Loss of White Matter Integrity in Major Tracts Can Lead to Severe Impairments in Varying Cognitive Functions.

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Tractography in a healthy young adult

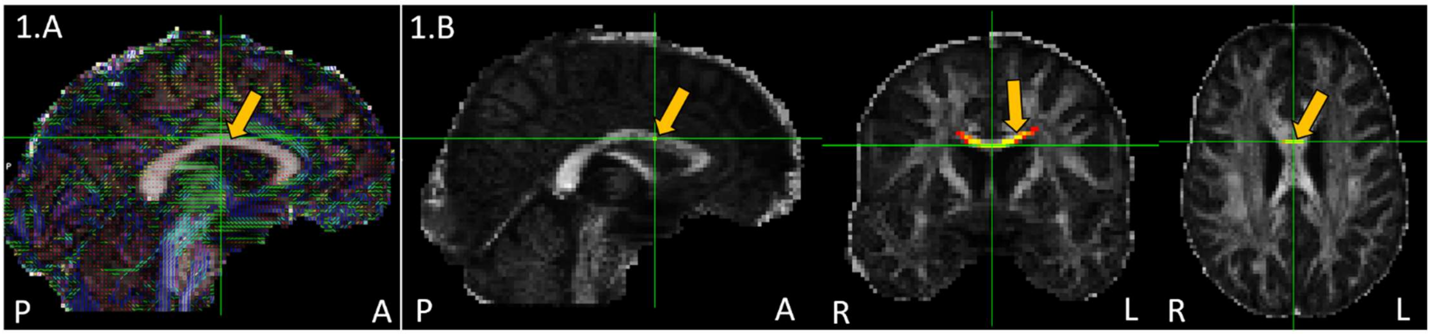

Figure 1 – Corpus callosum DTI and probabilistic tractography in a young healthy adult with a Siemens 3.0T magnet MRI scan. *1.A: Diffusion tensor imaging (DTI) in sagittal view with a FA value of 0.79 at [59 61 44]. P indicates posterior and A indicates anterior side of the brain. Yellow arrow points to the corpus collosum (CC) in red, indicating medial-lateral direction of diffusivity. 1.B: Probabilistic tractography of the CC in all three planes. Seed location at voxel [57 67 43]. L and R indicate radiological orientation. Yellow arrows point to the probabilistic tractography of the CC white matter tract made with FSLeyes.*

CC damage can be very detrimental to cognitive function and sensory-motor information transfer between hemispheres as seen in agenesis of the CC (ACC). Brown and Paul's 2019 study states that the malformation of the CC occurs within the 7^{th} and 20^{th} embryonic weeks due to disrupted neural development. This congenital disorder is characterized by the absence of parts or all of the CC, leading to decreased inter-hemispherical communication. This reduced communication is also the likely cause of the observed decrease of unfamiliar task and complex information processing, as well as the increased cognitive processing time. These core symptoms lead to deficits in recognizing facial emotions, spontaneous memory retrieval, learning visual and verbal information, as well as inferring others' emotional or mental states. This makes the social context challenging, and impairs the adaptive skills needed for daily life. However, most patients with ACC can still have interhemispheric transfer of uncomplex information such as visual and tactile information that are easily encoded, or familiar. The effects vary with the age of ACC patients as children are still going through significant myelination, meaning adults tend to show more of the mentioned symptoms, especially social deficits, though children may struggle in learning complex tasks. ACC is not defined by behavioral symptoms as they are usually mild, but by anatomy[1].

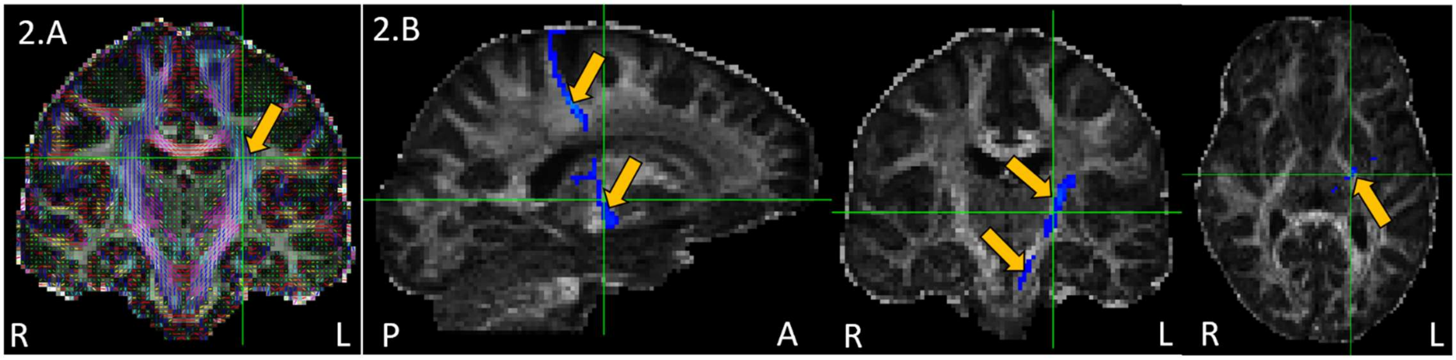

Figure 2 – Corticospinal tract DTI and probabilistic tractography in a young healthy adult with a Siemens 3.0T magnet MRI scan. *2.A: DTI in coronal view with a FA value of 0.44 at [70 55 41]. Yellow arrow points to the corticospinal tract (CST) in blue, indicating superior-inferior direction of diffusivity. 2.B: Probabilistic tractography of the CST in all three planes. Seed location at voxel [67 57 30]. Yellow arrows point to the probabilistic tractography of the CST white matter made with FSLeyes.*

CST damage can lead to heavy motor control impairments as seen in stroke patients, especially for limb motor function. Many individuals who have suffered from a stroke also get damage to the CST. These motor impairments arise from CST damage as it connects to the spinal cord, hence deteriorating the information transfer from the cortex to the spinal cord. This explains why stroke patients may suffer from motor impairments. Measuring CST integrity through FA distal to where the stroke happened with DTI can be very useful to quantify the amount of damage done by the stroke, hence ensuring a more appropriate treatment. FA tells us how intact white matter is, which we can use to determine how much white matter loss has occurred, therefore how much the CST (in this case) has been damaged by the stroke. Puig et al.'s 2017 study states that the extent of motor damage is highly dependent on the motor fibers and CST integrity. Recovery of lost motor functions from CST damage may consist of remodeling the CST to make it rely more on other motor tracts. This could work thanks to brain plasticity[2].

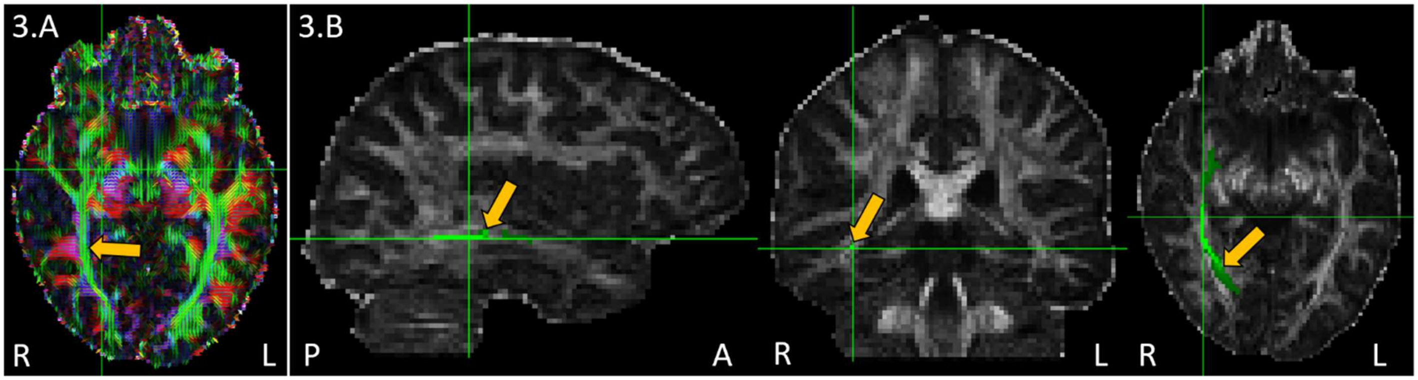

Figure 3 – Inferior frontal-occipital fasciculus DTI and probabilistic tractography in a young healthy adult with a Siemens 3.0T magnet MRI scan. *3.A: DTI in axial view with a FA value of 0.32 at [45 60 26]. Yellow arrow points to the inferior frontal-occipital fasciculus (IFOF) in green, indicating rostral-caudal direction of diffusivity. 3.B: Probabilistic tractography of the IFOF in all three planes. Seed location at voxel [38 46 24]. Yellow arrows point to the probabilistic tractography of the IFOF white matter made with FSLeyes.*

IFOF damage has been correlated with impairments in overall facial emotion recognition, hence disturbing social cognition. Philippi et al.'s 2009 study stated long association fiber tracts connecting emotion-related and visual structures (such as the IFOF) are likely involved in visual emotional processing. Patients suffering from right IFOF lesions demonstrated clear and specific impairments in emotional recognition from facial expressions; for example happiness, anger, disgust, surprise. Despite these patients' emotional recognition deficits, their memory, attention, perception and intelligence were intact, further pushing the idea that the IFOF plays a specific role for visual emotion recognition (by facial expression at least). The IFOF is part of a larger network for recognition of facial emotion and plays a critical role in it. However, the study mentions that it is possible that, instead of playing this specific role, it may only play a general role in either visual emotional stimuli, or retrieval of emotional information[3].

Tract-based spatial statistics (TBSS) in younger vs older adults

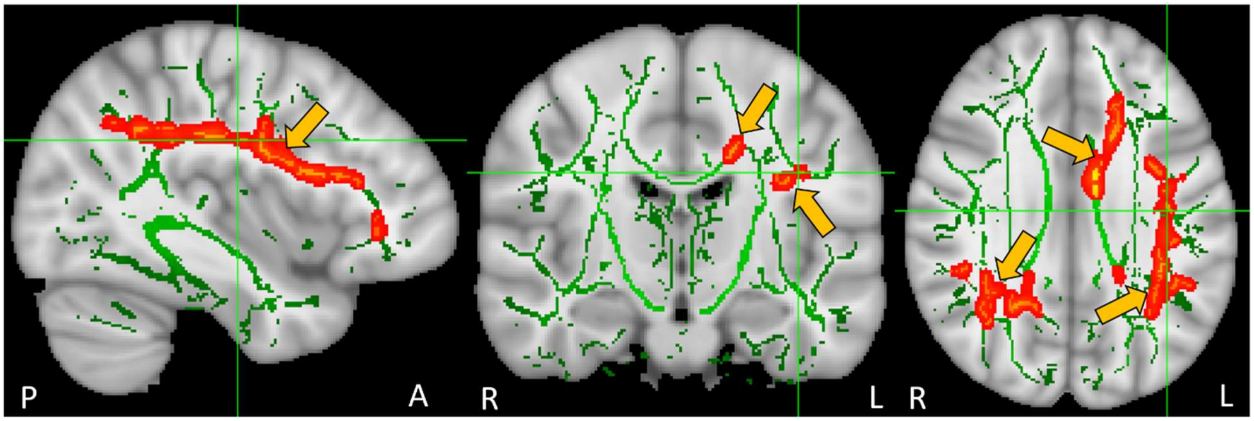

Figure 4 – Superior longitudinal fasciculus (SLF) TBSS differences between normal young adults (3 subjects around 25 years-old) and normal older adults (3 subjects around 65 years-old) with a Siemens 3.0T magnet MRI scan. *MNI coordinates of voxel location are [129 111 101]. Green areas represent the white matter skeleton. Yellow arrows indicate regions where the SLF has more fractional anisotropy (FA) in young adults than in older adults. Images made with FSLeyes.*

Amongst many other WM tracts, the SLF is also subject to age-related FA decrease. As the SLF has previously been studied to be associated with language due to its connections between ipsilateral frontal and opercular areas, and temporo-parietal language regions, Madhavan et al.'s 2014 study wanted to focus on a specific part of the SLF that connects to Wernicke's area which is involved in language comprehension. Many past studies have shown that FA decrease in language-related regions correlated with impairments in verbal fluency, learning grammar, and reading ability, as well as impaired word retrieval in normal ageing. However, in Madhavan et al.'s study, they found that there was no significant relationship between age and SLF FA, though this was likely due to sample size. They also found that SLF FA decreased in adults starting 30 years old and that males and females exhibited different patterns of FA decline. Males showed an earlier decline of FA than females, however their loss of WM integrity was not worse than females[4].

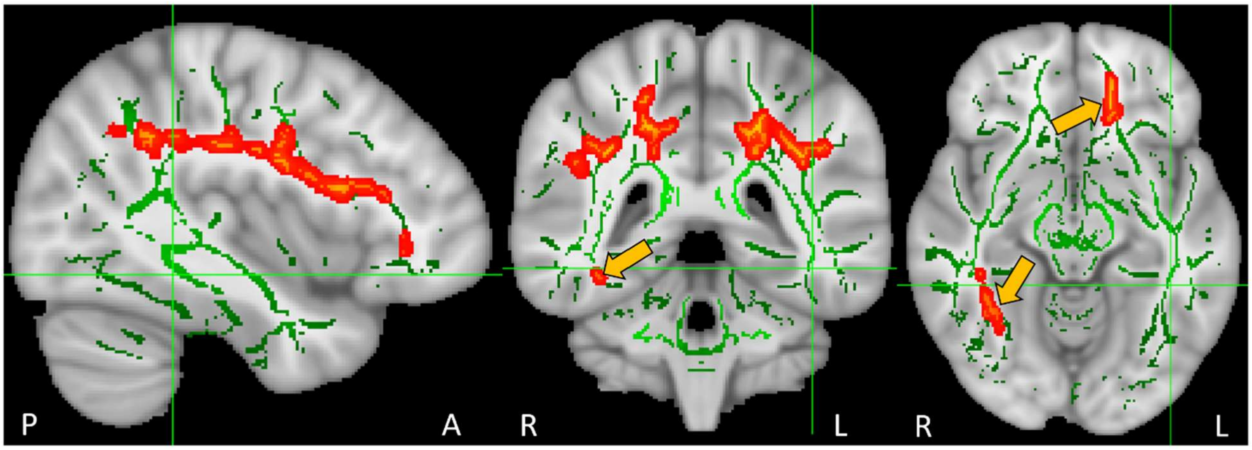

Figure 5 – Inferior longitudinal fasciculus (ILF) TBSS differences between normal young adults (3 subjects around 25 years-old) and normal older adults (3 subjects around 65 years-old) with a Siemens 3.0T magnet MRI scan. *MNI coordinates of voxel location are [130 85 61]. Green areas represent the white matter skeleton. Yellow arrows indicate regions where the ILF has more fractional anisotropy (FA) in young adults than in older adults. Images made with FSLeyes.*

In Perry et al.'s 2009 study on age related FA decrease in different WM tracts, they found that the ILF did not exhibit a significant correlation in FA decrease with age. However, they found that the ILF was an important part in psychomotor speed, attention and visual search (set shifting tasks) as it connects functional regions for visual memory. Age-related FA decrease in ILF significantly hindered performance in set-shifting tasks, but only in the right ILF. The importance of the right ILF in this study seems to relate to figure 5 as most differences seen between young and older adults in the ILF (at this voxel location) are seen on the right side of the brain. Overall, the age-related decrease in FA of the right ILF, though not very significant in this study, played a big role in the impaired performance in set-shifting tasks, still indicating its importance in WM integrity loss with age[5].

References

1. Brown WS, Paul LK. 2019. The Neuropsychological Syndrome of Agenesis of the Corpus Callosum. Journal of the International Neuropsychological Society. 25(3):324–330. doi: https://doi.org/10.1017/s135561771800111x.

2. Puig J, Blasco G, Schlaug G, Stinear CM, Daunis-i-Estadella P, Biarnes C, Figueras J, Serena J, Hernández-Pérez M, Alberich-Bayarri A, et al. 2017. Diffusion tensor imaging as a prognostic biomarker for motor recovery and rehabilitation after stroke. Neuroradiology. 59(4):343–351. doi: https://doi.org/10.1007/s00234-017-1816-0.

3. Philippi CL, Mehta S, Grabowski T, Adolphs R, Rudrauf D. 2009. Damage to Association Fiber Tracts Impairs Recognition of the Facial Expression of Emotion. Journal of Neuroscience. 29(48):15089–15099. doi: https://doi.org/10.1523/jneurosci.0796-09.2009.

4. Madhavan KM, McQueeny T, Howe SR, Shear P, Szaflarski J. 2014. Superior longitudinal fasciculus and language functioning in healthy aging. Brain Research. 1562:11–22. doi: https://doi.org/10.1016/j.brainres.2014.03.012.

5. Perry ME, McDonald CR, Hagler DJ, Gharapetian L, Kuperman JM, Koyama AK, Dale AM, McEvoy LK. 2009. White matter tracts associated with set-shifting in healthy aging. Neuropsychologia. 47(13):2835–2842. doi: https://doi.org/10.1016/j.neuropsychologia.2009.06.008.

6. FSL Course. 2018. Analysis Group, FMRIB. Oxford, United Kingdom. Available from: https://fsl.fmrib.ox.ac.uk/fslcourse/

7. Jenkinson M, Beckmann CF, Behrens TE, Woolrich ME, Smith SM. 2012. FSL. NeuroImage, 62:782-90.