Cerebral Perfusion as an Imaging Biomarker of Presymptomatic Genetic Frontotemporal Dementia: Preliminary Results from the Genetic Frontotemporal Dementia Initiative (GENFI)

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Background

Frontotemporal dementia (FTD) is a common cause of early onset dementia. While three genetic mutations are responsible for the majority of genetic FTD, imaging biomarkers that predict symptom onset are needed1. Recent work shows volumetric changes several years before the predicted age at disease onset2. Herein, we extend on this work by investigating whether perfusion patterns derived from non-invasive arterial spin labeling (ASL) MRI can be used as an early functional neuroimaging biomarker of presymptomatic genetic FTD.

Methods

Data were drawn from the GENetic Frontotemporal dementia Initiative (GENFI)2. From the first GENFI data freeze (n=220), 168 subjects had 3T ASL from which this analysis considers only the presymptomatic carriers and controls (n=144, Table 1). Cerebral blood flow (CBF)-maps were scaled to a mean grey matter (GM) CBF of 50 mL/100g/min per ASL sequence (four different ASL sequences were used) and registered to SPM12 3D T1 GM segmentations that were registered to MNI using DARTEL. In pre-selected ROIs associated with FTD, we investigated the effects of mutation status and years to expected age of disease onset on CBF, accounting for gender and family membership as fixed and random covariates. ROI CBF-values were corrected for partial volume fractions.

Results

Years to expected age of disease onset ($p<0.007$) was more correlated with CBF than age ($p<0.1$) alone. Although there was on average no CBF difference between carriers and non-carriers ($p>0.1$), there was an interaction effect between mutation carrier status and years to expected age of disease onset on CBF (Table 2). This interaction effect was significant for all ROIs except for the parietal and occipital cortices, anterior cingulate and putamen with the strongest effects being seen in the insula and the caudate nucleus (Figure 1).

Conclusions

CBF decreased as individuals approached the expected age of disease onset and this CBF decrease was accelerated in the presymptomatic mutation carriers compared to controls, in key regions implicated in FTD. These preliminary findings demonstrate the potential utility of non-invasive perfusion MRI as an early biomarker for genetic FTD.