Introduction

• Symptoms Without Evidence for Dopamine Deficiency (SWEDD) is the name given to a syndrome in which patients who appear clinically to have Parkinson’s disease have a “normal” DaT-SPECT scan, suggesting these individuals do not have degeneration of nigrostriatal dopaminergic circuitry.

• It is difficult for movement disorders specialists to clinically differentiate between patients with PD, who have abnormal DaT-SPECT scans and patients with SWEDD.

• Since patients with SWEDD and PD have different neuropathology they may have differences in their cognitive functions.

• The Parkinson’s Progression Markers Initiative (PPMI) clinical sites recruited over 600 subjects divided into participants with PD, Healthy Controls (HC) and SWEDD who were identified following a DaTSCAN not showing any abnormality. Movement, behavioral and cognitive function was studied in all subjects.

• This study focused on the neurobehavioral disorders that may differentiate individual SWEDDS compared to PD and HC.

Methods

• Participants: A sample of 417 from the PPMI dataset were studied. Subjects were divided into 3 groups; SWEDD (n=57), PD (n=178) and Healthy Controls (n=182).

• This sample represents a partial dataset that included all available subjects at the time of the analysis; no selection criteria were applied.

• Apparatus and Procedures: Montreal Cognitive Assessment (MoCA) score was used in order to compare global cognitive impairment across the sample. We attempted to determine what factors might account for differences in global cognition by analyzing the each domain of the MoCA.


• We evaluated mood changes using the Geriatric Depression Scale. We also compared patient’s perception of the impact of disease on daily function using the second part of the updated Movement Disorders Society Unified Parkinson’s Disease Rating Scale (MDS-UPDRS-II), and we evaluated color function across the sample using the motor subscale of the same scale (MDS-UPDRS-III).

Results

1. Cognitive Functions:

• Montreal Cognitive Analysis (MoCA)

  - As a group, the SWEDD cohort had lower mean global cognitive function (total MoCA score when compared to both the PD cohort (p = 0.045) and HC (P=0.002).

  - The F-test, used to evaluate variance between groups, indicated variance in the SWEDD sample was different from that of the PD sample (p = 0.0048).

  - In regard to the specific domains assessed by the MoCA (e.g., trail making, visuosconstructive skills, naming, memory, attention, sentence repetition, verbal fluency and abstraction), while SWEDD mean was less than PD in all cases, only “sentence repetition” showed a significant difference (p=0.008).

2.2 Mood:

• Analysis of the Geriatric Depression Scale revealed that there were no significant difference between the SWEDD and PD patients; however F-test once again disclosed differences between sample distributions in the patients with SWEDDs compared to PD.

3. Motor Exam and Perceived Functional Change:

• The subjects classified as SWEDD, while having similar objective motor findings as PD subjects (MDS-UPDRS III, motor exam, p<0.39), rated themselves as having significantly worse functional differences with both non-motor symptoms (MDS-UPDRS I, p < 0.001), and motor symptoms (MDS-UPDRS II, p < 0.001) typically associated with Parkinson’s disease.

<table>
<thead>
<tr>
<th>Domain</th>
<th>SWEDD</th>
<th>PD</th>
<th>Difference (SWEDD – PD)</th>
<th>HC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alternating Trail Making</td>
<td>0.8421</td>
<td>0.905</td>
<td>-0.0629 (p=0.242)</td>
<td>0.9344</td>
</tr>
<tr>
<td>Visuconstructual (Cube)</td>
<td>0.807</td>
<td>0.860</td>
<td>-0.0533 (p=0.333)</td>
<td>0.8579</td>
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<tr>
<td>Visuconstructual (Clock)</td>
<td>2.7779</td>
<td>2.8045</td>
<td>-0.0265 (p=0.660)</td>
<td>2.8634</td>
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<tr>
<td>Naming</td>
<td>2.9825</td>
<td>2.9832</td>
<td>-0.0008 (p=0.960)</td>
<td>2.9836</td>
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<tr>
<td>Attention</td>
<td>5.7368</td>
<td>5.7821</td>
<td>-0.0453 (p=0.650)</td>
<td>5.8852</td>
</tr>
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<td>Sentence Repetition</td>
<td>1.7193</td>
<td>1.9274</td>
<td>-0.2081 (p=0.008)</td>
<td>1.8852</td>
</tr>
<tr>
<td>Verbal Fluency</td>
<td>12.9298</td>
<td>12.8324</td>
<td>-0.0974 (p=0.800)</td>
<td>14.15</td>
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<tr>
<td>Abstract</td>
<td>1.9474</td>
<td>1.9497</td>
<td>-0.0024 (p=0.900)</td>
<td>1.9672</td>
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<td>Delayed Recall</td>
<td>3.3684</td>
<td>3.6704</td>
<td>-0.3020 (p=0.110)</td>
<td>3.8961</td>
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<tr>
<td>Orientation</td>
<td>5.9474</td>
<td>5.9777</td>
<td>-0.0303 (p=0.240)</td>
<td>5.989</td>
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<tr>
<td>MoCA (Overall)</td>
<td>27.1579</td>
<td>27.8883</td>
<td>-0.7304 (p=0.005)</td>
<td>28.2404</td>
</tr>
</tbody>
</table>

Table 1. Cognitive functions comparison using MoCA scores

• Other cognitive functions tests:

  - Individuals with SWEDD showed a clear decline in semantic fluency compared to individuals with DaTscan confirmed PD.

  - On the Hopkins Verbal Learning Test in total and delayed recall subtest, there was no significant difference between SWEDD and PD patients; however, the healthy controls had a significantly better performance than did the patients with SWEDD and PD.

  - The results of the other cognitive functions tests revealed no between group differences in the Benton’s Judgment of Line Orientation or Letter Number Sequencing tests (Table 2).

2. Mood:

• Analysis of the Geriatric Depression Scale revealed that there were no significant difference between the SWEDD and PD patients; however F-test once again disclosed differences between sample distributions in the patients with SWEDDs compared to PD.

3. Motor Exam and Perceived Functional Change:

• The difference between SWEDDS and PDs goes beyond DaTSCAN images.

• Cognitive function in SWEDD patients is more variable than PD subjects and mean cohort cognitive function is decreased in the SWEDD cohort compared to both the PD cohort and healthy controls.

• Subjects with SWEDD rate themselves as having a higher overall severity of both motor and non-motor symptoms typically associated with PD.

• High confidence of differences in sample distribution between SWEDD and PD among multiple tests suggest SWEDD represents a distinct syndrome, or possibly more than one syndrome.

• Taken together, these results suggest that deficits among SWEDD patients go beyond simple motor findings.

References


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