

Bilingualism modulates the white matter structure of language-related pathways

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ABSTRACT

Learning and speaking a second language (L2) may result in profound changes in the human brain. Here, we investigated local structural differences along two language-related white matter trajectories, the arcuate fasciculus and the inferior fronto-occipital fasciculus (IFOF), between early simultaneous bilinguals and late sequential bilinguals. We also examined whether early exposure to two languages might lead to a more bilateral structural organization of the arcuate fasciculus. Fractional anisotropy, mean and radial diffusivities (FA, MD, and RD respectively) were extracted to analyse tract-specific changes. Additionally, global voxel-wise effects were investigated with Tract-Based Spatial Statistics (TBSS). We found that relative to late exposure, early exposure to L2 leads to increased FA along a phonology-related segment of the arcuate fasciculus, but induces no modulations along the IFOF, associated to semantic processing. Late sequential bilingualism, however, was associated with decreased MD along the bilateral IFOF. Our results suggest that early vs. late bilingualism may lead to qualitatively different kind of changes in the structural language-related network. Furthermore, we show that early bilingualism contributes to the structural laterality of the arcuate fasciculus, leading to a more bilateral organization of these perisylvian language-related tracts.

1. Introduction

Learning is rooted in the brain's ability to reorganize itself in response to changing demands (Lövdén et al., 2010) and each new skill is, by and large, reflected as changes in neural connections. Learning and speaking a second language (L2) is a sustained experience, which may have a profound impact on the brain. Speaking multiple languages has been shown to lead to a variety of functional changes, and evidence of specific brain activation patterns related to bilingual language processing is abundant (for a recent review, see e.g. Costa and Sebastián-Gallés, 2014). While functional adaptations in response to L2 experience have been extensively investigated, there are fewer studies on L2-induced structural changes. However, a growing body of research has shown that bilingualism-induced functional changes are, in fact, often accompanied by anatomical changes in the brain structure (for reviews, see e.g., Li et al., 2014; Stein et al., 2014). Bilingualism has been associated with structural modulations in e.g.,

the left inferior parietal lobule (Mechelli et al., 2004), left inferior frontal gyrus (Stein et al., 2012), anterior temporal pole (Abutalebi et al., 2014) and the cerebellum (Pliatsikas et al., 2014), measured, for instance, as changes in grey matter density. The extent of these modulations has been found to be sensitive to L2 proficiency and the age of L2 acquisition (Stein et al., 2014). Similar age of acquisition and proficiency effects (e.g. Perani et al., 2003; Li et al., 2014) have also been reported in functional activation studies on L2 processing, particularly for the left inferior parietal and frontal areas.

Recent diffusion weighted magnetic resonance imaging (MRI) studies have also begun to investigate the possible structural white matter changes related to bilingualism. Diffusion tensor (DT) derived measures such as fractional anisotropy (FA) or radial and mean diffusivities (RD and MD respectively) have been used to describe the underlying microstructure and fibre organizations of the tracts. FA is a scalar measure between zero and one that describes the degree of anisotropy within a voxel. Values close to one indicate that the diffusion

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is highly restricted and only occurs along one orientation, while values near zero signify unrestricted diffusion, i.e., diffusion can occur in all orientations. Higher FA values are typically observed in regions where axons are densely packed and run parallel to each other, as water molecules cannot move across the axonal walls but are free to diffuse along them (Van Hecke et al., 2016). FA is highly sensitive to changes in the microstructural architecture, without providing insight about the specific type of change (Alexander et al., 2007). Factors that can modulate the FA include, but are not limited to, the degree of axonal myelination, axonal packing density, membrane permeability, the organizational coherence of the axons, and measurement technical details (Jones et al., 2013; Sairanen et al., 2017). In general, high FA values have been taken to indicate higher white matter integrity (Smith et al., 2006), although this interpretation has received considerable criticism of its vagueness (see e.g. Jones et al. 2013). RD and MD convey information about the diffusion magnitude and they are inherently related to FA, although both offer slightly different information: increased RD values have been linked to de- or dysmyelination of axons (Song et al., 2002), while MD is an inverse measure of the membrane density (Alexander et al., 2007). Furthermore, decreased MD in particular with increased FA has been suggested to reflect increasingly dense and ordered packing of the fibre tracts (Takahashi et al. 2000; Schmithorst et al. 2002).

Most DT studies on bilingualism have looked for global differences at the whole-brain level by utilizing Tract-Based Spatial Statistics (TBSS). This approach allows for comparing FA values, or any other tensor-derived values, with voxel-wise statistics at the centres of tracts common to all participants (Smith et al., 2004, 2006). These TBSS studies have reported a variety of sites responding to bilingualism, e.g., superior longitudinal fasciculus (Luk et al., 2011; Pliatsikas et al., 2015), inferior longitudinal fasciculus (Luk et al., 2011) and uncinate fasciculus (Luk et al., 2011). However, the two regions most consistently showing bilingualism-induced changes are the corpus callosum (CC) (Coggin et al., 2004; Luk et al., 2011; Mohades et al., 2012; Schlegel et al., 2012) and the inferior occipito-frontal fasciculus (IFOF) (Cummine and Boliek, 2013; Gold et al., 2013; Mohades et al., 2012). The IFOF is a long trajectory connecting the inferolateral and dorsolateral frontal cortex with the posterior temporal and occipital lobe (Catani et al., 2002; Jellison et al., 2004). It has been suggested to be relevant in semantic aspects of language processing (e.g. Duffau et al. 2005; Leclercq et al. 2010). Despite consistently reported differences for bilinguals vs. monolinguals at these locations, the directionality of the effect has varied. While some studies have shown increased FA for bilinguals in both locations (Luk et al., 2011; Pliatsikas et al., 2015), others have reported an opposite pattern of decreased FA for bilinguals (Cummine and Boliek, 2013; Gold et al., 2013; Kuhl et al., 2016). Due to contradictories in the findings, the exact effects of bilingualism on the IFOF remain ambiguous.

While analysis at the whole-brain level gives important information about the global effects of bilingualism, there are some restrictions related to this approach. First, the bilingual brain appears to be functionally less lateralized and more bilaterally balanced (Hull and Vaid, 2007) than the monolingual brain (but see e.g. Paradis, 1990). Since the CC is crucial in mediating information exchange between the two hemispheres, the reported changes in the CC fit well in line with the assumed more bilateral configuration of the bilingual brain. However, the salience of this effect might obscure smaller and more local tract-specific effects. Second, one step in the TBSS analysis pipeline involves skeletonizing the FA maps, a procedure aimed at improving comparability of the diffusion data across participants and between groups. This step leads to losing detailed participant-wise information about individual tracts and in some extreme cases can lead to entirely ill-posed comparisons if the projection of participant-wise tracts fails (Bach et al., 2014). Furthermore, the TBSS skeleton projection has been shown to be particularly vulnerable to distortions and misalignment in regions where pathways merge or the tract

structure is circular in form (like e.g. the uncinate fasciculus) (Bach et al., 2014).

One important language-related tract that might suffer from the TBSS skeletonization procedure due to its complex structure and circular form, is the arcuate fasciculus. It is a pathway connecting temporal, parietal and frontal language regions via one direct and two indirect trajectories between Broca's and Wernicke's regions (Catani et al., 2005). These three separable segments have been suggested to have designated functions of their own: the left direct segment, for instance, has been related to phonological language functions (Catani et al., 2005; Forkel et al., 2014; López-Barroso et al., 2013), while left indirect trajectories (specifically the posterior part) have been suggested to underlie semantic language functions (Binder and Desai, 2011; Catani et al., 2005). So far, only one (longitudinal) study (Mohades et al., 2015, 2012) has used a tract of interest (TOI) approach to locally compare FA values between groups of mono- and bilingual children. They investigated changes in four preselected TOIs associated with language processing and communication, among them the left arcuate fasciculus/superior longitudinal fasciculus and the left IFOF. They reported increased FA values for simultaneous bilinguals only along the left IFOF, but found no effects of bilingualism on the arcuate fasciculus in these child participants.

Considering the important role of the arcuate fasciculus in conveying information between two major language-related sites, the processing demands entailed by bilingualism might modulate the lateralization of this structure. In the right-handed population, the speech and language functions have been shown to demonstrate notable leftward asymmetries (e.g., Cabeza and Nyberg 2000), along with leftward structural lateralization patterns of the perisylvian language-related tracts (Glasser and Rilling, 2008; Nucifora et al., 2005). However, the degree of structural lateralization has been shown to vary between individuals from an extreme left lateralization to a relatively bilateral configuration (Catani et al., 2007). Furthermore, higher symmetry in the structure of the arcuate fasciculus has been found to predict better performance in verbal recall task (Catani et al., 2007). As bilinguals tend to exhibit more bilateral functional activations in linguistic tasks in general (for review, see e.g. Hull and Vaid, 2007), this functional symmetry might also be reflected in the underlying structural organization. However, to the best of our knowledge, there are no studies on the structural correlates of the bilingual functional language lateralization.

Here, we examined a) how early bilingualism affects local white matter structures along two major language trajectories and b) whether there are bilingualism-related structural lateralization differences in the arcuate fasciculus. More specifically, structural properties (FA, RD and MD values) of the IFOF and the three segments of the arcuate fasciculus (presented in Fig. 2A) were assessed bilaterally between early simultaneous bilinguals and late sequential bilinguals. These specific fibre bundles were chosen due to their strong links to language processing. Furthermore, the arcuate fasciculus connects the inferior parietal and frontal regions, which have been linked to bilingualism-induced grey matter changes. Additionally, as the arcuate fasciculus has been shown to reflect the degree of language lateralization, focusing on this structure enables comparisons of structural lateralization patterns between groups with differing bilingualism status.

2. Materials and methods

2.1. Participants

30 young right-handed adults (15 early Finnish-Swedish bilinguals; 15 late English second language speakers, Finnish as a native language), recruited via university mailing lists and matched for age (early bilinguals: $M=26.86$ years, $SD=5.67$, late bilinguals: $M=29.21$ years, $SD=4.54$) and gender (early bilinguals: 47% males, late bilinguals: 67% males) participated in the study. The early bilinguals had learned their

two languages before the age of 5 (mean L2 age of acquisition, $AoA=2.72$, $SD=2.00$), while late L2 speakers had no bilingual exposure before school (mean L2 $AoA=8.92$, $SD=.28$).

Both late and early bilingual groups had learned additional languages within the Finnish basic education program. The first language introduced at school was English at the age of 9 for both groups. For early bilinguals, English is thus their L3 (mean L3 $AoA=9.4$ years, $SD=.07$), whereas for late bilinguals it is L2. Moreover, the late bilinguals started learning the obligatory Swedish as their L3 on average at the age of 11 (mean L3 $AoA=11.2$ years, $SD=1.5$). In addition to these three languages (Finnish, Swedish and English), the early bilingual participants reported having studied, on average, 2.6 ($SD=1.1$) other languages and the late bilinguals 2.8 ($SD=1.2$) other languages. The groups did not differ with regard to the number of additional languages studied nor did they differ regarding the average number of years spent studying these additional languages ($M=7.3$ years, $SD=1.7$ and $M=7.1$ years, $SD=1.6$ for the early and late bilinguals respectively).

Both groups rated themselves as highly proficient in English in all four modalities and reported active usage of English in their everyday lives. The early bilingual group also reported using both their native languages frequently. For additional details regarding the participants' language background, see Table 1. Due to participants' identical exposure to foreign languages in school and to their similar L3 AoA , any emerging differences between the groups can be attributed to the difference in their bilingualism status during childhood (for similar groups, see e.g. Lehtonen et al. 2012). The choice of the participant groups was also motivated by Kaiser and colleagues (Kaiser et al., 2015), who proposed that the differences based on the age of L2 acquisition persist into adulthood and remain observable even though other languages are introduced later in life.

Two participants, one from each group, were excluded from the final analysis due to not meeting all background criteria (one had a medication for clinical depression, the other reported having an undiagnosed dyslexia). None of the remaining participants reported any neurological or psychiatric disorders nor had they medications that might affect the central nervous system. The participants gave their written informed consent to participate in the experiments. The experiments were performed in accordance with the Declaration of Helsinki. Ethical permission for the experiment was issued by the University of Helsinki Ethical Review Board of Humanities and Social and Behavioural Sciences.

2.2. MRI acquisition

Subjects were scanned with Siemens Skyra 3T MR (Erlangen, Germany) scanner using a 32-channel head matrix coil. The full brain single shot echo planar imaging (SS-EPI) sequence was used with following parameters: repetition time (TR) 9600 ms, echo time (TE) 81 ms, field-of-view 240 mm, voxel size $2 \times 2 \times 2 \text{ mm}^3$, b-value 1000 s/mm^2 , number of averages 1, and GRAPPA factor 2. Used diffusion gradient scheme was provided by the vendor and consisted of diffusion-weighted volumes in 64 non-collinear directions with one b0-volume. To enhance the reliability of the DT estimations, additional two b0-volumes were gathered in both posterior-anterior and anterior-posterior phase encoding directions.

2.3. DWI preprocessing and tractography

Data preprocessing was performed using FSL (Smith et al., 2004) installed on the Alcyon computing cluster (138 Xeon X5650 and 4 Xeon X7550 processors) at the University of Helsinki Department of Physics and the tensor estimations and tractography in ExploreDTI (Leemans et al., 2009). Full workflow is shown in Fig. 1. Tractography regions of interests (ROIs) were manually drawn based on anatomical landmarks to tract anterior, posterior, and long segments of arcuate

fasciculus (Catani et al., 2002) and IFOF (Catani and de Schotten, 2012) separately. Anatomically implausible tracts in frontal, superior, and posterior brain regions were excluded with proper NOT ROIs. Deterministic tractography was done with following parameters: minimum FA in seed point 0.2 and in tracing 0.1, maximum FA in tracing 1, maximum angle 55° , step size 0.5 voxels, tract minimum 35 mm and maximum 350 mm, and seedpoint supersampling $2 \times 2 \times 2$.

2.4. Statistical analysis

Statistical analysis was performed using IBM SPSS Statistics 22.0. To test the influence of bilingualism status on the mean tract-specific diffusion indices, a linear mixed regression model approach for analysis of variance was used with participants as random intercepts and pairwise post-hoc tests adjusted for multiple comparisons (Bonferroni). The mixed model approach allows for modelling of random variance due to inter-subject variability (random intercept), as well as accounting for missing data points. In the model, tract-specific mean FA, RD and MD values were treated as dependent variables, while Tract (4 tracts per hemisphere; direct, anterior, and posterior segments of arcuate fasciculus and IFOF) was defined as a repeated factor. The primary fixed effects were Group (early vs. late bilinguals) and Group by Tract interaction. Diagonal covariance matrix was used in all mixed model analyses.

To investigate possible structural lateralization differences between groups we adapted the analysis procedure described by Catani et al., (2007). The lateralization index was calculated by counting the number of reconstructed pathways within the direct segment for each hemisphere. A k-means cluster analysis was then performed to classify the participants into three groups representing the different lateralization configurations. A Fisher's exact test was used to assess the distribution of the lateralization across participants and between groups. For post-hoc comparisons, a contingency table analysis adjusted for multiple comparisons (Bonferroni) was used.

2.5. TBSS and tract-specific TBSS analysis

To facilitate comparisons to previous literature, a whole-brain level TBSS analysis was used to assess global bilingualism induced effects. FA, RD, and MD images were exported from ExploreDTI (Leemans et al., 2009) in NIfTI format and workflow described in FSL's userguide for TBSS (Smith et al., 2004, 2006) was applied to locate differences between groups. In TBSS analysis, the mean skeleton was thresholded using a value of 0.2, and FA, RD, and MD values were projected into subject-wise skeletons in MNI152 space. Skeletonized voxel-wise values were ranked to minimize impact of possible outliers in any group (Stjerna et al., 2015). Permutation tests (Winkler et al., 2014) were performed using Threshold-Free Cluster Enhancement (TFCE) (Smith and Nichols, 2009) with 20,000 permutations to locate differences between groups. Results were corrected for familywise errors due to multiple comparisons.

Tract-specific TBSS analysis allows for a more detailed mapping of the changes between groups by highlighting the exact voxels where the changes are located along the tracts. In this analysis, the mean skeleton was not thresholded but it was further restricted using binary masks of each studied segment of the arcuate fasciculus and the IFOF to reduce noise from non-relevant brain structures like corpus callosum in statistical testing. The binary masks were computed by registering all tractography results to MNI152 space and selecting voxels, which were present in the TBSS skeleton as well as in the corresponding tractography segment of at least one subject. The permutation testing was done to each skeleton segment as described above.

Table 1
Participants' language background.

Languages used during childhood			% Early bilinguals		% Late bilinguals					
Both languages at home			66.7		–					
FIN at home, SWE outside home			25.0		–					
SWE at home, FIN outside home			8.3		–					
Only FIN			–		100					
Acquired languages			Early bilinguals, M (SD)		Late bilinguals, M (SD)					
No. of additional languages studied			2.6 (1.1)		2.8 (1.2)					
Years of studying additional lang.			7.3 (1.7)		7.1 (1.6)					
Languages currently at home			% Early bilinguals		% Late bilinguals					
Monolingual home			54.6 ^a		92.3 ^b					
Bilingual home			45.4 ^c		7.7 ^d					
Languages at work			% Early bilinguals		% Late bilinguals					
Monolingual working environment			36.4 ^a		30.8 ^b					
Bilingual working environment			18.2 ^c		53.8 ^d					
Trilingual working environment			45.5 ^c		15.4 ^e					
Languages at social situations			% Early bilinguals		% Late bilinguals					
Monolingual communication			–		7.7 ^b					
Bilingual communication			41.7 ^c , 8.3 ^d		84.6 ^d					
Trilingual communication			50 ^e		7.7 ^e					
Language usage			% Early bilinguals		% Late bilinguals					
			FIN/SWE/ENG		FIN/SWE/ENG					
Overall			40.0/36.7/20.3		68.5/3.1/28.5					
Speaking			43.3/45.0/10.8		86.9/-/13.1					
Reading			32.5/30.8/34.2		50.8/2.3/45.4					
Listening			39.2/35.0/25.0		62.3/2.3/35.4					
Writing			31.7/45.0/20.8		66.9/3.8/30.0					
Language skills	% Excellent		% Very Good		% Good		% Moderate		% Below Moderate or less	
	Early	Late	Early	Late	Early	Late	Early	Late	Early	Late
Finnish										
Overall	83.3	92.3	16.7	7.7	–	–	–	–	–	–
Speaking	83.3	100	16.7	–	–	–	–	–	–	–
Reading	100	100	–	–	–	–	–	–	–	–
Listening	83.3	100	16.6	–	–	–	–	–	–	–
Writing	75	76.9	25	15.4	–	7.7	–	–	–	–
Swedish										
Overall	100	–	–	8.3	–	25	–	25	–	41.6
Speaking	100	–	–	7.7	–	23.1	–	15.4	–	54
Reading	100	7.7	–	23.1	–	30.8	–	23.1	–	17.4
Listening	91.7	7.7	8.3	–	–	53.8	–	–	–	23.1
Writing	75	7.7	25	–	–	30.8	–	23.1	–	38.5
English										
Overall	25	46.2	58.3	53.8	16.7	–	–	–	–	–
Speaking	25	46.2	50	53.8	25	–	–	–	–	–
Reading	50	69.2	41.7	30.8	8.3	–	–	–	–	–
Listening	27.3	76.9	72.7	23.1	–	–	–	–	–	–
Writing	33.3	46.2	41.7	46.2	25	7.7	–	–	–	–

^a Either Finnish or Swedish^b Only Finnish^c Finnish and Swedish^d Finnish and English^e Finnish, Swedish and English

3. Results

3.1. Tract-specific effects

A linear mixed model approach for analysis of variance was used to test the influence of the participants' bilingual status on tract-specific mean FA, RD and MD values separately. The primary fixed effects were Group (early vs. late bilinguals), Tract (4 tracts per hemisphere; direct, anterior, and posterior segments of arcuate fasciculus and the IFOF, in total 8 tracts) and Group by Tract interaction.

The analysis of FA values revealed a significant interaction between Tract×Group ($F(14)=33.522$; $p<.001$). Further pairwise comparisons showed that the early bilinguals had significantly higher FA values ($M=.489$, $SD=.011$) along the left direct segment of the arcuate fasciculus

compared to the late bilinguals ($M=.472$, $SD=.014$, $p=.001$). The Tract×Group interaction was also significant for both RD ($F(14)=12.642$; $p<.001$) and MD values ($F(14)=36.828$; $p<.001$). For MD values, the effect was driven by differences in the right posterior segment of the arcuate, where the late bilinguals had higher MD values ($M=7.6\times10^{-4}$ mm²/s, $SD=.16\times10^{-4}$ mm²/s) than the early bilinguals ($M=7.5\times10^{-4}$ mm²/s, $SD=.15\times10^{-4}$ mm²/s, $p=.017$). For RD, the post-hoc tests did not reveal any clear source of the effect. There was, however, a marginal difference between the groups in the left direct segment, where the late bilinguals had higher RD values ($M=5.4\times10^{-4}$, $SD=.17\times10^{-4}$) than the early bilinguals ($M=5.3\times10^{-4}$, $SD=.15\times10^{-4}$, $p=.081$). The significant mixed model results are shown in Fig. 2B.

To further explore whether the observed MD differences in the right posterior segment might be due to changes in fibre packing density, a

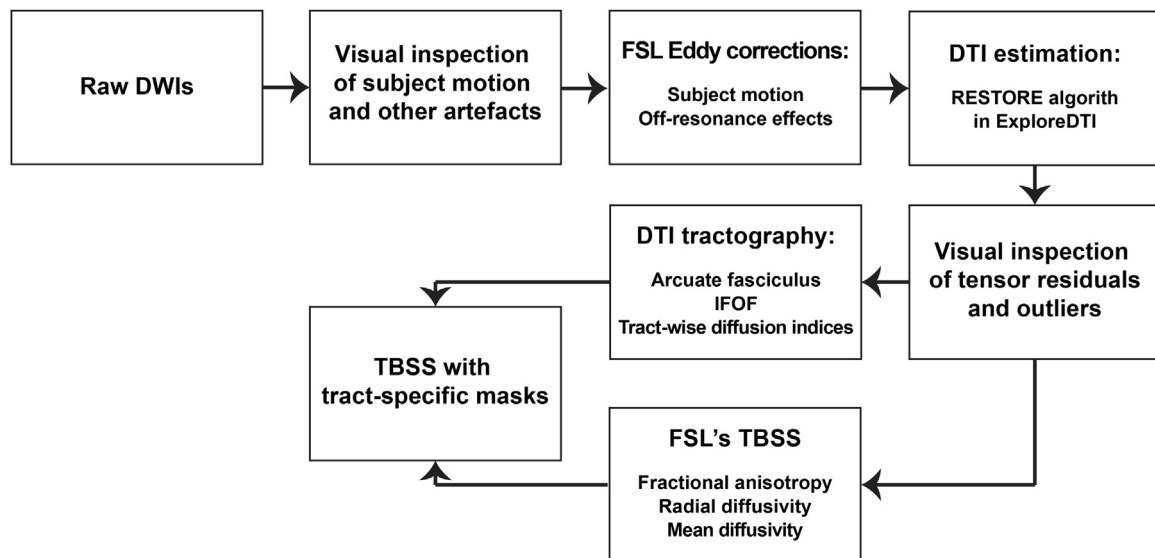


Fig. 1. The workflow from DTI preprocessing to TBSS and tract-specific TBSS analysis. The tract-specific TBSS analysis was achieved by restricting the FSL's TBSS analysis with tract-wise binary masks from DTI tractography.

post hoc Pearson's correlation analysis restricted to the right posterior segment was performed between the average MD and FA values for both groups separately. The analysis revealed a significant negative correlation between the two diffusion indices for early bilinguals ($r = -.521$, $N = 14$, $p = .031$, one tailed), but not for the late bilinguals ($r = -.009$, $N = 14$, $p = .49$, one tailed). This correlation is presented in Fig. 2C.

3.2. TBSS and tract-specific TBSS effects

The TBSS analysis on the whole-brain level did not reveal any significant differences when comparing FA, RD and MD values between

the early and late bilingual groups.

In the tract-specific TBSS analysis, binary masks of each tract were used to constrain the original TBSS analysis to include only voxels present in TOIs. This approach allowed for between-groups comparisons of voxel-wise FA, RD and MD values separately along each TOI by reducing noise from other brain structures. The tract-specific TBSS analysis revealed a group difference bilaterally over frontal parts of the IFOF, where early bilinguals had significantly higher ($p < .05$) MD values (mean MD = 7.7×10^{-4} mm²/s, SD = $.21 \times 10^{-4}$ mm²/s) than the late bilinguals (7.2×10^{-4} mm²/s, SD = $.22 \times 10^{-4}$ mm²/s) (Fig. 2D–F). This difference was the most pronounced over the right IFOF (N of

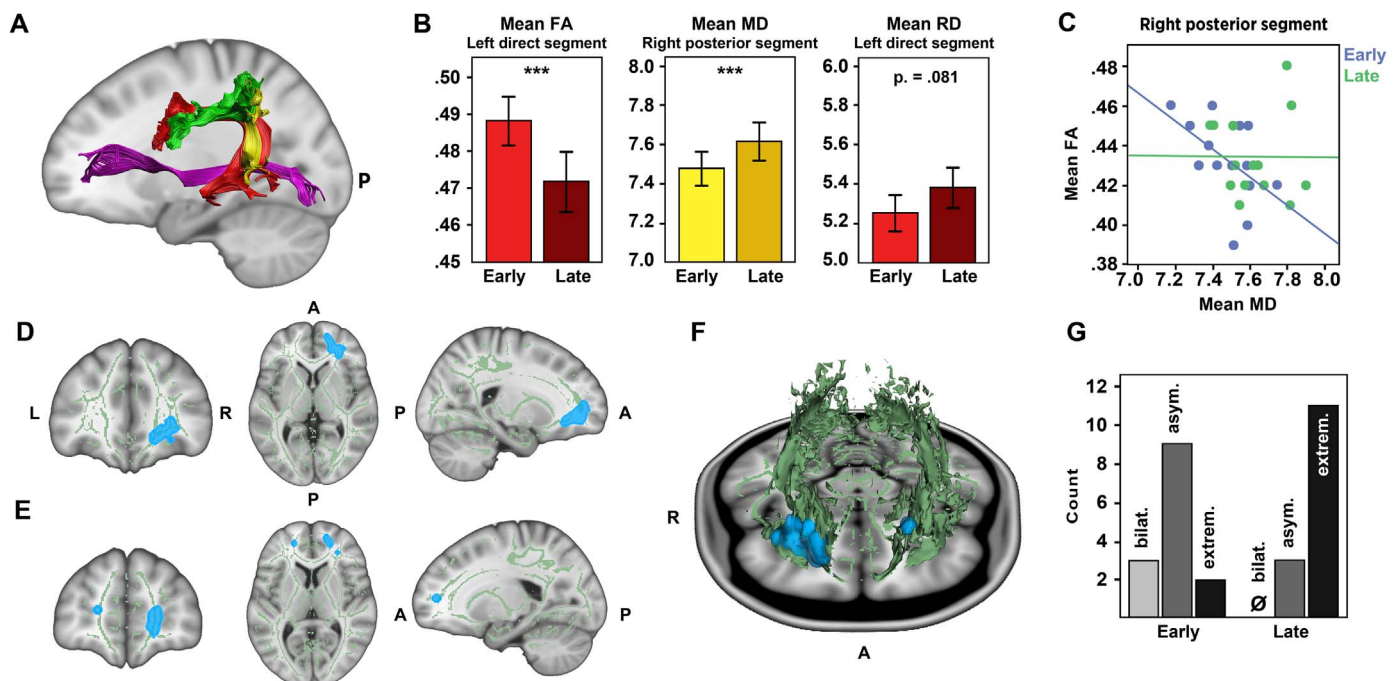


Fig. 2. The TOIs included in this study and the significant results from all statistical analyses. (A) The four TOIs: anterior (green), posterior (yellow) and direct (red) segment of the arcuate fasciculus and the IFOF (purple), overlaid on a standard MNI152 brain. (B) Mean FA, MD and RD values from tracts where significant differences between groups were observed with linear mixed model. (C) Correlation analysis between right posterior segment mean MD and FA values revealed a significant negative correlation ($r = -.521$) for the early bilingual (blue) group, but not for the late bilingual (green, $r = -.009$) group. (D) Significant differences in MD values over the right and (E) the left IFOF, observed with tract-specific TBSS analysis. Blue clusters mark the voxels within the skeleton, where $p < .05$. (F) 3D visualization of the difference clusters, overlaid on tract-specific white matter skeleton (green). For illustrative purposes, the blue clusters have been dilated. (G) Laterality pattern distributions between groups in the arcuate fasciculus, bilat.=bilateral configuration (light grey), asym.=leftward asymmetric lateralization (medium grey), extrem.=extreme left lateralization pattern (black).

significantly differing voxels on the right IFOF=279, and on the left IFOF=8). Subsequent post-hoc Pearson's correlation analysis restricted to the significantly differing voxels over the right IFOF was performed between the mean MD and FA values for both groups separately. This analysis revealed no significant correlations ($p=.204$ and $p=.116$ for early and late bilingual groups, respectively).

3.3. Laterality effects

To investigate whether bilingualism promotes more bilaterally balanced language tract configuration, a left-to-right ratio from the number of streamlines in the direct segment of the arcuate fasciculus was first calculated. A further k-means cluster analysis was then used to classify participants into the three laterality groups as described by Catani et al. (2007). Across all participants, the cluster analysis showed that the majority exhibited either an extreme left lateralization (46.4%, cluster centre of the lateralization index 1.82) or a strong leftward asymmetry of the direct segment of the arcuate fasciculus (42.9%, cluster centre of the lateralization index .86). In over half of the participants in the extreme left lateralization group, the direct segment in the right hemisphere could not be traced consistently. Only a handful of participants ($N=3$) presented a relatively symmetric left-right distribution of the direct segment (bilateral configuration) streamlines (10.7%, cluster centre of the lateralization index -.17). These findings are in line with the results presented by Catani et al. (2007).

A Fisher's exact test was then performed to assess the difference in the distribution of lateralization pattern between the early and late bilingual groups. An unequal distribution was revealed (Fisher's exact test=11.794; $p=.002$) and a further post-hoc contingency table analysis adjusted for multiple comparisons (Bonferroni) showed that the extreme left lateralization pattern was over-represented in late bilinguals relative to the early bilinguals ($p=.006$). Interestingly, all the participants with a bilateral pattern belonged to the early bilingual group, although this distribution did not reach statistical significance in the post-hoc testing. The results for the laterality effects are presented in Fig. 2G.

4. Discussion

We investigated a) how early bilingualism affects local white matter structures along major language trajectories and b) whether there are structural lateralization differences in the arcuate fasciculus, related to childhood bilingualism status. Whole-brain level and constrained tract-specific TBSS analyses along with linear mixed model analyses were used to compare diffusion indices between early simultaneous and late sequential bilingual speakers. Thus, we considered the L2 AoA to be the main source for the difference between the groups, as both groups had learned additional languages later in life (Kaiser et al., 2015). Distributions of lateralization patterns between groups in the arcuate fasciculus were compared using the approach described by Catani et al. (2007).

Importantly, we found bilingualism-induced modulations along the major language-related white matter trajectories. The lack of significant differences in the whole-brain TBSS analysis might be due to the fact that our effects were somewhat locally constrained, causing them to be lost in the overall variance at the whole-brain level. Moreover, some of the current effects were localized to structures that are hard to analyse reliably with the TBSS due to their complex architecture and circular form (Bach et al., 2014), thus making the TBSS practically blind to those effects. A further factor might be related to the bilingual samples used in this study. As both groups were highly proficient speakers of at least two languages, the differences between the groups induced by their different L2 AoA might have been too small to be present at the whole-brain level, motivating the implementation of tract-specific analyses.

The most notable modulations were observed along the left direct segment of the arcuate fasciculus, where the early bilinguals exhibited significantly higher mean FA values than the late bilingual speakers. This finding corroborates previous DT studies linking bilingual exposure to increased FA in several language-related white matter tracts (Luk et al., 2011; Mohades et al., 2012; Pliatsikas et al., 2015). As changes in FA can occur due to measurement techniques (Sairanen et al., 2017) and as a function of multiple white matter properties, such as changes in axonal packing density or in organizational coherence of the axons, the exact microstructural changes contributing to the observed difference are not evident from these results. However, since the direct segment of the arcuate fasciculus purportedly supports phonological language functions (Catani et al., 2005; López-Barroso et al., 2013), modulations in this particular segment might be due to early bilinguals facing increased phonological processing demands from early on. Moreover, the direct segment streamlines originate from the inferior frontal gyrus, which in addition to being related to phonological language processing, has also been shown to be sensitive to grey matter density modulations related to bilingual exposure (Stein et al., 2012). Although white matter changes have been proposed to occur independently of grey matter changes (Gold et al., 2013), there seems to be an intriguing concordance between the present finding and the previous grey matter results. Since there is no monolingual control group in our study, we cannot define whether a late exposure to L2 is also associated with some increase in FA along this segment, however, based on previous research (Pliatsikas et al., 2015) this might well be the case. Nevertheless, our results show that early exposure to two languages is associated with an increase in FA in this segment of the arcuate fasciculus.

Another difference was found along the right posterior segment of the arcuate fasciculus, where the early bilinguals exhibited significantly lower mean MD than the late bilinguals. For the early bilinguals, MD values correlated negatively with FA values. This negative relationship suggests that the current effect most likely reflects increasingly dense and ordered packing of the fibre tracts (Takahashi et al. 2000; Schmithorst et al. 2002) in response to long-term early bilingual exposure. However, this effect was not directly reflected in FA for the early bilinguals, possibly due to our relatively small sample size (Schmithorst et al., 2005). Aphasia studies have reported reduced comprehension of speech in relation to damage to the left posterior segment (Boatman et al., 2000; Damasio and Geschwind, 1984), suggesting that this segment might be important for auditory semantic comprehension (Catani et al., 2005). Whether the homologous right posterior segment might also support a similar function, is still unknown. Other studies have indicated that the right temporoparietal junction (i.e. the site from where the tracts of the posterior segment originate) might be important for higher-order cognitive processes, involving both language and social cognition, such as the theory of mind (Apperly et al., 2004; Catani and Bambini, 2014). Thus, as an alternative view, the right posterior segment may underlie some aspects of social functions. Supporting this idea, multilingual exposure has been proposed to facilitate effective communication skills (Fan et al., 2015) as bilingual children perform better than monolingual children on theory-of-mind tasks (Kovács, 2009; Rubio-Fernández and Glucksberg, 2012). Therefore, one could tentatively propose that the higher fibre organization found for early bilinguals along the right posterior segment might be due to enhanced socio-communicative aspects related to early bilingualism and the multilingual environment.

The third tract exhibiting white matter differences between the groups was the IFOF, which has been found to support semantic language functions (Duffau et al., 2005; Leclercq et al., 2010). The difference was observed bilaterally over the frontal parts of the tracts, although the effect was the most pronounced over the right IFOF, where early bilinguals had significantly higher MD than the late bilinguals. Unlike the MD difference over the right posterior segment, this effect was not correlated with FA in either group. MD on its own

denotes the overall diffusion rate in a voxel. As diffusion in constrained voxels is possible only in specific orientations, it lowers the overall diffusion rate and thus MD has been suggested to reflect the inverse of the membrane density (Alexander et al., 2007). However, as already discussed above, such interpretations linking diffusion indices to specific changes in the underlying white matter structure should not be made without reservations, as other structural modulation apart from the axonal density (together with measurement technical issues), might also be reflected in the observed MD values. Bearing this in mind, the current finding can be interpreted as either lower axonal packing for the early bilinguals or denser axonal packing for the late bilinguals, depending on the preferred point-of-view. In general, the former interpretation would corroborate studies reporting low FA for bilinguals compared to monolinguals along particular white matter tracts, including the bilateral IFOF (Cummine and Boliek, 2013; Gold et al., 2013; Kuhl et al., 2016). These results would, however, contradict the findings associating bilingualism with gained modulations in general (gained in this context refers to the pool of observations linking bilingualism to higher values of e.g., FA, grey matter density and cortical thickness. For comprehensive review, see e.g., García-Pentón et al., 2016). However, two of the aforementioned studies (Cummine and Boliek, 2013; Kuhl et al., 2016) suggested that the lack of increased FA for bilinguals in their results might be due to characteristics of their samples, as in both studies the bilinguals' L2 learning (Cummine and Boliek, 2013) and immersion times (Kuhl et al. 2016) were relatively short. They proposed that the increased FA associated with bilingualism may take time to develop and thus might not have been present in bilingual groups with restricted experience in L2. Yet the early bilinguals in our study had over 25 years of sustained bilingual experience, thus rendering this explanation unlikely to apply to our study. Therefore, we consider the latter interpretation to be more likely, i.e., that the late bilinguals had increased axonal packing density along the IFOF relative to the early bilinguals. This interpretation is in line with studies reporting that successive bilingualism modifies brain structure, while simultaneous bilingualism has no additional effect on brain development when measured e.g. as changes in cortical thickness or grey matter volume (Kaiser et al., 2015; Klein et al., 2014). Consequently, early simultaneous acquisition of two languages is assumed to result in more efficient neural networks (Kaiser et al., 2015), capable of accommodating two languages at once. However, learning L2 after the network has already been established to process one language requires additional modulations. Further evidence favouring this view comes from the work of Pliatsikas and colleagues (Pliatsikas et al., 2015), who reported increased FA for their highly immersed late bilinguals (L2 AoA=10 years) along the bilateral IFOF when comparing against monolinguals. Moreover, our interpretation also encompasses the results of Cummine and Boliek and those of Kuhl and colleagues (Cummine and Boliek, 2013; Kuhl et al., 2016), assuming their late bilingual groups would start to show an increase in FA along the IFOF after a sufficient L2 learning/immersion time. This hypothesis was indeed partly validated by Kuhl and colleagues, as in their subsequent analysis where the late bilingual sample was split according to the median of the immersion time, only the lower immersion subgroup persisted in exhibiting significant differences compared to the monolinguals. We therefore propose that the IFOF might be a trajectory that exhibits bilingualism-induced modulations only when L2 is acquired after gaining proficiency in L1.¹

Building on the current and previous research, we suggest that early simultaneous bilingualism may lead to qualitatively different kind of

changes than late sequential bilingualism in parts of the structural language-related network. Increased phonological processing load associated with language learning early in life seems to induce modulation of the white matter tracts along the left direct segment of the arcuate fasciculus, while the simultaneously increasing semantic processing demands are accommodated by adjusting the semantic neural network in a way that is not captured by DT measures alone. On the other hand, late sequential acquisition of L2 appears to tax the already established neural system and induces changes along the structures demanded by the task (Klein et al., 2014). Late sequential bilingualism could thus be characterized as steady increase in FA/axonal packing density over time a) along the same white matter tracts that respond to early simultaneous bilingualism and b) along some additional tracts such as the IFOF, for which the sensitive period to accommodate multiple languages at once without inducing structural modulations has already passed.

As per why increased phonological processing demands are accommodated differently from increased semantic processing demands in the simultaneously bilingual brain remains to be elucidated in future studies. One possibility is that since phonological processing is so closely linked to sensory activations from the auditory cortex, effective phonological processing requires boosting the structural link between the primary auditory cortex and the frontal speech processing areas (the direct segment of the arcuate fasciculus) in the developing brain. Semantic processing, however, can be seen to be less reliant on any single sensory processing area, making it possible to distribute the increased processing load between different parts of the semantic network. All in all, further research is needed to confirm these tentative interpretations.

Finally, the second aim of this study was to investigate whether bilingualism could be associated with a more bilaterally balanced configuration of the arcuate fasciculus. The results indeed showed that the late bilingual speakers are more likely to exhibit extreme left lateralization pattern than the early bilinguals. This finding suggests that early-onset bilingualism contributes to a more bilaterally balanced structural configuration of the perisylvian language tracts. It should be noted, however, that bilingualism is not unique in promoting larger and more structured composition of the right arcuate fasciculus. For instance, musical training (Bengtsson et al., 2005) and singing in particular (Halwani et al., 2011) have been shown to be associated with increased structural organization in the right arcuate fasciculus.

To summarize, our results demonstrate that the early simultaneous bilingualism is associated with several structural changes along the major language-related white matter trajectories. Importantly, our findings suggest that increased phonological processing demands induced by learning two languages at once are accommodated by increasing the FA along the phonology-related left direct segment of the arcuate fasciculus. On the other hand, the assumed concurrent semantic processing load does not appear to lead to structural changes in simultaneous bilinguals, but evokes modulations only in late sequential bilinguals. We therefore conclude that different aspects of L2 processing have unique microstructural signatures on the brain depending on the age of the second language acquisition. We are also the first to demonstrate that bilingualism affects the structural laterality of the arcuate fasciculus, promoting a less lateralized and more bilaterally balanced structural organization of the perisylvian language-related trajectories.

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¹ There are some contradictory findings that cannot be accounted for by our current interpretation: Two studies have reported increased FA along the IFOF in response to early simultaneous bilingualism (Luk et al., 2011; Mohades et al., 2012) and a third study reported decreased FA for highly proficient lifelong bilinguals (Gold et al., 2013). However, these studies were done with children (Mohades et al., 2012) and elderly participants (Gold et al., 2013; Luk et al., 2011).

Notes

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