

In vivo brainstem tau pathology is related to entorhinal amyloid pathology in middle-aged healthy participants

François Meyer^{1,2} | Narbutas Justinas¹ | Maxime Van Egroo^{1,3} | Chylinski Dapnée¹ | Mohamed Ali Bahri¹ | Koshmanova Ekaterina⁴ | Gabriel Besson¹ | Muto Vincenzo¹ | Schmidt Christina¹ | André Luxen¹ | Christophe Phillips¹ | Maquet Pierre^{1,2} | Vandewalle Gilles⁴ | Fabienne Collette¹ | Christine Bastin¹ | Eric Salmon^{1,2}

¹GIGA-CRC, University of Liège, Liège, Belgium

²Neurology Department, CHU of Liège, Liège, Belgium

³Maastricht University, Maastricht, Netherlands

⁴GIGA-Cyclotron Research Center-In Vivo Imaging, University of Liège, Liège, Belgium

Correspondence

François Meyer, GIGA-CRC, University of Liège, Liège, Belgium.

Email: francois.meyer@chu.ulg.ac.be

Abstract

Background: Braak's model of Alzheimer's disease (AD) progression suggests that the initial accumulation of hyperphosphorylated tau protein is seen in the locus coeruleus (LC). Tau pathology might be a good marker of subsequent cognitive decline in initially unimpaired participants. We capitalized on Braak's model to assess in a sample of cognitively unimpaired late-middle-aged individuals, the relationship between tau and A β accumulation in the locus coeruleus, basal forebrain (BF) and entorhinal cortex (ERC).

Method: 65 participants aged 50-70 years were enrolled in a multimodal cross-sectional study investigating the relationship between AD neuropathology, cognitive aging and cognitive complaints, and life style.

MRI acquisitions were performed on a 3-T scanner (MAGNETOM Prisma, Siemens). Tau and A β -PET were performed on an ECAT EXACT+ HR scanner (Siemens). [18F]THK5351-PET was used as a proxy of tau accumulation and A β -PET radiotracer was [18F]Flutemetamol.

Masks were used for entorhinal cortex (ERC), basal forebrain (BF) and locus coeruleus (LC). We extracted Tau and A β burden in each region of interest, for a total of ten neuroimaging AD biomarkers (LC-Tau, LC-A β , BF123-Tau, BF123-A β , BF4-Tau, BF4-A β , right and left ERC-Tau, right and left ERC-A β).

Statistical analyses. All statistical analyses were performed with SAS 9.4 for Windows (SAS Institute, Cary, NC, USA) using the GLIMIX model.

Result: We found direct correlations between LC-tau and left ERC-A β ($F = 6.86$, $p = .0112$) or LC-tau and right ERC-A β ($F = 14.12$, $p = .0004$), and also between LC-Tau and BF4-A β . However, a model including the interactions between LC-Tau, BF4-A β and ERC-A β , was not significant. Stepwise analysis confirmed a significant liability of the model to explain ERC-A β ($F = 5.86$, $p = .0048$ for left and $F = 6.83$, $p = .0005$ for right ERC, for which LC-tau had the main contribution ($F = 14.12$, $p = .0004$).

Conclusion: Our results showed a positive and significant correlation between Tau burden in the LC and amyloid burden in the ERC. The relationship between these two AD biomarkers was observed in healthy individuals without any cognitive impairment.