Contents lists available at ScienceDirect

NeuroImage

journal homepage: www.elsevier.com/locate/neuroimage

What you learn & when you learn it: Impact of early bilingual & music experience on the structural characteristics of auditory-motor pathways

Lucía Vaquero ^{a, c, *, 1}, Paul-Noel Rousseau ^{a, b, c}, Diana Vozian ^{a, c}, Denise Klein ^{b, c, 2}, Virginia Penhune ^{a, c, d, 2}

^a Laboratory for Motor Learning and Neural Plasticity, Department of Psychology, Concordia University, Montreal, QC, Canada

^b Montreal Neurological Institute, McGill University, Montreal, QC, Canada

^c Center for Research on Brain, Language and Music (CRBLM), Montreal, QC, Canada

^d International Laboratory for Brain, Music, and Sound Research (BRAMS), Montreal, QC, Canada

ARTICLE INFO

Keywords: Arcuate fasciculus Bilingualism Brain plasticity Music training Sensitive periods

ABSTRACT

Music and language engage the dorsal auditory pathway, linked by the arcuate fasciculus (AF). Sustained practice in these activities can modify brain structure, depending on length of experience but also age of onset (AoO). To study the impact of early experience on brain structure we manually dissected the AF in bilinguals with and without music training (MT) who differed in the AoO of their second language (L2), or MT. We found the usual left-greater-than-right asymmetry in the volume of the long segment (LS) of the AF across all groups. However, simultaneous exposure to two languages from birth enhanced this leftward asymmetry, while early start of MT (\leq 7) enhanced the right LS macrostructure, reducing the normative asymmetry. Thus, immersive exposure to an L2 in the first year of life can produce long-term plastic effects on the left LS, which is considered to be largely under genetic control, while deliberate music training in early childhood alters the right LS, whose structure appears more open to experience. These findings show that AoO of specific experience plays a key role in a complex gene-environment interaction model where normative brain maturation is differentially impacted by diverse intensive auditory-motor experiences at different points during development.

1. Introduction

Long-term, intense experiences such as music training or bilingualism produce structural and functional changes in the brain (Zatorre 2013; Klein et al. 2014; Li et al. 2014; Christie et al., 2017; Borsa et al., 2018; Del Maschio et al., 2018; DeLuca et al., 2019; Hayakawa and Marian 2019). These changes are likely dependent on factors such as length of experience and amount of exposure, but also crucially on the age of onset of learning (Penhune 2011; Birdsong 2018; Berken et al. 2016). Playing an instrument or speaking multiple languages involve mapping sounds to motor commands, recruiting auditory and motor regions such as the superior temporal gyrus, inferior parietal, inferior frontal and premotor areas, that are organized in the auditory dorsal stream (Hickok and Poeppel 2004, 2007; 2015; Zatorre et al. 2007; Rodríguez-Fornells et al. 2012; Zatorre 2013). Structural changes in dorsal-stream regions have been observed in both trained musicians and bilinguals (Mechelli et al. 2004; Chen et al. 2008a, 2008b; Bermudez et al. 2009; Ressel et al. 2012). Further, differences in premotor and inferior frontal regions have been found to be dependent on the age at which music training or bilingual experience occurs (Bailey et al. 2014; Klein et al. 2014). The white-matter tract connecting dorsal stream regions is the arcuate fasciculus (AF) (Vaquero et al. 2017). Long-term training in music and language has been found to alter this pathway, with greater structural connectivity for bilinguals compared to monolinguals in the left hemisphere (Hämäläinen et al. 2017), and for musicians compared to non-musicians in the right hemisphere (Halwani et al. 2011). However, the impact of age of onset of such training has not been fully explored. Further, because bilingual and musical experiences begin at different ages, the current approach allowed the examination of the effect of intensive auditory-motor experience at different points in development. Developmental studies show that the AF matures in late childhood (10–14 years; Budisavljevic et al. 2015; Tak et al. 2016), although debate

https://doi.org/10.1016/j.neuroimage.2020.116689

Received 27 August 2019; Received in revised form 18 January 2020; Accepted 25 February 2020 Available online 29 February 2020

1053-8119/© 2020 The Authors. Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/byne-nd/40/).





^{*} Corresponding author. Laboratory for Motor Learning and Neural Plasticity, Concordia University, 7141 Sherbrooke St. West, H4B 1R6, Montreal, QC, Canada. *E-mail addresses:* lucvaq01@ucm.es, lucia.vaquero.z@gmail.com (L. Vaquero).

¹ Currently at: Complutense University of Madrid (Spain).

² Senior authors: Klein and Penhune are to be considered co-senior authors.

around maturational timelines for the different AF segments is still open. A left-greater-than-right (L > R) asymmetry in volume, particularly of the long or direct segment (LS), has been consistently observed, even in early childhood (Powell et al. 2006; Catani et al., 2007; Rodrigo et al. 2007; Lebel and Beaulieu 2009; Häberling et al. 2013; Tak et al. 2016). The LS is the branch of the AF that forms a direct connection between posterior auditory cortex and inferior frontal gyrus. A twin study showed that both genetic and environmental factors influence the adult micro- and macro-structural properties of the LS (Budisavljevic et al. 2015). In addition, previous reports have demonstrated a relationship between individual differences in the AF structure and short-term language or music learning (López-Barroso et al., 2013; Vaquero et al. 2018), as well as with long-term bilingual or musical experience (Hämäläinen et al. 2017; Halwani et al. 2011). Early bilinguals (age of onset or AoO < 5years) show enhanced white matter (WM) microstructure in the left LS, suggesting that early intensive second language (L2) experience can drive plasticity in this pathway (Hämäläinen et al. 2017) which has been linked to phonological processing -the integration of linguistic sounds and actions (López-Barroso et al. 2013). Similarly, the right LS has been observed to be enhanced in musicians (Halwani et al. 2011) and thought to be related to music learning and auditory-motor integration in musical contexts (Loui et al. 2011; Vaquero et al. 2018).

Here, we extend this line of investigation by examining the effect of AoO of bilingual and musical experience on the structure of the three branches of the AF. Taking advantage of the rich linguistic environment in Montreal, we used diffusion-tensor imaging (DTI) to dissect the AF in bilinguals with and without musical training. All groups were matched for bilingual proficiency and sub-divided based on their AoO of first and second language learning or music training: Simultaneous Bilingual Non-Musicians (NM), Sequential Bilingual NM, Early-Trained (ET) Musician Bilinguals and Late-Trained (LT) Musician Bilinguals. Because all our participants were bilingual, we were able to explore possible additive effects of these two intensive auditory-motor experiences that begin at two different points during development. Early start of bilingualism and musicianship were expected to affect the structural properties of the left and right AF, respectively. Across all groups, we found the expected L > Rasymmetry in the volume of the AF, particularly in the LS. Crucially, however, we found that Simultaneous Bilingual NM had an enhancement of that asymmetry possibly linked to the impact of simultaneous exposure to two languages during the first year of life. In comparison ET Musician Bilinguals showed a reduced leftward asymmetry with a relatively larger volume of the right LS probably related to intensive music training in early childhood. Together, these findings provide support for a complex gene-environment interaction model in which multiple factors influence the plastic effects observed after long-term training (Ullén et al., 2016), and in which AoO and the specific type of training seems crucial. Further, it suggests that variability in the left AF appears to be more genetically determined, while the structure of the right AF seems more open to environmental influence. Moreover, our findings provide the basis for a more sophisticated model of sensitive period effects by showing that long-term plasticity depends on region-specific differences in malleability by experience, the age at which experience occurs and the type of learning experience.

2. Materials & methods

2.1. Participants

All participants (n = 62, 34 female) in this study were bilinguals who spoke either English or French as their L2 (see Table 1 and Supplementary Table S1 for language, music and demographic characteristics). The large majority had English or French as their L1 (83.87% of total). A small number (n = 10) had other languages as their L1. Other languages spoken as a L3 varied, and only a 30.65% of all participants were exposed or non-fluently spoke an L3/L4 (see Table S1).

Half of the participants were also trained musicians (Musician Bilinguals: N = 31, 15 female) and the other half were non-musicians (NM Bilinguals: N = 31, 19 female). Musician Bilinguals were selected to have a minimum of 10 years of music practice (mean = 15.74) and 8 years of formal training (mean = 12.23) and were actively practicing at the time

Table 1

Demographic information of the sample. Means and SD (in brackets) are provided and significant differences between groups are indicated by the * (and, when more than a pair of groups show significant differences, these are marked with circles, triangles and 5-pointed stars). All values are rounded to two decimals. Abbreviations: Yrs, years; AoO, age of onset; train, training; L2, second language; No., number; lang, languages; SES, socio-economic status; ed., education; n.s., not significant.

	Mean age	Sex	Yrs. of education	AoO music train.	Yrs. music experience	No. instruments played	AoO of L2	Yrs. L2 exposure	No. lang. fluently spoken	Self-rated (spoken) L2 fluency	SES (Mother's ed.)
Bilingual Non- musicians	25.03 (4.25)	19 female, 12 male	14.06 (2.83)	11.33 (2.72) [n=18/31]	1.26 (1.43)	0.71 (0.74) [n=18/31]	5.84 (5.01)	19.19 (6.21)	2.00 (0.00)	5.98 (0.88)	3.89 (1.47)
Bilingual Musicians	23.06 (4.63)	15 female, 16 male	14.03 (3.08)	7.19 (2.39)	15.74 (4.26)	1.94 (1.06)	4.50 (4.32)	18.67 (4.81)	2.13 (0.57)	5.48 (1.52)	4.00 (1.10)
Significance	n.s.	n.s.	n.s	p < .001	p < .001	p < .001	n.s.	n.s.	n.s.	n.s.	n.s.
Simultaneous Bilingual NM	23.22 (3.07)	5 female, 4 male	14.78 (2.73)	12.00 (2.74) ⁰ [n=5/9]	1.43 (1.50)* 🖈	0.78 (0.67) ⁰ [n=5/9]	0.39 (0.60) ^{o 🗴}	22.83 (3.08)	2.00 (0.00)	6.56 (0.53) [*]	5.25 (0.89) ^{* c}
Sequential Bilingual NM	25.77 (4.50) ⁰	14 female, 8 male	13.77 (2.88)	11.08 (2.78)☆ [n=13/22]	1.19 (1.43) ^{°∆}	0.68 (0.78) ☆∆ [n=13/22]	8.06 (4.22)*☆	17.71 (6.59)	2.00 (0.00)	5.75 (0.90)	3.35 (1.31) ⁰
Early-trained- Musician bilinguals	21.18 (2.65) ^{* 0}	10 female, 7 male	13.35 (2.83)	5.47 (1.07) ^{*°} ☆	15.65 (2.62) ^{* °}	1.53 (0.62) ^{*∆}	3.53 (3.38)*	17.65 (3.63)	2.25 (0.68)	5.94 (1.30)	3.73 (0.96)*
Late-trained- Musician bilinguals	25.36 (5.51)*	5 female, 9 male	14.86 (3.28)	9.29 (1.77)*	15.86 (5.77) ^{☆∆}	2.43 (1.28)**	5.77 (5.18) ⁰	20.00 (5.92)	2.00 (0.39)	4.93 (1.64) *	4.36 (1.21)
Significance	p < .01	n.s.	n.s.	p < .001	<i>p</i> < .001	p < .05	<i>p</i> < .001	n.s.	n.s.	p < .05	p < .005

of the experiment (mean hours of practice per week = 13.57).

The NM Bilingual group was sub-divided into Simultaneous Bilingual NM (those who were exposed to L2 from birth; N = 9, 5 females) and Sequential Bilingual NM (those who acquired their L2 later; N = 22, 14 females). Simultaneous Bilingual NM were all exposed to their two languages from birth, although some of them reported their AoO of L2 in relation to the moment they actually started to speak (AoO range: 0–1.5). All Sequential Bilingual NM were exposed and started to learn their L2 after the age of 2 (AoO range: 2–20). Despite the lack of a clear cut-off for defining simultaneous and sequential bilinguals in previous literature (Genesee and Nicoladis, 2007), our definition of simultaneous bilinguals is similar to that described in previous reports (Klein et al., 2014; Berken et al., 2016, 2017).

The Musician Bilingual group was sub-divided into early-trained (ET Musician Bilinguals: those who began their music training before age 7; N = 17, 10 females, AoO range: 4–7) and late-trained (LT Musician Bilinguals: who began training after age 7; N = 14, 5 females, AoO range: 8–14). ET and LT Musician Bilingual groups were matched for years of musical experience (ET-musicians mean = 15.65, SEM = 0.64, LT-musicians mean = 15.86, SEM = 1.54, t(29) = -0.13, p = .89), years of formal training (ET-musicians mean = 13.06, SEM = 0.76, LT-musicians mean = 11.21, SEM = 0.79, t(28.51) = 1.68, p = .10), and hours of current weekly practice (ET-musicians mean = 11.53, SEM = 2.13, LT-musicians mean = 16.04, SEM = 3.89, t(20.49) = -1.02, p = .32) as verified by independent sample t-tests (See Table 1). Distribution of AoO of both trainings in both Bilingual NM and Musician Bilingual groups can be seen in Supplementary Fig. S1.

Since we were interested in isolating the effect of age of start of both types of audio-motor experience, the four groups were matched for years of L2 exposure/use, number of languages fluently spoken, age, gender and years of education (See Table 1). ET- and LT-musician bilingual groups contained both simultaneous and sequential bilinguals. Overall, language background was more variable for musicians than non-musicians (See Table S1).

All participants were self-identified right handers and had no known history of auditory, neurological or psychiatric disorder. Participants gave written informed consent. The procedures of this investigation were approved by the Research Ethics Board of the Montreal Neurological Institute (MNI) and was carried out in agreement with the principles of the Declaration of Helsinki.

2.2. Experimental procedure

2.2.1. Imaging acquisition and analysis

Images were acquired using a 3.0 T S Magnetom TrioTim syngo MR B17 scan at the McConnell Brain Imaging Center of the MNI (Montreal, Canada). The scan session consisted of: a localizer, a T1-weighted sequence, a resting state sequence, and the Diffusion Weighted protocol. Only the details for the diffusion-weighted images are reported here. Diffusion-weighted images were acquired using a twice-refocused spinecho sequence, with the following parameters: Repetition Time (TR) = 10000 ms; Echo Time (TE) = 90 ms; FOV = 256 x 256; matrix size = 128 x 128; slice thickness = 2.0 mm; no gap; 73 axial slices; voxel size was 2 x 2 \times 2 mm. Diffusion was measured along 64 non-collinear directions, using a b value of 1000 s/mm², and including a b = 0 as the first volume acquired.

To pre-process the diffusion-weighted images, first, the brain was virtually extracted from the rest of the head using FSL's Brain Extractor Tool (Smith, 2002; Smith et al., 2004; Woolrich et al., 2009). Then, motion and eddy-current correction were performed using FMRIB's Diffusion Toolbox (FDT), part of the FMRIB Software Library (FSL 5.0.1, www.fmrib.ox.ac.uk/fsl/). To take into account the corrections made at the previous stage, the b-vectors gradient matrix was then rotated by using the *fdt_rotate_bvecs* software included in the FMRIB Software Library. The diffusion tensors were then reconstructed using Diffusion Toolkit's least-square estimation algorithm for each voxel, and Fractional

Anisotropy (FA) was calculated (Ruopeng Wang, Van J. Wedeen, Martinos Center for Biomedical Imaging, Massachusetts General Hospital, http: //www.trackvis.org/). Radial Diffusivity (RD) maps were also calculated by averaging the two minor eigenvectors extracted from the diffusion tensors obtained in the previous preprocessing step.

Deterministic tractography across the whole brain was performed using Diffusion Toolkit, with an interpolated streamlines algorithm using 35° as the maximum curvature threshold and a minimum FA threshold of 0.2. The fibre direction is assumed here to correspond to the principal eigenvector (the eigenvector with the largest eigenvalue). This vector was colour coded (green for posterior-anterior, blue for superior-inferior and red for left-right directions) in order to generate a colour-coded FA map. Dissections were carried out by the first author in the native space of each subject and in both hemispheres, by using Trackvis software, following the methodology used in previous studies (Catani et al. 2005, 2007; López-Barroso et al. 2013; Vaquero et al. 2017, 2018). Regions of interest (ROIs) were defined on the FA and FA colour-coded maps according to individual anatomical landmarks. Tractography carried out on each subject's anatomy, using the native space of every participant, is considered to be more faithful to the white-matter anatomy and to better preserve individual differences that can be neglected in an atlas-based type of dissection, being, at the same time, as accurate as dissections performed on normalized data (Adluru et al., 2013; López-Barroso et al., 2013).

To dissect the AF, the first ROI was drawn in the coronal view, anterior to the central sulcus, comprising the fibres going to the inferior frontal gyrus (IFG). The second ROI was depicted in the axial view covering the white matter underlying the superior and middle temporal gyri (S/MTG). Finally, the third ROI was delineated on the sagittal view to include the fibres traveling to supramarginal and angular gyri (inferior parietal or IPG). These ROIs were combined to define the three rami of the AF: the long/direct segment (between IFG and S/MTG), the anterior segment (linking IFG and IPG), and the posterior segment (connecting S/MTG with IPG). When needed, artefactual fibres were removed using exclusion ROIs.

2.2.2. Behavioural testing

Participants completed an initial questionnaire providing information about their health and MRI compatibility; language background information (such as number of languages spoken, self-rating of their fluency in those languages, AoO of their languages); and musical background (years of music training, AoO of musical training). Additional information regarding their musical background was provided via the Music Experience Questionnaire (MEQ, Bailey and Penhune 2010), which also reflected years of formal music education, current hours of practice per week, and number of instruments played.

The variable 'number of languages fluently spoken' (see Table 1) was based on a self-rated score (scale: 1 to 7). A language was considered as "fluent" when this score was \geq 5. One early-trained and one late-trained musician bilingual rated their L2 fluency with a value < 5 due to lack of current practice at the time of the experiment, but were recoded as fluent by the experimenters because their years of L2 exposure were comparable to others who rated their proficiency as fluent, and their age of L2 acquisition was early in life. This was done because we felt that it was more accurate to indicate that these participants had an additional language that was likely relatively fluent, despite its rating. Verbal fluency (VF), both phonemic and semantic, was tested for all participants in English and, for those who spoke it, in French. In English, participants were asked to name as many words as possible starting with the letter A and pertaining to the category 'animals', while in French, letter L and 'fruits' category were used. Scores were calculated by using the total number of utterances. Fluency scores for participants L2 -whether English or French- were used for analysis, when possible; details of distribution and between-group differences in this variable can be found in Table S3.

Musical abilities were tested using the Melody Discrimination (Foster

and Zatorre 2010) and Rhythm Synchronization (Bailey and Penhune 2010) tasks. The Melody Discrimination Task requires participants to listen to two short melodic sequences and indicate whether they are the same or different. The task has two levels of difficulty: simple and transposed. There is also a parallel control task where participants must discriminate between two sequences of syllables. Participants completed 30-trial blocks for each condition, and the task order was counterbalanced with randomized trials within each block. Performance was measured via percent correct responses. We calculated a composite score for correct responses in both Simple and Transposed conditions, as well as a score for the Control/Syllable condition. The Rhythm Synchronization task requires participants to listen to and then reproduce short musical rhythms by tapping in synchrony with their right index finger on the left button of a computer mouse. Rhythms varied across three levels of metrical complexity (2 rhythms per level, with 3 repetitions per rhythm). Performance was measured using the inter-tap interval (ITI) deviation (Bailey and Penhune 2012). This measure indicates the extent of deviation from the actual interval between each pair of woodblock notes, providing information about how well the participant reproduces the temporal structure of the model rhythms. Both tasks were programmed in Presentation (Neurobehavioral Systems, http://www.neu robs.com/) and presented using a laptop computer, a set of headphones and a computer mouse.

Matrix Reasoning (MR) and Letter-Number Sequencing (LNS) subtests from the WAIS-IV (Weschler Adult Intelligence Scale, Weschler 2008) were used as proxy to assess potential differences between the groups in general IQ and auditory working memory, respectively. Scaled scores from these two tests were included in subsequent analyses. To assess executive functions, participants performed a Simon Task (Bialystok et al. 2008; Kousaie et al. 2014) implemented in E-Prime 2.0.10.353 software (Psychology Software Tools, Inc. [E-Prime 2.0]. (2013). Retrieved from http://www.pstnet.com). The Simon task contained four experimental conditions: (i) control, (ii) reverse, (iii) conflict congruent and (iv) conflict incongruent. The 4 different conditions were presented 4 times; the task was divided into two blocks and every condition was presented twice in each block, for 48 trials, in a fixed order. The measure included in the analysis was the 'Simon interference' which measures the effect of the location of the arrow during the conflict conditions (facilitation or distraction) and is calculated by subtracting reaction times from the incongruent trials to the reaction times in the congruent trials (congruent - incongruent).

Finally, Socio-economic status (SES) was determined based on mother's education (Braveman et al., 2001; Hackman and Farah, 2009; Vable et al., 2018), assigning a value from 1 to 6 as follows: 1, primary school; 2, secondary education (middle or high school); 3, CEGEP (Collège d'Enseignement Général et Professionnel, 'general and vocational college', a pre-university and technical college in the province of Québec) or DEP (Diplôme d'éstudes professionnelles, 'professional studies diploma'); 4, College, undergraduate or Bachelor's degree; 5, Graduate degree: Master's; 6, Graduate degree: PhD or MD.

2.3. Statistical analysis

Analyses were restricted to tract volume, fractional anisotropy (FA) and radial diffusivity (RD) measures since previous investigations have shown that these parameters are highly sensitive to individual differences in healthy participants (López-Barroso et al. 2013; Ripollés et al. 2017; Vaquero et al. 2017, 2018). Tract volume informs about the macrostructural organization of the tract, while FA and RD are markers of the microstructural organization, related to axon architecture (i.e., packing and diameter) and myelin content of the tract (Song et al. 2002, 2005; Klawiter et al. 2011; Zatorre et al. 2012; López-Barroso et al. 2013; Ripollés et al. 2017). Tract volume, FA and RD were extracted from the three rami of the AF in each hemisphere. Since ET and LT groups contained both simultaneous and sequential bilinguals, the DTI analysis was controlled for the AoO of L2 in order to take that fact into account and to

isolate the effect of AoO of music training. Group differences in volume, FA and RD were thus explored using a repeated measures ANCOVA, with hemisphere as repeated measure and AoO of L2 as the control covariate. Using deterministic tractography it is common not to find some segments, especially in the right hemisphere (Catani and Mesulam 2008). Thus, the ANCOVAs were performed separately for every segment and DTI measure (i.e., volume in Long segment, FA in Long segment, RD in Long segment, volume in Anterior segment, etc.), in order to avoid list-wise deletions that would have happen by using an omnibus repeated measures ANCOVA taking the three segments at once. Post-hoc comparisons in these analyses were Bonferroni corrected for multiple comparisons with a *p*-value < .05.

To investigate behavioural group differences in music perception and production, neuropsychological, and executive function measures, one-way ANOVAs were carried out for each individual variable, except for: (i) Matrix Reasoning (MR), that was included in a one-way ANCOVA to control for AoA of L2, since MR and AoO of L2 were observed to correlate significantly (p < .05); and (ii) the two measures from the Melody Discrimination task, that were included in a repeated measures ANOVA (conditions as repeated measure). Post-hoc analyses were Bonferroni corrected for multiple comparisons with a *p*-value < .05.

In addition, for the imaging variables showing significant group differences, a lateralization index (LIndex) was calculated following a formula previously used (López-Barroso et al. 2013; Vaquero et al. 2017): (values on the left – values on the right)/(values on the left +values on the right). We used this LIndex in subsequent analyses to explore group per hemisphere interactions and relationships with experience-related measures. For the latter, Pearson correlations were performed between the LIndex and the AoO of both L2 acquisition and musical training, as well as with the verbal fluency in participants' L2 (average of phonemic and semantic fluency, only for bilingual NM groups). Correlations were considered significant with a Bonferroni corrected *p*-value < .05. All analyses were run using IBM SPSS Statistics 25. *P*-values were adjusted for non-sphericity using the Greenhouse-Geisser test when appropriate.

3. Results

3.1. Behavioural results

Bilinguals with and without musical training were compared on a Melody Discrimination task and on a Rhythm Synchronization task. On the Melody Discrimination Task, a repeated measures ANOVA showed a main effect of condition (F(1,55) = 27.42, p < .001), indicating a difference between the composite melody score and the control condition, as well as a significant group by condition interaction (F(3,55) = 24.58, p < .001), showing that musician bilinguals outperformed the Bilingual NM groups in the melody simple and melody transposed conditions –Composite melody score– (ET-musician bilinguals mean = 86.46 ± 4.09 , vs. Simultaneous bilingual NM mean = 59.38 ± 8.26 , p < .001; LT-musicians mean = 83.63 ± 5.21 , vs. Simultaneous mean = 83.63 ± 5.21 , vs. Sequential bilingual NM mean = 83.63 ± 5.21 , vs. Sequential mean = 62.73 ± 10.03 , p < .001), while no difference was found for the control (syllable discrimination) condition).

On the Rhythm Synchronization task, a one-way ANOVA (ITI deviation: F(3,57) = 16.58, p < .001) showed that ET-musician bilinguals outperformed Sequential bilingual NM (ET-musicians mean = 0.264 ± 0.056 s, vs. Sequential bilingual NM mean = 0.341 ± 0.041 s, p < .001), and LT-musicians outperformed both groups of bilingual NM (LT-musicians mean = 0.230 ± 0.057 s, vs. Simultaneous mean = 0.313 ± 0.043 s, p < .005; LT-musicians mean = 0.230 ± 0.057 s, vs. Sequentials mean = 0.341 ± 0.041 s, p < .001). Results for both musical tasks are depicted in Fig. 1.

All scores on cognitive tests were in the normal range for all groups based on standard scores for participants' age and education. However,



Fig. 1. Bar graphs depicting the behavioural group-difference results on the Melody Discrimination and Rhythm Synchronization tasks. A) Group differences in the composite score for the Simple melody and Transposed melody conditions on the melody discrimination task. Y axis shows percentage correct responses. B) Group differences on the rhythm synchronization task, by means of Inter-tap-Interval or ITI-deviation (in seconds). Significance is marked with asterisks; see legend.

groups significantly differed on Matrix Reasoning as determined by oneway ANCOVA controlling for AoO of L2 (F(3,55) = 8.36, p < .001); this result was driven by differences between both groups of Musician Bilinguals and the Sequential Bilingual NM who had the lowest scores (ETmusician bilinguals mean = 13.41 ± 2.50 , vs. Sequential bilingual NM mean = 9.36 ± 2.82 , p < .005; LT-musician bilingual = 13.38 ± 2.18 , vs. Sequential bilingual NM mean = 9.36 ± 2.82 , p < .005). One-way ANOVA also showed significant differences in Letter-Number Sequencing (F(3,57) = 3.97, p < .05) between the ET-musician bilinguals and the Sequential bilingual NM (ET mean = 14.29 ± 3.72 , Sequential mean = 11.00 ± 3.45 , p < .05). Regarding executive functions, no significant between-group differences were found for the Simon effect (F(3,55) = 0.27, p = .84).

3.2. Arcuate fasciculus connectivity results

Two participants in the Sequential Bilingual NM group showed no left LS when performing the reconstruction of the AF. Hence, as it is usual practice for this deterministic method of dissection, those 2 participants were removed from the analysis, leaving an n = 20 in the Sequential Bilingual NM group (see Supplementary Results and Table S2). Results with the final sample (n = 60) showed a main effect of hemisphere for volume in the LS (F(1,54) = 47.35, p < .001) and the Posterior segment (F(1,54) = 11.25, p < .005), such that volume in the left hemisphere was greater across the four groups (see Fig. 2A).

Interestingly, a significant group by hemisphere interaction was found for volume in the LS (F(3,54) = 3.87, p < .05). Post-hoc pairwise comparisons using the Bonferroni correction showed that this interaction was driven by a significant difference between ET Musician Bilinguals and Simultaneous Bilingual NM in the volume of the right LS $(4.19 \pm 2.11 \text{ vs. } 1.30 \pm 1.41, \text{ p} < .05)$. We further explored this interaction by calculating the lateralization index (LIndex: Left-Right/ Left + Right) of volume in the LS. The LIndex takes into account the ratio of Left/Right volume, which makes it an ideal measure to further investigate the observed between-group differences, as well as to perform more informative correlations than with the individual hemispheric values. Thus, comparison across groups in this case also revealed a significant difference (F(3,54) = 5.17, p < .005), with posthoc tests using the Bonferroni correction showing again a significant difference between ET-Musician Bilinguals and Simultaneous Bilingual NM (p < .005), such that Simultaneous Bilingual NM showed a strong left lateralization of the volume values in the LS (LIndex = 0.76 \pm 0.24) and ET-Musician Bilinguals presented an almost perfectly symmetrical distribution (LIndex = 0.24 \pm 0.33) (See Fig. 2B). To be certain that the observed differences in volume of the LS were not a result of differences in the volumes of the ROIs used to define it, we compared the volumes of left and right IFG and STG ROIs and compared them across groups and found no significant differences (Left IFG: F(3,57) = 0.74, p = .53; Right IFG: F(3,57) = 2.33, p = .08; Left STG: F(3,57) = 0.12, p = .95; Right STG: F(3,57) = 1.20, p = .32).

No significant differences were found for fractional anisotropy (FA) or radial diffusivity (RD) measures for any of the segments, and thus, no further analyses were carried out with these variables. Additional information regarding the distribution of missing AF segments in our sample is in Supplementary Materials and Table S2.

3.3. Relationship between structural connectivity & AoO of training

The observed differences in AF volume of the left and right hemispheres for Simultaneous Bilingual NM and ET-Musician Bilinguals suggest a differential effect of AoO for music and bilingual experience. To test this hypothesis, we first performed correlations between the LIndex and AoO of L2 and L2 Verbal Fluency in the Bilingual NM group, and then for AoO of music training and AoO of L2 in the Bilingual Musician group. In the Bilingual NM group, neither AoO of L2 (r = -0.15, p = .44) nor L2 Verbal Fluency (r = -0.02, p = .92) were correlated with the LIndex. This suggests that the neuroplastic effects of early bilingual experience on the volume of the LS are most prominent within the first year of life, preventing us from finding a significant correlation using the full range of AoO of L2.

Then, we performed correlations for the Musician Bilingual groups alone between LIndex of volume in the LS and AoO of music training and AoO of L2. Correlations were significant for AoO of music training (r =0.46, p < .01) but not for AoO of L2 (r = 0.34, p = .07). This indicated that the earlier the start of music training, the closer to 0 were the LIndex values, meaning that the symmetrical pattern of lateralization found for the ET-Musician Bilinguals is likely explained by this early start of musical training. To confirm that this was specific to the early-trained musician group, we explored this same correlation with the ET- and LT-musician bilingual groups separately and found that it remained indeed significant only for the ET group (ET: r = .61, p < .01; LT: r =0.08, p = .78). This suggests that between the ages of 4 and 7 years, early start of music training has a greater effect on volume of the LS than training after that window. See Fig. 3.

4. Discussion

In the current study, we examined the differential effects of the AoO of bilingual experience and music training on the arcuate fasciculus which connects auditory, multisensory and motor regions in the dorsal stream. To do so, we manually dissected this tract in highly proficient bilinguals who differed, first, in their AoO of L2 and, secondly, in their musical experience and AoO of music training. Across all groups, the volume of the long segment of the AF was larger on the left, indicating that leftward lateralization is a consistent anatomical feature in the population that is likely under genetic control. This leftward



Fig. 2. Main structural results. A) Depiction of left and right volume values for the Long segment across the 4 experimental groups. Main effect of hemisphere and significant group per hemisphere interaction (for the volume in the right LS between ET Musician Bilinguals and Simultaneous Bilingual NM, specifically) are marked. B) Further exploration of the group per hemisphere interaction through the lateralization index: values closer to 1 mean left-lateralization, closer to 0 symmetrical, closer to -1 right-lateralization. Significant difference between ET musician bilinguals and simultaneous bilingual NM is marked. Abbreviations: ET, early-trained; NM, non-musicians.

lateralization was enhanced in simultaneous bilinguals without musical training, suggesting that exposure to a second language from birth promotes the development of auditory-motor connections in a pathway crucial for language (López-Barroso et al. 2013; François et al. 2016). In contrast, early start of music training in childhood resulted in enhancement of the LS in the right hemisphere, reducing the normative leftward lateralization. In addition, earlier AoO of music training predicted this more symmetrical pattern of lateralization, which demonstrates that music experience in early childhood exerts an effect on auditory-motor circuits known to be important for linking sounds to actions. Together, these findings illustrate the interaction of normative maturation and diverse intensive auditory-motor experience at different points during development.

The LS of the AF is the pathway underlying the flow of information from posterior auditory cortices to premotor and inferior frontal regions. A crucial role in language acquisition has been described for this pathway, especially in the left hemisphere, and it is considered to be the basis of a bidirectional sound-to-action feedback loop (Rodríguez-Fornells et al. 2012: López-Barroso et al. 2013; François et al. 2016). Disruptions of this tract have been described to lead to deficits in processing of both language (Agosta et al. 2013; Sierpowska et al. 2017) and music (Loui et al. 2009; Sihvonen et al. 2017). Our finding of a leftward asymmetry of the LS across all groups is consistent with a number of previous results (Powell et al. 2006; Catani et al. 2007; Rodrigo et al. 2007; Lebel and Beaulieu 2009; Häberling et al. 2013; Tak et al. 2016). This asymmetry has been linked to language dominance (Annet, 1985, and McManus, 1991, as cited in Geschwind et al. 2002; Catani et al. 2007; Matsumoto et al. 2008; Häberling et al. 2013) and for the LS of the AF in particular has been found to be present early in childhood (Budisavljevic et al. 2015; Tak et al. 2016). Twin studies suggest a strong genetic component to this asymmetry, but with a sizable environmental influence (Häberling et al. 2013; Budisavljevic et al. 2015).

Our finding that Simultaneous Bilinguals without music training have a greater leftward asymmetry of the LS is in line with previous reports (Hämäläinen et al. 2017). Although this group was relatively small, all showed a strong leftward asymmetry for this AF segment (see Fig. 3C). This clearly demonstrates that intensive L2 experience within the first year of life influences the development of this pathway and supports the concept that there is an early sensitive period for language acquisition (Lenneberg 1967; Hensch 2005; Pierce et al. 2014). Our study goes further to show this pattern in a controlled comparison with a group that also presents an extensive experience in another type of auditory-motor training. The LS connects the IFG to posterior auditory regions, and the current and previous findings indicate that bilingual experience exerts a neuroplastic effect on both regional architecture and network connectivity. These plastic changes could be explained by refinement of maturational processes due to bilingual exposure from birth (Berken et al. 2017), since it is known that pruning of language-related connections relies on activity-dependent stabilization of functionally crucial networks (Innocenti and Price 2005; Friederici 2009). To test whether the asymmetry of the LS was related to AoO of L2, we correlated these values in the full group of bilingual NM, where there was adequate variability to assess possible effects (range of AoO: 0-20 years). However, no significant correlation was found. This result suggests that plastic effects related to L2 exposure must occur very early in life, probably during the first year of life (Pierce et al. 2014). Another possible explanation is that, in addition to AoO of L2 acquisition, other factors related to bilingualism such as language proficiency, social diversity of language use, or number of languages spoken, may also modulate the plastic processes involved in brain reorganization and interact with the effect of age of commencement (Perani et al., 1998, 2003; Abutalebi et al., 2005; Gullifer et al., 2018). The unbalanced size of our four groups, especially affecting the Simultaneous Bilingual NM, implies that the findings must be interpreted with caution pending replication. Additional studies are thus needed with more homogeneous groups, where there is also less exposure to third or fourth languages. This might be easier to do in other bilingual communities and regions, and could allow for inclusion of additional linguistic variables, such as verbal-fluency or proficiency measures.

In comparison with the Simultaneous Bilingual NM, ET Musician Bilinguals had a larger volume of the right LS, and thus a reduced leftward asymmetry. Crucially, the degree of asymmetry was negatively predicted by AoO of music practice, indicating that earlier training results in a reduction in the normative leftward asymmetry. This suggests that the neuroarchitecture of the LS in the right hemisphere is still malleable in early childhood and can be changed by intensive experience. These findings fit with previous evidence of sensitive periods for music experience, similar to those for L2 learning, but which occur during a later period of development (Penhune 2011; Vaquero et al. 2016). There



(caption on next column)

Fig. 3. Correlations between the lateralization index for volume values in the Long segment of the AF and age of onset of training. A) Correlation with the AoO of music training, only for the musician bilingual groups (significant). B) Correlation with the AoO of L2, only for musician bilingual groups (not significant). For both A) and B) panels, in light green is detailed the correlation line corresponding to the additional correlation performed only with the ET-Musician Bilingual group, and the same colour is used to depict every subject in the ET-Musician Bilingual group; in dark green, the additional correlation performed only for the LT-Musician Bilingual group is depicted, with participants in this group being represented by dots of this same colour. C) Correlation with the AoO of L2, only for the bilingual NM groups (not significant). Light blue shows the regression line corresponding to the additional correlation performed only with the Simultaneous Bilingual NM group, as well as participants in this group; in dark blue, the additional correlation performed only for the Sequential Bilingual NM group and the dots corresponding to participants in this group. Abbreviations: AF, arcuate fasciculus; AoO, age of onset; L2, second language; ET, early-trained; LT, late-trained.

is no clear consensus regarding maturational time-lines or genetic versus environmental influences for the different segments of the AF. However, based on previous reports exploring age effects on the different AF segments (Budisavljevic et al. 2015; Tak et al. 2016), the LS seems to be the last to mature and most probably would have still been developing while our ET Musician Bilinguals started their musical training (Budisavljevic et al. 2015; Tak et al. 2016). Furthermore, it seems that age does not predict the architecture of this segment in the right hemisphere (Tak et al. 2016), indicating that experience may play a significant role. Together, this evidence suggests that during early childhood the right LS is more susceptible to environmental influence than the left whose structure seems more genetically determined and only malleable by training in very early infancy. Obviously, it is possible that those who undertake music training at an early age might have a more symmetrical organization of the LS than those who begin later, even before the start of the training. However, only a long-term longitudinal study could address this question.

Our results are consistent with a multifactorial gene-environment interaction model which hypothesizes that expert performance and its plastic effects on the brain depend on additive and multiplicative interactions between deliberate practice and other variables, such as physical, cognitive or personality traits, that are influenced by genetic factors (Ullén et al. 2016). In light of our current findings, we propose that AoO of training is also a crucial variable within this model since, depending on the maturational stage at which specific training takes place, some structures and networks will be more malleable and sensitive to change due to experience. Specifically, the four-group comparison performed here for the AF macrostructural properties highlights the specific effect of early commencement of music training in comparison to the early commencement of L2 acquisition, while suggesting that learning music later on does not drastically change the typical, more genetically determined, asymmetric pattern of lateralization of AF volume values (see Fig. 4).

The right dorsal auditory-motor network connected by the AF has been previously described as being involved in pitch, contour and prosody processing, as well as in music learning (Loui et al. 2011; Albouy et al. 2013; Sammler et al. 2015; Sihvonen et al. 2016). In addition, the right AF is one of the most important pathways recruited during music perception and learning (Halwani et al. 2011; Loui et al. 2011; Vaquero et al. 2018). Furthermore, AoO of music training during early childhood has been found to result in better adult performance on musical tasks (Watanabe et al. 2007; Bailey and Penhune 2010, 2012; Vaquero et al. 2016) and to be related to increased cortical surface area in the right ventral premotor cortex which is connected to posterior auditory and parietal cortex through the AF (Bailey et al. 2014; Habibi et al. 2018).

More broadly, the differential impact of early language and music training on brain structure is likely the result of the nature and timing of experience. Simultaneous bilingual experience starts even before the



Fig. 4. Summary of findings/conclusions and derived hypothesized time-course of brain structural changes on the long segment of the AF, depending on the life-time moment in which training takes place: L2 experience during early infancy enhances the leftward asymmetry (L much thicker than R); music training during early childhood enhances the volume of the right long segment, altering that normative asymmetry (L 'almost' equal in volume than R); L2 or music training starting after these distinct sensitive periods does not seem to alter the usual asymmetric pattern (L > R) elicited by normal maturation. Abbreviations: L2, second language; L, left; R, right.

moment of birth, and is immersive and constant. This type of experience may thus promote plasticity even in networks, such as the left LS, that are more strongly under genetic control. In comparison, music training can only begin once motor control is adequately acquired, typically no earlier than age 3-4 years. Unlike early bilingual experience, music training is deliberate, and is likely selected by and promoted in children with some pre-existing interest and skills. Musical training is also less immersive than bilingual experience, although placing similar demands on auditory-motor networks. So why might music training still promote additional brain plasticity? Music training implies significant amounts of deliberate practice, with repeated prediction, feedback and error correction (crucial functions of the dorsal pathway), and performance itself is likely rewarding (Penhune 2019). Thus, music training may promote plasticity later in childhood because it is a more conscious and deliberate process than the practice of two languages in a highly bilingual context, and because it requires higher precision of processing, repetition and focused attention (Patel 2011).

In the current study, no between-group differences were found for microstructural properties of the AF (i.e., FA, RD). Our results point to an effect of age of start of audio-motor trainings only on the volume of the tract. This volumetric effect may be due to changes in the packing properties of the tract, the thickness and morphology of the myelin sheaths, or the vasculature architecture surrounding the AF (Zatorre et al., 2012). These plastic mechanisms would mainly affect the macrostructural organization of the tract (i.e., FA/RD values).

Behaviourally, our musical tests helped us characterize our sample by showing a musical advantage for the Musician Bilingual group (supporting previous findings, Chen et al 2008a,b; Foster and Zatorre 2010; Bailey et al. 2014), but no between-group differences in the control condition of syllable discrimination. In contrast with previous studies (Bailey et al., 2014; see Penhune, 2011 for a review), no differences were found between ET and LT musicians regarding their performance on the music tasks. Although previous reports showed robust differences, they were typically small, and our current sample size or cohort variability may have prevented us to observe this difference.

Although the whole sample exhibited normative–range scores on the cognitive tests, Musician bilinguals, overall, showed better scores in auditory working memory (Letter-Number Sequencing) and Matrix Reasoning, but not in executive function, when compared to their non-

musician counterparts. Importantly, though, no specific difference for these cognitive variables was found between ET-musician bilinguals and Simultaneous bilingual NM, the groups crucially differing at the brain structural level.

4.1. Conclusion

In summary, by comparing two well-controlled groups of highlytrained bilinguals differing in their music experience, the present experiment was able to explore and disentangle the differential effects of two auditory-motor trainings and, more important, of their crucially different AoO. In conclusion, our findings reveal the interaction between normative maturation and two forms of intensive auditory-motor experience that begin at different points during development. We show that simultaneous exposure to two languages in infancy accentuated the leftward asymmetry of the LS, despite the fact that previous evidence has shown that the adult structure of this region is under largely genetic control. Further, music training during early childhood (ages 4–7 years) altered the macrostructure of the right LS, reducing the normative leftward asymmetry, consistent with evidence that it may be more malleable by environmental influences. We believe these findings are important first steps in contributing to our understanding of plasticity in crucial WM pathways underlying auditory-motor integration for language and music. Further, they begin to provide a more sophisticated understanding of sensitive periods and the interaction between brain maturation and experience. We thus conclude that AoO of specific experience plays a key role in a complex gene-environment interaction model where long-term plasticity depends on region-specific differences in malleability by experience, the age at which experience occurs and the type of learning experience.

5. Funding

This work was supported by grants to VP from NSERC (RGPIN/ 04225-2015) and CIHR (MOP-11541), by an NSERC grant to DK (RGPIN, 2014-05371), and by funding from the CRBLM to DK and VP via the Fonds de recherché du Québec –Nature et technologies and –Société et culture. LV was partially funded by the Fonds de recherche du Québec – Nature et technologies (i.e., Merit scholarship program for foreign students –PBEEE–), the Quebec's Bio-Imaging Network (i.e., QBIN's Postdoctoral Scholarship for Foreign Students), and the Auditory Cognitive Neuroscience Network within the Erasmus Mundus Program.

Declaration of competing interest

None declared.

CRediT authorship contribution statement

Lucía Vaquero: Conceptualization, Formal analysis, Investigation, Writing - original draft, Writing - review & editing, Project administration. Paul-Noel Rousseau: Formal analysis, Investigation, Writing original draft, Project administration. Diana Vozian: Investigation, Writing - original draft. Denise Klein: Conceptualization, Writing original draft, Writing - review & editing, Supervision, Funding acquisition. Virginia Penhune: Conceptualization, Writing - original draft, Writing - review & editing, Supervision, Funding acquisition.

Acknowledgements

The authors would like to thank Dr. Shanna Kousaie for their help in scoring and interpreting data regarding the Simon task; Joseph Thibodeau for his help in programming the experimental tasks; Brian Gunther for his help in preparing and scoring behavioural and cognitive tests; and the MRI technicians at the Brain Imaging Center of the MNI for their professionalism and smooth work during the scanning sessions. We also wish to thank all the participants for their engagement in the study, as well as the funding organizations.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.neuroimage.2020.116689.

References

- Abutalebi, J., Cappa, S.F., Perani, D., 2005. What can functional neuroimaging tell us about the bilingual brain? In: Kroll, Judith F., de Groot, Annette M.B. (Eds.), The Oxford Handbook of Bilingualism. Oxford University Press, Oxford (UK), pp. 497–515.
- Adluru, N., Zhang, H., Tromp, D.P.M., Alexander, A.L., 2013. Effects of DTI spatial normalization on white matter tract reconstructions. Mar 13 Proc. SPIE Int. Soc. Opt. Eng. 8669. https://doi.org/10.1117/12.2007130.
- Agosta, F., Galantucci, S., Canu, E., Cappa, S.F., Magnani, G., Franceschi, M., Falini, A., Comi, G., Filippi, M., 2013. Disruption of structural connectivity along the dorsal and ventral language pathways in patients with nonfluent and semantic variant primary progressive aphasia: a DT MRI study and a literature review. Brain Lang. 127 (2), 157–166.
- Albouy, P., Mattout, J., Bouet, R., Maby, E., Sánchez, G., Aguera, P.E., Daligault, S., Delpuech, C., Bertrand, O., Caclin, A., Tillman, B., 2013. Impaired pitch perception and memory in congenital amusia: the deficit starts in the auditory cortex. Brain 136 (Pt 5), 1639–1661.
- Bailey, J.A., Penhune, V.B., 2010. Rhythm synchronization performance and auditory working memory in early-and late-trained musicians. Exp. Brain Res. 204 (1), 91–101.
- Bailey, J., Penhune, V.B., 2012. A sensitive period for musical training: contributions of age of onset and cognitive abilities. Ann. N. Y. Acad. Sci. 1252 (1), 163–170.
- Bailey, J.A., Zatorre, R.J., Penhune, V.B., 2014. Early musical training is linked to gray matter structure in the ventral premotor cortex and auditory-motor rhythm synchronization performance. J. Cogn. Neurosci. 26 (4), 755–767.
- Berken, J.A., Chai, X., Chen, J.K., Gracco, V.L., Klein, D., 2016. Effects of early and late bilingualism on resting-state functional connectivity. J. Neurosci. 36 (4), 1165–1172.
- Berken, J.A., Gracco, V.L., Klein, D., 2017. Early bilingualism, language attainment, and brain development. Neuropsychologia 98, 220–227.
- Bermudez, P., Lerch, J.P., Evans, A.C., Zatorre, R.J., 2009. Neuroanatomical correlates of musicianship as revealed by cortical thickness and voxel-based morphometry. Cerebr. Cortex 19 (7), 1583–1596.
- Bialystok, E., Craik, F., Luk, G., 2008. Cognitive control and lexical access in younger and older bilinguals. J. Exp. Psychol. Learn. Mem. Cogn. 34 (4), 859–873.
- Birdsong, D., 2018. Plasticity, variability and age in second language acquisition and bilingualism. Front. Psychol. 9, 81.
- Borsa, V.M., Perani, D., Della Rosa, P.A., Videsott, G., Weekes, B.S., Franceschini, R., Abutalebi, J., 2018. Bilingualism and healthy aging: aging effects and neural maintenance. Neuropsychologia 111, 51–61.

- Braveman, P., Cubbin, C., Marchi, K., Egerter, S., Chavez, G., 2001. Measuring socioeconomic status/position in studies of racial/ethnic disparities: maternal and infant health. Publ. Health Rep. 116 (5), 449–463.
- Budisavljevic, S., Dell'Acqua, F., Rijsdijk, F.V., Kane, F., Picchioni, M., McGuire, P., Toulopoulou, T., Georgiades, A., Kalidindi, S., Kravariti, E., Murray, R.M., Murphy, D.G., Craig, M.C., Catani, M., 2015. Age-related differences and heritability of the perisylvian language networks. J. Neurosci. 35 (37), 12625–12634.
- Catani, M., Jones, D.K., ffytche, D.H., 2005. Perisylvian language networks of the human brain. Ann. Neurol. 57 (1), 8–16.
- Catani, M., Allin, M.P., Husain, M., Pugliese, L., Mesulam, M.M., Murray, R.M., Jones, D.K., 2007. Symmetries in human brain language pathways correlate with verbal recall. Proc. Natl. Acad. Sci. U. S. A. 104 (43), 17163–17168.
- Catani, M., Mesulam, M., 2008. The arcuate fasciculus and the disconnection theme in language and aphasia: history and current state. Cortex 44 (8), 953–961.
- Chen, J.L., Penhune, V.B., Zatorre, R.J., 2008a. Moving on time: brain network for auditory-motor synchronization is modulated by rhythm complexity and musical training. J. Cogn. Neruosci. 20 (2), 226–239.
- Chen, J.L., Penhune, V.B., Zatorre, R.J., 2008b. Listening to musical rhythms recruits motor regions of the brain. Cereb. Cortex 18 (12), 2844–2854.
- Christie, G.J., Hamilton, T., Manor, B.D., Farb, N.A.S., Farzan, F., Sixsmith, A., Temprado, J.J., Moreno, S., 2017. Do lifestyle activities protect gainst cognitive decline in aging? A review. Frot. Aging Neurosci. 9, 381.
- Del Maschio, N., Sulpizio, S., Gallo, F., Fedeli, D., Weekes, B.S., Abutalebi, J., 2018. Neuroplasticity across the lifespan and aging effects in bilinguals and monolinguals. Brain Cognit. 125, 118–126.
- DeLuca, V., Rothman, J., Bialystok, E., Pliatsikas, C., 2019. Redefining bilingualism as a spectrum of experiences that differentially affects brain structure. Proc. Natl. Acad. Sci. U.S.A. 116 (15), 7565–7574.
- Foster, N.E., Zatorre, R.J., 2010. Cortical structure predicts success in performing musical transformation judgments. Neuroimage 53 (1), 26–36.
- François, C., Ripollés, P., Bosch, L., García-Alix, A., Muchart, J., Sierpowska, J., Fons, C., Solé, J., Rebollo, M., Gaitán, H., Rodríguez-Fornells, A., 2016. Language learning and brain reorganization in a 3.5-year-old child with left perinatal stroke revealed using structural and functional connectivity. Cortex 77, 95–118.
- Friederici, A.D., 2009. Pathways to language: fiber tracts in the human brain. Trends Cognit. Sci. 13 (4), 175–181.
- Genesee, F., Nicoladis, E., 2007. Bilingual first language acquisition. In: Hoff, Erika, Shatz, Marilyn (Eds.), Blackwell Handbook of Language Development. Blackwell Publishing LTD, pp. 324–342. https://doi.org/10.1002/9780470757833.ch16 (Chapter 16).
- Geschwind, D.H., Miller, B.L., DeCarli, C., Carmelli, D., 2002. Heritability of lobar brain volumes in twins supports genetic models of cerebral laterality and handedness. Proc. Natl. Acad. Sci. U. S. A. 99 (5), 3176–3181.
- Gullifer, J.W., Chai, X.J., Whitford, V., Pivneva, I., Baum, S., Klein, D., Titone, D., 2018. Bilingual experience and resting.state brain connectivity: impacts of L2 age of acquisition and social diversity of language use on control networks. Neurospcyhologia 117, 123–134.
- Hackman, D.A., Farah, M.J., 2009. Socioeconomic status and the developing brain. Trends Cognit. Sci. 13 (2), 65–73.
- Häberling, I.S., Badzakova-Trajkov, G., Corballis, M.C., 2013. Asymmetries of the arcuate fasciculus in monozygotic twins: genetic and nongenetic influences. PloS One 8 (1), e52315.
- Habibi, A., Damasio, A., Ilari, B., Veiga, R., Joshi, A.A., Leahy, R.M., Haldar, J.P., Varadarajan, D., Bhushan, C., Damasio, H., 2018. Childhood music training induces change in micro and macroscopic brain structure: results from a longitudinal study. Cerebr. Cortex 28 (12), 4336–4347.
- Halwani, G.F., Loui, P., Rüber, T., Schlaug, G., 2011. Effects of practice and experience on the arcuate fasciculus: comparing singers, instrumentalists, and non-musicians. Front. Psychol. 2, 156.
- Hämäläinen, S., Sairanen, V., Leminen, A., Lehtonen, M., 2017. Bilingualism modulates the white matter structure of language-related pathways. Neuroimage 152, 249–257.
- Hayakawa, S., Marian, V., 2019. Consequences of multilingualism for neural architecture. Behav. Brain Funct. 15 (1), 6.
- Hensch, T.K., 2005. Critical period plasticity in local cortical circuits. Nat. Rev. Neurosci. 6 (11), 877–888.
- Hickok, G., Poeppel, D., 2004. Dorsal and ventral streams: a framework for understanding aspects of the functional anatomy of language. Cognition 92 (1), 67–99.
- Hickok, G., Poeppel, D., 2007. The cortical organization of speech processing. Nat. Rev. Neurosci. 8 (5), 393–402.
- Hickok, G., Poeppel, D., 2015. Neural basis of speech. Handb. Clin. Neurol. 129, 149–160. Innocenti, G.M., Price, D.J., 2005. Exuberance in the development of cortical networks. Nat. Rev. Neurosci. 6 (12), 955–965.
- Klawiter, E.C., Schmidt, R.E., Trinkaus, K., Liang, H.F., Budde, M.D., Naismith, R.T., Song, S.K., Cross, A.H., Benzinger, T.L., 2011. Radial diffusivity predicts demyelination in ex-vivo multiple sclerosis spinal cords. Neuroimage 55 (4), 1454–1460.
- Klein, D., Mok, K., Chen, J.K., Watkins, K.E., 2014. Age of language learning shapes brain structure: a cortical thickness study of bilingual and monolingual individuals. Brain Lang. 131, 20–24.
- Kousaie, S., Sheppard, C., Lemieux, M., Monetta, L., Taler, V., 2014. Executive function and bilingualism in young and older adults. Front. Behav. Neurosci. 8, 250.
- Lebel, C., Beaulieu, C., 2009. Laterization of the arcuate fasciculus from childhood to adulthood and its relation to cognitive abilities in children. Hum. Brain Mapp. 30 (11), 3563–3573.
- Lenneberg, E.H., 1967. The Biological Foundations of Language. John Wiley & Sons, New York City (NY).

Li, P., Legault, J., Litcofsky, K.A., 2014. Neuroplasticity as a function of second language learning: anatomical changes in the human brain. Cortex 58, 301–324.

Loui, P., Alsop, D., Schlaug, G., 2009. Tone deafness: a new disconnection syndrome? J. Neurosci. 29 (33), 10212–10220.

- Loui, P., Li, H.C., Hohmann, A., Schlaug, G., 2011. Enhanced cortical connectivity in absolute pitch musicians: a model for local hyperconnectivity. J. Cognit. Neurosci. 23 (4), 1015–1026.
- López-Barroso, D., Catani, M., Ripollés, P., Dell'Acqua, F., Rodríguez-Fornells, A., de Diego-Balaguer, R., 2013. Word learning is mediated by the left arcuate fasciculus. Proc. Natl. Acad. Sci. U. S. A. 110 (32), 13168–13173.
- Matsumoto, R., Okada, T., Mikuni, N., Mitsueda-Ono, T., Taki, J., Sawamoto, N., Hanakawa, T., Miki, Y., Hashimoto, N., Fukuyama, H., Takahashi, R., Ikeda, A., 2008. Hemispheric asymmetry of the arcuate fasciculus: a preliminary diffusion tensor tractography study in patients with unilateral language dominance defined by Wada test. J. Neurol. 255 (11), 1703–1711.
- Mechelli, A., Crinion, J.T., Noppeney, U., O'Doherty, J., Ashburner, J., Frackowiak, R.S., Price, C.J., 2004. Neurolinguistics: structural plasticity in the bilingual brain. Nature 431 (7010), 757.
- Patel, A.D., 2011. Why would musical training benefit the neural encoding of speech? The OPERA hypothesis. Front. Psychol. 2, 142.
- Penhune, V.B., 2011. Sensitive periods in human development: evidence from musical training. Cortex 47 (9), 1126–1137.
- Penhune, V.B., 2019. Musical expertise and brain structure: the causes and consequences of training. In: Thaut, Michel, Hodges, Donald (Eds.), The Oxford Handbook of Music and the Brain. Oxford University Press, Oxford (UK), pp. 1–22.
- Perani, D., Paulesu, E., Sebastián-Gallés, N., Dupoux, E., Dehaene, S., Bettinardi, V., Cappa, S.F., Fazio, F., Mehler, J., 1998. The bilingual brain. Proficiency and age of acquisition of the second language. Brain 121, 1841–1852.
- Perani, D., Abutalebi, J., Paulesu, E., Brambati, S., Scifo, P., Cappa, S.F., Fazio, F., 2003. The role of age of acquisition and language usage in early, high-proficient bilinguals: an fMRI study during verbal fluency. Hum. Brain Mapp. 19, 170–182.
- Pierce, L.J., Klein, D., Chen, J.K., Delcenserie, A., Genesee, F., 2014. Mapping the unconscious maintenance of a lost first language. Proc. Natl. Acad. Sci. Unit. States Am. 111 (48), 17314–17319.
- Powell, H.W., Parker, G.J., Alexander, D.C., Symms, M.R., Boulby, P.A., Wheeler-Kingshott, C.A., Barker, G.J., Noppeney, U., Koepp, M.J., Duncan, J.S., 2006. Hemispheric asymmetries in language-related pathways: a combined functional MRI and tractography study. Neuroimage 32 (1), 388–399.
- Ressel, V., Pallier, C., Ventura-Campos, N., Díaz, B., Roessler, A., Ávila, C., Sebastián-Gallés, N., 2012. An effect of bilingualism on the auditory cortex. J. Neurosci. 32 (47), 16597–16601.
- Ripollés, P., Biel, D., Peñaloza, C., Kaufmann, J., Marco-Pallarés, J., Noesselt, T., Rodríguez-Fornells, A., 2017. Strength of temporal White matter pathways predicts semantic learning. J. Neurosci. 37 (46), 11101–11113.
- Rodrigo, S., Naggara, O., Oppenheim, C., Golestani, N., Poupon, C., Cointepas, Y., Mangin, J.F., Le Bihan, D., Meder, J.F., 2007. Human subinsular asymmetry studied by diffusion tensor imaging and fiber tracking. AJNR Am. J. Neuroradiol. 28 (8), 1526–1531.
- Rodríguez-Fornells, A., Rojo, N., Amengual, J.L., Ripollés, P., Altenmüller, E., Münte, T.F., 2012. The involvement of audio-motor coupling in the music-supported therapy applied to stroke patients. Ann. N. Y. Acad. Sci. 1252, 282–293.
- Sammler, D., Grosbras, M.H., Anwander, A., Bestelmeyer, P.E., Belin, P., 2015. Dorsal and Ventral pathways for prosody. Curr. Biol. 25 (23), 3079–3085.
- Sierpowska, J., Gabarrós, A., Fernández-Coello, A., Camins, À., Castañer, S., Juncadella, M., Morís, J., Rodríguez-Fornells, A., 2017. Words are not enough:

nonword repetition as an indicator of arcuate fasciculus integrity during brain tumor resection. J. Neurosurg. 126 (2), 435–445.

- Sihvonen, A.J., Ripollés, P., Leo, V., Rodríguez-Fornells, A., Soinila, S., Särkämö, T., 2016. Neural basis of acquired amusia and its recovery after stroke. J. Neurosci. 36 (34), 8872–8881.
- Sihvonen, A.J., Ripollés, P., Särkämö, T., Leo, V., Rodríguez-Fornells, A., Saunavaara, J., Parkkola, R., Soinila, S., 2017. Tracting the neural basis of music: deficient structural connectivity underlying acquired amusia. Cortex 97, 255–273.
- Smith, S.M., 2002. Fast robust automated brain extraction. Hum. Brain Mapp. 17 (3), 143–155.
- Smith, S.M., Jenkinson, M., Woolrich, M.W., Beckmann, C.F., Behrens, T.E., Johansen-Berg, H., Bannister, P.R., De Luca, M., Drobnjak, I., Flitney, D.E., Niazy, R.K., 2004. Advances in functional and structural MR image analysis and implementation as FSL. Neuroimage 23, S208–S219.
- Song, S.K., Sun, S.W., Ramsbottom, M.J., Chang, C., Russell, J., Cross, A.H., 2002. Dysmyelination revelead through MRI as increased radial (but unchanged axial) diffusion of water. Neuroimage 17 (3), 1429–1436.
- Song, S.K., Yoshino, J., Le, T.Q., Lin, S.J., Sun, S.W., Cross, A.H., Armstrong, R.C., 2005. Demyelination increases radial diffusivity in corpus callosum of mouse brain. Neuroimage 26 (1), 132–140.
- Tak, H.J., Kim, J.H., Son, S.M., 2016. Developmental process of the arcuate fasciculus from infancy to adolescence: a diffusion tensor imaging study. Neural Regen. Res. 11 (6), 937–943.
- Ullén, F., Hambrick, D.Z., Mosing, M.A., 2016. Rethinking Expertise: a multifactorial gene-environment interaction model of expert performance. Psychol. Bull. 142 (4), 427–446.
- Vable, A.M., Eng, C.W., Mayeda, E.R., Basu, S., Marden, J.R., Hamad, R., Glymour, M.M., 2018. Mother's education and late-life disparities in memory and dementia risk among US military veterans and non-veterans. J. Epidemiol. Community Health 72 (12), 1162–1167.
- Vaquero, L., Hartmann, K., Ripollés, P., Rojo, N., Sierpowska, J., François, C., Càmara, E., van Vugt, F.T., Mohammadi, B., Samii, A., Münte, T.F., Rodríguez-Fornells, A., 2016. Structural neuroplasticity in expert pianists depends on the age of musical training onset. Neuroimage 126, 106–119.
- Vaquero, L., Rodríguez-Fornells, A., Reiterer, S.M., 2017. The left, the better: whitematter brain integrity predicts foreign language imitation ability. Cerebr. Cortex 27 (8), 3906–3917.
- Vaquero, L., Ramos-Escobar, N., François, C., Penhune, V., Rodríguez-Fornells, A., 2018. White-matter structural connectivity predicts short-term melody and rhythm learning in non-musicians. Neuroimage 181, 252–262.
- Watanabe, D., Savion-Lemieux, T., Penhune, V.B., 2007. The effect of early musical training on adult motor performance: evidence for a sensitive period in motor learning. Exp. Brain Res. 176 (2), 332–340.
- Woolrich, M.W., Jbabdi, S., Patenaude, B., Chappell, M., Makni, S., Behrens, T., Beckmann, C., Jenkinson, M., Smith, S.M., 2009. Bayesian analysis of neuroimaging data in FSL. Neuroimage 45, S173–S186.
- Weschler, D., 2008. Weschler Adult Intelligence Scale–Fourth Edition (WAIS-IV). NCS Pearson.
- Zatorre, R.J., Chen, J.L., Penhune, V.B., 2007. When the brain plays music: auditorymotor interactions in music perception and production. Nat. Rev. Neurosci. 8 (7), 547–558.
- Zatorre, R.J., Fields, R.D., Johansen-Berg, H., 2012. Plasticity in gray and white: neuroimaging changes in brain structure during learning. Nat. Neurosci. 15 (4), 528–536.
- Zatorre, R.J., 2013. Predispositions and plasticity in music and speech learning: neural correlates and implications. Science 342 (6158), 585–589.