Introduction

Why are biomarkers so important for FTD?

Frontotemporal dementia (FTD) is a progressive, neurodegenerative condition with 30% of cases caused by an autosomal dominant gene mutation, including in progranulin (GRN), chromosome 9 open reading frame 72 (C9orf72) or microtubule-associated protein tau (MAPT). As clinical trials are fast approaching, identification of robust and easily accessible biomarkers is paramount to monitor treatment response.

Neurofilament light (NFL), a constituent of the neural cytoskeleton, is a marker of neuronal death and axonal degeneration. Glial fibrillary acidic protein (GFAP) is a filamentous structure expressed by mature astrocytes. It is a marker of astrogliosis, which is the abnormal proliferation of astrocytes in response to neuronal damage. Both biomarkers can be measured in CSF and blood-based samples including plasma and serum.

Aim

Investigating GFAP and NFL within GENFI

To test plasma levels of the markers GFAP and NFL in patients from the GENFI cohort. Establish biomarker differences in FTD mutation carriers versus controls and investigate correlations with psychological and imaging measures.

Methods

Participants from the GENFI cohort

<table>
<thead>
<tr>
<th>Group</th>
<th>Mean (IQR)</th>
<th>Median (IQR)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Controls</td>
<td>32.45 (4.31)</td>
<td>30.75 (4.31)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>C9</td>
<td>117.01 (24.24)</td>
<td>116.30 (24.24)</td>
<td>0.2871</td>
</tr>
<tr>
<td>GRN</td>
<td>31.09 (7.79)</td>
<td>30.30 (7.79)</td>
<td>0.0024</td>
</tr>
<tr>
<td>MAPT</td>
<td>31.09 (7.79)</td>
<td>30.30 (7.79)</td>
<td>0.0024</td>
</tr>
</tbody>
</table>

Table 1. Participant characteristics

Measurement of plasma biomarkers

Markers were multiplexed using the Neurology 4-plex assay on the Single Molecule Array (SIMOA) platform. 469 plasma samples were included in total and measured in duplicates using one batch of reagents.

Results

Plasma GFAP levels are increased in Symptomatic FTD Mutation Carriers within the GENFI Cohort

GFAP and NFL were measured in 469 plasma samples from the GENFI cohort. Plasma GFAP levels were significantly higher in the GRN mutation carriers compared to controls and MAPT mutation carriers. GFAP correlated with age and psychological measures in all groups. Cross-sectional imaging data correlated with GFAP in most brain regions across various groups. Longitudinal atrophy of brain regions known to be affected in FTD were only seen in the GRN mutation carriers. These findings further strengthen the hypothesis that inflammation plays a key role in FTD, in particular in the GRN mutation carriers. Further investigation of longitudinal changes in plasma GFAP is required, to determine its use as a biomarker.

Conclusions

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