



White matter asymmetries in human situs inversus totalis

Lieselot Mannaert¹ · Helena Verhelst^{1,2} · Robin Gerrits^{1,2} · Stephanie Bogaert^{2,3} · Guy Vingerhoets^{1,2} 

Received: 18 January 2019 / Accepted: 6 June 2019 / Published online: 13 June 2019
© Springer-Verlag GmbH Germany, part of Springer Nature 2019

Abstract

Diffusion weighted imaging (DWI) was used to investigate white matter asymmetries in participants with situs inversus totalis (SIT) and matched controls. Regardless of visceral condition, hemispheric differences were found for the arcuate fasciculus (ARC) and the superior longitudinal fasciculus (SLF), which are involved in language and visuospatial functioning, respectively. The ARC appears lateralized to the left hemisphere, analogous to the left lateralization of functional areas associated with language. The SLF, on the other hand, is lateralized to the right, corresponding with rightward lateralization of visuospatial functioning. Interestingly, SIT participants show a significantly lower number of streamlines in the Uncinate Fasciculus (UNC). In addition, UNC volume appears associated with measures of cognitive performance, a finding in line with previously reported performance differences between SIT participants and controls.

Keywords Situs inversus totalis · White matter asymmetry · Lateralization · Arcuate fasciculus · Uncinate fasciculus · Superior longitudinal fasciculus

Introduction

Situs inversus totalis (SIT) is a rare anatomical condition in which the internal organs are in mirrored position compared to their typical location with the heart on the left and the liver on the right (Grimes and Burdine 2017). The condition may go unnoticed for decades until it is discovered by chance during medical examination for an unrelated event. In others, the condition is revealed soon after birth because associated congenital heart disease required surgical intervention. Still others are diagnosed with primary ciliary dyskinesia (PCD), a genetic dysfunction of hair-like cells in respiratory and genital tracts that cause chronic bronchitis and rhinitis, and subfertility (Bush et al. 1998). Fifty percent of patients with PCD have SIT, as hypomotility of nodal cilia during embryogenesis is believed to result in a randomization of visceral situs (Leigh et al. 2009).

Recently, we compared brain structural and functional asymmetries in 15 participants with SIT and 15 matched control participants. We aimed to investigate whether humans show an association between visceral and brain asymmetries, an observation reported in other animal species (Goto et al. 2010). Results showed that visceral reversal in humans has only limited effects on typical brain asymmetry. Structural and functional asymmetries associated with language revealed no significant differences with control participants (Vingerhoets et al. 2018b). On the other hand, the ‘Yakovlevian’ brain torque, a population-wide lobar asymmetry seen in most human brains, was generally reversed in participants with SIT and appeared predominantly driven by SIT participants without primary ciliary dyskinesia. In addition, the SIT-group showed significantly more frequent atypical functional segregation, in which one or two cognitive functions present with atypical hemispheric dominance while others show typical lateralization (Vingerhoets et al. 2018a).

Thus far our anatomical reports on this cohort focused mainly on brain structural and functional language-related asymmetries. Here, we turn to results from diffusion weighted imaging (DWI) and explore white matter asymmetries of major association tracts in the SIT and control group. High anatomical consensus exists for five tracts (Hua et al. 2008; Oishi et al. 2011; Webb 2017; Haines

✉ Guy Vingerhoets
guy.vingerhoets@ugent.be

¹ Department of Experimental Psychology, Ghent University, Henri Dunantlaan 2, 9000 Ghent, Belgium

² Ghent Institute for Functional and Metabolic Imaging (GfMI), Ghent University, Ghent, Belgium

³ Department of Radiology, Ghent University Hospital, Ghent, Belgium

and Mihailoff 2018): arcuate fasciculus (ARC), inferior fronto-occipital fasciculus (IFO), inferior longitudinal fasciculus (ILF), superior longitudinal fasciculus (SLF), and the uncinate fasciculus (UNC). Furthermore, hemispheric differences in these five tracts have been reported in white matter asymmetry studies in healthy participants. For example, Ocklenburg and Güntürkün (2018) reviewed leftward lateralization of ARC and hemispheric differences of sub-components of UNC and SLF; Thiebaut de Schotten et al. (2011b) found leftward asymmetry for ILF and for the long segment of the ARC, but rightward asymmetry for the IFO; and the results of Slater et al. (2019) showed left lateralization of ARC and UNC and right lateralization of IFO. We present hemisphere data on fractional anisotropy (FA) and number of streamlines (NoS), two adequate measures in DTI which are frequently reported in WM asymmetry research (Van Hecke et al. 2016). Two main questions will be addressed: (1) do these white matter tracts show significant between hemisphere differences, and (2) do we find white matter differences between participants with SIT and matched controls.

Method

Participants

Following institutional and ethical approval the databases of Ghent University Hospital and Middelheim Hospital Antwerp were searched for the term ‘situs inversus’ in radiological protocols of patients aged 18–70 years. Fifteen participants with situs inversus totalis were included after written informed consent was obtained according to the Declaration of Helsinki. The SIT cohort consisted of 15 individuals, 7 women and 8 men that were between 18 and 50 years old. A group of healthy control participants was also recruited that were individually matched for gender, age, years of formal education, and handedness with the SIT participants (7 women, 8 men, 19–51 years old). All participants underwent the same research protocol. Detailed information on participant recruitment and demographic and medical details can be found elsewhere (Vingerhoets et al. 2018a, b).

Cognitive performance

Cognitive performance was measured using a Dutch adaptation of the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS), (Randolph 2002). For SI06 and CO17, French and Italian adaptations were used, respectively. The RBANS comprises ten cognitive subtests and provides index scores for five domains: immediate memory, visuospatial/constructional, language, attention, and

delayed memory. The index scores are reported as standard scores with a mean of 100 and a standard deviation of 15.

MRI data

A 3.0 T TIM Trio (release VB17) and a standard 32-channel head coil (Siemens Healthineers, Erlangen, Germany) were used for MRI data acquisition. The parameters for DWI were as follows: a twice refocused single-shot echo-planar diffusion pulse sequence with an isotropic image resolution of 2.5 mm³, one non-diffusion weighted b₀ image, 64 different non-collinear directions with $b = 1200$ s/mm², 60 contiguous slices, TR/TE = 10,800/83 ms, FOV = 240 mm, matrix size 96 × 96, bandwidth 1736 Hz/Px, epi factor = 96, PAT = 3, and acquisition time = 12:36 min (see also Vingerhoets et al. 2018b).

WM tracts

The DWI brain scans were processed using Eddy (Anderson and Sotiropoulos 2016) from FDT (FMRIB diffusion toolbox, which is part of FSL). First, the images were pre-processed, correcting for eddy current distortions and head motion using a 12-parameter affine registration to a reference volume (non-diffusion weighted volume). The gradient directions were rotated accordingly (Leemans and Jones 2009). Euler integration was used to perform deterministic tractography (Basser et al. 2000), with a step size of 1 mm. The stopping criteria for reconstructing fiber pathways were either when the FA-value in a voxel was lower than 0.20 or when the angle between two consecutive tractography steps was greater than 35°.

TrackVis was used to delineate the fiber tracts (Wang et al. 2007). For the ARC, two ROIs were selected in accordance with Kamali et al. 2014. The first one was placed on a bundle of association white matter (coded as green on the color maps) passing through the fronto-temporal junction on the coronal slice. The second ROI consisted of projection fibers passing through the temporal plane on the axial slice. To delineate the SLF, the classification of Makris et al. (2005) was used. He argued that the SLF consists of four sub-components: SLF I, SLF II, SLF III, and the Arcuate Fasciculus. In the present study, we focus on the SLF II component of the SLF, which is primarily involved in visual processing and spatial attention. Hereafter, the SLF II component will be referred to as SLF. The first ROI for the SLF was the same as for the ARC. The second one was situated in the angular gyrus and consisted of a bundle of association white matter on the coronal slice. For the UNC, two ROIs were placed, a coronal inclusion ROI at the fronto-temporal junction and an inclusion ROI in the temporal plane. (Van Hecke et al. 2016). To delineate the ILF, an inclusion ROI was placed at the temporal lobe on the coronal slice

and another large coronal inclusion ROI was placed in the parieto-occipital area. Furthermore, an exclusion ROI was placed at the fronto-temporal junction on the coronal slice (Van Hecke et al. 2016). For the IFO, there were two coronal inclusion ROIs placed. The first at the fronto-temporal junction, but posterior to the UNC, and the second in the parieto-occipital area (Van Hecke et al. 2016). After the delineation of all tracts in each subject, NoS and FA were computed. Furthermore, lateralization indices were calculated both for NoS and for FA. This was done by dividing the difference in NoS or FA between the right and left hemispheres by the sum of NoS or FA of both hemispheres: $(R-L)/(R+L)$.

Data analysis

The data was analyzed in R version 3.4.2 using a 2×2 repeated measures MANOVA. The first factor, Group, is a between-subjects factor with two levels, the SIT group and the control group. The second factor, Hemisphere, is a within-subjects factor with two levels that refers to the left or right hemisphere. Ten dependent variables were examined: the number of streamlines and the FA-value of each of the five tracts. Subsequently, post hoc tests were conducted to check the influence of Group and Hemisphere on each of the dependent variables. The p values of the post hoc tests were corrected using false discovery rate correction (FDR).

Results

First, we looked at the repeated measures MANOVA omnibus effect with all ten dependent variables. Both the main effect of Group ($F(10,47) = 5.71$, $p = 0.00027$, $\eta^2 = 0.48$) and the main effect of Hemisphere ($F(10,47) = 4.31$, $p = 0.00002$, $\eta^2 = 0.55$) were significant. However, the Group \times Hemisphere interaction did not reach significance ($F(10,47) = 1.23$, $p = 0.297$). Since both main effects were of interest, we looked further into the effect on each of the dependent variables using post hoc repeated measures ANOVA. For the ARC, there was a main effect of Hemisphere for both NoS ($F(1,56) = 20.9$, $p_{\text{adj}} = 0.0003$, $\eta^2 = 0.27$), see also Vingerhoets et al. (2018b), and FA ($F(1,56) = 6.74$, $p_{\text{adj}} = 0.0401$, $\eta^2 = 0.1$).

In particular, there were significantly more streamlines and higher FA in the left hemisphere (NoS: $M = 171.93$, $SD = 94.6$; FA: $M = 0.47$, $SD = 0.03$) compared to the right hemisphere (NoS: $M = 72.57$, $SD = 72.1$; FA: $M = 0.39$, $SD = 0.16$), see Fig. 1a. Also, for the SLF, a main effect of Hemisphere was found for NoS ($F(1,56) = 11.46$, $p_{\text{adj}} = 0.0065$, $\eta^2 = 0.16$), showing higher NoS in the right hemisphere ($M = 172.2$, $SD = 109.46$) compared to the left hemisphere ($M = 90.67$, $SD = 81.08$), see Fig. 1a. No effect for FA was found ($F(1,56) = 1.98$, $p_{\text{adj}} = 0.33$). For all other tracts, the main effect of Hemisphere was not significant.

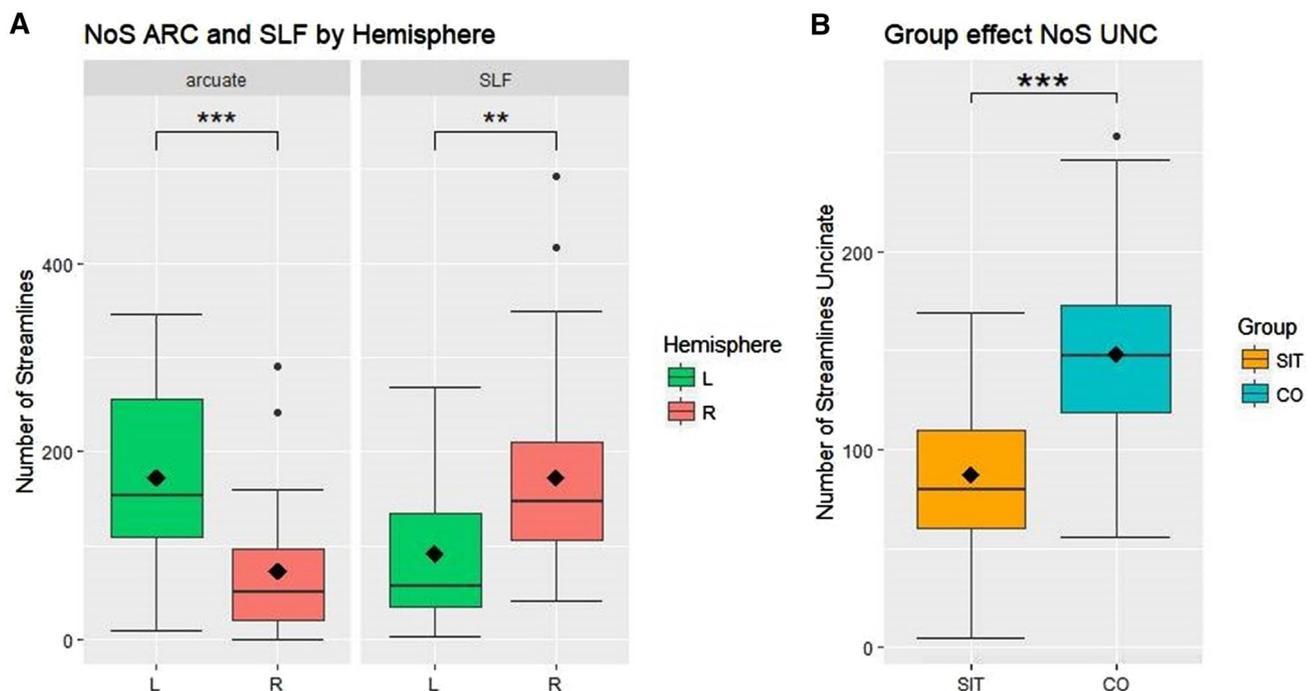


Fig. 1 **a** Hemispheric differences for ARC and SLF with higher FA and higher NoS in the left hemisphere for ARC and higher NoS in the right hemisphere for SLF. **b** Group differences for UNC with higher

NoS for the SIT group (SIT) compared to the control group (CO). * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

Hence, the omnibus main effect of Hemisphere appears to be driven by the number of streamlines of the ARC and the SLF and the FA-value of the ARC. The main effect of Group was only significant for NoS of the UNC ($F(1,56)=28.52$, $p_{\text{adj}}=0.00002$, $\eta^2=0.31$), with the NoS being higher in the control group ($M=171.27$, $SD=49.37$) compared to the SIT-group ($M=85$, $SD=47.53$). Hence, there are differences in white matter between the SIT and control group, which are expressed in a lower number of streamlines in the uncinate fasciculus for the SIT group compared to the control group (Fig. 1b). Within the SIT group, no WM differences were found between SIT participants with primary ciliary dyskinesia and SIT participants without primary ciliary dyskinesia ($F(10,19)=1.192$, $p=0.355$).

Since previous research revealed that SIT is associated with lower cognitive performance compared to controls (Vingerhoets et al. 2018a) and the current findings reveal between-group differences in the uncinate fasciculus, we wanted to check whether the NoS in the UNC is associated with cognitive performance. A repeated measures MANCOVA was conducted with five dependent variables, which were the five cognitive domain scores of the RBANS. The model consisted of two predictors: a continuous variable (NoS) and a factor (Hemisphere). We found a main effect of NoS ($F(5,52)=2.5$, $p=0.042$, $\eta^2=0.2$) on cognitive performance, but no main effect of

Hemisphere ($F(5,52)=0.09$, $p=0.993$) nor an interaction effect ($F(5,52)=0.34$, $p=0.887$). Post hoc ANCOVA analysis revealed that the effect was significant for Immediate Memory ($F(1,56)=7.32$, $p_{\text{adj}}=0.023$, $\eta^2=0.12$) and visuospatial/constructional ($F(1,56)=12.59$, $p_{\text{adj}}=0.004$, $\eta^2=0.19$), with better performances being associated with higher NoS (Fig. 2).

Discussion

In the present study, we found evidence for (1) hemispheric white matter differences, specifically in the ARC and in the SLF; and (2) white matter differences between participants with SIT and matched controls, characterized by a lower NoS in the UNC in SIT. In addition, higher NoS in the UNC is associated with higher performance on tasks of immediate memory and visuospatial/constructional ability.

Previous research already reported hemispheric differences in WM tracts. Catani et al. (2010) found a higher NoS in the right IFO and there is consensus that the ILF shows leftward asymmetry for both FA (Ashtari et al. 2007; Catani et al. 2010) and volume (Wakana et al. 2007). The ARC is asymmetrical as well, with higher FA (e.g. Büchel et al. 2004) and a larger volume (e.g. Good et al. 2001) in the

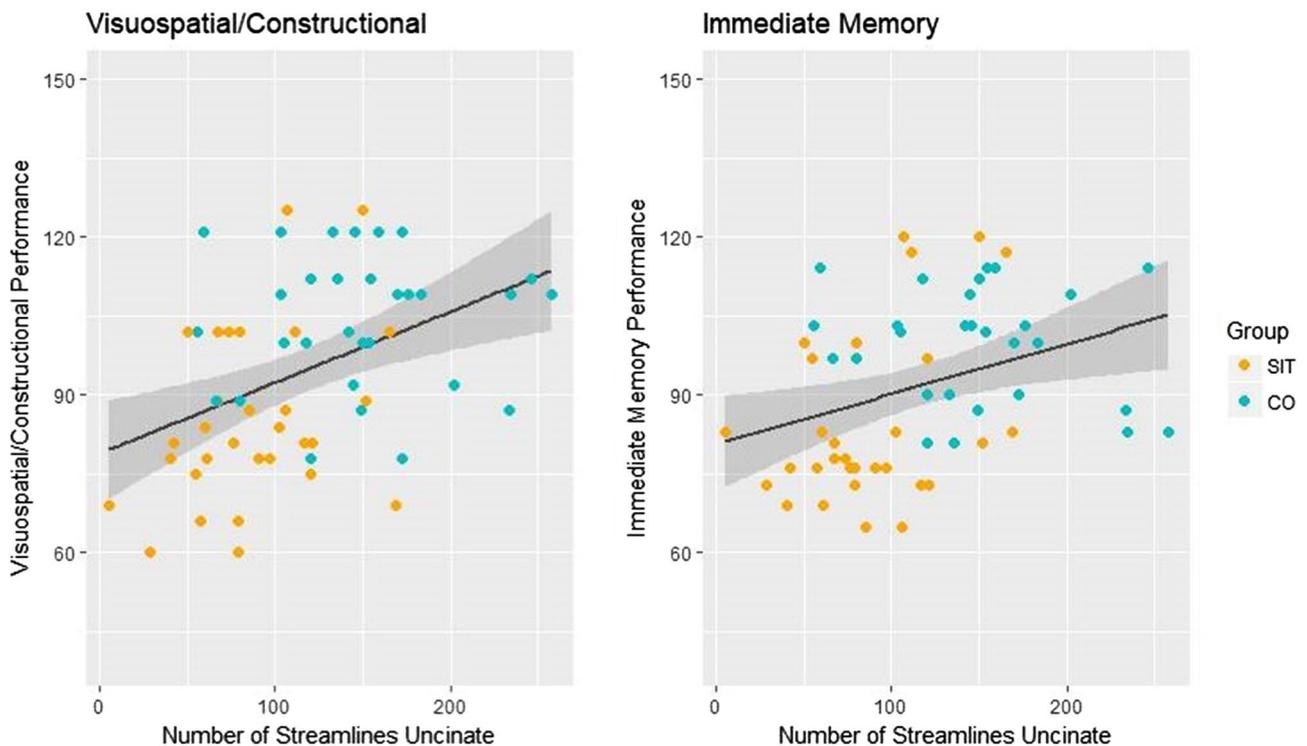


Fig. 2 Visuospatial/Constructional performance (left) and immediate memory (right) in function of NoS in the UNC

left hemisphere, which seems to be in accordance with its putative role in language (Catani and Mesulam 2008; Rilling et al. 2008). Although we did not find any differences between the left and right hemisphere for the ILF or the IFO, we did find significant effects for the ARC with higher levels for both FA and NoS in the left hemisphere compared to the right hemisphere. The present study, therefore, confirms leftward lateralization of the ARC.

Similar to typical left hemispheric dominance for language, spatial attention is known to be functionally lateralized to the right hemisphere. An important white matter tract in spatial attention is the SLF II component of the SLF. For example, Thiebaut de Schotten et al. (Thiebaut de Schotten et al. 2011a) found that lateralization of the SLF II is associated with an asymmetry in behavioral performance on a visuospatial task. He also pointed out that there is a trend towards rightward lateralization of the SLF II. The current study confirms the rightward asymmetry of the SLF II, though only for NoS and not for FA. Again, these results indicate that white matter and functional asymmetry are intertwined.

As for the UNC, there is some ambiguity in the literature about its hemispheric differences. Some researchers report asymmetry to the right hemisphere (e.g. Good et al. 2001; Highley et al. 2002), while others report leftward asymmetry (e.g. Hervé et al. 2006; Rodrigo et al. 2007). In the present study, no evidence for hemispheric asymmetry of the UNC was found. However, SIT participants showed lower NoS in the UNC compared to control participants. Similar alterations in the UNC have been described for various clinical groups in other research, for example in participants with Autism Spectrum Disorder (Ameis 2015; Kumar et al. 2010; Pugliese et al. 2009), participants with a social anxiety disorder (Phan et al. 2009), and participants with Alzheimer's disease (Yasmin et al. 2008). Overall, these pathologies seem to be associated with alterations in the UNC, mostly expressed in lower FA and lower NoS in the UNC. Since several of these pathologies are accompanied by cognitive deficits, the question arises whether there is a link between alterations in the UNC and cognitive performance. Interestingly, the present data seem to confirm this relation, as the fewer NoS in the UNC, the lower the performance on visuospatial/constructional and on immediate memory tasks. Especially the latter behavioral effect is in agreement with the UNC's presumed function. The UNC connects anterior temporal with orbital and polar frontal regions and has strong connections with the limbic system (Thiebaut de Schotten et al. 2012). It has been involved in social and emotional processing, in memory, and in language processing, (Mega et al. 1997; Von Der Heide et al. 2013). Hence, memory is one of the UNC's core functions and it seems that if the UNC's volume is reduced, memory performance is affected as well. The association between lower UNC volume in SIT and reduced

performance on selected cognitive domains is noteworthy but does not explain the global suboptimal cognitive performance reported in this cohort before (Vingerhoets et al. 2018a). Certainly, no causal interpretation is warranted here as reduced UNC volume might be the consequence of suboptimal cognition or related to an intermediate neurodevelopmental variable. This is the largest neuro-imaging study on SIT to date. The still relatively small number of participants precludes more sophisticated analysis of the data and limits interpretation until replication in a larger cohort is provided.

Funding This study was funded by the Fonds Wetenschappelijk Onderzoek-Vlaanderen by FWO-grant n° G.0114.16 N assigned to Guy Vingerhoets.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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

References

- Ameis SH (2015) Altered white matter connectivity as a neural substrate for social impairment in Autism Spectrum Disorder. *Cortex* 62:158–181. <https://doi.org/10.1016/J.CORTEX.2014.10.014>
- Andersson JLR, Sotiropoulos SN (2016) An integrated approach to correction for off-resonance effects and subject movement in diffusion MR imaging. *NeuroImage* 125:1063–1078. <https://doi.org/10.1016/J.NEUROIMAGE.2015.10.019>
- Ashtari M, Cottone J, Ardekani BA, Cervellione K, Szeszko PR, Wu J, Chen S, Kumra S (2007) Disruption of white matter integrity in the inferior longitudinal fasciculus in adolescents with schizophrenia as revealed by fiber tractography. *Arch Gen Psychiatry* 64(11):1270. <https://doi.org/10.1001/archpsyc.64.11.1270>
- Basser PJ, Pajevic S, Pierpaoli C, Duda J, Aldroubi A (2000) In vivo fiber tractography using DT-MRI data. *Magn Reson Med* 44(4):625–632
- Büchel C, Raedler T, Sommer M, Sach M, Weiller C, Koch MA (2004) White matter asymmetry in the human brain: a diffusion tensor MRI study. *Cereb Cortex* 14(9):945–951. <https://doi.org/10.1093/cercor/bhh055>
- Bush A, Cole P, Hariri M, Mackay I, Phillips G, O'Callaghan C, Wilson R, Warner JO (1998) Primary ciliary dyskinesia: diagnosis and standards of care. *Eur Respir J* 12(4):982–988
- Catani M, Mesulam M (2008) The arcuate fasciculus and the disconnection theme in language and aphasia: history and current state. *Cortex J Devoted Study Nerv Syst Behav* 44(8):953–961. <https://doi.org/10.1016/j.cortex.2008.04.002>

- Catani M, Forkel S, Thiebaut de Schotten M (2010) Asymmetry of white matter pathways. The two halves of the brain. The MIT Press, Cambridge, pp 177–210
- Good CD, Johnsrude I, Ashburner J, Henson RNA, Friston KJ, Frackowiak RSJ (2001) Cerebral asymmetry and the effects of sex and handedness on brain structure: a voxel-based morphometric analysis of 465 normal adult human brains. *NeuroImage* 14(3):685–700. <https://doi.org/10.1006/nimg.2001.0857>
- Goto K, Kurashima R, Gokan H, Inoue N, Ito I, Watanabe S (2010) Left–right asymmetry defect in the hippocampal circuitry impairs spatial learning and working memory in iv mice. *PLoS One* 5(11):e15468. <https://doi.org/10.1371/journal.pone.0015468>
- Grimes DT, Burdine RD (2017) Left-right patterning: breaking symmetry to asymmetric morphogenesis. *Trends Genet* 33(9):616–628. <https://doi.org/10.1016/j.tig.2017.06.004>
- Haines DE, Mihailoff GA (2018) The Telencephalon. *Fundam Neurosci Basic Clin Appl* 225–240:e1. <https://doi.org/10.1016/B978-0-323-39632-5.00016-5>
- Hervé P-Y, Crivello F, Percey G, Mazoyer B, Tzourio-Mazoyer N (2006) Handedness and cerebral anatomical asymmetries in young adult males. *NeuroImage* 29(4):1066–1079. <https://doi.org/10.1016/j.neuroimage.2005.08.031>
- Highley JR, Walker MA, Esiri MM, Crow TJ, Harrison PJ (2002) Asymmetry of the uncinate fasciculus: a post-mortem study of normal subjects and patients with schizophrenia. *Cerebral Cortex* (New York, 1991) 12(11):1218–1224
- Hua K, Zhang J, Wakana S, Jiang H, Li X, Reich DS, Calabresi PA, Pekar JJ, van Zijl PCM, Mori S (2008) Tract probability maps in stereotaxic spaces: analyses of white matter anatomy and tract-specific quantification. *NeuroImage* 39(1):336–347. <https://doi.org/10.1016/j.neuroimage.2007.07.053>
- Kamali A, Flanders AE, Brody J, Hunter JV, Hasan KM (2014) Tracing superior longitudinal fasciculus connectivity in the human brain using high resolution diffusion tensor tractography. *Brain Struct Funct* 219(1):269–281. <https://doi.org/10.1007/s00429-012-0498-y>
- Kumar A, Sundaram SK, Sivaswamy L, Behen ME, Makki MI, Ager J, Janisse J, Chugani HT, Chugani DC (2010) Alterations in frontal lobe tracts and corpus callosum in young children with autism spectrum disorder. *Cereb Cortex* 20(9):2103–2113. <https://doi.org/10.1093/cercor/bhp278>
- Leemans A, Jones DK (2009) The *B* -matrix must be rotated when correcting for subject motion in DTI data. *Magn Reson Med* 61(6):1336–1349. <https://doi.org/10.1002/mrm.21890>
- Leigh MW, Pittman JE, Carson JL, Ferkol TW, Dell SD, Davis SD, Knowles MR, Zariwala MA (2009) Clinical and genetic aspects of primary ciliary dyskinesia/Kartagener syndrome. *Genet Med* 11(7):473–487. <https://doi.org/10.1097/GIM.0b013e3181a53562>
- Makris N, Kennedy DN, McInerney S, Sorensen AG, Wang R, Caviness VS, Pandya DN (2005) Segmentation of subcomponents within the superior longitudinal fascicle in humans: a quantitative, in vivo, DT-MRI study. *Cerebral Cortex* 15(6):854–869. <https://doi.org/10.1093/cercor/bhh186>
- Mega MS, Cummings JL, Salloway S, Malloy P (1997) The limbic system: an anatomic, phylogenetic, and clinical perspective. *J Neuropsychiatry Clin Neurosci* 9(3):315–330. <https://doi.org/10.1176/jnp.9.3.315>
- Ocklenburg S, Güntürkün O (2018) Structural hemispheric asymmetries. *Later Brain*. <https://doi.org/10.1016/B978-0-12-803452-1.00009-6>
- Oishi K, Faria AV, van Zijl PCM, Mori S (2011) MRI atlas of human white matter. Academic Press
- Phan KL, Orlichenko A, Boyd E, Angstadt M, Coccaro EF, Liberzon I, Arfanakis K (2009) Preliminary evidence of white matter abnormality in the uncinate fasciculus in generalized social anxiety disorder. *Biol Psychiatr* 66(7):691–694. <https://doi.org/10.1016/j.biopsych.2009.02.028>
- Pugliese L, Catani M, Ameis S, Dell'Acqua F, Thiebaut de Schotten M, Murphy C, Robertson D, Deeley Q, Daly E, Murphy DGM (2009) The anatomy of extended limbic pathways in Asperger syndrome: a preliminary diffusion tensor imaging tractography study. *NeuroImage* 47(2):427–434. <https://doi.org/10.1016/j.neuroimage.2009.05.014>
- Randolph C (2002) Repeatable battery for the assessment of neuropsychological status. Pearson Assessment, London, UK
- Rilling JK, Glasser MF, Preuss TM, Ma X, Zhao T, Hu X, Behrens TEJ (2008) The evolution of the arcuate fasciculus revealed with comparative DTI. *Nat Neurosci* 11(4):426–428. <https://doi.org/10.1038/nn2072>
- Rodrigo S, Oppenheim C, Chassoux F, Golestani N, Cointepas Y, Poupon C, Seamh F, Mangin JF, Le Bihan D, Meder J-F (2007) Uncinate fasciculus fiber tracking in mesial temporal lobe epilepsy. Initial findings. *Eur Radiol* 17(7):1663–1668. <https://doi.org/10.1007/s00330-006-0558-x>
- Slater DA, Melie-Garcia L, Preisig M, Kherif F, Lutti A, Draganski B (2019) Evolution of white matter tract microstructure across the life span. *Hum Brain Mapp*. <https://doi.org/10.1002/hbm.24522>
- Thiebaut de Schotten M, Dell'Acqua F, Forkel SJ, Simmons A, Vergani F, Murphy DGM, Catani M (2011a) A lateralized brain network for visuospatial attention. *Nat Neurosci* 14(10):1245–1246. <https://doi.org/10.1038/nn.2905>
- Thiebaut de Schotten M, Ffytche DH, Bizzi A, Dell'Acqua F, Allin M, Walshe M, Murray R, Williams SC, Murphy DGM, Catani M (2011b) Atlasing location, asymmetry and inter-subject variability of white matter tracts in the human brain with MR diffusion tractography. *NeuroImage* 54(1):49–59. <https://doi.org/10.1016/j.NEUROIMAGE.2010.07.055>
- Thiebaut de Schotten M, Dell'Acqua F, Valabregue R (2012) Monkey to human comparative anatomy of the frontal lobe association tracts. *Cortex* 48(1):82–96. <https://doi.org/10.1016/J.CORTE.2011.10.001>
- Van Hecke W, Emsell L, Sunaert S (2016) Diffusion tensor imaging : a practical handbook
- Vingerhoets G, Gerrits R, Bogaert S (2018a) Atypical brain functional segregation is more frequent in situs inversus totalis. *Cortex* 106:12–25. <https://doi.org/10.1016/j.cortex.2018.04.012>
- Vingerhoets G, Li X, Hou L, Bogaert S, Verhelst H, Gerrits R, Siugzdaite R, Roberts N (2018b) Brain structural and functional asymmetry in human situs inversus totalis. *Brain Struct Funct* 223(4):1937–1952. <https://doi.org/10.1007/s00429-017-1598-5>
- Von Der Heide RJ, Skipper LM, Klobusicky E, Olson IR (2013) Dissecting the uncinate fasciculus: disorders, controversies and a hypothesis. *Brain* 136(6):1692–1707. <https://doi.org/10.1093/brain/awt094>
- Wakana S, Caprihan A, Panzenboeck MM, Fallon JH, Perry M, Gollub RL, Hua K, Zhang J, Jiang H, Dubey P, Bliz A, van Zijl P, Mori S (2007) Reproducibility of quantitative tractography methods

- applied to cerebral white matter. *NeuroImage* 36(3):630–644. <https://doi.org/10.1016/j.neuroimage.2007.02.049>
- Wang R, Benner T, Sorensen AG, Wedeen VJ (2007) Diffusion toolkit: a software package for diffusion imaging data processing and tractography. *Proc Intl Soc Mag Reson Med* 15:3720
- Webb WG (2017) Organization of the nervous system I. *Neurol the Speech Lang Pathol* 10:13–43. <https://doi.org/10.1016/B978-0-323-10027-4.00002-6>
- Yasmin H, Nakata Y, Aoki S, Abe O, Sato N, Nemoto K, Arima K, Furuta N, Uno M, Hirai S, Masutani Y, Ohtomo K (2008) Diffusion abnormalities of the uncinate fasciculus in Alzheimer's disease: diffusion tensor tract-specific analysis using a new method to measure the core of the tract. *Neuroradiology* 50(4):293–299. <https://doi.org/10.1007/s00234-007-0353-7>

Publisher's Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.