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Effects of bilingualism on white matter integrity in older adults

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ABSTRACT

Bilingualism can delay the onset of dementia symptoms and has thus been characterized as a mechanism for cognitive or brain reserve, although the origin of this reserve is unknown. Studies with young adults generally show that bilingualism is associated with a strengthening of white matter, but there is conflicting evidence for how bilingualism affects white matter in older age. Given that bilingualism has been shown to help stave off the symptoms of dementia by up to four years, it is crucial that we clarify the mechanism underlying this reserve. The current study uses diffusion tensor imaging (DTI) to compare monolinguals and bilinguals while carefully controlling for potential confounds (e.g., I.Q., MMSE, and demographic variables). We show that group differences in Fractional Anisotropy (FA) and Radial Diffusivity (RD) arise from multivariable interactions not adequately controlled for by sequential bivariate testing. After matching and statistically controlling for confounds, bilinguals still had greater axial diffusivity (AD) in the left superior longitudinal fasciculus than monolingual peers, supporting a neural reserve account for healthy older bilinguals.

Introduction

Speaking two languages on a regular basis has been shown to lead to domain-general cognitive changes that persist across the lifespan (for recent reviews, see Bialystok, 2017; Grundy et al., 2017). However, it is unclear what neural mechanism might underlie these behavioral changes and whether this mechanism persists into old age. Uncovering such a mechanism is crucial in light of the increasing size of the elderly population. For example, in Canada the proportion of seniors aged 60–79 rose from 4.2% of the population in 2012 to 4.7% in 2016 (Statistics Canada, 2017). This rise in the size of the older adult population is associated with increases in the number of individuals suffering with dementia or cognitive decline. Importantly, there is converging evidence from multiple sources that symptoms of dementia and cognitive decline appear later in lifelong bilinguals than in comparable monolinguals. Older adult bilinguals are diagnosed with Alzheimer's disease (AD) on average four years later than their monolingual peers (Bialystok et al., 2007; Craik et al., 2010; Alladi et al., 2013). A study by Brookmeyer et al. (2007) demonstrated that a 1-year delay in symptoms would yield 11.8 million fewer cases of Alzheimer's disease worldwide by 2050. Clearly there is a need to expose the structural and functional brain differences that may underlie bilinguals' ability to protect cognitive function with aging and stave off dementia symptoms.

A consistent finding in the AD literature is a reduction in white matter integrity with disease progression. The anterior aspect of the corpus callosum and the superior longitudinal fasciculi are both sensitive to the progression of AD (Bartzokis et al., 2004; Rose et al., 2000; Bozzali et al., 2002). These white matter regions are also consistently remodeled by second-language experience in young adults. Structural magnetic resonance imaging (MRI) has revealed that young adult bilinguals have greater white matter volume than their monolingual peers. These differences are particularly reliable in the corpus callosum, and may allow bilinguals to exchange cross-hemispheric information more efficiently than monolinguals (e.g., Coggins et al., 2004; Felton et al., 2017).

More recently, the advent of diffusion tensor imaging (DTI) has allowed for a more detailed examination of water flow along gradients in the neurological pathways in the brain. This methodological development has allowed researchers to characterize white matter microstructural integrity using summary measures of the diffusion tensor (but see Jones et al., 2013; for an alternative interpretation). Anisotropic water

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diffusion along the primary eigenvector (λ_1), that is, parallel to a white matter tract is an index of axial diffusivity (AD) and has been shown to measure axon integrity, with higher values indicating better integrity. Isotropic water diffusion, largely influenced by increasing flow perpendicular to the primary diffusion gradient indicates radial diffusivity (RD: λ_2, λ_3) and is associated with demyelination such that higher values are generally associated with poorer integrity. The most widely reported measure, however, is the combination of the former two measures. This measure, called fractional anisotropy (FA), indexes the overall microstructural health of the white matter in a voxel and is calculated from a combination of the three eigenvalues, $\lambda_1, \lambda_2, \lambda_3$, by the following formula: $\sqrt{(3/2)}* \sqrt{[(\lambda_1 - \lambda_{123})^2 + (\lambda_2 - \lambda_{123})^2 + (\lambda_3 - \lambda_{123})^2]} / \sqrt{(\lambda_1^2 + \lambda_2^2\ \lambda_3^2)}$, where λ_{123} is the mean of the eigenvalues. Therefore, FA is not a simple ratio of AD and RD but rather a complex summary of diffusion along the axon derived from the other two vectors. All three measures thus contribute meaningful information about white matter structure. Although greater FA is generally thought to index healthier white matter integrity, it is possible for changes to emerge in RD or AD without any effect on FA values. Accordingly, it is important to examine all three white matter components from the DTI analysis.

Studies using DTI to measure white matter integrity in young adults have revealed effects of bilingualism echoing the volumetric data. A recent study by Pliatsikas et al. (2015), for example, showed that bilingual young adults expressed greater FA values than monolinguals in most regions of the corpus callosum, bilaterally in the inferior frontal occipital fasciculus, and external capsules. Training studies have also produced compelling evidence for white matter remodeling. Schlegel et al (2012) demonstrated that second-language training of Chinese by native English speakers over an eight-month period led to a linear increase in FA located predominantly in the anterior corpus callosum. To the degree that they successfully acquired their new language as measured by test scores, the students showed a steeper FA slope, indicating a more rapid remodeling of white matter. Parallels may also be drawn between how bilingualism and musicianship reshape the brain – and, in particular, the corpus callosum. As with bilinguals, musicians also appear to have larger corpus callosum volumes, an effect that is sensitive to the age at which the musician first acquired the skill (Schlaug et al., 1995; Wan & Schlaug, 2010). Echoing the arguments from the bilingual literature, the strengthening of the corpus callosum in musicians is also thought to reflect greater inter-hemispheric communication (e.g., Barrett et al., 2013).

Whether these increases in white matter integrity persist into the older adult years is still a matter of debate but essential for understanding the potential basis for cognitive reserve found for older bilinguals. Only two studies have examined how bilingualism impacts white matter integrity in the aging brain and these two studies report conflicting findings. The first study by Luk et al. (2011) showed that in a small but well-matched sample (N = 14 per group), bilingual older adults had higher FA values than monolinguals in the corpus callosum and bilateral superior and inferior longitudinal fasciculi, consistent with the young adult data. A second study by Gold et al. (2013) matched participants from a larger monolingual sample to a group of 20 bilinguals.[1] Whereas Luk et al. reported increased FA in corpus callosum and bilateral superior longitudinal fasciculi, Gold et al. reported the opposite: monolinguals were more likely to have higher FA values in a distributed set of regions including the corpus callosum, the inferior and superior fronto-occipital fasciculi, and the fornix. The authors noted that there were no regions in which bilinguals showed higher FA than monolinguals, but that bilinguals had higher RD values in most of these same regions. The latter finding that RD was higher for bilinguals was likely what drove the FA ratio, and led Gold and colleagues to conclude that their sample of bilinguals displayed remarkable cognitive reserve in the face of white matter atrophy relative to the monolingual sample.

One possible reason for the lack of consensus among group comparisons in neuroimaging studies is suboptimal matching. While many studies in neuroscience do attempt to rigorously match groups on behaviors and background variables to rule out the possibility that these other factors explain their findings, many others either do not, or simply present a subset of demographic variables without comment. Of those studies that do report matching groups, some indicate that they used *t*-tests to assess the (lack of) group differences in confounding variables, but often the matching procedure is not reported. More recently, techniques have been developed to carefully match groups on multiple variables simultaneously. One such technique, propensity score matching, fits a logistic regression to multiple confounds simultaneously and thus accounts for multivariate interactions among confounding variables that may differ between groups. We argue that there is a pressing need for more transparency about *how* participants are matched if we to assure that differences can be attributed to group characteristics and effects can be replicated. Propensity score matching is superior to sequential univariate group comparisons as it actively accounts for interactions between variables which may themselves differ by group.

Given the need to clarify the mechanism underlying bilinguals' ability to delay dementia symptoms, we investigated whether evidence for white matter differences following a lifetime of bilingual language use could be found in a large sample of older adults. We carefully matched monolingual and bilingual participants to control for multivariate interactions among potentially confounding variables, something previous studies have not done. Based on the evidence from younger adults, we expected to find greater white matter integrity for bilinguals than monolinguals in the corpus callosum, superior longitudinal fasciculi, and inferior fronto-occipital fasciculi. Such differences would contribute to our understanding of the factors responsible for neural reserve in general and the preserved cognitive function found for older bilinguals in particular.

Method

Participants

Sixty-one healthy older adults were recruited from the community. Thirty-one (11 men) of these participants were determined to be bilingual and 30 (8 men) were determined to be monolingual based on an extensive background questionnaire called the *Language and Social Background Questionnaire* (LSBQ; Anderson et al., 2017). Anderson et al. (2017) provide a method for calculating summary factor scores from which bilingual status can be determined, however validation of this method has not yet been extended to older adults. We therefore report English speaking and understanding and second-language speaking and understanding scores for each group (see Table 1). Importantly, English scores were equivalent for the two groups but second-language scores were significantly different. Screening for bilingual status was conducted via telephone interview and participants who could not be reliably categorized as monolingual or bilingual did not take part in the study. All participants were right handed and had no history of heart disease, psychological or neurological disease, or other MRI contraindications (see Table 1 for descriptive statistics). Bilinguals were lifelong bilinguals who were residents of Canada at the time of testing. We also asked participants "were any periods in your life when you did not use your second language?" If so, "how long?" The majority of the bilingual participants continually used their second language (64%) throughout their lives, a relationship that emerged even more strongly in the matched sample (72%).

[1] Gold et al. (2013) matched participants for sex, education level age, and scores on ISP, Cattell IQ, MMSE, Vocabulary (PPVT), Digit span forward and backward, Spatial span forward and backward, Logical memory I and II and Task-switching RT and % errors. Luk et al. (2011) matched on age, gender, years of education, weekly hours of computer use, MMSE, Shipley English scores, Verbal fluency, Design Fluency, Stroop response time and Trail-Making response time. In both studies, matching success was assessed by a non-significant between-groups *p*-value for each measure.