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Relationship between β-amyloid and structural network topology in decedents without dementia

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Study objective

This study investigated associations between amyloid-β (Aβ) load and postmortem structural network topology in non-demented decedents.

What is known and what this paper adds

Past studies into associations between Aβ load and brain network topology have relied on imperfect proxies for Aβ accumulation. This study used within-subjects post-mortem MRI and direct measurements of Aβ load on histopathology to study the association.

Participants and setting

These analyses included data from 14 subjects (mean age at death, 72.6 ± 7.2 years), selected from the Normal Aging Brain Collection Amsterdam (NABCA) database. Selection criteria were lack of neurodegenerative diagnoses, availability of in situ MRI without signs of overt neurodegenerative or major vascular disease, and availability of a neuropathological diagnosis with pathology meeting criteria for only none or low AD pathological change according to the NIA-AA guidelines.

Design, size, and duration

In situ MRI images were obtained including 3D T1-weighted images (for cortical gray matter (GM) segmentation), 3D-FLAIR (for detection of white matter abnormalities), and 2D echo-planar diffusion tensor imaging (DTI) for probabilistic tractography and structural network construction. Network topology measures of centrality (degree), integration (global efficiency), and segregation (clustering and local efficiency) were calculated. At autopsy, tissue sections from 12 cortical regions were sampled and immunostained for Aβ and (p-)tau, and the area percent histopathological load was measured. Linear mixed-effects models were used to analyze associations between Aβ loads and network topology measures.

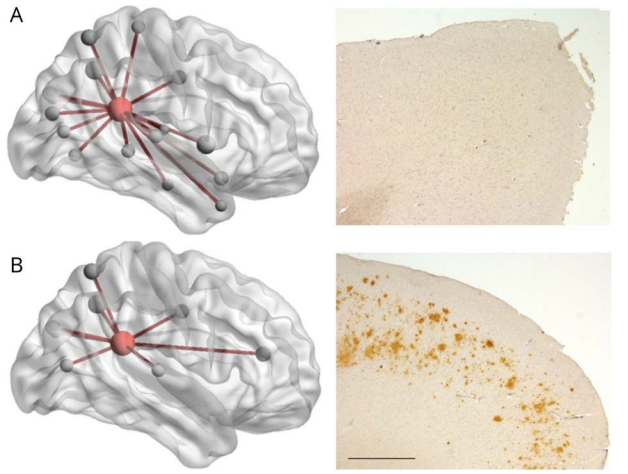
Primary outcome measures

The primary outcome was the association between Aβ loads and network topology measures.

Main results and the role of chance

Aβ was present in 79% of cases and predominantly consisted of diffuse plaques, (p-)tau was sparsely present. The analyses showed independent negative associations between Aβ loads and global efficiency ($\beta = -0.83 \times 10^{-3}$; $p = 0.014$), degree ($\beta = -0.47$; $p = 0.034$), and clustering ($\beta = -0.55 \times 10^{-2}$; $p = 0.043$), and a positive association between Aβ loads and local efficiency ($\beta = 3.16 \times 10^{-3}$; $p = 0.035$). Regionally, these results were significant in the posterior cingulate cortex (PCC) for degree ($\beta = -2.22$, $p < 0.001$) and local efficiency ($\beta = 1.01 \times 10^{-2}$, $p = 0.014$), and precuneus for clustering ($\beta = -0.91 \times 10^{-2}$, $p = 0.017$). There was no relationship between (p-)tau and network topology.

Figure Two non-neurological cases with differential pathological burden and network topology



Bias, confounding, and other reasons for caution

The investigators had no cognitive status data for the decedents. The present study had a small sample size.

Study funding/potential competing interests

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A draft of the short-form article was written by M. Dalefield, a writer with Editage, a division of Cactus Communications. The corresponding author(s) of the full-length article and the journal editors edited and approved the final version.