INVESTIGATING THE INTEGRITY OF MAJOR WHITE MATTER TRACTS IN APHASIA

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AIMS OF THE CURRENT STUDY

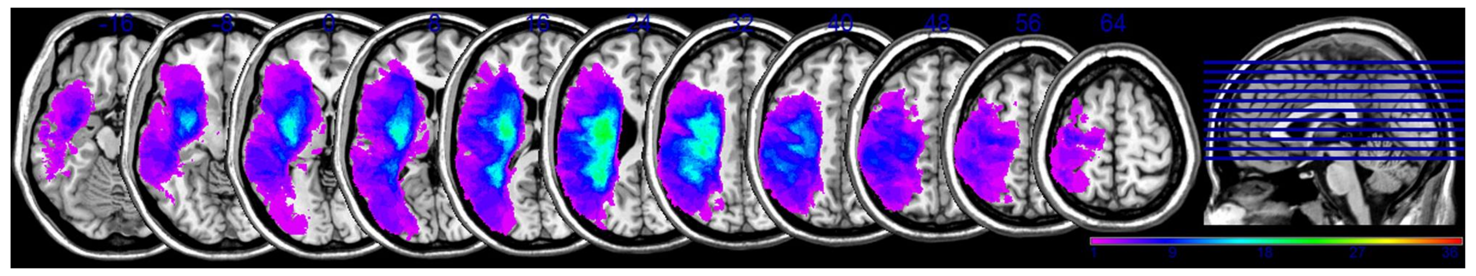
1. **Compare integrity of major white matter tracts of both hemispheres between individuals with aphasia and healthy age-matched controls.**
2. **Investigate the relationship between integrity of major white matter tracts and language deficits (comprehension and production at the word and sentence level) in aphasia.**

Novelty of the study:

- Investigation of major tracts in both hemispheres purportedly supporting language: **Arcuate Fasciculus (AF), Inferior Longitudinal Fasciculus (ILF), Inferior Frontal-Occipital Fasciculus (IFOF), Uncinate Fasciculus (UF), Corpus Callosum (CC)** with Superior Occipital-Frontal Fasciculus (SOFF) for comparison**;**
- Use of comprehensive in-vivo measures of microstructural integrity extracted from diffusion-weighted scans: **fractional anisotropy (FA), mean diffusivity (MD), radial diffusivity (RD), axial diffusivity (AD);**
- Exploration of individual tract segments.

PARTICIPANTS

Individuals with aphasia – 37 individuals with different types and severity of aphasia due to single or multiple left hemisphere stroke not earlier than four months prior to scanning (18 males, 19 females; M_{age} = 54 years, SD = 10.53, age range: 34 - 78 years; $M_{months\ post\text{-}onset}$ = 26.38, SD = 21.40 months, post-onset range: 4 - 100 months). All were right-handed and native speakers of Russian.



Lesion overlay for 37 individuals with aphasia. The greatest degree of overlap is seen in the periventricular white matter underlying the frontal, temporal, parietal lobes and in the perisylvian cortex and insula.

All individuals with aphasia were assessed with a standardized language test in Russian on subtests targeting word and sentence level comprehension (comprehension of single words, sentences and commands) and production (naming and sentence construction) (Tsvetkova et al., 1981; see Ivanova et al., 2015 for detailed description of the test).

Control group – 11 age-matched neurologically-healthy right-handed native speakers of Russian (6 males, 5 females; M_{age} = 53 years, SD = 8.56, age range: 35 - 65 years).

NEUROIMAGING

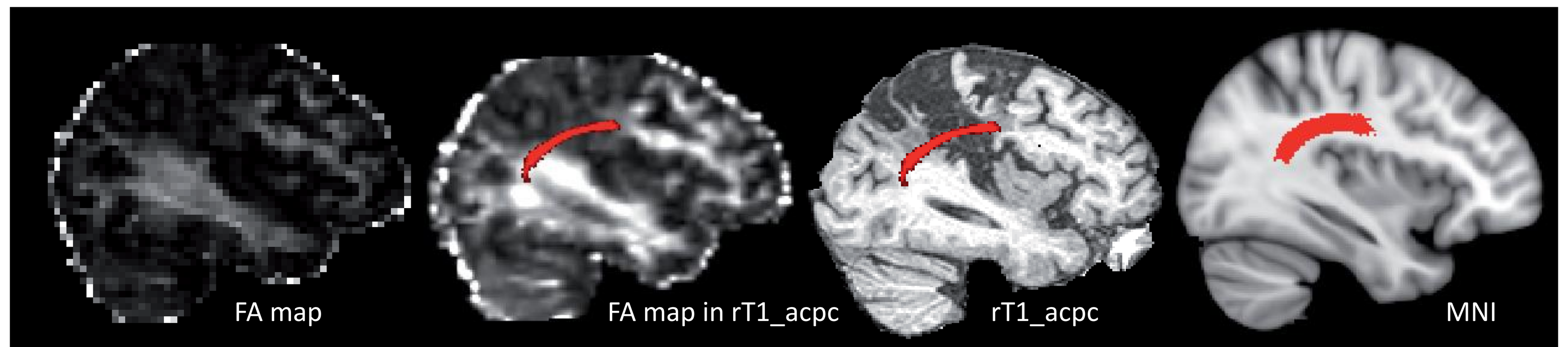
MRI data acquisition

- High-resolution structural T_1 –weighted volume of the whole brain was acquired (1x1x1mm voxels)
- DTI data were acquired using a spin echo, single shot EPI pulse sequence: acquisition matrix = 70x70, FOV = 192x192 mm, slice thickness = 2.7 mm, resulting in 2.7x2.7x2.7 mm voxels, TR = 6000 ms, TE = 95 ms, GRAPPA factor = 2, EPI factor = 70, b = 1000 s/mm^2, gradient directions = 20 and one b0, number of repetitions = 2.

DTI data preprocessing and analysis

Analyses of DTI metrics of selected white matter tracts was done by warping the tract masks from a standardized atlas to the individual space and extracting selected DTI metrics (analogous to Zhang et al, 2010 and Lunven et al., 2015). This transformation included the following steps performed in FSL:

1. Transform of individual diffusion maps (FA, MD, RD, AD) to T1 space with cost function masking of the lesion;
2. Computation of the transform from T1 to MNI with cost function masking of the lesion;
3. Application of the inverse transform from the previous step for tracts chosen from standardized atlases (JHU White Matter Tractography Atlas and Juelich Histological Atlas) in MNI space (tracts were initially thresholded with probability of .25 and binarized);
4. Use of transformed tracts as ROI for extraction of FA, MD, RD and AD values in T1 space.



An example of left AF tract as it is transformed from MNI space to rT1_acpc and laid over T1 and FA map

RESULTS & DISCUSSION

1. Comparison of integrity of major white matter tracts of both hemispheres between individuals with and without aphasia.

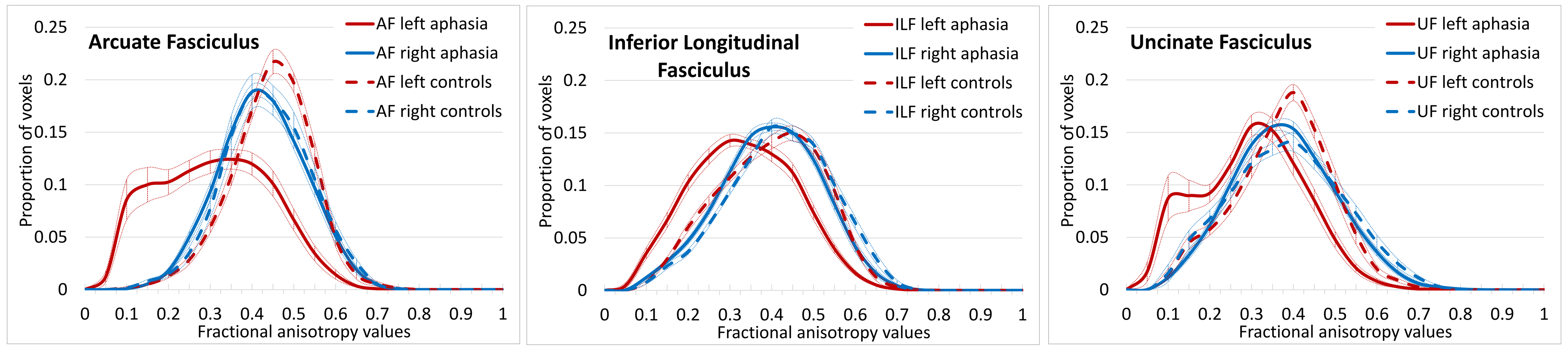
Mean (SD) DTI indices for each white matter tract for the aphasia and the control groups, and results of between group comparisons.

		FA		MD [× 10^{-3} mm^2/s]		AD [× 10^{-3} mm^2/s]		RD [× 10^{-3} mm^2/s]	
		Aphasia	Control	Aphasia	Control	Aphasia	Control	Aphasia	Control
AF	left	.29 (.09) **	.42 (.01)	1.13 (0.34) **	0.75 (0.02)	1.40 (0.30) **	1.09 (0.02)	0.99 (0.36) **	0.57 (0.02)
	right	.40 (.04)	.41 (.02)	0.79 (0.06) *	0.75 (0.02)	1.13 (0.05)	1.07 (0.04)	0.63 (0.06) **	0.57 (0.02)
ILF	left	.31 (.05) **	.37 (.02)	0.96 (0.16) **	0.81 (0.02)	1.25 (0.15) **	1.12 (0.04)	0.82 (0.17) **	0.64 (0.02)
	right	.37 (.03) *	.39 (.01)	0.84 (0.04) *	0.80 (0.03)	1.17 (0.05)	1.13 (0.04)	0.68 (0.04) **	0.62 (0.03)
IFOF	left	.31 (.05) **	.39 (.02)	1.05 (0.22) **	0.81 (0.02)	1.35 (0.20) **	1.15 (0.04)	0.90 (0.23) **	0.62 (0.02)
	right	.37 (.03) *	.39 (.02)	0.87 (0.06) *	0.82 (0.03)	1.21 (0.06)	1.17 (0.04)	0.70 (0.06) **	0.63 (0.03)
UF	left	.28 (.08) **	.35 (.03)	1.11 (0.35) **	0.83 (0.03)	1.38 (0.31) **	1.14 (0.03)	0.97 (0.38) **	0.67 (0.04)
	right	.35 (.03)	.36 (.03)	0.86 (0.05)	0.83 (0.05)	1.18 (0.05)	1.15 (0.05)	0.70 (0.06)	0.67 (0.05)
SOFF	left	.27 (.09)	.31 (.03)	1.20 (0.42) **	0.80 (0.05)	1.47 (0.40) **	1.03 (0.08)	1.06 (0.44) **	0.66 (0.04)
	right	.32 (.04)	.31 (.03)	0.87 (0.08) *	0.79 (0.05)	1.14 (0.12) *	1.03 (0.09)	0.74 (0.07) **	0.66 (0.04)
CC	body	.35 (.05) **	.42 (.04)	1.21 (0.14) **	0.99 (0.11)	1.59 (0.11) **	1.43 (0.08)	1.01 (0.15) **	0.76 (0.12)
	genu	.38 (.05)	.42 (.04)	1.02 (0.10) **	0.90 (0.06)	1.41 (0.08) **	1.31 (0.07)	0.82 (0.12) **	0.68 (0.07)
	splenium	.39 (.06) **	.47 (.03)	1.23 (0.12) **	1.05 (0.09)	1.69 (0.10) **	1.57 (0.08)	0.99 (0.13) **	0.77 (0.10)

Note. Significance levels of comparisons between groups: **$p \leq .001$; *$p < .01$

Individuals with aphasia compared to controls had:

- Significantly lower FA values for all left hemisphere tracts, except SOFF;
- Significantly lower FA values in ILF and IFOF in the right hemisphere;
- Significantly higher MD, AD, RD values for all left hemisphere tracts, with a less consistent picture and overall less prominent but still significant differences for the right hemisphere tracts;
- Significantly lower mean FA values and significantly higher MD, RD, AD values for all left hemisphere tracts compared to the intact right hemisphere tracts.



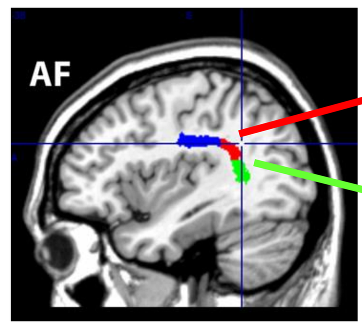
Average FA histograms for AF, ILF and UF of the left (red) and right (blue) hemispheres for the aphasia (solid lines) and the control (dashed lines) groups. Dotted lines represent the FA histograms one standard error above and below the mean.

2. Investigation of the relationship between integrity of major white matter tracts and language comprehension and production in aphasia.

Partial correlations taking age, time post onset and lesion size into account were used to investigate the relationship between major tracts and language scores.

Only FA measures for the left AF, ILF, and IFOF were significantly related to language measures:

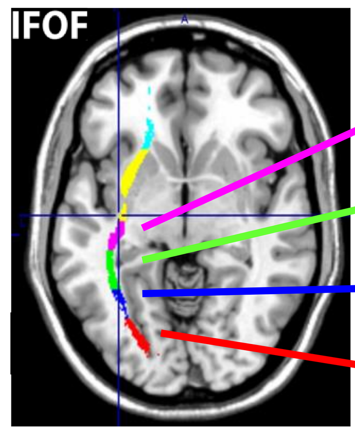
- **AF** integrity related to **production deficits** (word level: r = .503, p =.002; sentence level: r = .442, p =.009). But when analyzed by individual segments:



Related to **production** at the word and sentence level (r = .415* and r = .374*, respectively)

Related to **comprehension** and **production** at the word and sentence level (comprehension: r = .644** and r = 642**; production: r = .528** and r = 508**)

- **ILF** and **IFOF** integrity related to **comprehension deficits** (ILF: r = .524, p =.001; IFOF: r = .504, p =.002). But when analyzed by individual segments:



Related to **comprehension** and **production** at the word and sentence level (comprehension: r = .588** and r = 391*; production: r = .452* and r = 473*)

Related to **comprehension** at the word and sentence level (r = .459** and r = .386*)

Related to **comprehension** at the word and sentence level (r = .348* and r = .359*)

Related to **comprehension** at the word and sentence level (r = .355* and r = .401*)

HIGHLIGHTS:

- Fiber pathways – AF, ILF, IFOF, but not UF, SOFF and CC – play an important role in supporting different language functions;
- Temporal tracts – ILF and IFOF – are vital for language processing, in particular, comprehension;
- Clear functional juxtaposition of dorsal versus ventral tracts as proposed in dorsal-ventral models of language processing does not seem feasible;
- It is an oversimplification to regard fasciculi as indivisible entities and determine functional relevance of the whole tract, as analysis of individual tract segments demonstrated differential relationship with language production and comprehension in aphasia;
- Distal changes in the unlesioned right hemisphere were demonstrated and need to be investigated further.

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