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Brain metabolism and tau pathology impact cognition in a Memory Clinic cohort

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BACKGROUND

Evidence suggests that tau pathology (T) and neurodegeneration (N) strongly correlate with cognitive impairment, as compared to amyloid-b plaques (A). The contribution of Alzheimer's Disease (AD) biomarkers (A, T, N) in explaining cognitive dysfunction and predicting rates of cognitive decline in a Memory Clinic cohort is not clear yet.

AIMS

- examine the independent and combined effects among neuroimaging AD biomarkers and cognitive performance and decline
- assess the prognostic value of each A/T/N PET biomarkers

METHODS

- Participant: 94 subjects from the Geneva Memory Clinic
- Imaging data: tau-PET, FDG-PET, amyloid-PET, T1 MRI (within one year)
- Cognitive data: MMSE baseline and follow-up (1.69y±0.85, N=64)

Imaging measures:

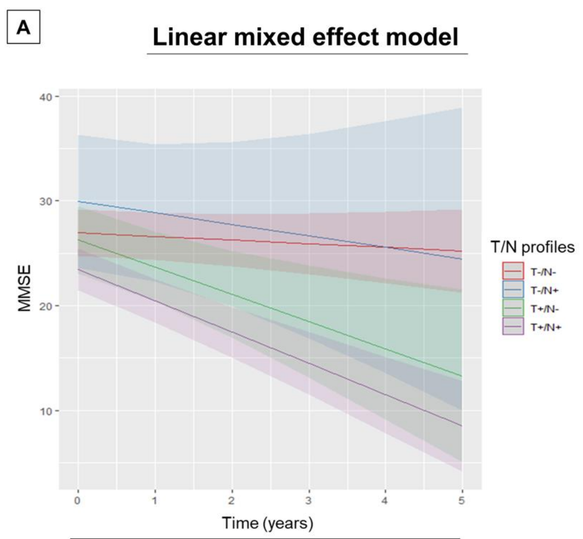
- A/T/N measures (standardized uptake value ratio for PET and volumes/thickness for MRI) were extracted in AD-related regions
- A/T/N were used both as dichotomous and continuous variables.

Statistical analysis:

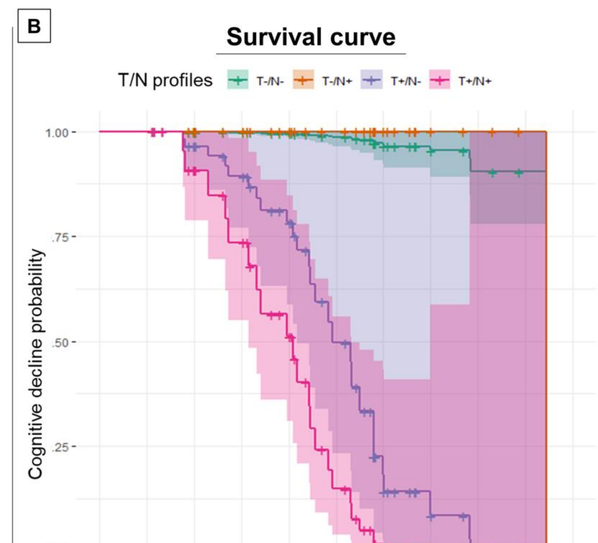
- Linear regression models were applied to test the independent association between A/T/N and MMSE
- Mediation analyses were performed to test the combined association of T/N on cognition.
- Linear mixed models and Cox proportional hazards regression were applied to assess the prognostic value T/N profiles

RESULTS

- The N_{FDG} in lateral temporal regions had the strongest association with MMSE (p=0.551; p<0.001), followed by T in the same regions (r= -0.487; p<0.001)
- Neocortical T had the strongest association with MMSE annual rate of change (r=-0.602; p<0.001)
- N mediated more strongly the baseline association between T and MMSE, compared to the one between T and MMSE changes
- T+/N+ and T+/N- groups showed a faster cognitive decline over time (A) and an increased risk for cognitive decline compared to the T-/N- group (B)



Group	β	p-values
T-/N-	-0.34	NA
T-/N+	-1.12	0.0564
T+/N-	-2.78	**0.003**
T+/N+	-2.75	**<0.001**



CONCLUSION

Our results are consistent with T and N synergistically contributing to cognitive impairment.
However, N drives concurrent cognitive dysfunction while neocortical T drives longitudinal cognitive decline.
The main finding is the added value of tau PET in predicting cognitive worsening compared to other AD neuroimaging biomarkers.
The superior value of T for predicting cognitive changes supports tau-PET as a prognostic tool in Memory Clinics.

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