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NEUROIMAGING

Microstructural assessment of the locus coeruleus-entorhinal cortex pathway and association with ATN markers in patients with cognitive impairment

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Abstract

Background: This study investigated microstructural features of the locus coeruleus to entorhinal cortex pathway (LC-EC) in relation to amyloid (A), tau (T), neurodegeneration (N) markers and cognitive impairment in memory clinic patients.

Method: 124 participants were recruited from the Geneva Memory Clinic (n=30 cognitively unimpaired – CU; n=80 MCI and n=14 dementia - CI) and underwent clinical assessment, 3T MRI scan including diffusion weighted imaging, amyloid PET, and tau PET. Diffusivity indices (fractional anisotropy - FA, mean, axial and radial diffusivities - MD, AxD, RD) were assessed in the LC-EC pathway using a probabilistic atlas. A, T, N markers were assessed both as continuous and dichotomous measures. Differences in LC-EC microstructure according to ATN markers and diagnosis were assessed with ANOVA models (FDR correction). Linear regression models were used to test whether LC-EC pathway microstructure predicted cognitive impairment independently of ATN markers.

Result: Lower FA ($p=0.020$) and higher MD, RD and AxD ($p<0.005$) was observed in participants with tau positivity in the EC (T_{EC}+, Braak stage ≥1) compared to tau negative subjects (T_{EC}-). Higher MD, RD and AxD was observed in neurodegeneration positive (N+, medial temporal atrophy) versus negative (N-) participants ($p<0.001$), and CI versus CU ($p<0.016$). There was no difference in LC-TE microstructure between amyloid positive (A+) and negative (A-) subjects ($p>0.05$) nor between tau positive (T+; Braak stage ≥4) and negative (T-) subjects ($p>0.05$). The regression model showed that RD of the LC-EC tract was associated with clinical diagnosis and mini mental state examination score independently of ATN markers ($p<0.05$).

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Conclusion: Our results indicate that LC-EC microstructural measures, specifically RD, are sensitive in detecting CI and provide complementary information over ATN biomarkers. Associations with T suggest that LC-TE microstructural alterations show regional specificity in the EC.