[^{11}C]PBR28 inflammatory PET imaging in genetic frontotemporal dementia

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Background

There is a growing focus on the role of neuroinflammation in frontotemporal dementia (FTD). Microglial burden at post-mortem is significantly increased in all forms of genetic FTD but most extensively in *GRN* mutation carriers, whose CSF levels of inflammatory biomarkers are also increased.

The [^{11}C]PBR28 PET ligand is a putative marker of inflammation which binds to a translocator protein (TSPO) expressed by activated microglia. [^{11}C]PBR28 binding is increased in neurodegenerative diseases but has not been investigated in FTD.

Methods

Cohort

Participants included ten individuals with a diagnosis of genetic behavioural variant FTD (4 *GRN*, 4 *C9orf72*, 2 *MAPT;* mean age 63.4, SD 6.6) and five age-matched healthy controls (mean age 61.8, SD 2.9).

Imaging

Dynamic PET data were acquired continuously for 90 minutes following injection of [^{11}C]PBR28. An arterial plasma input function was generated from arterial blood samples. Participants also underwent volumetric T1-weighted MR imaging.

Analysis

Non-displaceable binding potential (BP_{ND}) values were generated using a simplified reference tissue model with the cerebellum as a reference region. Regions of interest (ROIs) were defined on the co-registered T1-weighted MR image.

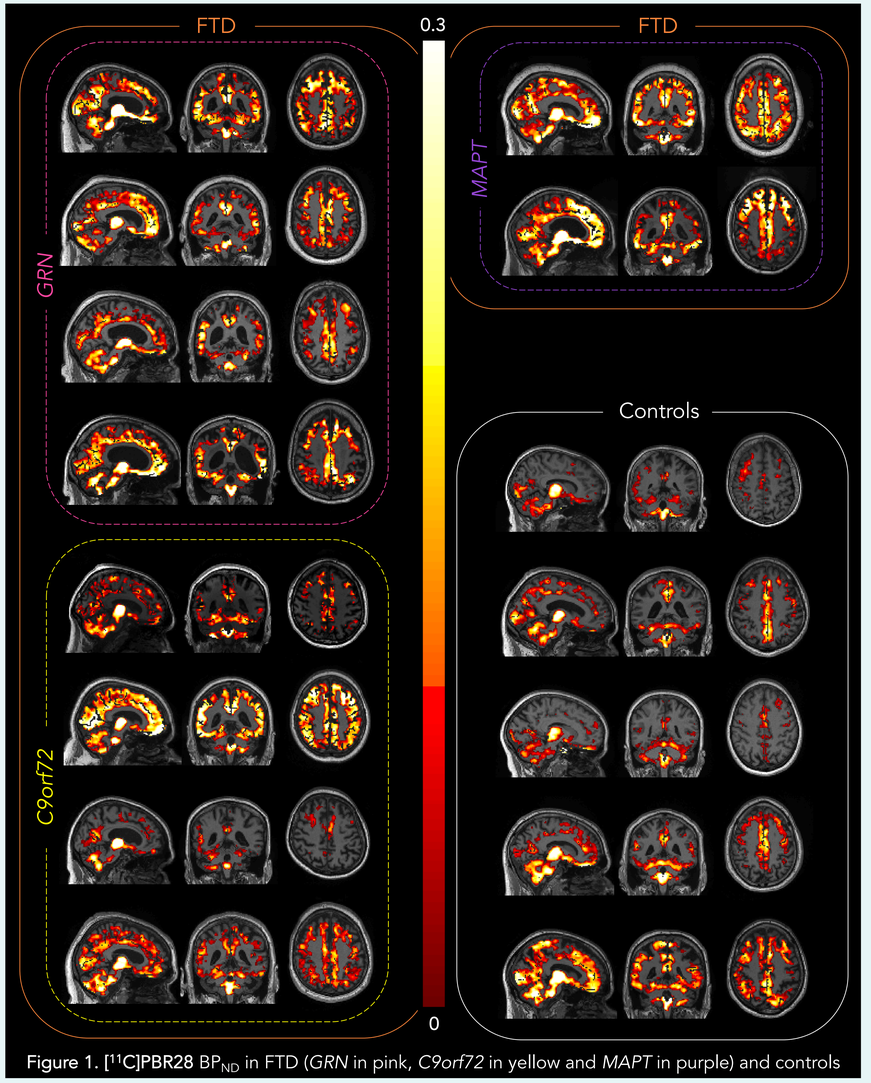

Figure 1. [^{11}C]PBR28 BP_{ND} in FTD (*GRN* in pink, *C9orf72* in yellow and *MAPT* in purple) and controls

Results

FTD vs controls

BP_{ND} was variable between individuals with genetic FTD (Figure 1). Mann-Whitney group comparisons revealed significantly greater signal in the temporal lobe (p = 0.04), posterior cingulate (p = 0.01) and putamen (p = 0.03) in FTD (Figure 2). ROC curve analyses revealed that posterior cingulate BP_{ND} best discriminated groups (AUC = 0.90, p = 0.01).

Genetic FTD

Separate comparisons in *GRN* and *C9orf72* groups revealed significant increases specifically in *GRN* mutation carriers vs controls in these three ROIs (temporal lobe p = 0.03, posterior cingulate p = 0.03 and putamen p = 0.02).

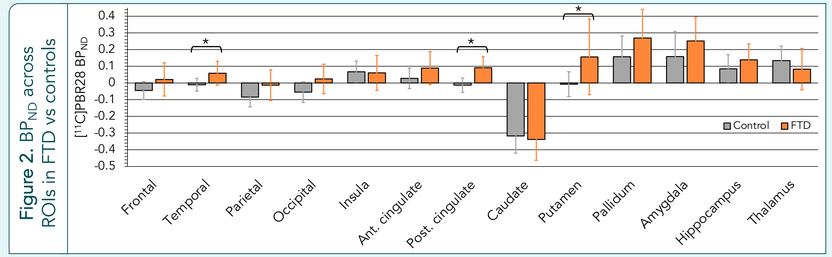

Figure 2. BP_{ND} across ROIs in FTD vs controls

Conclusions

There is increased inflammatory PET signal in individuals with genetic FTD, probably led by increased binding in *GRN* mutation carriers. Regional distribution of [^{11}C]PBR28 involved areas known to be affected in *GRN*-FTD. Microglial activation may be a useful biomarker to better understand *GRN*-FTD pathogenesis and as a potential outcome measure in future therapeutic trials.

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