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Asymmetry of the Frontal Aslant Tract is Associated with Lexical Decision

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Abstract

The frontal aslant tract (FAT) is a recently documented white matter tract that connects the inferior and superior frontal gyri with a tendency to be more pronounced in the left hemisphere. This tract has been found to play a role in language functions, particularly verbal fluency. However, it is not entirely clear to what extent FAT asymmetry is related to performance benefits in language-related tasks. In the present study, we aimed to fill this gap by examining the correlations between asymmetric micro- and macro-structural properties of the FAT and performance on verbal fluency and lexical decision tasks. The results showed no correlation between the FAT and verbal fluency; however, lexical decision was correlated with FAT laterality. Specifically, greater left lateralization in both micro- and macro-structural properties was related to faster lexical decision response times. The results were not due merely to motor or decision-making processes, as responses in a simple discrimination task showed no correlation with laterality. These data are the first to suggest a role for the FAT in mediating processes underlying lexical decision.

Introduction

The frontal aslant tract (FAT) is a recently identified white matter tract in the human brain (Catani et al. 2012). The FAT connects the inferior frontal gyrus (Brodmann areas 44/45) to superior medial frontal regions including anterior cingulate cortex, supplementary motor area (SMA), and pre-supplementary motor area (pre-SMA), as corroborated by magnetic resonance imaging (MRI) functional connectivity between these regions (e.g., Crosson et al. 2001; see Dick et al. 2019, for a review). The FAT is typically left-lateralized in terms of volume in right-handed individuals (Catani et al. 2012), suggesting a role in language functions, as the same lateralization has been observed also for other language-related tracts, including the long segment of the arcuate fasciculus (Thiebaut de Schotten et al. 2011b).

Indeed, a role in speech fluency has been confirmed for the left FAT by a number of clinical studies using intraoperative electrical stimulation during tumor resection (Fujii et al. 2015; Kemerdere et al. 2016; Kinoshita et al. 2015; Vassal et al. 2014). These studies showed that direct stimulation of the left FAT consistently resulted in speech disturbances (e.g., speech arrest, speech inhibition, stuttering). Further, Kinoshita and colleagues (2015) found that patients with post-operative speech disturbances had smaller distances between the tumor resection site and the left FAT than those without this type of deficit; no right-hemisphere patients showed language-related post-operative disturbances. Additionally, the average distance between tumor resection cavity and the left FAT was positively correlated with semantic and phonemic fluency, but not naming ability (also see Chernoff et al., 2018 for analogous results).

Additional evidence that the left FAT is implicated in fluency comes from studies on patients with aphasia. In patients with primary progressive aphasia (PPA), the mean length of utterance and speech rate were correlated with proxy measures of white matter micro-structural integrity of the left FAT such as fractional anisotropy (FA) and/or radial diffusivity (RD) (Catani et al. 2013; also see Mandelli et al. 2014). These measures did not correlate with grammatical processing or picture naming abilities. Correlations between verbal fluency abilities and the integrity of the left FAT (measured with lesion percentage and FA) were also seen in an examination of 51 post-stroke patients (Li et al. 2017). An additional study of post-stroke aphasic patients found that the white matter signal intensity (from a T1 scan) in the left FAT/anterior segment was the best predictor of speech fluency compared to other left hemisphere tracts involved in speech and language (Basilakos et al. 2014).

Beyond fluency, the left FAT seems well-positioned to contribute to lexical retrieval processes given its end points in the inferior frontal gyrus (IFG) and pre-SMA, which have been linked to lexical processing. The former is assumed to be associated with effortful processes such as retrieval, manipulation, and selection of phonological representations (Fiez et al. 1999). In particular, left Brodmann area (BA) 45 is related to semantic aspects of language processing, and the more posterior left BA 44 is related to phonological and syntactic processing and speech programming (Amunts et al. 2004). Moreover, FA in left BA 45 has shown a negative association with lexical decision speed (Gold et al. 2007).

Left pre-SMA has been associated through fMRI studies with internally-guided generation of lexical items, but only items with pre-existing representations in the brain (Crosson et al. 2001, 2003). This region is also activated during semantic decision tasks (Binder et al. 1997) and lexical decision tasks, especially for low frequency words (Carreiras et al. 2006, 2009).

Finally, a neurosurgical study found that stimulation at the level of the pre-SMA and extending to the FAT in the left hemisphere resulted in morphological over-regularization in a noun-based verb generation task (Sierpowska et al. 2015). The authors suggested that the stimulation acted by inhibiting more demanding lexical retrieval processes.

While the evidence above focuses on the left hemisphere, there is some indication that inter-hemispheric dynamics are important for lexical retrieval processes. For instance, healthy participants are faster in picture naming after inhibitory cathodal transcranial direct current stimulation (tDCS; vs. sham) of the right IFG, a result mostly due to fewer tip-of-the-tongue instances (Rosso et al. 2014). The interpretation of this finding was that, as the right hemisphere was inhibited by tDCS, inter-hemispheric rivalry towards the left hemisphere was decreased. FMRI data were also collected during a word repetition task in the same participants. Effective connectivity analyses with dynamic causal modeling of these data showed hemispheric rivalry directly from right Broca's area to the left homologous area, and indirectly from left to right Broca's through the SMAs.

A similar role for interhemispheric dynamics has been found for fluency in relation to the FAT. In a study employing repetitive transcranial magnetic stimulation (rTMS) over left and right BA 47 (Smirni et al. 2017), performance on a phonemic fluency task was impaired after stimulation to left BA 47 (compared to sham), but improved after stimulation to right BA 47, although it must be noted that neuronavigation was performed with a probabilistic head model and not with the individual MRI. The authors suggested rTMS applied to the right hemisphere suppressed the inter-hemispheric inhibitory interactions.

Although task performance usually benefits from a division of labor between the two hemispheres (Banich and Belger 1990; Belger and Banich 1998), inter-hemispheric cooperation has been observed for complex, more demanding tasks, especially in the prefrontal cortex (e.g., Höller-Wallscheid et al. 2017), and may be beneficial for performance (Belger and Banich 1998; Berryman and Kennelly 1992).

Several studies have demonstrated that taking into account the inter-hemispheric asymmetries of intra-hemispheric white matter pathways is important to explain variability in performance across individuals for various cognitive functions, including language and attention systems (see Ocklenburg et al. 2016, for a review). As an example, the degree of structural a/symmetry of the arcuate fasciculus, in terms of micro-structure (FA) and/or macrostructure (volume, fiber density) is correlated with language-related functioning, with the direction of the advantage depending on the type of task. Catani and colleagues (2007) found that a more symmetric arcuate fasciculus was associated with an advantage in verbal recall, while Lebel and Beaulieu (2009) found that children with leftward asymmetry in the arcuate fasciculus outperformed those with rightward asymmetry in vocabulary and phonological processing tasks. The arcuate fasciculus structural asymmetry also correlates with the degree of brain functional lateralization (Ocklenburg et al. 2013; James et al. 2015), which notably also predicts verbal abilities (Gotts et al. 2013). Similar relationships have been observed for other tracts also in non-language domains. For instance, a leftward asymmetry of the inferior corona radiata is positively correlated with the performance in Attention Network Test (ANT), in particular with the executive control sub-component (Yin et al. 2013), while the direction of structural asymmetry of the superior longitudinal fasciculus (SLF) II predicts the direction of behavioral asymmetry in visuospatial attention tasks (Thiebaut De Schotten et al., 2011a; also see Budisavljevic et al. 2017b, for analogous results in visuomotor processing). Moreover, inter-individual differences in the asymmetry of the dorsal SLF tract predict the degree of lateralization in hand preference, visuospatial integration and fine motor control tasks (Howells et al. 2018).

However, little is known about whether and how inter-hemispheric white matter asymmetries in the FAT correlate with the ability to perform language tasks that have been associated with this tract. In this study, we tried to fill this gap by assessing correlations between asymmetric micro- and macro-structural properties of the FAT and performance on verbal fluency and lexical decision tasks. Given the previous findings that link these language abilities to the left FAT, we expected a correlation between leftward hemispheric FAT asymmetry and better performance on both of these linguistic tasks.

Methods

Participants

Twenty-nine healthy university students (19 females; mean age = 24.8, SD = 2.4, range 22-36) participated in the study. All participants were native Italian speakers with no known neurological or psychiatric problems. The Edinburgh Handedness Inventory (Oldfield 1971) was used to confirm that all participants were right-handed (mean score = 85, SD = 18, range 30-100). The study was approved by the ethical committees of the Scuola Internazionale Superiore di Studi Avanzati (SISSA), "Istituto IRCCS E. Medea – La Nostra Famiglia", and Azienda Ospedaliera di Padova. All participants gave written informed consent and were compensated for their time.

Verbal Fluency Task

Participants completed a verbal fluency task in which they were asked to name as many items as possible belonging to a category in 60 seconds[1]. Each participant completed six categories, three semantic categories and three letter categories, in their native language, Italian. The specific

[1] Verbal fluency data were only available for 22 of the participants.

categories were drawn from a list of nine possible categories for each type, (adapted from Schwieter and Sunderman 2011; see Appendix for all categories used)[2]. Each category began with fixation cross for 500 ms, followed by a 100 ms beep (400 Hz) and then the category name was presented on the screen. Participants were given 60 seconds to name as many items belonging to the category as possible. The conclusion of the 60 seconds was signaled with another 100 ms beep. A blank screen appeared for 3000 ms before the next category. Participants were instructed that they would see two types of categories (semantic and letter) and have 60 seconds to name as many items as they could in the given category. They were also told that repetitions, words with the same root, and proper names would not be counted. Before completing the experimental categories, participants completed two practice categories (P and utensili da cucina-*kitchen items*) with an experimenter present to clarify any difficulties.

The entire task was recorded using a digital recorder for offline transcription and coding. Transcription and coding were completed by a native Italian speaker. All responses initiated within the 60 second time limit for each category were transcribed and marked as either valid items or items to be excluded. For both category types responses were excluded that were: not a word in the language, not part of the category, repetitions of a previous response in the same category, and proper names. Further for semantic categories, repetitions of a concept (e.g., eggplant and aubergine) and superordinates when subordinates were also named (e.g., bird, pigeon, bluejay) were excluded. Finally, for letter categories, only one word with a given root was counted (e.g., fast, faster, fastest). The total number of valid items produced across the six categories (three semantic and three letter) was used at the measure of interest.

[2] In addition to their native Italian, participants also completed the task in two foreign languages. Only data from Italian are considered in the present analyses given the variability of these foreign languages (Dutch, English, French, German, and Spanish) as well as the participants' abilities in them (scores ranging from 3 to 5 on a scale of 1-5, with 5 representing native-like).

Lexical Decision Task

Participants completed a lexical decision task in which they had to judge whether presented letter strings were real Italian words or non-words. The items in the present study were taken from (Paulesu et al. 2000; and personal communication). The real word items were disyllabic nouns that had stress on the first syllable and were among the 7500 most frequent Italian words (e.g., collo-*neck*, mare-*sea*, porta-*door*). The non-word items were also disyllabic and were formed by changing one or two phonemes in the real words (e.g., coto, mave, borta). Stimulus trials began with a fixation screen presented for 1000 ms. A letter string was then presented and remained onscreen until a response was given. Participants were asked to give a judgment on the letter string as quickly and accurately as possible. A ‘word’ response was made with the index finger of one hand and a ‘non-word’ response with the index finger of the other hand; hand assignments were counterbalanced across participants. The task began with sixteen practice items followed by 160 experimental items, half of which were real words and half were non-words. Response times (RT) and accuracy were recorded; participants’ accuracy was very high (average 97%) and thus RT was used as the measure of interest.

Color and Shape Discrimination Task

Participants completed a discrimination task in which they needed to indicate for each presented stimulus either the color or the shape, performed in separate blocks. This task was similar to the Lexical Decision Task in that it required a forced-choice response from the participants, however, it did not require lexical processing. The stimuli consisted of red and blue hearts and stars presented individually on a white background. Trials began with a fixation cross presented for 1500 ms followed by a cue that indicated the present task. For color discrimination, the cue consisted of three colored rectangles (purple, orange, and yellow), while for shape discrimination, three black shapes (triangle, circle, and square) were used. In both cases the items were arranged linearly and appeared above the fixation cross location. The use of graphical cues had the benefit of limiting linguistic information. After either 100 or 1000 ms, distributed randomly and equally across the trials, the stimulus appeared in the center of the screen, below the cue, which remained onscreen. Participants were asked to indicate the color or shape as quickly and accurately as possible using the index fingers of their left and right hands. The four possible response-to-button mappings (left: red/heart, right: blue/star; left: red/star, right: blue/heart; left: blue/heart, right: red/star; left: blue/star, right: red/heart) were counterbalanced across participants. The trial ended when the participant made a response. Incorrect responses were followed by a 100 ms beep.

Participants completed two blocks of color discrimination and two blocks of shape discrimination; each block began with six practice trials, followed by 24 experimental trials. The blocks were presented using a sandwich design, meaning the first and last blocks required the same discrimination task, with the other task presented in the second and third blocks[3]. The specific assignment of tasks was counterbalanced across participants. Both response times and accuracy were recorded; RT was used as the measure of interest given the high accuracy rate of the participants (average 98%).

Diffusion Imaging Acquisition and Processing

Images were acquired on a 3-Tesla Philips Achieva whole-body scanner at the Santa Maria della Misericordia Hospital in Udine, Italy. Diffusion imaging was acquired with an 8-channel

[3] Between the second and third block, the participants completed a mixed-task block requiring a different discrimination task on each trial; performance on that block is not considered in the present study.

head coil using a single-shot, spin-echo, EPI sequence with the following parameters: TR = 9037 ms, TE = 70 ms, FOV = 240 mm x 223 mm, matrix size = 128 x 128, AP phase encoding, 57 contiguous axial slices (1.875 x 1.875 x 2.1 mm voxel resolution). For each slice, 64 diffusion-weighted images (b = 1000 s/mm^2) and one non-weighted image (b = 0) were acquired. Data processing and trackography were performed using ExploreDTI (http://www.exploredti.com). First, subject motion and geometric distortions induced by eddy currents were corrected in a single step through rotation of the b-matrix. Then, a b-spline interpolated streamline algorithm was used to perform whole brain tractography (stepsize: 1 mm; FA threshold: 0.2; angle threshold: 35°). The output from ExploreDTI was imported to TrackVis (http://www.trackvis.org), where virtual *in vivo* dissections were performed, using software written by Natbrainlab (Thiebaut de Schotten et al. 2011a).

Tract Dissection and Measures

Dissection of the frontal aslant tract was completed manually (by LB) using a two regions of interest (ROI) method. Following previous tractography studies (e.g., Catani et al. 2012; Budisavljevic et al. 2017a), ROIs were placed in the inferior frontal gyrus and superior frontal gyrus on the fractional anisotropy images in the three planes. In both cases, the ROI encompassed the entirety of the gyrus. These two regions were used as ‘AND’ ROIs in tracking the FAT. Streamlines that did not follow the known anatomy of the FAT were removed. The FAT was tracked in both the left and right hemispheres (Figure 1).

Figure 1.

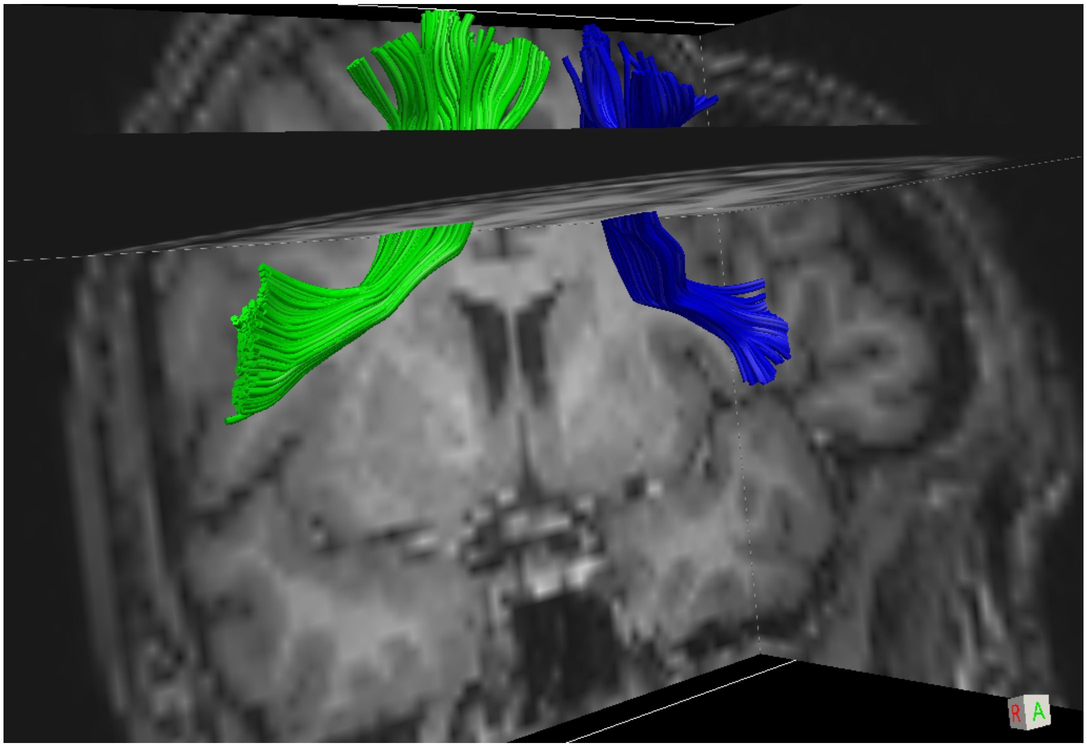

Figure 1: Right (in green) and left (in blue) Frontal Aslant Tract in a single participant overlaid on their T1-weighted MR image. The image is generated looking posteriorly, thus the right hemisphere is represented on the left side of the image and vice versa (the cube on the bottom right depicts the brain orientation: A = anterior; R = right).

Additionally, the anterior segment of the arcuate fasciculus was dissected to serve as a control tract. The arcuate fasciculus is a white matter pathway well-known for its role in language functions. This bundle can be divided into two pathways, a direct pathway connecting Broca's area to Werknicke's area and an indirect pathway mediated though the inferior parietal lobule (Catani et al., 2005). The anterior segment, which is considered part of the ventral branch of the superior longitudinal fasciculus (Martinos & Del Luca, 2014), was selected due to its comparability to the

FAT in terms of size and their shared endpoint in the inferior frontal gyrus. While the anterior segment is implicated in language functions (Catani & Mesulam, 2008), it has not been linked to lexical retrieval making it an ideal choice to demonstrate the specificity of any effects to the FAT. Similar to the FAT, the anterior segment was tracked (by LB) bilaterally using two 'AND' ROIs. These were placed in Broca's territory, encompassing the inferior frontal gyrus, middle frontal gyrus, and precentral gyrus, and in Geschwind's territory composed of the supramarginal and angular gyri. Streamlines that did not follow the known anatomy of the anterior segment were removed.

Three measures of interest were extracted for each tract: number of streamlines (NoS), volume, and fractional anisotropy. NoS and volume provide information about the macrostructural properties of white matter tracts. Both measures were considered to avoid the shortcomings related to either measure (see Budisavljevic et al. 2017b, for further discussion). FA was used as it is the most widely used proxy of white matter micro-structural properties. This measure indicates the degree of anisotropy in the diffusion process, ranging between 0 and 1. Values near 0 represent isotropic diffusion, while a value of 1 indicates diffusion along only one axis. In diffusion imaging, FA is taken as a proxy of fiber density, axonal diameter, and myelination of the white matter (Beaulieu, 2002). In order to examine the asymmetry of the tracts, a lateralization index (LI) was computed for each of the three measures using the following formula: LI = (Right – Left)/(Right + Left) (Thiebaut de Schotten et al. 2011a). Thus, positive LI values indicate right-lateralization and negative values left-lateralization. The lateralization of both the FAT and the anterior segment of the arcuate fasciculus was neutral across all three measures in our sample (FAT: $ps \geq .241$; anterior segment: $ps \geq .134$), that is, the tracts showed no trend of left- or right-lateralization across the participants (cf. Thiebaut de Schotten et al. 2011b; 2011b; Budisavljevic et al. 2017b).

Statistical Analyses

Statistical analyses were computed using IBM SPSS Statistics for Windows, Version 25.0. The two behavioral measures (Verbal Fluency, Lexical Decision RT) and three tract lateralization measures (NoS LI, volume LI, FA LI) were examined for normality with Kolmogorov-Smirnov tests. All measures were normally distributed ($p > .193$), except FA LI, for which there were three outliers. Removal of these participants resulted in a normal distribution for FA LI as well ($p > .200$). Pearson bivariate correlation analyses were used to examine the relationship between the behavioral measures and the lateralization measures. The six analyses were corrected for multiple comparisons using a False Discovery Rate (FDR) correction ($p < .05$). In addition, Pearson correlations were also computed between each behavioral measure and each white matter measure (i.e., NoS, volume, and FA) of the left and right FAT separately. Both corrected and uncorrected p-values are provided.

Results

Verbal fluency was not correlated with any of the lateralization measures (NoS: $r = -.258$, $p_{uncorr} = .247$, $p_{corr} = .346$; Volume: $r = -.237$, $p_{uncorr} = .288$, $p_{corr} = .346$; FA: $r = .183$, $p_{uncorr} = .439$, $p_{corr} = .439$). Lexical Decision instead correlated with all three lateralization indices (NoS: $r = .424$, $p_{uncorr} = .022$, $p_{corr} = .044$; Volume: $r = .475$, $p_{uncorr} = .027$, $p_{corr} = .072$; FA: $r = .539$, $p_{uncorr} = .004$, $p_{corr} = .024$; see Figure 2). These correlations indicated that faster RTs on the Lexical Decision task were associated with left lateralization. The potential influence of lexical status on these relationships were examined with correlation analyses between the three lateralization indices and the RTs for words and non-words separately. Both words (NoS: $r = .367$, $p_{uncorr} = .050$, $p_{corr} = .050$; Volume: $r = .392$, $p_{uncorr} = .036$, $p_{corr} = .043$; FA: $r = .540$, $p_{uncorr} = .004$, $p_{corr} = .021$) and non-words (NoS: r = .431, p_{uncorr} = .020, p_{corr} = .030; Volume: r = .493, p_{uncorr} = .007, p_{corr} = .021; FA: r = .483, p_{uncorr} = .012, p_{corr} = .024) correlated with all three lateralization measures. Finally, to confirm that the correlation was specific to lexical processes rather than motoric and/or decision-making processes, we examined the correlation between RT in the color and shape discrimination task and lateralization. This task was not correlated with any of the lateralization measures (NoS: r = .316, p_{uncorr} = .095, p_{corr} = .095; Volume: r = .318, p_{uncorr} = .093, p_{corr} = .095; FA: r = .341, p_{uncorr} = .089, p_{corr} = .095).

Figure 2.

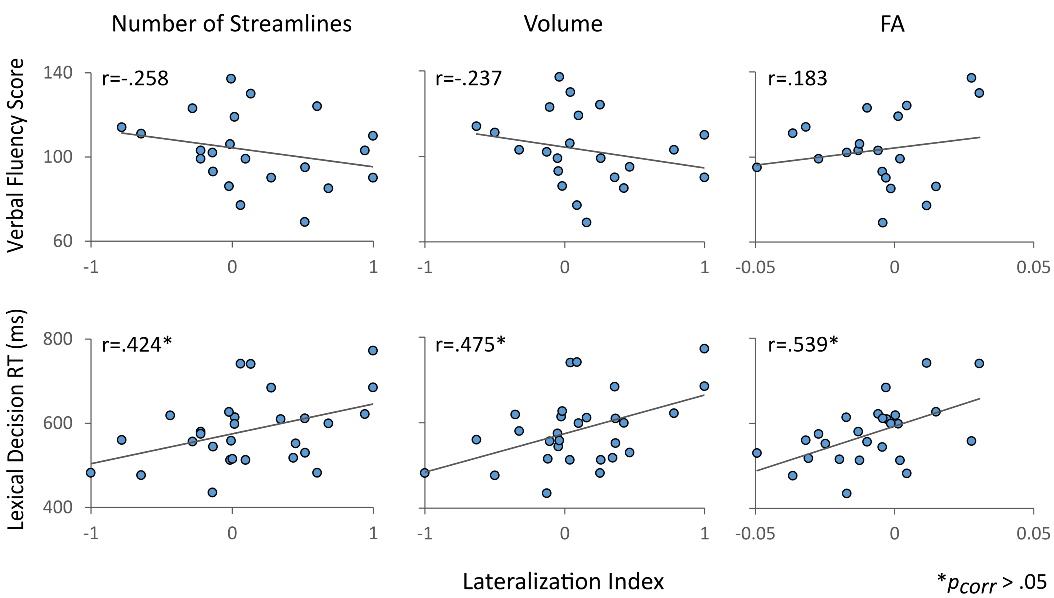

Figure 2: Correlations between the behavioral measures and tract lateralization measures. The top row shows correlations between verbal fluency score and the three lateralization measures, none of which were significant. The bottom row shows correlations between lexical decision RT and the three lateralization measures; all three were significant, however, only the correlation with FA LI survived correction for multiple comparisons. This correlation indicated that faster RTs were associated with greater left lateralization.

Additionally, in order to understand whether verbal fluency or lexical decision may be related with the degree of laterality rather than with its (left vs. right) direction, we also assessed correlations between the behavioral tasks and the absolute laterality values; no significant correlations were found (all *p*s > .217).

Further, given that previous studies found a relation between language abilities and the left FAT, specifically, we also tested the correlations between the behavioral measures and the three tract measures in each hemisphere. Verbal fluency showed a correlation with the volume of the left FAT, however, this did not survive correction for multiple comparisons (r = .426, p_{uncorr} = .048, p_{corr} = .162). No other correlations reached significance before or after multiple comparison correction ($ps_{uncorr} \geq .054$, $ps_{corr} \geq .162$).

Finally, to confirm the specificity of the correlation to the FAT, we performed the same correlations using a control tract, the anterior segment of the arcuate fasciculus. No significant correlations were found between performance on the lexical decision task and the lateralization of this tract (NoS: r = -.010, p_{uncorr} = .960, p_{corr} = .960; Volume: r = .150, p_{uncorr} = .439, p_{corr} = .848; FA: r = .118, p_{uncorr} = .565, p_{corr} = .848).

Discussion

In the present study, we examined the relationship between the FAT white matter structure and language functions, specifically verbal fluency and lexical decision, in healthy adults. Contrary to our hypotheses, which were mainly derived from findings with brain damaged patients, our results showed no correlation between the lateralization indices of FAT micro- and macro-structure and verbal fluency; however, lexical decision was correlated with the laterality of the FAT.

Specifically, faster lexical decision latency was associated with greater left lateralization of both the macrostructure (i.e., number of streamlines and volume) and the microstructure (i.e., fractional anisotropy) of the FAT. These results could not be explained as generally due to motor and/or decision-making processes, as responses in a simple discrimination task showed no correlation with laterality. Neither were these results explained by correlations with only the left FAT. Further, the results were specific to the FAT, and not found in another tract known to support language functions, namely, the anterior segment of the arcuate fasciculus. To the best of our knowledge, our results are the first to suggest a relation between FAT asymmetry and processes underlying lexical decision.

Verbal fluency was correlated with the volume of the left FAT only, extending the findings gathered primarily on clinical populations (Basilakos et al. 2014; Catani et al. 2013; Kinoshita et al. 2015) to healthy subjects, although this result did not survive multiple comparison correction. Importantly, the absence of correlation between FAT lateralization and performance in verbal fluency was unexpected, if one infers from results coming from clinical studies (e.g., Catani et al. 2013; Kinoshita et al. 2015). However, the present result is in line with previous work suggesting no correlation between speech fluency and the left FAT in healthy individuals (Kronfeld-Duenias et al. 2016). This finding could be tentatively interpreted as due to the fact that this type of task is clearly left-lateralized in the prefrontal cortex (Gaillard et al. 2000; Schlösser et al. 1998), and thus it does not suffer much from interference from the right hemispheric homologous regions. On the other hand, there is evidence that word recognition, which is required in lexical decision tasks, involves interhemispheric exchange (Mohr et al. 1994; also see Ibrahim and Eviatar 2012) and is associated with inferior frontal activations extending bilaterally to the right hemisphere (e.g., Park et al. 2012). Although bilateral inferior frontal activation might be required when the task becomes more challenging, for instance when it requires extensive semantic processing (Edwards et al. 2005) and decision making (Gan et al. 2013), inter-hemispheric collaboration could turn out to be detrimental for performance under less demanding contexts (cf. Banich and Belger 1990). Perhaps because of this, lexical decision processes may suffer more from inter-hemispheric interference. Having a strongly left-lateralized FAT may act as a safeguard against this interference from the right homologous region, which is more dedicated to complementary, possibly interfering processes, such as general action control, especially in the visuo-spatial domain (Dick et al. 2019).

A potential limitation of this study concerns the makeup of the participants, most of whom were multilingual. As multilingualism may affect the lateralization of some cortical regions and white matter tracts (e.g., Felton et al. 2017; Hämäläinen et al. 2017), the results may not generalize to a monolingual population and would need to be specifically investigated. Though, bilinguals and multilinguals represent more half of the world's population (Grosjean, 2010). An additional limitation is the relatively low sample size. Despite this, we were still able to show positive results. Final samples of 20 participants (for the verbal fluency tasks) or 26 (for the lexical decision task) did not allow us, however, to further investigate potentially interesting issues that would have required to split out our sample even further. Such issues include if and how sex differences or the degree of multilingualism modulate the relationship between the FAT and language functions. Future studies should address these and similar research questions.

In conclusion, the present study confirms the importance of investigating inter-hemispheric asymmetries for white matter pathways in order to understand inter-individual variability in cognitive task performance. Our findings clearly showed that a more left-lateralized frontal aslant tract is beneficial for performance in a verbal task such as lexical decision. Further studies are needed to more directly corroborate whether this pattern is due to a reduction of interference originating from non-language functions implemented in contralateral regions connected by the homologous tract.

Ethical statement

Disclosure of potential conflicts of interest: The authors declare that they have no conflict of interest.

Research involving Human Participants and/or Animals: All procedures performed in studies involving human participants were in accordance with the ethical standards of the Ethics Committee of Scuola Internazionale Superiore di Studi Avanzati - SISSA, Trieste (Prot. # 6772) and Ethics Committee of Azienda Ospedaliera di Padova (Prot. # 2758P), and with the 1964 Helsinki declaration and its later amendments.

Informed consent: Informed consent was obtained from all individual participants included in the study.

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Appendix: Categories used in the Verbal Fluency task

Set	Categories
Semantic set 1	parti del corpo-*body parts*
	professioni-*occupations*
	strumenti musicali-*musical instruments*
Semantic set 2	animali-*animals*
	legume-*vegetables*
	abbigliamento-*clothing items*
Semantic set 3	mezzi di trasporto-*methods of transportation*
	sport-*sports*
	frutta-*fruits*
Letter set 1	A, M, F
Letter set 2	E, T, G
Letter set 3	O, D, L