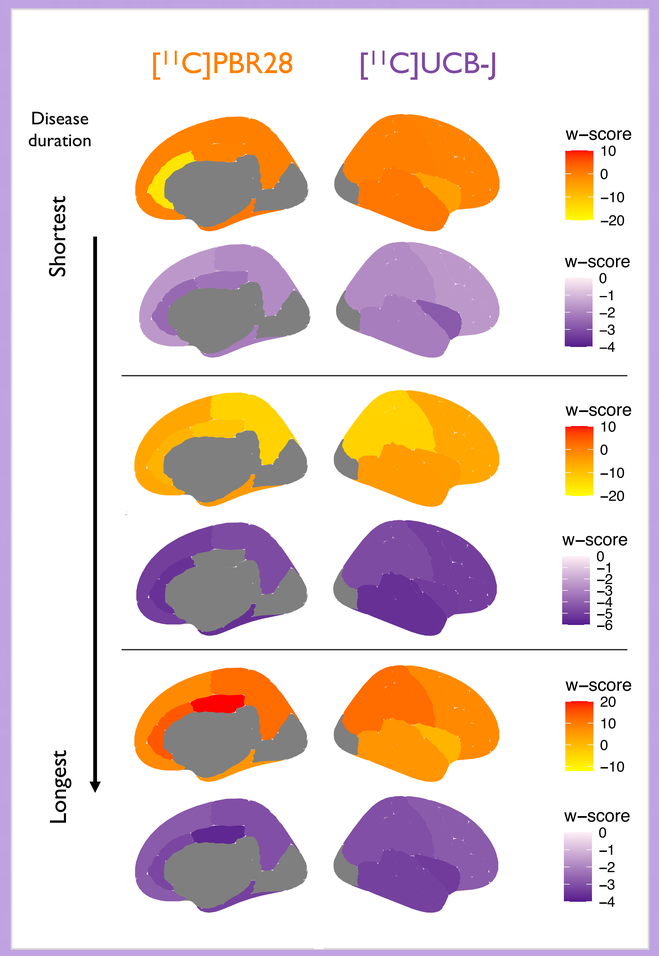
Inflammatory and synaptic PET provide more sensitive biomarkers of *C9orf72*-FTD than structural MRI



Variability between individuals may be explained by disease duration

Inflammatory and synaptic PET imaging in bvFTD caused by a repeat expansion in *C9orf72* (*C9orf72*-FTD)

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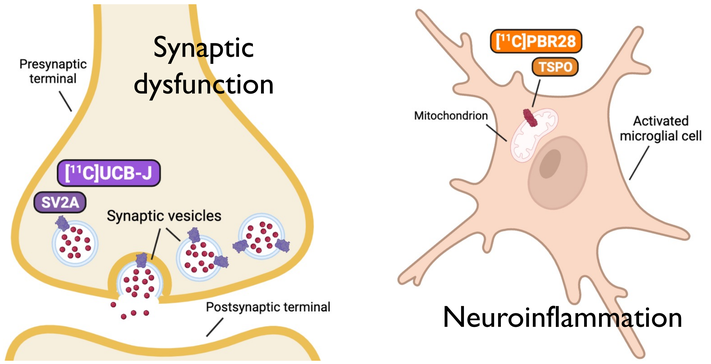
1. Background

Pathophysiological neurodegenerative mechanisms include neuroinflammation and synaptic dysfunction. PET tracers can investigate these *in vivo*.



2. Methods

Dynamic data from three male participants with *C9orf72*-FTD (mean age 62.7 years) who underwent [^{11}C]PBR28 and [^{11}C]UCB-J PET scans within 13 months were compared with data from age-matched controls (*n*=5 PBR28; *n*=17 UCB-J).

BP_{ND} was calculated for PBR28 using the cerebellum as a reference region; DVR-1 were calculated for UCB-J using the centrum semiovale. Regions of interest were defined on structural MRI.

W-scores were computed from PET and MRI data from each control cohort using age as a covariate with values >1.65 and <-1.65 considered abnormal.

3. Results

PBR28 w-scores indicated significant neuroinflammation. Differences in BP_{ND} were greater than in volume in FTD-associated regions in the case with the longest disease duration (16 years). Inversely, there were greater differences in volume than in BP_{ND} in the individual with the shortest disease duration in most regions (1 year).

UCB-J w-scores indicated significant synaptic dysfunction and were lower than w-scores of volume in all cortical regions. Differences in PBR28 were greater than differences in UCB-J in the case with the longest disease duration in most regions. Inversely, differences in UCB-J were greater than differences in PBR28 in the case with the shortest disease duration.

4. Conclusions

Inflammatory and synaptic PET may provide more sensitive biomarkers of *C9orf72*-FTD than MRI.

Variability in PET signal for both tracers within this genotype may be explained by disease duration. Greater differences in UCB-J than PBR28 earlier in the disease suggest synaptic dysfunction may precede neuroinflammation. Future research should evaluate these tracers within other FTD genotypes.

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