The correlation of in vivo tau with amyloid beta, hypometabolism, and cortical atrophy in chronic TBI subjects

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INTRODUCTION

- Traumatic brain injury (TBI) is associated with an earlier age of onset of Alzheimer's disease (AD) [1].
- Recent neuropathologic studies have characterized post-TBI dementia as a polypathology consisting of a variety of misfolded proteins [2].

OBJECTIVE

The objective of this work was to examine the topography and severity of *in vivo* neurofibrillary tau and its colocalization with amyloid beta (Aβ) plaques, hypometabolism, and cortical atrophy in subjects with a history of TBI.

METHODS

Subjects

- 22 subjects with a history of traumatic brain injury (21-61 years, 21M/1F) were recruited at the University of Pittsburgh.
- Each subject was classified based on their trauma exposure frequency into three categories:

Few	(<4 exposures)
Intermediate	(4-10 exposures)
Numerous	(>10 exposures)

Imaging

- Structural T1-weighted MRI scans were acquired on a 3T Siemens TIM Trio scanner.
- [F-18]AV-1451 PET images were acquired over 75-105 min post-injection on a Siemens mCT-Flow Biograph PET/CT scanner.
- [C-11]PiB PET and [F-18]FDG PET images were acquired over 40-70 min and 35-60 min post-injection, respectively, on a Siemens ECAT HR+ PET scanner.

Statistics

- MRI data were processed through FreeSurfer v5.3 to generate cortical regions of interest (ROIs) and associated cortical thickness measures.
- [F-18]AV-1451, [C-11]PiB, and [F-18]FDG standardized uptake value ratio (SUVR) images and regional measures were generated using cerebellar grey matter (GM) as reference.
- [F-18]AV-1451 and [C-11]PiB SUVR images were visually classified as positive(+) or negative(-) for the presence of tau and Aβ, respectively.
- Pearson correlations were assessed for each PET-positive subject across all ROIs between [F-18]AV-1451 SUVR and [C-11]PiB SUVR, [F-18]FDG SUVR, and cortical thickness.

RESULTS

Two subjects were classified as both AV-1451(+) and PiB(+):

Case 1: 60-year old male, *numerous* concussive and sub-concussive exposures throughout 45-year career in scholastic and collegiate athletics.

Case 2: 54-year old male, *numerous* concussive and sub-concussive exposures throughout 26-year career in explosive ordinance disposal.

Table 1. FreeSurfer ROIs of greatest AV-1451 retention.

Case 1		Case 2	
FreeSurfer ROI	**AV-1451 SUVR**	**FreeSurfer ROI**	**AV-1451 SUVR**
Cuneus	2.39	BanksSTS	3.11
Lateral Occipital	2.28	Precuneus	2.97
Superior Parietal	2.19	Superior Parietal	2.86
BankSTS	2.17	Fusiform	2.81
Precuneus	2.05	Lateral Occipital	2.76
Lingual	2.02	Supramarginal	2.72
Fusiform	2.00	Postcentral	2.63

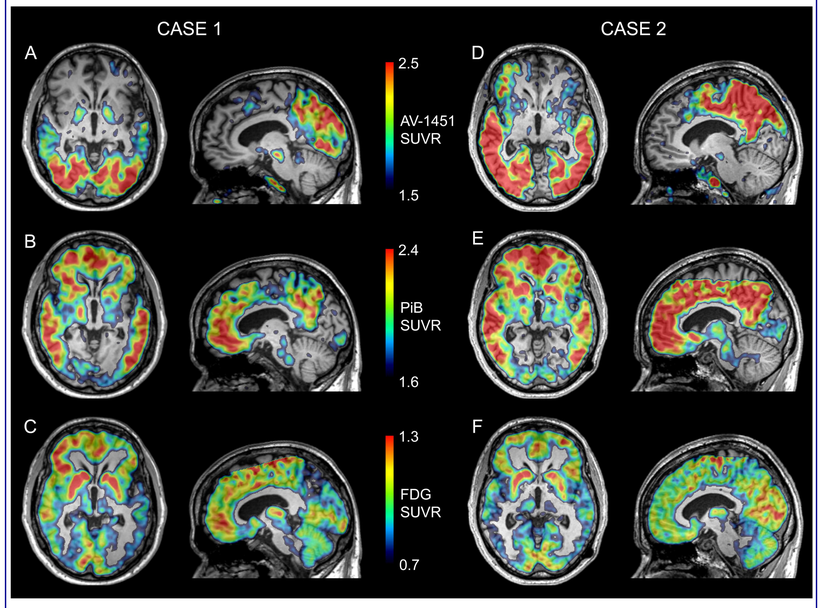

Figure 1. SUVR images of AV-1451, PiB, and FDG for Case 1 and Case 2. In Case 1, AV-1451 retention (A) is most prominent in the occipitoparietal and occipitotemporal areas both medially and laterally. In Case 2, AV-1451 retention (D) is most prominent in lateral temporoparietal areas. In both cases, PiB retention (B,E) is notable throughout the cortex, with the occipital lobe relatively spared, in a characteristic AD pattern.

RESULTS

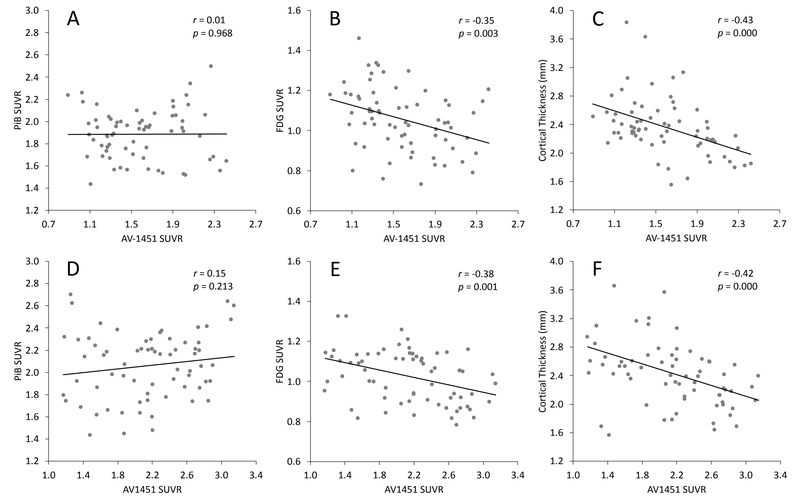

Figure 2. Regional correlations between AV-1451 SUVR and PiB SUVR, FDG SUVR, and cortical thickness for Case 1 (A-C) and Case 2 (D-F). In both cases significant negative correlations are observed between AV-1451 SUVR and FDG SUVR, and AV-1451 SUVR and cortical thickness. No significant relationship is observed between AV-1451 SUVR and PiB SUVR in either case.

CONCLUSIONS

- The topography and severity of [F-18]AV-1451 uptake, [C-11]PiB uptake, [F-18]FDG hypometabolism, and cortical atrophy seen in these cases is consistent with patterns previously reported in typical and atypical variants of AD, including posterior cortical atrophy.
- While limited by sample size, these findings suggest structural MR, [F-18]AV-1451, [C-11]PiB, and [F-18]FDG imaging hold promise for detecting trauma-related neurodegeneration in vivo.

REFERENCES

[1] Schaffert et al. (2018) Traumatic brain injury history is associated with an earlier age of dementia onset in autopsy-confirmed Alzheimer's disease. **[2]** Kenney et al. (2018) Dementia after moderate-severe traumatic brain injury: coexistence of multiple proteinopathies. **[3]** Xia et al. (2017) Association of in vivo [18F]AV-1451 tau PET imaging results with cortical atrophy and symptoms in typical and atypical Alzheimer disease.

ACKNOWLEDGEMENTS

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