A selective ageing effect on the frontal lobe connections

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Purpose. With aging the neuronal loss and small vessel alteration lead to progressive white matter damage associated with cognitive decline in the elderly (1). Cognitive decline affects predominantly executive functions, and brain changes seem to distribute unevenly, concerning predominantly the frontal region (2). The study of the frontal connections is of particular interest for the neurosciences of aging. Previous studies using tract specific measurements revealed a slow decrease with aging in FA for frontal callosal tracts (3) and for the average value of long tracts connecting the frontal lobe (4) affecting more prominently the frontal portion of these tracts (5). Using voxel-based statistics, FA has been found to correlate negatively with aging, especially within the frontal lobes (6). Here we explored whether this progressive decline affects the whole frontal white matter or specific tracts in the frontal lobe.

Material and methods. Diffusion weighted datasets from 47 healthy volunteers aged 22-70 (M:F 24:23) were acquired on a 3T Siemens Verio TIM system equipped with a 32-channel head coil with the following parameters: voxel size 2x2x2 mm, matrix 128x128, slices 60, NEX 1, TE 90 ms, b-value 1500 s/mm2, 60 diffusion-weighted directions and 6 non-diffusion-weighted volumes, using a spin-echo EPI sequence. Cardiac Gating was applied with effective TR of 24 R-R intervals. Diffusion datasets were corrected for motion and eddy current distortions (7) and then process with a Spherical Deconvolution algorithm based on the damped Richardson-Lucy algorithm (8, 9). Tractography was performed following the method described in (10). We dissected fifty-five frontal tracts including U-shaped fibers. For each dissection fractional anisotropy (FA, 11) and hindrance modulated orientational anisotropy (HMOA, 9) was extracted as an indirect measure of the tract integrity and correlated with the age of the participants regressing out the level of education.

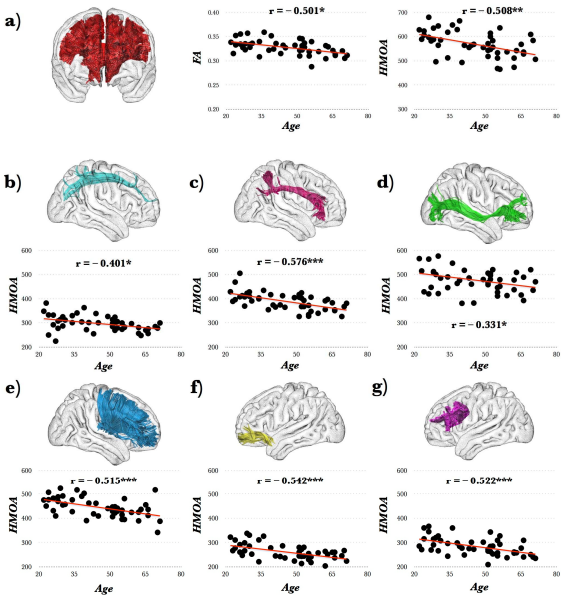

Figure 1. Correlation between age of the participants and tract specific measurements. a) frontal corpus callosum b) first branch of the right superior longitudinal fasciculus; c) third branch of the right superior longitudinal fasciculus; d) right inferior fronto-occipital fasciculus; e) right fronto-thalamic projections; f) left frontal orbito-polar tract; g) left frontal inferior longitudinal fasciculus. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$ false discovery rate corrected for multiple comparison.

Results. Aging was significantly associated with a decrease of FA ($r = -0.501$*) and HMOA ($r = -0.508$**) in the frontal projections of the corpus callosum. Aging was also associated with a decrease of HMOA in the right frontal lobe including the SLF I ($r = -0.401$**) and SLF III ($r = -0.576$***) branches of the superior longitudinal fasciculus, inferior fronto-occipital fasciculus ($r = -0.331$*), fronto-thalamic projections ($r = -0.515$***). HMOA measure also decreased with aging in the left hemisphere for the frontal inferior longitudinal fasciculus ($r = -0.542$***) and the frontal orbito-polar tract ($r = -0.542$***).

Discussion and Conclusion. We confirmed preliminary evidences reporting reduced integrity in the frontal portion of the corpus callosum associated with aging (3). This commissural decline may explain the increased reaction time associated with aging reported in tasks requiring interhemispheric transfer (12).
Our results also suggest for the first time that aging alters significantly specific long and short tracts in the frontal lobes which brings up interesting hypotheses on a pathophysiological explanation for aging decline in visuospatial and verbal working memory, memory encoding and retrieval, reward-based associative learning that can be tested in the elderly (6).

Reference. (1) Pantoni, Lancet Neurol (2010). (2) Bishop et al. Nature (2010). (3) Lebel, S et al. Neuroimage (2010). (4) Jones et al. Hum Brain Mapp (2006). (5) Davis et al. NeuroImage (2009). (6) Cabeza and Dennis, Principles of Frontal Lobe Function, 2nd Edition (2012) (7) Smith et al., Neuroimage (2004). (8) Dell'acqua et al., Neuroimage (2010). (9) Dell'Acqua et al. Hum Brain Mapp (2013). (10) Catani et al. Cortex (2012). (11) Basser and Pierpaoli J Magn Reson B (1996). (12). Reuter-Lorenz and Stanczak Developmental neuropsychology (2000).