Relationship between cerebral amyloid burden and cerebral microstructure measured by quantitative MRI in healthy aging

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The presence of Alzheimer's disease (AD) biomarkers in the brain of healthy older individuals has been associated with decreased myelin and increased iron deposits in the brain (Bartzokis, 2011). Novel Magnetic Resonance Imaging (MRI) techniques, like quantitative multiparameter mapping (MPM), allow to gain insight in the microstructure of the brain and could help to address the link between myelin and iron in the brain (Callaghan et al., 2014) and AD biomarkers. Our aim was, therefore, to relate the amount of myelin and iron content to the cortical amyloid burden. We acquired MPM sequences in a 3T scanner and [18F]flutemetamol positron-emission tomography (PET) images in 55 cognitively healthy adults (35 women), aged 50-70 (mean: 59.5 ± 5.5). We used MPM to infer myelin content, based on magnetization transfer saturation (MT) and longitudinal relaxation rate (R1), and iron content, based on effective transverse relaxation rate (R2*). Cortical beta-amyloid burden was measured with [18F]flutemetamol PET. Multiparameter maps were created and normalised with the hMRI

(Balteau et al., 2018) toolbox for MATLAB (The Mathworks Inc, Natick, MA, USA). Correlations between MPM maps and amyloid burden were conducted with SPM12 framework (Wellcome Trust Centre for Neuroimaging, London) $p<.05$ FWE corrected.

As expected (Dean et al., 2017), we observed a link between increased amyloid burden and increased iron content in frontal areas mainly but also in parietal and occipital areas. However, there was an unexpected negative correlation between amyloid burden and white matter iron content in the left superior temporal area. Moreover, a positive association between amyloid burden and myelin content was found in the frontal and temporal lobes in both grey and white matter. Furthermore, R1 values, which depend on both iron and myelin storage, present positive correlations with amyloid burden in both grey and white matter of frontal, temporal and occipital areas.

The finding that increased iron in frontoparietal and occipital areas are associated with increased amyloid burden fits with previous studies. However, current results also indicate that individuals with higher cortical amyloid burden have higher myelin water fraction in frontotemporal areas. This would suggest that, in cognitively healthy middle-aged individuals, the presence of amyloid in the brain, which represents a risk factor for AD, is accompanied by both cerebral microstructural decline in some areas and enhanced –possibly compensatory- microstructure properties in other areas.

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Bibliography

1. Balteau, E., Tabelow, K., Ashburner, J., Callaghan, M.F., Draganski, B., Helms, G., Kherif, F., Leutritz, T., Lutti, A., Phillips, C., Reimer, E., Ruthotto, L., Seif, M., Weiskopf, N., Ziegler, G., and Mohammadi, S. (2018). hMRI -- A toolbox for using quantitative MRI in neuroscience and clinical research. Weierstraß-Institut für Angewandte Analysis und Stochastik Leibniz-Institut im Forschungsverbund Berlin e. V. Berlin. 10.20347/WIAS.PREPRINT.2527

2. Bartzokis, G (2004). Age-related myelin breakdown: a developmental model of cognitive decline and Alzheimer's disease. *Neurobiol. Aging*, 25 (2004), pp. 5-18
3. Callaghan, M. F., P. Freund, B. Draganski, E. Anderson, M. Cappelletti, R. Chowdhury, J. Diedrichsen, T. H. B. Fitzgerald, P. Smittenaar, G. Helms, A. Lutti, and N. Weiskopf (2014). "Widespread age related differences in the human brain microstructure revealed by quantitative magnetic resonance imaging." *Neurobiol. Aging* 35.8, pp. 1862–1872.
4. Dean, D. C. III, Hurley, S.A., Kecskemeti, S.R., O'Grady, J.P., Canda, C., Davenport-Sis, N.J., Zetterberg, H., Blennow, K., Asthana, S., Sager, M.A., Johnson, S.C., Alexander, A.L. and Bendelin, B.B (2017). Association of amyloid pathology with myelin alteration in preclinical Alzheimer disease. *JAMA Neurol*; 74:41–9.