p-291

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Event-based modeling of in vivo MRI measures is associated with pathologic burden in frontotemporal lobar degeneration due to tau

Christopher Olm, Sarah Burke, Claire Peterson, Edward Lee, John Trojanowski, Lauren Massimo, David Irwin, Murray Grossman, James Gee

State of the art:
Monitoring disease progression in frontotemporal lobar degeneration due to tau (FTLD-tau) is a vital aspect of understanding data from clinical treatment trials. Event-based modeling (EBM) is a data-driven analysis method that can determine the characteristic sequence of imaging changes, "events", occurring during neurodegeneration. Gray matter (GM) volumes derived from T1-weighted MRI, and perfusion measures, quantified as cerebral blood flow (CBF) derived from arterial spin labeling (ASL) MRI, are both informative of disease in FTLD, though may be sensitive to different disease processes.

Methodology:
42 patients with autopsy-confirmed FTLD-tau and 167 healthy controls (HC) with available T1-weighted images were identified. A subset of patients (N=15) and HCs (N=22) also had ASL. All patients had quantitative digital histopathology performed on select GM regions at autopsy. MRI images were processed, producing regional measures of GM-volume and CBF. EBM was used to: 1) validate the characteristic sequence of GM-volumes of autopsy-confirmed FTLD-tau, 2) establish the characeteristic sequence of CBF, 3) estimate each patient's disease stage by GM-volumes, 4) estimate each patient's disease stage by CBF. Linear regressions related pathological burden to EBM-estimated disease phase for GM-volumes and ASL-CBF.

Results:
EBM for GM-volumes generated a characteristic sequence that replicated autopsy-confirmed findings. The same sequence was found for CBF. GM-volume-based EBM-estimated disease stage was associated with pathologic burden ($p=0.026$).

Conclusion:
We provide the first evidence that EBM can reproduce pathologically-confirmed T1-volumetric phasing results, and that EBM-estimated stage may be related to pathologic burden. CBF displays a similar sequence of perfusion deficit phases.

Conflicts of interest

None