)=13.10$, $p<0.05$; right ($F(1,7)=12.11$, $p<0.05$), and left PT ($F(1,7)=12.07$, $p<0.05$). Significant interactions of word-noise and incongruous-congruous effects in left PT ($F(1,7)=17.12$, $p<0.05$) and left STS ($F(1,7)=17.00$, $p<0.05$) were driven by a significant words>noise effect for both left PT (post-hoc paired samples $t(7)=3.43$, $p<0.01$) and STS ($t(7)=3.86$, $p<0.006$). No regions demonstrated significant incongruous > congruous effects during the 90-100 ms time window. **b.** dSPM estimates are greater to incongruous than congruous words from 250-300ms (tan bar) in left PT ($t(7)=2.46$, $p<0.044$), and aITS ($t(7)=2.61$, $p<0.035$), with trends in the STS ($t(7)=2.16$, $p<0.068$) and pSTS ($t(7)=1.97$, $p<0.089$). In the right hemisphere, effects were obtained for PT ($t(7)=2.40$, $p<0.048$), pSTS ($t(7)=2.74$, $p<0.029$) and pITS ($t(7)=2.32$, $p<0.053$), with a trend in STS ($t(7)=2.24$, $p<0.060$). Regions of Interest (ROIs: Supplementary Materials, fig. 3): STS = superior temporal sulcus, PT = planum temporale, p = posterior, a = anterior, ITS = inferior temporal sulcus. *=$p<0.05$; #=trend.

The localization of early word>noise effects estimated from MEG correspond closely to the areas showing hemodynamic activation associated with prelexical processing, and more specifically spectrotemporal analysis in the dorsal superior temporal gyrus and phonological processing in the middle and posterior superior temporal sulcus (Hickok and Poeppel, 2007; Price, 2010). Similarly, the localization of later incongruous>congruous effects estimated from MEG correspond to those found with hemodynamic methods to be active during lexico-semantic processing, reflecting a hypothesized ventral and anterior pathway for speech recognition (Hickok and Poeppel, 2007; Binder *et al.*, 2009; Price, 2010). Both word>noise and incongruous>congruous MEG differences are bilateral with left predominance, consistent with hemodynamic activations (Hickok and Poeppel, 2007; Binder *et al.*, 2009; Price, 2010).

Our results indicate that word-selective activity begins ~60ms after word onset and peaks at ~100ms within bilateral superior temporal and planar cortices (‘M100w’), followed by more widespread semantic activity beginning at ~180ms and sustained for ~300ms (‘N400m’) (**Figure 1**). Since the time-varying acoustic features of each stimulus word were precisely matched in a corresponding noise stimulus, the M100w presumably reflects the lexically relevant features of a word sound. Since differential word>noise activity begins at ~61ms and it takes ~13ms for auditory information to arrive in the cortex, the distinguishing acoustic information must be contained within the first ~48ms of the word sound. This requires that the distinctive feature be at a relatively low segmental level, at least initially. Presumably, like early fusiform responses to visual words (McCandliss *et al.*, 2003) and faces (Halgren *et al.*, 2000), the M100w may be encoding the essential elements which are later combined arbitrarily into symbols pointing to semantics.

By ~180ms when semantic effects are seen, enough of the word has been presented so that it is possible to predict how it might be completed. Specifically, our results are consistent with several lexical processing models which have proposed that at least the initial syllable of a word (~150 ms) must be analyzed before contact is initiated with the lexicon (Frauenfelder and Tyler, 1987; Marslen-Wilson, 1987; Zwitserlood, 1989), which is also consistent with the timing of initial top-down sentence context influences on phonemic processing (Groppe *et al.*, 2010). However, it is long before the acoustic stimulus contains enough information to definitively and uniquely identify the word. Thus, lexico-semantic modulation likely reflects the multiple lexical possibilities consistent with the initial ~169ms (=182-13) of the stimulus, as predicted by some models of speech understanding (Norris *et al.*, 2000; Marslen-Wilson, 1987)

Our study shows that the first ~120ms of word-selective activity is unaffected by the presence of a lexico-semantic information generated by a picture context. Thus, it is not consistent with models of speech processing that posit a continuous interaction between acousto-phonemic and lexico-semantic levels of processing (Frauenfelder and Tyler, 1987; McClelland and Elman, 1986; Morton, 1969). However, due to the overlapping anatomical substrates of the M100w and N400m, it is not possible with the current data to exclude top-down effects after 182ms. Thus, our data are consistent with either completely autonomous acousto-phonemic processing (Norris *et al.*, 2000), or acousto-phonemic processing that remains autonomous until the first syllable is identified (Marslen-Wilson, 1987).

The ability to measure the neural substrate for auditory word encoding has broad applications. Further investigation is needed to determine the sensitivity of the M100w to different prelexical features. Characterizing this response in development and those who suffer from language impairment may improve our understanding of these disorders (Tallal, 2004), and identify those at risk for developing them (Kuhl, 2004).

3.1: Methods Summary

3.1.1: Subjects

Eight healthy right-handed, monolingual English-speaking adults (3 males; 21-29 years) gave informed, written consent, approved by the UCSD Institutional Review Board.

3.1.2: Tasks

In the primary task, an object picture (<5% visual angle) appeared for the entire 1300ms trial duration (600-700ms intertrial interval). 500ms after picture onset, either a congruously or incongruously paired word or noise stimulus was presented binaurally (1,000 trials, 250 per condition). Participants pressed a button to congruous sounds. Response hand alternated between 100 trial blocks. Words were highly-imageable nouns recorded by a female native speaker. White noise was band-passed and amplitude-modulated to match the acoustic structure of a corresponding word in total power in each of 20 equal bands from 50-5000 Hz, and the exact time versus power waveform for 50-247, 248-495Hz and 496-5000Hz (Shannon *et al.*, 1995). Sounds (mean duration=

445±63ms; range= 304-637ms; 44.1kHz; normalized to 65dB average intensity) were presented binaurally through plastic tubes fitted with earplugs. Following this task, subjects listened to 180 1000Hz binaural tones at 1Hz while maintaining fixation. Data from one subject were lost due to an equipment malfunction.

3.1.3: Neuroimaging

Procedures were as described previously (Leonard *et al*., 2010; Travis *et al*., 2011). 204 planar gradiometer channels distributed over the scalp were recorded at 1000Hz with minimal filtering (0.1-200Hz). Sources were estimated using a linear minimum-norm approach, noise normalized to a pre-baseline period (Dale *et al*., 2000; Liu *et al*., 2002). Candidate cortical dipoles and the boundary element forward solution surfaces were located in each subject from 3D T1-weighted MRI. Regional timecourses were extracted from the resulting maps, and were tested for between-condition differences.

3.2: Supplementary Results - additional details

3.2.1: Behavioral Performance

Behavioral responses were recorded primarily to ensure that subjects maintained attention during the experiment. Response times and performance accuracy were adequately recorded for all eight subjects. Most subjects were highly accurate at identifying congruous word conditions (97% correct ± 6.21) and correctly omitted responses for incongruous word conditions (99.6 % correctly omitted ± 0.52). Since subjects were instructed to respond whenever what they heard matched the visual object they were viewing, we also observed a high proportion of responses to congruously matched noised conditions, however, accuracy was more variable (67.5% correct ± 30.87). Subjects were significantly more accurate at identifying matched word trials than matched noise, determined by a within-subjects 2-tailed, paired *t*-test ($t(7)$ 3.18 $p<0.01$). Subjects were also significantly faster in responding to matched words as opposed to matched noise conditions, determined by a within-subjects 2-tailed, paired *t*-test ($t(7)$ 11.03 $p<0.00001$). Average head movement over the session was 5.3±3.6mm (2.9±1.1mm for the passive listening experiment).

3.3: Supplementary Figures

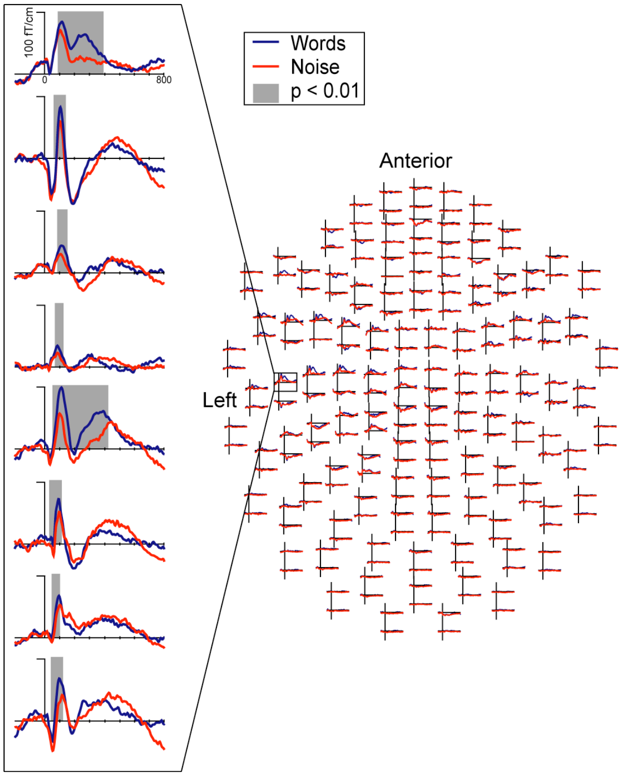

Figure S3.1: Significant M100w response is consistent across all subjects (n=8). **a**. The same left temporal gradiometer channel shows a significant words > noise response beginning ~100ms in all subjects. Shaded areas represent the first cluster of significance in the event-related time-course for each subject, as determined by Monte Carlo between-condition statistics (*p*<0.01) (Maris and Oostenveld, 2007). **b.** Head plot showing sensor-level group average of responses to words and noise, and the location of the left temporal gradiometer that demonstrates a similar early response in all 8 participants.

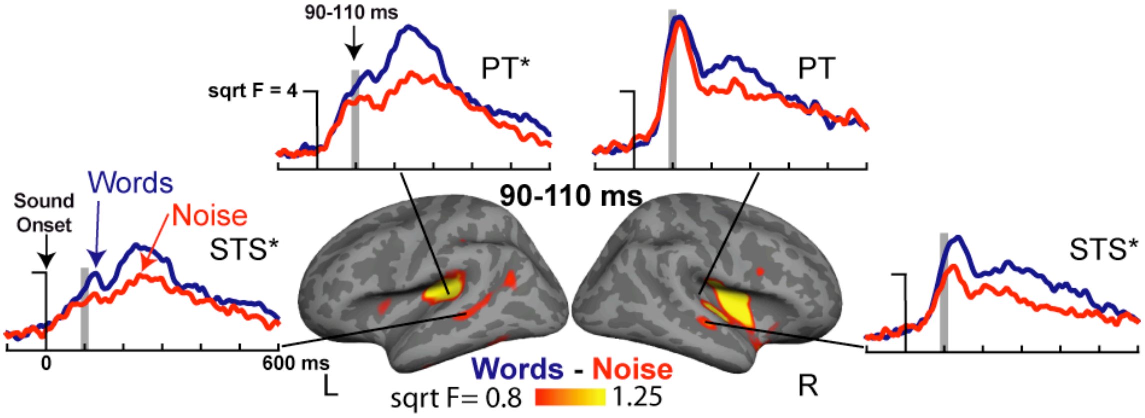

Figure S3.2: Replication of the M100w in a different task, with a different set of words, spoken by a different person. In a separate session, nine right-handed, monolingual English speaking adults (5M; mean age = 30.26 ± 6.67 years, range = 20-41) listened passively to a different set of words and matched noise stimuli. Stimuli consisted of 200 one-syllable words (nouns, verbs, and adjectives), 100 nonwords derived by changing the final phoneme, and 200 noise stimuli generated as described above (573ms average duration, range 373-829ms, 1500-1800ms SOA). 100 words repeated once during the experiment. A different speaker from the primary task recorded the stimuli. **a.** *Center:* Estimated cortical localization of group average activity using dSPM (n=9) showing a words > noise response with similar spatio-temporal characteristics as the early word-selective response in figs 1 and 2. Color bars represent square-root of F values, which are a measure of signal-to-noise. **b.** In bilateral STS and left PT, the M100w is significant from 90-110ms in estimated regional group time-course activity (*surround*). Time courses with * indicate regions where a significant difference was observed. Specifically, ROI analyses revealed significant word > noise activity between 90 and 110ms for all subjects in left planum temporale ($t(8)=2.23$, $p<0.05$), and left ($t(8)=2.54$, $p<0.03$) and right ($t(8)= 2.64$, $p<0.03$) superior temporal sulci.

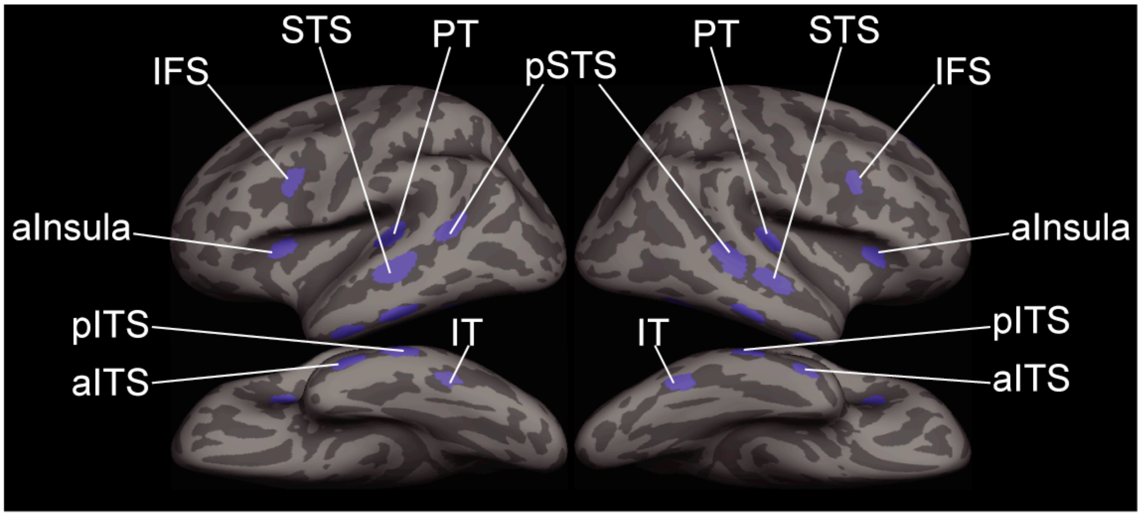

Figure S3.3: Eight bilateral regions of interest (ROI) used to examine early word vs noise and later semantic priming response. This approach is generally quite conservative since it does not allow for inconsistent spatial distribution or latency across subjects. Specific ROI locations were determined based on *a priori* hypotheses about the data. Two ROIs located bilaterally in the superior temporal areas were selected to examine the early M100w. For these ROIs, average square root of F-values from the mean activity that occurred during the peak of the first early response (90-110ms) were entered into a repeated-measures ANOVA with word-form (words vs. noise) and semantics (incongruous vs. congruous) as within subject factors. In addition to these areas, six other ROIs were selected bilaterally in posterior superior temporal and inferior temporal regions to examine later-stage semantic effects. Our *a priori* hypothesis predicted that only significant effects would obtain for incongruous > congruous words, but not for semantically primed noise. Therefore, in order to minimize effects of multiple testing, we performed paired within-subjects 2-tailed *t*-tests for each bilateral ROI for the mean activity occurring only to mismatched and matched words obtained from the 50ms (250-300ms) time window between 200-400ms. To test the task- and stimulus specificity of early words and noise differences, ROI analyses were also performed on estimated activity to words and noise presented during the passive listening task. Within-subjects 2-tailed, paired *t*-tests were performed on the mean activity to words and noise conditions that occurred between (90-110ms) in the two bilateral superior temporal ROIs. IFS = Inferior frontal sulcus; STS = Superior temporal sulcus; PT = Planum temporale; p = posterior; a = anterior; ITS = Inferior temporal sulcus; IT = Inferotemporal.

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3.5: Acknowledgements

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CHAPTER 4:

Additional Studies and Notes

The work presented in this dissertation represents the most successful and promising data and theoretical interpretations from the previous five years of graduate study. In addition to these published and soon-to-be-submitted papers, we considered alternative theories and performed additional experiments, some of which were successful, and some of which were not. In this section, I will discuss some of this work to help put the main studies in a broader context, to allow readers to consider studies that produced negative results, and also to set the stage for future studies that will clarify issues in this dissertation.

4.1: Proficiency

One of the greatest difficulties in bilingualism research is adequately characterizing subjects and their language abilities. Even for Spanish-English bilinguals, an increasingly common group in the United States, there does not exist any standard measure of language history and proficiency, in part because developing such a tool requires standard definitions of the concept of language proficiency. As discussed in Chapter 2, proficiency is not a single measurable entity; it is closely related to daily use, age of acquisition, and likely interacts with order of acquisition. Furthermore, it is reasonable to measure proficiency in each language domain separately. Many bilinguals may be balanced in their oral comprehension abilities, but they may be significantly less proficient at reading or speaking one of their languages. Additionally, a bilingual's ability to utilize grammatical structures may be separate from his or her facility with understanding single words in each language (and importantly for the studies presented here, the underlying connections from words in each language to higher level conceptual representations may be more or less fully developed than other aspects of language). At this time, we do not know of any single language measure (objective or otherwise) that adequately captures these nuances.

In the course of designing our studies, we made several decisions regarding how to deal with these issues. Most notably, we relied heavily on a self-assessment questionnaire to determine language proficiency (adapted from Marian *et al.*, 2007; see Chapter 1.6.3). This questionnaire is designed to acquire a comprehensive view of each participant's language history, including how much and in what contexts they used each language during childhood, adolescence, and adulthood, and it breaks down proficiency into reading, speaking, and understanding, allowing us to attempt to identify subjects who are balanced in certain domains and modalities. In general, we were satisfied with this method, as it consistently confirmed our impressions of subjects' overall language dominance (which is the measure we ended up using to classify subjects in the first two studies). Although some subjects indicated better reading abilities in their supposedly non-dominant language, their neural responses for auditory words were similar to those for written words, suggesting that they either mischaracterized their reading abilities (which was the case for the bilinguals who participated in the study that normed the questionnaire, Marian *et al.*, 2007) or the self-assessment measures were not sensitive to the level of language that our task and neurophysiological methods probed.

Attempts to correlate subjects' neural responses with their self-assessed proficiency (both overall dominance and for each linguistic domain) produced null results, perhaps suggesting that the questionnaire does indeed measure aspects of language that are not targeted by our semantic task. Part of this may be due to the fact that each subject likely interpreted the 1-10 proficiency scales differently, making it impossible to compare responses across subjects. Furthermore, although we attempted to provide an accurate translation of the questionnaire in both English and Spanish, some subjects may have interpreted the scales differently across languages, which could mean that the magnitudes of their self-reported proficiency differences are inaccurate. It may be prudent for future questionnaires to specify certain aspects of language (e.g., understanding single words, speaking sentences with multiple clauses, reading literature versus magazines, etc.) so that subjects are able to be more consistent in their assessments.

The seemingly most straightforward way to deal with these issues is to use a more objective measure of language proficiency. Originally, we had wanted to use a vocabulary assessment such as the Boston Naming Test (Kaplan *et al.*, 1983), however the design flaws with the Spanish-language version discouraged that route (Kohnert *et al.*, 1998). Another measure, verbal fluency, which tests a subject's ability to name items that either begin with a certain letter or that are members of a particular category (e.g., animals with four legs) did not seem to be appropriate, as most existing tests are designed with neuropsychological outcomes in mind, which are not necessarily appropriate for assessing healthy populations.

For the experiments in Chapter 2, we collected proficiency data for reading and oral comprehension using the Woodcock-Muñoz Language Survey – Revised (WMLS-R; Woodcock *et al*., 2005), which had been recommended by several people who specialize in bilingual education. The WMLS-R data from more than 20 subjects did not match up with their self-assessment responses, and perhaps more importantly, did not reflect our impressions of many subjects' language dominance. Several subjects who scored higher in Spanish were very clearly English-dominant based on our interaction with them (including their reading abilities). Even if we had considered the test to be an accurate proficiency measure, like the self-assessment questionnaire, WMLS-R scores did not correlate with MEG data in key regions of interest. For these reasons, we chose not to include the objective measure in Chapter 2, and we also relied heavily on group effects instead of within-subject correlations.

There is no question that a better objective proficiency measure is required to determine the true effects of proficiency on brain activity. One of our current goals in the next set of bilingual studies is to find (and perhaps even create) a tool that accurately portrays subjects' vocabulary and conceptual knowledge, and that reflects aspects of the underlying neural processes that can be measured using MEG.

4.2: Replication

One of the original goals of what became Chapter 2 was a direct replication and extension of the results in Chapter 1. In addition to finding a similar pattern in an independent group of Spanish-dominant subjects, we also wanted to present auditory words so that we could compare those results with the data from the English-dominant subjects presented in Chapter 2. Using the same methods as described in that chapter, we tested ten Spanish-dominant subjects who were theoretically similar to the group in Chapter 1 (the new Spanish-dominant group was recruited using similar mechanisms as the first group, primarily from local community colleges). Presented with both visual and auditory words in the semantic size judgment task, while words in both languages evoked activity primarily in the classical language network, there were no significant language-related effects. The procedure and stimuli for the visual condition were identical to those in Chapter 1, and the new subjects indicated on their self-assessment questionnaires that they were indeed Spanish-dominant. This inability to replicate remains perplexing, however there are at least two possibilities for why we did not achieve positive results.

The first possibility is that despite the subjects' perceptions of being Spanish-dominant, they could be more accurately classified as balanced bilinguals. Behavioral cross-language priming asymmetries essentially disappear as bilinguals achieve balanced proficiency in their two languages (Duñabeitia *et al.*, 2010), and it is possible that the underlying neural differences also diminish. This interpretation is consistent with our positive results in the first two chapters. Our finding that language dominance determines the relative amount of activity in the extended network regardless of order of acquisition suggests that when the two languages are equally dominant (and hence, highly proficient), the extended network may not be necessary for processing words in either language. It is possible that the second group of Spanish-dominant subjects was in this state of language dominance, and therefore did not show between-language differences.

The second possibility relates to a more general characteristic of the subjects we recruited. Unlike all of our other subject groups, some of these participants exhibited an abnormal pattern of repetition effects, where repeated words evoked greater responses than new words. At the group analysis level, there were few brain regions with significant new>repeat effects, and many areas (particularly in the right frontal cortex) that showed repeat>new effects during a slightly later time window than the typical N400 repetition suppression effect. It is not clear why this was the case, however we hypothesize that a future replication of Chapter 2 with Spanish-dominant subjects would not have these issues.

Still, it remains quite powerful that Chapter 2 replicated the effects in Chapter 1 in a different type of bilingual population and across modalities. Although the effects are weaker in Chapter 2 (perhaps related to the subjects being more balanced in proficiency), the change in the pattern apparently related to language dominance is compelling evidence for a real and replicable effect.

4.3: Task-related Effects

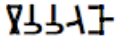
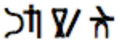
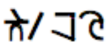
One consistent criticism of the bilingual studies relates to the task that we used to evoke lexico-semantic representations. We chose this task because it had been used previously in MEG with monolingual English speakers (Marinkovic *et al*., 2003), and because it allowed us to examine aspects of higher level conceptual representations. However, the task asks subjects to decide whether items fit into a shoebox, which requires an inherent activation of visual and spatial information. The fact that many of the brain regions that make up the extended network are in secondary visual areas that are typically associated with visual object and feature processing poses the question of whether the task and stimulus modality are driving the recruitment of these areas. Our finding in Chapter 2 that auditory words evoke activity in the extended network argues against this interpretation, and furthermore the fact that such activity is modulated by language proficiency suggests that it is not purely a reflection of visual processing. Still, finding activity in these areas using a different task would be more compelling.

To address this issue, we designed a task that rapidly presented subjects with single written words (~1 per second). Subjects were instructed to press a button when they saw a rare target stimulus that was a member of the category of animals. Repetition suppression was included in the same manner as in the size judgment task, and words were presented in Spanish and English both separately and in a mixed language condition. All MEG and MRI procedures were identical to those described previously.

Unfortunately, we did not find significant language- or repetition- related effects in the group of ten Spanish-dominant subjects described in the previous section. On the one hand, this confirms our hypothesis that there was something odd about this subject group that was not related to the specific task or stimuli. While the activity in both tasks localized to the classical language areas, it was not modulated by repetition in the normal manner, and we were thus unable to draw conclusions regarding the recruitment of the extended network in this task.

An additional purpose of the target detection task was to characterize the response properties of the left and right fusiform region during early visual word encoding in bilinguals. We therefore also presented subjects with pronounceable pseudowords, non-pronounceable pseudowords, and false fonts, which are letters that have been scrambled visually to be unintelligible (but which are sensorily matched to the words that are presented in the same task; see **Table 4.1**). While we found the expected words>false fonts effect in left posterior fusiform for both Spanish and English at ~170 ms, there were no significant language-related differences at this time. This negative finding further adds to the evidence that these bilinguals may have been more balanced than the other two groups we tested, as we predicted that higher language proficiency would mean less early activity in right posterior fusiform cortex.

Table 4.1: Example stimuli used in the target detection task. Words, pronounceable pseudowords, non-pronounceable pseudowords, and false fonts were presented in a pseudo-random order. The three non-word conditions were created based on real words and letter frequency data for both Spanish and English, and stimuli were presented in both a blocked language and a mixed language condition. A subset of the real words repeated several times throughout the experiment to induce a repetition suppression response.

Word	Pronounceable pseudoword	Non-pronounceable pseudoword	False font
APPLE	KLORB	CNTGP	
CHAIR	STEMP	LRTVD	
RING	VENK	SXFZ	

4.4: Speech-specificity of the M100w

In Chapter 3, we present the first evidence for a neural process that is sensitive to the degree to which an auditory stimulus is word-like, analogous to the visual word form process for written words. This study is exciting for a number of reasons, including the future work that will be required to specify the response characteristics of the M100w (see below for a discussion of future directions). One issue that is particularly important is to determine whether the M100w is a response that occurs exclusively to speech that is generated by human vocal cords. While speech is unique in nature in terms of its ability to convey meaningful information through sound waves, its physical acoustic properties are not entirely different from other sounds. While it seems to be the case that the M100w is involved in decoding acoustic stimuli into a linguistic code that can be processed by lexico-semantic brain areas, it is possible that it reflects a more general auditory process for selecting time- and frequency- varying information that has similar properties as speech (e.g., rapidly changing frequencies in the range of ~100-1000 Hz).

Our data suggest that the M100w is not specific to a particular set of words or a particular speaker (see Chapter 3, **Figure S3.2**). However, it remains to be seen whether a similar difference occurs at ~100 ms to meaningless speech-like stimuli and matched noise. Future work will use synthetic speech stimuli that can be manipulated specifically to create such acoustic characteristics. If meaningless sounds evoke a greater response than their matched noise in a similar network of superior temporal and superior planar regions at ~100 ms, this would suggest that the M100w is not speech-specific, though it may still be an important process for selecting words from the acoustic input.

4.5: Future Directions

In this chapter, I have outlined several issues and weaknesses related to the data and interpretations presented in the first three chapters. Many of these weaknesses can be addressed through additional work, some of which has been described here. In addition to these future studies, there are several other questions that will not only help clarify the present findings, but will also lead to a more comprehensive understanding of the neural dynamics of word processing. Some of these studies are currently underway, and others are planned for the future.

Just as we have used bilingualism as a tool to expand our knowledge of both early visual word encoding and late lexico-semantic processing, it will be important to characterize early auditory word processing in bilinguals. In Chapter 2.4.3, we found that Spanish and English evoke different activity during the earliest word processing stage in the auditory modality. As we learned in Chapter 3, the timing of this activity corresponds to the M100w, which is involved in determining how word-like an auditory stimulus is. Do bilinguals use the M100w (or a related process) to identify which language they are hearing during the earliest word encoding stage? Spanish and English are phonetically and phonemically different, so it may be the case that the brain is capable of selecting the language based on pre-lexical properties detected by the M100w. (Presenting stimuli in a mixed language condition is essential for determining the level at which the brain separates the two languages.) It may also be the case that language proficiency modulates the degree of activity in bilateral superior temporal and superior planar areas, which could suggest that the M100w acts differently depending on the brain's experience with a particular language. Such an interpretation would also suggest that even if the M100w reflects a process that is not speech-specific, it is shaped by expertise with specific stimuli.

Related to this, it is unclear how early the M100w emerges during language acquisition. In addition to studying this question in bilinguals, it may be possible to examine the development of the M100w in infants. In a recent study, we found that 12- to 18- month old infants have N400-like lexico-semantic activity that is similar to adults, despite knowing on average fewer than 100 words (Travis *et al*., 2011). Do infants also have an adult-like M100w? If not, how is the later processing stage so advanced? If so, does it emerge concurrently with N400 processes, or does it emerge prior to higher level lexico-semantic processes, facilitating the development of these later stages? The techniques we have developed to study MEG in infants will allow us to address these questions directly.

Finally, at the intersection of questions related to modality-specific processing and bilingualism, we are interested in examining word processing in American Sign Language (ASL). Many ASL signers are congenitally deaf and acquire sign as a native language, either from birth or in the years that follow. If the language acquisition process is similar for truly native signers as it is for hearing populations, the neural processing stages should also be similar. Our preliminary data with a group of native signers (individuals who are born deaf to deaf parents, and therefore receive sign input from birth) suggest that the lexico-semantic processing stage is similar in both its spatial and temporal dynamics as speech (Leonard & Ferjan Ramirez *et al*., In Preparation). Analogous to the previous questions regarding infants, is there an early word-form encoding process for signs, perhaps an M100s? To test this question, we will develop a sensory-matched control analogous to the matched noise used in Chapter 3. Although this is a difficult stimulus to create (it is necessary to control for time-varying spatial frequencies within sub-regions of the video clips), it requires many of the same considerations as what we encountered for speech. It is likely that there is an early visual process that detects the degree to which a stimulus is sign-like, though its temporal dynamics and locations in the brain are currently unknown.

ASL can also be used to probe the phenomenon of bilingualism from a different perspective. Many signers are born hearing and acquire a spoken language normally, and then go on to learn ASL as a second language. These multimodal bilinguals provide an opportunity to probe how proficiency and other factors affect languages that are processed in different modalities. Do the two languages interact to a lesser or greater degree if they do not necessarily share modality-specific neural resources? Does learning a visuo-motor language affect the way speech is processed differently than if both languages are auditory? We are beginning a series of studies that will examine spoken, signed, and written word processing in subjects who are native English speakers learning ASL as a second language, and we hope to address these questions.

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CONCLUSIONS

In this dissertation, I have attempted to expand our knowledge of the various stages of word processing, taking into account the fact that monolingual English-speaking individuals may not be representative of the general population. This is especially true internationally where most people grow up speaking more than one language, which allows them to participate in global discussions and transactions. The United States has traditionally lagged behind the rest of the world in the proportion of our population that is bilingual, however changing demographics are causing us to catch up. Although language distributions are somewhat difficult to measure due to different questions being used over time, it is clear that monolingualism is a decreasing trend, especially among younger age categories, and especially in Latino communities (Shin & Kominski, 2010). According to newly-released data from the 2010 decennial census, Hispanic and Asian populations are growing faster than any other (Humes *et al*., 2011), and with these increases comes greater linguistic diversity.

Whether or not one finds this diversity to be an opportunity for the United States to continue in its role as an innovative leader in the global economy, there is no reason to ignore or dismiss the facts. In some states, it is only a matter of years before English is no longer the sole language spoken by the majority, and it would be unwise to maintain the linguistic status quo in education, health care, and community development without considering these changes.

In the case of education, it is imperative that we provide opportunities for bilingual children to advance at the same rate as their monolingual peers. At a time when budget cuts are forcing schools to eliminate programs that administrators consider unnecessary (but that parents, teachers, and students know are essential), it is more important than ever to ensure that English as a Second Language (ESL) programs are preserved (Waters, 2001). Children who are not placed in ESL and bilingual education programs fare significantly worse than their peers who are in such programs, even those that are the least effective (Thomas & Collier, 2003). However, we must not simply continue with programs that are insufficient or in some cases, harmful to students' abilities in both languages. What are the ideal circumstances under which children successfully acquire a second language? How can these conditions be replicated in the classroom? How can we improve ESL programs, and even better, how can we integrate their lessons into the classroom so that children with a native language other than English are not burdened further by being separated from their peers several hours a week? Can these improvements be applied to adults who have recently immigrated, and who are past the so-called critical or sensitive periods for language acquisition (Lenneberg, 1967)? Should we measure the effectiveness of these programs in contexts other than academic achievement? These are all questions that deserve our attention and resources because without addressing them, we face the prospect of generations of children who never fully acquire the languages that are crucial to their social, emotional, and financial well being.

Educational psychology research has begun to reveal the importance of immersion in a linguistic environment, but this method is only effective when English-language learners (ELLs) have exposure to both of their languages daily, and only when immersion occurs over the long term (Thomas & Collier, 2003; Cummins, 2005). Extensive longitudinal studies by Thomas and colleagues have affirmed the importance of full and successful acquisition of the native language, even if that is not the primary language of instruction, which is consistent with the psycholinguistic literature suggesting that second language development relies heavily on a solid native language foundation (Meschyan and Hernandez, 2002; Mayberry, 2007). However, recent intervention studies have clarified this notion by pointing out that there are highly interactive processes between the two languages, and that at least in terms of literacy measures, simultaneous (but not redundant) instruction in both languages leads to better outcomes as long as L1 reading skills increase at a sufficient rate (Escamilla *et al.*, 2007). Unfortunately, even the most effective bilingual education programs only marginally close the gap for ELLs. A more comprehensive understanding of the underlying acquisition and representation processes in each of a bilingual's two languages (and crucially, how they interact across languages) may lead to more effective interventions that take advantage of how the bilingual brain organizes information.

In the case of health care, it is obviously important that both patients and health care providers are able to communicate effectively so that the proper treatments can be administered. However, there are also many cases where understanding the basic principles of bilingualism in the brain are essential for treating disorders that affect language. To give an idea of how little we understand language disorders in bilingual and multilingual populations, performing a literature search on Google Scholar returns an inordinate number of individual case studies with dyslexic patients. There have been relatively few controlled studies of dyslexia in bilinguals compared to monolinguals, and even fewer among child populations (Durkin, 2000). It is therefore not surprising that diagnostic tests and treatments are not tailored to bilinguals, and may therefore be ineffective. Indeed, many current diagnostics attempt to understand the extent of a disorder by testing patients in a language they may hardly comprehend! Investigating the neural basis of reading and phonological decoding in bilinguals may help us understand whether and how the two languages are differentially affected, and in particular, studies examining the spatiotemporal properties of these processes will help identify the stages at which each language is impacted. For example, our finding that right VOT is more active when healthy adults read words in their less proficient language could provide a useful focus for future studies of dyslexia. Do bilinguals with dyslexia activate bilateral VOT at ~150 ms? Do they show less activation in left VOT like their monolingual dyslexic counterparts (Pugh *et al*., 2001; Shaywitz *et al*., 1998; Shaywitz *et al*., 2002; Paulesu *et al*., 2001)? Is the M100w (Travis & Leonard *et al*., In Preparation) affected in dyslexia and other disorders like specific language impairment, and how does the pattern change if the individual speaks more than one language? By investigating these questions, we may gain a better understanding of how and when the brain fails to decode the relevant information, which will lead to the development of more accurate and appropriate measures to diagnose and treat these disorders.

The two most common questions I get when people find out I research language and bilingualism are, “am I hurting my child by raising them bilingual?” (NO: see Bialystok, 2010; Craik *et al*., 2010), and “why are you interested in bilingualism?” The answer to the second question is that bilingualism poses a serious set of challenges to our current educational and mental health systems, and we need to find ways to address these issues. It can be difficult to find a research topic that both advances our knowledge of basic scientific principles and has potentially far-reaching effects on social and cultural institutions, and it is exciting to be working at this intersection. While there are many steps between neurophysiology and educational policy, it is advisable to ground the latter in the former because language and learning happen in the brain. As science advances toward a deeper and applied understanding of individual variability in genetics, function, and behavior, it is not difficult to imagine educational tools and clinical diagnostic tests that are specially tailored to each individual. Understanding how factors such as proficiency affect the underlying processing dynamics will be crucial to developing these mechanisms, and will ultimately lead us to a more profound notion of the human experience.

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