Mismatch Negativity Links to Information Processing in Multiple Sclerosis (MS)
Felicia Jackson, B.S.; Leigh Charvet, Ph.D.; Maria G. Amella, B.S.; Greg Hajcak Proudfit, Ph.D.; Lauren Krupp, MD, FAAN

Objective
To evaluate the mismatch negativity (MMN) component of the event-related potential (ERP) as a biomarker of cognitive function in adults with multiple sclerosis (MS).

Background
- Cognitive impairments affect more than half of all individuals with MS and there is a need for biomarkers.
- The MMN is a negative deflection in the ERP that is automatically evoked with a difference in sensory inputs.
- MMN has the advantage of being recorded under passive conditions and does not depend on participant attention.
- Blunted MMN is an indicator of abnormalities in early sensory processing and has been associated with cognitive impairment and risk for decline in a range of neurodegenerative disorders.
- The Symbol Digit Modalities Test (SDMT) has been shown to be correlated with specific neural changes reported using fMRI.

Methods

EEG Data Collection
- MMN was elicited in a 20 minute passive auditory oddball task with 3 tone conditions: Standards, Duration Deviants and Frequency Deviants
- 1,750 tones were presented:
  - 90% Standard Tones (50ms, 633 Hz)
  - 5% Duration Deviant Tones (100ms, 633 Hz)
  - 5% Frequency Deviant Tones (50ms, 1000 Hz).
- Duration Deviant MMN was scored as the mean amplitude from 150 to 250 ms at electrode site Fz.
- Analyses were conducted on the difference wave of Duration Deviant tones minus Standard tones (Duration Difference).

Results

Neuropsychological Assessment
- Of the measures included in the study, the groups only significantly differed on the SDMT.

<table>
<thead>
<tr>
<th>Domain</th>
<th>Measure</th>
<th>MS</th>
<th>Control</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estimated IQ</td>
<td>WRAT-3 Reading Level (standard)</td>
<td>105.0 ± 6.1</td>
<td>103.9 ± 8.2</td>
<td>0.70</td>
</tr>
<tr>
<td>Speeded Information</td>
<td>Processing</td>
<td>-1.0 ± 1.2</td>
<td>0.41 ± 0.9</td>
<td>0.002*</td>
</tr>
<tr>
<td>Verbal Learning</td>
<td>SRT Total Learning (r score)</td>
<td>0.29 ± 1.6</td>
<td>0.63 ± 1.3</td>
<td>0.30</td>
</tr>
<tr>
<td>Visualse Learning</td>
<td>SRT Total Learning (r score)</td>
<td>49.7 ± 19.35</td>
<td>55.9 ± 10.4</td>
<td>0.10</td>
</tr>
<tr>
<td>Working Memory</td>
<td>WAIS-IV Letter Number (scaled)</td>
<td>9.5 ± 3.0</td>
<td>10.6 ± 3.4</td>
<td>0.36</td>
</tr>
</tbody>
</table>

Mismatch Negativity (MMN)
- Duration Difference MMN did not significantly differ in MS participants relative to controls.
- SDMT performance significantly correlated with the Duration Difference MMN ($r = -0.38$, $p = 0.05$), but not with Frequency Difference MMN ($r = 0.08$).
- No other cognitive measure was significantly correlated with the Duration Difference MMN.

Conclusions
- MMN is associated with impaired SDMT performance.
- MMN may serve as a biomarker of cognitive impairment in MS.

References

Participants
- Participants were 14 individuals with MS compared to 15 locally-recruited healthy controls. MS and control groups did not differ in age (51.4 ± 9.5 vs. 52.5 ± 12.6 years, $p = 0.81$), gender (10 women in each group), or years of education (14.6 ± 2.1 vs. 15.4 ± 2.2 p=0.34).
- For the MS group, EDSS scores ranged from 2.0 to 6.5 with a median of 4.0. Mean duration of diagnosis was 15.9 ± 10.5 years.
- Both groups completed cognitive testing and an electrophysiology (EEG) session.

Neuropsychological Assessment
- Tests included the SDMT, as well as the WRAT-3 reading (for estimated premorbid IQ), SRT (verbal learning), BVMT-R (visual learning), and WAIS-IV Letter Number Sequencing (working memory).

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