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ORIGINAL ARTICLE

Poorer clinical outcomes for older adult monolinguals when matched to bilinguals on brain health

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Abstract

Previous studies have reported bilingualism to be a proxy of cognitive reserve (CR) based on evidence that bilinguals express dementia symptoms ~ 4 years later than monolinguals yet present with greater neuropathology at time of diagnosis when clinical levels are similar. The current study provides new evidence supporting bilingualism's contribution to CR using a novel brain health matching paradigm. Forty cognitively normal bilinguals with diffusion-weighted magnetic resonance images recruited from the community were matched with monolinguals drawn from a pool of 165 individuals in the Alzheimer's Disease Neuroimaging Initiative (ADNI) database. White matter integrity was determined for all participants using fractional anisotropy, axial diffusivity, and radial diffusivity scores. Propensity scores were obtained using white matter measures, sex, age, and education as predictive covariates, and then used in one-to-one matching between language groups, creating a matched sample of 32 participants per group. Matched monolinguals had poorer clinical diagnoses than that predicted by chance from a theoretical null distribution, and poorer cognitive performances than matched bilinguals as measured by scores on the MMSE. The findings provide support for the interpretation that bilingualism acts as a proxy of CR such that monolinguals have poorer clinical and cognitive outcomes than bilinguals for similar levels of white matter integrity even before clinical symptoms appear.

Keywords Bilingualism · Cognitive reserve · Diffusion weighted imaging · White matter integrity

Lifelong bilingualism has been shown to confer executive control benefits for older adults, allowing bilinguals on average to outperform monolingual peers (Bialystok et al. 2016). Although positive effects for bilinguals compared to monolinguals are less likely to be found in young adults (e.g., Paap and Greenburg 2013; Paap and Sawi 2014; von Bastian, Souza and Gade 2016), research with children has produced both positive and null results (e.g., Dick et al 2019; Duñabeitia et al. 2014; see Leivada et al. 2020 for a review on the "phantom-like" effects of bilingualism). However, the positive effects of bilingualism are more reliably found for older adults, particularly when taking into account language proficiency and exposure (see Zhang et al. 2020 for a review). This adaptation in cognitive systems for older bilinguals is thought to result from the demands associated with managing two languages and selecting appropriate responses to satisfy current contextual cues. Managing two languages in one's mind has been likened to "mental juggling" (Kroll 2008), as each language in a bilingual's repertoire remains simultaneously active while reading, hearing, and speaking, even in single language contexts (Dijkstra 2005; Marian and Spivey 2003; Kroll et al. 2006). Further, language selection in bilinguals is modulated by the cingulo-frontoparietal network—the same control network that monolinguals use for performing nonverbal tasks such as Simon or flanker tasks, providing functional neural evidence linking these two activities (e.g., Abutalebi and Green 2008; Anderson, Chung-Fat-Yim et al. 2018a; Luk, Green et al. 2011b). Robust evidence also demonstrates that speaking two or more languages is associated with a delay in symptoms of dementia of between 3 and 5 years compared to monolinguals (e.g., Alladi et al. 2013; Bialystok et al. 2007; Chertkow et al. 2010; Woumans et al. 2015; Zheng et al.

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2018). Two recent meta-analyses support the claims from these studies that bilingualism delays the onset of dementia by 4.7 years (CI 3.3–6.1; Anderson et al. 2020; Brini et al. 2020) but does not prevent bilingual individuals from developing dementia, a pattern consistent with cognitive reserve (Stern 2002). However, as it is with behavioural results, some studies have failed to find any differences between monolinguals and bilinguals in clinical diagnoses (Lawton et al 2015; Sanders et al 2012; see Mukadam et al. 2017 for a meta-analysis, but see Grundy and Anderson 2017 for a rebuttal), although continuous measures of bilingual practice and immersion more accurately predicts positive effects of bilingualism than do comparisons across groups (see Del Maschio et al. 2018, for a review).

In light of the positive behavioural and neuropsychiatric findings, there has been a strong interest in exploring structural and functional brain differences attributable to bilingualism. Perani et al. (2017) used PET to show that in a patient sample matched on disease duration, bilingual patients with Alzheimer's disease (AD) had more severe cerebral hypometabolism than monolingual patients, a measure that the authors attributed to reduced synaptic function and density. Despite this, bilinguals outperformed monolinguals on short- and long-term verbal memory and visuospatial tasks. Another study compared monolingual and bilingual patients with AD using computed tomography scans (Schweizer et al. 2012). Patients were matched on age, education, occupational status, and clinical level of dementia, yet bilingual patients showed greater medial temporal atrophy than the monolingual group. Importantly, despite this greater atrophy bilinguals were indistinguishable from monolinguals on cognitive status measures derived from standardized tests.

Although grey matter structure has been widely studied, white matter integrity is critical for cognitive functioning, particularly as atrophy occurs with ageing (Bennett and Madden 2014). Diffusion tensor imaging (DTI) is used to measure the directional displacement of water along neural pathways in the brain and thus provides a measure of microstructural integrity. Fractional anisotropy (FA), axial diffusivity (DA), and radial diffusivity (DR) are measures that reflect the overall health of white matter and respectively correspond to the anisotropic diffusion along an axon, diffusion along the primary axis, and isotropic diffusion perpendicular to the primary axis. A useful heuristic is that higher FA values roughly correspond to greater white matter integrity, while a higher DR value is associated with demyelination of axons and thus poorer integrity (see Madden et al. 2009, for a review). The interpretation of DA, however, is less clear. Conflicting results have been reported in the literature with findings of both DA increases and decreases linked to age-related changes (Burzynska et al. 2010; Cox et al. 2016; Sexton et al. 2014). Notably, increased DA has also been reported as a necessary stage in neuronal loss (Acosta-Cabronero et al. 2012), especially related to microglial processes such that DA decreases as an initial response to axonal loss, but subsequently increases with the clearance of cell debris (Burzynska et al. 2010; see also Michielse et al. 2010; Sexton et al. 2014, for similar patterns). This pattern of change in DA over time may explain the difference in findings, as the age at which an individual is tested will in part influence DA values and the direction of change.

Only a few studies have compared bilingual and monolingual white matter integrity in older age, with contrasting results. Luk, Bialystok, et al. (2011a) showed that older adult bilinguals had greater FA values in the corpus callosum and bilateral superior and inferior longitudinal fasciculi than their monolingual peers. No group differences were found in DA, but monolinguals had greater DR in the body of the corpus callosum—some in areas that overlapped where bilinguals showed greater FA values. This greater white matter integrity in the bilingual group than the monolingual group was found even when both groups were matched on age, education, and gender, with similar neuropsychological performance on standardized tests. In contrast, a study by Gold et al. (2013) involving older adults reported opposite findings—monolinguals had greater FA values than bilinguals in the corpus callosum, superior and inferior longitudinal fasciculus, and fornix whereas bilinguals showed greater DR in the inferior fronto-occipital fasciculus and corpus callosum than monolinguals. As with Luk, Bialystok, et al. (2011a), there were no group differences in DA. However, in a sample of cognitively healthy older adults, Anderson, Grundy, et al. (2018b) found that monolinguals had greater FA values, while bilinguals had higher DA and DR values, largely consistent with the results reported by Gold et al. (2013). The two groups were then matched on seven background measures using propensity score matching (PSM), after which only the greater DA findings in bilinguals remained. The higher values were present in a range of white matter tracts including the midbody and splenium of the corpus callosum, and the left superior temporal longitudinal fasciculus. The findings of Anderson, Grundy, et al. replicated those of Gold et al. in the unmatched sample, but more stringent matching criteria led to findings in the same region as that found by Luk, Bialystok et al. higher DA values for bilinguals in the left superior longitudinal fasciculus for Anderson, Grundy et al. and higher FA values for bilinguals in this same region for Luk, Bialystok, et al. The differences in white matter integrity between these studies may possibly be explained by the participants' ages (a mean of approximately 64 years in the study by Gold et al. to a mean of 75 years of age in the study by Anderson, Grundy et al.), as it has been previously noted that age is a determinant in white matter measures (Burzynska et al. 2010; Michielse et al. 2010; Sexton et al. 2014). However, the scarcity of research investigating this

issue in regard to bilingualism means there is currently no consensus. The question is important because it addresses the key tenets of how bilingualism modifies white matter integrity across the lifespan in particular and the neurological changes associated with increasing cognitive impairment in general.

The concept of cognitive reserve helps to explain the disjunction between preserved cognitive functioning and clinical pathology as has been reported for bilinguals (e.g., Brini et al. 2020). Reserve is thought to be the cumulative improvements to or maintenance of neural resources brought about by lifetime exposures like education, occupational complexity, or social engagement, such that individuals are better able to cope with neural decline. Education, in particular, has been extensively studied and posited as a socio-behavioural proxy of reserve, with findings that include higher risk of dementia in those with low education, and slower cognitive and functional decline in those with high educational attainment (for reviews see Meng and D'Arcy 2012, and Stern 2009). The findings suggest that education, as a proxy of cognitive reserve, acts to protect against the damaging effects of brain atrophy in both disease and ageing. This dissociation between brain state and cognitive level is the signature of cognitive reserve (Bialystok et al. 2018; Stern 2009).

As noted earlier, bilingualism is associated with a delay in onset of symptoms of dementia by approximately 4 years and thus has been posited to be another proxy of cognitive reserve. Early life experience in two languages is associated with a lower incidence of mild cognitive impairment (MCI) than is found for those with minimal second-language learning (Wilson et al. 2015). Recently, bilingualism has also been shown to influence conversion times from MCI to dementia such that bilinguals converted faster to dementia than monolinguals (Berkes et al. 2020). Although this finding seems counterintuitive, faster conversion and decline once cognitive issues appear is in line with predictions made by cognitive reserve theory. Due to the greater accumulation of neuropathology in those with higher levels of reserve (i.e., bilinguals), the inflection point of decline occurs later than those with low reserve (i.e., monolinguals). The endpoint of cognitive impairment, however, remains similar regardless of reserve. Thus, there is a steeper slope, or faster decline, for those who are able to withstand the detrimental effects of neuropathology for a longer time. This finding of sharper decline is not unique to bilingualism and has also been shown using the previously mentioned proxy of education (e.g., Scarmeas et al. 2006; Stern et al. 1999).

Cognitive reserve — defined in terms of bilingualism for the current study — attenuates age-related decline presumably through the strengthening of neural networks. This strengthening refers both to the accumulation of neural resources prior to decline (through disease or typical age-related decline) and to compensation in alternate networks in response to task demands (see Cabeza et al. 2018, for a review). Typically, studies match participants on cognitive level and then examine the corresponding brain integrity associated with specific cognitive outcomes. However, this approach does not address what the cognitive outcomes would be for monolinguals in older age who showed the same level of neuropathology. This is the question for the present study.

The present study reverses the usual convention of matching participants on cognitive health to compare brain integrity. Instead, bilinguals and monolinguals were matched on white matter integrity and then cognitive health was evaluated. First, a principal component analysis (PCA) was conducted on white matter parameters to extract a component across each of these correlated measures which captured the variation in average white matter diffusivity and reduced multicollinearity and multiple comparisons. Then, a sample of cognitively healthy older adult bilinguals were matched on white matter to a subset of monolinguals using PSM. Finally, a randomization analysis was used to compare cognitive health. If bilingualism leads to cognitive reserve, then monolinguals matched to cognitively healthy bilinguals on white matter integrity will show less favorable cognitive outcomes than bilinguals as measured by clinical diagnoses and cognitive measures. This reversal of the usual approach to matching is novel in the literature. It is also suited to studies that have collected samples of "healthy" older adults which can then be matched to individuals in large databases which include a wider spectrum of cognitive abilities and brain states.

Method

Participants

Forty cognitively healthy older adult bilinguals and 38 cognitively healthy older adult monolinguals were recruited from the community for a prior study (Anderson, Grundy et al. 2018b). Screening for language status was conducted via telephonic interviews using the *Language and Social Background Questionnaire* (LSBQ; Anderson, Mak et al. 2018c). All participants were right-handed with no known neurological impairments or MRI contraindications. Diffusion-weighted scans were subsequently performed and the resulting images were analysed. When compared by group, bilingual participants showed lower FA and higher DA values than monolinguals in regions that included, but were not limited to, the anterior corpus callosum, corona radiata, and superior temporal longitudinal fasciculus. That is, when matched for cognitive level, bilinguals showed more neuropathology than monolinguals as found in previous research.

To reverse the standard approach, the data from these bilingual individuals were then used as the baseline to match a new group of monolinguals with similar values for white matter integrity.

Data for monolinguals were obtained from the Alzheimer's Disease Neuroimaging Initiative (ADNI) database (*adni.loni.usc.edu*), specifically from the ADNI-3 study. Detailed language and social background information were not as readily available as that obtained from the LSBQ, so categorization as monolingual involved some assumptions. Patients were selected for inclusion if their primary language and preferred language of testing were both English. Additionally, they were considered monolingual if they were identified as white or African American and were neither Latino nor Hispanic. It is impossible to rule out the possibility of other language use, but the ethnic, racial, and language criteria provided make it unlikely that these individuals used languages aside from English to a significant degree in their daily lives. After individuals in the database were identified to fit the inclusion criteria, participants for the study were selected through serial search. Participants who had T1-weighted, FLAIR, and axial DTI files available were chosen, for a total of 165 monolingual older adults.

Data acquisition

Bilingual participants were scanned at York University using a Siemens Trio 3 T scanner with a 32-channel head coil. DTI scans were whole-brain 64-direction diffusion-weighted images, with TR = 9200 ms, TE = 86 ms, voxel size of 2.0 mm^3, and FOV = 192 mm.

Monolingual participants taken from the ADNI database were tested at various sites across the United States and Canada, but all used a GE, Siemens, or Phillips scanner. DTI scans were whole-brain 48-direction diffusion-weighted images, obtained with TR = 7200 ms, TE = 56, and voxel size of 2.0 mm^3 for all scanner models. All scans were screened at Mayo Clinic for quality control before being accepted into the ADNI database.

Data processing

The same protocol for MRI processing was applied separately for the bilingual and monolingual groups. Processing was performed in part using the MRtrix3 package (www.mrtrix.org), which included the initial step of de-noising using the dwidenoise function. To utilize TOPUP, a synthetic b = 0 image was created following the Synb0-DisCo protocol (Schilling et al. 2019) and subsequently merged with a real b = 0 image obtained during scan acquisition. The results from TOPUP were then used for eddy distortion correction using the eddy function in FSL. Denoising was again done on the eddy output using *dwidenoise*, and residual maps were examined for quality control. Scans with high residual noise were excluded at this point as this indicated that EDDY had done a poor job modeling the data ($n = 8$ bilinguals, $n = 4$ monolinguals). Following this, a diffusion tensor was fit using the DTIFIT command from FSL. Finally, Tract-Based Spatial Statistics (TBSS; Smith et al. 2006) included in FSL was utilized on the FA images from the DTIFIT output. Each participant's FA images were aligned to a $1 \times 1 \times 1$ mm standard space utilizing nonlinear registration, and subsequently all merged together into a single 4D image. The mean of all FA images was created, as well as a thinned FA skeleton representing the centers of tracts common to all participants. This methodology was then applied to DA and DR data, and tracts were identified post-hoc using the John Hopkins University DTI based probabilistic white matter atlas included in FSL.

The numbers of participants included after following these steps were 32 bilinguals and 161 monolinguals after removing participants with scans that were not of sufficient quality (e.g., containing slice drop out).

Analyses and results

Once whole brain values of FA, DA, and DR were obtained for every participant, principal components analysis (PCA) was conducted. Briefly, PCA uses an orthogonal transformation to simplify complex data while preserving any trends or patterns (Lever et al. 2017). Furthermore, PCA is "blind" in that it finds patterns without prior knowledge of group inclusion or treatment. FA, DA, and DR measures were the input variables, with close to 80% of the variance in the data accounted for by the first principal component (Fig. 1). For the first principal component, a loading score was derived per participant (similar to the concept of "factor scores" from factor analysis) which reflected each person's relative position in this multivariate space, and this was used in the subsequent PSM step. Thus, the PCA provided a single overall assessment of white matter integrity that captured about 80% of the variation.

To compare cognitive health (i.e., clinical diagnosis) between the two groups, PSM was used to explicitly match bilinguals to monolinguals. PSM is a useful method for sampling from a large reservoir of control participants (monolinguals) to create a smaller subsample with a distribution of covariates that is similar to the distribution in the treated group (bilinguals) (Rosenbaum and Rubin 1983). A propensity score is calculated and used as a balancing score wherein participants with similar propensity scores will have similar baseline covariate values regardless of the treatment group. Although there does not seem to be a consensus on which variables to include in the propensity score model, theoretical models suggest including any variables that may

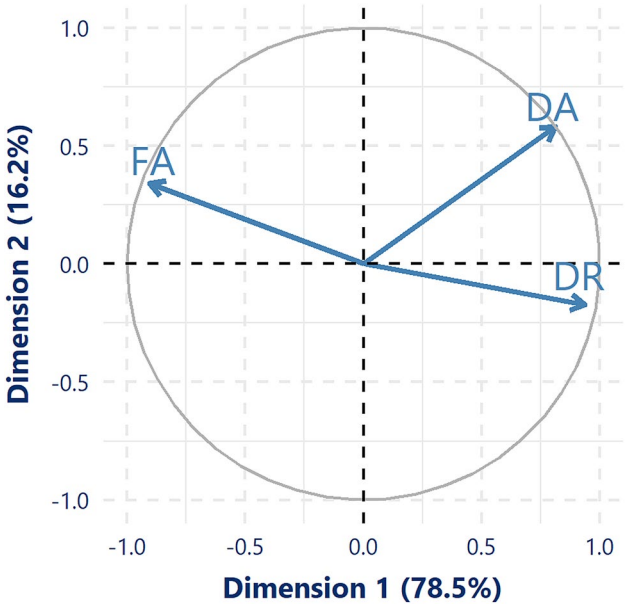

Fig. 1 Variables factor map of principal component analysis using fractional anisotropy (FA), axial diffusivity (DA), and radial diffusivity (DR) measures as input variables

influence treatment assignment (Austin 2011). Additionally, one-to-one matching is the most common implementation of PSM such that pairs of control and treated participants are created with similar propensity scores. In this way, the sample of control participants should be reduced to match the treatment group, in the present case producing 32 participants in each group.

For the analyses, the MatchIt package in R (Ho et al. 2007) was used using the following formula: matchit(Group ~ Sex + Education + Age + PCA, data, method = "nearest", distance = "logit", discard = "treat"). Sex, education, age, and first principal component scores were included as baseline covariates to predict treatment conditions, with the 'discard' option specified such that any bilinguals who were sufficiently different from the propensity score model would be excluded. The final sample after this step included 32 bilinguals and 32 monolinguals for which analyses were then performed.

Due to the nature of the current study, comparing clinical diagnoses between bilinguals and monolinguals would yield little of value. Bilingual participants were selected for the original study on the basis of having reported being cognitively normal (CN), whereas monolingual participants were chosen at random from a larger pool which encompassed CN, MCI, and AD diagnoses. As shown in Table 1, the distribution of these diagnostic categories in the unmatched monolingual sample was as follows: 117 considered to be CN, 34 MCI, and 10 with AD. However, the measurement of interest is the diagnoses of monolinguals *after* they have been matched on bilingual brain health measures compared to the diagnoses of the original larger monolingual sample that was randomly selected. To accomplish this, a cognitive profile score was created and assigned for each participant. A score of 0 indicates a diagnosis of CN, while a score of 1 indicates impairment (i.e., MCI or AD). MCI and AD were not differentiated in value because any impairment past normal cognition was noteworthy. The unmatched monolingual sample had a mean cognitive profile score of 0.27 compared to a mean score of 0.41 for the matched monolingual sample. That is, ~ 27% of unmatched monolinguals had a diagnosis of MCI or AD, whereas ~ 41% of matched monolinguals had received a clinical diagnosis of impairment.

To compare the proportion of cognitively impaired individuals in the matched sample to the overall sample, a null distribution was created using the *infer* package in R (https://github.com/tidymodels/infer) by running 1000 permutations of random samples of monolinguals using the "true"

Table 1 Demographic information and mean brain measures (with standard deviations) for the full unmatched monolingual sample, bilingual sample, and matched monolingual sample

Group	*N*	Age in years	Education in years	MMSE	Fractional anisotropy	Axial diffusivity	Radial diffusivity	PCA scores	Cognitive profile
Monolinguals (unmatched)	161 (58% F)	71.3 (7.1)	16.8 (2.3)	28.3 (2.7)	0.48 (0.03)	1.2×10^{-3} (0.03×10^{-3})	5.5×10^{-4} (0.4×10^{-4})	−0.36 (1.4)	CN = 117 (73%) MCI = 34 (21%) AD = 10 (6%)
Bilinguals	32 (72% F)	73.5 (3.8)	16.1 (2.8)	29.4 (0.7)	0.42 (0.02)	1.2×10^{-3} (0.02×10^{-3})	6.6×10^{-4} (0.5×10^{-4})	1.79 (1.1)	**CN = 32 (100%)**
Monolinguals (matched)	32 (69% F)	73.1 (6.5)	16.3 (2.5)	26.7 (4.4)	0.45 (0.02)	1.2×10^{-3} (0.04×10^{-3})	6.1×10^{-4} (0.4×10^{-4})	1.32 (1.2)	**CN = 19 (59%) MCI = 8 (25%) AD = 5 (16%)**

The relevant comparison in Cognitive Profile between the bilinguals and matched monolinguals is indicated in bold

CN Clinically normal, *MCI* Mild cognitive impairment, *AD* Alzheimer's disease

proportion of 0.27, against which the sample proportion of 0.41 was compared.

Demographic information, DTI measures, and PCA scores for the full monolingual sample, bilingual sample, and matched monolingual sample are presented in Table 1. The matched dataset had a balance improvement of 62% on propensity scores in that matched monolingual propensity scores ($M = 0.34$) more closely matched bilingual propensity scores ($M = 0.49$) than when using those of the full monolingual sample ($M = 0.10$). Other predictive covariates were also improved from a range of 75% for education levels to 80% for age.

T-tests were performed to compare the bilingual and matched monolingual groups on the covariates entered in the PSM model. There were no significant differences between groups on education, $t(62) = 0.29$, $p = 0.78$, $d = 0.07$, age, $t(62) = 0.33$, $p = 0.74$, $d = 0.08$, or PCA scores, $t(62) = 1.61$, $p = 0.11$, $d = 0.4$. A chi-square test also revealed no difference in proportions of sex between the two groups, $p = 1$. Due to possible protocol and scanner differences between testing sites, an additional ANOVA test examining PCA scores in the matched sample as a function of site was conducted. There was no significant difference in the overall model, $F(16, 47) = 1.43$, $p = 0.17$, $\eta^2 = 0.33$, nor were any pairwise comparisons between sites significant using a Tukey adjustment, $ps > 0.05$.

Once predictive covariates and brain health were matched between groups, two variables of interest were considered: cognitive performance as measured by MMSE scores and clinical diagnoses of participants. First, a one-way ANOVA revealed a significant difference in MMSE scores, $F(1, 62) = 12.17$, $p < 0.001$, $\eta^2 = 0.16$, where bilinguals had higher mean MMSE scores ($M = 29.4$) than monolinguals ($M = 26.7$).

Second, the proportion of individuals in each of the three groups described as CN, MCI, and AD are reported in Table 1. A randomization-based test for a single proportion was used to compare the proportion of cognitively impaired participants in the matched sample to the overall sample of monolinguals from the ADNI database (Fig. 2). The matched monolingual sample had significantly poorer clinical outcomes (i.e., higher scores on the cognitive profile score reflecting MCI and AD) than that predicted by a null distribution generated from resampling the unmatched sample, $p < 0.001$. Thus, the matched monolingual sample was more cognitively impaired than would be expected in a theoretical population of both cognitively normal and impaired individuals.

Discussion

Previous studies have focused on bilingualism as a form of cognitive reserve by using different types of measures including (but not limited to) executive functioning (see

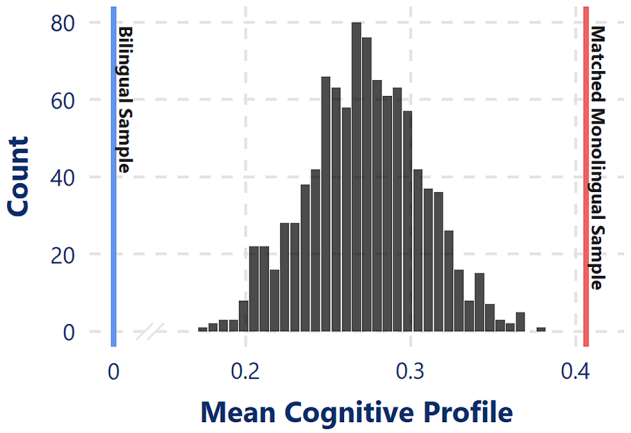

Fig. 2 Randomisation-based null distribution of mean cognitive profiles (where 0 = 'Healthy' and 1 = 'Unhealthy') with matched monolingual sample (red line) and bilingual sample (blue line)

Bialystok 2017 for review), brain imaging (e.g., Abutalebi et al. 2014, 2015), or dementia onset (e.g., Alladi et al. 2013; Bialystok et al. 2007; Chertkow et al. 2010; Woumans et al. 2015). These studies typically match participants on age and cognitive level and generally report that, when compared to monolinguals, bilinguals show greater brain atrophy but better (or equivalent) cognitive outcome. However, this approach leaves unanswered the question about how different levels of brain health correspond to cognitive outcomes in these two groups, the reverse of the question that is usually examined. In other words, how would monolingual older adults cope with the levels of brain integrity found for bilinguals? The present study aimed to fill that gap.

A crucial measure of brain health is white matter integrity, but there is a lack of consistency regarding how these measures and cognitive performance are impacted by bilingualism with ageing. In the study by Luk, Bialystok et al. (2011a), bilinguals had better white matter integrity than monolinguals as measured by higher FA values in the corpus callosum and superior and inferior longitudinal fasciculi. By contrast, Gold et al. (2013) found that bilinguals had poorer white matter integrity than monolinguals, showing lower FA values in the same regions found by Luk, Bialystok et al., as well as in the fornix. The findings by Anderson, Grundy et al. (2018b) are less clear: stricter matching criteria using PSM resulted in higher DA values for bilinguals than monolinguals in parts of the corpus callosum and the left superior temporal longitudinal fasciculus. Unlike the findings of Luk, Bialystok et al. and Gold et al., no differences in FA were found. The interpretation by Anderson, Grundy et al. was that DA enhances white matter integrity as "an index of diffusion along the primary gradient that is associated with positive cognitive outcomes", and thus bilinguals had better white matter integrity than monolinguals. However, studies examining white matter integrity in older age show

that DA values increase with age past the 6th decade of life (Michielse et al. 2010), and that groups with Alzheimer's dementia show higher DA values than those without (Bosch et al. 2012; Salat et al. 2010). Rather than high DA values being an indicator of maintained neural integrity as claimed by Anderson, Grundy et al., evidence suggests that it may in fact be the reverse, i.e., poorer brain health. The loadings of variables in the factor plot from the current study support the interpretation that DA and DR are associated with cognitive decline, as they correlate together along dimension 1 but negatively correlate with FA in the same dimension, which is presumably associated with cognitive health (Fig. 1). The overall PCA scores provide a holistic assessment of white matter integrity while simultaneously accounting for most of the variance in the original variables.

In all three previous studies of white matter and bilingualism, both bilinguals and monolinguals were considered cognitively healthy older adults. This assumption was confirmed, in part, by similar cognitive performances across groups within each of the studies. Yet, despite this cognitive and clinical similarity, bilinguals were more likely to present with poorer white matter integrity than monolinguals (e.g., Anderson, Grundy et al. 2018b; Gold et al. 2013) rather than the reverse (e.g., Luk, Bialystok et al 2011a). This was true for the participants in the study by Anderson, Grundy et al., from which the bilingual group in the current study were drawn. What is not addressed by these studies is what would be the cognitive outcomes for monolinguals if their brain integrity was at the level of bilinguals. Put another way, what would the cognitive and clinical outcomes be for monolinguals if they "swapped brains" with bilinguals?

The current study was designed to investigate this question. After matching older adult monolingual participants to bilinguals on sex, age, education, and brain integrity (as measured by a primary PCA score) it was shown that monolinguals whose brain parameters were matched to bilinguals showed more advanced clinical decline. This was reflected in more clinical diagnoses of MCI and AD than what would be expected by chance within the monolingual matched sample and lower cognitive performance, as seen by poorer MMSE scores. To our knowledge, this is the first study to examine cognitive and clinical outcomes between bilinguals and monolinguals by using this "brain swap" technique to match individuals on brain health rather than the reverse.

Despite the relatively poorer neural health of bilinguals than monolinguals in the studies by Gold et al. (2013) and Anderson, Grundy et al. (2018b), bilinguals still had comparable cognitive performance. In the present study, monolinguals showed poorer cognitive performance and poorer clinical outcomes when matched to bilinguals on brain health, a finding consistent with our predictions regarding the contribution of bilingualism to cognitive reserve. Bilinguals performed near ceiling on MMSE scores, while monolinguals' scores in the matched sample were borderline to MCI (despite being matched for age, sex, education, and brain health). These results suggest that monolinguals are less able to cope with neural degeneration than bilinguals.

White matter integrity was selected as the measure by which to judge brain health, in part as it provides an index of connectedness between neural networks, and as an extension of the work by Anderson, Grundy et al (2018b). However, from the perspective of cognitive reserve, using other measures of brain health such as cortical thickness or cerebral atrophy would theoretically lead to a similar pattern of results as seen in the current study. A study by Pettigrew et al. (2017) examined cortical thickness in cognitively normal individuals using cognitive reserve as a factor in predicting progression to MCI. Their findings showed that higher mean cortical thickness at baseline was associated with a reduced risk of clinical symptom onset within 7 years of initial scan, and higher cognitive reserve was similarly associated with reduced symptom onset in general. However, an interaction between the two factors suggested that individuals with low cognitive reserve were more likely to develop clinical symptoms further out from baseline than those with high cognitive reserve, i.e., high reserve individuals were better able to compensate for cortical atrophy that occurs in the earlier stages of disease progression. If one considers that the participants in this study by Pettigrew et al. were an average age of ~ 57 years at baseline, then their results suggest that testing high reserve against low reserve individuals in later years of life, and consequently atrophy, would lead to similar results as the present study.

Considering that the present results seem to rule out whole-brain white matter integrity as the mechanism by which bilingualism modulates cognitive reserve (i.e., white matter integrity is poor in bilinguals despite normal cognition and thus other measures must be responsible for cognitive maintenance), three studies examining cerebral atrophy in bilingual and monolingual older adults are worth mentioning here. In the first, Abutalebi et al. (2015) found greater grey matter volume in the left and right inferior parietal lobules for cognitively normal bilinguals compared to their monolingual peers. The second study, by Costumero et al. (2020), found reduced parenchymal brain volume for bilinguals than monolinguals in a sample of patients with MCI. The third study, by Schweizer et al. (2012), showed greater cerebral atrophy in bilinguals than monolinguals in a sample of patients with probable AD. In all three studies, the language groups were matched on cognitive status. Together, it appears that in older age the stage at which measures are taken could greatly impact the conclusions that are drawn. Older adult bilinguals may have greater grey matter volume in normal cognition but undergo cerebral atrophy at a quicker rate than monolinguals once they progress to MCI and AD. This is in line with cognitive reserve theories and

may point to the mechanism by which bilinguals are better able to cope with decline while maintaining cognitive performance, via an accumulation of neural resources prior to decline.

For the current study, the MMSE was used as an indicator of cognitive level as it was available in both the bilingual and ADNI samples. Meta-analyses of studies examining the effect of bilingualism on clinical status and dementia show that a majority use the MMSE as a measure of cognitive performance (Anderson et al. in press; Brini et al. 2020), although some have argued that there are issues with the MMSE as a diagnostic tool due to its low sensitivity, requiring the use of other tests in tandem for optimal results (e.g., Berkes et al. 2020; Mitchell 2009). Ideally, the bilingual group in the current study would have been tested on the neuropsychological battery used in the ADNI sample to align cognitive performance to the monolingual group across a wider array of measures, although this was not possible in the present study.

The current study also has other limitations. As mentioned earlier, monolingual patients were selected from the ADNI database and as such did not have objective language measures to fully confirm language usage or proficiency. Future studies would be better served by having more detailed language information from participants, including but not limited to all languages known or studied along with proficiency, ages of acquisition, and daily language exposure. Other limitations inherent in the ADNI database is the usage of different MRI scanner models across hospital sites. Variability in data between sites could be due to differences in acquisition protocols, scanning parameters, and scanner manufacturers. However, a positive feature of the ADNI dataset is a standardised scanning protocol across collection sites to minimise differences inherent in scanner model, alongside quality control at the Mayo clinic to ensure minimal differences in scans across sites. Reassuringly, the analyses examining effects of site on PCA scores in the current study did not reveal any significant trends. Regardless, future studies should aim to collect all images using the same scanner model and software, or failing that option, follow the advice of Fortin et al (2017) to harmonize data collected across different sites.

The current study adds unique evidence to support the claim that bilingualism is a cognitive reserve factor. In contrast to typical studies of cognitive reserve in which neural markers are outcome measures, in this case, individuals were matched on *neural parameters* derived from diffusion tensor imaging and diagnostic status was compared. Bilingual status was associated with an ~ 40% reduced chance of having a diagnosis of either MCI or Alzheimer's disease. Furthermore, these results cannot be explained by sex, age, or education, suggesting that bilingualism confers a unique protective benefit. Bilingualism and its associated benefits across neural networks (e.g., Bialystok et al. 2012; Brini et al. 2020) seem, at a minimum, to postpone deleterious effects of ageing and poor brain health, whereas monolinguals are more likely to suffer the consequences of earlier cognitive decline. The current findings provide new evidence that bilingualism protects individuals from negative clinical outcomes in the face of ageing and neural degeneration.

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Code availability Available upon request.

Compliance with ethical standards

Conflict of interest None.

Ethics approval The research study was approved by York University's Ethics Review Board and conforms to the standards of the Canadian Tri-Council Research Ethics guidelines.

Consent to participate Bilingual participants signed written consent before the study and verbal assent throughout out. Monolingual participants were selected from the ADNI database where consent procedures were handled by ADNI.

Consent for publication All authors consent to publication.

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