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Musical Sophistication and Multilingualism: Effects on Arcuate Fasciculus Characteristics

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ABSTRACT

The processing of auditory stimuli which are structured in time is thought to involve the arcuate fasciculus, the white matter tract which connects the temporal cortex and the inferior frontal gyrus. Research has indicated effects of both musical and language experience on the structural characteristics of the arcuate fasciculus. Here, we investigated in a sample of $n = 84$ young adults whether continuous conceptualizations of musical and multilingual experience related to structural characteristics of the arcuate fasciculus, measured using diffusion tensor imaging. Probabilistic tractography was used to identify the dorsal and ventral parts of the white matter tract. Linear regressions indicated that different aspects of musical sophistication related to the arcuate fasciculus' volume (emotional engagement with music), volumetric asymmetry (musical training and music perceptual abilities), and fractional anisotropy (music perceptual abilities). Our conceptualization of multilingual experience, accounting for participants' proficiency in reading, writing, understanding, and speaking different languages, was not related to the structural characteristics of the arcuate fasciculus. We discuss our results in the context of other research on hemispheric specializations and a dual-stream model of auditory processing.

1 | Introduction

Music and language are both auditory stimuli which are structured in time. Their processing thus involves both the auditory cortex and the inferior frontal gyrus (Golestani et al. 2006; Kunert et al. 2015; Nan and Friederici 2013; Schneider et al. 2005; for a different view on the role of the inferior frontal gyrus in music processing, see also Chen et al. 2023) which are connected through a white matter tract referred to as the arcuate fasciculus (AF). The AF supports the processing of auditory stimuli via two routes: (1) a long pathway, also called the direct

AF or the long segment of the AF, and (2) an indirect pathway, also referred to as the indirect AF or the indirect segments of the AF, namely a posterior segment connecting the auditory cortex to the inferior parietal lobule and an anterior segment connecting the inferior parietal lobule with the inferior frontal gyrus.

The AF has been studied both in the context of music processing and language processing tasks and skills. For example, volume and fractional anisotropy (FA) values in the ventral part of the direct AF, which directly connects the middle temporal gyrus to the inferior frontal gyrus, correlate with

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Summary

- Different aspects of musical sophistication relate to arcuate fasciculus' volume (emotional engagement), volumetric asymmetry (musical training and music perceptual abilities), and fractional anisotropy (music perceptual abilities).
- The relationship between multilingual experience and structural characteristics of the arcuate fasciculus remains unclear.
- Results provide indications for hemispheric specializations and a dual-stream model of music processing.

performance in both a pitch-based grammar learning task (Loui, Li, and Schlaug 2011) and a structural planning of harmonic sequences (Bianco et al. 2016). Further, left AF FA values and volumetric asymmetry relate to phonological skills in children (Yeatman et al. 2011), and mean diffusivity of the anterior segment of the AF has been linked to grammar learning abilities (Kepinska et al. 2017). The lateralization of the AF is also associated with hemispheric language dominance such that participants whose language dominance is mainly represented in one hemisphere show volumetric asymmetry corresponding to the dominant hemisphere (Matsumoto et al. 2008; Vassal et al. 2016).

1.1 | Experience and the Arcuate Fasciculus

Researchers have also examined how different levels of musical and language *experience* may relate to structural characteristics of the AF. Higher volume and FA values of the right direct AF have been found for musicians compared to nonmusicians (Vaquero et al. 2020), particularly in the *dorsal* part which directly connects the superior temporal gyrus to the inferior frontal gyrus (Halwani et al. 2011), with FA values in the right AF correlating with the amount of piano practicing in adulthood (Bengtsson et al. 2005). These findings converge with reports of greater rightward FA asymmetry for musicians compared to nonmusicians (Li, Zatorre, and Du 2021). Further, FA values in the right direct AF but not in the left AF correlate with the learning rate of a melodic task in nonmusicians (Vaquero et al. 2018). However, others have also reported lower FA for musicians compared to nonmusicians (Acer et al. 2018), or greater rightward FA symmetry for nonmusicians compared to musicians (Oechslin et al. 2010).

Understanding of the influence of language experience on structural characteristics of the AF are also mixed. Some have reported on FA differences in the left AF between early and late bilinguals (Hämäläinen et al. 2017), while others have found no such differences between monolingual, early bilingual, and late bilingual participants (Mohades et al. 2012). One study found an absence of AF lateralization in a sample of 30 trilingual participants (Yazbek et al. 2021), while several others noted leftward asymmetry (Fernández-Miranda et al. 2015; Vassal et al. 2016). These different findings suggest that an effect of language experience on the AF cannot be ruled out. Further, the neuroplastic effect of additional

language experience often occurs in the first year of life (Vaquero et al. 2020). However, a recent paper also showed changes in the right AF after intensive second language learning in young adults (Wei et al. 2024) and others have shown that reduced leftward volumetric asymmetry may be more advantageous to verbal memory (Catani et al. 2007).

Few studies have studied contrasts between the musical and language experience or the effects of combined musical and language experience. To the best of our knowledge, only one study has contrasted musical and language experience (Vaquero et al. 2020). This work recruited musicians and non-musicians who were either simultaneous or sequential bilinguals and found the greatest leftward volumetric asymmetry in the direct AF for simultaneous bilingual nonmusicians. There was almost no asymmetry for early-trained musician bilinguals (this group included both simultaneous and sequential bilinguals). No group effects on asymmetry were found for the anterior or posterior segments. These results are consistent with prior work suggesting that language experience may influence structural characteristics of the left direct AF (Hämäläinen et al. 2017; Yeatman et al. 2011) while musical experience may influence structural characteristics of the right direct AF (Halwani et al. 2011; Loui, Li, and Schlaug 2011). This pattern of asymmetry mirrors other findings on music- and language-processing related asymmetries of the auditory network (for a review, see Zatorre 2022).

Despite some research indicating that musical and language experience are linked (Nayak et al. 2022), only very few studies have considered the effects of musical and language experience in the same sample by investigating singing experience. Singing experience combines musical and language experience to some extent, as greater musical experience as a singer through expanded foreign language repertoire naturally includes additional engagement with language (Perron, Vaillancourt, and Tremblay 2022). To this effect, a study of choir singers indicated higher leftward FA asymmetry in a segment of the AF localized to the posterior temporal lobe (Perron et al. 2021). Similarly, a study comparing professional or trainee singers to instrumentalists, that is, participants with presumably greater music and language experience to participants with greater music experience, indicated higher leftward volume asymmetry for singers but an inverse relationship between the amount of singing training and the FA value of the left dorsal AF (Halwani et al. 2011). Thus, combined musical and language experience may further accentuate direct AF characteristics, particularly its volume and FA.

1.2 | Conceptualizing Musical and Language Experience

Our goal was to study the relationship between structural characteristics of the direct AF and musical and language experience in a single sample of participants, using continuous conceptualizations of musical and language experience. Such conceptualizations allow us to move beyond the trained musician/untrained nonmusician and the bilingual/monolingual binary categorization. In the case of musical experience, a continuous conceptualization allows us to study distributions

in participants who despite never having received formal music training may show a high degree of active and emotional engagement with music, as well as music perceptual and singing abilities, which may be summarized under the term *musical sophistication*. These attributes can be measured using the validated Goldsmiths Musical Sophistication Index (Gold-MSI, Müllensiefen et al. 2014). Indeed, researchers have shown that structural characteristics of the left AF may relate to male participants' active engagement with music as measured using the relevant Gold-MSI subscale (Mehrabinejad et al. 2021).

To the best of our knowledge, no other report of relationships between Gold-MSI subscales and white matter characteristics exists. Some studies however relate Gold-MSI subscale values to other brain characteristics. The musical training and emotional engagement subscales for example are both associated with variations in the functional connectivity of the bilateral precentral gyri (Cui et al. 2023) and greater volume of the inferior frontal gyrus in healthy older adults (Chaddock-Heyman et al. 2021). The latter result in particular suggests a potential correlation between musical sophistication and AF characteristics. However, no association between the active engagement and musical training subscales were reported with a whole-brain measure (Matziorinis, Gaser, and Koelsch 2022).

Others have studied possible associations between AF characteristics and a continuous conceptualization of musical reward sensitivity as measured using the Barcelona Music Reward Questionnaire (BMRQ, Mas-Herrero et al. 2013), which in turn is positively correlated with musical sophistication (Kreutz and Cui 2022). The volume of the tract between the left superior temporal gyrus and left anterior insula which likely includes parts of the AF seems to relate to the BMRQ (Loui et al. 2017). Indeed, another report indicates a possible relationship between left AF fiber characteristics and the BMRQ (Matthews et al. 2024).

A continuous conceptualization of language experience may take into consideration different aspects of language proficiency, that is, proficiency in reading, writing, understanding, and speaking a language (Kaushanskaya, Blumenfeld, and Marian 2020), and may also account for typological differences between the languages in which a participant is proficient (Kepinska, Caballero, et al. 2023). Such a continuous conceptualization of language experience which may be termed *multilingualism* has been shown to, for example, relate to structural characteristics of the auditory cortex (Kepinska, Dalboni Da Rocha, et al. 2023).

1.3 | Current Study

As outlined above, research indicates effects of musical training on and relationships with music cognition tasks with characteristics of the direct segment (Bianco et al. 2022; Vaquero et al. 2018, 2020). Previous studies have differed in their choice of a segmentation approach though. For instance, some have studied characteristics of the anterior and posterior segments in addition to characteristics of the long or direct segments (see e.g., Catani and Mesulam 2008; Catani, Jones,

and Ffytche 2005; Chen et al. 2018; Vaquero et al. 2020, 2021) while others divided the white matter tract into even smaller segments to support localization efforts (see e.g., Perron et al. 2021). Yet the direct segment of the AF seems to be more important compared to the anterior and posterior segments for music perceptual abilities (Vaquero et al. 2021). In our study, we therefore examine whether continuous conceptualizations of musical and language experience correspond to white matter characteristics of the dorsal or the ventral part of the direct AF.

The separation of a dorsal and ventral part of the direct AF (as described for instance by Bianco et al. 2022; Fernández-Miranda et al. 2015; Halwani et al. 2011; Glasser and Rilling 2008; Loui, Li, and Schlaug 2011; see also Nakajima et al. 2020) is particularly relevant for our study given that musical sophistication encapsulates different abilities and aspects of musical experience. In turn these attributes correspond to the proposed functions of the dorsal and ventral streams in a dual-stream model of music processing (Loui 2015). The dorsal stream is hypothesized to support fine-grained auditory-motor mappings, a function which is crucial to making music, whereas the ventral stream is hypothesized to support sound object identification and may thus be crucial to perceiving music (Baumann et al. 2007; Loui 2015). Indeed, differing levels of experience in music making correspond to differences in the dorsal stream (Dittinger et al. 2018; Halwani et al. 2011), whereas differences in pitch perception abilities co-occur with differences in ventral AF characteristics (Loui, Alsop, and Schlaug 2009).

These productive and perceptual aspects of musical sophistication are differentiated within the Gold-MSI. The musical training and singing abilities subscales assess respondents' experience with making music and their vocal skills respectively and may thus predominantly assess dorsal stream functions. In contrast, the perceptual abilities subscale assesses respondent's skills in judging and differentiating sounds and may thus predominantly assess ventral stream functions. Thus, we ask here: (1) do musical sophistication and/or multilingualism relate to AF volume and volumetric asymmetry, and (2) do musical sophistication and/or multilingualism relate to FA values and FA asymmetry of the AF? Findings will help us better understand the interplay of musical and language experience and their relation to structural characteristics of the white matter tract connecting brain areas linked to the processing of music and language.

2 | Methods

2.1 | Participants

Data were collected from 86 young adult participants after obtaining informed consent. All participants were enrolled at the same, selective university and may thus be considered highly educated. We excluded two participants from analysis due to incidental findings, bringing our final sample size to $n = 84$ ($M = 20.95$ years, $SD = 3.13$ years). Of the included participants, 47 participants were female, 37 were male. Note that analyses on the relationship of 73 of the included participants' resting-state fMRI data with musical sophistication are published elsewhere (Cui et al. 2023).

2.2 | Data Acquisition and Processing

2.2.1 | Experience: Gold-MSI and LEAP-Q

Participants completed the Goldsmiths Musical Sophistication Index (Gold-MSI, Müllensiefen et al. 2014), which provides a summary scale of general sophistication as well as subscales on active engagement, emotions, perceptual abilities, singing abilities, and musical training. We refer to these subscales below as *musical sophistication aspects*. We calculated these values as described by Müllensiefen et al. (2014), then z-scored the resulting values to use them as predictors in our statistical models.

Participants further completed the Language Experience and Proficiency Questionnaire (LEAP-Q, Kaushanskaya, Blumenfeld, and Marian 2020). On this questionnaire, participants report their proficiency in reading, writing, understanding, and speaking for each known language. Additionally, participants report the age of acquisition and their total exposure to each of their known languages. We used participants' responses on the LEAP-Q to calculate measures of multilingualism.

First, for each language reported to be known by the participants, we calculated an average proficiency score based on their reported reading, writing, understanding, and speaking skills (on a scale between 0 and 10). If data were missing, we assumed a proficiency of 10 for the native language (one participant), and a proficiency of 1 for all other languages (five participants). Next, for each participant, we calculated one measure of multilingualism by combining the average proficiency scores of participants' different languages into a *language experience* index per participant. This was computed with Shannon's entropy equation (Shannon 2001).

To further account for differences between the languages, we calculated a second measure of multilingualism which included information on lexical distances between the languages (henceforth *typological language experience*). Here, following methodology outlined in Kepinska, Caballero, et al. (2023), we collected lexical distances between each participant's languages through the ASJP Database (<http://asjp.clld.org/>, Wichmann, Holman, and Brown 2018). When participants noted "Chinese" as a language, this was coded as "Mandarin," and when they noted "Arabic" as a language, this was coded as "Standard Arabic." When participants noted "ASL" as a language, the highest distance occurring in the database was used as the lexical distance between ASL and the participants' other languages. Next, using Rao's quadratic entropy equation (Rao 1982), we combined the summed lexical distances between all language pairs for each participant by weighing them by their respective proficiency score.

We calculated four more indices using both Shannon's entropy and Rao's quadratic entropy equations: A language experience index for which each language's age of acquisition was used as a weight (lower age of acquisition, on a logarithmic scale, received higher weights) and a typological language experience index, again where age of acquisition, transformed as above, was used as weight, as well as a language experience index for which each language's total exposure was used as a weight (higher total

exposure received higher weights) and a typological language experience index, again where total exposure was used as a weight. All indices were z-scored to use them as predictors in our statistical models.

2.2.2 | DTI

We obtained from each participant: (1) a high-resolution T1 scan (TR = 7.4 ms, TE = 3.7 ms, flip angle $\theta = 6^\circ$, FOV = 256 mm, 160 slices, 1 mm thickness, scan time = 3.2 min), as well as (2) diffusion weighted scans using a high-angular resolution diffusion imaging sequence across 60 non-collinear diffusion gradients (b -value = 700 s/mm², TR/TE = 7015/60 ms, voxel size = 2 × 2 mm, FOV = 224 × 224 × 154 mm, slice thickness = 2.2 mm), and (3) three T2 scans with a b -value of 0 (TR = 5266 ms, TE = 68 ms, acquired voxel size = 2.2 mm × 2.2 mm × 2.2 mm reconstructed in plane to 2 mm with 0 mm slice gap, FOV = 224 × 226 mm, scan time = 5.5 min).

FMRIB's FSL suite 5.0.9 (Smith et al. 2004) was used to pre-process raw images. To correct for eddy currents and head motion, a 3D affine registration was used (Jenkinson and Smith 2001). The b -vectors gradient matrix was rotated in the process of using these tools. We used *bet* for brain extraction (Smith 2002) before estimating eigenvectors and eigenvalues of diffusion tensors for each voxel and FA values were calculated using the *dtifit* function in FSL. The probability distribution for fiber direction was calculated for each voxel using *bedpostx* (Behrens et al. 2007). Similar pre-processing pipelines have been used by others interested in AF characteristics (Bianco et al. 2016; Halwani et al. 2011; Perron et al. 2021; Vaquero et al. 2021).

The segmentation procedure of the AF described here mimics the one described by Halwani et al. (2011) and others (Bianco et al. 2016; Fernández-Miranda et al. 2015; Loui, Li, and Schlaug 2011; Loui et al. 2017), though for consistency's sake we opted for an atlas-based approach to create seed (superior temporal gyrus and middle temporal gyrus) and waypoint/target (inferior frontal gyrus) masks rather than defining these regions through hand drawing. Masks were created based on the Harvard-Oxford Structural Atlas (Desikan et al. 2006) in MNI-space, then co-registered to T1 space. Afterwards, masks were co-registered to diffusion space at the participant level, then thresholded at 50% and binarized.

Probabilistic tractography was then applied to trace the dorsal branch of the AF (STG to IFG) and the ventral branch of the AF (MTG to IFG), using the *probtrackx2* function in FSL (Behrens et al. 2007) with the default settings of the curvature threshold at $c = 0.2$. The resulting tract was thresholded at 10% and then binarized for both branches on the left and right hemisphere to create tract masks. The volume and mean and standard deviation of FA values were calculated for each tract mask, as well as volumetric and FA asymmetry by applying the formula $asymmetry = (left - right) / (left + right)$ (Perron et al. 2021), such that positive values indicate leftward and negative values indicate rightward asymmetry. For visualization purposes and voxelwise follow-up analysis, tracts were transformed back into MNI space.

2.3 | Statistical Models

All analyses were carried out in R version 4.3.0 (R Core Team 2022). To assess relationships between musical and language experience, we correlated musical sophistication aspects, language experience, and typological language experience. Separate linear regressions were then conducted to test whether: (1) AF volume (in proportion to whole-brain volume) and AF volume asymmetry, (2) FA and FA asymmetry are predicted by musical sophistication aspects and/or (typological) language experience.

The final model for each analysis was selected via a three-stage process. First, an initial model was created to assess each outcome measure as a function of tract, hemisphere (where applicable), and all musical sophistication aspects. Variance inflation factor, calculated using the car package (Fox, Weisberg, and Price 2001), was assessed as an indicator of possible multicollinearity. After confirming that multicollinearity was low, we proceeded to the second stage.

During the second stage, we added an index of language experience. Given that each language experience index is highly related to its typological version (see below), we compared models to determine first which language experience index should be included (based on proficiency, age of acquisition, or exposure), and then whether the typological language experience index should be included in the final model. Where models resulted in similar values, the model with the more parsimonious language experience index was selected, that is, the non-typological index.

During the third and last stage, variations of the most parsimonious model determined from the steps above were created with terms for participant sex and participant age. To determine the final model for each outcome measure, models were compared using the Akaike Information Criterion (AIC, Akaike 1974) to determine whether these additional models improved model fit. Variance inflation factors and model iterations can be found in the Appendix S1 (Tables S1–S3).

For AF volume, the final model was determined to include tract, hemisphere, all musical sophistication aspects, language

experience based on proficiency, and sex (9 predictors). For AF volume asymmetry, the final model was determined to include tract, all musical sophistication aspects, language experience, and age (8 predictors). For FA, the final model was determined to include tract, hemisphere, all musical sophistication aspects, language experience based on proficiency, and sex (9 predictors). For FA asymmetry, the final model was determined to include tract, musical sophistication aspects, and language experience (7 predictors). To accompany each model, resultant effect sizes (Cohen's f^2) were calculated using the sensemakr package in R (Cinelli, Ferwerda, and Hazlett 2019).

We further followed up our FA model with exploratory voxelwise analyses using *randomize* (Winkler et al. 2014) with 5000 permutations and threshold-free cluster enhancement, given that region-specific effects of music experience and language experience on FA have been shown before (see e.g., Bengtsson et al. 2005; Halwani et al. 2011; Perron et al. 2021). Thus, we explored where in the AF the FA values were related to musical sophistication and/or language experience while controlling for sex and age.

3 | Results

All musical sophistication aspects were highly correlated with each other, $r(82)=0.478$ to $r(82)=0.768$, $ps < 0.001$. Participants' mean and standard deviation for each subscale, along with the range of values that can be achieved, as well as Pearson's r -values between subscales are reported in Table 1.

Participants' cumulative language proficiency is shown in Figure 1. All language experience indices were highly correlated with each other, $r(78)=0.472$ to $r(78)=0.974$, $ps < 0.001$. Participants' mean and standard deviation for each index and Pearson's r -values between the indices are reported in Table 2.

The correlation between language experience and singing abilities approached significance, $r(79)=0.193$, $p=0.084$. All other correlations between language experience indices and musical sophistication aspects were not significant, $ps > 0.100$.

TABLE 1 | The range of values that can be achieved, and participants' mean and standard deviation of each Gold-MSI subscale and Pearson's r for their correlations.

	Active engagement	Perceptual abilities	Musical training	Emotions	Singing abilities
Subscale range	[9–63]	[9–63]	[7–49]	[6–42]	[7–49]
Active engagement	$M=40.21$ $SD=8.68$				
Perceptual abilities	$r(82)=0.688$	$M=48.88$ $SD=8.74$			
Musical training	$r(82)=0.583$	$r(82)=0.768$	$M=28.58$ $SD=10.96$		
Emotions	$r(82)=0.664$	$r(82)=0.562$	$r(82)=0.478$	$M=34.06$ $SD=5.04$	
Singing abilities	$r(82)=0.562$	$r(82)=0.717$	$r(82)=0.639$	$r(82)=0.479$	$M=32.56$ $SD=8.80$

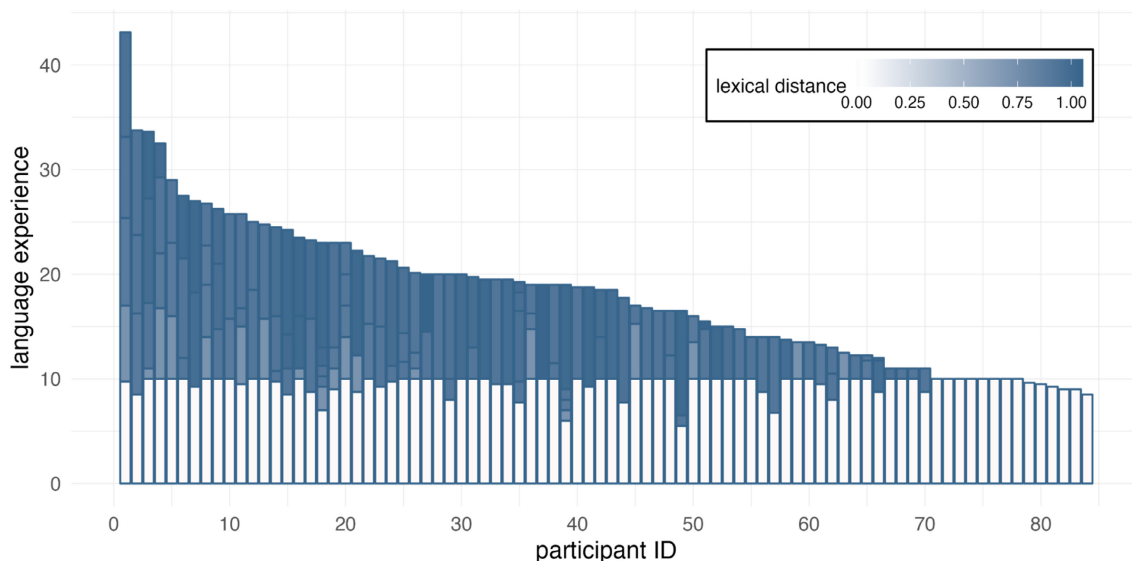


FIGURE 1 | Illustration of the participants' language experience. Each bar represents a single participant's overall language experience; the height of the stacked bars within each bar represents the self-reported proficiency for individual languages (the taller the bar, the higher the proficiency), per LEAP-Q (Kaushanskaya, Blumenfeld, and Marian 2020). The height of the white part indicates participants' English proficiency. Proficiency in other languages is represented by the height of the blue part within each bar; the shade of blue stands for the lexical distance of each language to English: The darker the shade, the more lexically distant from English the language. Prior to plotting, data were sorted by the overall language experience values; consequently, data of participants with most diverse language experience can be found on the left-hand side of the figure, and the right-hand side includes data from monolinguals (i.e., with knowledge of only one language).

TABLE 2 | Participants' mean and standard deviation of each language experience and typological language experience index and Pearson's r for their correlations.

		Language experience			Typological language experience		
		prof	acq	exp	prof	acq	exp
Language experience	prof	$M=0.79$ $SD=0.44$					
	acq	$r(79)=0.970$	$M=0.85$ $SD=0.49$				
	exp	$r(78)=0.573$	$r(78)=0.562$	$M=0.47$ $SD=0.34$			
Typological language experience	prof	$r(79)=0.952$	$r(79)=0.917$	$r(78)=0.659$	$M=0.41$ $SD=0.20$		
	acq	$r(79)=0.930$	$r(79)=0.960$	$r(78)=0.644$	$r(79)=0.960$	$M=0.44$ $SD=0.22$	
	exp	$r(78)=0.481$	$r(78)=0.472$	$r(78)=0.974$	$r(78)=0.612$	$r(78)=0.588$	$M=0.27$ $SD=0.20$

Note: Indices were based on participants' self-reported proficiency (prof), age of acquisition (acq), or total exposure (exp).

Tractography outcomes, that is, participants' dorsal and ventral AF on the left and right hemispheres, are shown in Figure 2. For visualization purposes, the outcomes were transformed into MNI space.

3.1 | Volume and Volumetric Asymmetry

Participants' AF volume is visualized in Figure 3, separately for the dorsal and ventral tract and left and right hemispheres. Output from our linear regression conducted to test whether AF

volume was related to musical sophistication and/or language experience is shown in Table 3. This analysis revealed that the overall model was significant, $R^2=0.26$, $F(9, 314)=12.12$, $p<0.001$, and that tract, hemisphere, the Gold-MSI Emotions subscale, and sex were significant predictors (see Table 3, also for effect sizes). For illustrative purposes, we have graphed residual values from our regression conducted on AF volume across participants' Gold-MSI Emotions values, separately for the dorsal (orange) and ventral (blue) tracts, the left and right hemisphere, and male (shown in lighter shaded diamonds) and female (shown in darker shaded circles) participants in Figure 4. As can be seen by the estimated

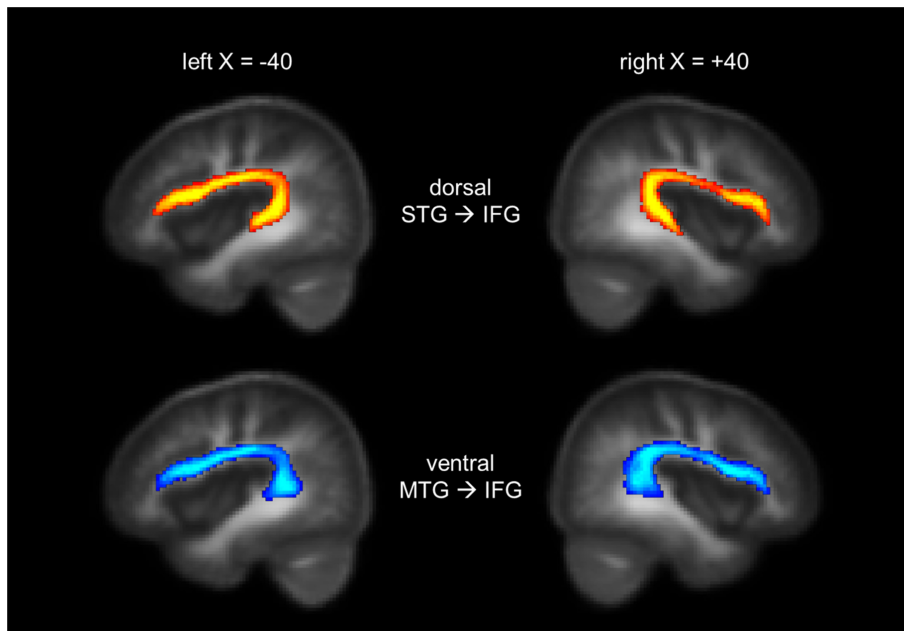


FIGURE 2 | Probabilistic tractography outcome averaged over all participants shown in MNI space. Dorsal and ventral AF are shown in the left and right hemisphere overlaid on the average FA map.

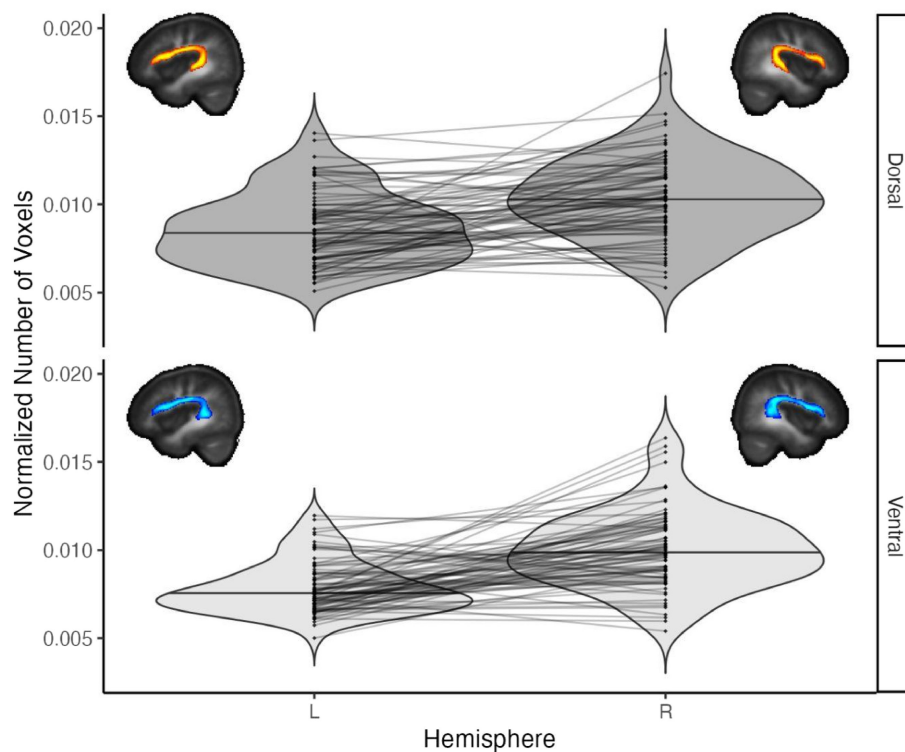


FIGURE 3 | Normalized number of voxels (i.e., against whole-brain number of voxels) for each AF tract of interest across hemispheres. Individual participants are represented by individual dots, with lines showing the same participant across hemispheres for visualization purposes.

slopes, the positive relationship between the Gold-MSI Emotions subscale values and the normalized AF volume seems to be driven predominantly by the relationship between these variables in male participants' right hemisphere.

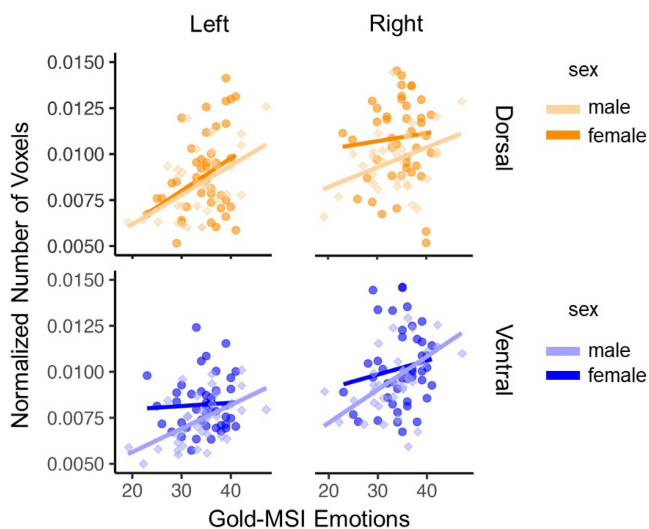
Output from our linear regression conducted to test whether AF volume asymmetry was predicted by musical sophistication

and/or language experience is shown in Table 4. This analysis revealed that the overall model was significant, $R^2=0.10$, $F(8, 153)=2.17$, $p=0.032$, and that the Gold-MSI Musical Training subscale, the Gold-MSI Perceptual Abilities subscale, and age were significant predictors (see Table 4, also for effect sizes). For illustrative purposes, we have graphed residual values resulting from our regression on AF volume asymmetry across

TABLE 3 | Linear regression conducted to assess whether AF volume was predicted by tract, hemisphere, musical sophistication aspects, language experience, and sex.

Predictors	AF volume			
	Estimates (95% CI)	Standard error	<i>p</i>	Cohen's f^2
(Intercept)	0.00818 (0.00772–0.00864)	0.00023	< 0.001	
Hemisphere (right)	0.00196 (0.00152–0.00240)	0.00022	< 0.001	0.248
Tract (ventral)	–0.00057 (–0.00100 to –0.00013)	0.00022	0.011	0.021
Gold-MSI Emotions	0.00046 (0.00016–0.00076)	0.00015	0.003	0.029
Gold-MSI Training	0.00013 (–0.00022 to 0.00047)	0.00018	0.465	< 0.01
Gold-MSI Singing	–0.00002 (–0.00035 to 0.00031)	0.00017	0.917	< 0.01
Gold-MSI Active	–0.00032 (–0.00067 to 0.00003)	0.00018	0.070	0.011
Gold-MSI Perceptual Abilities	–0.00024 (–0.00066 to 0.00017)	0.00021	0.252	< 0.01
Language experience	0.00017 (–0.00005 to 0.00040)	0.00012	0.134	< 0.01
Sex (female)	0.00060 (0.00015–0.00106)	0.00023	0.010	0.021
Observations		324		
R^2/R^2 adjusted		0.2578/0.2365		

Note: Resultant effect sizes were calculated using the `sensemakr` package in R (Cinelli, Ferwerda, and Hazlett 2019).

**FIGURE 4** | Residual values of normalized number of voxels (i.e., against whole-brain number of voxels) across Gold-MSI Emotions values for each AF tract of interest and hemisphere. Female participants are represented by darker shaded circles, and male participants are represented by lighter shaded diamonds.

participants' Gold-MSI Musical Training, Gold-MSI Perceptual Abilities, and age respectively in Figure 5. The shift away from

leftward asymmetry as a function of the Gold-MSI Musical Training subscale values (left column of panels) is noticeable in the dorsal tract. Conversely, the shift towards leftward asymmetry as a function of the Gold-MSI Perceptual Abilities subscale values (middle column of panels) is noticeable in the ventral tract.

3.2 | FA and FA Asymmetry

Participants' FA values are visualized in Figure 6, separately for the dorsal and ventral tract and left and right hemispheres. Output from our linear regression conducted to test whether FA was related to musical sophistication and/or language experience is shown in Table 5. This analysis revealed that the overall model was significant, $R^2=0.44$, $F(9, 314)=27.42$, $p<0.001$, and that tract, hemisphere, the Gold-MSI Perceptual Abilities subscale, and sex were significant predictors (see Table 5, also for effect sizes). For illustrative purposes, we have graphed residual values of the regression model on AF values across participants' Gold-MSI Perceptual Abilities values, separately for the dorsal (orange) and ventral (blue) tracts, the left and right hemisphere, and male (shown in lighter shaded diamonds) and female (shown in darker shaded circles) participants, in Figure 7. Greater FA values were found in the ventral tract, also as a function of Gold-MSI Perceptual Abilities subscale values, though more so for female participants.

TABLE 4 | Linear regression conducted to assess whether AF volume asymmetry was predicted by tract, musical sophistication aspects, language experience, and age.

Predictors	AF volume asymmetry			Cohen's f^2
	Estimates (95% CI)	Standard error	p	
(Intercept)	-0.284 (-0.431 to -0.137)	0.074	< 0.001	
Tract (ventral)	-0.021 (-0.062 to 0.019)	0.020	0.294	< 0.01
Gold-MSI Emotions	0.001 (-0.027 to 0.028)	0.014	0.958	< 0.01
Gold-MSI Training	-0.044 (-0.077 to -0.011)	0.017	0.009	0.046
Gold-MSI Singing	0.005 (-0.026 to 0.035)	0.015	0.765	< 0.01
Gold-MSI Active	-0.026 (-0.057 to 0.005)	0.016	0.102	0.018
Gold-MSI Perceptual Abilities	0.048 (0.010-0.086)	0.019	0.014	0.040
Language experience	-0.008 (-0.029 to 0.013)	0.011	0.452	< 0.01
Age	0.009 (0.002-0.016)	0.003	0.010	0.045
Observations		162		
R^2/R^2 adjusted			0.1022/0.0552	

Note: Resultant effect sizes were calculated using the sensemakr package in R (Cinelli, Ferwerda, and Hazlett 2019).

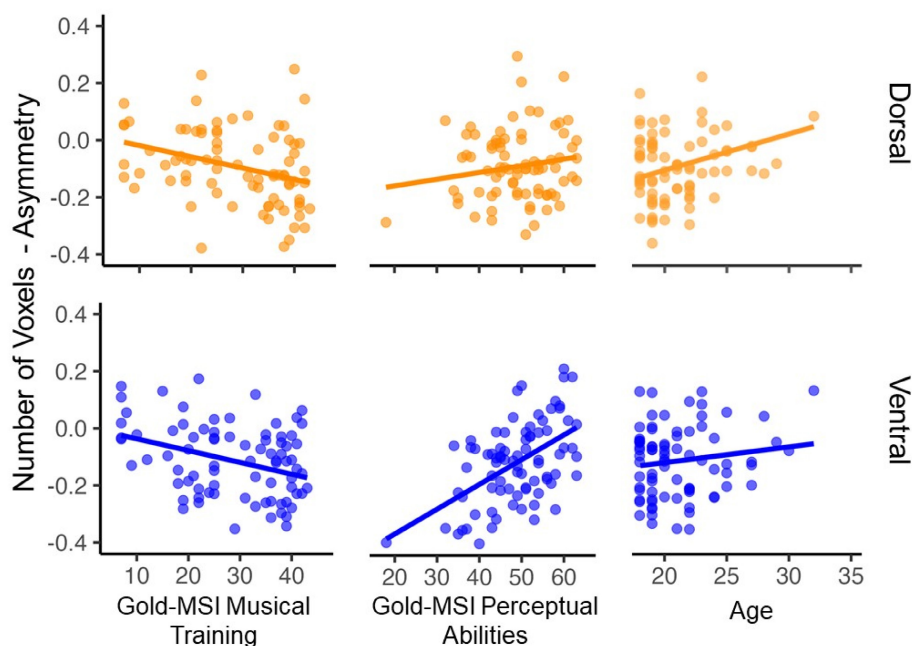


FIGURE 5 | Residual values of AF volume asymmetry across Gold-MSI Musical Training values, Gold-MSI Perceptual Abilities values, and age for each tract of interest.

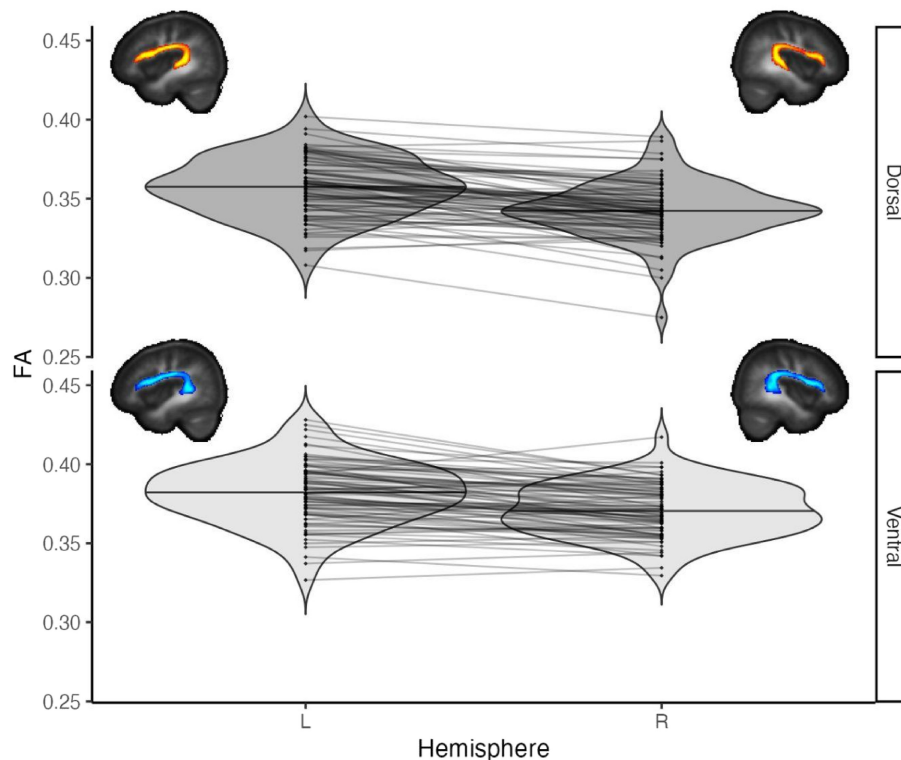


FIGURE 6 | FA values for each AF tract of interest across hemispheres. Individual participants are represented by individual dots, with lines showing the same participant across hemispheres for visualization purposes.

Results of the exploratory voxelwise analyses on where in the AF we might find relationships between musical sophistication and language experience with FA values are reported in Table 6 when the p -value was $p < 0.100$. There was a significant positive relationship between FA values in a cluster of voxels in the right dorsal AF and active engagement, $p = 0.028$, and a trend for a negative relationship between FA values in a cluster of voxels in the left dorsal AF and active engagement, $p = 0.078$. Further, there was a significant negative relationship between FA values in a cluster of voxels in the left ventral AF and active engagement, $p = 0.009$. Lastly, there was a trend for a positive relationship between FA values in a cluster of voxels in the left dorsal AF and language experience, $p = 0.083$.

The overall model used to test whether FA asymmetry was predicted by musical sophistication and/or language experience was not significant, $R^2 = 0.08$, $F(7, 154) = 2.03$, $p = 0.055$. The output is shown in Table 7.

4 | Discussion

We studied the effects of diverse levels of musical and language experience on the structural characteristics of the direct pathway of the AF in a sample of $n = 84$ young adults. We highlight noteworthy findings about the AF overall first before discussing the effects of musical and language experience in dedicated sections.

Contrary to the commonly found leftward volumetric asymmetry of the AF (Fernández-Miranda et al. 2015; Vassal et al. 2016;

though rightward asymmetry has also been reported, see, e.g., Wilkinson et al. 2017, and may be related to language dominance, see Matsumoto et al. 2008), the volume of the right AF in our dataset was higher than that of the left AF. One possible explanation for these different patterns in the literature are differing segmentation and tractography approaches (Bain et al. 2019).

Given our particular interest in the contributions of productive experience and perceptual abilities to the dorsal and ventral tracts of the direct AF, we did not trace the indirect pathway connecting the inferior frontal gyrus and the auditory cortex via the inferior parietal lobule. Instead, we based our pre-processing pipeline and its segmentation and tractography approach on those described in a previous report relevant to our research questions. There, singers, that is, participants with presumably high music and language experience, were directly compared to instrumentalists, that is, participants with high music experience only (Halwani et al. 2011). The differentiation between a dorsal and ventral tract within the direct AF has further been shown to be relevant for the distinction between tasks of music production and music perception (Bianco et al. 2022; Loui et al. 2017), as well as phonological and lexical-semantic activations in language tasks (Glasser and Rilling 2008).

Another possible explanation for the rightward volumetric asymmetry in our sample is a higher proportion of musically trained participants which we also discuss in greater detail below. This possible explanation for our results merits further investigation especially with musically trained samples. Though the average percentile norm of the musical training scores in our sample is the 55th percentile, the median percentile norm of the musical training scores

TABLE 5 | Linear regression conducted to assess whether FA was predicted by hemisphere, tract, Gold-MSI subscales, language experience, and biological sex.

Predictors	FA			Cohen's f^2
	Estimates (95% CI)	Standard error	p	
(Intercept)	0.3618 (0.3577–0.3659)	0.0021	<0.001	
Hemisphere (right)	−0.0131 (−0.0170 to −0.0092)	0.0020	<0.001	0.138
Tract (ventral)	0.0261 (0.0222–0.0300)	0.0020	<0.001	0.548
Gold-MSI Emotions	0.0024 (−0.0003 to 0.0051)	0.0014	0.081	<0.01
Gold-MSI Training	−0.0001 (−0.0032 to 0.0030)	0.0016	0.961	<0.01
Gold-MSI Singing	0.0000 (−0.0030 to 0.0030)	0.0015	0.992	<0.01
Gold-MSI Active	−0.0028 (−0.0059 to 0.0003)	0.0016	0.079	<0.01
Gold-MSI Perceptual Abilities	0.0042 (0.0005–0.0079)	0.0019	0.027	0.016
Language experience	0.0007 (−0.0013 to 0.0028)	0.0010	0.474	<0.01
Sex (female)	−0.0093 (−0.0134 to −0.0052)	0.0021	<0.001	0.063
Observations		324		
R^2/R^2 adjusted		0.4407/0.4247		

Note: Resultant effect sizes were calculated using the `sensemkr` package in R (Cinelli, Ferwerda, and Hazlett 2019).

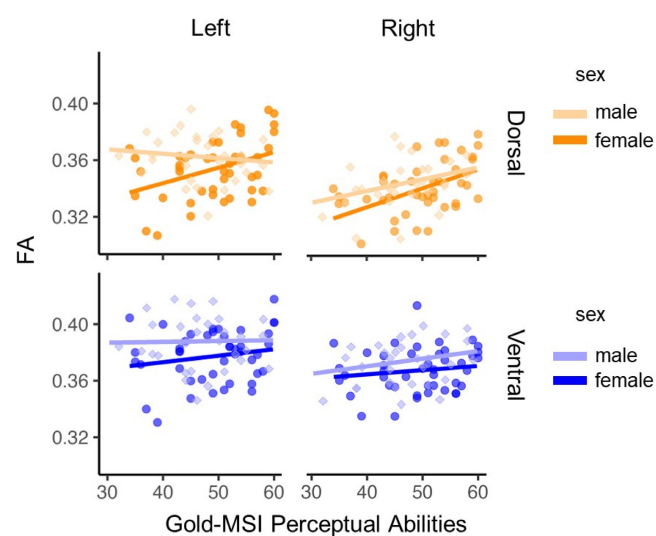


FIGURE 7 | Residual FA values across Gold-MSI Perceptual Abilities values for each AF tract of interest and hemisphere. Female participants are represented by darker shaded circles, and male participants are represented by lighter shaded diamonds.

is the 62nd percentile. Others have noted the possibility of greater rightward volumetric asymmetry with greater verbal memory and reduced leftward volumetric asymmetry in female compared to male participants (Catani et al. 2007). Nonetheless, multilingualism, which is associated with greater verbal memory (Fyndanis et al. 2023), and sex were not significant predictors of volumetric asymmetry in our sample. However, the proportion of female to male participants (47 female; 37 male) and proportion of multilingual to monolingual participants (70 multilingual; 11 monolingual) in the current sample may have contributed to our findings.

Further, contrary to what others have reported (Bain et al. 2019; Lebel and Beaulieu 2009; Reynolds et al. 2019; Song et al. 2015), we found an effect of age on volumetric asymmetry (see Table 3), such that with increasing age we found greater leftward volumetric asymmetry. However, given the small range of ages represented in our dataset (17–32 years of age) we are cautious in interpreting this finding. Consideration of this variable in studies of experience on structural characteristics of the brain may be prudent in the future, especially as others have also reported in an adolescent dataset a sex-dependent relationship between age and FA (Schmithorst, Holland, and Dardzinski 2008). Specifically,

TABLE 6 | Results of exploratory voxelwise analyses.

Predictor	Voxels	Tract	Maximum intensity	Center of gravity	<i>p</i>
Active engagement (positive)	82	Right dorsal	[38 62 41]	[36.5 62.1 41.8]	0.028
	10	Right dorsal	[34 74 42]	[34.2 73.9 42.6]	0.063
	6	Right dorsal	[40 50 38]	[40.2 50.2 38.5]	0.083
	2	Right dorsal	[36 49 38]	[36.5 49.0 38.0]	0.086
	1	Right dorsal	[40 53 39]	[40.0 53.0 39.0]	0.095
Active engagement (negative)	189	Left ventral	[61 64 37]	[60.0 64.3 40.1]	0.009
Active engagement (negative)	7	Left dorsal	[61 62 40]	[60.7 60.3 42.1]	0.078
Language experience (positive)	4	Left dorsal	[58 44 45]	[57.5 43.7 45.5]	0.083

Note: Voxel coordinates are given in MNI standard space.

TABLE 7 | Linear regression conducted to assess whether FA asymmetry was predicted by tract, Gold-MSI subscales and language experience.

Predictors	FA asymmetry			Cohen's f^2
	Estimates (95% CI)	Standard error	<i>p</i>	
(Intercept)	0.0211 (0.0170–0.0253)	0.0021	<0.001	
Tract (ventral)	−0.0062 (−0.0121 to −0.0003)	0.0030	0.038	0.028
Gold-MSI Emotions	0.0008 (−0.0032 to 0.0048)	0.0020	0.704	<0.01
Gold-MSI Training	0.0059 (0.0013–0.0106)	0.0024	0.013	0.041
Gold-MSI Singing	−0.0013 (−0.0058 to 0.0031)	0.0022	0.550	<0.01
Gold-MSI Active	−0.0011 (−0.0057 to 0.0034)	0.0023	0.623	<0.01
Gold-MSI Perceptual Abilities	−0.0059 (−0.0114 to −0.0003)	0.0028	0.040	0.028
Language experience	−0.0001 (−0.0032 to 0.0029)	0.0015	0.943	<0.01
Observations		162		
R^2/R^2 adjusted		0.0843/0.0427		

Note: Resultant effect sizes were calculated using the sensemakr package in R (Cinelli, Ferwerda, and Hazlett 2019).

adolescent females displayed a positive correlation and adolescent males displayed a negative correlation between age and FA for the right AF as well as greater FA in adolescent males compared to adolescent females in the right AF overall (Schmithorst, Holland, and Dardzinski 2008). Our own finding of greater FA in male compared to female participants (see Table 4) suggests that this pattern may extend from adolescence into young adulthood.

Together with other results indicating sex-dependent patterns in FA values in the AF (e.g., Häberling, Badzakova-Trajkov, and Corballis 2013; Jung et al. 2019; Mehrabinejad et al. 2021), this indicates the need for additional caution in extrapolating findings from studies on smaller samples with uneven distributions of male and female participants (e.g., only male participants were

considered in Bengtsson et al. 2005, and the proportion of female to male participants was different in the group of singers who participated in the study of Halwani et al. 2011 compared to the proportion of female to male participants in the instrumentalist and nonmusician groups). However, as our study was not designed to study sex-dependent effects of musical and language experience on the AF, we are limited in interpreting this finding.

4.1 | Musical Experience and the Arcuate Fasciculus

We noted different effects of different aspects of musical experience on the characteristics of the AF: Participants' Gold-MSI

Emotions values positively related to their AF volume, Gold-MSI Musical Training values were significantly related with a shift away from leftward volumetric asymmetry, and Gold-MSI Perceptual Abilities values were significantly related with leftward volumetric asymmetry and negatively related to FA values. We contextualize these findings below.

The emotional engagement subscale of the Gold-MSI includes items such as “I sometimes choose music that can trigger shivers down my spine” (Müllensiefen et al. 2014). This Gold-MSI subscale may thus map well to the emotion evocation subscale of the BMRQ, which includes items such as “I sometimes feel chills when I hear a melody that I like” (Mas-Herrero et al. 2013). Though we did not employ the BMRQ, our results converge with others that suggest a relationship between musical reward sensitivity and characteristics of (parts of) the left AF (Loui et al. 2017; Matthews et al. 2024). Closer inspection of our data however, reveals that the relationship between participants’ self-reported emotional engagement and AF volume may be driven by male participants whose right AF more readily shows this pattern than their left AF, or the AF of female participants (see Figure 4). Future studies investigating a possible link between AF characteristics and emotional engagement should therefore consider including both the Gold-MSI and BMRQ and differentiating between white matter tract connecting the superior temporal gyrus and inferior frontal gyrus (the dorsal tract of the AF mapped here) and the white matter tract connecting the superior temporal gyrus and the anterior insula, which neighbors the inferior frontal gyrus (mapped by Loui et al. 2017, in their study on musical anhedonia).

The shift away from the more commonly found leftward volumetric asymmetry (Fernández-Miranda et al. 2015; Vassal et al. 2016) with more musical training found in our sample aligns with reports of less leftward asymmetry in early-trained musicians (Vaquero et al. 2020). Our data further support conclusions of others, who have argued for a particular effect of music training on the right-hemispheric AF (Halwani et al. 2011) as well as on the right inferior frontal gyrus (Chaddock-Heyman et al. 2021; Sluming et al. 2002) and the right auditory cortex (Habibi et al. 2020; Kleber et al. 2016; Wengenroth et al. 2014). It has been suggested that the effect of music training on the right-hemispheric AF and the regions connected by it could be due to the bimanual nature of many instruments, as music-cued left-hand motor training seems to affect the structural characteristics of only the contralateral, right-hemispheric AF (Moore et al. 2017), over and above other hemispheric specializations for music (Zatorre 2022).

In our data, the shift towards rightward volumetric asymmetry was found more readily in the dorsal tract (see Figure 5). Halwani et al. (2011) suggested that the dorsal tract represents a system which is particularly reliant on fine-grained auditory feedback to adjust auditory-motor mappings, compared to the ventral tract which may represent a coarser system. Our data can thus be interpreted as evidence for effects of music experience on the right dorsal AF volume, resulting in less leftward asymmetry with more musical training, that is, extended experience using auditory feedback to adjust auditory-motor mappings. Therefore, our findings also converge with reports of increased functional connectivity in the dorsal stream in professional musicians (Ditinger et al. 2018).

In contrast, greater perceptual abilities seem to correspond to greater leftward volumetric asymmetry, particularly in the ventral tract. A functional relevance of the ventral tract for sound object identification and pitch perception abilities has been previously discussed (Baumann et al. 2007; Loui 2015; Loui, Alsop, and Schlaug 2009). Our results support this idea and further suggest that greater left-hemispheric ventral AF volume may indicate music perceptual abilities more broadly. Our findings thus support a dual-stream model of auditory processing (Hickok 2012) realized as volumetric asymmetry in the dorsal and ventral tract of the AF which depends on productive experience and perceptual abilities respectively.

Greater perceptual abilities in our participants were also associated with higher FA values, again, more so in the ventral compared to the dorsal tract. Interestingly, this result seems to be driven by female rather than male participants, suggesting sex-specific relationships between aspects of musical sophistication and structural characteristics of the AF. To the best of our knowledge, only one study has reported on the possibility of such relationships (Mehrjabin et al. 2021). However, the pattern of relationship reported there was different, such that in male participants only a relationship between active engagement with music and a measure of anisotropy was found. Our results stand in contrast to the previously reported pattern. Therefore, our study further points towards the importance of considering sex in studies of the AF. This is also supported by reports of a greater proportion of intrahemispheric fibers relative to inter-hemispheric fibers in male brains (Ingallhalikar et al. 2014) but fewer cases of extreme leftward volumetric asymmetry in female brains (Catani et al. 2007), and greater FA in males compared to females in the AF specifically (Jung et al. 2019).

Despite the absence of whole-tract effects of participants’ active engagement, we found in our exploratory voxelwise analysis that the FA values in different clusters of voxels were related to participants’ active engagement with music. Specifically, the FA values in a cluster of 82 voxels in the right dorsal AF related positively to active engagement, while FA values in a cluster of 189 voxels in the left ventral AF related negatively to active engagement. These effects seem comparable to those reported by others, that is, a positive relationship between FA values in the right AF and the amount of time spent practicing piano (Bengtsson et al. 2005) and a negative relationship between FA values in the left AF and the amount of singing training (Halwani et al. 2011). However, the Gold-MSI assesses active engagement by asking participants about the time and money spent seeking out (new) music. While practicing and training can be viewed as active engagement with music, the Gold-MSI scale is designed to capture nuanced data that illustrates effort put into seeking (new) musical experiences.

4.2 | Language Experience and the Arcuate Fasciculus

Despite the large variability in our sample’s multilingual language experience (see Figure 1), our results do not provide convincing evidence for continuously quantified multilingual language experience to be parametrically related to the structure of the AF. This was the case for all included measures, whether based on proficiency, age of acquisition, exposure, or

accounting for typological distance between languages, and for both dorsal and ventral portions of the AF. One could interpret the absence of such a relationship as implying that the effect of singing experience reported by others (compared to experience playing an instrument and no musical experience in Halwani et al. 2011; and compared to no singing experience in Perron et al. 2021) may be driven by the musical rather than language aspects of singing experience. We consider three alternative explanations for this pattern of results: (1) the age-specific effects of language exposure on the AF, (2) our sample size, and (3) our segmentation approach.

The neuroplastic effect of additional language experience may occur in the first year of life (Vaquero et al. 2020; though see also Ronderos et al. 2024, who suggest that a protracted development of the white matter pathways is associated with language). Indeed, Hämäläinen et al. (2017) showed that early (relative to late) second language exposure could be associated with increased FA along the direct segment of the AF (see below). When seen in adults, the neuroplastic effect of multilingualism seems to follow only after intense training (Wei et al. 2024). Yet, in the current study, participants' cumulative language experience calculated based on proficiency and cumulative language experience based on age of acquisition of different languages per participant did not differ in their model contributions (see Appendix S1).

Discrepancies between our results and those of others who have posited an effect of language experience on brain structure and function may also be due to our smaller sample size (compared to $n=92$ in Kepinska, Caballero, et al. 2023, or $n=136$ in Kepinska, Dalboni Da Rocha, et al. 2023). Further, discrepancies between our results and those of others might stem from differences in the approach to AF segmentation. Here, following the procedure of Halwani et al. (2011), we opted to segment the AF into a dorsal and a ventral tract (see also Fernández-Miranda et al. 2015). This differentiation into dorsal and ventral tracts may be more relevant to musical experience than language experience (see above). It is possible that language experience has a different signature in the AF distributed in the short (indirect) and long (direct) segments, as proposed by Catani, Jones, and Ffytche (2005) and used by Hämäläinen et al. (2017). Thus, our analysis approach may not have been sensitive to the potential effects of language experience. Note that in our exploratory voxelwise analysis, the trending effect of language experience on the dorsal AF FA values could be localized to the medial portion of the tract in the left hemisphere. This aligns with exposure-dependent effects on FA in the left-hemispheric AF reported by Hämäläinen et al. (2017) specifically, and the left-hemispheric specialization for language functions in general (e.g., Gernsbacher and Kaschak 2003).

4.3 | Limitations and Future Directions

Future research may consider the combined effects of musical sophistication and multilingualism on additional white matter tracts beyond the direct AF (see above). Effects of experience on tract characteristics have for example been reported for the corpus callosum, both for music (Acer et al. 2018; Bengtsson

et al. 2005; Elmer, Hänggi, and Jäncke 2016; Giacosa et al. 2016; Mehrabinejad et al. 2021; Schläffke et al. 2020; Schmithorst and Wilke 2002; Steele et al. 2013) and language (Anderson et al. 2018; Elmer et al. 2011; Gold, Johnson, and Powell 2013; Kuhl et al. 2016; Luk et al. 2011; Mohades et al. 2012, 2015; Pliatsikas, Moschopoulou, and Saddy 2015; Schlegel, Rudelson, and Tse 2012). Here, we chose to consider effects on the AF given the purported role of this white matter tract in music and language, and thus the possible effects of musical and language experience on characteristics of this tract.

As noted earlier, future research may consider the impact of age and sex in investigations of the effects of musical and language experience on white matter characteristics by studying these effects in samples which have been specifically balanced for such purposes, as well as the impact of segmentation and tractography approach (see above). While continuous conceptualizations of experience offer a promising approach to account for the variability within groups of participants (consider for example a standard deviation of 8.5h relative to an average of 30.7h of instrument practice in the expert pianists studied by Oechslin, Gschwind, and James 2018, or the wide range of multilingual experience in non-monolingual participants in our sample), they also require larger sample sizes. Though evidently our sample size of $n=84$ young adults was large enough to detect effects of musical experience, one limitation of our study as discussed above is its smaller sample size compared to those that have shown effects of language experience on brain structure (Kepinska, Dalboni Da Rocha, et al. 2023). Future research aiming to study the effects of language experience may thus want to opt for a larger group of participants (see above).

Lastly, longitudinal research is required to truly determine whether the correlates we report here are causal effects of experience on the AF or whether the structural characteristics of this white matter tract may influence participants' propensity for gaining musical experience. While it has been suggested that differences in language skills may correspond to changes in AF characteristics over time rather than the AF characteristics at a given timepoint (Yeatman et al. 2012), recent indications of neuroanatomical dispositions manifested in the auditory cortex towards musical aptitude for example (Schneider et al. 2023) suggest the possibility of AF characteristics determining the propensity for gaining experience.

5 | Conclusions

In this study, we report effects of musical and language experience on the structural characteristics of the AF. Using continuous conceptualizations of such experience we show a relationship between musical experience and (whole-brain normalized) tract volume, volumetric asymmetry, and FA values. The associations of specific aspects of musical sophistication with AF characteristics were manifested in the ventral and dorsal tracts, lending support to a dual-stream model of auditory processing. Language experience was not related to any of the studied characteristics. Our results thus appear to suggest that the effects of singing experience, which can be considered a combination of musical and language experience, are driven by the musical aspect of singing.

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Ethics Statement

This project was reviewed and approved by the University of British Columbia Office of Research Ethics.

Consent

Participants provided informed consent prior to their participation.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

Data will be shared on request to the corresponding author.

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Supporting Information

Additional supporting information can be found online in the Supporting Information section.