An Investigation into the Formation and Histology of Focal Basal Ganglia Mineralization with quantitative MRI

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Target Audience: This study characterizes a potential imaging biomarker for cerebral microvascular disease using quantitative MRI, which could have further applications in ageing research.

Purpose: Multifocal T2*-weighted (T2*w) hypointensities in the basal ganglia (Fig. 1) are linked to focal mineralization[1] and are commonly found in the vascular territories of the lenticulostriate arteries.[2] Recently, they have been proposed as a novel imaging biomarker for microvascular disease and ageing.[3] Little is known about their formation and histology. Therefore we quantified their progression with age, as well as their appearances on R2*, R2' and frequency shift maps (high-pass filtered B_0 maps).

Methods: Three hundred subjects (183 females; 64 ± 11 years) without history or signs of neuropsychiatric disorders were scanned on a Siemens Tim Trio 3T MRI scanner with a six- or twelve-echo spoiled gradient echo sequence (TE = 4.9 ms, ΔTE = 4.9 ms, 0.9 × 0.9 × {2 or 4} mm, 208 × 256 × {64 or 32}, FA = 15°), a dual-echo spin echo sequence (TE1 = 10 ms, TE2 = 73 ms, TR = 5.3s, 0.9 × 0.9 × 3 mm, 192 × 256 × 40) and a T1-weighted MPRAGE sequence (TI = 900 ms, TE = 2.19 ms, TR = 1.9 s, 1 × 1 × 1 mm, 224 × 256 × 176). R2* and R2 maps[4] were obtained by fitting monoexponential or linear functions voxelwise to the gradient-echo or logarithmized spin-echo magnitude data and R2' maps[5] by subtracting R2* from R2 maps. Frequency shift maps[6] were created by homodyne filtering (Gaussian filter with 3 mm full width at half maximum) of the gradient-echo phase data and estimating the linear phase change per voxel over time. Basal ganglia T2*w hypointensities were automatically segmented with a novel, unsupervised version of a supervised thresholding method.[7] The atlas based method first created masks for the putamen, globus pallidus and internal capsule, and then masks for all basal ganglia T2*w hypointensities in these regions. Two spatial probability maps[2] of basal ganglia T2*w hypointensities were generated for subjects with age < 65 years and ≥ 65 years. Individual basal ganglia T2*w hypointensities were identified using connected component analysis.[2] Their locations, volumes normalized by the intracranial volume (ICV), and median R2* and R2' relaxivity rates and frequency shifts relative to the surrounding, normal-appearing tissue were then calculated.

Results: Spatial probability maps (Fig. 2) showed that basal ganglia T2*w hypointensities mostly occurred within the globus pallidus of subjects < 65 years but also frequently in the inferior genu of the internal capsule and posterior putamen of subjects ≥ 65 years. These features were on average larger in the globus pallidus than in other structures with a volume of 10.9 (5.1…25.7) ppm ICV compared to 7.3 (4.2…17.4) ppm ICV. Skipped Spearman's correlation[8] revealed that the total volume of basal ganglia T2*w hypointensities significantly increased with age (ρ = 0.31; total volume [ppm ICV] = 1.7 × age - 49.5). Median R2* and R2' relaxivity rates, and frequency shifts of T2*w hypointensities in the globus pallidus and other structures relative to the surrounding, normal-appearing tissue were 28.4 ± 12.8 s^{-1}, 27.5 ± 12.4 s^{-1}, 0.9 ± 1.5 Hz, and 36.8 ± 15.4 s^{-1}, 32.4 ± 13.8 s^{-1}, 0.9 ± 1.6 Hz, respectively.

Discussion: Spatial probability maps indicated that basal ganglia T2*w hypointensities appear earlier and are bigger in the globus pallidus than in other structures, which might be related to the iron content of normal-appearing tissue[4] or different mechanisms behind their formation. Their size increase with age could be a related to progressive mineralization in and around the deep penetrating arteries.[9] R2*, R2' and frequency shift maps confirm that the underlying tissue predominantly contains aggregated and mostly paramagnetic trace metals, which is consistent with previous histochemical studies.[9]

Conclusion: In a cohort of 300 community-dwelling subjects, basal ganglia T2*w hypointensities are paralleling the process of ageing. Basal ganglia T2*w hypointensities are likely caused by focal mineralization, which is possibly of vascular origin. More work is required to show relationships of these features to cognitive function and small vessel disease.

References: 1. Harder SL. *et al.* AJNR 2008 29(1):176-83; 2. Glatz A. *et al.* NeuroImage 2013 82(100):470-80; 3. Penke L. *et al.* Neurobiol Aging 2012 33(3):510-17; 4. Langkammer C. *et al.* Radiology 2010 257(2):455-62; 5. Sedlacik J. *et al.* NeuroImage doi:10.1016/j.neuroimage.2013.08.051; 6. He X. *et al.* PNAS 2009 106(32):13558-63; 7. Glatz A. *et al.* ECR2013 Poster doi:10.1594/ecr2013/C-2293; 8. Cyril PR. *et al.* Front Psychol 2013 3:606; 9. Casanova MF. *et al.* Psychiatry Res 2003 121(1):59-87

Fig. 1: An example of T2*-weighted hypointensities in the globus pallidus.

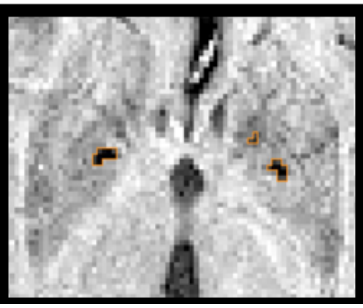

Fig. 2: Spatial probability maps of basal ganglia T2*w hypointensities for age < 65 years (A) and age ≥ 65 years (B) overlaid onto T1-weighted volumes of representative subjects.