Longitudinal magnetic resonance spectroscopy and cognitive impairment in Parkinson’s disease

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1 Parkinson’s disease (PD) at a glance

- **PD**: A neurodegenerative movement disorder.
- **Prevalence**: Affects up to 2% of individuals over 60.
- **Risk factors**: Age.
- **Diagnosis**: Clinical & neuropsychological assessment
- **Symptoms**: Motor: tremor, slow movement, rigidity; Cognitive: impairments in multiple domains, including attention, executive, function, and memory; Others: sleep disturbances and swallowing difficulties.
- **Treatment**: Medications & Surgical (motor symptoms only).

2 The problem

As the disease progresses, cognitive impairments become more manifest in many patients, ultimately leading to dementia in the majority. However, there is considerable variation (range 2-20 years) between onset of the initial motor disorder and the emergence of dementia. Importantly, this delay provides a window for potential therapeutic intervention.

Detecting cognitive impairment at its earliest stages would facilitate the most appropriate and timely intervention aimed at slowing the progression to dementia.

However, the assessment of neuroprotective and disease-modifying therapies in PD has been hampered by a lack of clinically useful, reliable neurobiomarkers.

3 The proposed solution

Magnetic Resonance Spectroscopy (MRS) provides an attractive option to identify a neurobiomarker of cognitive impairment in PD.5

4 Aim

To examine whether MRS of posterior cingulate cortex (PCC) can track the metabolic changes associated with cognitive impairment in Parkinson’s disease.

5 Methods

- All subjects completed a neuropsychological battery and were classified as healthy controls (HC), PD with normal cognition (PND), PD with mild cognitive impairment (PDMCI), or PD with dementia (PDD) (Table 1).
- At baseline, 179 subjects underwent MRS spectroscopy examinations.
- The follow-up stage involved re-imaging 173 controls and non-demented subjects up to 4 years after their initial assessment.
- 2 × 2 × 3cm³ MRS voxel was placed on the posterior cingulate cortex of the brain (Figure 1).
- We quantified 4 metabolites and their ratios (Table 2).

6 Results

- Cognition performance scores significantly varied at baseline and over time among the groups.
- MRS markers showed no significant group difference at baseline.
- At follow-up, neither a significant change in MRS markers nor a relationship between the MRS markers and the change in the cognitive status were identified (Table 3).

7 Conclusion

- With a large sample size and comprehensive neuropsychological assessment, we were unable to identify any significant change in MRS parameters relating to cognitive status at baseline or over time.
- Our findings suggest that MRS of the PCC at least, is not a clinically useful biomarker of longitudinal change in cognitive impairment in Parkinson’s disease.

Table 1. Demographic and neuropsychological data by group at baseline

<table>
<thead>
<tr>
<th></th>
<th>Controls</th>
<th>PND</th>
<th>PDMCI</th>
<th>PDD</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>49</td>
<td>77</td>
<td>33</td>
<td>20</td>
</tr>
<tr>
<td>Sex (M/F)</td>
<td>33/16</td>
<td>51/26</td>
<td>21/12</td>
<td>17/3</td>
</tr>
<tr>
<td>Age (years)</td>
<td>68(8)</td>
<td>64(8)*</td>
<td>70(5)</td>
<td>73(7)*</td>
</tr>
<tr>
<td>Education</td>
<td>13(2)</td>
<td>13(2)</td>
<td>13(3)</td>
<td>12(2)</td>
</tr>
<tr>
<td>Disease duration(years)</td>
<td>NA</td>
<td>2(3)</td>
<td>5(3)</td>
<td>18(8)</td>
</tr>
<tr>
<td>Cognitive Z score</td>
<td>0.63(0.37)</td>
<td>0.26(0.43)**</td>
<td>-0.72(0.39)**</td>
<td>-1.71(0.59)**</td>
</tr>
<tr>
<td>McCA</td>
<td>27(1.9)</td>
<td>26(2)**</td>
<td>27(2.4)**</td>
<td>17(1.8)**</td>
</tr>
</tbody>
</table>

- Values are mean (sd). *p<0.05 & **p<0.001 between control and PD groups at baseline. LED = Livedopa Equivalent Dose. McCA = Montreal Cognitive Assessment. Z score = represents the global cognition.

Table 2. The brain metabolites and their physiological significance.

<table>
<thead>
<tr>
<th>Metabolite</th>
<th>Physiological Significance</th>
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<tbody>
<tr>
<td>N-Acetylaspartate</td>
<td>Neuronal integrity marker</td>
</tr>
<tr>
<td>Cho</td>
<td>Gicellular membrane breakdown marker</td>
</tr>
<tr>
<td>NAA/Cr</td>
<td>Represents energy storage, relatively stable in most diseases</td>
</tr>
<tr>
<td>Cho</td>
<td>Glial cell marker</td>
</tr>
<tr>
<td>myo-Inositol</td>
<td>Increased mi indicates an ongoing glissis</td>
</tr>
</tbody>
</table>

![Figure 1](image1.png) Axial, coronal, and sagittal (left to right) MRI structural images showing the voxel location and an example MR Spectrum.

![Figure 2](image2.png) Trajectory of global cognitive Z score over time by cognitive group (top) and NAA/Cr ratio (bottom).


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