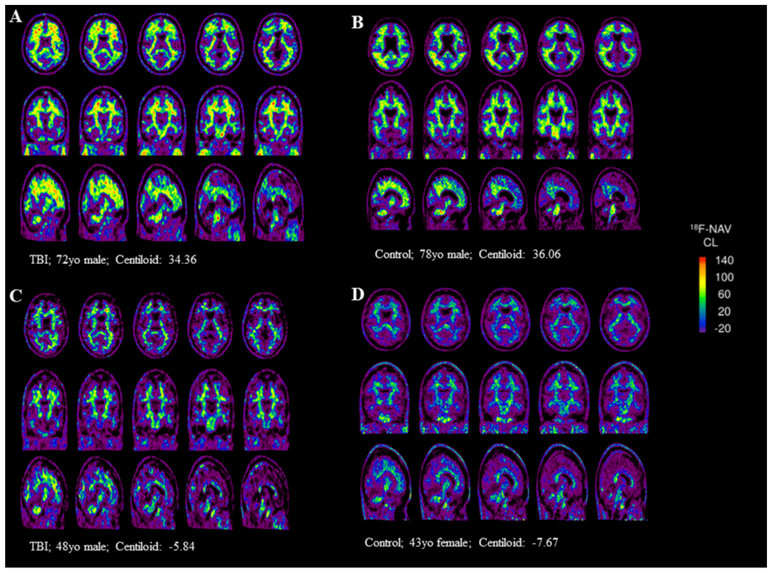


Amyloid-β and Tau Imaging in Chronic Traumatic Brain Injury: A Cross-Sectional Study

PRIMARY OBJECTIVE

To assess amyloid-β and tau burden in long-term TBI survivors and healthy controls using PET imaging.

SECONDARY OBJECTIVE

To examine PET data in relation to time since injury and age at injury.

BACKGROUND & RATIONALE

- TBI has been increasingly promoted as a risk factor for Alzheimer's disease.
- Evidence of amyloid-β and tau beyond the initial years post injury is inconclusive.
- There is conflicting evidence from PET, CSF and post-mortem studies of elevated amyloid-β and tau pathology in chronic TBI survivors compared to controls.
- The relationships between amyloid-β and tau pathology and injury characteristics, such as time since injury and age at injury, are also unclear.

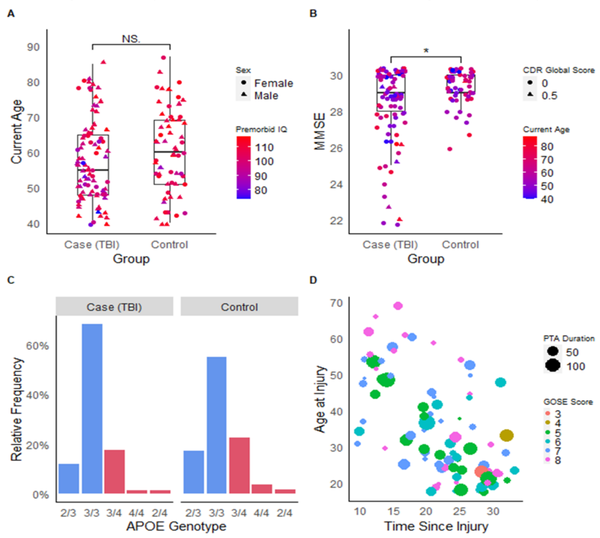
A SINGLE MODERATE TO SEVERE TRAUMATIC BRAIN INJURY WAS NOT ASSOCIATED WITH HIGHER BURDEN OF AMYLOID-B OR TAU PATHOLOGIES IN THE CHRONIC POST INJURY PERIOD (≥ 10 YEARS) RELATIVE TO HEALTHY CONTROLS

METHODS

- 18F-NAV4694 (amyloid-β) and 18F-MK6240 (tau) tracers.
- Amyloid-β deposition was quantified using the Centiloid scale.
- Tau deposition was quantified using the standardized uptake value ratio (SUVR) in four regions of interest (ROI).
  - Mesial Temporal (Me): entorhinal cortex, hippocampus, parahippocampus, amygdala
  - Temporoparietal (Te): inferior and middle temporal, fusiform, supramarginal and angular gyri, posterior cingulate/precuneus, superior and inferior parietal, lateral occipital
  - Meta-Temporal: entorhinal cortex, hippocampus proper, parahippocampus, amygdala, fusiform, inferior and middle temporal gyri, temporo-occipital region, angular gyrus
  - Rest of neocortex (R): dorsolateral and ventrolateral prefrontal, orbitofrontal cortex, gyrus rectus, superior temporal, and anterior cingulate

SAMPLE

- 87 individuals with TBI (71.3% male, 28.7% female; M 57.53 years, SD 11.53).
  - Average age of injury was 35.36 years (SD 14.02, Range 18 - 69); average time since injury was 21.72 years (SD 6.35, Range 10 - 33).
- 59 healthy controls (59.3% male, 40.7% female; M 60.34 years, SD 11.97).



RESULTS

- No association of TBI with amyloid-β burden.
  - TBI participants and controls did not differ in Centiloid value (B= 2.99, SE = 1.62, [95% CI: -0.217, 6.196], p = 0.067).
- TBI was not associated with higher tau SUVR in any of the ROIs.
  - Group did significantly predict SUVR in all four regions (Me, p = 0.001; Te, p < 0.001; Meta-temporal, p < 0.001; R, p < 0.001) but this was driven by higher SUVR for controls (Me, B = 0.103; Te, B = 0.074; meta-temporal, B = 0.094; R, B = 0.08).
- The association between group and PET quantification was not changed in any of our additional analyses:
  - Sample restricted to those 60 years and over.
  - Extended covariate list included - risk factors for Alzheimer's disease (age, sex, family history of neurodegenerative disease, vascular risk score, FSIQ, sleep quality, APOE Ɛ4 status and lifetime diagnosis of MDD/PTSD).
  - Lesion threshold applied - for focal injuries.

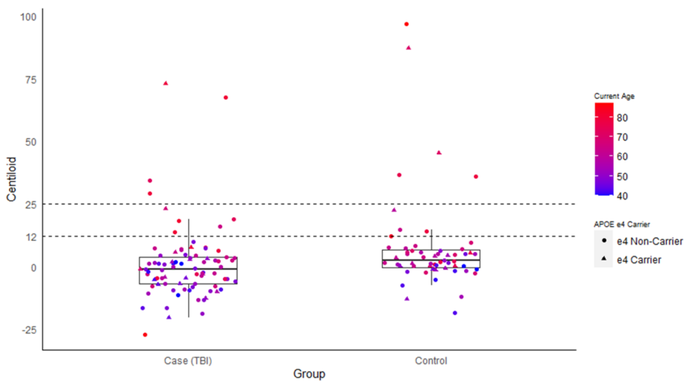


Figure. TBI does not increase 18F-NAV4694 Amyloid-β Centiloid values. Box plots showing the median Centiloid values for individuals with TBI and controls. The dashed lines represent the cut-offs of 25 and 12 Centiloids.

- No association between time since injury and amyloid-β or tau burden.
  - Time since injury was not significantly associated with Centiloid value (B = 0.230, SE = 0.192, [95%CI: -0.151, 0.611], p = 0.234), or tau SUVR in any region (Me, p = 0.297; Te, p = 0.214; meta-temporal, p = 0.332; R, p = 0.057).
- Visual assessment of the association between PET data and age at injury shows no clear trends.

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