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NEUROIMAGING

The volume of the accessory-basal nucleus of the amygdala reduces with tau pathology in AD, but remains normal in non-AD conditions

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Abstract

Background: In AD, tau pathology starts in the medial temporal lobe, including the amygdala-hippocampal complex. The amygdala is composed of subnuclei that until recently could not be distinguished in-vivo. This has recently been achieved and implemented in FreeSurfer 7. We aimed to investigate the relative atrophy of the amygdala subnuclei in AD and non-AD disorders, and to evaluate the association with tauopathy.

Methods: We recruited 131 participants who underwent 3D-T1 brain MRI and ^{18}F-MK6240 tau-PET. Amyloid status (A-/A+) was determined using plasmatic SiMOA assays or cerebrospinal fluid analyses. The participants were classified after neuropsychological evaluation as cognitively normal (CN) individuals (n = 23 A-CN, n = 23 A+CN), prodromal AD (n = 48 A+MCI), AD dementia (n = 24 A+dementia), or non-AD disorders (n = 13, A-MCI/dementia). We tested differences in the global amygdala volume, and amygdala subnuclei volumes according to clinical diagnoses and visual tau-PET Braak-stages. We also assessed the relationship between subnuclei volumes, cognition, and tauopathy in the temporal lobe, covarying age, sex, and global amygdala volume.

Results: We observed that the global amygdala volume was reduced in the A+MCI group compared to CN (A+/A), and further reduced in AD dementia. In contrast, A+CN and A-CN had similar volumes (Fig.1A). The global amygdala volume was reduced in Braak III-IV compared to 0-I-II. Individuals with Braak V-VI had similar amygdala volumes than Braak III-IV (Fig.1B). After adjusting for the global amygdala volume, only the cortical, medial, and accessory-basal nuclei volumes were significantly reduced in A+MCI (versus A-CN). Furthermore, the accessory-basal nucleus volume was reduced in A+MCI/dementia group (n = 72) compared to A-MCI/dementia (which was not different from CN ((n = 46), Fig.2). Among A+ participants, temporal tau was negatively associated with the volume of the same three nuclei and the central nucleus, even after

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adjusting for the amygdala volume. These subnuclei volumes were associated with cognitive performance (Fig.3).

Conclusion: The atrophy of amygdala, especially the cortical, medial, and accessory-basal nuclei, is observed in symptomatic AD, and is associated with temporal tau pathology. Whereas the volumes of the global amygdala and most subfields are also reduced in non-AD disorders, the volume of the accessory-basal nucleus was reduced only in symptomatic AD patients.

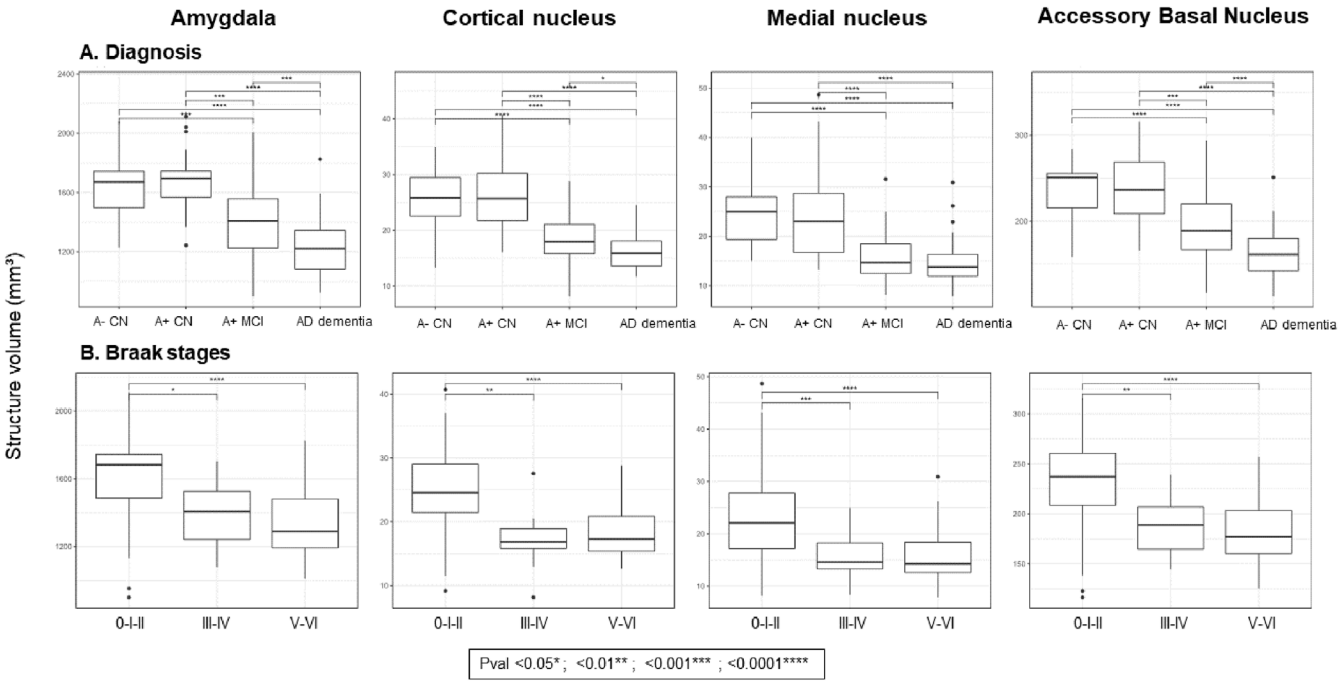

Figure 1 : Volumetric MRI Boxplots for volumes of amygdala and cortical, medial and accessory basal nuclei regarding diagnosis or Braak stage. Horizontal lines represent the medians, boxes represent upper and lower quartiles.

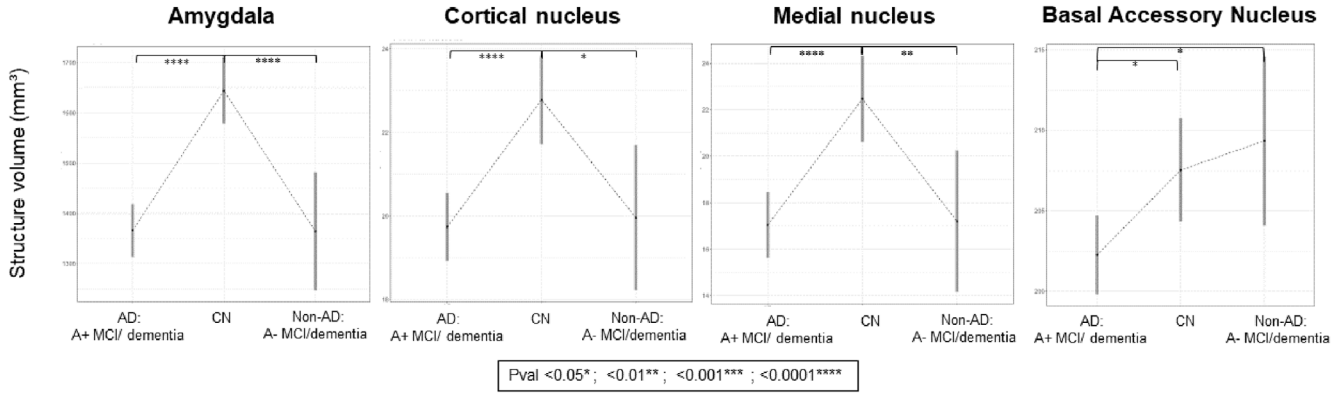

Figure 2 : Amygdala and subnuclei volumes adjuted for amygdala volume regarding diagnosis. Black dots represent the mean value, grey bars represent the confience interval (95%).

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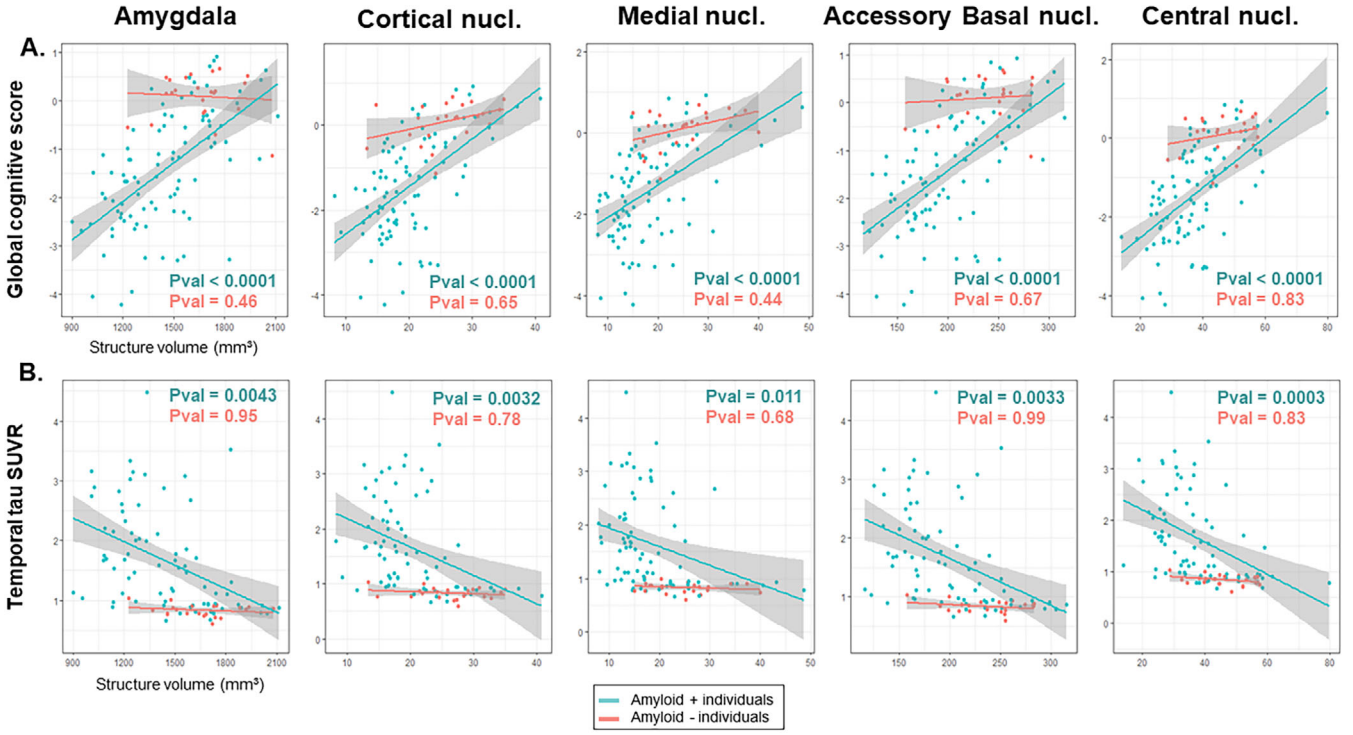

Figure 3 : Linear relationship between amygdala subnuclei volumes, cognitive score, and tau pathology in the temporal lobe (covarying age, sex, and global amygdala volume)

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