Magnetization Transfer Imaging in Brain Corticospinal Tract is Associated with Clinical Walking Performance in Multiple Sclerosis

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Background

- Up to 85% of individuals with MS report gait disturbance as their main complaint. (Kelleher et al. 2010)
- Walking is frequently tested in the clinic as a measure of physical function.
- EDSS
  - Walking evaluation based on distance and assistance level
  - No measure of:
    - Time to complete walking tasks
    - Quality of walking
    - Functional tasks during walking
Background

- Previous work in Diffusion Tensor Imaging (DTI) and Magnetization Transfer Ratio (MTR) has focused on impairment measures (strength) and has shown:
  - An association between strength and:
    - Spinal cord MTR of the lateral column
    - Spinal cord FA of whole spinal cord ROIs
  - Brainstem corticospinal tract (CST) MTR dissociates stronger vs. weaker muscle strength
- Walking represents a global disability measure and may be more practical for monitoring change over time and with intervention.

Objectives

- Explore the relationship of clinical measures of walking and CST-specific MRI measures.
- Determine the extent that quantitative measures of walking may add to basic clinical measures (age, gender, symptom duration and EDSS).

Hypotheses

- Tract-specific imaging measures of the CST will be related to walking.
- Quantitative measures of walking will add information about the MRI that is complimentary to basic clinical information.
Demographics

<table>
<thead>
<tr>
<th></th>
<th>Age Mean(SD)</th>
<th>Gender</th>
<th>Symptom Duration Mean(SD)</th>
<th>EDSS Median (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>MS n=23</strong></td>
<td>49.1 (11.5)</td>
<td>12F; 11M</td>
<td>14.1 (10.2) Years</td>
<td>4.0 (1-6.5)</td>
</tr>
<tr>
<td><strong>Control n=20</strong></td>
<td>52.2 (10.4)</td>
<td>13F; 7M</td>
<td>--</td>
<td>--</td>
</tr>
</tbody>
</table>

Clinical Measures
- Fall History
- Strength
- Sensation
- Walking
  - Timed Up and Go (TUG)
  - Timed 25 Foot Walk (T25W)
  - Two Minute Walk Test (2MWT)

MRI Measures
- **Phillips 3T Scanner**
- **Diffusion Tensor Imaging (DTI)**
  - 33 direction
  - FOV: 212 x 154 x 212
  - 70 slices
  - 2.2 SENSE
  - TR = 7173 ms
  - Scan Resolution 96x96
- **Magnetization Transfer Ratio (MTR)**
  - FOV: 212 x 154 x 212
  - 70 slices
  - Scan Resolution 144x140
  - TR: 64.411 ms
Results

Table 1. Comparisons Between Individuals with MS and Controls

<table>
<thead>
<tr>
<th></th>
<th>MS Mean(SD)</th>
<th>Control Mean(SD)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Falls (# past month)</td>
<td>0.43 (0.51)</td>
<td>0</td>
<td>p=0.0009 ‡</td>
</tr>
<tr>
<td>Hip Flexion Strength (lbs)</td>
<td>34.1(14.8)</td>
<td>46.6(10.5)</td>
<td>p=0.0025</td>
</tr>
<tr>
<td>Vibration Sensation (vu)</td>
<td>7.5(3.5)</td>
<td>3.2(2.4)</td>
<td>P=0.0002 ‡</td>
</tr>
<tr>
<td>TUG (s)</td>
<td>8.1(2.5)</td>
<td>5.9(1.0)</td>
<td>p=0.0006</td>
</tr>
<tr>
<td>T25W (s)</td>
<td>5.7(2.4)</td>
<td>4.2(0.65)</td>
<td>p=0.0102 ‡</td>
</tr>
<tr>
<td>2MWT (m)</td>
<td>162.6(45.5)</td>
<td>199.4(32.4)</td>
<td>p=0.0067</td>
</tr>
</tbody>
</table>

‡ Indicates Mann-Whitney Tests; all others T-tests

Results

Table 2. Correlations between Clinical Measures and MRI Measures

<table>
<thead>
<tr>
<th></th>
<th>MTR Mean(SD)</th>
<th>Λ⊥ Mean(SD)</th>
<th>Λ∥ Mean (SD)</th>
<th>Fractional Anisotropy Mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TUG</td>
<td>-0.4297(0.0071)</td>
<td>0.2948(0.0613)</td>
<td>0.1772(0.2873)</td>
<td>-0.2877(0.0681)</td>
</tr>
<tr>
<td>T25W</td>
<td>-0.3972(0.0101)</td>
<td>0.3404(0.0294)</td>
<td>-0.0970(0.5461)</td>
<td>-0.4085(0.0080)</td>
</tr>
<tr>
<td>2MWT</td>
<td>0.2889(0.0828)</td>
<td>-0.3059(0.0656)</td>
<td>-0.1420(0.4017)</td>
<td>0.2209(0.1889)</td>
</tr>
<tr>
<td>EDSS</td>
<td>0.1812(0.2570)</td>
<td>0.3829(0.0135)</td>
<td>0.3639(0.0193)</td>
<td>-0.1530(0.3395)</td>
</tr>
<tr>
<td>Hip Flexion Strength</td>
<td>0.2256(0.1561)</td>
<td>-0.1301(0.4175)</td>
<td>0.2476(0.1186)</td>
<td>0.2319(0.1445)</td>
</tr>
</tbody>
</table>

Spearman’s R-value (p-value)
Results

- Can walking measures provide information that is not obtained from basic clinical data?
  - age, gender, symptom duration, EDSS

- We analyzed the data to determine the unique contribution of:
  1. Basic clinical information to MRI.
  2. Basic clinical information + walking measures to MRI.

MTR and Walking Measures

**Basic Clinical Measures alone:**
- $R^2 = -0.01489$

**Model with TUG, falls & age:**
- $R^2 = 0.2657$
  - TUG $p=0.000811$
  - Falls $p=0.004645$
\[ \lambda \] and Walking Measures

Basic Clinical Measures alone:

- \( R^2 = 0.2469 \)

Model with TUG, symptom duration & EDSS:

- \( R^2 = 0.3268 \)
  - TUG \( p=0.0257 \)
  - Symptom duration \( p=0.0134 \)
  - EDSS \( p=0.0299 \)

Fractional Anisotropy and Walking Measures

Basic Clinical Measures alone:

- \( R^2 = 0.055 \)

Model with T25W and symptom duration:

- \( R^2 = 0.2153 \)
  - T25W \( p=0.000957 \)
Summary

Quantitative measures of walking (T25W, TUG):
- Are related to MRI measures (MTR, λ, FA).
- Add additional information to the EDSS that is relevant to MRI measures.
- Are specific to the primary complaint (walking) of our patients.

Conclusions

- Our data links the CST to walking measures and highlights MTR as an important addition to structural MRI protocols.
- Evaluating structure-function relationships is important for the development of quantitative outcome measures that are specific to patient complaints.
Future Directions

- Establish Minimal Detectable Change (MDC) for these walking measures in MS
- Expand the analysis to include volumetric imaging
- Understand the relationship of MRI to falls data
- Determine the predictive value of MRI and clinical measures in evaluating intervention responsiveness

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References


