

## 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 detection of sensory change.
- 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

### Participants

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

### Neuropsychological Assessment

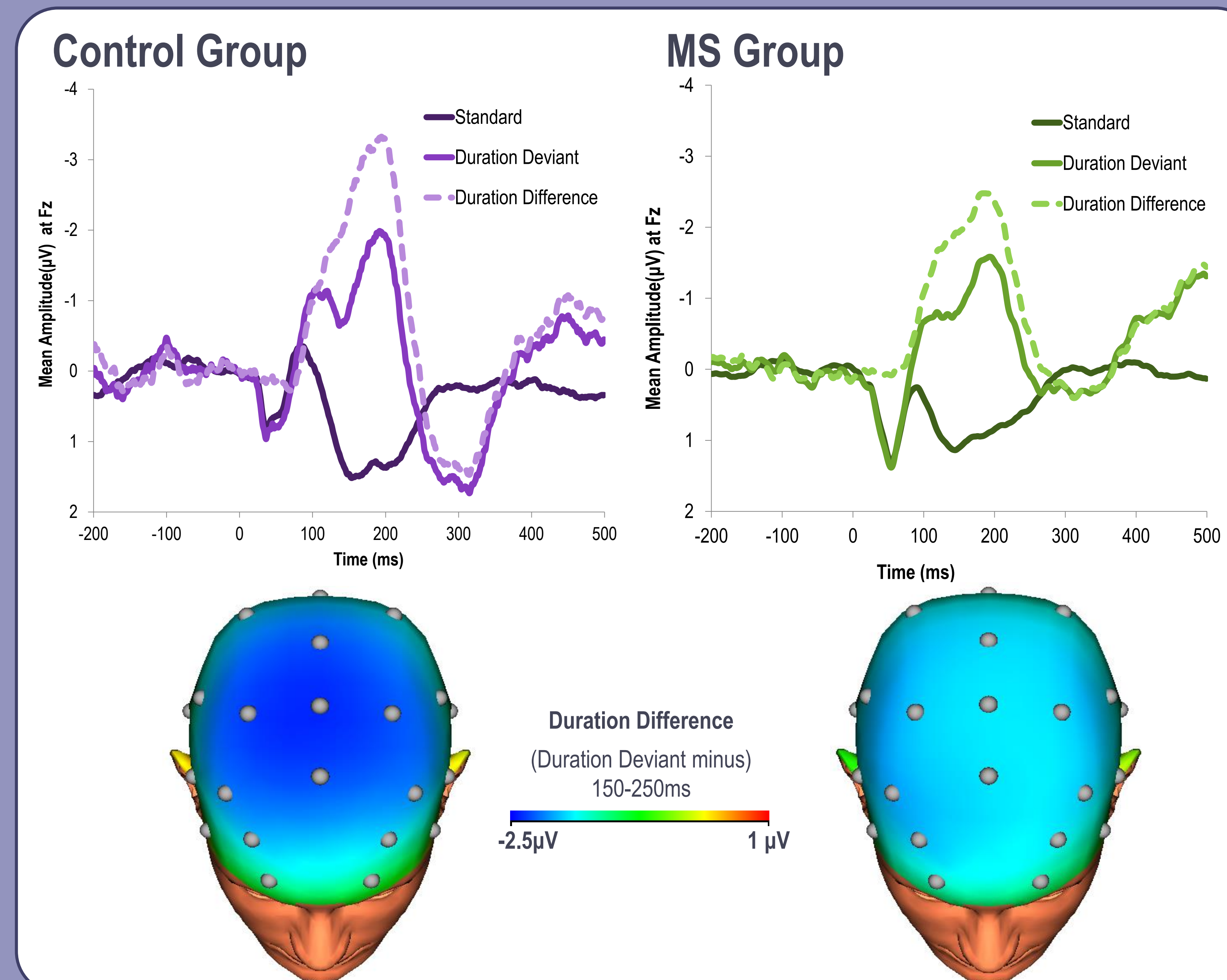
- Tests included the SDMT, as well as the WRAT-3 reading (for estimated premorbid IQ), SRT (verbal learning), BVMT-R (visual learning), and WAIS-IV Letter Number Sequencing (working memory).

## 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



## Results

### Neuropsychological Assessment

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

Domain	Measure	MS	Control	p value
Estimated IQ	WRAT-3 Reading Level (standard score)	105.0 ± 6.1	103.9 ± 8.2	0.70
Speeded Information Processing	SDMT (z score)	-1.0 ± -1.2	0.41 ± 0.9	0.002*
Verbal Learning	SRT Total Learning (z score)	-0.29 ± 1.6	0.63 ± 1.3	0.10
Visual Learning	BVMT-R Total Learning (t score)	49.7 ± 9.35	55.9 ± 10.4	0.10
Working Memory	WAIS-IV Letter Number (scaled)	9.5 ± 3.0	10.6 ± 3.4	0.36

### 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

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