Background

Inflammation as a contributor to disease pathogenesis
- Progranulin involved in inflammatory pathways
- Increased sTREM2 in GRN CSF
- sTREM2 enhances microglial activation
- Astrocytic marker YKL-40 increased in FTD CSF

PET imaging of neuroinflammation
- Radiotracers bind TSPO, expressed by active microglia
- $^{11}$C]PK11195 binding increased in FTD, consistent with disease topography, but shows non-specific binding and poor sensitivity
- $^{11}$C]PBR28 binding is increased in ALS, but has not been previously explored in FTD

Methods

All participants had intravenous bolus injection of $^{11}$C]PBR28 before 90 min dynamic PET acquisition in 3D mode. An arterial plasma input function was generated for each participant. All participants also underwent T1-weighted volumetric MRI. A SRTM was used to generate $BP_{ND}$ values (Gunn et al. 1997), using the cerebellum as a reference region. Analyses were performed using MIAKAT™. ROIs were defined on the co-registered MR image. Linear regression analyses with 95% bias-corrected bootstrapped confidence intervals with 1000 repetitions were used to compare $BP_{ND}$ between groups.

<table>
<thead>
<tr>
<th>Group</th>
<th>N</th>
<th>Age at scan (years M [SD])</th>
<th>Gender (Male:Female)</th>
<th>TSPO binding (Medium:High)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Genetic FTD</td>
<td>7</td>
<td>61.7 (6.4)</td>
<td>6:1</td>
<td>6:1</td>
</tr>
<tr>
<td>Healthy controls</td>
<td>4</td>
<td>61.8 (3.3)</td>
<td>3:1</td>
<td>3:1</td>
</tr>
</tbody>
</table>

Results

Regional $BP_{ND}$ values significantly greater in genetic FTD than healthy controls are in orange.

- $BP_{ND}$ values were significantly higher in genetic FTD than healthy controls in four cortical regions: frontal (mean difference 0.08), temporal (0.07), parietal (0.13) and cingulate (0.08)
- Stratification by genetic mutation revealed highest $BP_{ND}$ in MAPT mutation carriers, then GRN mutation carriers (see Figure 2)
- $BP_{ND}$ of $^{11}$C]PBR28 in C9orf72 mutation carriers was comparable to that of controls

Conclusions

This data demonstrates increased binding of $^{11}$C]PBR28 in a cohort of individuals with genetic FTD compared with age- and gender-matched healthy controls. The distribution of increased binding reflects the pattern of atrophy associated with bvFTD. MAPT mutation carriers exhibited the greatest binding, consistent with pathological findings. Analyses with an increased sample size will explore differential genetic binding patterns and associated measures.

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