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Tracking Training-Related Plasticity by Combining fMRI and DTI: The Right Hemisphere Ventral Stream Mediates Musical Syntax Processing

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Abstract

As a functional homolog for left-hemispheric syntax processing in language, neuroimaging studies evidenced involvement of right prefrontal regions in musical syntax processing, of which underlying white matter connectivity remains unexplored so far. In the current experiment, we investigated the underlying pathway architecture in subjects with 3 levels of musical expertise. Employing diffusion tensor imaging tractography, departing from seeds from our previous functional magnetic resonance imaging study on music syntax processing in the same participants, we identified a pathway in the right ventral stream that connects the middle temporal lobe with the inferior frontal cortex via the extreme capsule, and corresponds to the left hemisphere ventral stream, classically attributed to syntax processing in language comprehension. Additional morphometric consistency analyses allowed dissociating tract core from more dispersed fiber portions. Musical expertise related to higher tract consistency of the right ventral stream pathway. Specifically, tract consistency in this pathway predicted the sensitivity for musical syntax violations. We conclude that enduring musical practice sculpts ventral stream architecture. Our results suggest that training-related pathway plasticity facilitates the right hemisphere ventral stream information transfer, supporting an improved sound-to-meaning mapping in music.

Key words: extreme capsule, music, right hemisphere, syntax, ventral stream

Introduction

Musical training develops the comprehension of musical syntax, and therefore the ability to perceive any violation of its rules. The underlying neuroanatomical white matter pathways of this higher order cognitive capacity remain unknown.

In the context of training-related adaptations, so far, the study of neural pathway architecture using diffusion tensor imaging (DTI) rather focused on the comparison of musicians to nonmusicians (reviews by Munte et al. 2002; Zatorre 2013; Moore et al. 2014), than on different levels of musical

proficiency. This involved motor (Schmithorst and Wilke 2002; Bengtsson et al. 2005; Han et al. 2009; Imfeld et al. 2009; Engel et al. 2014; Ruber et al. 2015; Giacosa et al. 2016), associative (Halwani et al. 2011; Dohn et al. 2015), auditory (Oechslin et al. 2009; Halwani et al. 2011; Loui et al. 2011; Engel et al. 2014), inter-hemispheric (Schmithorst and Wilke 2002; Steele et al. 2013), and cerebellar fiber connections (Abdul-Kareem et al. 2011).

Here, we explore training-related brain plasticity following different levels of musical training and proficiency. To study the anatomical connections between relevant areas for music syntax processing, we applied DTI tractography between functionally defined regions from a previous functional magnetic resonance imaging (fMRI) study in the same participants (Oechslin et al. 2013).

Far less studies exist on anatomical substrates of higher-level music processing compared with those of language. Nevertheless, music and speech processing share basic sensory encoding units (e.g., James 2012; Perrachione et al. 2013; Chandrasekaran et al. 2014) based on similar acoustic (spectrotemporal) features. Despite these shared basic units, hemispheric specialization occurs with respect to ventrolateral frontal areas: syntax processing in speech preferentially involves the left hemisphere (e.g., Friederici et al. 2000; Friederici et al. 2003; Vernooij et al. 2007; Herrmann et al. 2009; Propper et al. 2010; Bornkessel-Schlesewsky and Schlesewsky 2013).

However, music-syntactic processing rather takes place in the right hemisphere. Processing sound or tones and processing musical syntax are intrinsically different processes. Specifically for musical syntax processing that requires fine-grained higher order pitch perception, right hemisphere dominance in temporal—and to a lesser extent—in ventrolateral frontal areas is well established (Zatorre 2001; Koelsch and Mulder 2002; Brown et al. 2006; Tillmann et al. 2006; James et al. 2008; Perani et al. 2010; Klein and Zatorre 2011; Jantzen et al. 2014; Jentschke et al. 2014; Musso et al. 2015; Cha et al. 2016). Clinical studies further support these observations (Johnsrude et al. 2000; Hyde et al. 2006; Albouy et al. 2013). Right hemispheric dominance enhances with musical expertise (Koelsch et al. 2002; Koelsch et al. 2007; James et al. 2008; Jantzen et al. 2014), although already present in newborns to some extent (Perani et al. 2010).

In contrast to anatomical connections in the left hemisphere for language, possible right hemisphere anatomical connections enabling higher-level music processing, remain unknown. A few studies investigated the functional neuroanatomy of the right hemispheric temporo-frontal (TF) pathway system in the context of language processing and development (Saur et al. 2010; Perani et al. 2011; Rilling et al. 2011). Functional neuroimaging studies further support the idea of a direct right TF connection, supposed to serve the encoding of different aspects of prosodic speech information (Meyer et al. 2004; Kotz et al. 2006; Mitchell and Ross 2013). Given the shared spectrotemporal features of pitch modulations in prosodic speech and music (Coutinho and Dikken 2013; Patel 2014), a commonly used right ventral stream pathway could explain previously reported advantages of musically trained people in speech prosody processing (Thompson et al. 2003; Marques et al. 2007; Hausen et al. 2013).

Previous research successfully demonstrated the existence of a hardwired left-hemispheric dorsal-ventral-pathway system, considered as the neuroanatomical substrate of language production and comprehension (Glasser and Rilling 2008; Saur et al. 2008; Makris and Pandya 2009; Wong et al. 2011; Brauer et al.

2013; Friederici and Gierhan 2013; Griffiths et al. 2013). Numerous functional brain imaging studies (reviews by Hickok and Poeppel 2007; Friederici 2012; Poeppel et al. 2012; Hickok and Poeppel 2015) corroborated its left lateralization. Whereas dorsal pathway fibers (via the arcuate fasciculus) map sound to articulation, the ventral route (via the extreme capsule [EmC]) was assigned to linguistic sound-to-meaning mapping and speech syntax processing. An archetype of this dual pathway system of auditory processing occurs in nonhuman primates, representing the cornerstones for the evolution of human communication skills (Rilling et al. 2008; Rauschecker and Scott 2009).

In the present study, we focused on the right hemisphere pathway system possibly underlying musical syntax processing by analyzing DTI tractography based on previous fMRI results of the same participants (Oechslin et al. 2013). These fMRI data unveiled modulation of an ensemble of right hemisphere brain regions (middle temporal gyrus [MTG], anterior insula [INS], and the pars opercularis [POp]), by musical syntax violation salience and by degree of musical expertise (nonmusicians [N], amateurs [A], and experts [E]). The fMRI contrasts in this study focused exclusively on music syntax processing, controlling for basic music and sound processing. To study right TF fiber connections, we performed DTI tractography by implementing these areas revealed by fMRI as seeds and targets, respectively. In view of previous data on the involvement of the left ventral stream in higher order language processing (Saur et al. 2008; Turken and Dronkers 2011), we hypothesized a right hemisphere homolog TF pathway subserving musical syntax processing. Additionally, given that musical expertise yielded enhanced sensitivity for musical syntax violations (Oechslin et al. 2013), we assumed that training-related modulations of right TF fibers may predict the accuracy of musical syntax processing.

Methods

Participants

We recruited 3 groups of participants characterized by different degrees of musical expertise: 20 expert pianists, mainly advanced conservatory students and also some established performers and teachers, who received training at the Conservatoires of Geneva, Lausanne, Paris, and Zürich (E: mean age = 24.5, SD = 4.5; 10 females), 20 amateur pianists, defined as being still musically active, however, regular instrumental practice never exceeded 10 h per week (A: mean age = 22.2, SD = 3.1; 10 females), and 19 nonmusicians, who never received any extracurricular musical education (N: mean age = 24, SD = 4; 9 females). The groups were matched by age, gender, fluid intelligence, instrument of practice, and age of training onset. All N and A were university students, except for one academic lecturer and one secondary school student. All participants were positively tested for right-handedness (Oldfield 1971). Importantly, E and A did not differ by means of starting age of musical training (E: mean age = 6.2; SD = 1.9; A: mean age = 7.0, SD = 1.4). Current practice intensity (estimated training hours/week between 18 and 25 years of age) was significantly different between E and A (E: mean = 30.7, SD = 8.5; A: mean = 4.4, SD = 2.9; $T_{38} = 12.4$, $P < 0.001$, $d = 4.1$). For comprehensive retrospective data on training intensity (back to the age period 10–12 years), we refer to Oechslin et al. (2013).

Behavioral Sensitivity for Harmonic Violations

The here implemented behavioral performance data was assessed in a previously reported fMRI study with the same

participants (Oechslin et al. 2013). In this former fMRI experiment, we used specifically composed string quartets with manipulated terminal chords (in-key transgressions) that were either regular (R, composed of the first degree with fundamental bass, I), subtly transgressed (T_{sub} , composed of the first degree in first inversion: I⁶), or apparently transgressed (T_{app} , composed of the fourth degree in first inversion: IV⁶). By a forced-choice 2 alternative task our participants indicated by button press whether the pieces' terminations sounded satisfactory or not. Accordingly, rater performance was reported as sensitivity (d-prime) for harmonic syntax violations (Fig. 3 in Oechslin et al. 2013). In contrast to a highly established measure for musical aptitude (Gordon 1989), our task could discriminate between all 3 levels of musical expertise [consider Oechslin et al. (2013) for example stimuli and a comprehensive description of the task and related results]. We thus calculated linear regression models to test the predictability of the sensitivity for musical syntax violations by individual pathway volumes (Fig. 2C).

We would like to emphasize that the fMRI results of this task (Oechslin et al. 2013) are the fruit of rigorous contrasts that focused exclusively on music syntax processing, that is, subtracting brain responses to regular terminal chords (involving basic music and sound processing) from the responses to the transgressed terminal chords ($T_{\text{sub-R}}$ and $T_{\text{app-R}}$). As a result, only right-hemispheric activations appeared, associated to higher-level auditory processing.

Diffusion Tensor and Structural Image Acquisition

Image acquisition was performed on a 3-T scanner (Siemens Trio, Erlangen, Germany). Diffusion-weighted images were acquired using a monopolar Stejskal-Tanner sequence (TR = 8300 ms, TE = 83 ms; reconstructed matrix: 128 × 128 pixels, 64 axial slices with a voxel size of 2 × 2 × 2 mm along 63 independent directions, using a b value of 1000 s/mm²). The sequence was run twice and for every acquisition one b_0 image was recorded. For each individual, we additionally recorded a T_{app} -weighted high-resolution, magnetization-prepared rapid gradient-echo (MPRAGE) structural image (TR = 1900 ms, TE = 2.27 ms, TI = 900 ms, flip angle = 9°, FoV = 256 × 256 mm, voxel size = 1 × 1 × 1 mm, 192 slices).

DTI Data Preprocessing and Probabilistic Fiber Tracking

All data processing was performed by using the FSL (version 4.1.9) software library (<http://fsl.fmrib.ox.ac.uk/fsl>). The 2 acquisitions of each participant were concatenated, corrected for eddy distortions and head movement using eddy current correction [FDT toolbox (Behrens et al. 2003)]. Then, the data were skull-stripped by using BET (Smith 2002). BEDPOSTX (standard options) served to estimate the 2 most likely diffusion directions by using Bayesian estimation, including a model that accounts for the possibility of crossing fibers within each voxel (Behrens et al. 2007). In order to create a mask for a later exclusion of cerebrospinal fluid (CSF), we first ran DTIFIT and fed the resulting S0 image to the NEW SEGMENT tool (default options) delivered with SPM8 (<http://www.fil.ion.ucl.ac.uk/spm>). Probabilistic fiber tracking was performed by PROBTRACKX in diffusion space (curvature threshold = 0.2; number of steps per sample = 5000; step length = 0.5; number of samples = 25 000; applied exclusion mask: CSF, $p_{\text{thres}} = 50$). Sphere ROIs (radius = 8 mm), originally reported in MNI space by Oechslin et al. (2013) (MTG [63 -7 -20], INS [30 23 1], POP [42 8 28]), were transformed into diffusion space by applying individual warp fields using the *invwarp* function (reference brain: FMRIB58_FA_1 mm). They were located on the junction of gray

and white matter, as defined by a FA value of >0.2. For each of the 2 tracts in the right hemisphere, MTG_POP and MTG_INS, we performed probabilistic fiber tracking twice, so that each ROI served once as seed and once as target ROI, resulting in a probability tractogram for each tracking direction. These probability tractograms [MTG to POP, $p(x)$; POP to MTG, $p(y)$] were normalized by the identified number of connections (division by *waytotal*) and then combined in order to create the definite tract [$p(x) \cup p(y)$]. The combined tractogram was thresholded ($p_{\text{thres}} = 0.05$) and binarized. The tract volume was measured (number of voxels) for each individual ($n = 59$). Finally, individual tractograms were transferred into MNI space (using the *applywarp* function) and averaged across all participants, in order to create a group probability map, which was thresholded at >30% for illustration purposes (cf., Fig. 1: mean probabilistic group tracts and surface renderings).

Investigation of Ventral Pathway Consistency

In order to further investigate the volumetric properties of the MTG_POP tract (the tract showing significant group differences; Fig. 2), we evaluated its pathway consistency. For that aim, we took into account the probabilistic tract representations revealed by the 2 fiber tracking directions: from MTG to POP [$p(x)$] and from POP to MTG [$p(y)$]. The literature on probabilistic DTI tractography is heterogenous concerning fiber tracking directions: whereas some defined the tract in one direction only [seed-to-target (e.g., Glasser and Rilling 2008; Ethofer et al. 2012)], others defined the tract in both directions (Saur et al. 2008). We made use here of the specific difference between both approaches. The combination of the probability of tracking in both directions is given as the tract union [$t_u = p(x) + p(y) - p(x) \times p(y)$], and the core part of the tract with the most consistent fiber bundle of the pathway corresponds to the combined probability (intersecting volume) of both tracking directions [tract core $t_c = p(x) \times p(y)$]. It is therefore possible to calculate the volume of the tract, where fibers are traveling only in either of the directions, representing the more peripheral, less systematic fiber contributions [tract dispersion $t_d = t_u - t_c$]. Finally, the relationship of the volumes of the tract core and the tract dispersion t_c and t_d yield a measure of tract consistency ($C = t_c/t_d$). High tract consistency indicating a well-defined tract is therefore given by a large tract core (t_c) volume in relation to a small tract dispersion (t_d) volume.

As a last step, we applied linear regression analyses to test whether and to which degree tract consistency (C) predicted musical syntax processing accuracy (d-prime for T_{sub} and T_{app}).

Results

By means of probabilistic fiber tracking, we identified 2 fiber bundles of the ventral pathway, one connecting the MTG with the INS, and one connecting MTG with the POP of the inferior frontal gyrus, respectively (Fig. 1A). A selected coronal slice ($y = 7$) provides a detailed view of the precise allocation of the 2 identified pathways (Fig. 1B). Both tracts are closely related to each other (Figs 1C and 2B): connecting TF MTG_POP fibers run dorsally in parallel to those of the MTG_INS through the EmC, and the 2 pathways separate before entering the deep part of anterior INS.

Morphometric analyses of MTG_POP and MTG_INS tract volumina revealed a reduction of MTG_POP tract volume (number of voxels) in the musicians' groups (A, E) compared with the N group (Fig. 2A). Accordingly, a two-way ANOVA with the factors *Expertise* (N, A, E) and *Tract* (MTG_POP, MTG_INS) revealed a significant main effect *Tract* ($F_{2,56} = 55.641$, $P < 0.001$, $\eta^2_p = 0.498$)

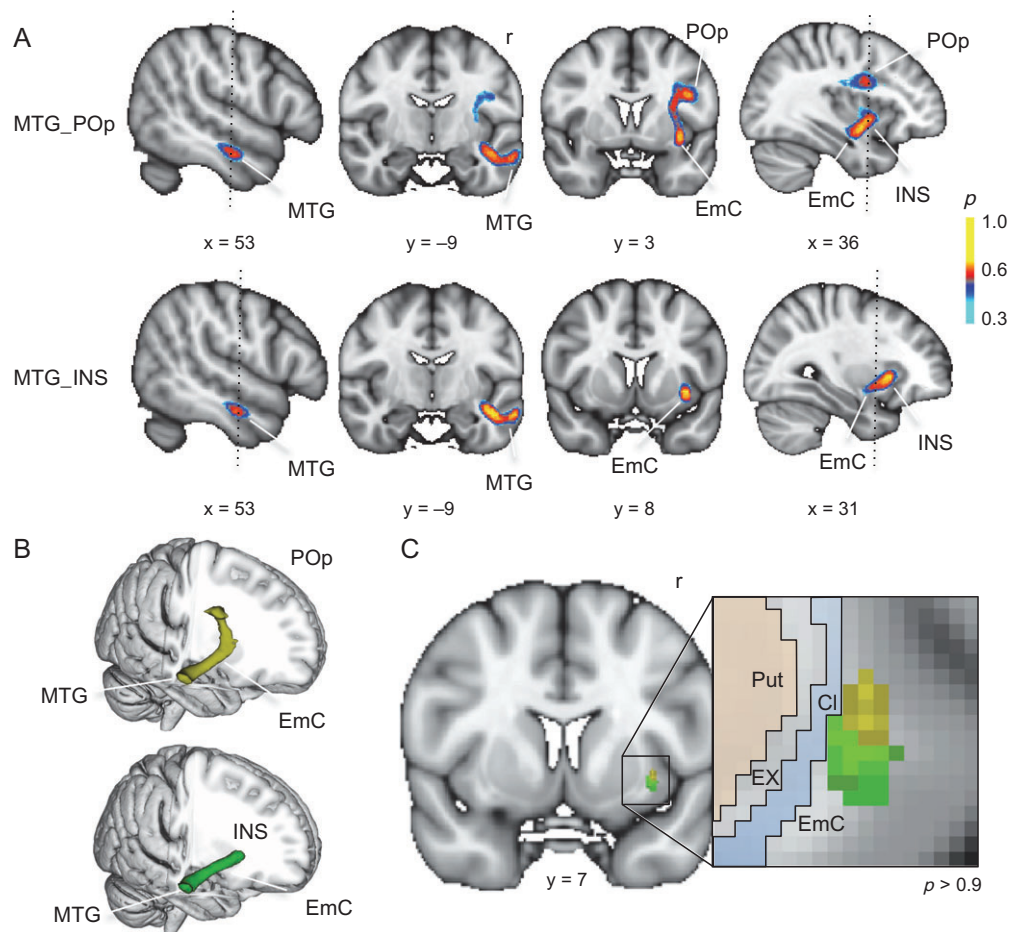


Figure 1. (A) Results of probabilistic fiber tracking of the 2 tracts (upper row: MTG_POP; lower row: MTG_INS), running in parallel through the EmC connecting the MTG with the INS, and with the POp of the inferior frontal gyrus, respectively. Group probability maps of both tracts were computed by averaging 59 individual fiber connections. Colorbar coding: probability range (p) = 0.3–1.0. Slices are labeled by MNI coordinates. (B) Separate 3D rendering of the 2 tracts. (C) Cross sections of core fibers (overlap $p > 0.9$ is displayed) of the 2 tracts are delineated in a close-up on a selected coronal view ($y = 7$) (yellow: MTG_POP; green: MTG_INS). A selected coronal slice allows a detailed inspection of the precise allocation of the 2 identified pathways. EX, external capsule; Cl, Claustrum; Put, Putamen.

and interaction *Expertise* \times *Tract* ($F_{2,56} = 3.612$, $P = 0.033$, $\eta^2_P = 0.114$), but no significant main effect of *Expertise* ($F_{2,56} = 2.646$, $P = 0.080$, $\eta^2_P = 0.086$). We additionally performed 2 single one-way ANOVAs, for each tract separately: *Expertise* (MTG_INS) turned out not significant ($F_{2,56} = 0.729$, $P = 0.487$, $\eta^2_P = 0.025$). *Expertise* (MTG_POP), however, showed a significant relationship between musical expertise and the MTG_POP tract volume ($F_{2,56} = 3.461$, $P = 0.038$, $\eta^2_P = 0.110$), characterized by a relatively high effect size. Additional post hoc two-sample *t*-tests (2-tailed) could assign these musical expertise related effects to a significant volume reduction in the MTG_POP pathway only between N and A ($N > A$: $t_{37} = 2.555$, $P = 0.015$, $N > E$: $t_{37} = 1.644$, $P = 0.109$, $A > E$: $t_{37} = 0.867$, $P = 0.391$; Bonferroni corrected for multiple comparisons). No significant group differences were found in the MTG_INS volume. In sum, this data suggest that only the MTG_POP pathway underwent musical training-related volumetric adaptations.

As a next step, we applied regression analyses to test whether tract volume of the MTG_POP pathway predicted accuracy in musical syntax processing (Oechslin et al. 2013). As dependent variables, we implemented individual sensitivity values (*d*-prime) for either subtle (T_{sub}) or apparent (T_{app}) transgressed final chords of musical pieces, violating harmonic expectations established

by the prior musical context. Including all 59 participants in this analysis, the models significantly revealed that people with smaller MTG_POP volume showed higher accuracy in identifying transgressed musical endings (T_{sub} : $b = -0.294$, $t_{58} = -2.323$, $P = 0.024$; T_{app} : $b = -0.366$, $t_{58} = -2.966$, $P = 0.004$) (cf., plotted regressions in Fig. 2B). In contrast, no significant prediction was revealed by MTG_INS tract volume (T_{sub} : $b = 0.168$, $t_{58} = 1.268$, $P = 0.203$; T_{app} : $b = 0.116$, $t_{58} = 0.885$, $P = 0.380$).

In order to further investigate the finding that smaller tract volume was associated to higher musical proficiency, we characterized tract consistency (C) by dissociating and comparing the highly reliable core from the less systematic peripheral tract fibers. The hereby obtained dissection of the entire MTG_POP pathway volume into tract core (t_c) and tract dispersion (t_d) (see Methods section) (Fig. 3A), revealed significant main effects of musical *Expertise* ($F_{2,56} = 3.461$, $P = 0.038$, $\eta^2_P = 0.110$). To evaluate a systematic variation of t_c and t_d volumes by level of musical expertise, we calculated the following two-factorial 3×2 ANOVA for repeated measures [*Expertise* (N, A, E) \times *Tract_Part* (t_c , t_d)]. The data revealed significant main effects of musical *Expertise* ($F_{2,56} = 3.461$, $P = 0.038$, $\eta^2_P = 0.110$), *Tract_Part* ($F_{2,56} = 214.644$, $P < 0.001$, $\eta^2_P = 0.793$) and a significant interaction *Expertise* \times *Tract_Part* ($F_{2,56} = 6.831$, $P = 0.002$, $\eta^2_P = 0.196$).

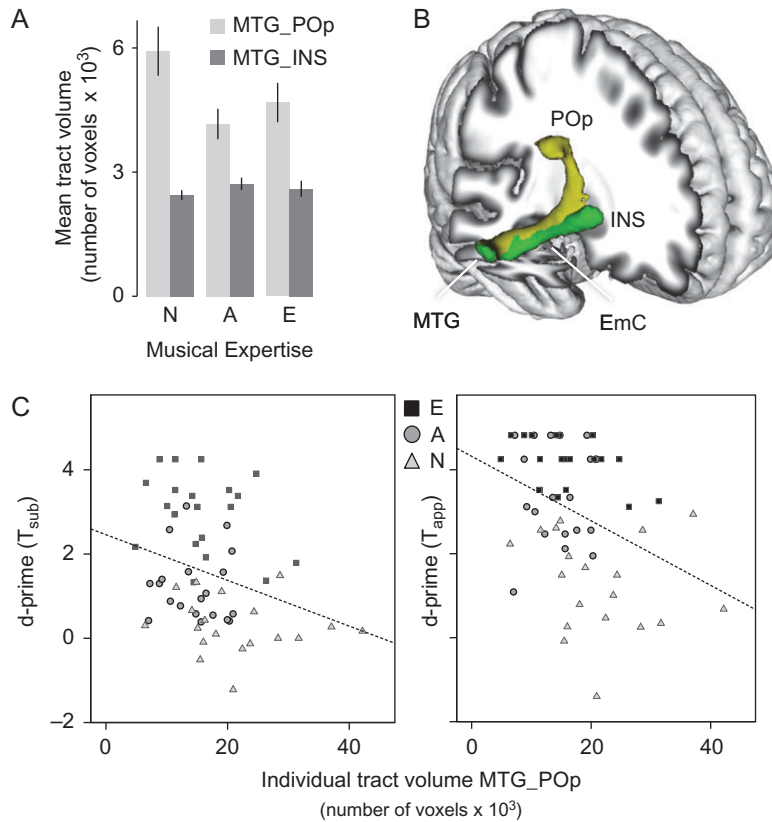


Figure 2. (A) Mean tract volumes of MTG_POp (light gray) and MTG_INS (dark gray) are plotted (\pm SEM) for each group. (B) The proximal relation of the 2 tracts is outlined by here-combined 3D renderings (yellow: MTG_POp; green: MTG_INS). (C) Scatterplots (including all participants, $n = 59$) and regression lines indicate the negative relationship between sensitivity (d-prime) for harmonic violations in musical pieces and MTG_POp volume; on the left side for subtle (T_{sub}) and on the right side for apparent (T_{app}) harmonic transgressions (E [rectangles], A [circles], and N [triangles]).

For t_c volume (but not t_d volume), post hoc two-sample t -tests revealed significant group differences $N > A$ ($t_{37} = 2.951$, $P = 0.005$) and $N > E$ ($t_{37} = 2.250$, $P = 0.030$), meaning that the volumes of the core and of the dispersed fibers of MTG_POp were qualitatively different for the 3 groups of expertise (Fig. 3B). Furthermore, t_c and t_d volumes were significantly correlated ($r = 0.444$, $P < 0.001$) (Fig. 3C). The measure for tract consistency ($C = t_c/t_d$) trended to a significant main effect of Expertise ($F_{2,56} = 2.782$, $P = 0.070$, $\eta^2_p = 0.090$); a post hoc two-sample t -test revealed a significant group difference $E > N$ ($t_{37} = 2.324$, $P = 0.026$), whereas tract consistency of the A group was located in intermediate position (Fig. 3D). In addition, by performing 2 separate linear regression models, we tested whether and to which degree tract consistency C (the independent variable) of MTG_POp predicted accuracy in detecting harmonic syntax violations (d-prime T_{sub} , T_{app} ; the 2 dependent variables). Including all 59 participants, linear regression models significantly revealed that higher C predicted better accuracy in identifying transgressed musical endings (T_{sub} : $b = -0.364$, $t_{58} = 2.950$, $P = 0.003$; T_{app} : $b = 0.322$, $t_{58} = 2.564$, $P = 0.013$) (Fig. 3E).

White matter integrity of MTG_POp, as measured by the microstructural properties fractional anisotropy (FA), radial diffusivity (RD), and longitudinal diffusivity (LD) in both tract subvolumes (t_c and t_d), further corroborated these results (Supplementary Fig. 1). There was a significant difference of mean FA in the tract core compared with the tract dispersion in A ($P = 0.016$) and E ($P = 0.000$), but not in the N group. This higher global tract integrity was mainly due to the relatively lower RD in the tract core and higher RD in the tract

dispersion (difference significant for E only, $P = 0.002$) while in all 3 groups, LD was significantly higher in tract core than in tract dispersion (N, $P = 0.003$; A, $P = 0.001$; E, $P = 0.0004$; all tests were paired t -tests under correction for multiple comparisons using false discovery rate (Hochberg and Benjamini 1990), q -value = 0.033).

Discussion

In this study, we investigated the functional neuroanatomy of higher-level musical syntax processing by performing probabilistic DTI tractography between task-specific fMRI activations in 3 groups of participants that differed by degree of musical expertise and proficiency (Oechslin et al. 2013). The here presented analysis revealed a right hemisphere ventral stream, connecting functionally defined key regions in the temporal and ventrolateral prefrontal cortex. Ventral stream fibers, in nonhuman primates, consist of a bundle of long bidirectional association fibers between the temporal and frontal lobe, running through the EmC (Petrides and Pandya 2007), connecting the middle superior temporal region, via the rostral insular cortex, with the orbitofrontal (inferior ramus) and the ventrolateral prefrontal cortex (superior ramus) (Schmahmann and Pandya 2006). As outlined in the Introduction section, functionally and anatomically, this connection is considered the right homolog to the left ventral stream of the language processing architecture (Hickok and Poeppel 2007; Saur et al. 2008; Brauer et al. 2011; Rilling 2014). Accordingly, we found here that coactivated right hemisphere areas during a

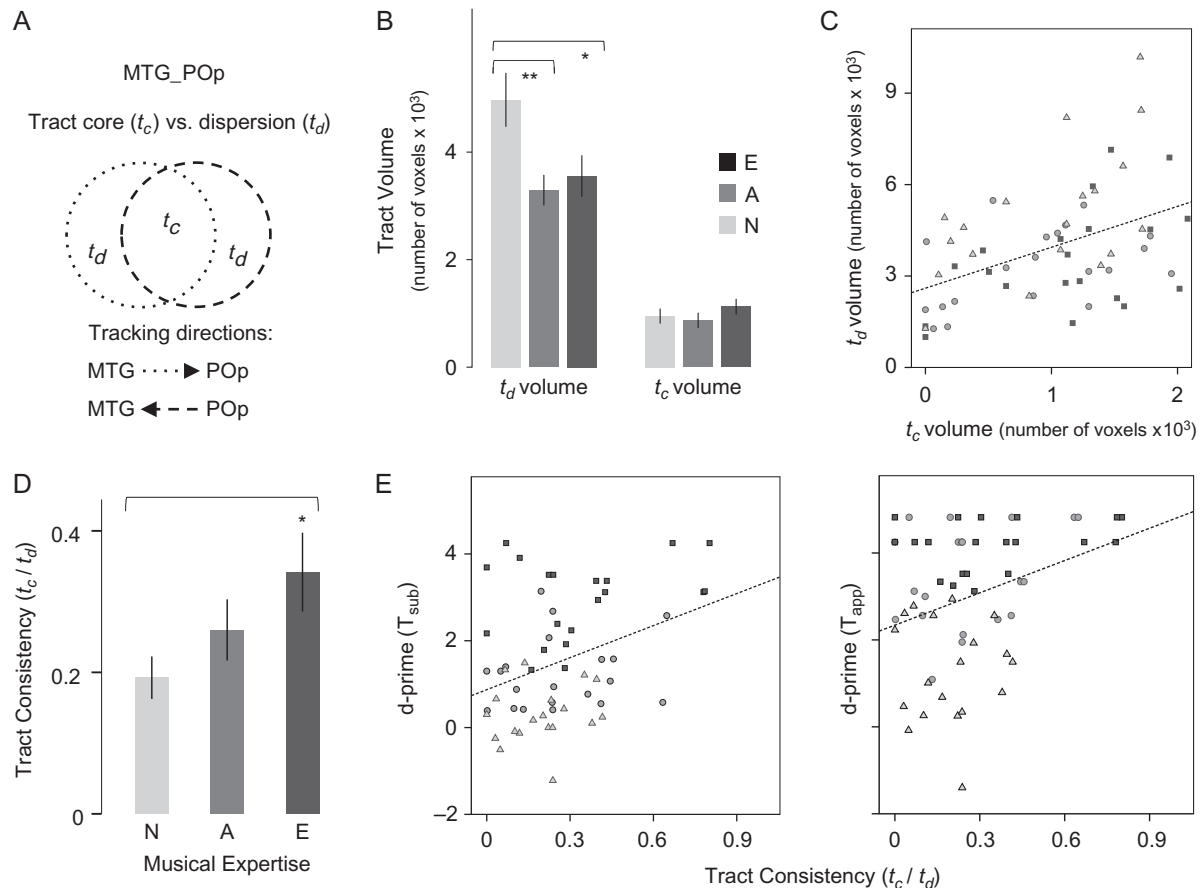


Figure 3. (A) A schematized cross-section of the 2 probabilistic maps related to tracking directions of MTG_POP is provided. Tract core (t_c) represents the overlapping and tract dispersion (t_d) the nonoverlapping parts. (B) Mean volumes (\pm SEM) of t_c and t_d are plotted separately for each group. (C) This scatterplot (including all participants, $n = 59$) and regression line indicates the relationship between t_c and t_d volumes (E [rectangles]; A [circles]; N [triangles]). (D) Here the mean tract consistency ($C = t_c/t_d$) (\pm SEM) is plotted separately for each group (N, A, E). (E) Scatterplots (including all participants, $n = 59$) and regression lines indicate the relationship between sensitivity (d-prime) for harmonic violations in musical pieces and tract consistency; on the left side for subtle (T_{sub}) and on the right side for apparent (T_{app}) harmonic transgressions. Asterisks indicated significant t-tests for independent samples (* $P < 0.05$, ** $P < 0.01$).

musical syntax violation task (MTG, INS, POP) (Oechslin et al. 2013) are connected by 2 separate fiber bundles (Fig. 1: MTG_POP, MTG_INS) via the ventral route through EmC; the exact morphological embedding of these 2 pathways in relation to medially neighboring subcortical structures (claustrum [Cl], EmC, putamen [Put]) was outlined in detail (Fig. 1B) and unveiled that MTG_POP fibers form a discrete connection running dorsally attached in parallel to MTG_INS fibers. This fundamental discovery henceforth provides the neuroanatomical “missing link” to numerous studies investigating cognitive functions underlying musical structure analysis and music syntax processing (Maess et al. 2001; Koelsch et al. 2002; Tillmann et al. 2003; Brown et al. 2006; Tillmann et al. 2006; James et al. 2008; Klein and Zatorre 2011; Herholz et al. 2012; Koelsch et al. 2013; James et al. 2014; Jantzen et al. 2014).

Our data on rigorously matched groups differing in training intensity provide substantial evidence on the influence of musical training on plasticity of MTG_POP fibers. The MTG_POP bundle showed reduced volume in musicians (A, E) compared with musically nonexperienced participants (N) (Fig. 2A). Moreover, linear regression models confirmed the importance of MTG_POP for musical syntax processing (Fig. 2B): smaller MTG_POP pathway volume predicted higher behavioral sensitivity for musical syntax violations. In contrast, the MTG_INS

pathway volume was not related to these performance data. This result confirms the general notion that, in contrast to insular and orbitofrontal areas (corresponding to the termination of EmC’s inferior ramus), the ventrolateral frontal region is of key importance for musical syntax processing (Maess et al. 2001; Tillmann et al. 2003; Koelsch 2011).

However, it was unexpected to find that smaller tract volume corresponded to musical expertise, because it seems unlikely that reduced tract volume improves information transfer (rather vice versa). In turn, we considered that smaller tract volume, associated to musical expertise (Fig. 2A), might reflect increasingly clear-cut tract morphology; or in other words, that increased tract volume, associated with poor sensitivity for syntax violations (Fig. 2B) might reflect less systematic tract morphology and fiber alignment in the ventral stream pathway. To test this assumption, we further tracked down the path properties of MTG_POP fibers to disclose individual tract consistency by taking advantage of the bidirectionally performed probabilistic tractography (cf., Methods section). Given the 2 directions of fiber tracking, we calculated for every participant the tract consistency ($C = t_c/t_d$), expressing the ratio of the double visited volume (during fiber tracking in both directions; tract core, t_c) and the only once visited, nonoverlapping parts (tract dispersion, t_d) of the MTG_POP fibers (cf., schematization in Fig. 3A). Confirming our

initial assumption the N group showed a significantly increased volume of tract dispersion (t_a) in contrast to the musicians' groups (Fig. 3B). On the other hand, the tract core (t_c) volume was only marginally significantly enhanced in the E group. Instead, tract consistency (C), the volume ratio between the tract core and tract dispersion, proved to be the crucial: the data compellingly revealed gradually increased tract consistency as a function of musical expertise (Fig. 3D), while higher tract consistency predicted increased sensitivity for musical syntax violations (Fig. 3E). Therefore, this result suggests that the major influence of musical expertise on the ventral stream morphology is a sharpening of the pathway architecture.

Our finding that musical training modulates the right ventral stream, and furthermore, that its pathway morphology directly relates to behavioral performance in musical syntax processing represents a groundbreaking corroboration of training-related plasticity and yields a number of important implications. First of all, this study provides general evidence for the neuroanatomical correlate enabling information transfer necessary for higher-level musical syntax comprehension. Then, our findings demonstrate the impact of musical training on the nature of fiber architecture, and in turn explain why musical training potentially supports speech prosody processing (Thompson et al. 2003; Marques et al. 2007; Hausen et al. 2013). Finally, it yields equally a new perspective on different medical conditions with implication of the right hemisphere higher-level auditory processing, assumed to be mediated through the right ventral stream. This includes for example neurological conditions associated to dysfunctional processing of melody or intonation such as tone deafness or congenital amusia (Loui et al. 2008, 2009; Hyde et al. 2011; Peretz 2013; Loui 2016) and perceptive aprosodia, the inability to convey emotional prosody (Pell 2006; Ross and Monnot 2008). In fact, previous research, supporting the hypothesis that music and language have a common origin as an emotional protolanguage (Darwin 1859; Fitch 2006), revealed that subjects suffering of amusia also manifest difficulties in decoding emotional prosody (Thompson et al. 2012; Kantrowitz et al. 2014). The present findings hence imply a crucial role of right ventral pathway fibers in higher-level pitch processing by means of context integration, and encourage future investigations to use combined fMRI and DTI to unveil dysfunctional white matter architectonics related to these neurological conditions.

Limitations

Although DTI tractography has been used extensively to study white matter connectivity, in view of the present application, this technique, however, has 2 inherent shortcomings: the difficulty to distinguish different fascicles in areas where tracts run in parallel (Catani et al. 2003) and to map the fiber architecture in areas with fiber crossings (Wedeen et al. 2008). Several diffusion imaging techniques have been developed to account for the latter issue, for example, diffusion spectrum imaging (Wedeen et al. 2005), q-ball imaging (Tuch et al. 2003), and spherical deconvolution (Dell'acqua et al. 2010; Thiebaut de Schotten et al. 2011).

Supplementary Material

Supplementary material is available at *Cerebral Cortex* online.

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