DALFAMPRIDINE MAY ENHANCE THE EFFECTS OF PHYSICAL THERAPY ON GAIT IN PEOPLE WITH MULTIPLE SCLEROSIS

Prue Plummer1, Whitney Huryta2, Jessica Reynolds3, Silva Markovic-Plese1, Barbara Giesser4

1University of North Carolina at Chapel Hill, Chapel Hill, NC; 2Pivot Physical Therapy, Burlington, NC; 3Allied Rehab, Wake Forest, NC; 4University of California Los Angeles, Los Angeles, CA

RATIONALE
- Dalamanpridine extended-release (DER) is a drug that improves gait speed in some people with MS.
- The therapeutic benefit of DER occurs in only 38% of patients.
- Physical therapy (PT) can also improve gait speed in MS and may be a valuable adjunct to DER.

OBJECTIVE
To estimate the effect size of combining DER with PT on gait speed in people with MS, and to compare the effects to PT without DER.

METHODS
Participants:
- 8 people with MS with self-reported walking difficulty
- 4x4 starting DER (usual care), 4x4 not taking DER (Table 1)

DER Intervention: 10 mg twice per day, as prescribed
PT Intervention:
- One-on-one multicomponent exercise and gait training with a physical therapist, 2x/week for 6 weeks, 40 mins per session
- Functional strengthening, balance, gait (treadmill and overground), and dual task training

Primary and secondary outcome measures were assessed at weeks 0, 3, 9, 12. Participants taking DER continued medication in the follow up period.

Table 1. Participant characteristics

<table>
<thead>
<tr>
<th>Group/subject</th>
<th>Age (years)</th>
<th>Gender</th>
<th>MS Type</th>
<th>MS duration (years)</th>
<th>Fear of falling # falls last year</th>
</tr>
</thead>
<tbody>
<tr>
<td>DER+PT 1</td>
<td>59</td>
<td>F</td>
<td>RRMS</td>
<td>6</td>
<td>Y</td>
</tr>
<tr>
<td>DER+PT 2</td>
<td>59</td>
<td>F</td>
<td>RRMS</td>
<td>1.2</td>
<td>N</td>
</tr>
<tr>
<td>DER+PT 3</td>
<td>42</td>
<td>F</td>
<td>RRMS</td>
<td>4.3</td>
<td>Y</td>
</tr>
<tr>
<td>DER+PT 4</td>
<td>38</td>
<td>F</td>
<td>RRMS</td>
<td>2</td>
<td>Y</td>
</tr>
<tr>
<td>DER+PT total</td>
<td>49.5 (SD 11.1)</td>
<td>F</td>
<td>RRMS</td>
<td>6.1 (SD 4.3)</td>
<td>5.5 (SD 5.2)</td>
</tr>
<tr>
<td>PT 1</td>
<td>63</td>
<td>F</td>
<td>SPMS</td>
<td>15.5</td>
<td>N</td>
</tr>
<tr>
<td>PT 2</td>
<td>65</td>
<td>F</td>
<td>RRMS</td>
<td>5.8</td>
<td>N</td>
</tr>
<tr>
<td>PT 3</td>
<td>53</td>
<td>M</td>
<td>PPMs</td>
<td>0.5</td>
<td>N</td>
</tr>
<tr>
<td>PT 4</td>
<td>29</td>
<td>F</td>
<td>RRMS</td>
<td>6</td>
<td>Y</td>
</tr>
<tr>
<td>PT total</td>
<td>52.5 (SD 16.5)</td>
<td>F</td>
<td>RRMS</td>
<td>6.7 (SD 6.3)</td>
<td>1.8 (SD 1.0)</td>
</tr>
</tbody>
</table>

SELF-SELECTED SINGLE-TASK AND DUAL-TASK GAIT SPEED

Figure 1. 25FW changes in (A) seconds and (B) percent change from baseline. Bars = SEM
- All DER participants fell below the 20% improvement clinically important threshold after 3 weeks of DER (mean: 12.8%, range: 5.8-19.4%)
- Significantly greater improvement in T25FW from week 3-9 in DER group (p=0.004)
  - DER+PT increase 20.7% (95% CI: 3.8-37.6)
  - PT group by 6.8% (95% CI: 3.4-10.3)
- Overall week 0-9 increase in T25FW was 30.5% for DER+PT, with all participants exceeding clinically important “responder” threshold of 20% improvement.

SECONDARY OUTCOMES

Figure 3. Changes in (A) ABC and (B) MSWS-12 scores
- Balance self-efficacy (ABC score)
  - Both groups significantly improved in balance self-efficacy in week 3-9 (no change week 0-3)
  - Significantly greater improvement in the DER+PT group (21.6 points) than the PT group (7.0 points) (p=.003)

Self-perceived walking disability (MSWS-12)
- No change in self-rated disability in DER+PT group week on DER only (week 0-3), consistent with actual gait speed changes
- DER+PT group significantly improved week 3-9
- No change in PT group, but these participants had lower perceived walking disability, on average, at baseline

SUMMARY
- PT may enhance the effects of DER on gait speed in people with MS who do not reach the responder threshold for a meaningful improvement on DER alone
- DER may enhance the effects of PT and exercise, since the benefits of PT were greater in those taking DER
- There was large variation between participants, so larger studies are needed to obtain more precise estimates of treatment effects

References & Acknowledgements
2. Plummer Int J MS Care 2016;18:105-115

The authors thank Gozde Ilgum and Jasmine Martin for conducting the evaluations, and Amy Thomas, Corinne Bohlig, Alexis Williams, and Ellesse Nickles for assistance providing PT interventions. We sincerely thank the staff at Steps For Recovery and the Campbell University Department of Physical Therapy for providing intervention facilities. This research was supported by the National MS Society (PP-1503-03458, Plummer).

2. Plummer Int J MS Care 2016;18:105-115