White matter maturation in the temporoparietal junction and its connection to prefrontal cortex support the emergence of Theory of Mind

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Introduction

- **ToM development:** The ability to represent the mental states of other agents, i.e. their thoughts and believes, is considered to be a hallmark of human cognition.[1] This ability is referred to as Theory of Mind (ToM) and understanding others' false beliefs (FB) is considered to be a crucial test of it.[2] A developmental breakthrough in ToM is consistently observed between the age of 3 and 4 years, when children start passing such FB tests.[3] To date, however, we lack an understanding of the neural mechanisms which support this crucial step in the development of social cognition.
- **Functional neural ToM network:** In adults, a number of fMRI studies on FB understanding have shown functional activation in a network including the temporoparietal junction (TPJ), the superior temporal sulcus (STS), the precuneus (PC) and the medial prefrontal cortex (MPFC).[4] This network has also been reported to be activated for ToM in 6- to 11-year-old children.[5] Concerning white matter (WM) connectivity of the ToM network, a patient study suggests that the integrity of the arcuate fascicle (AF) and the cingulum are important for ToM.[6]
- **The present study:** Here, we study how WM development relates to ToM abilities in the critical age period of 3 to 4 years (ys), when explicit FB understanding develops.

Methods

Participants: 17 aged 3- to 3.5 ys and 26 aged 4- to 4.5 ys.

Behavioral tasks:

- Standard explicit FB tasks: false location[7] and false content[8]
- Standardized language test: SETK 3-4
- Battery of executive function (EF) tests[9]
- Implicit anticipatory looking FB test[9]

White matter analysis:

- Tract-Based Spatial Statistics (TBSS)[10]: Correlation of explicit FB performance with fractional anisotropy (FA) projected to a skeleton.
- Commonality Analysis: including FA, age, language, EF and implicit FB as predictors for explicit FB. This analysis allows to determine the variance explained uniquely by one predictor or in common by several predictors. Goals: (1) Separate effects into age-independent and age-related FA effects; (2) Control for other cognitive abilities and earlier-developing implicit FB.
- Tractography: Probabilistic tractography from TBSS seeds based on Constrained Spherical Deconvolution (CSD).[11] Streamline density was then correlated with FB performance. Goal: Specify how the obtained tracts were related to FB understanding.

Results

1

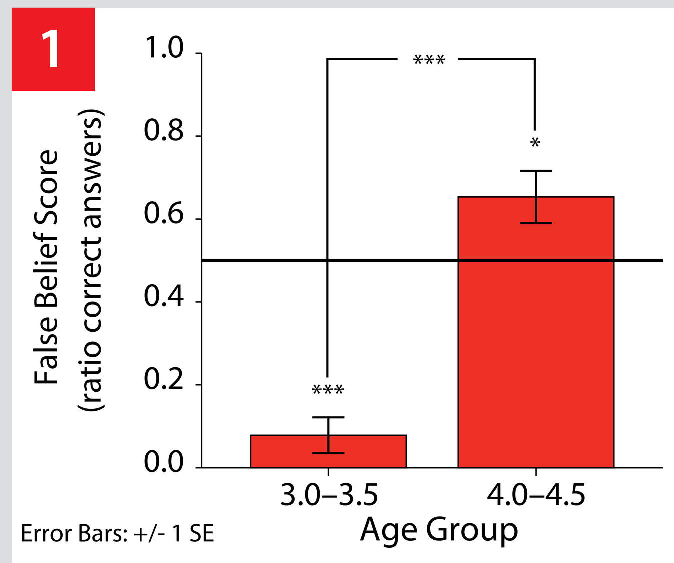

Figure 1: Behavioral results: 3-year-olds perform significantly below chance and 4-year-olds significantly above chance in the explicit FB tests.

2

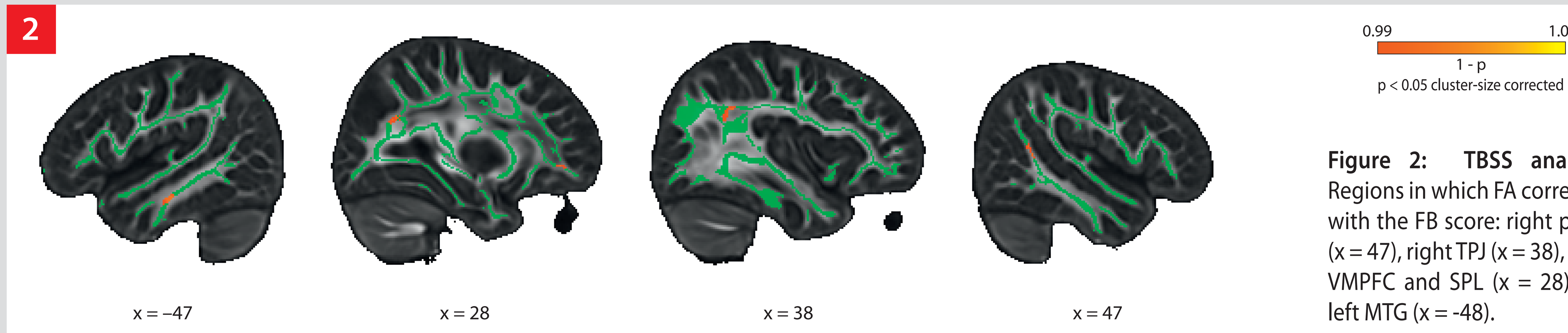

Figure 2: TBSS analysis: Regions in which FA correlates with the FB score: right pMTG (x = 47), right TPJ (x = 38), right VMPFC and SPL (x = 28) and left MTG (x = -48).

3

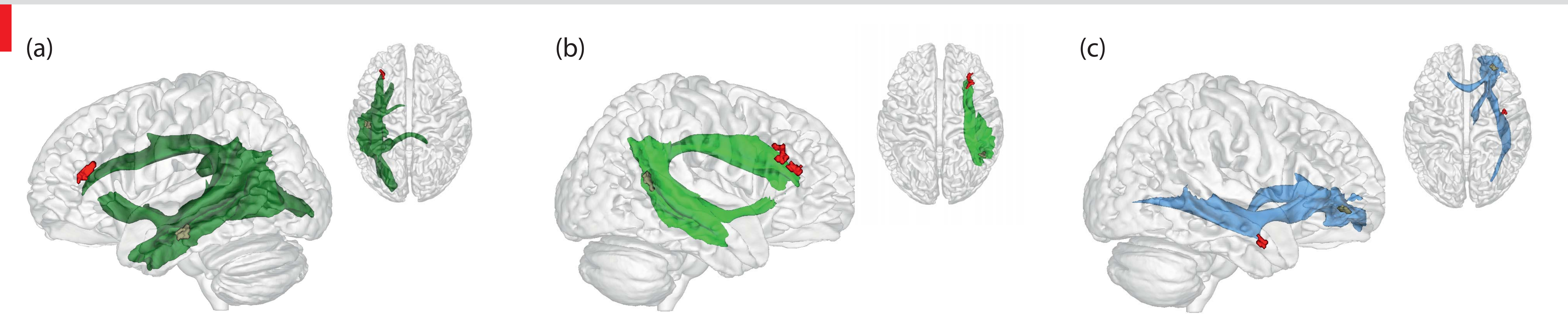

Figure 3: In red: significant correlation of FB and streamline density of the fibre tracts found seeding in the TBSS regions :
(a) Left inferior frontal gyrus (IFG) at the anterior tip of the left AF
(b) Right IFG at the anterior tip of the right AF
(c) Right MTG along the IFOF
The effects are independent of age and co-developing abilities.

$p < 0.05$ cluster-size corrected
Bonferroni corrected for number of tracts

Table 1

	(A) TBSS Analysis				(B) Commonality Analysis			(C) Tractography
	MNI coordinates centre of gravity			Cluster Size	Mean explained variance (& overlap) of significant contributions incl. FA			
Region: WM in/near	x	y	z	(in vox)	FA + Age	FA + Age + impl FB	FA + Age + Lang + EF	WM Tracts
rTPJ	37	-50	30	66	7.4% (0.95)	n.s.	2.2% (0.91)	AF
rpMTG/ TPJ	47	-51	14	49	6.8% (0.90)	1.3% (0.65)	n.s.	AF
lMTG	-48	-18	-20	63	7.5% (0.98)	n.s.	n.s.	AF
lITG	-33	-13	-13	63	6.2% (0.92)	n.s.	n.s.	IFOF, ILF, fornix
lSTG	-38	-32	2	35	6.4% (0.94)	n.s.	n.s.	IFOF
rVMPFC	28	46	-4	31	4.3% (0.71)	n.s.	n.s.	IFOF, CC (prefrontal)
rSPL	28	-64	28	34	6.5% (0.97)	1.3% (0.53)	n.s.	CC (parietal)
lThalamus	-3	-12	0	18	9.8% (1.00)	n.s.	n.s.	aTR

FA – fractional anisotropy, EF – executive functions, impl FB – implicit false belief, Lang – language, TPJ – temporoparietal junction, MTG – medial temporal gyrus, ITG – inferior temporal gyrus, STG – superior temporal gyrus, VMPFC – ventromedial prefrontal cortex, SPL – superior parietal lobule, AF – arcuate fascicle, IFOF – inferior fronto-occipital fascicle, ILF – inferior longitudinal fascicle, CC – corpus callosum, aTR - anterior thalamic radiation, r – right, l – left, p – posterior.

Table 1: (A) Regions in which FA correlates with the explicit false belief (FB) score in the TBSS analysis (see Fig. 2). **(B)** Mean explained variance in FB by contributors including FA in a commonality analysis including age, FA, language, EF and implicit FB as predictors for the explicit FB score. In brackets: proportion of overlapping voxels with significant contribution. **(C)** WM tracts found with probabilistic tractography seeding in the TBSS regions (see Fig. 3).

Summary Results

- FB understanding correlates with age-driven FA changes in right TPJ, bilateral MTG, VMPFC and precuneus (SPL) in 3- and 4-year-olds, also when language, EF and implicit FB are controlled for.
- Seeding in these regions yields dorsal and ventral connections between TPJ and PFC (AF and IFOF) as well as cross-hemispheric connections through the CC (connecting the precuneus and the VMPFC bilaterally).
- In particular the connectivity between the TPJ and the anterior IFG through the AF and in the right MTG along the IFOF correlate with the children's FB understanding, independently of age and other co-developing abilities.

Conclusion

- WM maturation in the regions functionally activated for ToM in adults play a crucial role for the developmental breakthrough in explicit false belief understanding between the age of 3 and 4 years.
- The degree to which the TPJ is connected to the anterior IFG supports the emergence of false belief understanding in the critical age when the ability develops.
- We therefore suggest a mechanism in which the connection between the belief processing region TPJ and hierarchical embedding in IFG through the arcuate fascicle paves the way for the developmental breakthrough in representational ToM.

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