

SUPPLEMENTARY MATERIAL

S1. Protocol for delineation of the three segments of the arcuate fasciculus

The *long* tract of the arcuate fasciculus was isolated with a frontal AND gate in the coronal plane 1mm anterior to the upper boundary of the corpus callosum and around the periventricular anterior/posterior running fibres located lateral to the projection fibres of the corona radiata. A second, temporal AND gate was placed in the axial plane, lateral to the posterior horn of the lateral ventricle, 4mm posterior to the last slice where the fibre curves around the posterior and medial extent of the Sylvian fissure, the AND gate extending around the majority of the temporal lobe (Figure S1A). The *anterior* tract was isolated using the frontal gate implemented for the long segment and a parietal AND gate placed on the sagittal plane, 3mm lateral to the emergence of the fibres arching around the Sylvian fissure to include the region medial to the supramarginal gyrus, (Figure S1B). The posterior tract was isolated using the parietal and temporal gates (Figure S1C). The posterior tract was isolated using the parietal and temporal gates (Figure S1C).

NOT gates were applied to remove any spurious tracts and tract areas external to the defined gates were excluded to include the main body of each tract in analysis. Both left and right segments were isolated with this protocol.

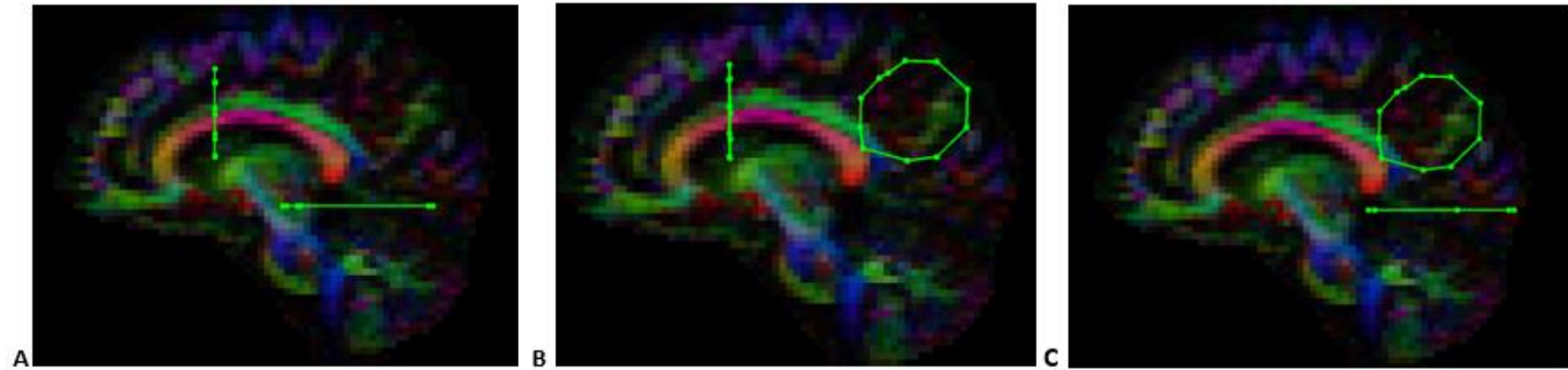


Figure S1: (A) Frontal and temporal AND gates placed on DEC-FA map to isolate the long tract of the arcuate fasciculus (AF); (B) the frontal gate in addition to the parietal gate were used to extract the anterior tract; (C) the parietal gate was used in conjunction with the temporal gate to isolate the posterior tract of the AF

S2. FreeSurfer Processing – Cortical analysis

Based on a linear combination of voxel intensities and local geometric constraints, the cerebral white matter (WM) is first segmented, divided into 2 hemispheres, and the brain stem and cerebellum removed. Tessellation is then performed to produce a triangle-based mesh of the WM surface and refined to alleviate the voxel-based nature of the initial curvature. The WM surfaces are deformed outward to generate the pial (GM/CSF intersection) surface. Topologic defects in the surface are corrected using an automated topology fixer. Visual quality checks were then performed and inaccuracies manually edited and corrected by reprocessing. The cortical surface is then spherically inflated so that the entire cortical surface is exposed, including deep tissue inside the sulci. Using combined information from the pial and WM surfaces, cortical thickness, surface area and volume are calculated at each vertex. Seven language-related bilateral cortical regions, where the arcuate fasciculus is known to project to, were isolated from each individual cortex using an automated parcellation process based on the Desikan-Killany cortical atlas (Desikan et al., 2006) implemented in FreeSurfer (Figure 1). The *pars opercularis*, *pars triangularis* and *pars orbitalis* were chosen as the rostral cortical regions where frontal projections of the long and anterior AF segment terminate. Temporal terminations of the long and posterior segment were identified as *the superior, middle and inferior temporal gyri* (Rilling et al., 2008, Dick & Tremblay, 2012). The *supramarginal gyrus* was identified as the posterior termination of the anterior segment and the superior lateral termination of the posterior segment.

S3. Results of normal distribution testing using Shapiro–Wilk

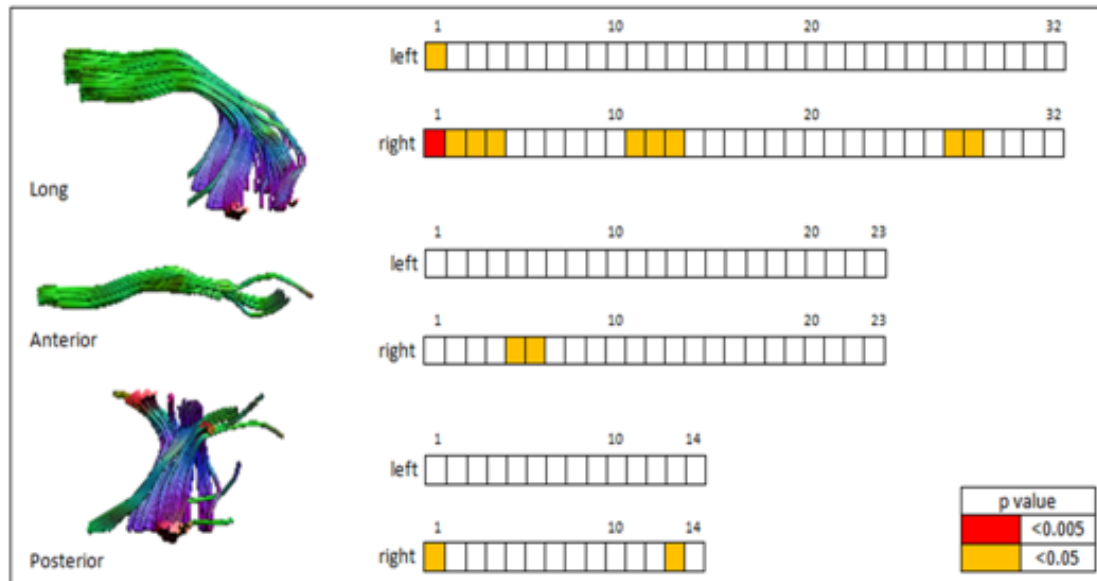
Cognition: Verbal learning was normally distributed ($w=0.97, p=0.45$). Verbal fluency was non-normal ($w=0.93, p=0.005$), however became normally distributed following log transformation ($w=0.96, p=0.10$).

Arcuate fasciculus: Left and right AF segments were all normally distributed ($w=0.95-0.99, p=0.06-0.99$).

Cortex: The cortical thickness of the right hemisphere pars opercularis was non-normally distributed ($w=0.94, p=0.02$) but became so after log transformation ($w=0.96, p=0.16$). All other cortical regions were normally distributed ($w=0.94-0.99, p=0.07-0.95$). The cortical surface area of the right hemisphere pars triangularis ($w=0.92, p=0.004$) and ITG ($w=0.94, p=0.02$) were non-normal both becoming significant following log transformation for the pars triangularis ($w=0.96, p=0.16$) and square transformation for the ITG ($w=0.96, p=0.1$). All other regions were normally distributed for surface area ($w=0.92-0.99, p=0.07-0.96$) and cortical volume ($w=0.96-0.99, p=0.07-0.90$).

Lateralization index: The lateralization index of all three AF segments were normally distributed ($w=0.97-0.98, p=0.18-0.61$). All lateralization indices (LI) of cortical thickness were normally distributed ($w=0.93-0.98, p=0.19-0.87$) excepting the LI of the pars triangularis ($w=0.92, p=0.005$), MTG ($w=0.94, p=0.02$) and ITG ($w=0.94, p=0.014$). All LIs of the cortex using surface area measures were normally distributed ($w=0.96-0.99, p=0.19-0.98$) with the exception of the STG ($w=0.77, p=0.00$). Using cortical volume, the LI of all cortical regions were normally distributed ($w=0.96-0.99, p=0.19-0.98$) except for the STG ($w=0.85, p=0.00$). Non-parametric tests were used when analyzing the non-normally distributed LI variables as it was not possible to successfully transform these data.

S4. Sections along each of the three segments of the AF that had significant group differences (uncorrected p values are shaded p<0.05)



S5. Results of investigations of the Fractional Anisotropy of the Arcuate Fasciculus

(A)

There were no significant differences between the individuals with psychosis and healthy controls in the FA of the long, anterior or posterior segments ($F=0.001-1.15, p=0.29-0.77$), nor at any individuals points investigated along the three AF segments which survived FDR correction

(B)

Relationship to Verbal Cognition: In the individuals with psychosis, greater FA in the right long segment was positively associated with log transformed verbal fluency ($r=0.57, p=0.011$). There were no significant associations between FA of the bilateral long, anterior or posterior AF segments and verbal learning ($r=-0.34-0.12, p=0.14-0.81$) or verbal fluency ($r=-0.28-0.36, p=0.14-0.72$) in either group. There were no associations between points along each segment and verbal learning ($r=-0.64-0.54, p=0.003-0.89$) or verbal fluency ($r=-0.22-0.26, p=-0.22-0.92$), following FDR correction.

(C)

Patterns of lateralization (FA)

		t, p	Difference from 0	Direction	VL** r,p	VF** r,p
Healthy Controls	LI Long	3.84,0.01*	0.078	Left	-0.04,0.85	-0.33,0.14
	LI Anterior	-3.86,0.001*	-0.071	Right	-0.12,0.59	0.19,0.41
	LI Posterior	0.85,0.42	0.044	Left	0.29,0.21	-0.06,0.79
Psychosis	LI Long	3.2, 0.004*	0.04	Left	-0.34,0.17	-0.27,0.28
	LI Anterior	-2.27,0.03	-0.018	Right	-0.01,0.96	-0.34,0.17
	LI Posterior	0.73,0.47	0.043	Left	-0.31,0.21	0.21,0.40

Legend: LI = lateralisation index; * = significantly different from zero and survived FDR correction; ** = relationship of LI to verbal learning and verbal fluency, covarying for age and gender.

Group Differences in Lateralization Patterns (FA): A univariate ANOVA revealed that there was no significant differences between individuals with psychosis and healthy controls in the lateralisation index of the long ($F=0.06, p=0.81$), anterior ($F=0.61, p=0.44$) or posterior tract ($F=0.68, p=0.42$).

S6. Lateralization index (using measures of cortical thickness, surface area and volume) of seven language related cortical regions in healthy controls (A)

and

individuals with psychosis (B).

A

	Cortical Thickness			Cortical Surface area			Cortical volume		
	T	p	Mean Diff	T	p	Mean Diff	T	p	Mean Diff
Pars opercularis	-1.56	0.13	-0.011	4.11, 0.0004*	0.79		4.42,0.0001*		0.074
Pars triangularis	1.55	0.14	0.007	-4.77,0.7e-5*	-0.064		-4.34,0.0002*		-0.06
Pars orbitalis	-0.53	0.60	-0.004	-9.11,0.0e-5*	-0.114		-6.91,0.0e-5*		-0.11
STG	0.56	0.58	0.003	2.54,0.018*	0.017		2.68,0.013*		0.017
MTG	-0.22	0.83	-0.001	-3.93,0.001*	-0.035		-3.91,0.001*		-0.044
ITG	3.93	0.001*	0.013*	5.07,0.00004*	0.044		5.25,0.00002*		0.051
Supramarginal gyrus	0.009	0.99	0.0001	1.40,0.17	0.017		1.93,0.07		0.022

Legend: Note: Mean diff = mean difference from 0 - positive values indicate a leftward asymmetry, negative values indicate a rightward asymmetry; * = significantly different from zero

B

	Cortical Thickness			Cortical Surface area			Cortical volume		
	t	p	Mean Diff	t	p	Mean Diff	t	p	Mean Diff
Pars opercularis	-0.48	0.64	-0.004	6.30	0.3e-6*	0.113	6.70	0.01e-6*	0.125
Pars triangularis	-1.26	0.22	-0.009	-4.6	0.00015*	-0.071	-4.13	0.0005*	-0.084
Pars orbitalis	0.70	0.49	0.006	-8.87	0.0e-6*	-0.122	-7.69	0.0e-6*	-0.101
STG	0.48	0.64	0.003	1.53	0.14	0.025	2.63	0.016*	0.044
MTG	0.59	0.56	0.003	-6.32	0.3e-5*	-0.066	-5.01	0.00006*	-0.07
ITG	0.66	0.52	0.004	2.11	0.047*	0.0283	1.78	0.09	0.027
Supramarginal gyrus	-1.49	0.15	-0.009	-0.29	0.77	-0.05	-0.54	0.59	-0.10

Legend: Note: Mean diff = mean difference from 0 - positive values indicate a leftward asymmetry, negative values indicate a rightward

asymmetry; * = significantly different from zero; STG = superior temporal gyrus; MTG = middle temporal gyrus; ITG = inferior temporal gyrus.

S7. Group differences in the lateralization index of cortical regions

	Cortical Thickness			Cortical surface area			Cortical volume		
	Controls	Psychosis	F, p	Controls	psychosis	F, p	Controls	Psychosis	F, p
	m±SE	m±SE		m±SE	m±SE		m±SE	m±SE	
Pars opercularis	-0.012±0.007	-0.002±0.008	0.69,0.41	0.08±0.019	0.11±0.021	1.24,0.27	0.073±0.018	0.126±0.02	3.75,0.059
Pars triangularis	0.008±0.006	-0.01±0.006	4.33,0.043	-0.06±0.02	-0.077±0.02	0.66,0.42	-0.06±0.02	-0.09±0.02	1.67,0.21
Pars orbitalis	-0.004±0.008	0.006±0.008	0.72,0.40	-0.11±0.01	-0.13±0.01	0.39,0.53	-0.10±0.02	-0.11±0.02	0.021,0.89
STG	0.002±0.005	0.004±0.006	0.074,0.79	0.017±0.01	0.025±0.006	0.21,0.65	0.02±0.01	0.044±0.013	1.77,0.19
MTG	-0.002±0.006	0.004±0.006	0.45,0.51	-0.03±0.01	-0.07±0.011	5.23,0.027	-0.044±0.01	-0.07±0.014	1.80,0.19
ITG	0.013±0.005	0.004±0.006	1.39,0.24	0.05±0.01	0.03±0.01	1.72,0.19	0.05±0.01	0.03±0.01	2.40,0.13
Supramarginal gyrus	-0.001±0.006	-0.007±0.006	0.44,0.51	0.02±0.02	-0.003±0.02	0.59,0.45	0.02±0.02	-0.007±0.017	1.31,0.26

Legend: mean ± standard error reported; STG = superior temporal gyrus; MTG = middle temporal gyrus; ITG = inferior temporal gyrus.

S8. *Post-hoc* Investigation of Positive Symptoms

Post-hoc analyses were conducted to investigate the relationship between any significant findings in the AF and associated cortical regions with the PANSS positive symptom total score and P3 of the PANSS which assesses hallucinatory behavior specifically. Furthermore, significant neuroanatomical associations with verbal cognition were further explored by separating the psychosis group into those who ever experienced auditory verbal hallucinations (AVH, $n=9$) and those who never experience AVHs ($n=13$). No significant associations were found between brain regions and positive symptoms ($r=-0.54-0.37, p=0.03-0.96$), however the significant association between the lateral index of the pars opercularis volume and verbal learning found in the psychosis group appeared to be driven by those who experienced AVH ($r=-0.91, p=0.004$), in comparison to those who never experienced AVHs ($r=-0.30, p=0.40$).

Verbal learning and verbal fluency (log) did not correlate with PANSS positive total score or P3 of the PANSS ($r=-0.32-0.21, p=0.23-0.94$).