Genetically identical twins show comparable tau PET load and spatial distribution

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Abstract: Tau accumulation starts during the preclinical phase of Alzheimer's disease and is closely associated with cognitive decline. For preventive purposes, it is important to identify factors associated with tau accumulation and spread. Studying genetically identical twin-pairs may give insight into genetic and environmental contributions to tau pathology, as similarities in identical twin-pairs largely result from genetic factors, while differences in identical twin-pairs can largely be attributed to non-shared, environmental factors. This study aimed to examine similarities and dissimilarities in a cohort of genetically identical older twin-pairs in 1) tau load and 2) spatial distribution of tau, measured with [18F]flortaucipir PET.

We selected 78 genetically identical twins (39 pairs; average age 73 ± 6), enriched for amyloid-β pathology and APOE ε4 carriership, who underwent dynamic [18F]flortaucipir PET. We extracted binding potentials (BPND) in entorhinal, temporal, widespread neocortical and global regions, and examined within-pair similarities in BPND using age and sex corrected intra-class correlations. Furthermore, we tested whether twin-pairs showed a more similar spatial [18F]flortaucipir distribution compared to non-twin pairs, and whether the participant's co-twin could be identified solely based on the spatial [18F]flortaucipir distribution. Last, we explored whether environmental (e.g. physical activity, obesity) factors could explain observed differences in twins of a pair in [18F]flortaucipir BPND.

On visual inspection, Alzheimer's disease-like [18F]flortaucipir PET patterns were observed, and although we mainly identified similarities in twin-pairs, some pairs showed strong dissimilarities. [18F]flortaucipir BPND was correlated in twins in the entorhinal ($r = 0.40$; $p = 0.01$), neocortical ($r = 0.59$; $p < 0.01$) and global ($r = 0.56$; $p < 0.01$) regions, but not in the temporal region ($r = 0.20$; $p = 0.10$). The [18F]flortaucipir distribution pattern was significantly more similar between twins of the same pair (mean $r = 0.27$; SD = 0.09) than between non-twin pairings of participants (mean $r = 0.01$; SD = 0.10) ($p < 0.01$), also after correcting for proxies of off-target binding. Based on the spatial [18F]flortaucipir distribution, we could identify with an accuracy of 86% which twins belonged to the same pair. Finally, within-pair differences in [18F]flortaucipir BPND were associated with within-pair differences in depressive symptoms ($0.37<\beta<0.56$), physical activity ($-0.41<\beta<-0.42$) and social activity ($-0.32<\beta<-0.36$) (all $p < 0.05$).

Overall, identical twin-pairs were comparable in tau load and spatial distribution, highlighting the important role of genetic factors in the accumulation and spreading of tau pathology. Considering also the presence of dissimilarities in tau pathology in identical twin-pairs, our results additionally support a role for (potentially modifiable) environmental factors in the onset of Alzheimer's disease pathological processes, which may be of interest for future prevention strategies.

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