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

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RATIONALE

- Dalfampridine extended-release (DER) is a drug that improves gait speed in some people with MS[1]
- The therapeutic benefit of DER occurs in only 38% of patients[1]
- Physical therapy (PT) can also improve gait speed in MS and may be a valuable adjunct to DER[2,3]

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
- n=4 starting DER (usual care), n=4 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.

Primary outcome measure:

- Timed 25 Foot Walk Test (T25FW): fastest safe speed

Secondary outcome measures:

- Single task gait speed (self-selected speed)
- Dual task gait speed (walking with "clock task")
- MSWS-12: self-perceived walking ability
- ABC scale: balance self-efficacy

GAIT SPEED OUTCOMES

Table 1. Participant characteristics

Group/subject	Age (years)	Gender	MS Type	MS duration (years)	Fear of falling	# falls last year
DER+PT 1	59	F	RRMS	6	Y	1
DER+PT 2	59	F	RRMS	12	N	7
DER+PT 3	42	F	RRMS	4.3	Y	2
DER+PT 4	38	F	RRMS	2	Y	12
DER+PT total	**49.5 (SD 11.1)**			**6.1 (SD 4.3)**		**5.5 (SD 5.1)**
PT 1	63	F	SPMS	15.5	N	1
PT 2	65	F	RRMS	5.8	N	1
PT 3	53	M	PPMS	0.5	N	3
PT 4	29	F	RRMS	5	Y	2
PT total	**52.5 (SD 16.5)**			**6.7 (SD 6.3**		**1.8 (SD 1.0)**

TIMED 25-FOOT WALK

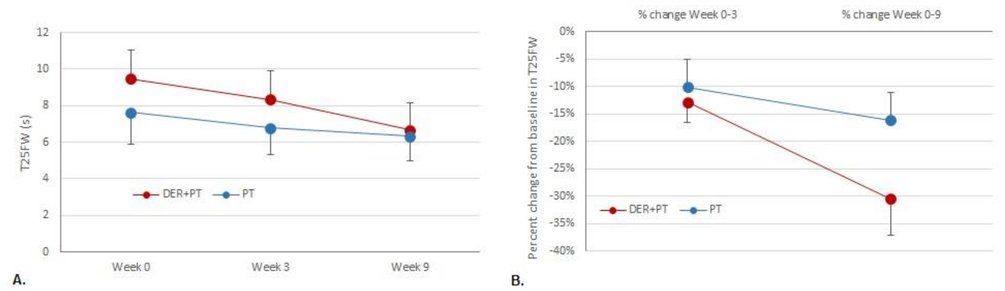

Figure 1. T25FW changes in (A) seconds and (B) percent change from baseline. Bars = SEM

- 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=.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

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

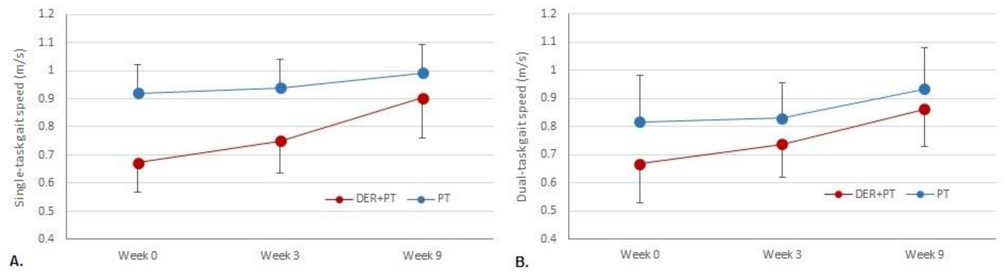

Figure 2. Gait speed changes in (A) single-task self-selected speed and (B) dual-task self-selected speed. Bars = SEM

- Single-task gait speed: significant Group x Time interaction (p=.02, η_p^2=0.48)
  - DER+PT significant increase in gait speed week 3-9 (**0.15 m/s,** SD 0.09)
  - PT group no change
- Dual-task gait speed: main effect of Time (p=.005, η_p^2=0.59)
  - Significant increase in dual-task gait speed during PT phase (week 3-9, **0.10 m/s**)

SECONDARY OUTCOMES

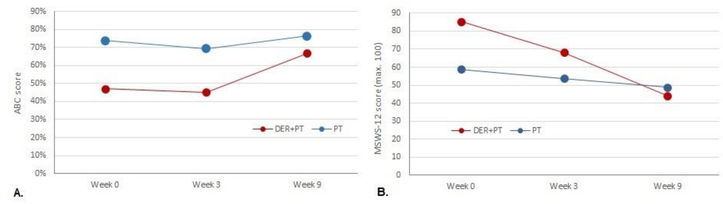

Figure 3. Changes in (A) ABC and (B) MSWS-12 scores

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

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2. Plummer *Int J MS Care* 2016;18:105-115
3. Vaney et al. 2012. *Neurorehabil Neural Repair* 2012;26:212-221
4. Goodman et al. *Neurology* 2008;71:1134-1141

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