Cognitive Impairment and Magnetic Resonance Changes in Multiple Sclerosis

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Background

- MS inflammatory lesions interrupt white matter tracts, resulting in impaired cognition
- Studies have identified associations between cognitive performance, cortical lesions and regional gray matter atrophy
- Longitudinal studies comparing MRI abnormalities and cognitive decline have relied upon brain MRIs acquired every 6-12 months
Hypotheses

Cognition will be more impaired in the presence of acute contrast-enhancing lesions compared to no active lesions.

Cortical atrophy over 2 years will be associated with impaired cognition.

Materials & Methods

• 75 subjects with RRMS

• MRIs were performed monthly for at least the first year of this 2-year study

• Comprehensive neurocognitive battery was administered at 0, 6, 12, and 24 months
### Cognitive Sets and Represented Domains

<table>
<thead>
<tr>
<th>Set</th>
<th>Domain</th>
<th>Subtest</th>
</tr>
</thead>
<tbody>
<tr>
<td>(A) Information Processing/Memory</td>
<td>Visual Learning</td>
<td>Ruff Figural Fluency Test error ratio</td>
</tr>
<tr>
<td></td>
<td>Auditory Processing</td>
<td>PASAT</td>
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<td>California Verbal Learning Test trials 1-5 total</td>
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<td>Processing Speed</td>
<td>WAIS-III Digit Symbol</td>
</tr>
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<td>(B) Visual-Spatial/Executive Function</td>
<td>Visual-spatial</td>
<td>WMS-III Spatial Span</td>
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### Criteria for Cognitive Impairment

**None**
- Impairment on 0-1 Individual Tests

**Mild**
- Impairment on 2-3 Individual Tests
  - Significant Impairment 1/3 Sets

**Moderate**
- Impairment on 4-5 Individual Tests
  - Significant Impairment 2/3 Sets

**Severe**
- Impairment on ≥6 Individual Tests
  - Significant impairment 3/3 Sets
  - Impaired = 1 SD
  - Significant Impairment = 2 SD
• T1-weighted fat-saturated sequences acquired with Gadolinium were reviewed using Amira® imaging software.

• Maximal lesion volume (mm$^3$) of the CEL was measured using volume rendering, indicated by the purple circle

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**SIENAX**

• FSL program that segments various brain regions
• All brain volumes were normalized to the skull
Normalized Brain Volume Variability Over 2 years

- % change in volume over 2 years was determined

- **Categories included:**
  - Whole brain
  - White matter
  - Peripheral Grey (Cortex)
  - Ventricle

**Example:** Patient 16

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Active Gadolinium-enhancing Lesion vs. Cognitive Impairment

- MRI scans at the time of cognitive testing were evaluated by volume of Gadolinium enhancement

- Cognitive tests were performed at 0, 6, 12, and 24 months

- MRI Gadolinium enhancement was categorized by total volume (mm$^3$):
  1. 1.0 to 199
  2. 200 to 399
  3. 400 to 599
  4. 600 to 799
  5. 800 and above
Cognitive Performance vs. Gd Volume

- Patients with Gd enhancement at the time of cognitive testing were more likely to be impaired on information processing/memory ($p<0.01$)
  - Seen with Gd >800 mm$^3$
  - Effect was mild impairment
  - Driven by PASAT

- No drop in performance based upon total Gd lesion volume was observed for:
  - Visual-spatial/executive
  - Verbal memory/attention

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Ventricular Enlargement and White Matter Loss
vs.
Gadolinium-enhancing lesion volume

Gadolinium Enhancing Lesion Volume vs. Normalized Ventricle Volume

• Gd lesion volume at baseline was predictive of 2-year % increase in ventricular volume ($p < 0.01$)
Gadolinium Enhancing Lesion Volume vs. Normalized White Matter

- Gd lesion volume at baseline was predictive of 2-year % change in white matter volume ($p < 0.05$)

Gd volume at baseline vs. 2-year % change in whole brain and peripheral grey (cortex)

- No significant relationship was found between Gd volume at baseline vs. 2-year % change whole brain

- No significant relationship was found between Gd volume at baseline vs. 2-year % change peripheral grey (cortex)
Ventricular and White Matter Volume % Change vs. Cognitive Impairment

- Increases in ventricular volume over 2 years was correlated with deficits in:
  1. Information processing and memory at 24 months**
  2. Overall cognitive impairment at 24 months*

- Decreases in white matter volume over 2 years was correlated with deficits in:
  1. Overall cognitive impairment at 24 months*

*p < 0.05, **p < 0.01

Conclusions

- Processing speed may be mildly impacted when active lesion volume is high in this early MS cohort

- Gd lesion volume at baseline predicted ventricular and white matter atrophy over 2 years

- Two year cognitive impairment was related to ventricular and white matter atrophy over 2 years

- Of the cognitive sets, information processing speed seemed most associated with some MRI changes

- In this dataset, cortical volumes did not appear to be predictive of cognition over 2 years
Future Directions

• The majority of this early MS cohort showed mild to no impairment during cognitive testing over 2 years

• Thus, a 10-year follow-up assessment could demonstrate additional correlations between volume change and cognitive performance as a result of disease progression

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![Table 1](image-url)