Fall 2016

Association between bilingualism and functional brain connectivity in older adults

Edmarie Guzmán-Veléz
University of Iowa

Follow this and additional works at: https://ir.uiowa.edu/etd
Part of the Psychology Commons

ASSOCIATION BETWEEN BILINGUALISM AND FUNCTIONAL BRAIN CONNECTIVITY IN OLDER ADULTS

by

Edmarie Guzmán-Vélez

A thesis submitted in partial fulfillment
of the requirements for the Doctor of Philosophy
degree in Psychology (Clinical Psychology) in the
Graduate College of
The University of Iowa

December 2016

Thesis Supervisor: Professor Daniel Tranel

Graduate College
The University of Iowa
Iowa City, Iowa

CERTIFICATE OF APPROVAL

PH.D. THESIS

This is to certify that the Ph.D. thesis of

Edmarie Guzmán-Vélez

has been approved by the Examining Committee for
the thesis requirement for the Doctor of Philosophy degree
in Psychology (Clinical Psychology) at the December 2016 graduation.

Thesis Committee:

Daniel Tranel, Thesis Supervisor

Michelle W. Voss

Bob McMurray

Molly Nikolas

Natalie L. Denburg

To my beautiful and loving grandma, mama Eva. Life deprived you from having an education, and gave you the responsibility of raising your siblings and later your 9 kids with barely nothing. You have successfully overcome every single obstacle that has been placed in your way, and you have done so with love, passion, and with the outmost humbleness. You taught me through example to fight for what I want, to be persistent, to have fun and enjoy life, to be grateful for I have, and most importantly, to value my family and friends. You have said that if you were to be young again you would like to be like me, but I strive every day to be just like you, working hard to be a better person and to obtain the education and professional success that you have always yearned for. This is for you, an accomplishment that I know if you are extremely proud of.

ACKNOWLEDGEMENTS

I have been blessed to have many people in my life that have made this long (and occasionally frustrating) journey fun and totally worthwhile. First, I want to thank my parents for their unconditional love and support. I bet it was not easy to hear your daughter say she was moving to a place named Iowa to pursue a career in something called clinical neuropsychology (and to now hear that she is going to Boston!). Yet you always had my back, celebrated with me my successes (and made sure that everyone on Facebook knew about them), and cheered me up whenever I missed home and felt like running away. Also, to my brother, who I'm sure missed his big sister a whole lot. I also want to thank my partner in crime, Héctor, for reading and critiquing my drafts, for helping me have fun when I felt stressed, and for cooking and cleaning while I spent hours reading and writing. Thanks to my cohort, my COR sisters, and friends for all their support, especially to my almost lifelong sisters Nancy, Cyd, and Sheila who have supported me since I was 5 years old. To the rest of my family, who always know how to make me happy and remind me every day of how lucky I am.

I also want to thank all students in the Health, Brain & Cognition Lab, especially to Tim for providing scripts and answering my 1000 questions. To Dr. Kramer's Lab, especially Aga, Susan, and Gill…thank you, thank you. Thanks to the National Science Foundation and Graduate College for funding my education throughout these years. Thanks to all faculty members who have supported me throughout these years, including my committee members who helped me create a very cool project. To all of the students that I have had the privilege of mentoring and sharing my passion with. Thanks to my participants, patients, and clients who inspire me and help give purpose to my research, and to all the teachers and professors who have helped me acquire the skills and knowledge needed to pursue my research questions. Finally, I want to thank Dan for

giving me the chance to learn about neuropsychological research in 2008 as a SROP student when I had no idea what neuropsychological research really was, and for believing in me again in 2010, and every day ever since. Thank you for helping me become a better scientist.

ABSTRACT

Older bilingual adults typically perform better than monolinguals in tasks of executive control, and are diagnosed later with dementia. Studies have also shown structural and functional brain differences between bilinguals and monolinguals. However, it remains poorly understood how language history influences the functional organization of the aging brain. The current study investigated; 1) differences in resting-state functional connectivity between monolinguals and bilinguals in the Default Mode Network (DMN), Frontoparietal Network (FPN), Executive Control Network (ECN), Language Network (LANG), and a network consisting of structures associated with tasks of executive control coined the Bilingual Control Network (BCN); 2) the relationship of cognitive performance with functional connectivity of the BCN; and 3) whether proficiency, age of second language acquisition, degree of second language exposure, and frequency of language use predicts the network's functional connectivity. Healthy older bilinguals (N=10) were matched pairwise for age, sex and education to healthy older monolinguals (N=10). All participants completed a battery of cognitive tests, a language history questionnaire, and a 6-minute functional scan during rest. Results showed that groups did not differ in cognitive performance, or in the functional connectivity of the FPN, ECN, LANG, or BCN. However, monolinguals had significantly stronger functional connectivity in the DMN compared to bilinguals. Later age of second language acquisition and lower proficiency were also associated with greater DMN functional connectivity. None of these variables predicted BCN's functional connectivity. However, bilinguals showed stronger functional connectivity with other structures outside of the canonical networks compared to monolinguals. Finally, vocabulary scores, local switch cost accuracy and reaction time were negatively correlated with BCN's functional connectivity. Overall, these findings illustrate differences in functional brain

organization associated with language experience in the DMN, while challenging the "bilingual advantage" hypothesis. The results also suggest a possible neural mechanism by which bilingualism might mediate cognitive reserve.

PUBLIC ABSTRACT

As cross-cultural boundaries fade away, business, relationships, employment, education, and the desire for new adventures, have lead to an increasing necessity to communicate in languages other than our mother tongue. Studies suggest that the benefits of being bilingual, or of speaking more than one language, transcend those associated with facilitating communication. Specifically, it has been suggested that bilinguals of all ages are better than monolinguals at executive control tasks (i.e. attention, switching, and inhibition). Scientists have proposed that it is the constant switching of languages what leads to better performance in executive control tasks. This is supported by neuroimaging studies showing that bilinguals engage many of the same brain structures on tasks of language switching and executive control. More recently, studies have suggested that bilingualism protects against dementia onset, as reflected by lifelong bilinguals being diagnosed with dementia (e.g. Alzheimer's disease) years after monolinguals. These findings have raised great interest in both the scientific and the non-scientific community given the increasing incidence of individuals with Alzheimer's disease in the United States and the lack of treatments or preventive measures. Although being bilingual does not cure or prevent the disease, it may allow individuals to enjoy a few more years of independency. However, the neural mechanisms underlying this phenomenon remain poorly understood.

The current study aimed to better understand how speaking more than one language and related variables (e.g. proficiency) influence the functional organization of the aging brain. Specifically, the study examined: 1) whether older bilinguals and matched monolinguals differed in the functional connectivity of multiple brain well-established networks observed during rest; 2) whether resting-state functional connectivity in regions proposed to be associated with executive control was significantly associated with performance in tests of cognition; and 3)

whether proficiency, age of second language acquisition, degree of exposure to a second language, and frequency of language predict resting-state functional connectivity of structures associated with executive control. Resting-state functional connectivity is acquired through functional magnetic resonance imaging (fMRI) and provides a tool to measure the functional integrity of component brain systems that are likely to have developed as a result of previous experiences. Stronger functional connectivity has been consistently associated with better cognitive functioning and with healthier aging.

My sample consisted of 10 monolinguals matched for sex, age, and education with 10 bilinguals of varying proficiency and language history. There were no significant differences between groups in cognitive functioning. Both groups also showed similar functional connectivity between structures associated with language, and in networks associated with executive control. However, monolinguals had stronger functional connectivity in the Default Mode Network, which has been associated with episodic memory, self-generated thought, and has been shown to be particularly susceptible to neurodegeneration. Further, those who were more proficient in their second language and had acquired it earlier in life had weaker functional connectivity in this network. Interestingly, exploratory analyses showed more widespread functional connectivity in bilinguals. Taken together, these findings raise the possibility that bilingualism might confer compensatory mechanisms to maintain cognitive functioning. That is, the experience of managing two or more languages may reorganize the brain functionally in such a way where if the brain suffers damage in an area usually involved in a function (in monolinguals), the function is not compromised in bilinguals because there are already connections to others areas that help maintain functioning. Findings also suggest that language variables such as proficiency influence the functional organization of the brain, emphasizing the importance of considering the heterogeneity within the bilingual group when studying cognition and brain function in this group. Similarly, given that there were no differences between groups in cognitive performance, this study also raises questions about whether bilingualism is actually advantageous or if it only means that it makes our brains look different.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

CHAPTER 1: BACKGROUND INFORMATION

One of the most fascinating characteristics the brain has is its flexibility and ability to adapt to change throughout the lifetime. Our experiences, both good (e.g. learning) and bad (e.g. injury), shape our brain and in turn, impact our behavior and thinking abilities. One experience that seems to significantly affect our brain and thinking is our ability to manage more than one language. There has been a growing interest in exploring how bilingualism might influence the brain's structure and function, and how these relate to cognitive functioning. Bilingualism has been traditionally characterized as the regular use of two (or more) languages (Grosjean, 1989); while monolingualism implies that individuals communicate in a single language regardless of whether they have been significantly exposed to another one. However, as will be further discussed, there exists tremendous heterogeneity within bilinguals; bilinguals differ in their age of second language acquisition and experience using both languages, among others.

Multiple studies have suggested that bilingualism is associated with better performance in executive control tasks across the lifespan, from toddlers to older adults, and with a delay in the onset of dementia (Bialystok, 2010; Bialystok, Craik, & Luk, 2012; Blom et al., 2014; Carlson & Meltzoff, 2008; Engel de Abreu, Cruz-Santos, Tourinho, Martin & Bialystok, 2012; Kousaie, Sheppard, Lemieux, Monetta, & Taler, 2014; Schroeder & Marian, 2012). Consistent with this literature, studies have also shown differences in brain structure and function between monolinguals and those who speak more than one language (Costa & Sebastian-Galles, 2014). However, other studies have failed to find differences in cognitive performance or in dementia onset as a function of amount of spoken languages (Costa, Hernández, Costa-Faidella, & Sebastian-Galles, 2009; Crane et al., 2009; Duñabeitia et al., 2013; Kousaie & Phillips, 2012; Paap & Greenberg, 2013; Paap, Johnson & Sawi, 2015; Zahodne et al., 2014). Therefore, there is a need for research to better examine the complex nature of bilingualism, and the circumstances under which it might influence cognitive performance and brain function.

Beginnings of Bilingualism Research

When the relationship between bilingualism and cognitive functioning began to be explored, there was a consensus in the community that argued in favor of bilingualism as having a detrimental effect on intellectual functioning. Many studies examining differences between bilinguals and monolinguals on standardized tests of IQ (Intelligence Quotient; e.g. Stanfor-Binet test of intelligence), consistently reported deficient IQ scores in the bilingual group (Saer, 1923; Smith, 1923). In fact, immigrants who landed at Ellis Island in the United States in the 19th century, and were given IQ tests in English, tended to perform poorly and were declared mentally unfit. Learning two languages was considered to add an additional burden to schoolchildren since they had to learn two sets of vocabulary and grammar, and so on.

The negative view of bilingualism and the notion of intellectual superiority in monolinguals compared to bilinguals were challenged by a study published in 1962 by Peal and Lambert. Unlike earlier studies, Peal and Lambert matched bilingual and monolingual children on variables that were known to correlate with intellectual functioning. By matching both groups on socioeconomic status (SES), sex, age, and educational background, and by giving the tests in the individual's proficient language, researchers could be more confident that differences observed between groups would most likely be due to differences in the number of languages spoken, and not to other factors. Contrary to what was expected, bilingual children performed better than monolinguals on virtually all tests, including tests measuring nonlinguistic abilities. Specifically, bilinguals performed better in tests that required symbol manipulation and reorganization. Peal and Lambert suggested that bilingual children performed better than monolingual children on most cognitive tests because they had greater mental flexibility, a notion that many researchers favor today. The authors concluded that bilinguals had “a language asset” instead of a “language handicap,” as had been previously suggested.

This study led to an unprecedented increase in more diverse and better-designed studies of bilingualism. Studies not only examined differences between bilinguals and monolinguals in tests of intellectual functioning, but expanded to other domains of functioning and began to consider the role of other factors including language proficiency, age at which the second language was acquired, frequency of use, and context in which the languages were learned. Moreover, studies began to further explore differences between groups using diverse methodologies including neuropsychological tests, other cognitive tests, and neuroimaging techniques. All of these studies have provided great insight into the complex nature of bilingualism.

Language Processing in Bilinguals

It is natural to wonder how it is that bilinguals process two languages. What happens to one language when a person is speaking in another? How do individuals handle the use of more than one language without letting one interfere with the other? Multiple models have been put forward to explain how bilinguals process both languages.

It was previously believed that bilinguals would “shut down” one language while they engaged in the other language. Today we know that this is not the case. Behavioral tests and neuroimaging techniques have provided compelling evidence showing that representations from both languages are active to some degree even when bilinguals are only communicating in one of them (Kroll, Bobb, Misra, & Guo, 2008; Marian, Spivey, & Hirsch, 2003).

For instance, the joint activation of two languages is supported by an experiment conducted by Marian and colleagues (2003), where highly proficient English-Russian bilinguals were instructed to “pick up” an object in either Russian or English while their eye movements were recorded. Participants were presented with four objects each time they were instructed to “pick up” an object, including the target object (e.g. a “speaker” if the instruction was to “pick up the speaker”), two filler objects, and the between-language competitor. The latter object was one whose name in the other language carried phonetic overlap with the name of the target object (e.g. “spichki” if the target object was “speaker”). Researchers suggested that if (the phonological uptake of) one language is in fact “switched off” while the other is being used, then participants should not move their eyes towards the between-language object more compared to the other objects (e.g. spichki, which means “matches” in Russian). Results showed that bilinguals made significantly more eye movements toward the between-language competitor compared with the filler objects, suggesting that bilinguals process their two languages in parallel even when direct linguistic input is provided in one language only. Studies have suggested that the joint activation of languages can be observed in strong monolingual contexts in proficient bilinguals (i.e. when the individual is only speaking, listening, writing or reading in one language without the stimuli of another language), independent of the languages’ writing system (Hoshino & Kroll, 2008; Thierry & Wu, 2007), or even when one language is spoken and the other is signed (Morford, Wilkinson, Villwock, Piñar, & Kroll, 2011).

The inhibition control model proposes that the simultaneous activation of representations from both languages in bilinguals results in a necessity to attend to one language while inhibiting the other non-target language in order to communicate effectively (Kroll et al., 2008). It has been proposed that the need for inhibitory control with simultaneous activation of both languages leads to what is referred to in the literature as the "bilingual advantage" (Bialystok et al., 2012) and to what Peal and Lambert referred to as "a language asset." This "bilingual advantage" refers to research showing that bilinguals usually perform better than monolinguals in tasks requiring inhibition, attention, anticipation, monitoring, working memory and task switching (Bialystok Craik, & Luk, 2008; Bialystok & Viswanathan, 2009; Bonifacci, Giombini, Bellocchi, & Contento, 2011; Carlson & Meltzoff, 2008; Luo, Craik, Moreno, & Bialystok, 2013). Overall, it has been proposed that the skills that are frequently employed by bilinguals in order to handle both languages—i.e. switching languages and inhibiting one language while attending to another—generalize to other nonlinguistic domains (i.e. based on tasks that are *not* mainly language tasks), a topic that will be further discussed later.

Bilingualism and "Nonlinguistic" Domains of Cognition

Most individuals would not find surprising that bilingualism (a linguistic experience) could have consequences for linguistic processing. What is unexpected, however, is that it seems to influence nonlinguistic cognitive processing as well. Multiple review articles highlight that many published studies show that bilinguals from all ages demonstrate better performance in tasks of executive control compared to monolinguals matched in age and other variables, presumably because they engage some of the same cognitive processes used to control language in the nonlinguistic tasks (Bialystok, 2010; Bialystok et al., 2012; Buchweitz & Prat, 2013). Executive control has been defined as a set of cognitive skills that include inhibition, switching attention, and working memory (Miyake, Friedman, Emerson, Witzki, Hemerter, & Wager, 2000). Research examining this set of cognitive skills and other higher-level cognitive functions (e.g. processing speed) in bilinguals is further discussed below.

Working memory. Working memory refers to information that is stored temporarily and is manipulated for complex cognitive operations (Lezak, Howieson, Bigler, & Tranel, 2012). Tasks of working memory involve an executive control mechanism that is recruited to be attentive and combat interference (Lezak et al., 2012). Therefore, it would be expected for bilinguals to perform better on these tasks compared to monolinguals given that it involves attention and interference management, both functions that are required in dual language processing. However, the available evidence is inconclusive.

In one study examining working memory in bilinguals, young and older bilingual adults were presented with a nonlinguistic task of working memory that consisted of repeating a sequence using 10 fixed blocks spread on a wooden base. In the forward condition, participants were asked to watch the experimenter tap the blocks in a certain order and then to repeat the sequence in the same order. In the backward condition, the sequence presented by the experimenter participants had to be repeated in the reverse order. No differences were observed between language groups for either the young or older group (Bialystok & Viswanathan, 2009). Similar findings were obtained for a self-ordered pointing task that required participants to remember which of 12 abstract drawings had been selected previously (Bialystok & Viswanathan, 2009). Other studies examining children and young adults have also failed to find differences between groups in similar tasks of working memory (Bialystok, 2010; Engel de Abreu, 2011; Giombini, Bellocchi, & Contento, 2011).

Contrary to these outcomes, other studies have reported better performance by bilinguals in tasks of working memory. For instance, a study by Blom et al. (2014) reported better performance by bilingual children in a visuospatial working memory task, where children had to recall the coordinates of dots that were shown on a series of screens with a red dot that appeared in a matrix. The same study reported that bilingual children outperformed monolingual children on a Backward Digit Recall task, a test of verbal working memory. Interestingly, other studies have found different outcomes based on whether the tasks are verbal or not. These studies tend to show a bilingual advantage for tasks of visuospatial working memory but not for verbal tasks of working memory (Luo et al., 2013).

Overall, there is no consensus on whether bilinguals perform better than monolinguals on working memory tasks. Outcomes seem to partially depend on the task that is administered. It is possible that even though all of the tasks measure working memory, they might also tap into other task-specific cognitive processes.

Finally, other types of memory—i.e. episodic and semantic memory—have been less studied in bilingual persons. Nonetheless, so far the evidence suggests that bilinguals perform worse than monolinguals in tests of semantic memory and possibly in tests of episodic memory, although there are mix findings regarding the latter (Bialystok, Craik, Green, & Gollan, 2009; Schroeder & Marian, 2012).

Processing speed. Findings from studies measuring processing speed have also been somewhat mixed. Contrary to working memory, studies of processing speed usually find a trend in favor of bilinguals, but results are not always statistically significant. In general, tests of processing speed assess the speed at which individuals can process information.

A study by Bonifacci and colleagues (2011) reported that bilingual children and young adults matched on age, sex and non-verbal IQ to monolinguals, did not perform significantly different than monolinguals in tests of Choice Reaction Time. Nonetheless, although statistically insignificant, bilinguals were faster than monolinguals. Other studies have reported significant differences between groups, with bilinguals performing faster than monolinguals on multiple tests of processing speed (Bialystok, 2010). The lack of significant findings in some studies can be partially explained by the fact that most of them do not consider the influence of language proficiency on processing speed. This is highly relevant given that other studies have shown that processing speed in bilinguals is moderated by language proficiency. Specifically, it has been observed that the more proficient the individual is in the second language, the faster the individual will perform in a task of processing speed (Leonard et al., 2011).

Inhibitory control. Performance on tests of task-switching has received generous attention in the bilingualism literature. Task-switching involves the ability to switch attention between one task and the other (Monsell, 2003). As previously discussed, bilinguals often have to switch from one language to the other, depending upon the context of interaction and interlocutors, a cognitively demanding skill that monolinguals do not necessarily develop. Similarly, it has been proposed that bilinguals are constantly inhibiting one language and selectively attending to the one they are using in order to communicate effectively. Interestingly, bilinguals consistently show enhanced performance in tasks that require similar skills.

Multiple studies have shown that bilinguals outperform monolinguals of all age groups on tasks of inhibition and interference suppression such as in flanker paradigms (Bialystok et al., 2008; Costa, Hernández, & Sebastian-Gallés, 2008), Stroop (Bialystok et al., 2008; Kousaie et al., 2014), and the Simon task (Bialystok et al., 2008; Kousaie et al., 2014). Similarly, bilinguals usually outperform monolinguals in task-switching as illustrated by performance in the Trail-Making Test Part B, where participants are required to connect symbols by alternating the sequence between numbers and letters (i.e. 1-A-2-B…12-L-13), as fast as they can without making mistakes. Bilinguals consistently perform faster and without more errors than monolinguals on this task (Bialystok, 2010). In fact, a study examining the relationship between language switching and nonlinguistic task-switching showed that habitual language switching is associated with general switching abilities in nonlinguistic tasks (Abutalebi, 2008). After administrating objective measures of language and nonlinguistic switching, and acquiring self-reported information about switching frequency in daily language use, researchers found an association between performance in language switching (in both subjective and objective measures) and nonlinguistic switching. Of note, smaller task-switching costs (errors) were observed only after controlling for SES, highlighting the importance of considering demographic variables in studies examining cognitive functioning (a point that will be discussed later).

Similar to processing speed tasks, language proficiency has also been found to be associated with performance on tests measuring task-switching, inhibition or interference suppression. Overall, studies show that the more proficient an individual is in a certain language, the less interference there is and the smaller the task-switching costs (Hernández, Martin, Barceló, & Costa, 2013; Marian, Blumenfeld, Mizrahi, Kania, & Cordes, 2013).

Further support for these findings comes from a meta-analysis that evaluated 63 papers examining the cognitive correlates of bilingualism (Adesope, Lavin, Thompson, & Ungerleider, 2010). The authors found a moderate positive overall association between bilingualism and performance on metalinguistic and metacognitive awareness, abstract and symbolic representation, attentional control and problem solving. Furthermore, they reported that better performance by bilinguals was not associated with geography; that is, studies from United States reported findings similar to the ones reported in China or in European countries. Researchers also reported that bilinguals performed better than monolinguals in tests of abstract and symbol representations, attentional control and problem solving regardless of the spoken language pairings (e.g. English-Spanish, English-Chinese). All of these findings held true even after considering SES, illustrating that bilingualism is associated with cognitive benefits regardless of the SES of participants, another factor that is commonly associated with better cognitive functioning.

Challenging the "Bilingual Advantage"

As reported for some studies of processing speed and working memory, an increasing number of research studies have found similar performance between bilinguals and monolinguals of different age groups on tasks measuring executive control. Studies have failed to find differences between groups in tests of inhibition (Costa et al., 2009; Duñabeitia et al., 2013; Kousaie & Phillips, 2012; Paap & Greenberg, 2013; Paap et al., 2015), attention (Anton et al., 2014; Kousaie & Phillips, 2012; Paap & Greenberg, 2013; Paap et al., 2015), and task-switching (Kousaie & Phillips, 2012; Paap & Greenberg, 2013; Paap et al., 2015). Researchers whose data show similar performance in tasks of executive control between bilinguals and monolinguals, ascribe findings supporting a "bilingual advantage" to a confirmation bias to report positive findings, publication bias, task selection, and experimental design (De Bruin, Treccani, & Della Sala, 2014).

Adesope and colleagues (2010) assessed the potential for publication bias in their meta-analysis, recognizing that nonsignificant findings are sometimes archived in drawers or published in less accessible literature. Their analyses revealed that thousands of additional studies would be needed to invalidate their findings and hundreds to nullify the effects reported from the meta-analysis, which showed better performance by bilinguals in some cognitive domains compared to monolinguals (as discussed in the previous section).

Other studies that have not found a "bilingual advantage" argue that findings from multiple studies supporting the cognitive benefits of bilingualism can be attributed to factors such as formal educational attainment, SES, culture and immigration, and less so to the bilingual experience. However, studies have reported a "bilingual advantage" even after controlling for all the aforementioned variables (i.e. formal education, culture, immigration status, among others) (Adesope et al., 2010; Bialystok & Viswanathan, 2009; Calvo & Bialystok, 2014; Engel de Abreu et al., 2012). Some of these have specifically shown independent effects of bilingualism and SES (Calvo & Bialystok, 2014; Prior & Gollan, 2011). Better performance in executive control tasks has also been observed in bilingual children from lower-income and less educated families compared to middle-class monolinguals (Carlson & Meltzoff, 2008) and in young children growing up in underprivileged conditions and environments that might negatively impact or even impede healthy brain development and impact executive control performance (Engel de Abreu et al., 2012). This suggests that the advantages of bilingualism can transcend social disadvantages that often challenge children's cognitive development. Nonetheless, it cannot be ignored that all of these factors also influence cognitive functioning, and thus must be taken into consideration when examining the relationship between bilingualism and cognitive function.

Overall, although significant findings in favor of a "bilingual advantage" have been found after considering multiple demographic variables, some studies still fail to observe this phenomenon even after controlling for these variables. The increasing inconsistency in findings has led researchers to question whether a "bilingual advantage" actually exists or whether it is restricted to specific circumstances.

Bilingualism and Linguistic Tasks

Lastly, it is important to note that monolinguals consistently perform better than bilinguals on some cognitive domains, many of which have a heavier linguistic demand relative to the ones discussed thus far. These differences have been consistently found independent of demographic variables and other factors.

Similar to language acquisition in monolinguals, acquiring two languages early in development seems to be as effortless, efficient, and successful. However, the size of the developing vocabularies differs between monolingual and bilingual children. There is compelling evidence showing that, on average, bilingual children know significantly fewer words than monolingual children, in each language (more when combining both languages) (Bialystok, 2010; Blom et al., 2014; Calvo & Bialystok, 2014; Carlson & Meltzoff, 2008). Results from the English Peabody Picture Vocabulary Test (PPVT), which was administered to monolingual English-speaking children between the ages of 3 and 10 and bilingual children whose first language was English, showed that receptive vocabulary was reliably higher for monolinguals compared to bilinguals (Bialystok et al., 2010). In an earlier study, Bialystok and colleagues (2008) administered the same vocabulary test (PPVT) to both young and older adults whose first language was English. Similar to children, PPVT scores standardized for age were higher for monolinguals compared to bilinguals in both age groups, demonstrating smaller vocabulary size in bilingual's each language across the lifespan.

The same study also reported that monolinguals outperformed bilinguals in the Boston naming task. Consistent with these findings, other studies have shown that overall bilingual individuals take longer and produce more errors than monolinguals on tasks of naming (Bialystok et al., 2008; Gollan, Fennema-Notestine, Montoya, & Jernigan, 2007; Kousaie et al., 2014).

Studies have also suggested that bilinguals perform worse than monolinguals in tests of verbal fluency, possibly because verbal fluency is associated with vocabulary size. Similar to naming tests, bilingual adults generate fewer words than monolinguals in tests of category and letter fluency, especially in category fluency tasks (Bialystok et al., 2008, 2010; Kousaie et al., 2014). However, studies have shown that when bilinguals are as proficient as monolinguals in the language spoken by them, both groups perform similarly in category fluency tests, which has been suggested to depend more on vocabulary size, and better than monolinguals on letter fluency, which has been associated with cognitive control (Bialystok et al., 2009). Further, as observed in naming tests, it is also possible that bilinguals sometimes perform worse in verbal fluency tasks because they are also slower at retrieving words. It has been proposed that bilinguals show slower word retrieval because they have to deal with two competing languages.

Taken together, it can be argued that the bilingualism literature as a whole shows that bilinguals process information differently from monolinguals, performing worse on some cognitive tasks (e.g. vocabulary, naming), and better in others (e.g. task-switching, inhibition). This is consistent with findings showing that, and as will be discussed next, bilinguals recruit brain resources *differently* from monolinguals (Kroll & Bialystok, 2013).

Neural Correlates of Bilingualism

Language processing in the bilingual brain. Defining bilingualism is not an easy endeavor since, as can be inferred by the previously discussed studies, bilingualism encompasses a broad typology of speakers. There are bilinguals who learn two languages from birth; others who learn a second language in a formal setting early or late in life; those who learn it by migrating to a different country; and they can all differ in their proficiency in each language. All of these factors play a role in how the brain of a bilingual is shaped.

Early studies of brain organization in bilinguals found that global aphasia could be induced in bilinguals by using sodium Amytal injection to paralyze the dominant left hemisphere

(Berthier, Starkstein, Lylyk, Leiguarda, 1990; Gomez-Tortosa, Martin, Gaviria, Charbel, & Ausman, 1995). This led researchers to believe that both languages are represented in the dominant left hemisphere. This would be consistent with the literature showing that brain areas such as the ventrolateral frontal cortex, the posterior parietal cortex, and temporal cortex in the left hemisphere are associated with monolingual language processing (Friederici, 2011; Kelly et al., 2010). However, lesion studies began to report right-hemisphere involvement depending on the age of second language acquisition (Marrero et al., 2002). Studies examining bilingualism in patients with aphasia and in patients with dementia also began to notice different patterns of language recovery (and deterioration) across individuals (Larner, 2012; Méndez, Perryman, Pontón, & Cummings, 1999). For instance, some studies reported cases of individuals with dementia who showed marked language impairment for the individual's second language with relative preservation of the first language (Méndez et al., 1999). Many of these studies suggested that differences in recovery and deterioration between bilinguals were due to variability in proficiency, age of second language acquisition, and frequency of language use, among other factors. These findings led to the notion that bilinguals had differentiated neural patterns of activation for each language, or even a neural network that represented each language (Kovelman, Baker, & Petitto, 2008).

However, recent studies argue against two separate language neural networks, and instead propose that similar brain structures are engaged when bilinguals use either of the two languages (Abutalebi et al., 2007; Simmonds, Wise, & Leech, 2011; Stein et al., 2012). Further, the extent of neural overlap between both languages has been suggested to primarily depend on second-language proficiency and to some extent, on the age of second language acquisition (Abutalebi et al., 2007; Mechelli et al., 2004; Simmonds et al., 2011). Interestingly, research suggests that the effect of age of acquisition diminishes or even disappears when early or late learners are equated in proficiency (Hernández & Li, 2007; Leonard et al., 2011; Perani et al., 1998). In turn, proficient bilinguals, independent of age of acquisition, show greater grey matter density in language-related regions (i.e. inferior frontal gyrus) and a striking similarity in brain activation across different languages, again supporting a common network for bilingual language processing (Stein et al., 2012). These findings are further supported by research showing similar deterioration of lexical processing in both languages in bilinguals with Alzheimer's disease, Mild Cognitive Impairment, and non-fluent progressive aphasia (Costa et al., 2012; Druks & Weekes, 2014).

Taken together, research suggests that specific left frontal, temporal and parietal regions, together with some subcortical structures (i.e. basal ganglia) seem to be functionally involved in the processing of both first and second languages, and that engagement of occipital areas and the hippocampus during language processing decrease as second language proficiency increases (Leonard et al., 2010, 2011).

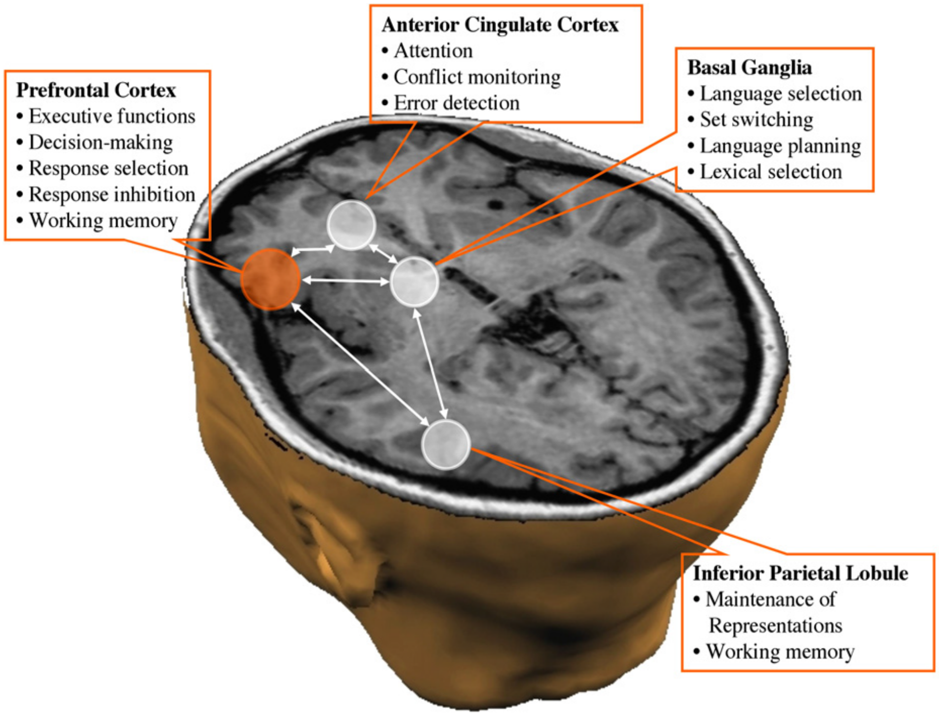
As discussed, multiple studies have suggested that bilinguals perform better than monolinguals in executive control tasks. Next, we consider neural correlates that might underlie this "bilingual advantage."

Neural correlates of cognitive control. In 2000, before the relationship between bilingualism and measures of executive control had been explored extensively, Fabbro and colleagues reported the case of a lifelong Friulian-Italian bilingual who was diagnosed with a tumor in the white matter in the left frontal lobe at the age of 56 years. The authors reported that the patient had an unprecedented "compulsive tendency to alternate utterances in Italian and utterances in Friulian," (p.652) illustrating pathological switching. Researchers concluded that abnormal switching between languages was affected by the lesion in the anterior cingulate, and left frontal and prefrontal structures. Further, they suggested that the system responsible for language switching is independent of language (given that the patient did not show symptoms of aphasia) and instead, it is part of a more general system. Similar to the study by Fabbro and colleagues (2000), other studies have shown that damage to the prefrontal cortex and basal ganglia are involved in pathological language switching (Buchweitz et al., 2013).

In a comprehensive review by Abutalebi and Green (2007), the authors proposed a neurocognitive model of bilingual language switching based on multiple neuroimaging studies of switching between two languages and translation. The proposed model is depicted in Figure 1.

Abutalebi and Green (2007) proposed that this subcortical-cortical circuit sustains the cognitive demand of managing two languages, including inhibiting one language while suppressing the “irrelevant” language. Furthermore, they suggested that the prefrontal cortex, anterior cingulate cortex, basal ganglia, and inferior parietal lobule, which are involved in language switching, are also involved in cognitive control, a finding that was supported in a quantitative meta-analysis examining cognitive control of language switching in bilinguals (Luk, Green, Abutalebi, & Grady, 2011).

Figure 1. Neural Regions Associated with Cognitive Control



Note: Reproduced from Abutalebi & Green, 2007

A study by Gold and colleagues (2013) further illustrates the relationship between regions involved in cognitive control and those engaged in language processing. In this study researchers examined the functional neuroanatomical basis of bilingual cognitive control advantages in a group of lifelong younger and older proficient bilinguals who had learned a second language before the age of 10, and spoke both languages on a daily basis. Monolinguals and bilinguals were matched across multiple demographic and neuropsychological scores, most of which have been proposed to influence cognitive control performance—e.g., educational attainment, SES and intelligence. Groups similar in age did not significantly differ in regional brain volume. Results revealed that bilingual older adults performed better than older monolinguals in a task-switching experiment (i.e., were significantly faster at switching between perceptual tasks) while showing lower activation in the left dorsolateral prefrontal cortex, the left ventrolateral prefrontal cortex and the anterior cingulate cortex, a pattern that was similar to the one observed in younger adults. These areas have been previously associated with a network of regions engaged during task-switching performance (Gold, Kim, Johnson, Kryscio, & Smith, 2013) and language processing, further supporting the model depicted by Abutalebi and Green (2007). The authors interpret the finding of better performance in task-switching with lower activation in the three aforementioned regions, as demonstration of higher neural efficiency conferred by lifelong bilingualism. Neural efficiency has been proposed to be one of the mechanisms associated with cognitive reserve (see Bilingualism and Reserve), and it suggests that some individuals with neuropathology can maintain cognitive functioning by making more efficient use of the same networks engaged by healthy individuals (Bartrés-Faz & Arenaza-Urquijo, 2011; Steffener, Reuben, Rakitin, & Stern, 2011).

White matter integrity and functional connectivity. Differences in white matter integrity and functional connectivity between monolinguals and individuals who had successfully managed two languages since an early age (before the age of 11 years) were investigated by Luk and colleagues (2011). Bilingual older adults did not differ from monolinguals in a range of demographic variables including age and years of formal education, or in neuropsychological performance on standardized tests. The results showed higher white matter integrity in bilingual older adults, primarily in the corpus callosum connecting the two hemispheres but also extending to the bilateral superior longitudinal fasciculi (bidirectional tract connecting the frontal, temporal, parietal, and occipital lobes), right inferior frontal-occipital fasciculus (tract that passes backward from the frontal lobe all the way into the occipital lobe), and the uncinate fasciculus (bidirectional tract that connects the lateral orbitorfrontal cortex and the rostral frontal cortex with the anterior temporal lobe). Decline in white matter microstructure has been associated with aging (Hakun, Zhu, Brown, Johnson, & Gold, 2015), and worse performance in cognitive tasks including language functioning (Madhavan, McQueeny, Howe, Shear, & Szaflarski, 2014), executive functioning (Charlton et al., 2008), processing speed and memory (for a review see Gunning-Dixon & Raz, 2000).

The researchers then proceeded to conduct a resting-state functional connectivity analysis, which allows researchers to examine how anatomically separated structures can be functionally linked (van den Heuvel & Hulshoff Pol, 2010). These functionally linked regions form multiple complex networks that have been individually associated with cognitive functions such as executive control, self-generated thought, among others (see Introduction to the Current Study for more information about resting-state functional connectivity). Researchers aimed to examine whether there was stronger functional connectivity in grey matter regions near areas where they found group differences in white matter integrity.

Results showed similar synchronous activity with contralateral regions at rest for bilinguals and monolinguals. However, bilinguals had stronger functional connectivity between bilateral temporal gyri, right inferior parietal lobule, precuneus, bilateral middle occipital gyri, and left caudate, many of which are not typically associated with executive control. On the other hand, monolinguals showed greater functional connectivity between the left inferior frontal region and other anterior areas (e.g. right superior frontal gyrus, bilateral precentral gyri, among others). Thus, compared to monolinguals who had stronger functional connectivity within the frontal lobes and closer neighboring regions, bilinguals showed more distributed resting-state functional connectivity and in overlapping regions to where white matter structural differences were observed.

The authors suggested that these findings reflect how enriched experience (i.e. bilingualism) protects white matter against age-related deterioration (Luk, Bialystok, Craik, & Grady, 2011). They also suggested that these results indicate white matter could provide reserve by compensating for grey matter damage, which in turn results in sustained cognitive performance in lifelong bilinguals.

The same group of researchers later published a research article that examined resting-state functional connectivity in the same cohort of healthy lifelong older bilinguals and older monolinguals (Grady, Luk, Craik, & Bialystok, 2015). Specifically, they measured functional connectivity in: 1) The Default Mode Network (DMN), which has been related to episodic memory retrieval, self-referential processes, social cognition and mind wandering (Andrews-Hanna, Smallwood, & Spreng, 2014); 2) The Frontoparietal Network (FPN), which has been associated with engagement in task-initiation and error-related activity (Scolari, Seidl-Rathkopf, & Kastner); and 3) The Salience Network, which has been implicated in integrating sensory data with internal states (Seeley et al., 2007). Groups were matched for age, gender, neuropsychological variables, and English proficiency, and bilinguals were on average 1 year more educated than monolinguals. In order to test differences in functional connectivity between groups, researchers analyzed the data using seed Partial Least Squares, a multivariate approach that reveals correlations between functional activity in a brain region chosen a-priori and activity across all other regions of the brain (Grigg & Grady, 2010; McIntosh & Lobaugh, 2004). The posterior cingulate cortex (PCC) was used as the region of interest for the DMN, while the anterior insula/frontal operculum (aIFO) was used as the major node for the FPN and the Salience Network.

Consistent with their hypotheses, the DMN and the FPN were significantly more strongly functionally connected in bilinguals compared to monolinguals, whereas there were no significant differences between groups for the Salience Network. Authors suggested that these findings are in line with outcomes from their previous study (Luk et al., 2014) where they found better-maintained white matter between hemispheres and between anterior-posterior brain regions in lifelong bilinguals.

Given that stronger functional connectivity within multiple networks has been associated with better cognitive performance, findings from the aforementioned studies could be taken as evidence supporting the “bilingual advantage.” For instance, stronger functional connectivity in the DMN has been associated with better performance in episodic memory tests (Andrews-Hanna et al., 2014), and it has been suggested to be particularly prone to aging-related neurodegeneration and Alzheimer’s disease neuropathology (Chhatwal et al., 2003). Therefore, one interpretation of these findings is that the experience of managing two languages on a regular basis since an early age strengthens the functional connection between regions within the DMN and FPN in order to maintain performance even when the brain has been exposed to some kind of insult (i.e. neuropathology). However, none of these studies examined the relationship between the functional connectivity of these networks with cognitive performance. Most importantly, the studies by Luk et al. (2014) and Grady et al. (2015) tested the same sample, which was composed of lifelong, highly proficient bilinguals who reported using both languages on a regular basis, a sample that is likely not representative of bilinguals worldwide. Bilinguals vary in proficiency, age of second language acquisition, and on how frequently they use both languages, all factors that could potentially influence functional connectivity between different brain regions, given that they have been shown to impact brain structure and function (associated with tasks) (Garbin et al., 2011; Jasinska & Petitto, 2013; Luk & Bialystok, 2012; Mechelli et al., 2004). Thus, there is a need for research to better characterize how and under what circumstances might bilingualism confer an "advantage."

Bilingualism and Cognitive Reserve

An increasing body of literature has provided evidence for bilingualism as a contributing factor to cognitive reserve. Cognitive reserve refers to individual differences in the ability to adaptively use brain resources to cope with neuropathology and maintain cognitive functioning (Bartrés-Faz et al., 2011; Stern, 2009). Therefore, if two individuals of similar age, sex and with comparable neuropathology (e.g., similar brain atrophy) are evaluated, the one with high cognitive reserve will perform better in tests of cognitive functioning, presumably by using brain resources more effectively.

Research suggests that different traits and exposures contribute to cognitive reserve during the life course, including formal educational attainment, occupational attainment, premorbid intelligence, SES, early-life linguistic ability, and cognitive activities (Koenen, et al., 2009; Reed et al., 2011; Sattler, Toro, Schönknecht, & Schröder, 2012; Snowdon et al., 1996). It is important to acknowledge that none of these variables protects individuals from developing neuropathology or other brain damage. Instead, they appear to mitigate the impact of neuropathology on the clinical expression of diseases such as Alzheimer's disease.

More recently, studies have reported a relationship between bilingualism and delayed symptom onset of dementia (for a review see Guzmán-Vélez & Tranel, 2014). That is, on average, bilinguals are diagnosed with dementia or mild cognitive impairment years after monolinguals, even after considering variables such as education, immigration status and SES (Ossher, Bialystok, Craik, Murphy, & Troyer, 2013). For instance, two retrospective studies reported an average delay of 4 to 5 years in the onset of symptoms of dementia in a bilingual group compared to the monolingual group (Alladi et al., 2013; Bialystok, Craik, & Freedman, 2007). These results were observed even after controlling for immigration status, educational attainment, occupation, rural vs. urban dwelling, sex, and cardiovascular risk factors, among others. Other studies have further contributed to the literature by adding that more proficient individuals show clinical manifestations of the disease later compared to less proficient individuals (Gollan et al., 2011).

Further evidence for a relationship between bilingualism and cognitive reserve comes from neuroimaging studies comparing groups of older bilinguals and monolinguals. In one of these studies, lifelong bilingual patients with Alzheimer's disease were matched with monolingual patients on measures of cognitive function including the Behavioral Neurology Assessment and Mini-Mental State Examination (MMSE), age of diagnosis, years of formal education and on a measure of activities of daily living (Schweizer, Ware, Fischer, Craik, & Bialystok, 2012). A head computed tomography (CT) scan revealed that bilingual patients had significantly more medial temporal lobe atrophy than monolingual patients (and possibly more Alzheimer's disease neuropathology in this region). Despite having more atrophy, bilingual patients' cognitive and daily functioning did not differ from that of monolinguals. Consistent with these findings, a recent study examining white matter integrity and gray matter volumetric patterns in older lifelong bilinguals and monolinguals found that bilinguals maintained cognitive performance despite moderate neurodegeneration (Gold, Johnson, & Powell, 2013). In this study, researchers examined healthy older bilinguals and monolinguals whose first language was English, and matched them for age, sex, education, SES, intelligence, MMSE, and multiple neuropsychological scores. Although no significant differences in gray matter were observed, findings showed that bilinguals had significantly lower white matter integrity in tracts that are prominently affected in Alzheimer's disease (i.e., fornix, inferior longitudinal fasciculus, among others) even when they performed similar to monolinguals in a range of neuropsychological tests.

Attention should be allocated to the fact that these findings are not uniform, and some studies have failed to find a strong relationship between bilingualism and cognitive reserve (Crane et al., 2009, 2010; Zahodne et al., 2014). Nonetheless, most studies offer convergent evidence supporting the hypothesis that bilingualism modifies the relationship between neuropathology and cognitive functioning, possibly because of the extra constant exercise that bilinguals impose in their brain by constantly managing more than one language.

CHAPTER 2: INTRODUCTION TO THE CURRENT STUDY

The vast majority of studies to date examining brain function in bilinguals have employed task-related functional magnetic resonance imaging (fMRI) to measure how different cognitive functions relate to different patterns of brain activation. Although tasks are usually designed to measure a specific domain of cognitive functioning (e.g. memory, language, executive functioning), they often differ in exactly what they are measuring. For instance, two tasks of working memory could also each be measuring different additional cognitive processes and thus, recruiting different neural networks, all of which can lead to inconsistent findings (Chan, Shum, Toulopoulou, & Chen, 2008; Khng & Lee, 2014). Similarly, some tasks are more cognitively demanding than others, also impacting neural recruitment. Another way to understand differences between groups in brain function without having the potential confounding effects of tasks is to look at resting-state functional connectivity.

Resting-state functional connectivity serves to characterize functional brain networks comprised of regionally separate but temporally connected regions of the brain in a non-invasive way (Ferreira & Busatto, 2013; Voss et al., 2010). It allows researchers to study the brain's underlying organization and function given that it is conducted while individuals are not engaged in a task. The term "resting" does not refer to an absence of thought; instead, it refers to the brain when it is not engaged in experimental manipulation. In simple terms, resting state functional connectivity provides a tool to measure the functional integrity of component brain systems that are likely to have developed as a result of previous experiences, and for which the brain continually expends energy maintaining through recurrent synaptic activity. In this way, the functional architecture of brain systems observed during rest is thought to describe the functional components upon which evoked functional responses are built. In turn, it has been suggested that functional connectivity is an expression of the network behavior underlying higher-level cognitive function. There are multiple brain networks that are consistently found across studies using different populations and that have been associated with different cognitive functions: 1) The Executive Control Network (ECN), which has been related to maintenance of task rule and goal-directed action; 2) The FPN, associated with engagement in task-initiation and error-related activity; and 3) The DMN, which has been associated with self-generated cognition. In a similar way, studying the functional connectivity of different regions of the brain that have been proposed to be associated with language processes in bilingualism could help shed more light into the neural correlates of this linguistic phenomenon, including how (and whether) these connections differ from those of monolinguals.

Only two studies have been published to date examining resting-state functional connectivity in bilinguals (Grady et al., 2014; Luk et al., 2011). However, it is yet to be examined whether the structures that have been associated with bilingual language control (i.e. anterior cingulate cortex, prefrontal cortex, basal ganglia and inferior parietal lobule) are functionally connected at rest (forming an integrated system), or whether these regions are associated with distinct networks during the resting state. Similarly, it has not been examined how brain regions known to be associated with monolingual language processing (i.e. left ventrolateral frontal region, posterior parietal and temporal regions) are functionally connected in bilingual and monolinguals, whether these patterns of functional connectivity differ between groups, and how much the functional networks overlap with (or are distinct from) regions associated with language control in bilinguals. Furthermore, no study to date has investigated a sample of bilinguals that vary in proficiency, frequency of second language use, and age of second language use, given that published studies of resting-state functional connectivity have only reported data from lifelong bilinguals who report using both languages on a daily basis. Having a more heterogeneous sample of bilinguals can help refine our understanding of the relationship between bilingualism and functional brain health.

CHAPTER 3: SIGNIFICANCE

Bilingual and multi-language use characterizes a majority of the population worldwide (Grosjean, 1989). It is estimated that two-thirds of the world's children grow up in bilingual environments. In United States only, approximately 21% of the population aged 5 years or older speaks a language at home other than English (Census Bureau, 2011), a population that is likely to increase given the growing cultural diversity of the country. Yet, despite the statistics and the significant amount of knowledge about differences in both cognition and brain organization between bilinguals and monolinguals and the sizeable amount of bilinguals worldwide, the vast majority of the research in cognitive science is conducted only with monolingual subjects. By mostly studying monolinguals, it is possible then that the research that is available is less applicable to bilinguals, and therefore to the majority of the population worldwide. Learning more about the differences in brain function and cognitive test performance between monolingual and bilingual individuals could help inform the field about how the number of spoken languages and related variables (proficiency, age of second language acquisition) can influence research study outcomes. For instance, it raises questions about how the amount of spoken languages might impact results from intervention studies, and diagnostic procedures involving cognitive testing, among others (Thordardottir, 2010). Therefore, it is important that cognitive scientists try to better characterize the differences between monolinguals and bilinguals in both cognitive performance, as well as in brain structure and function.

Much of the research examining bilingualism has been conducted with children and young adults as participants. Less is known about differences in brain structure and function between monolingual and bilingual older adults, a population that is projected to increase significantly in the years ahead (Census Bureau, 2011). Further, only two studies to date have examined differences between monolinguals and bilinguals in functional brain systems using a resting-state functional connectivity approach. Further, to my knowledge, no study has investigated the relationship between resting-state functional connectivity and cognitive function in a group of bilinguals, or how functional connectivity between regions associated with monolingual language processing and with cognitive control differs between groups. The proposed study aims to address each of the aforementioned gaps in the literature for the first time, in a population that has received almost no attention in the bilingualism field. It also aims to help clarify the circumstances under which there might be a "bilingual advantage."

CHAPTER 4: SPECIFIC AIMS AND HYPOTHESES

The proposed study was designed to examine resting-state functional connectivity in distinct brain networks shown to be involved in language production and cognitive control in groups of older bilinguals and monolinguals, and its relationship to performance in cognitive tasks. Specifically, the proposed study aimed to investigate the following three aims.

Aim 1

The first aim of the proposed study examined resting-state functional connectivity between structures that have been associated with language and cognitive control, in older monolinguals and bilinguals.

Specifically, it aimed to determine whether there are differences between monolinguals and bilinguals in the functional connectivity of brain regions associated with cognitive and language control in bilinguals during rest (Abutalebi and Green, 2007; Figure 1), including the anterior cingulate cortex, prefrontal cortex (including the inferior frontal gyrus and middle frontal gyrus), basal ganglia (e.g. caudate) and inferior parietal lobule. This group of regions will be referred as the Bilingual Control Network (BCN). Furthermore, the study explored functional connectivity of brain regions that are considered "classical" language areas (LANG), including the left inferior frontal gyrus, superior temporal gyrus, middle temporal gyrus, and the inferior parietal gyrus (Friederici, 2011; Kelly et al., 2010). I also examined whether there were between-group differences in functional connectivity in the ECN, the FPN, and the DMN.

Expected results for aim 1. I hypothesized that functional connectivity between the regions from the BCN, the ECN, the FPN, and the DMN would be significantly different between monolinguals and bilinguals, with stronger connectivity between the regions in the bilingual group. I predicted that no differences between groups would be observed in the functional connectivity of LANG network.

Aim 2

The second aim was to investigate the association between resting-state functional connectivity of brain regions from the BCN and performance in cognitive tests, and whether this association differed between bilinguals and monolinguals. That is, the proposed study examined the relationship between functional connectivity of brain regions within the BCN, and performance on tasks of vocabulary, task switching, spatial working memory, episodic memory, processing speed, reasoning, and spatial processing in the bilingual and monolingual groups.

Expected results for aim 2. I hypothesized that average functional connectivity of brain regions within the BCN would be positively associated with performance on tests of task-switching, spatial working memory, and processing speed, given that task-related fMRI studies have shown an association between these cognitive functions and regions comprising the BCN. Further, I predicted that the network would be more strongly correlated with cognitive performance in bilinguals relative to monolinguals. Average functional connectivity of the BCN was not expected to be associated with performance on tests of vocabulary, reasoning, episodic memory, or spatial processing.

Aim 3

The third aim examined the relationship between functional connectivity of the BCN and multiple language variables including language proficiency, age of second language acquisition, degree of second language exposure, and frequency of second language use.

Expected results for aim 3. I hypothesized that there would be a relationship between language proficiency, age of second language acquisition, degree of second language exposure, and frequency of second language use, and the average functional connectivity of the BCN. Specifically, I predicted that higher proficiency would be associated with stronger functional connectivity; earlier age of second language acquisition would be related to stronger functional connectivity; more exposure would be associated with stronger functional connectivity; and higher frequency of second language use would be associated with stronger functional connectivity. Language proficiency was expected to be the most strongly associated with the average functional connectivity of brain regions that comprise the BCN compared to the other variables.

CHAPTER 5: METHODS AND MATERIALS

Participants

The current study analyzed the *baseline* data obtained at the Lifelong Brain and Cognition Laboratory at the University of Illinois in Urbana-Champaign (UIUC), Illinois. Via a cross-institute collaboration, the Health, Brain & Cognition Lab at the University of Iowa, has access to data collected during long-term intervention programs. These intervention programs aim to further characterize the behavioral and brain changes associated with participating in either of the following two interventions: 1) Acting intervention (ACT); and 2) Fit and Active Senior Trial (FAST). These datasets consist of individuals from 60 to 85 years of age recruited from the community, who have completed a demographics questionnaire, a battery of MRI scans, as well as an extensive battery of neuropsychological tests that measure different domains of cognitive functioning.

As an attempt to only include healthy older individuals, the following exclusion criteria were used to select participants for the ACT and FAST studies: 1) cognitive impairment as determined by a score of < 23 on the modified MMSE (MMSE-2); 2) evidence of neurological disease, dementia, or psychiatric disorder within the past two years; 3) alcohol or drug abuse within the past two years; 4) cardiovascular disease or history of heart problems; 5) terminal illness; 6) self-reported severe vision problems; 7) inability to hear dialogue spoken by other subjects; 8) use of recreational drugs within the past six months; 9) has participated in any sort of exercise intervention in the last two years; or 10) history of central nervous system disease or brain injury. Subjects recruited for the FAST intervention were also excluded if they self-reported regular physical activity of more than two times per week in the last six months (prior to recruitment). Given that the study protocol included an MRI scan, subjects who self-reported claustrophobia or had implanted devices (e.g. pacemakers, cochlear implants, aneurysm clips, etc.) were excluded from the study. In addition, subjects were screened in a mock MRI system to ensure that they felt comfortable spending time in the magnet. Those who did not feel comfortable in the magnet and were not willing to proceed with the scan were excluded from the study.

The Language and Social Background Questionnaire (LSBQ; see below for more details) was sent to 249 individuals from the FAST and ACT cohorts via mail or email, 104 of which completed and returned the questionnaire to the researcher at the University of Iowa. Those who responded did not differ from responders in age, sex, or years of education. It is possible that those who did not respond had no desire to be involved in research, questioned the legitimacy of the emails (thought it was a scam), were busy, or were not satisfied with the compensation (a chance to win one of two Amazon.com gift cards). Since there were no demographical differences between those who responded and those who did not, responders can be considered to be a representative sample of the pool of individuals eligible for the study.

Participants were assigned to the bilingual or monolingual group based on information acquired from the LSBQ. Specifically, participants were assigned to a group based on their answer to the question: Overall, how would you describe your level of bilingualism/multilingualism? There were five possible answers, 1, 25, 50, 75 and 100, where 1 represented completely monolingual and 100 completely bilingual/multilingual. Participants who chose '1' were classified as monolinguals, meaning that they only spoke one language. Those who self-identified as monolinguals also denied having been significantly exposed to a second language. Participants were assigned to the bilingual group if they identified a '50' or higher. These individuals reported being able to communicate in at least two languages.

Out of the 104 individuals who returned the LSBQ, 10 were assigned to the bilingual group (M_{age} = 65.3, SD = 5.08; $M_{education}$ = 17.5, SD = 5.27; M_{MMSE} = 28.7, SD = 1.7). Each of these individuals were then manually matched (by the principal investigator) for sex, age and education to a monolingual (n = 10; M_{age} = 64.5, SD = 3.50; $M_{education}$ = 16.3, SD = 2.91; M_{MMSE} = 29.2, SD = .92). No pair differed in age or years of education by more than two years. Six of the 10 individuals in the bilingual group identified English as their second language, and German, Chinese, Urdu, or French as their first language. The other four participants identified English as their first language, and French, Italian, German or Spanish as second language. Age of second language acquisition in the bilingual group ranged from birth to age 20 (M = 9.6 years, SD = 6.59), with four individuals having acquired their second language before 7 years of age, five between the ages of 12 and 15, and one at the age of 20. Seven individuals in the bilingual group reported having lived in a country outside of the United States during their lifetime, and six of these individuals were born outside the United States. Monolinguals were all born in the United States, and identified the United States as their only country of residence during their lifetime.

Procedure

As presented in Table 1, all subjects completed the studies' protocol on four separate days. Overall, each subject completed a demographic questionnaire, the MMSE, a mock MRI procedure, a battery of neuropsychological tests that lasted approximately four hours (see "Neuropsychological Tests" for more details) and an MRI scan.

Table 1. Study's Protocol

Day	Protocol
Day 1	Sign informed consent; Demographic assessments; MMSE; mock MRI procedure
Day 2 & 3	Battery of neuropsychological tests (approximately 2 hours each session)
Day 4	MRI scan
Follow-up	Completion of the Language and Social Background Questionnaire

This study was approved by the Institutional Review Board at the University of Iowa and the University of Illinois in Urbana-Champaign.

Assessment of Bilingualism

At present, there is no standard measure of bilingualism. However, recent studies have used the LSBQ to collect data that can better characterize bilinguals' history and use of languages (Luk & Bialystok, 2013). The LSBQ was originally developed by the Cognition and Development Lab at York University in Ontario for Canadians, in order to obtain a subjective measure of social activities and language history. For the purposes of this study, I only administered the language section of the questionnaire (see Appendix A). Previous research has reported a correlation between English proficiency (as a second language) as measured by vocabulary tests, and self-rated proficiency in the LSBQ (Luk & Bialystok, 2013), suggesting that self-reported language proficiency is often a reliable estimate of "actual" language proficiency.

The language section of the LSBQ elicits information about each subject's occupation, use of psychoactive medications, immigration history, and education, in addition to language use. Subjects who self-identified as bilingual or who reported being exposed to a second language were asked to state how many and what languages they speak, at what age they learned each language, how often they use each language, how competent they consider they are in each language, and in which contexts they speak each language. Proficiency was measured by averaging scores from the question, “Relative to a highly proficient speaker’s performance, rate your proficiency level on a scale of 0 – 100 for the following activities conducted in ANOTHER language (“second language,” in order of proficiency),” where 100 represented the highest level of proficiency. In turn, frequency of second language use was calculated by assigning a value (0, 25, 50, 75, or 100) to each of the possible answers for the question, “Of the time you spend engaged in each of these activities, how much of that time is spent using this language (second language)?” These values were then averaged to create a score that represents the frequency of second-language use. Higher values represent higher frequency of second language use. Furthermore, answers to the question, “Overall, how would you describe your level of bilingualism/multilingualism,” were used as a measure of the level of exposure to a second language.

The LSBQ was either mailed or emailed to participants. The online questionnaire was created through REDCap (Research Electronic Data Capture) hosted at the University of Iowa (Harris, Taylor, Thielke, Payne, Gonzalez, Conde, 2009). REDCap is a secure, web-based application designed to support data capture for research studies. The LSBQ was only administered in English since it was the common language spoken by all participants.

Neuropsychological Tests

All subjects completed a battery of neuropsychological tests in English on two days. Most tests were chosen from the Virginia Cognitive Aging Project (Salthouse et al., 2003, 2005, 2013). Two other tests that have been frequently used in the literature were also added to the battery. Individuals who participated in the ACT intervention completed a test battery that is different from the one completed by individuals in the FAST study. Table 2 lists and describes the tests that were administered to each group.

Table 2. Neuropsychological Tests by Cognitive Domain

Tests	Description
Episodic Memory	
Logical memory stories A and B	Number of units of information recalled across two stories.
Paired associations	Amount of response terms recalled when presented with a stimulus term.
Free word recall	Number of words recalled in 4 trials of a word list.
Working Memory	
*Spatial working memory**	Remember the location of previously presented black dots as quickly and accurately as possible.
Processing Speed	
*Digit symbol substitution**	Match symbols with their corresponding numerical digit.
Pattern comparison	Comparison of pairs of line patterns
Letter comparison	Comparison of pairs of letter patterns
Task Switching	
*Task switching test**	Flexibly shift visuo-spatial attention between two different features: high/low or odd/even.
Vocabulary	
Word vocabulary	Define different words.
Picture vocabulary	Name the object in the picture.
Synonyms	Indicate the best synonym of the target word.
Antonyms	Indicate the best antonym of the target word.
Reasoning	
Matrix reasoning	Indicate the response that completes the matrix or series.

Table 2—continued

Shipley abstraction test	Indicate the words or numbers that best completes the sequence.
Letter sets	Identify which five sets of letters in unrelated to the others.
Spatial Processing	
Spatial relations	Identify the correspondence between a 3-D figure and alternative 2-D figures.
Paper folding	Identify the pattern of holes that would result from a sequence of folds and a punch through folded paper.
Form boards	Indicate what combinations of shapes are needed to fill a larger shape.

Note. Individuals in the FAST group completed all neuropsychological tests described in Table 1. However, individuals in the ACT group only completed those tests followed by an asterisk (*). Therefore, those tests with an asterisk (*) are the only tests that were completed by both groups.

As can be observed in Table 2, the tests that were administered can be categorized in one of the following six domains of cognitive functioning: memory, processing speed, task switching, vocabulary, reasoning, and spatial processing. Each of these tests has been shown to be strongly associated to the cognitive domain that it intends to measure (Salthouse et al., 2003, 2005, 2008, 2013). Each of the tests presented in Table 2 have been validated with adults of all age groups, including older adults (Salthouse et al., 2003, 2005, 2008, 2013). Each test has also been shown to be sensitive to age-related cognitive decline (Salthouse & Ferrer-Caja, 2008).

The task-switching test required participants to switch between judging whether a number was low or high, or was odd or even (Baniqued et al., 2013). Each number was presented individually for 1500 ms against a pink or blue background at the center of the screen. The same number did not appear twice in succession. If the background was blue, participants were instructed to report as quickly as possible whether the letter was high or low. Instead, if the background was pink, the participants were instructed to report whether the number was odd or even. This task primarily measures switch cost during dual-task blocks, which are calculated by subtracting the average reaction time for repeat trials from the average reaction time for switch trials for each individual. It also measures global switch cost, which is calculated by subtracting average reaction time during the single-task block from average reaction time in the mixed or switching task blocks. Finally, accuracy measures of both switch costs will be taken into consideration, as well as composite scores of both accuracy and reaction time. This task is similar to that of Kramer, Hahn, and Gopher (1999). This version of the task was administered using E-prime software (Psychology Software Tools, www.pstnet.com).

On the spatial working memory test, participants viewed an arrangement of two, three or four dots presented on the screen. Set sizes two and three were presented for 500 ms and set size four was presented for 1000 ms on each trial. They were then instructed to remember this array. Following a 3000 ms delay a red probe dot was presented for 2000 ms, and participants were asked to indicate whether the location of the red probe dot matched the location of one of the black dots previously shown for that trial. There were 40 trials of each set size (20 match and 20 non-match) presented in a random order for each participant. The primary measure of this task is the average accuracy from all set size conditions (Baniqued et al., 2013).

Resting State fMRI

MRI acquisition. All images were acquired during a single session on a 3T Siemens Trio Tim system with 45 mT/m gradients and 200 T/m/sec slew rates (Siemens, Erlangen, Germany). T2*-weighted resting state images were acquired with a fast echo-planar imaging (EPI) sequence with blood oxygenation level dependent (BOLD) contrast (6min, TR = 2s, TE = 25ms, flip angle = 80 degrees, 3.4 x 3.4 mm^2 in-plane resolution, 35 4mm-thick slices acquired in ascending order, Grappa acceleration factor = 2, 64 × 64 matrix), while the participants were asked to lay still with their eyes closed. Additionally, dual-echo gradient field maps were acquired to account for geometric distortions caused by magnetic field inhomogeneity (Jezzard and Balaban, 1995). The gradient field maps were collected as 35, 4 mm-thick slices, 3.4 x 3.4 mm^2 in-plane resolution, TR = 700ms, TE = 10/12.46 ms, and flip angle = 35 degrees. Resting state and field-map images were obtained parallel to the anterior-posterior commissure plane with no inter-slice gap.

High-resolution structural MR scans were acquired using a 3D MPRAGE T1-weighted sequence (TR = 1900 ms; TE = 2.32 ms; TI: 900 ms; flip angle = 9°; matrix = 256 × 256; FOV = 230 mm; 192 slices; resolution = 0.9 × 0.9 × 0.9 mm; GRAPPA acceleration factor 2) and used as an intermediate step in registration of functional images to standard MNI space.

Data processing. All imaging processing and analyses were carried out with an in-house script library containing tools from FSL 5.0.4 (Functional Magnetic Resonance Imaging of the Brain's Software Library, http://www.fmrib.ox.ac.uk/fsl), AFNI (http://afni.nimh.nih.gov/afni), FreeSurfer (http://surfer.nmr.mgh.harvard.edu), and MATLAB (The MathWorks, Natick, MA, USA). First, raw DICOM images were converted to a NIfTI using FreeSurfer's *mri_convert* tool and then reoriented to RPI orientation with FSL's *fslorient*. Next, voxels (basic unit of volume in an fMRI image) containing non-brain tissue were stripped from the T1 structural images using FSL's BET (Brain Extraction Technique) algorithm (Smith, 2002). The skull-stripped anatomical images were then manually inspected and corrected for errors resulting from the BET algorithm. A 6 degree-of-freedom rigid-body head motion correction was applied to the resting-state fMRI EPI data using AFNI's *3dvolreg* function, which produced six parameters of head motion (root-mean-squares of translational and rotational movement: X, Y, Z, pitch, roll, and yaw directions) for subsequent regression of spurious variance. Gradient field map images were first skull-stripped with BET and then processed for subsequent EPI unwarping using FSL's *fsl_prepare_fieldmap.* The processed field maps were then applied to the motion corrected EPIs using FSL's *epi_reg* for simultaneous EPI distortion correction and registration to the T1. The resting-state fMRI data were further refined by removing non-brain tissue with BET, spatially smoothing using a 6.0 mm three-dimensional Gaussian kernel of full-width at half-maximum.

Using AFNI's *3dBandpass* the pre-processed time series data were then temporally filtered ensuring that fMRI data fell within the frequency band of $.008 < f < 0.08$ Hz, which reduces unwanted noise such as high frequency physiological signals (e.g., cardiac pulse) and low frequency scanner drift. The frequency band was chosen to best represent the spontaneous, low frequency fluctuation of the BOLD fMRI signal in the brain (Leopold et al., 2003; Salvador et al., 2005). Following temporal filtering, the mean time series was then extracted from three sources of non-neuronal variance: white matter signal from a region in a deep white matter structure, cerebrospinal fluid signal from a region in the lateral ventricle, and the global signal derived from a whole-brain mask. These nuisance signals were used as covariates to control for physiological artifacts in the brain that may confound functional connectivity measures. Together with the three nuisance signals, the six head motion parameters obtained from the rigid body motion correction were bandpassed with the same temporal filter applied to the fMRI data and included as nuisance regressors (Hallquist et al., 2013). Altogether, the 9 bandpassed nuisance regressors (white matter, CSF, global, and motion parameters) were then entered into a multiple regression (using FSL's FEAT tool) as independent variables predicting the observed fMRI data as a dependent variable. Finally, using the residual time series data from the nuisance regression, any volumes containing excessive head motion were "scrubbed" following a procedure described by Power and colleagues (Power et al., 2012).

Regions of interest. Matlab was used to perform functional connectivity analysis based on seeds, also known as regions of interest (ROIs), in regions comprising the BCN, and independently, in LANG, the FPN, the ECN, and the DMN. I constructed 14mm diameter spheres for each ROI in the BCN and LANG based on coordinates from previously published data (see Figure 2; Di Martino et al., 2008; Kelly et al., 2009; Hurley, Bonakdarpour, Wang, & Mesulam, 2015; Luk et al., 2011; Monti et al., 2014; Tomasi & Volkow, 2012; Tu et al., 2015).

Table 3. ROIs in Each Network

Region	*X*	*Y*	*Z*
Bilingual Control Network			
L anterior cingulate cortex	-5	14	42
L caudate	-13	15	9
L putamen	-28	1	3
L inferior frontal gyrus	-38	31	-14
L medial frontal gyrus (BA9)	-44	13	29
L middle frontal gyrus (BA46)	-48	23	23
L inferior parietal lobule	-54	-54	20
Classical Language Network			
L inferior frontal gyrus	-38	31	-14
L superior temporal gyrus	-51	-51	30
L middle temporal gyrus	-66	-38	-4
L inferior pariental lobule	-54	-54	20
Default Mode Network			
L medial prefrontal cortex	-6	62	-4
L lateral parietal cortex	-46	-64	32
L posterior cingulate cortex	-6	-54	32
L superior frontal gyrus	-24	24	42
R posterior cingulate cortex	6	-60	32
R medial prefrontal cortex	6	62	-4
R superior frontal gyrus	22	28	44

Table 3—continued

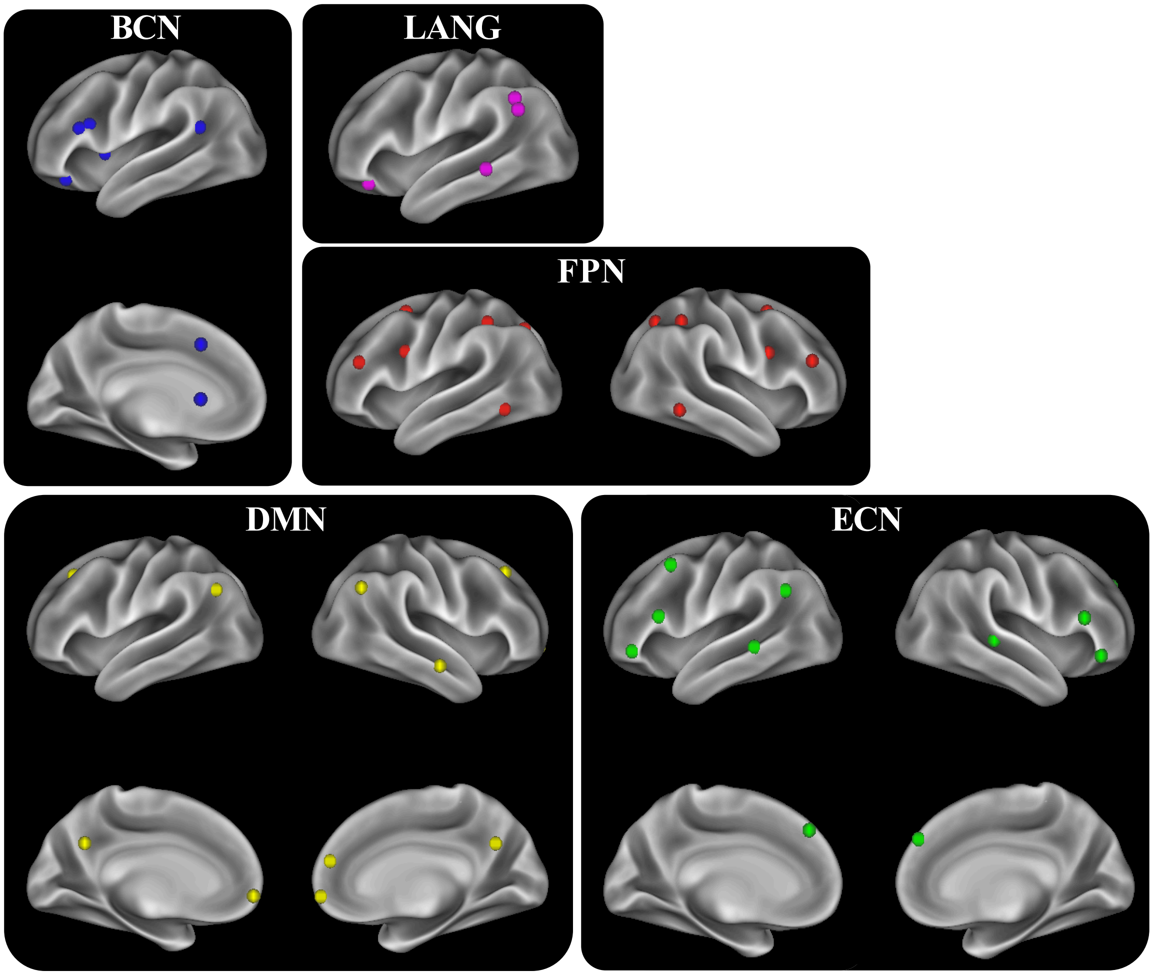
R lateral parietal cortex	50	-62	34
R dorsalmedial prefrontal cortex	6	50	20
R middle temporal gyrus	62	-10	-16
Frontoparietal Network			
L posterior intraparietal sulcus	-28	-68	48
L anterior intraparietal sulcus	-40	-46	46
L middle temporal gyrus	-52	-60	-8
L frontal eye field	-26	2	54
L motor cortex	-48	6	30
L middle frontal gyrus	-46	34	22
R posterior intraparietal sulcus	30	-66	48
R anterior intraparietal sulcus	38	-46	46
R middle temporal gyrus	58	-52	-10
R frontal eye field	28	4	54
R motor cortex	48	10	28
R middle frontal gyrus	46	34	22
Frontal Executive Network			
L superior frontal gyrus	-6	42	44
L middle frontal gyrus	-44	12	48
L inferior frontal gyrus	-52	20	20
L anterolateral prefrontal cortex	-46	42	-6
L middle temporal gyrus	-58	-38	0
L angular gyrus	-50	-60	32
R superior frontal gyrus	6	50	38
R anterolateral prefrontal cortex	48	36	-10
R inferior frontal gyrus	54	26	18
R superior temporal gyrus	52	-32	0

Note. R = right; L = left; *X* = right/left; *Y* = anterior/posterior; *Z* = superior/inferior; BA = Brodmann Area (regions of the cerebral cortex defined by its cytoarchitecture). X, Y, Z coordinates are specified for standard MNI (mm) space.

ROIs for the DMN, FPN, and the ECN were derived from a group-level ICA conducted by researchers in the Health, Brain & Cognition Lab at the University of Iowa. Group-level ICA was applied to the pre-processed resting-state fMRI data using FSL's MELODIC with automatic dimensionality estimation. This data-driven analysis method decomposed the resting-state fMRI data into 13 independent spatiotemporal components (IC) common across 236 older adults (from FAST) and 49 younger adults. I identified 3 ICs as cognitively-relevant resting state networks that are established in the literature: 1) DMN, 2) FPN, and 3) ECN. For each of these 3 networks identified by ICA, I constructed 14-mm diameter spheres centered on the peak coordinates within the IC (listed in Table 3; illustrated in Figure 2). Together these ROIs served as a set of a priori seeds for the analysis of pairwise correlations within and across ROIs from networks of interest.

All target ROIs were first created in standard MNI (2 mm) space and then registered to native (functional) space through a multi-stage procedure: First, individual EPIs were registered to their high-resolution structural T1 space using the boundary-based registration (BBR) algorithm (Greve & Fischl, 2009). Registration of the EPIs from individual high-resolution structural space to standard MNI space was then accomplished by FNIRT nonlinear registration with the default 10 mm warp resolution (Andersson, Jenkinson, & Smith, 2007a, b). The two resulting transformations were concatenated and then applied to the original functional image to create a functional image in standard MNI space; a reverse transform was used to register the seeds from standard MNI space to each participant's native functional space.

Figure 2. Regions of Interest



Note. Each 14mm sphere represents the approximate location of each ROI in the corresponding network.

Data Analysis

Neuropsychological tests. Statistical Package for Social Science (SPSS) was used to analyze results from neuropsychological tests. Test scores were transformed into standardized scores (z-scores). I then averaged the z scores of tests that belonged to the same cognitive domain (see Table 2) in order to create a composite score that represents each cognitive domain. Tests within a cognitive domain are highly correlated with each other (and not with tests from other cognitive functions) and have been shown to be a valid measure of that particular cognitive domain (Salthouse et al., 2003, 2005, 2013). Accuracy scores and reaction times were computed for both the task-switching and the spatial working memory tests. Two-tailed independent samples *t* tests were computed to compare the scores for each cognitive domain between the monolingual and bilingual groups. Effect sizes were calculated using Cohen's *d*. Confidence intervals of the difference between groups are also reported.

Resting-state functional connectivity. The first hypothesis for *Aim 1* was that bilinguals would have stronger functional connectivity between regions within the BCN, ECN, FPN, and DMN compared to monolinguals, and that no between-group differences would be observed for LANG. I used two approaches to test this hypothesis: 1) a targeted pairwise ROI analysis (data-driven); and 2) a group analysis of voxel-wise seed maps (exploratory).

Initially, for each individual, the average normalized timeseries of the fluctuating BOLD signal in each set of voxels within an ROI was extracted by Matlab and used to calculate an average timeseries for each ROI. For within-network ROI-to-ROI comparisons, the correlation values for specified ROI pairs within a network were computed for each individual. These Pearson's correlation *r* values were then transformed to z-scores using the Fisher *r* to *z* transformation. To obtain a summary of the overall functional connectivity within proposed networks of interest, for each individual I averaged the functional connectivity estimates for all ROI pairs in a given network. These average network Fisher's *z* scores represent the functional connectivity between the ROI's of a specified network of interest. Subsequently, two-tailed independent samples *t* tests were calculated to compare average *z* scores of each network between the monolingual and bilingual groups. Effect sizes were calculated using Cohen's *d*. Confidence intervals of the difference between groups are reported.

I also conducted an exploratory analysis to further examine group-differences in the functional connectivity of the BCN, the LANG, the ECN, the FPN, and the DMN seeds with other brain regions. For this analysis, I used seeds that were composed of the anchor regions (ROIs most highly correlated with other ROIs within a given network) for each network (i.e. multi-seeds). When each of these multi-seeds is analyzed against the timeseries from every other voxel in the brain, they are often strongly functionally connected to other regions within the intended network. These seeds were named LANG multi-seed, DMN multi-seed, ECN multi-seed, and FPN multi-seed. Given that the left middle frontal gyrus was the region most strongly correlated with the other ROIs within the BCN, I only used the left middle frontal gyrus as a seed for the BCN.

Data from each chosen seed (or multi-seed) was analyzed against the timeseries from every voxel in the brain to produce a statistical map of regions that are highly correlated with the seed (based on Pearson's correlation which was then transformed to a Fisher's *z*). Individual-subject level correlation maps were registered to standard MNI (2 mm) space using transformation matrices from the multi-stage registration procedure described previously. Once in standard space, the seed maps from individual subjects were concatenated to form a 4D image file (subject as the fourth dimension) and this 4D image was input to a between-subjects ordinary least-squares (OLS) regression using FSL's *flameo* (Beckmann, Jenkinson,, & Smith, 2003), with group entered as a factor. Multiple comparisons for the resulting group-level statistical maps were controlled by thresholding group contrast maps at $Z > 2.33$, with cluster correction of $p < 0.05$ (Worsley, Evans, Marrett, & Neelin, 1992). This resulted in thresholded Z-statistic maps representing significant differences between monolinguals and bilinguals.

In order to address *Aim 2* and test whether functional connectivity in the BCN was positively correlated with performance on tests of task-switching, spatial working memory, and processing speed, but not with the other cognitive functions (e.g. reasoning, episodic memory), I conducted a two-tailed correlation analysis. Correlation coefficients were calculated for each group to evaluate the relationship between average *z* scores for ROIs from the BCN (as determined in Aim 1) and performance on cognitive tests (e.g. composite scores of episodic memory, vocabulary, reasoning, processing speed, spatial processing), the accuracy and reaction time score for the spatial working memory task, and accuracy and reaction time scores for the task-switching test.

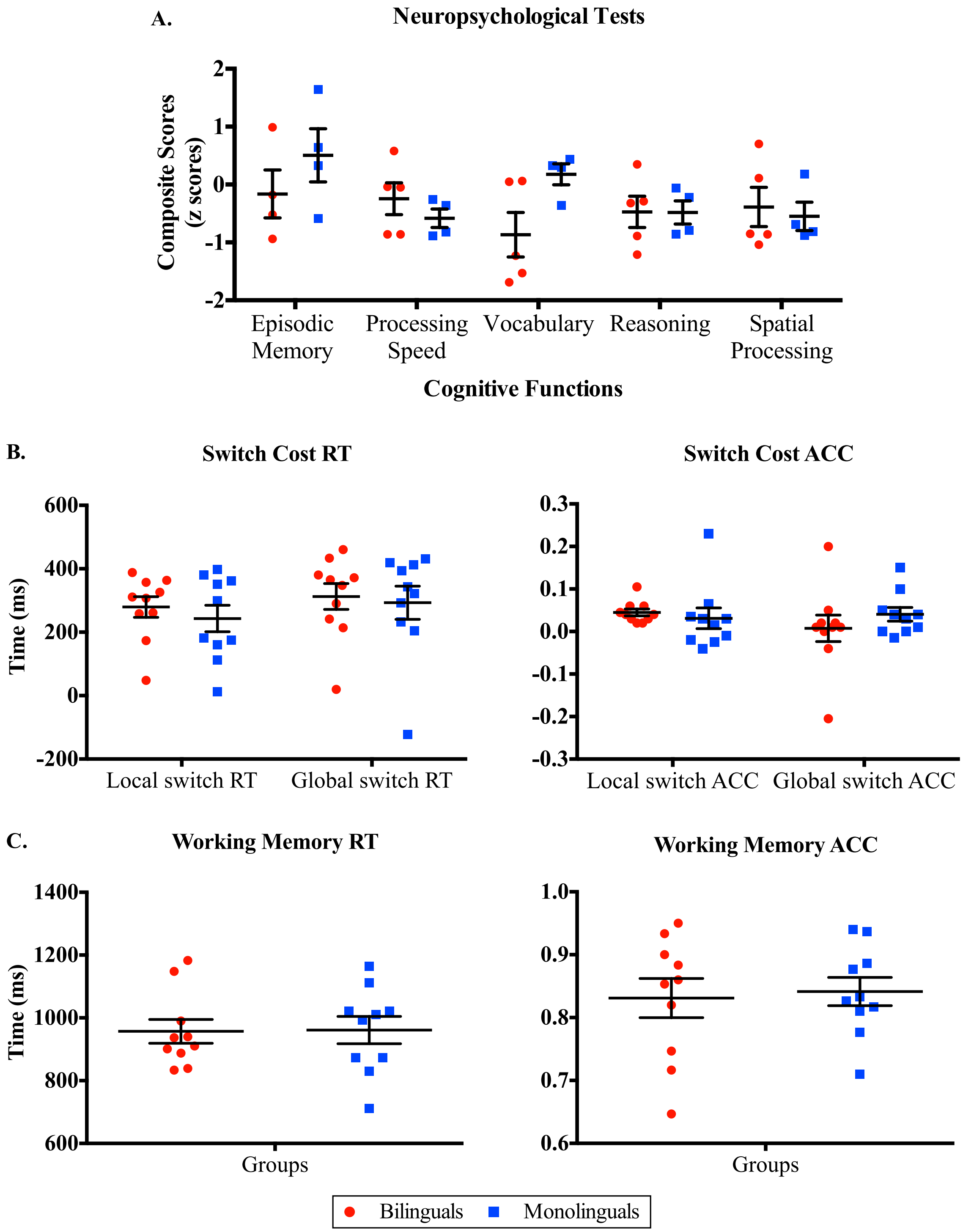
Finally, the hypothesis for *Aim 3* was that different language variables (e.g. proficiency, age of second language acquisition) would significantly predict functional connectivity in the BCN. This hypothesis was tested by conducting a regression analysis with average *z* estimates for ROI pairs from the BCN (as determined in Aim 1) as the dependent variable, and language proficiency, age of second language acquisition, degree of exposure to a second language, and frequency of second language use as independent variables.

CHAPTER 6: RESULTS

Performance in Cognitive Tests

I first examined whether bilinguals and monolinguals differed in their performance on cognitive tests (see Figure 3). Given that participants from the ACT and FAST studies did not complete the same battery of neuropsychological tests (see Table 2), some of the composite scores are not available for a subgroup of the sample (see Table 4 for sample size per cognitive domain). Episodic memory ($t(10) = 1.33$, $p = .21$, $d = 0.79$, 95% CI [-0.41, 1.62]), processing speed ($t(11) = -0.39$, $p = .70$, $d = 0.22$, 95% CI [-0.80, 0.56]), spatial processing ($t(11) = 0.89$, $p = .39$, $d = 0.50$, 95% CI [-0.41, 0.97]), and reasoning composite ($t(11) = 0.27$, $p = .79$, $d = 0.15$, 95% CI [-0.71, 0.91]) scores did not significantly differ between bilinguals and monolinguals. Similarly, spatial working memory accuracy values ($t(18) = 0.19$, $p = .85$, $d = 0.09$, 95% CI [-0.08, 0.09]) and reaction time ($t(18) = -0.07$, $p = .95$, $d = 0.03$, 95% CI [-117, 125]), local switch cost reaction time ($t(18) = -0.69$, $p = .50$, $d = 0.31$, 95% CI [52.8, -147]), local switch cost accuracy ($t(18) = -0.54$, $p = .60$, $d = 0.24$, 95% CI [-0.07, 0.04]), global switch cost reaction time ($t(18) = -0.29$, $p = .77$, $d = 0.13$, 95% CI [66.4, -159]), and global switch cost accuracy ($t(18) = 0.93$, $p = .36$, $d = 0.42$, 95% CI [-0.04, 0.11]) values did not significantly differ between groups. Composite scores for vocabulary almost reached statistical significance ($t(5) = 2.26$, $p = .07$, $d = 1.38$, 95% CI [-0.11, 1.98]), with monolinguals having a higher score compared to bilinguals (see Figure 3).

Figure 3. Performance in Cognitive Tests



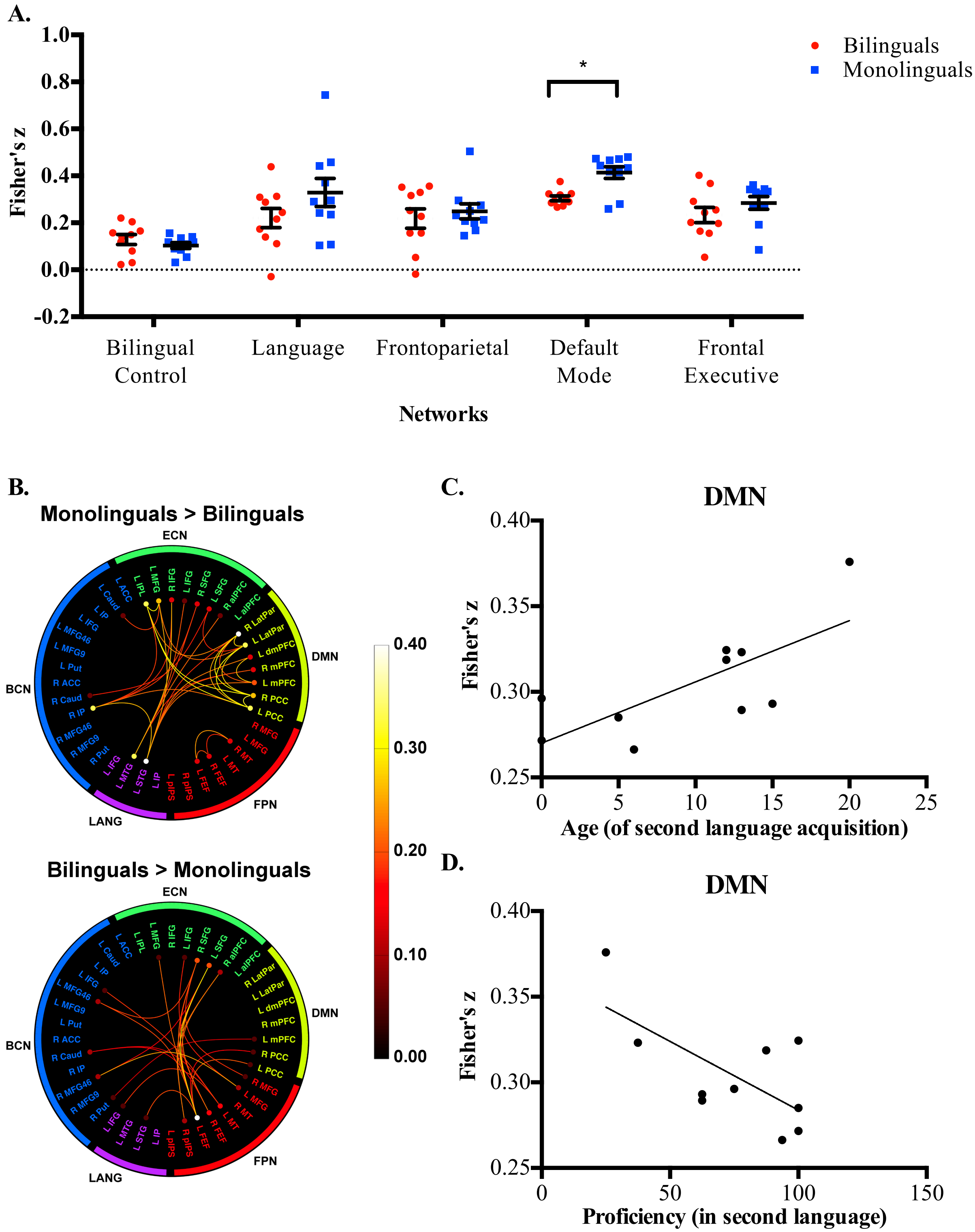
Note. RT = Reaction Time; ACC = Accuracy. Bilinguals and monolinguals did not significantly differ in their performance on cognitive tests. A) Represents group averages and individual composite scores for different domains of cognition. B) Represents group averages and individual values for local and global switch cost ACC (where higher is worse), and local and global switch cost RT (where higher is worse). C) Represents group averages and individual values for RT (where higher is worse) and ACC (where lower is worse) in the working memory task. Error bars represent standard error of the mean.

Resting-state Functional Connectivity Based on ROI-to-ROI Pairs

To address *Aim 1*, differences in resting-state functional connectivity between bilinguals and monolinguals were first explored using a data-driven approach in which the average pair-wise correlations (converted to Fisher's z) among all ROIs within a given network were compared between groups. As shown in Figure 4A, there were no significant between-group differences in the resting-state functional connectivity of the BCN ($t(18) = -1.03$, $p = .32$, $d = 0.46$, 95% CI [-0.08, 0.03]), the LANG ($t(18) = 1.50$, $p = .15$, $d = 0.67$, 95% CI [-0.04, 0.26]), the FPN ($t(18) = .59$, $p = .56$, $d = 0.27$, 95% CI [-0.08, 0.14]), or the ECN ($t(18) = 1.21$, $p = .54$, $d = 0.27$, 95% CI [-0.04, 0.14]). However, resting-state functional connectivity of the DMN was significantly different between groups, with monolinguals exhibiting stronger connectivity between ROIs within the DMN compared to bilinguals ($t(18) = 4.03$, $p = .001$, $d = 1.80$, 95% CI [0.05, 0.17]).

Circular graphs were constructed (Figure 4B) to further illustrate group-related functional connectivity differences between all possible ROI pairs from both within and between networks (all $p < .05$, two-tailed). Of note, I did not correct for multiple comparisons at the level of individual ROI pairs because the goal of this analysis was to evaluate whether there was a systematic pattern of network structure in these groups. Therefore, this approach emphasizes assessing *qualitative* patterns across multiple pairs of ROIs instead of focusing on results from specific pairs. These figures further illustrate that ROIs within the DMN are more strongly functionally connected in the monolingual group compared to the bilingual group. They also show a qualitative difference between groups in the functional connectivity of structures within the FPN and ECN, with bilinguals illustrating stronger functional connectivity between these networks, both of which have been associated with executive control. Furthermore, consistent with Figure 4A, ROIs within the BCN seem to be similarly functionally connected with one another in both groups.

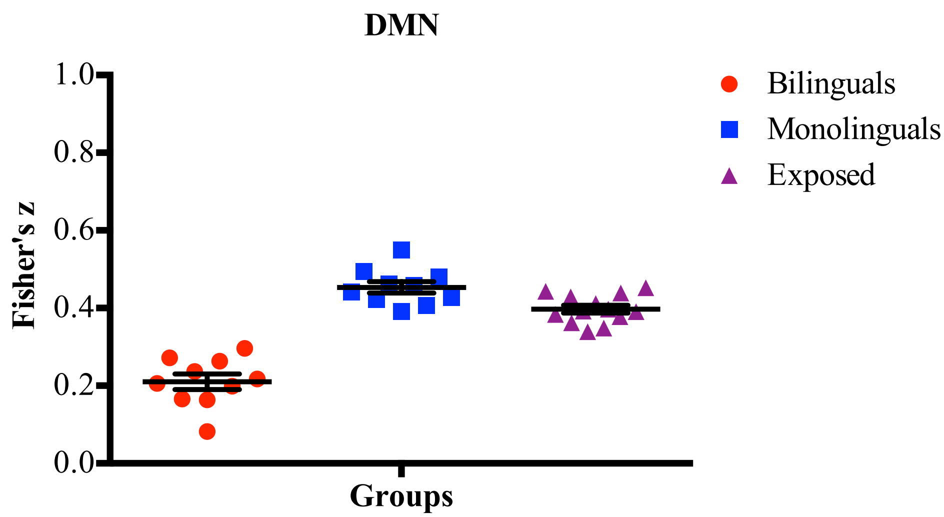
Figure 4. Resting-state Functional Connectivity of Multiple Networks



Note. Graphs represent functional connectivity of different brain regions within a network. A) Graph illustrated individual and group average Fisher's z scores for each network. There was a significant difference between monolinguals and bilinguals in the DMN; $p = .001$. Error bars represent standard error of the mean. B) Circular graphs present group-related functional connectivity differences between all possible ROI pairs from both within and across networks. Lighter colors represent stronger connectivity for one group compared to the other. Circular graph in the superior part represents greater functional connectivity in the monolingual group compared to the bilingual groups, whereas the one in the inferior part represents greater functional connectivity in the bilingual group compared to the monolingual group. C) Scatterplot represents the association between age of second language acquisition and functional connectivity in the DMN for bilinguals. D) Scatterplot represents the association between proficiency in the second language and functional connectivity in the DMN for bilinguals.

In order to further characterize our findings, I conducted a Pearson's r correlation that tested whether proficiency in the second language, frequency of second language use, or age of second language acquisition significantly correlated with functional connectivity in the DMN in the bilingual group. Interestingly, age of second language acquisition was positively correlated with functional connectivity in the DMN (Figure 4C; $r(9) = .73$, $p = .02$), while second-language proficiency was negatively correlated with functional connectivity in the DMN (see Figure 4D; $r(9) = .73$, $p = .02$). In addition, I explored whether functional connectivity in the DMN significantly differed between individuals who had been significantly exposed to a second language to the extent where they can understand but not speak the second language, bilinguals, and monolinguals. Figure 5 illustrates how individuals who had been significantly exposed to a second language did not differ from monolinguals in DMN functional connectivity, yet significantly differed from bilinguals ($t(9) = 13.26$, $p = < .0001$, $d = 0.67$, 95% CI [0.16, 0.23]). Taken together, results show that monolinguals have stronger functional connectivity in the DMN on average compared to bilinguals, and that within the bilingual group, the more "monolingual-like" someone is the more their functional connectivity resembles that of the monolingual group.

Figure 5. Degree of Second Language Exposure and DMN

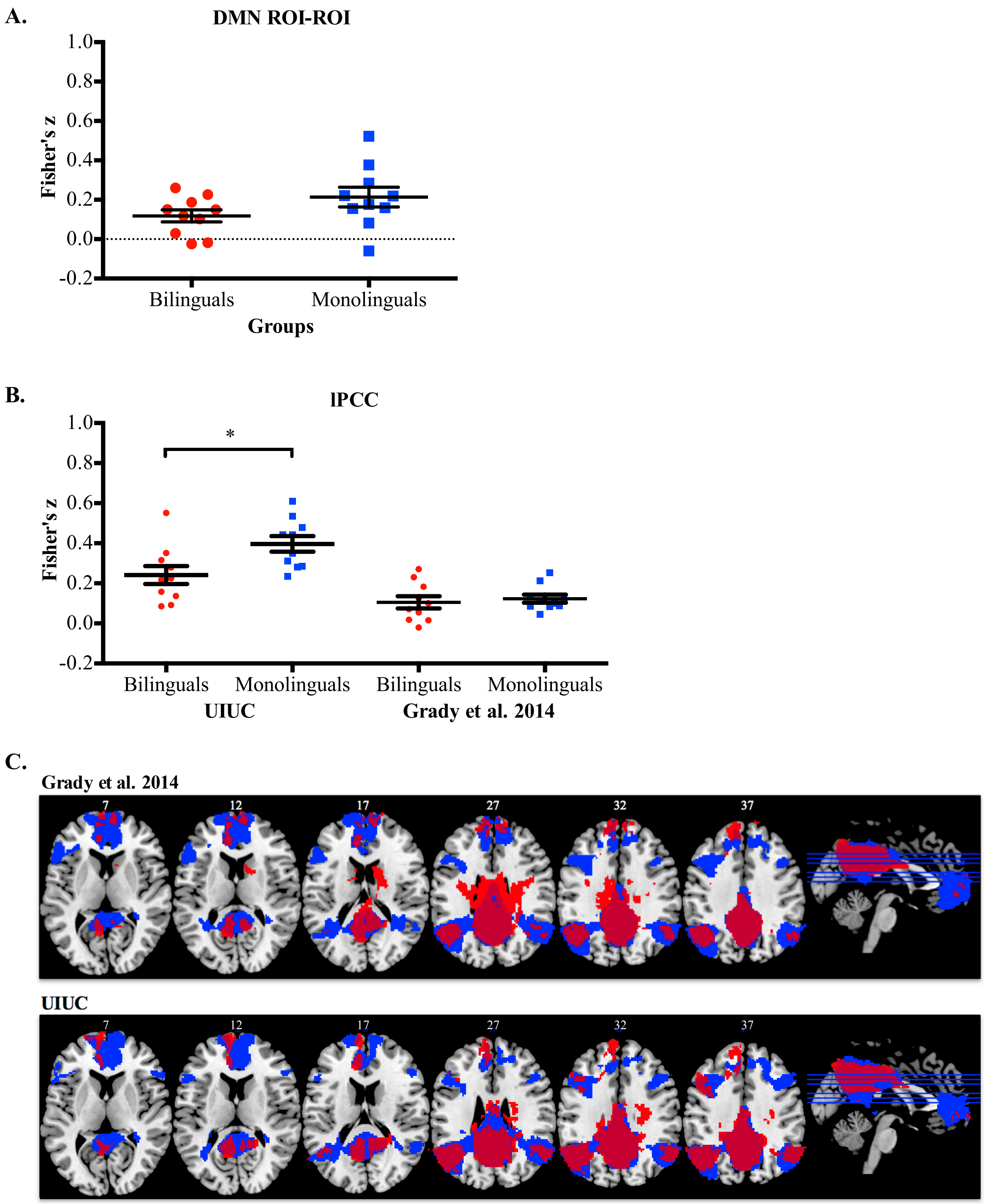


Note. Graph depicts differences in functional connectivity of the DMN between groups that have been exposed to a second language to different degrees. There were not significant differences between monolinguals and those who had been exposed to a second language ($p > .05$). However, there were significant differences between bilinguals and individuals in the exposed group ($p < .0001$). Error bars represent standard error of the mean.

Replicating Findings from Grady et al. 2014

Given that the results seemed to contradict findings reported by Grady et al. (2014), I endeavored to replicate their findings, in part to assess whether our findings were an artifact of the chosen seeds. Grady et al. (2014) examined differences between resting-state functional connectivity in the DMN between lifelong bilinguals and monolinguals by comparing the functional connectivity of the left posterior cingulate cortex (lPCC; which has been previously identified as an anchor region for this network) with other regions in the brain. I attempted to replicate Grady et al. (2014) findings by: 1) creating 14mm diameter spheres using coordinates reported by Grady et al. (2014) for ROIs within the DMN; 2) averaging ROI-to-ROI correlations (where Pearson's correlation *r* values were transformed to Fisher's *z*) within the DMN and comparing group averages using a two-tailed independent samples *t* test; 3) determining the average correlation of the lPCC with the DMN by correlating the average normalized timeseries of the lPCC (using seeds from UIUC and from Grady et al. independently) with that of every other ROI within the DMN, and comparing group averages for each lPCC using a Student *t* test; and 4) analyzing the average timeseries of the lPCC against the timeseries from every voxel in the brain to compare groups on their functional connectivity with the lPCC with an exploratory seed-based analysis.

Figure 6. Functional Connectivity of Default Mode Network



Note. Figures compare DMN's functional connectivity based on seeds by Grady et al. 2014 and from the current study. A) There are no significant differences between groups in functional connectivity if the DMN using ROIs reported by Grady et al. 2014. B) Average ROI-to-ROI pairs of the lPCC with all other regions within the DMN, for ROIs reported by Grady et al. 2014 and our seeds. There is a statistically significant difference between groups when using our seeds (p = .02). Error bars represent standard error of the mean. C) Upper panel represents mean functional connectivity map based on Grady et al. (2014) lPCC seed. Lower panel represents mean functional connectivity map based on our lPCC seed. Red = mean functional connectivity in the DMN for bilinguals; Blue = mean functional connectivity in the DMN for monolinguals. The left side represents the left hemisphere and the right side represents the right hemisphere.

As depicted in Figure 6A, within network ROI-to-ROI pair averages of the DMN from the Grady study ROIs again show stronger functional connectivity in the monolingual group compared to the bilingual group. Although these results are not statistically significant ($t(18)$ = 1.62, p = .12, d = 0.73, 95% CI [-0.03, 0.22]), the direction of the average values is consistent with findings presented in Figure 4. Of note, there is more variability within each group, particularly in the monolingual group, compared to the data reported in Figure 4. Similarly, monolinguals displayed stronger connectivity between the lPCC and other regions within the DMN compared to bilinguals when the analyses were conducted with our seeds ($t(18)$ = 2.62; p = .02, d = 0.22, 95% CI [0.03, 0.28]); no significant differences were observed when using seeds reported by Grady et al. ($t(18)$ = .50; p = .63, d = 1.17, 95% CI [-0.06, 0.10]) (Figure 6B). Notably, functional connectivity for the DMN was stronger when using my seeds ($M_{monolinguals}$ = .41) compared to those reported by Grady et al. (2014) ($M_{monolinguals}$ = .21), suggesting that my seeds may capture the DMN better. Figure 6C further illustrates (qualitatively) the difference between groups in the functional connectivity of the DMN, and how these differ based on the seeds that were employed to conduct the analyses (i.e. lPCC). As can be observed, the functional connectivity of the lPCC (from both research groups) with other brain regions comprising the

DMN, form a network that is more consistent with the typical DMN map for monolinguals compared to bilinguals.

Taken together, although ROI-to-ROI analysis using Grady study ROIs did not show statistically significant differences between groups, functional connectivity in the DMN is consistently stronger in monolinguals compared to bilinguals.

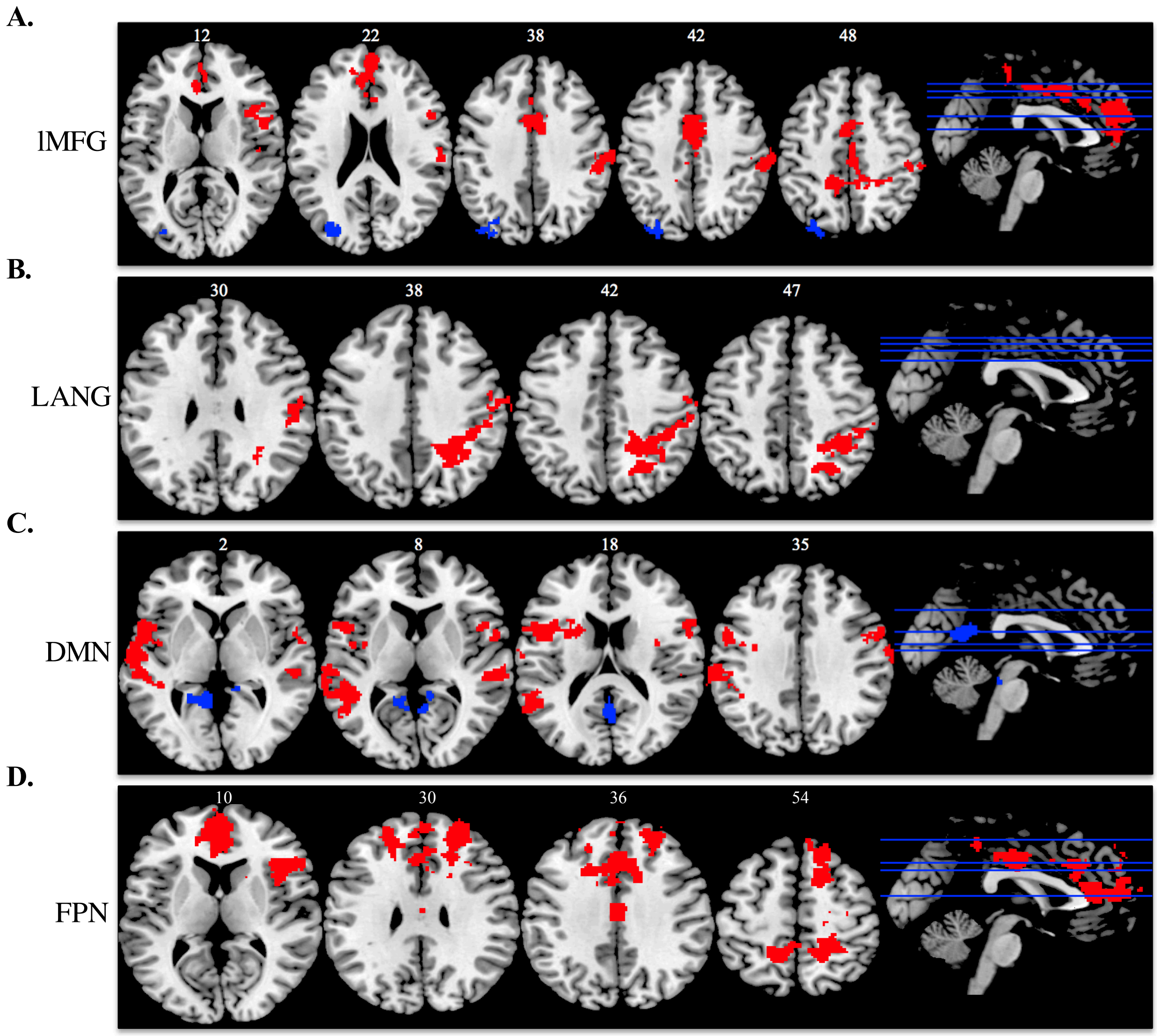
Exploratory analysis of differences in functional connectivity between bilinguals and monolinguals

Differences in functional connectivity at rest between groups was further explored by examining connectivity maps using the left middle frontal gyrus (BA9), LANG multi-seed, DMN multi-seed, ECN multi-seed, and FPN multi-seed, and analyzing each one against the timeseries from every voxel in the brain.

Regions with stronger functional connections with the left middle frontal gyrus in the bilingual group (compared to the monolingual group) include the posterior cingulate cortex, left anterior cingulate cortex, left superior frontal gyrus, bilateral postcentral gyrus, right superior parietal lobe, and bilateral precuneus (Figure 7A), whereas monolinguals showed stronger functional connectivity in the left lateral occipital cortex, bilateral lingual gyrus, left intracalcerine cortex, and bilateral occipital pole. Regions with stronger correlations to the LANG multi-seed in bilinguals included the right parietal lobule, right superior postcentral gyrus, right lateral occipital cortex, and right supramarginal gyrus (Figure 7B). Monolinguals showed stronger functional connectivity in the left parahippocampal gyrus and left temporal fusiform.

As illustrated in Figure 7C, the DMN multi-seed had stronger connections to the left temporal lobe, bilateral inferior frontal gyrus, right superior temporal gyrus, left supramarginal gyrus, left angular gyrus, right precentral gyrus, left middle temporal gyrus, and right postcentral gyrus in the bilinguals compared to the monolinguals. There were stronger connections in the right precuneus in the monolingual group. Furthermore, the left middle prefrontal cortex, anterior cingulate cortex, bilateral dorsolateral prefrontal cortex, and right inferior frontal gyrus were more strongly correlated with the FPN multi-seed in bilinguals compared to monolinguals (Figure 7D). Monolinguals had stronger connections in the left occipital pole and left orbitofrontal lobe compared to bilinguals. No significant differences between groups were seen for the ECN multi-seed. Taken together, bilinguals showed broader connectivity between each chosen ROI and other regions throughout the brain compared to the monolingual group. Particularly, many of the chosen ROIs were more strongly functionally connected with brain regions within the parietal lobe in the bilingual group. These findings are discussed to a greater extent in the following section.

Figure 7. Functional Connectivity Maps



Note. Functional connectivity maps using seeds from each network. Red = stronger functional connectivity in bilinguals compared to monolinguals; Blue = stronger functional connectivity in monolinguals compared to bilinguals. The left side represents the left hemisphere and the right side represents the right hemisphere. All slices are in *z* plane in MNI space. A) left middle frontal gyrus (BA9); B) Language Network; C) Default Mode Network; D) Frontoparietal Network.

Differentiation Between Networks

Follow-up analyses were conducted to explore whether groups differed in the extent to which networks were distinct from each other (showing a clear differentiation of networks). In other words, I wanted to know whether networks overlapped more in one group compared to the other. To examine this, the average multi-seed timeseries for each network was correlated with the average multi-seed timeseries of each other network. Pearson's correlation r values were then transformed to z-scores using the Fisher r to z transformation. Each fisher's z score represents the relationship between two given networks. Independent samples t tests (two-tailed) were then calculated to compare z scores between the monolingual and bilingual groups. Bonferroni correction was used to account for multiple comparisons. Effect sizes were calculated using Cohen's d. Confidence intervals of the difference between groups are also reported.

There was greater differentiation between the Language Network and ECN in the bilingual group compared to the monolingual group ($t(18) = -3.12$, $p = .006$, $d = 1.47$, 95% CI [-0.51, -0.10). Figure 4B further illustrates stronger connectivity between structures in the LANG and structures in the ECN in the monolingual group. No statistically significant differences were found for the other networks ($p > .05$).

Resting-state Functional Connectivity and Cognitive Performance

For *Aim 2*, I explored the relationship between functional connectivity in the BCN and performance on tests of cognition. Correlation analyses yielded significant findings for local switch cost accuracy ($r(9) = -.66$, $p = .04$), and local switch cost reaction time ($r(9) = -.66$, $p = .04$) in the bilingual group but not in the monolingual group, suggesting that amount of spoken languages may be associated with the function of some of the brain regions in the BCN. All other associations tested were non-significant (see Table 4).

Table 4. Correlation Between the BCN and Cognitive Test Scores

	Bilinguals			Monolinguals		
	n	Pearson correlation	Sig.	n	Pearson correlation	Sig.
Episodic Memory	4	.79	.11	8	.53	.09
Processing Speed	5	.13	.42	8	.23	.29
Vocabulary	5	-.87	.06	8	.30	.23
Reasoning	5	.24	.35	8	.53	.09
Spatial Processing	5	.81	.05	8	.62	.05
Spatial Working Memory (Accuracy)	10	.41	.12	10	.24	.25
Spatial Working Memory (Reaction time)	10	-.53	.06	10	.30	.20
Local Switch Cost (Accuracy)	10	-.66	.04*	10	-.04	.46
Global Switch Cost (Accuracy)	10	.26	.24	10	-.09	.41
Local Switch Cost (Reaction time)	10	-.66	.04*	10	.23	.27
Global Switch Cost (Reaction time)	10	-.21	.28	10	.27	.23

Note. $*p < .05$

Proficiency, Age of Second Language Acquisition, and Frequency of Use

To examine *Aim 3*, a linear regression analysis was conducted to explore whether multiple language-related variables predicted functional connectivity of the BCN at rest. Neither proficiency in their second language ($\beta = 0.19$, $t(6) = 0.23$, $p = .83$), frequency of second language use ($\beta = 0.04$, $t(6) = 0.04$, $p = .97$), age of second language acquisition ($\beta = 0.15$, $t(6) = 0.23$, $p = .83$), or degree of exposure to a second language ($\beta = 0.15$, $t(45) = 0.97$, $p = .34$) predicted functional connectivity of the BCN.

CHAPTER 7: DISCUSSION

Research evaluating cognitive differences between bilinguals and monolinguals has reported better executive control in bilinguals, and a delay in dementia onset in bilinguals compared to monolinguals. However, some studies have challenged the "bilingual advantage" and instead propose that results showing cognitive differences in favor of bilinguals might be confounded by variables such as SES, immigration status, and use of inappropriate statistics. Much remains unknown regarding how the experience of managing more than one language might influence the brain's function, and how these relate to cognitive function. Furthermore, most of the literature focuses on young bilinguals, especially children, and less attention has been given to how bilingualism influences behavior and brain function during older age. The current study aimed to address these limitations in the literature by examining: 1) whether older bilinguals and matched monolinguals differed in the functional connectivity of multiple brain networks observed during rest; 2) whether functional connectivity in regions proposed to be associated with language control was significantly associated with performance in tests of cognition; and 3) whether proficiency, age of second language acquisition, degree of exposure to a second language, and frequency of second language use relate to functional connectivity in the BCN.

Older bilinguals were carefully matched with monolinguals for age, sex, and education. Groups did not differ in cognitive performance. In fact, except for vocabulary, both groups had similar variability and mean values on the different cognitive domains. These similarities in cognitive performance between groups allow me to better understand differences in brain activity as a function of bilingualism. That is, I can now inquire, with things being similar (i.e. age, sex, education, cognitive performance), is the brain of a bilingual, as measured by resting-state functional connectivity, different from that of a monolingual, and in what way? Given that resting state functional connectivity is also increasingly shown as a consistent correlate of mild cognitive impairment and dementia (Binnewizend et al., 2012; Seeley, Crawford, Zhou, Miller, & Greicius, 2009; Sheline & Raichle, 2013), such differences may also shed light on potential mechanisms for the proposed protective role of bilingualism against risk for these age-related neurological diseases.

As hypothesized, functional connectivity in the LANG did not significantly differ between groups, suggesting that bilingualism does not significantly influence the functional association between regions typically linked to language production and comprehension. This is consistent with studies showing that bilinguals engage the classical language areas to a similar degree as monolinguals (Berken et al., 2015; Fabbro et al., 2000).

Contrary to my predictions, there were no differences in resting-state functional connectivity between groups in the BCN, the FPN, or the ECN. Although regions within the BCN have been associated with cognitive control and the management of two languages, these were not strongly connected to each other (as illustrated in Figure 4A), suggesting that the functional integrity of this network may not be well characterized during the resting state. Furthermore, the data suggests that neither proficiency in the second language, age of second language acquisition, degree of exposure to a second language, or frequency of second language use are significantly associated with connectivity in this network. Therefore, although previous studies have shown larger task-evoked changes in BOLD signal in the left inferior frontal gyrus, prefrontal cortex, basal ganglia, inferior parietal lobe, and anterior cingulate cortex in bilinguals compared to monolinguals during tasks of executive control and language management, these regions do not necessarily form a cohesive resting network that characterizes those who speak more than one language, regardless of their language history (e.g. proficiency, age of second language acquisition, etc.; Seeley et al., 2007).

Despite the absence of a significant difference in functional connectivity between groups for the BCN, functional connectivity in this network was negatively correlated with local switch cost accuracy and local switch cost reaction time in bilinguals but not monolinguals. That is, the stronger the functional connectivity between regions within the BCN, the better accuracy and reaction time during switching in bilinguals. Regions within the BCN such as the left anterior cingulate cortex, caudate, and frontal cortex, have been previously associated with language switching (Garbin et al., 2011). That is, fMRI studies (see Abutalebi et al., 2007 for a review) have shown changes in BOLD signal in structures within the BCN when bilinguals engage in language switching. There is empirical evidence suggesting that regions associated with language switching (such as those in the BCN) in bilinguals are the same as those involved in domain-general or "nonlinguistic" task-switching (Abutalebi et al., 2007; Garbin et al., 2011), including the aforementioned brain regions. Therefore, it is understandable why stronger functional connectivity between these structures is associated with lower local switch cost (i.e. better accuracy and reaction time during switching) in bilinguals and not in monolinguals, given that monolinguals do not have the necessity to switch between languages.

The lack of significant differences in resting-state functional connectivity in the ECN and FPN might be related to the absence of significant differences between groups in tasks associated with executive control. However, Grady et al. (2014) found stronger functional connectivity in the FPN in lifelong bilinguals compared to monolinguals, even when these groups were matched for neuropsychological variables. Contrary to their study, my sample was not composed of only lifelong bilinguals. Instead, bilinguals in my study varied in age of second language acquisition, proficiency, and frequency of second language use. I discuss the potential effect of these variables in cognitive functioning, as well as in brain structure and function in more detail below.

To my surprise, the DMN was significantly more strongly functionally connected in monolinguals compared to bilinguals. This was true even after using Grady and colleagues' (2014) ROIs and conducting multiple follow-up analyses. An established body of literature has pinpointed the DMN as supporting different aspects of self-generated cognition, such as reflecting, thinking about past events, or planning future ones, as well as episodic memory retrieval and social cognition (Andrews-Hanna et al., 2014; Sheline & Raichle, 2013; Uddin, Kelly, Biswal, Castellanos, & Milham, 2009).

The DMN is quite sensitive to aging; that is, there is lower functional connectivity in this network in older adults. The gradual loss of integrity in this network is more palpable in a variety of neurodegenerative diseases, including Alzheimer's disease and other forms of dementia (Chhatwal et al., 2013). The progressive degradation of this network parallels the gradual impairment in memory and ability to self-generate thoughts in individuals with Alzheimer's disease. Although statistically insignificant, bilinguals in my study performed worse than monolinguals in tests of episodic memory on average. Although there wasn't a significant relationship between episodic memory composite scores and DMN functional connectivity, it is interesting (and consistent with the literature) that the group with poorer functional connectivity in the DMN also had worse scores for episodic memory. Taking this into consideration, one might wonder if bilinguals are more prone to neuropathology and whether this is why they have poorer functional connectivity in the DMN. However, there is no reason to believe that this is the case since the prevalence of these neurodegenerative diseases is not higher in bilinguals.

Given the unlikeliness of bilinguals being at a higher risk for developing neuropathology, other possibilities must be considered. As mentioned previously, participants in the studies by Luk et al. (2013) and Grady et al. (2014) were all lifelong bilinguals living in Toronto, Canada. Researchers of these studies described participants as having acquired their second language before the age of 11 and as having used both languages on a regular basis throughout their lifetime. This group of researchers not only reported overall stronger functional connectivity and white matter integrity in this cohort of lifelong bilinguals, but they also reported (in another study) differences in cortical thickness between groups. Specifically, they showed that bilinguals had greater white matter in the frontal lobe compared to monolinguals, and no relationship between temporal pole (associated with the retrieval of proper names; Tranel, 2009) volume and age in bilinguals, whereas monolinguals showed greater decrease with age in temporal pole cortical thickness (Olsen et al., 2015). Authors suggest that altogether these findings show that lifelong bilingualism might attenuate the effects of aging in the brain. Participants from these three studies had multiple similarities to the bilinguals from my study: 1) they were similar in age and education; 2) they did not significantly differ in cognitive performance; 3) they spoke a variety of languages; and 4) they were mostly immigrants. However, as previously mentioned, bilinguals from the previous three studies were all lifelong bilinguals, whereas I had a more heterogeneous sample composed of bilinguals with diverse language histories.

Perhaps the strength or functional coupling of different structures in the brain depends on the language history of the individual. This is supported by my data, which shows that age of second language acquisition and proficiency in the second language were significantly associated functional connectivity in the DMN. Those who self-reported less proficiency in their second language or acquired the second language later in life, had stronger functional connectivity in the

DMN. Consistently, those who reported being exposed to a second language, to the extent where they could understand it but not speak it, had similar functional connectivity in the DMN as those who reported having very little to almost no exposure to a second language. In other words, those who were more "monolingual-like," even within the bilingual group, had stronger functional connectivity in the DMN. Yet, why would this be the case, and why do my findings contradict those by Grady et al. (2014)?

One possibility is that bilinguals in both studies might have differed in their language use, which could have potentially impacted the functional connectivity findings. In a recent study, researchers recruited young Cantonese-Mandarin bilinguals who had similar proficiency in both languages and had acquired both languages at birth, and manipulated their exposure to their second language during a 30-day period (summer vacation) (Tu et al., 2015). All participants completed a free narration task in an fMRI scan before (when they were exposed to both languages to a similar extent) and after the 30-day period. They found a significant negative correlation between second language exposure and BOLD signal in the left ACC, a brain regions that has been previously associated with the monitoring and controlling of languages in bilinguals. Furthermore, although insignificant, second language exposure was negatively correlated with the engagement of areas involved in language control, including the left middle frontal gyrus and the left pars opercularis. In other words, a significant decrease in the frequency of use of one of the languages led to an increase in the engagement of multiple brain regions that have previously associated with language control, emphasizing the significant impact of language use in the brain.

Bilinguals in the study by Grady and colleagues reported using both languages on a regular basis. On the contrary, bilinguals in my study resided in Urbana-Champaign, a context that does not necessarily allow or provide the opportunity for the regular use of both languages. In fact, many of the published studies that have failed to find a delay in dementia onset in bilinguals have been conducted in the United States (Crane et al., 2009, 2010; Zahodne et al, 2014), whereas those that have favored bilingualism as a form of cognitive reserve tend to come from countries that are characterized by the their multilingual population (e.g. Canada, India, Iran, among others) (Bialystok et al., 2007, 2008; Freedman et al., 2014). Even though bilinguals in my study reported continuing to make use of both languages to some degree, it may be possible that a low frequency of use is not enough to maintain a "bilingual advantage." Indeed, if bilinguals do not use both languages on a regular basis, then they might not be switching between languages regularly. Given that it has been proposed that it is this action of switching between languages what confers the bilingual advantage, it is possible that failure to see stronger functional connectivity or better cognitive performance in bilinguals is due to a lower frequency of language switching in bilinguals from the current study (Freedman et al., 2014; Tu et al., 2015).

It is also possible that the ongoing conscious experience of managing two languages might influence self-generated cognition, which may explain differences in functional connectivity during the resting state in the DMN coupled with robust differences in favor of bilinguals across several networks shown in exploratory analyses (Figure 7). Bilinguals may be engaging in different internal thought processes compared to monolinguals, such as switching or mixing languages when they think. This is supported by the fact that those who are less proficient in their second language had greater functional connectivity, potentially because they are only engaging one language. The constant inhibition or switching of languages at rest might therefore modify the neural correlates of self-generated thought.

Along these lines, although bilinguals in my study did not differ in cognitive performance or functional connectivity in most networks, except the DMN, they showed stronger functional connectivity with other structures in the brain compared to monolinguals (Figure 7). Multiple studies have suggested that one mechanism by which different lifestyle or demographic factors confer a cognitive reserve is by neural compensation. A study by Wook Yoo et al. (2015) examined the neural mechanisms of cognitive reserve, as measured by educational attainment, by conducting a network flow analysis of binary white matter brain networks with normal controls and patients with Alzheimer's disease. Results showed that normal controls with higher educational attainment showed a sub-network that consisted of parieto-frontal, perieto-temporal, parieto-limbic and parieto-central connections, with the left supramarginal gyrus as the hub node (not observed in individuals with lower educational attainment). The authors suggest based on these observations that, "cognitive reserve may be based on the ability of network reorganization to secure the information flow within the brain network. The existence of multiple alternative routes could be interpreted to have neural compensation or back-up plans for the brain" (p. 8).

Many of the regions reported by Wook Yoo et al. (2015) overlap with some of the regions I found to be more strongly functionally connected with the different chosen ROIs in bilinguals (e.g. supramarginal gyrus, superior parietal lobe, precuneus, angular gyrus). Perhaps the experience of managing more than one language might instigate the formation of other networks or of connectivity between regions not seen in monolinguals, and this might function as a form of neural compensation that mediates cognitive reserve. Therefore, it is plausible that the experience of managing more than one language, especially switching languages, enables the formation of another network associated with self-generated thought or episodic memory, so that these processes (some of the first to be affected in Alzheimer's disease and other dementias) are not compromised when neuropathology or neurodegeneration associated with aging affects regions comprising the DMN.

So far I have examined the possibility that these findings support bilingualism as a form of cognitive reserve (through neural compensation), or that the lack of significant differences between groups in cognitive performance and the average functional connectivity of multiple networks associated with executive control might be due to different variables, such as the frequency of language switching in bilinguals. However, it is necessary to also consider that the lack of significant differences between groups for most variables and the stronger functional connectivity in monolinguals compared to bilinguals might reflect that bilingualism does not always confer an advantage. Other studies have also failed to find data in favor of a “bilingual advantage” (Costa, Hernández, Costa-Faidella, & Sebastian-Galles, 2009; Crane et al., 2009; Duñabeitia et al., 2013; Kousaie & Phillips, 2012; Paap & Greenberg, 2013; Paap, Johnson & Sawi, 2015; Zahodne et al., 2014). In addition, a recent article reported that only 29% of studies challenging the “bilingual advantage” are published in peer-reviewed journals (de Bruin et al., 2015), suggesting that multiple studies that have also failed to find differences between groups in favor of bilinguals, or a lack of differences, are unavailable to the community given that these are either not submitted for publication or do not make it past the editorial process. In a recent review article, Paap and colleagues (2015) argue that the “bilingual advantage” is driven by variables such as immigration status, SES, use of incorrect statistics, among others, and that the evidence provided so far is not strong enough to conclude that bilingualism enhances executive control. Taken this into consideration, it is possible that the lack of differences between groups for most variables in my study evidences that bilingualism might not always confer an advantage, and instead, might enhance executive control only under certain circumstances (perhaps when they use both languages on a regular basis). These findings emphasize the multifaceted nature of bilingualism. It may not be accurate to speak about bilingualism as a categorical variable. Instead, research should consider the wide variability within bilingualism and how this variability might be associated with differences in cognition and the brain's function and structure.

Conclusion

There are millions of bilinguals around the world. Yet, it is still unclear how the experience of managing more than one language affects the brain's organization and function. Multiple published studies suggest that the management of two or more languages offers an advantage that surpasses the ability to communicate in different languages. That is, much of the research suggests that bilinguals are better at tasks of executive control and that bilingualism might delay the onset of dementia. However, there is a growing debate about whether bilingualism in fact enhances executive control, and what might be the circumstances under which there might be a bilingual advantage.

Findings from the current study suggest that bilingualism is associated with more widespread functional connectivity in the brain, potentially reflecting a form of neural compensation. However, given that bilinguals did not perform better than monolinguals on any cognitive task, and that there is no reason to believe that bilinguals might have greater neuropathology or neurodegeneration, these data could be interpreted as meaning that bilingualism does not confer an advantage (as measured by stronger functional connectivity in diverse networks that have been associated with executive control). It seems that stating that bilingualism, or the ability to speak more than one language (as defined by Grosjean and as operationalized in many studies) leads to an advantage in executive control or to more brain efficiency, might be too strong of a claim. Instead, research should examine more carefully how cognitive performance and resting state functional connectivity in different networks is influenced by multiple language variables including frequency of use of both languages. This deserves further examination with a bigger sample (see Limitations of the Current Study). Altogether, these data raise interesting possibilities about how the heterogeneity within bilingualism could influence brain function and structure.

CHAPTER 8: STRENGTHS & LIMITATIONS

Strengths of the Current Study

The current study had multiple strengths. I had a rich battery of cognitive tests that allowed me to evaluate multiple cognitive domains. I was also able to match individuals between groups for multiple variables that could potentially influence cognitive functioning or brain activity, including sex, education, and age. Furthermore, bilinguals in this study varied in language history, which allowed me to examine, for the first time to my knowledge, how these variables relate to functional connectivity between multiple brain regions. Furthermore, I was also able to investigate whether being exposed to a second language is associated with differences in functional connectivity. Finally, I explored differences between groups in functional connectivity by conducting both data-driven and exploratory analyses that are frequently used by different groups of researchers, and are therefore comparable to the resting-state functional connectivity literature. The use of data-driven and exploratory approaches permits a more comprehensive examination of the functional connectivity between multiple brain regions.

Limitations of the Current Study

Several limitations must be acknowledged. First, my sample size was small, which raises the possibility of false-negatives and false-positives. This raises the possibility that I might have found significant differences between groups if my sample had been bigger, and that therefore, the lack of differences between groups in many variables might be due to not having enough power. However, other studies investigating resting-state functional connectivity in older bilinguals have had a similar sample size (e.g. 14 bilinguals). Further, my sample size was big enough to detect a significant difference in the DMN's functional connectivity ($1\text{-}\beta = 0.86$; $d =$

1.80) and there was a big effect size for most variables. Nonetheless, a bigger sample would be required to state with more confidence that there are no statistically significant differences between groups for many of the examined variables.

Second, all instructions and tests were administered in English. Although all participants reported being fluent in English, it is possible that their performance in tests might have differed if these were conducted in their first language (when different from English). Third, language proficiency was measured using self-report. While self-report measures are strongly correlated with objective measures of proficiency, a more accurate estimate of language proficiency (for each language) can be obtained by conducting a test of vocabulary or reading. Fourth, participants were not debriefed at the end of the MRI scan, which prevented me from learning what they were thinking about while they were in the scanner and the extent to which they switched between languages in their thought processes during the resting state scan. Fifth, based on the exclusion criteria, it is possible that some individuals had abused alcohol or drugs at some point in their lifetime, which could have potentially affected their cognitive functioning. However, there is no reason to think that there could have been any differences in alcohol or drug consumption between groups. Finally, participants differed in their first and second language, many of which pertained to different language families (i.e. Spanish vs. Chinese). There are mixed findings pertaining to whether the spoken languages make a difference or not in brain activity and cognitive performance. Nonetheless, it is a factor that should be taken into consideration in future studies.

CHAPTER 9: FUTURE DIRECTIONS

The current study raises many interesting opportunities for future studies, particularly related to better understanding what factors associated with the management of two or more languages might confer the bilingual advantage. First, studies should further examine the association between functional connectivity and proficiency, age of second language acquisition, and frequency of language use, in a larger and even more variable sample (in language history). Based on my results and those from Grady et al. (2014), it was estimated that in order to have a power (1-β) of 0.80, a sample of 20 individuals per group would be required. Further, in addition to categorizing "degree of bilingualism" based on self-report, future studies should complement this by administrating tests that estimate proficiency in both of the individual's languages, such as a valid reading or vocabulary test (e.g. Shipley vocabulary test). Future studies should also collect detailed histories of language use (in each language), possibly through interviews and questionnaires. Along these lines, in order to better control for potential confounding variables and for the sake of feasibility (in terms of the administration of tests), all participants should speak the same two languages. This is particularly possible in areas where there are big communities of individuals from similar cultural backgrounds.

In order to gain a better understanding of the participants' cognitive functioning, a comprehensive battery of valid cognitive tests measuring multiple cognitive domains should be administered in the language in which the individual is most proficient. In addition to the tests that were administered in the current study, the Stroop Task and a test of attention or inhibition, could be administered in order to compare results with the broader literature on bilingualism and cognitive function.

Furthermore, although it is customary to scan individuals while they are at rest for 6 minutes, recent studies have suggested that scanning subjects for 10 minutes or more can optimize within-subject reproducibility of functional connectivity patterns across the brain (Gonzalez-Castillo et al., 2014). Scanning subjects at rest for a longer period of time has several practical limitations, however. For instance, participants are more likely to move, become impatient, among others, adding more noise to the data. Further, the benefits of scanning individuals during rest for a longer time are more meaningful for individual differences analysis and less so for group-based contrasts of networks. Therefore, although it is unclear whether I would obtain better data by scanning participants for 10 minutes, it might be worth conducting a longer scan if the resources are available.

Given my findings of lower functional connectivity in the DMN, it would be informative to debrief participants after the scanning session in order to learn what they were thinking about, in what language, and whether they caught themselves switching or mixing languages in their thoughts. Another possibility would be to prime the person before the scan to switch languages in their thoughts, and then to prime the same person to think in his or her most proficient language. Further, given that I did not find differences in functional connectivity in the BCN between bilinguals and monolinguals, it would be interesting to scan the same individuals at rest and later while they conduct language control tasks to examine whether there is task-evoked functional connectivity in BCN regions, and how these might be influenced by the different language variables.

Future studies should also explore how white matter integrity and cortical thickness vary as a function of proficiency, age of second language acquisition, and frequency of language use. Neuroimaging methods such as diffusion tensor imaging (DTI), could help better understand the role of white matter integrity in the brain's functional integrity and organization, possibly extending our knowledge of how bilingualism might contribute to cognitive reserve.

REFERENCES

Abutalebi, J. (2008). Neural aspects of second language representation and language control. *Acta Psychologica (Amst), 128*, 466-478. doi: 10.1016/j.actpsy.2008.03.014

Abutalebi, J., & Green, D. (2007). Bilingual language production: The neurocognition of language representation and control. *Journal of Neurolinguistics, 20*, 242-275. doi: 10.1016/j.jneuroling.2006.10.003

Abutalebi, J., Keim, R., Brambati, S. M., Tettamanti, M., Cappa, S. F., De Bleser, R., & Perani, D. (2007). Late acquisition of literacy in a native language. *Human Brain Mapping, 28*, 19-33. doi: 10.1002/hbm.20240

Adesope, O. O., Lavin, T., Thompson, T., & Ungerleider, C. (2010). A systematic review and meta-analysis of the cognitive correlates of bilingualism. *Review of Educational Research, 80*, 207-245. doi: 10.3102/0034654310368803

Alladi, S., Bak, T. H., Duggirala, V., Surampudi, B., Shailaja, M., Shukla, A. K., …Kaul, S. (2013). Bilingualism delays age at onset of dementia, independent of education and immigration status. *Neurology, 81*, 1938-1944. doi: 10.1212/01.wnl.0000436620.33155.a4.

Andersson, J.L.R., Jenkinson, M., & Smith, S. (2007a). Non-linear optimisation. *FMRIB Analysis Group Technical Reports.*

Andersson, J.L.R., Jenkinson, M., & Smith, S. (2007b). Non-linear registration, aka spatial normalisation. *FMRIB Analysis Group Technical Reports.*

Andrews-Hanna, J. R., Smallwood, J., & Spreng, R. N. (2014). The default network and self-generated thought: Component processes, dynamic control, and clinical relevance. *Annals of the New York Academy of Sciences*, *1316*, 29–52. http://doi.org/10.1111/nyas.12360

Anton, E., Duñabeitia, J. A., Estevez, A., Hernandez, J. A., Castillo, A., Fuentes, L. J., . . . Carreiras, M. (2014). Is there a bilingual advantage in the ANT task? Evidence from children. *Frontiers in Psychology, 5*, 398. doi: 10.3389/fpsyg.2014.00398

Baniqued, P. L., Lee, H., Voss, M. W., Basak, C., Cosman, J. D., Desouza, S., . . . Kramer, A. F. (2013). Selling points: What cognitive abilities are tapped by casual video games? *Acta Psychologica (Amst), 142*, 74-86. doi: 10.1016/j.actpsy.2012.11.009

Bartrés-Faz, D., & Arenaza-Urquijo, E. M. (2011). Structural and functional imaging correlates of cognitive and brain reserve hypotheses in healthy and pathological aging. *Brain Topography*, *24*, 340–357. doi:10.1007/s10548-011-0195-9

Beckmann, C.F., Jenkinson, M., & Smith, S.M. (2003). General multilevel linear modeling for group analysis in FMRI. *NeuroImage, 20*, 1052-1063.

Berken, J. A., Gracco, V. L., Chen, J.-K., Watkins, K. E., Baum, S., Callahan, M., & Klein, D. (2015). Neural activation in speech production and reading aloud in native and non-native languages. *NeuroImage*, *112*, 208–217. http://doi.org/10.1016/j.neuroimage.2015.03.016

Berthier, M. L., Starkstein, S. E., Lylyk, P., & Leiguarda, R. (1990). Differential recovery of languages in a bilingual patient: A case study using selective Amytal test. *Brain and Language, 38*, 449-453.

Bialystok, E. (2010). Bilingualism. *Wiley Interdisciplinary Reviews: Cognitive Science*. doi: 10.1002/wcs.43

Bialystok, E., Craik, F. I. M., & Freedman, M. (2007). Bilingualism as a protection against the onset of symptoms of dementia. *Neuropsychologia*, *45*, 459–464. doi:10.1016/j.neuropsychologia.2006.10.009

Bialystok, E., Craik, F. I. M., Green, D. & Gollan, T. (2009). Bilingual minds. *Psychological Science in the Public Interest*, *10*, 89-129.

Bialystok, E., Craik, F. I. M., & Luk, G. (2008). Cognitive control and lexical access in younger and older bilinguals. *Journal of Experimental Psychology: Learning, Memory, and Cognition, 34*, 859-873. doi: 10.1037/0278-7393.34.4.859

Bialystok, E., Craik, F. I. M., & Luk, G. (2012). Bilingualism: Consequences for mind and brain. *Trends in Cognitive Science, 16*, 240-250. doi: 10.1016/j.tics.2012.03.001

Bialystok, E., & Viswanathan, M. (2009). Components of executive control with advantages for bilingual children in two cultures. *Cognition, 112*, 494–500. doi:10.1016/j.cognition.2009.06.014

Bick, A. S., Goelman, G., & Frost, R. (2011). Hebrew brain vs. English brain: Language modulates the way it is processed. *Journal of Cognitive Neuroscience, 22*, 2280-2290. doi: 10.1162/jocn.2010.21583

Binnewijzend, M. A. A., Schoonheim, M. M., Sanz-Arigita, E., Wink, A. M., van der Flier, W. M., Tolboom, N., … Barkhof, F. (2012). Resting-state fMRI changes in Alzheimer's disease and mild cognitive impairment. *Neurobiology of Aging*, *33*, 2018–2028. http://doi.org/10.1016/j.neurobiolaging.2011.07.003

Blom, E., Kuntay, A. C., Messer, M., Verhagen, J., & Leseman, P. (2014). The benefits of being bilingual: Working memory in bilingual Turkish-Dutch children. *Journal of Experimental Child Psychology, 128*, 105-119. doi: 10.1016/j.jecp.2014.06.007

Bonifacci, P., Giombini, L., Bellocchi, S., & Contento, S. (2011). Speed of processing, anticipation, inhibition and working memory in bilinguals. *Developmental Science, 14*, 256-269.

De Bruin, a., Treccani, B., & Della Sala, S. (2014). Cognitive Advantage in Bilingualism: An Example of Publication Bias? *Psychological Science, 26,* 99-107. http://doi.org/10.1177/0956797614557866

Buchweitz, A., & Prat, C. (2013). The bilingual brain: Flexibility and control in the human cortex. *Physics of Life Review, 10*, 428-443. doi: 10.1016/j.plrev.2013.07.020

Census Bureau. (2013). Language use in the United States: 2011. Retrieved from http://www.census.gov/prod/2013pubs/acs-22.pdf

Calvo, A., & Bialystok, E. (2014). Independent effects of bilingualism and socioeconomic status on language ability and executive functioning. *Cognition, 130*, 278-288. doi: 10.1016/j.cognition.2013.11.015

Carlson, S. M., & Meltzoff, A. N. (2008). Bilingual experience and executive functioning in young children. *Developmental Science, 11*, 282-298. doi: 10.1111/j.1467-7687.2008.00675.x

Chan, R. C. K., Shum, D., Toulopoulou, T., & Chen, E. Y. H. (2008). Assessment of executive functions: Review of instruments and identification of critical issues. *Archives of Clinical Neuropsychology : The Official Journal of the National Academy of Neuropsychologists*, *23*, 201–216. http://doi.org/10.1016/j.acn.2007.08.010

Charlton, R. A., Landau, S., Schiavone, F., Barrick, T. R., Clark, C. A., Markus, H. S., & Morris, R. G. (2008). A structural equation modeling investigation of age-related variance in executive function and DTI measured white matter damage. *Neurobiology of Aging*, *29*, 1547–1555. http://doi.org/10.1016/j.neurobiolaging.2007.03.017

Chhatwal, J. P., Schultz, A. P., Johnson, K., Benzinger, T. L. S., Jack, C., Ances, B. M., … Sperling, R. A. (2013). Impaired default network functional connectivity in autosomal dominant Alzheimer disease. *Neurology*, *81*, 736–744. http://doi.org/10.1212/WNL.0b013e3182a1aafe

Crane, P. K., Gibbons, L. E., Arani, K., Nguyen, V., Rhoads, K., McCurry, S. M., … White, L. (2009). Midlife use of written Japanese and protection from late life dementia. *Epidemiology, 20*, 766–774. doi:10.1097/EDE.0b013e3181b09332

Crane, P. K., Gruhl, J. C., Erosheva, E. A., Gibbons, L. E., McCurry, S. M., Rhoads, K., … White, L. (2010). Use of spoken and written Japanese did not protect Japanese-American men from cognitive decline in late life. *The Journals of Gerontology Series B: Psychological Sciences and Social Sciences, 65*, 654-666. doi: 10.1093/geronb/gbq046

Costa, A., Calabria, M., Marne, P., Hernandez, M., Juncadella, M., Gascon-Bayarri, J., . . . Rene, R. (2012). On the parallel deterioration of lexico-semantic processes in the bilinguals' two languages: Evidence from Alzheimer's disease. *Neuropsychologia, 50*, 740-753. doi: 10.1016/j.neuropsychologia.2012.01.008

Costa, A., Hernandez, M., Costa-Faidella, J., & Sebastian-Galles, N. (2009). On the bilingual advantage in conflict processing: Now you see it, now you don't. *Cognition, 113*, 135-149. doi: 10.1016/j.cognition.2009.08.001

Costa, A., Hernandez, M., & Sebastian-Galles, N. (2008). Bilingualism aids conflict resolution: Evidence from the ANT task. *Cognition, 106*, 59-86. doi: 10.1016/j.cognition.2006.12.013

Costa, A., & Sebastián-Gallés, N. (2014). How does the bilingual experience sculpt the brain? *Nature Reviews. Neuroscience*, *15*, 336–345. http://doi.org/10.1038/nrn3709

Di Martino, a., Scheres, a., Margulies, D. S., Kelly, a. M. C., Uddin, L. Q., Shehzad, Z., … Milham, M. P. (2008). Functional connectivity of human striatum: A resting state fMRI study. *Cerebral Cortex*, *18*, 2735–2747. http://doi.org/10.1093/cercor/bhn041

Druks, J., & Weekes, B. S. (2013). Parallel deterioration to language processing in a bilingual speaker. *Cognitive Neuropsychology, 30*, 578-596. doi: 10.1080/02643294.2014.882814

Duñabeitia, J. A., Hernández, J. A., Antón, E., Macizo, P., Estévez, A., Fuentes, L. J., & Carreiras, M. (2013). The inhibitory advantage in bilingual children revisited. *Experimental Psychology, 11*, 1-18. doi: 10.1027/1618-3169/a000243.

Engel de Abreu, P. M. (2011). Working memory in multilingual children: Is there a bilingual effect? *Memory, 19*, 529-537. doi: 10.1080/09658211.2011.590504

Engel de Abreu, P. M. J., Cruz-Santos, A., Tourinho, C. J., Martin, R., & Bialystok, E. (2012). Bilingualism enriches the poor: Enhanced cognitive control in low-income minority children. *Psychological Science, 23*, 1364–1371. doi:10.1177/0956797612443836

Fabbro, F., Skrap, M., & Aglioti, S. (2000). Pathological switching between languages after frontal lesions in a bilingual patient. *Journal of Neurology, Neurosurgery, and Psychiatry, 68*, 650-652.

Ferreira, L. K., & Busatto, G. F. (2013). Resting-state functional connectivity in normal brain aging. *Neuroscience and Biobehavioral Reviews*, *37*, 384–400. http://doi.org/10.1016/j.neubiorev.2013.01.017

Freedman, M., Alladi, S., Chertkow, H., Bialystok, E., Craik, F. I. M., Phillips, N. a., … Bak, T. H. (2014). Delaying onset of dementia: Are two languages enough? *Behavioural Neurology*, *2014*. 1-8. http://doi.org/10.1155/2014/808137

Friederici, A. D. (2011). The brain basis of language processing: From structure to function. *Physiological Review, 91*, 1357-1392. doi: 10.1152/physrev.00006.2011

Garbin, G., Costa, A., Sanjuan, A., Forn, C., Rodriguez-Pujadas, A., Ventura, N., … Ávila, C. (2011). Neural bases of language switching in high and early proficient bilinguals. *Brain and Language*, *119*, 129–135. http://doi.org/10.1016/j.bandl.2011.03.011

Gollan, T. H., Fennema-Notestine, C., Montoya, R. I., & Jernigan, T. L. (2007). The bilingual effect on Boston Naming Test performance. *Journal of the International Neuropsychological Society, 13*, 197-208. doi: 10.1017/S1355617707070038

Gollan, T. H., Salmon, D. P., Montoya, R. I., & Galasko, D. R. (2011). Degree of bilingualism predicts age of diagnosis of Alzheimer's disease in low-education but not in highly educated Hispanics. *Neuropsychologia, 49*, 3826–3830. doi:10.1016/j.

Gold, B. T., Kim, C., Johnson, N. F., Kryscio, R. J., & Smith, C. D. (2013). Lifelong bilingualism maintains neural efficiency for cognitive control in aging. *The Journal of Neuroscience, 33*, 387-396. doi: 10.1523/JNEUROSCI.3837-12.2013

Gold, B. T., Johnson, N. F., & Powell, D.K. (2013). Lifelong bilingualism contributes to cognitive reserve against white matter integrity declines in aging. *Neuropsychologia. 51,* 2841-2846. doi: 10.1016/j

Gomez-Tortosa, E., Martin, E. M., Gaviria, M., Charbel, F., & Ausman, J. I. (1995). Selective deficit of one language in a bilingual patient following surgery in the left perisylvian area. *Brain and Language, 48*, 320-325.

Greve, D., & Fischl, B., 2009. Accurate and robust brain image alignment using boundary-based registration. *NeuroImage, 48*, 63-72.

Grigg, O., & Grady, C. L. (2010). Task-related effects on the temporal and spatial dynamics of resting-state functional connectivity in the default network. *PLoS ONE*, *5*. http://doi.org/10.1371/journal.pone.0013311

Grosjean, F. (1989). Neurolinguists, beware! The bilingual is not two monolinguals in one person. *Brain and Language, 36*, 3–15.

Gunning-Dixon, F. M., & Raz, N. (2000). The cognitive correlates of white matter abnormalities in normal aging: A quantitative review. *Neuropsychology, 14,* 224-232.

Guzmán-Vélez, E., & Tranel, D. (2014). Does bilingualism contribute to cognitive reserve? Cognitive and Neural Perspectives. *Neuropsychology*, *29,* 139-150 doi: 10.1037/neu0000105

Hakun, J. G., Zhu, Z., Brown, C. A., Johnson, N. F., & Gold, B. T. (2015). Longitudinal alterations to brain function, structure, and cognitive performance in healthy older adults: A fMRI-DTI study. *Neuropsychologia*, *71*, 225–35. http://doi.org/10.1016/j.neuropsychologia.2015.04.008

Hallquist, M., Hwang, K., & Luna, B. (2013). The nuisance of nuisance regression: spectral misspecification in a common approach to resting-state fMRI preprocessing reintroduces noise and obscures functional connectivity. *NeuroImage, 82*, 208-225.

Hernández, A. E., & Li, P. (2007). Age of acquisition: Its neural and computational mechanisms. *Psychological Bulletin, 133*, 638-650. doi: 10.1037/0033-2909.133.4.638

Hernández, M., Martin, C. D., Barceló, F., & Costa, A. (2013). Where is the bilingual advantage in task-switching? *Journal of Memory and Language*, *69*, 257–276.

Hoshino, N., & Kroll, J. F. (2008). Cognate effects in picture naming: Does cross-language activation survive a change of script? *Cognition, 106*, 501-511. doi: 10.1016/j.cognition.2007.02.001

Hurley, R. S., Bonakdarpour, B., Wang, X., & Mesulam, M.M. (2015). Asymmetric connectivity between the anterior temporal lobe and the language network. *Journal of Cognitive Neuroscience*, *27*, 464–473. http://doi.org/10.1162/jocn_a_00722

Jasinska, K. K., & Petitto, L. a. (2013). How age of bilingual exposure can change the neural systems for language in the developing brain: A functional near infrared spectroscopy investigation of syntactic processing in monolingual and bilingual children. *Developmental Cognitive Neuroscience*, *6*, 87–101. http://doi.org/10.1016/j.dcn.2013.06.005

Jezzard, P., & Balaban, R. (1995). Correction for geometric distortion in echo planar images from B0 field variations. *Magnetic Resonance in Medicine, 34*, 65-73.

Kelly, a M. C., Di Martino, A., Uddin, L. Q., Shehzad, Z., Gee, D. G., Reiss, P. T., … Milham, M. P. (2009). Development of anterior cingulate functional connectivity from late childhood to early adulthood. *Cerebral Cortex, 19*, 640–657. http://doi.org/10.1093/cercor/bhn117

Kelly, C., Uddin, L. Q., Shehzad, Z., Margulies, D. S., Castellanos, F. X., Milham, M. P., & Petrides, M. (2010). Broca's region: Linking human brain functional connectivity data and non-human primate tracing anatomy studies. *European Journal of Neuroscience, 32*, 383-398. doi: 10.1111/j.1460-9568.2010.07279.x

Kelly, R. E., Jr., Alexopoulos, G. S., Wang, Z., Gunning, F. M., Murphy, C. F., Morimoto, S. S., . . . Hoptman, M. J. (2010). Visual inspection of independent components: Defining a procedure for artifact removal from fMRI data. *Journal of Neuroscience Methods, 189*, 233-245. doi: 10.1016/j.jneumeth.2010.03.028

Khng, K. H., & Lee, K. (2014). The relationship between Stroop and stop-signal measures of inhibition in adolescents: Influences from variations in context and measure estimation. *PloS One*, *9*, e101356. http://doi.org/10.1371/journal.pone.0101356

Koenen, K. C., Moffitt, T. E., Roberts, A. L., Martin, L.T., Kubzansky, L., Harrington, H., … Caspi, A. (2009). Childhood IQ and adult mental disorders: A test of the cognitive reserve hypothesis. *The American Journal of Psychiatry, 166*, 50-57. doi: 10.1176/appi.ajp.2008.08030343

Kousaie, S., & Phillips, N. A. (2012). Ageing and bilingualism: Absence of a “bilingual advantage” in Stroop interference in a nonimmigrant sample. *Quarterly Journal of Experimental Psychology, 65*, 356-369. doi: /10.1080/17470218.2011.604788

Kousaie, S., Sheppard, C., Lemieux, M., Monetta, L., & Taler, V. (2014). Executive function and bilingualism in young and older adults. *Frontiers in Behavioral Neuroscience, 8*, 250. doi: 10.3389/fnbeh.2014.00250

Kovelman, I., Baker, S. A., & Petitto, L. A. (2008). Bilingual and monolingual brains compared: A functional magnetic resonance imaging investigation of syntactic processing and a possible "neural signature" of bilingualism. *Journal of Cognitive Neuroscience, 20*, 153-169. doi: 10.1162/jocn.2008.20011

Kramer A. F., Hahn S, Gopher D. (1999). Task coordination and aging: Explorations of executive control processes in the task switching paradigm. *Acta Psychologica. 101*, 339–378.

Kroll, J. F., & Bialystok, E. (2013). Understanding the consequences of bilingualism for language processing and cognition. *Journal of Cognitive Psychology (Hove), 25*. doi: 10.1080/20445911.2013.799170

Kroll, J. F., Bobb, S. C., Misra, M., & Guo, T. (2008). Language selection in bilingual speech: Evidence for inhibitory processes. *Acta Psychologica, 128,* 416-430. doi:10.1016/j.actpsy.2008.02.001

Larner, A. J. (2012). Progressive Non-Fluent Aphasia in a Bilingual Subject: Relative Preservation of "Mother Tongue." *The Journal of Neuropsychiatry and Clinical Neurosciences*, *24*, E9–E10. http://doi.org/10.1176/appi.neuropsych.11010019

Leonard, M. K., Brown, T. T., Travis, K. E., Gharapetian, L., Hagler, D. J., Jr., Dale, A. M., . . . Halgren, E. (2010). Spatiotemporal dynamics of bilingual word processing. *Neuroimage, 49*, 3286-3294. doi: 10.1016/j.neuroimage.2009.12.009

Leonard, M. K., Torres, C., Travis, K. E., Brown, T. T., Hagler, D. J. Jr., Dale, A. M., … Halgren, E. (2011). Language proficiency modulates the recruitment of non-classical language areas in bilinguals. PLoS ONE, 6, e18240- e18240. doi: 10.1371/journal.pone.0018240

Leopold, D., Murayama, Y., & Logothetis, N. (2003). Very slow activity fluctuations in monkey visual cortex: Implications for functional brain imaging. *Cerebral Cortex, 13*, 422-433.

Lezak, M., Howieson, D. B., Bigler, E., & Tranel, D. (2012). *Neuropsychological Assessment, Fifth Edition.* New York, NY: Oxford University Press.

Luk, G., & Bialystok, E. (2013). Bilingualism is not a categorical variable: Interaction between language proficiency and usage. *J Cogn Psychol (Hove), 25*, 605-621. doi: 10.1080/20445911.2013.795574

Luk, G., Bialystok, E., Craik, F. I. M., & Grady, C. L. (2011). Lifelong bilingualism maintains white matter integrity in older adults. *Journal of Neuroscience, 31*, 16808–16813. doi:10.1523/JNEUROSCI.4563-11.2011

Luk, G., Green, D. W., Abutalebi, J., & Grady, C. (2011). Cognitive control for language switching in bilinguals: A quantitative meta-analysis of functional neuroimaging studies. *Language and Cognitive Processes, 27*, 1479-1488. doi: 10.1080/01690965.2011.613209

Luo, L., Craik, F. I., Moreno, S., & Bialystok, E. (2013). Bilingualism interacts with domain in a working memory task: Evidence from aging. *Psychological Aging, 28*, 28-34. doi: 10.1037/a0030875

Madhavan, K. M., McQueeny, T., Howe, S. R., Shear, P., & Szaflarski, J. (2014). Superior longitudinal fasciculus and language functioning in healthy aging. *Brain Research*, *1562*, 11–22. http://doi.org/10.1016/j.brainres.2014.03.012

Mägiste, E. (1979). The competing language systems of the multilingual: A developmental study of decoding and encoding processes. *Journal of Verbal Learning and Verbal Behavior*, *18*, 79–89. http://doi.org/10.1016/S0022-5371(79)90584-X

Marian, V., Blumenfeld, H. K., Mizrahi, E., Kania, U., & Cordes, A. K. (2013). Multilingual Stroop performance: Effects of trilingualism and proficiency on inhibitory control. *International Multilingual Research Journal, 10*, 82-104. doi: 10.1080/14790718.2012.708037

Marian, V., Spivey, M., & Hirsch, J. (2003). Shared and separate systems in bilingual language processing: Converging evidence from eyetracking and brain imaging. *Brain and Language*, *86*, 70–82.

Marrero, M. Z., Golden, C. J., & Espe-Pfeifer, P. (2002). Bilingualism, brain injury, and recovery: Implications for understanding the bilingual and for therapy. *Clinical Psychology Review, 22*, 465-480.

Martin, C. D., Barcelo, F., Hernandez, M., & Costa, A. (2011). The time course of the asymmetrical " local" switch cost: Evidence from event-related potentials. *Biological Psychology*, *86*, 210–218. http://doi.org/10.1016/j.biopsycho.2010.12.001

Mendez, M. F., Perryman, K. M., Pontón, M. O., & Cummings, J. L. (1999). Bilingualism and Dementia. *The Journal of Neuropsychiatry and Clinical Neurosciences*, *11*, 411–412. http://doi.org/10.1176/jnp.11.3.411

McIntosh, A. R., & Lobaugh, N. J. (2004). Partial least squares analysis of neuroimaging data: Applications and advances. *NeuroImage*, *23*, 250–263. ://doi.org/10.1016/j.neuroimage.2004.07.020

Mechelli, A., Crinion, J. T., Noppeney, U., O'Doherty, J., Ashburner, J., Frackowiak, R. S., & Price, C. J. (2004). Neurolinguistics: Structural plasticity in the bilingual brain. *Nature, 431*, 757–757. doi:10.1038/431757a

Miyake, A., Friedman, N. P., Emerson, M. J., Witzki, A. H., Howerter, A., & Wager, T. D. (2000). The unity and diversity of executive functions and their contributions to complex "Frontal Lobe" tasks: A latent variable analysis. *Cognitive Psychology, 41*, 49-100. doi: 10.1006/cogp.1999.0734

Monsell, S. (2003). Task switching. *Trends in Cognitive Science, 7*, 134-140.

Monti, R. P., Hellyer, P., Sharp, D., Leech, R., Anagnostopoulos, C., & Montana, G. (2014). Estimating Time-varying Brain Connectivity Networks from Functional MRI Time Series. *NeuroImage*, *103*, 427–443. http://doi.org/10.1016/j.neuroimage.2014.07.033

Morales, J., Calvo, A., & Bialystok, E. (2013). Working memory development in monolingual and bilingual children. *Journal of Experimental Child Psychology, 114*, 187-202. doi: 10.1016/j.jecp.2012.09.002

Morford, J. P., Wilkinson, E., Villwock, A., Pinar, P., & Kroll, J. F. (2011). When deaf signers read English: Do written words activate their sign translations? *Cognition, 118*, 286-292. doi: 10.1016/j.cognition.2010.11.006

Ossher, L., Bialystok, E., Craik, F. I., Murphy, K. J., & Troyer, A. K. (2013). The effect of bilingualism on amnestic mild cognitive impairment. *Journals of Gerontology Series B: Psychological Sciences and Social Sciences, 68*, 8-12. doi: 10.1093/geronb/gbs038

Paap. K. R., & Greenberg, Z. I. (2013). There is no coherent evidence for a bilingual advantage in executive processing. *Cognitive Psychology, 66,* 232-258. doi: 10.1016/j.cogpsych.2012.12.002

Paap, K. R., Johnson, H. A., & Sawi, O. (2015). Bilingual advantages in executive functioning either do not exist or are restricted to very specific and undetermined circumstances. *Cortex; a Journal Devoted to the Study of the Nervous System and Behavior*, *69*, 265–278. http://doi.org/10.1016/j.cortex.2015.04.014

Peal E & Lambert, W. E. (1962). The relation of bilingualism to intelligence. *Psychological Monographs: General and Applied, 76*, 1-23.

Perani, D., Paulesu, E., Galles, N. S., Dupoux, E., Dehaene, S., Bettinardi, V., . . . Mehler, J. (1998). The bilingual brain: Proficiency and age of acquisition of the second language. *Brain, 121*, 1841-1852.

Prior, A., & Gollan, T. H. (2011). Good language-switchers are good task-switchers: Evidence from Spanish-English and Mandarin-English bilinguals. *Journal of the International Neuropsychological Society, 17*, 682-691. doi: 10.1017/S1355617711000580

Reed, B. R., Dowling, M., Tomaszewski Farias, S., Sonnen, J., Strauss, M., Schneider, J. A., … & Mungas, D. (2011). Cognitive activities during adulthood are more important than education in building reserve. *Journal of the International Neuropsychological Society, 17*, 615-624. doi: 10.1017/S1355617711000014

Saer, D. J. (1923). The effects of bilingualism on intelligence. *British Journal of Social Psychology*, *14*, 25-38.

Salthouse, T. A. (2005). Relations between cognitive abilities and measures of executive functioning. *Neuropsychology, 19*, 532-545. doi: 10.1037/0894-4105.19.4.532

Salthouse, T. A. (2013). Evaluating the Correspondence of Different Cognitive Batteries. *Assessment, 21*, 131-142. doi: 10.1177/1073191113486690

Salthouse, T. A., & Ferrer-Caja, E. (2003). What needs to be explained to account for age-related effects on multiple cognitive variables? *Psychological Aging, 18*, 91-110. doi: 10.1037/0882-7974.18.1.91

Salthouse, T. A., Pink, J. E., & Tucker-Drob, E. M. (2008). Contextual analysis of fluid intelligence. *Intelligence, 36*, 464-486. doi: 10.1016/j.intell.2007.10.003

Salvador, R., Suckling, J., Coleman, M., Pickard, J., Menon, D., & Bullmore, E. (2005). Neurophysiological architecture of functional magnetic resonance images of human brain. *Cerebral Cortex, 15*, 1332-1342.

Sattler, C., Toro, P., Schönknecht, P., & Schröder, J. (2012). Cognitive activity, education and socioeconomic status as preventive factors for mild cognitive impairment and Alzheimer's disease. *Psychiatry Research, 196*, 90–95. doi:10.1016/j.psychres.2011.11.012

Sheline, Y. I., & Raichle, M. E. (2013). Resting state functional connectivity in preclinical Alzheimer’s disease. *Biological Psychiatry*, *74*, 340–347. http://doi.org/10.1016/j.biopsych.2012.11.028

Schroeder, S. R., & Marian, V. (2012). A bilingual advantage for episodic memory in older adults. *Journal of Cognitive Psychology (Hove, England)*, *24*, 591–601. http://doi.org/10.1080/20445911.2012.669367

Schweizer, T. A., Ware, J., Fischer, C. E., Craik, F. I. M., & Bialystok, E. (2012). Bilingualism as a contributor to cognitive reserve: Evidence from brain atrophy in Alzheimer’s disease. *Cortex, 48*, 991–996. doi:10.1016/j.cortex.2011.04.009

Scolari, M., Seidl-Rathkopf, K. N., & Kastner, S. (2015). Functions of the human frontoparietal attention network: Evidence from neuroimaging. *Current Opinion in Behavioral Sciences*, *1*, 32–39. http://doi.org/10.1016/j.cobeha.2014.08.003

Seeley, W. W., Crawford, R. K., Zhou, J., Miller, B. L., & Greicius, M. D. (2009). Neurodegenerative diseases target large-scale human brain networks. *Neuron*, *62*, 42–52. http://doi.org/10.1016/j.neuron.2009.03.024

Seeley, W. W., Menon, V., Schatzberg, A. F., Keller, J., Glover, G. H., Kenna, H., … Greicius, M. D. (2007). Dissociable intrinsic connectivity networks for salience processing and executive control. *The Journal of Neuroscience : The Official Journal of the Society for Neuroscience*, *27*, 2349–2356. http://doi.org/10.1523/JNEUROSCI.5587-06.2007

Simmonds, A. J., Wise, R. J., & Leech, R. (2011). Two tongues, one brain: Imaging bilingual speech production. *Frontiers in Psychology, 2*, 166. doi: 10.3389/fpsyg.2011.00166

Smith, F. (1923). Bilingualism and mental development. *British Journal of Social Psychology*, *13*, 270-282

Snowdon, D. A., Kemper, S. J., Mortimer, J. A., Greiner, L. H., Wekstein, D. R., & Markesbery, W. R. (1996). Linguistic ability in early life and cognitive function and AD in late life. Findings from the Nun study. *JAMA: The Journal of the American Medical Association, 275*, 528-532

Power, J., Barnes, K., Snyder, A., Schlaggar, B., & Petersen, S. (2012). Spurious but systematic correlations in functional connectivity MRI networks arise from subject motion. *NeuroImage, 59*, 2142-2154.

Steffener, J., Reuben, A., Rakitin, B. C., & Stern, Y. (2011). Supporting performance in the face of age-related neural changes: Testing mechanistic roles of cognitive reserve. *Brain imaging and Behavior, 5*, 212–221. doi:10.1007/s11682-011-9125-4

Stein, M., Federspiel, A., Koenig, T., Wirth, M., Strik, W., Wiest, R., . . . Dierks, T. (2012). Structural plasticity in the language system related to increased second language proficiency. *Cortex, 48*, 458-465. doi: 10.1016/j.cortex.2010.10.007

Stern, Y. (2009). Cognitive reserve and Alzheimer's disease. *Neuropsychologia, 47*, 2015–2028. doi:10.1016/j.neuropsychologia.2009.03.004

Thierry, G., & Wu, Y. J. (2007). Brain potentials reveal unconscious translation during foreign-language comprehension. *Proceedings of the National Academy of Sciences, 104*, 12530-12535. doi: 10.1073/pnas.0609927104

Thordardottir, E. (2010). Towards evidence-based practice in language intervention for bilingual children. *Journal of Communication Disorders*, *43*, 523–37. http://doi.org/10.1016/j.jcomdis.2010.06.001

Tomasi, D., & Volkow, N. D. (2012). Resting functional connectivity of language networks: Characterization and reproducibility. *Molecular Psychiatry*, *17*, 841–854. http://doi.org/10.1038/mp.2011.177

Tranel, D. (2009). The left temporal pole is important for retrieving words for unique concrete entities. *Aphasiology*, *23*, 867–884. http://doi.org/10.1080/02687030802586498

Tu, L., Wang, J., Abutalebi, J., Jiang, B., Pan, X., Li, M., … Huang, R. (2015). Language exposure induced neuroplasticity in the bilingual brain: A follow-up fMRI study. *Cortex*, *64*, 8–19. http://doi.org/10.1016/j.cortex.2014.09.019

Uddin, L. Q., Kelly, a. M. C., Biswal, B. B., Castellanos, F. X., & Milham, M. P. (2009). Functional connectivity of default mode network components: Correlation, anticorrelation, and causality. *Human Brain Mapping*, *30*, 625–637. http://doi.org/10.1002/hbm.20531

Van den Heuvel, M. P., & Hulshoff Pol, H. E. (2010). Exploring the brain network: A review on resting-state fMRI functional connectivity. *European Neuropsychopharmacology : The Journal of the European College of Neuropsychopharmacology*, *20*, 519–34. http://doi.org/10.1016/j.euroneuro.2010.03.008

Voss, M. W., Erickson, K. I., Prakash, R. S., Chaddock, L., Malkowski, E., Alves, H., . . . Kramer, A. F. (2010). Functional connectivity: A source of variance in the association between cardiorespiratory fitness and cognition? *Neuropsychologia, 48*, 1394-1406. doi: 10.1016/j.neuropsychologia.2010.01.005

Worsley, K., Evans, A., Marrett, S., & Neelin, P. (1992). A three-dimensional statistical analysis for CBF activation studies in human brain. *Journal of Cerebral Blood Flow and Metabolism, 12,* 900-918.

Wook Yoo, S., Han, C. E., Shin, J. S., Won Seo, S., Na, D. L., Kaiser, M., … Seong, J.-K. (2015). A network flow-based analysis of cognitive reserve in normal ageing and Alzheimer's disease. *Scientific Reports*, *5*, 10057. http://doi.org/10.1038/srep10057

Zahodne, L. B., Schofield, P. W., Farrell, M. T., Stern, Y., & Manly, J. J. (2013). Bilingualism does not alter cognitive decline or dementia risk among Spanish-speaking immigrants. *Neuropsychology*, *28*, 238-246. doi: 10.1037/neu0000014