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In-vivo imaging of locus coeruleus integrity at ultra-high field: A feasibility study

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Abstract

Background: Increasing evidence suggests that neurodegeneration of the locus coeruleus (LC) is an early pathological feature of Alzheimer's Disease (AD). However, assessment of the LC *in-vivo* is hampered by its small size. Here we test the feasibility of characterizing LC's integrity *in-vivo* using ultra-high field MRI.

Method: Eight young controls (age: 23±3y, education: 17±2y) and 9 elderly subjects from the Geneva memory clinic cohort (age: 74±7y, education: 16±3y; MMSE: 26±2; diagnosis: 1 cognitively normal, 7 cognitively impaired; biomarker profile: 63% A+, 14% T+) underwent MRI on a 7T Siemens Magnetom scanner, including magnetization transfer (MT; voxel: 0.43x0.43x0.5mm) and diffusion tensor imaging (DTI; voxel: 1.3x1.3x1.4mm). A MT template was generated from all the MT images with the Advanced Normalization Tools software. A LC map was extracted from the template with semi-automated intensity thresholding. Individual MT and DTI images were warped to the MT template of the LC to measure: LC contrast ratio (CR) on MT; fractional anisotropy (FA) and mean diffusivity (MD) on DTI. These metrics were compared between groups and hemispheres using non-parametric tests.

Result: The LC volume (MT template) was 62mm^3, spanning 15mm rostro-caudally. Elderly showed higher CR than younger subjects (median [IQR]: 23 [21-28] vs 15 [12-19], p=0.008 on Mann Whitney U test). This difference was detected along most of the rostro-caudal LC axis (significance differences over 77% of the LC axis). In both younger and older subjects, the CR was greater in the left vs. right hemisphere (p=0.018 and p=0.015 respectively, Wilcoxon signed-rank test). MD was more heterogeneous and overall higher in the LC of elderly compared to younger subjects (median [IQR]: 1.7 [0.7-2.4] vs 0.94 [0.86-1.02], p=0.023 on Mann Whitney U test). FA showed neither group nor hemisphere differences.

Conclusion: These findings are consistent with previous LC literature at 3T. We confirmed that LC signal increases with age and reported a hemisphere asymmetry in LC signal. Microstructure atrophy with age is suggested by increased diffusivity. Data acquisition is ongoing with the aim to evaluate MT, DTI and fMRI differences across cognitively normal, AD and non-AD impaired groups. Funding: H2020-EU.3.1.1 (grant ID:667375), Swiss National Science Foundation (SNF-320030_169876).