UIC Department of Physical Therapy
UNIVERSITY OF ILLINOIS AT CHICAGO
COLLEGE OF APPLIED HEALTH SCIENCES

RIC
Rehabilitation Institute *of* Chicago

Combined pharmacological and physical interventions following neurological injury

T. George Hornby, PT, PhD

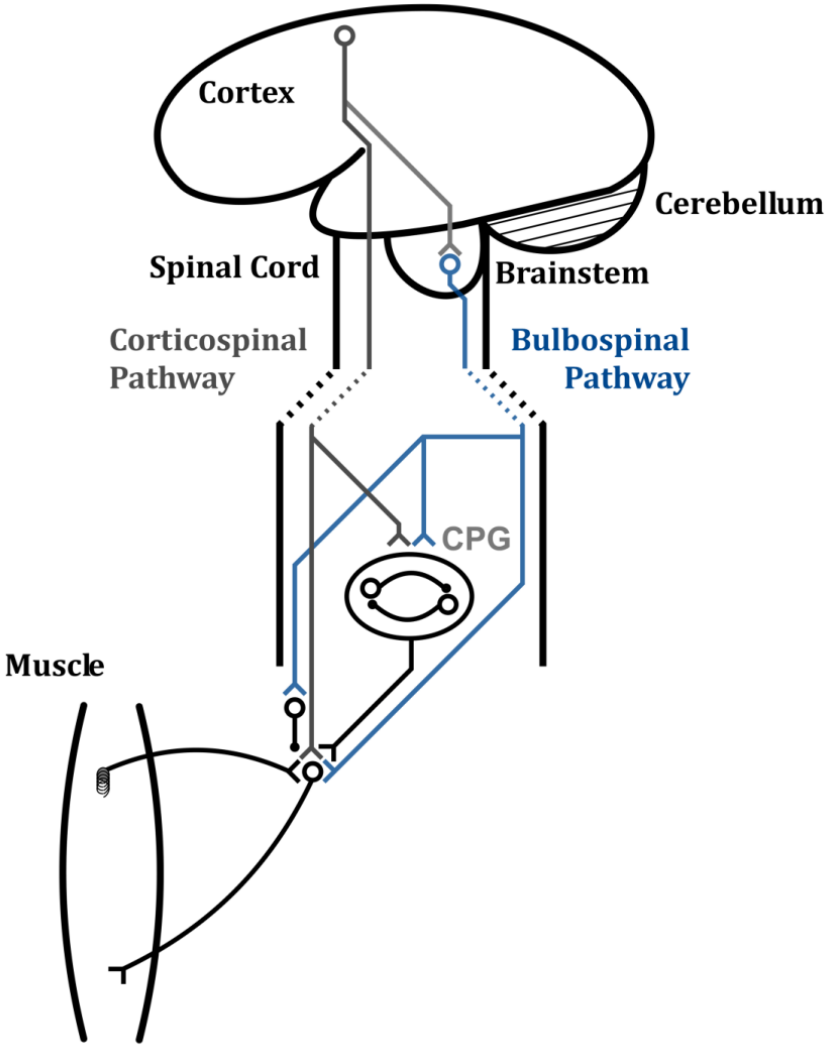
Associate Professor, Department of Physical Therapy and Kinesiology and Nutrition, University of Illinois at Chicago

Director, Locomotor Recovery Laboratory,
Research Scientist, Sensory Motor Performance Program,
Rehabilitation Institute of Chicago

Outline

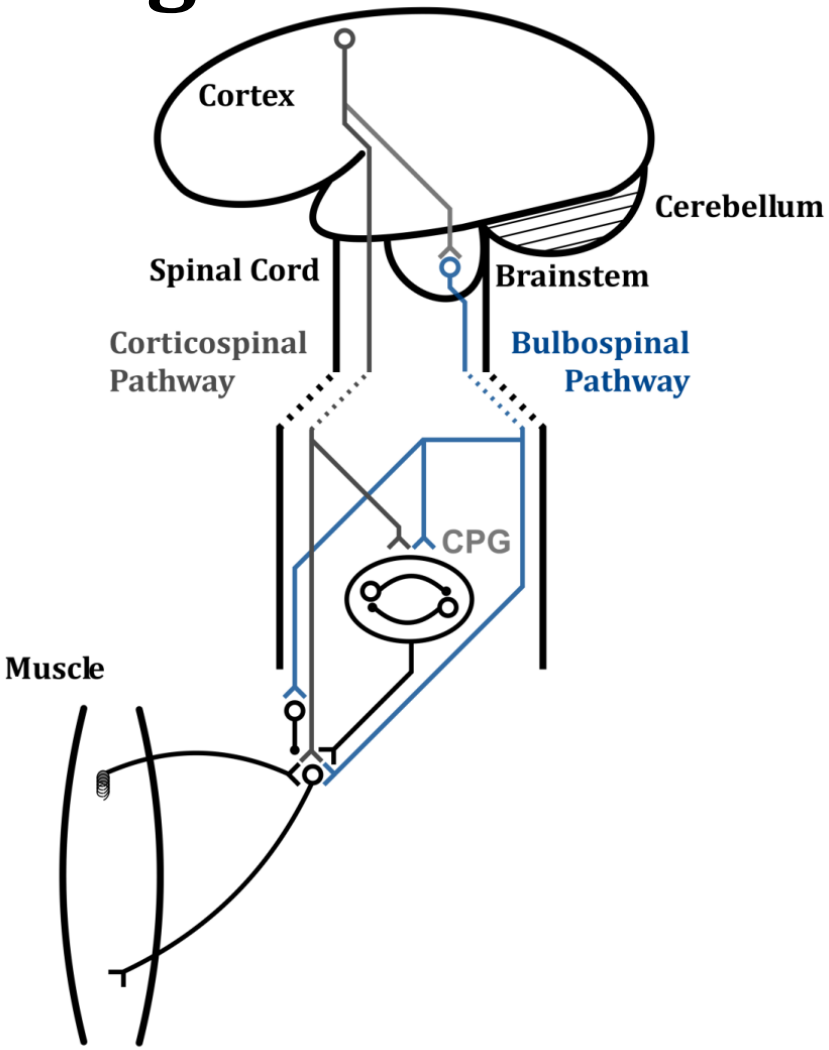
- Single dose agents do not significantly/substantially effect function
  - Divergent effects on volitional and reflex motor behaviors
  - No effect of functional task performance

- Effects of combined pharmacological and physical interventions



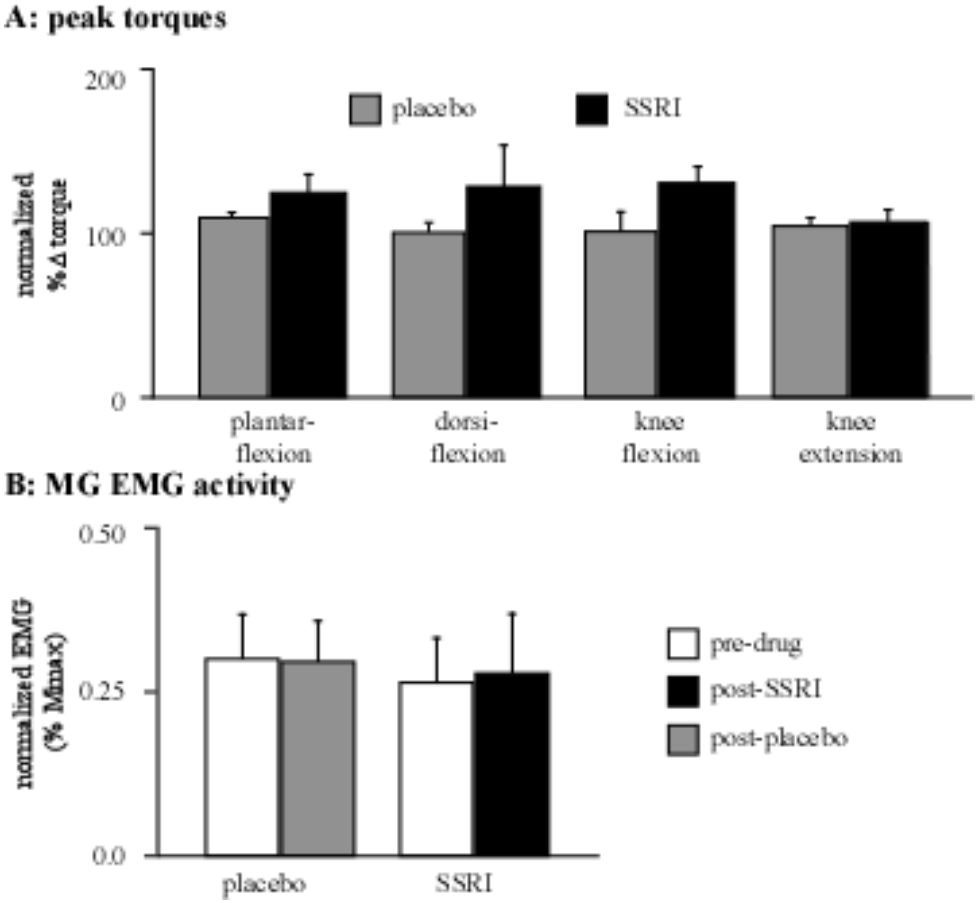
Influences of descending monoaminergic agents

- Bulbospinal pathways provide modulatory (5HT/NE) inputs to spinal circuits
  - Inhibit afferent/pain input (5HT1, NEα2)
  - Activate central circuits (5HT7, NEα2)
  - Modulate motoneurons (NEα1, 5HT2)
- Partially restore 5HT influences with broad-spectrum 5HT facilitators (SSRIs)
- Problem? Super-sensitivity, constitutively active 5HT receptors – recovery of volitional strength and reflex activity



Escitalopram influences volitional and reflex excitability

- SSRIs generate moderate increases in maximal volitional contractions in lower extremities (Gourab et al 2015; c.f,, however F. Chollet)



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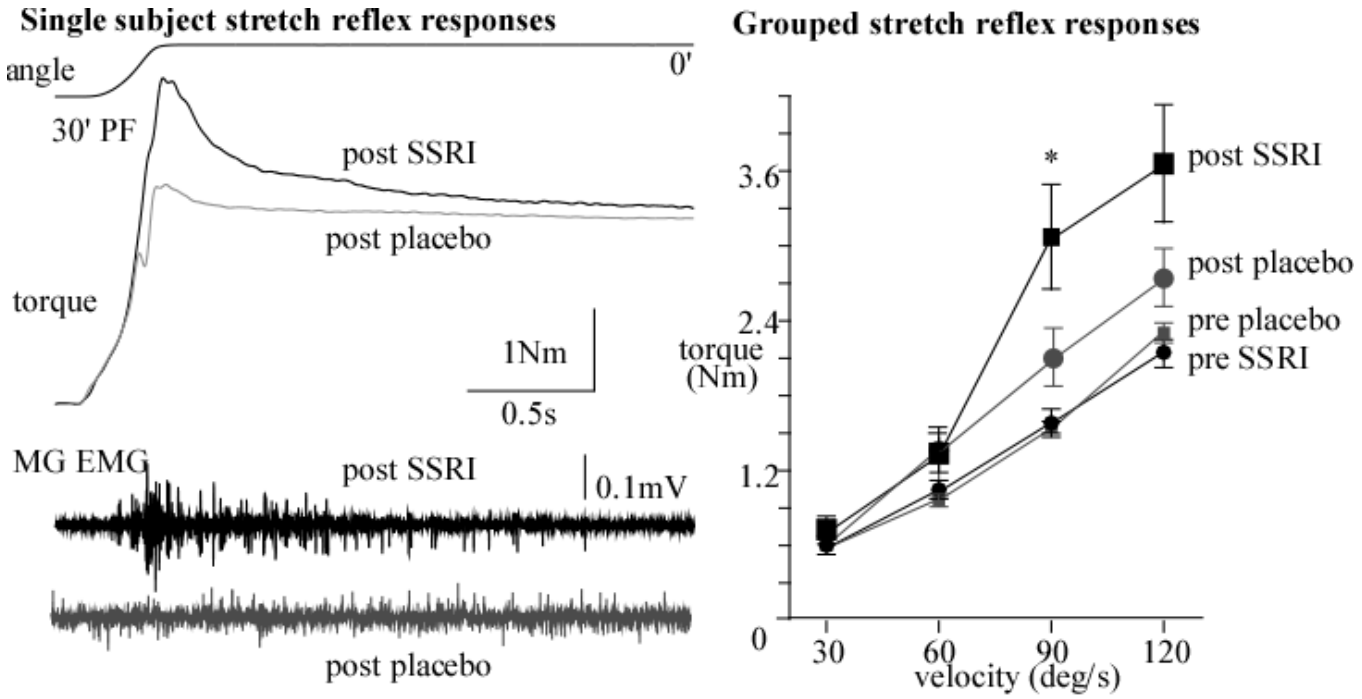

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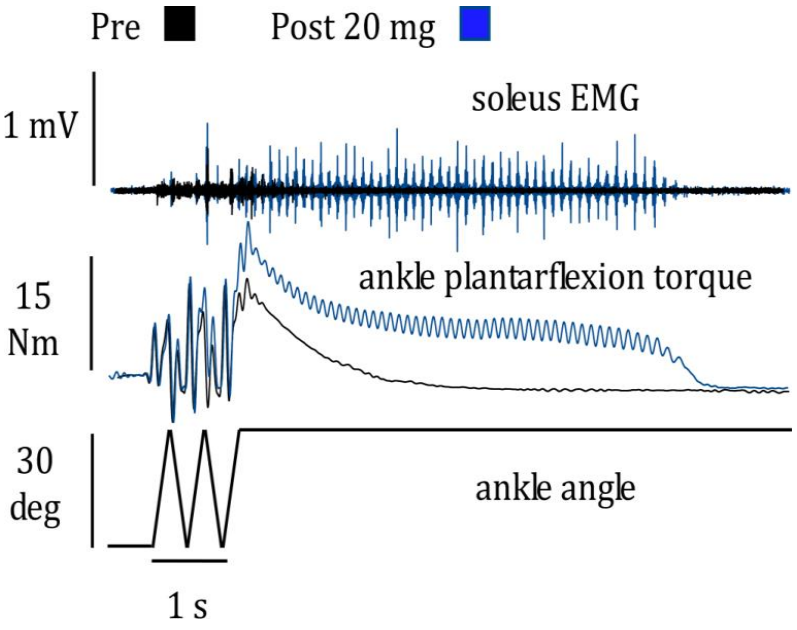

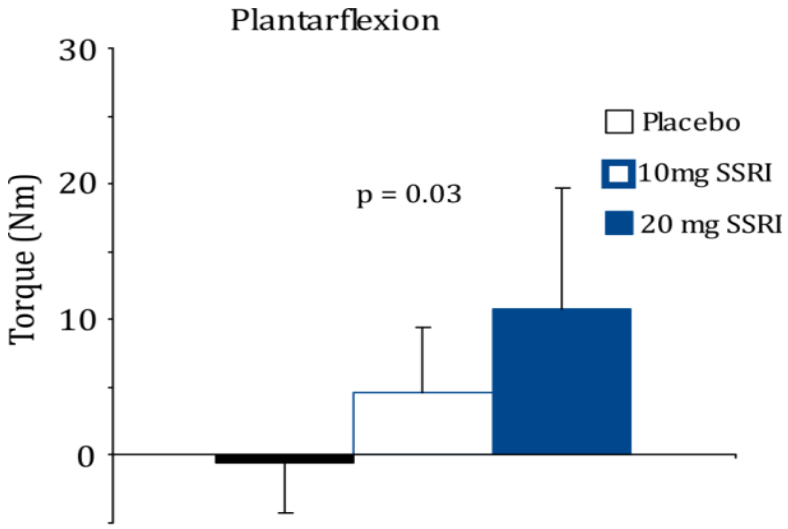

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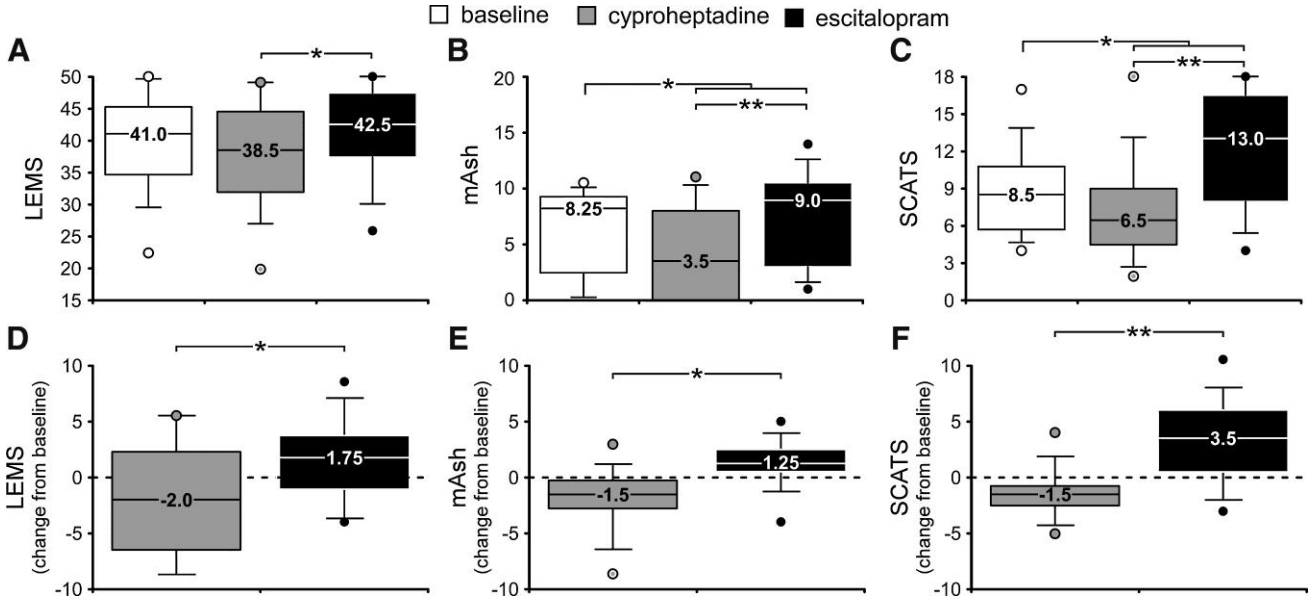
- Somewhat consistent with previous effects in upper extremity, although limited previous mention of increased abnormal responses (Stolp-Smith and Wainberg 1999)
  - Mono- to di-synaptic pathways
  - None to few intermediary interneurons

Cyproheptadine vs escitalopram

- Divergent responses of 5HT agents on volitional and reflex excitability (Thompson et al 2013 – incomplete SCI)



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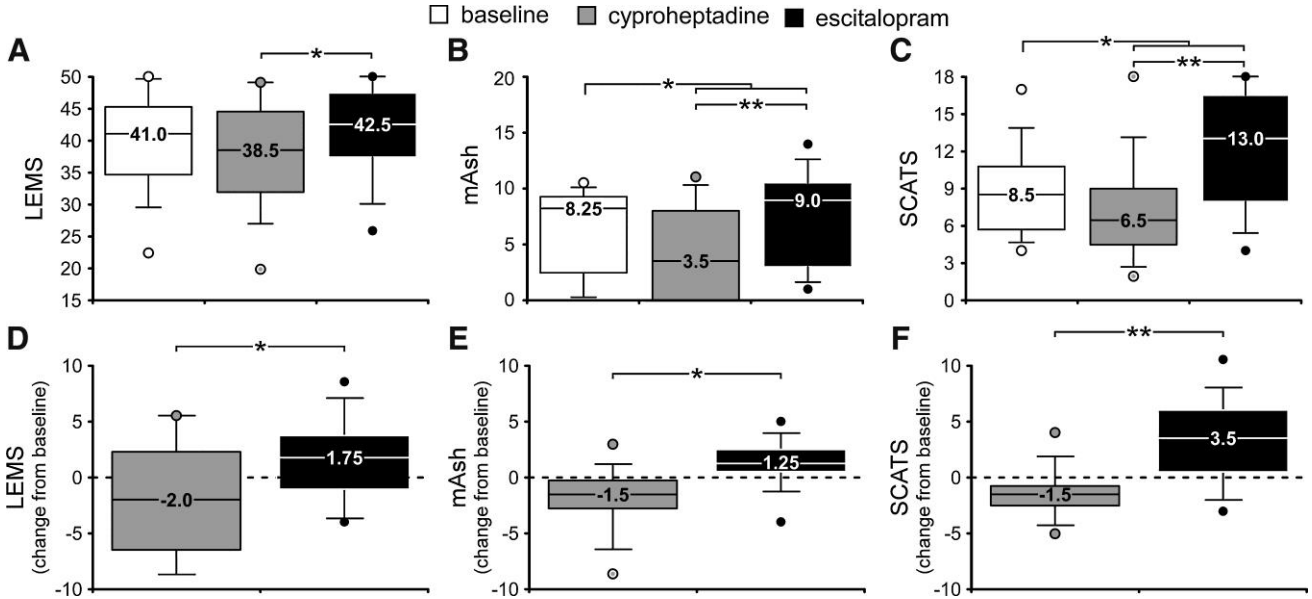
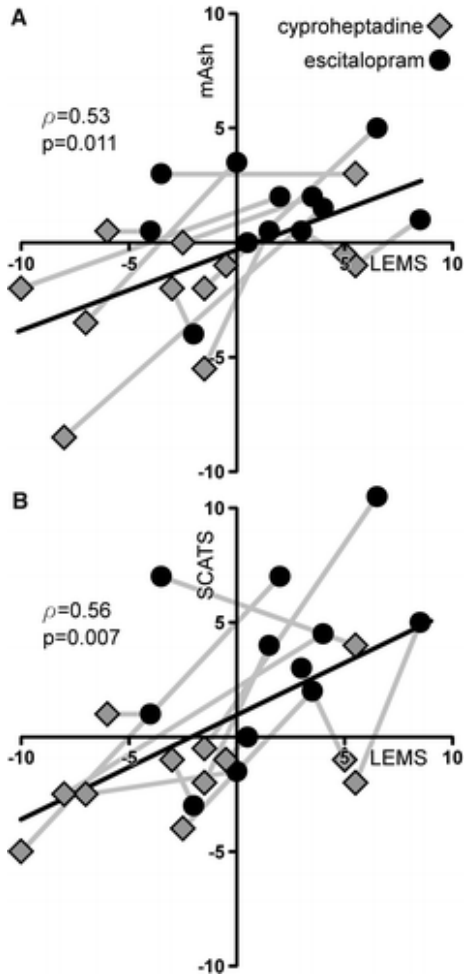
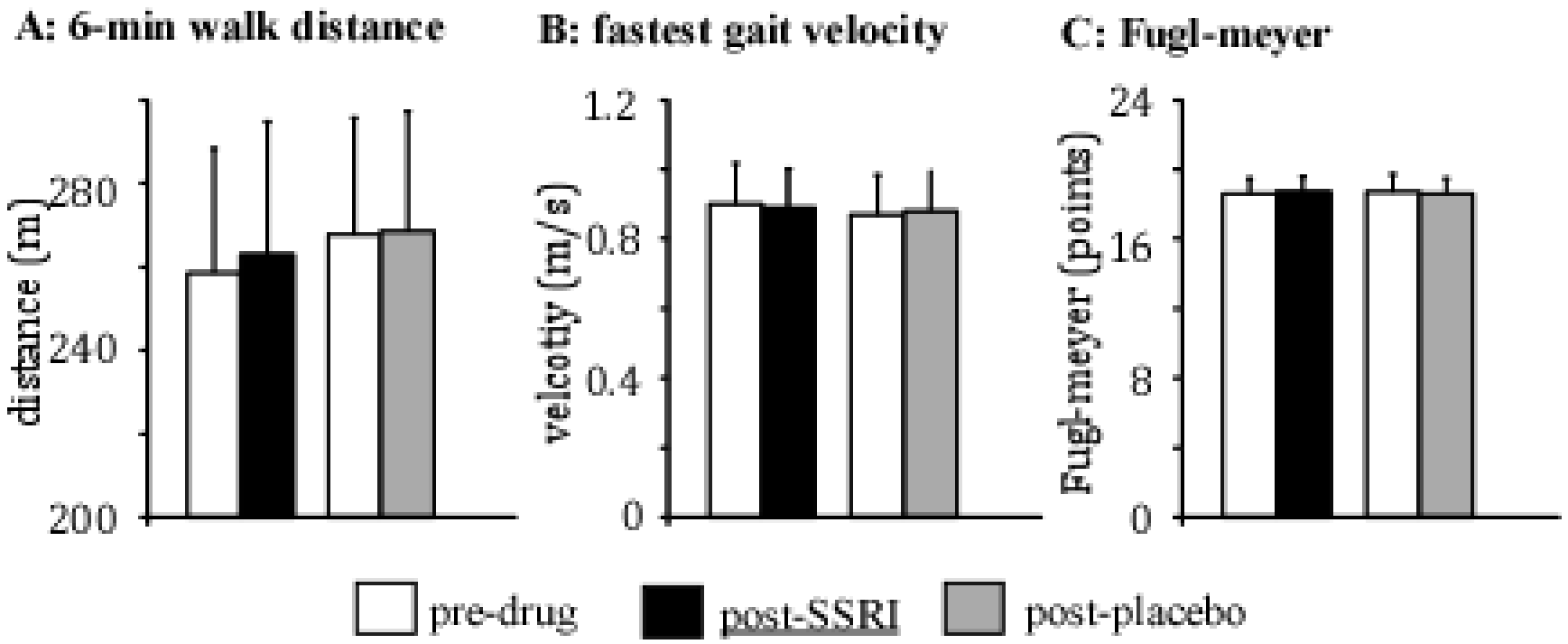




Cyproheptadine vs escitalopram

- Effects on locomotor performance
  - Stroke: Gourab et al 2015



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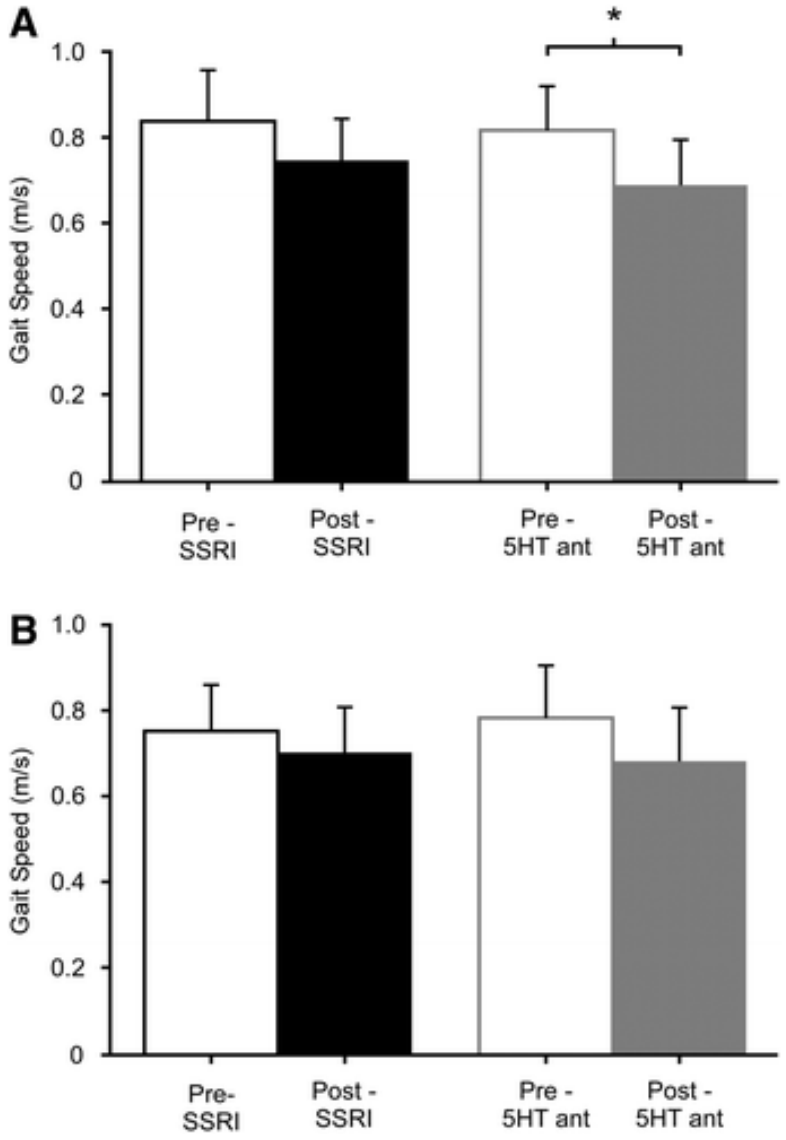
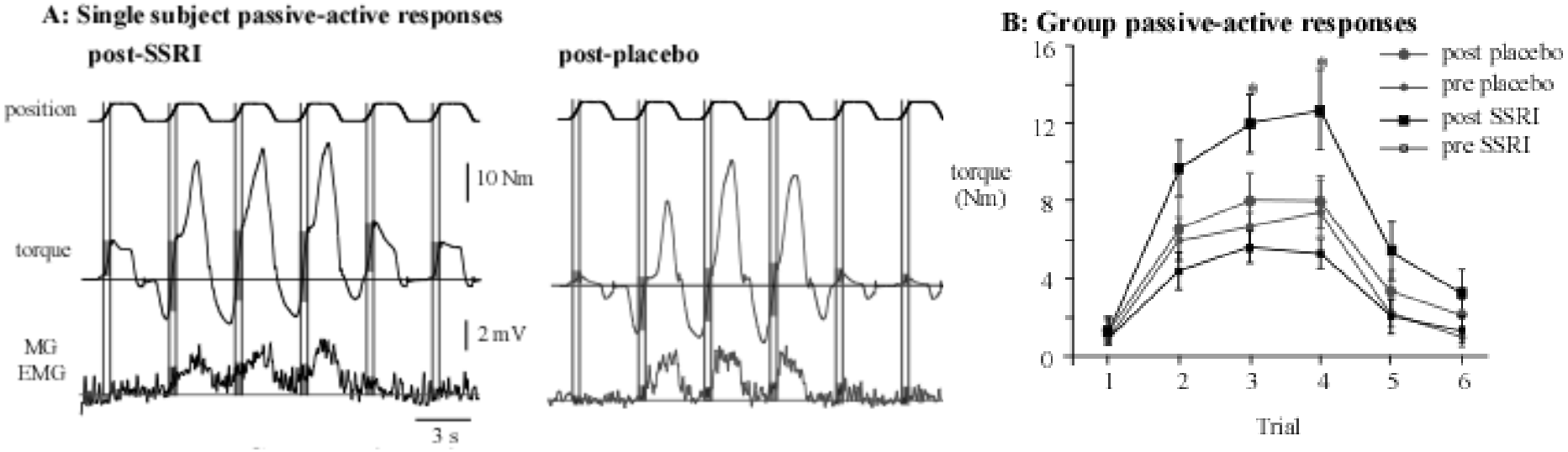


Cyproheptadine vs escitalopram

- Effects on locomotor performance
  - Stroke: Gourab et al 2015
  - SCI: Leech et al 2014
- Exaggerated effects with superimposed volitional activity (dorsiflexion MVCs with plantarflexor stretch)



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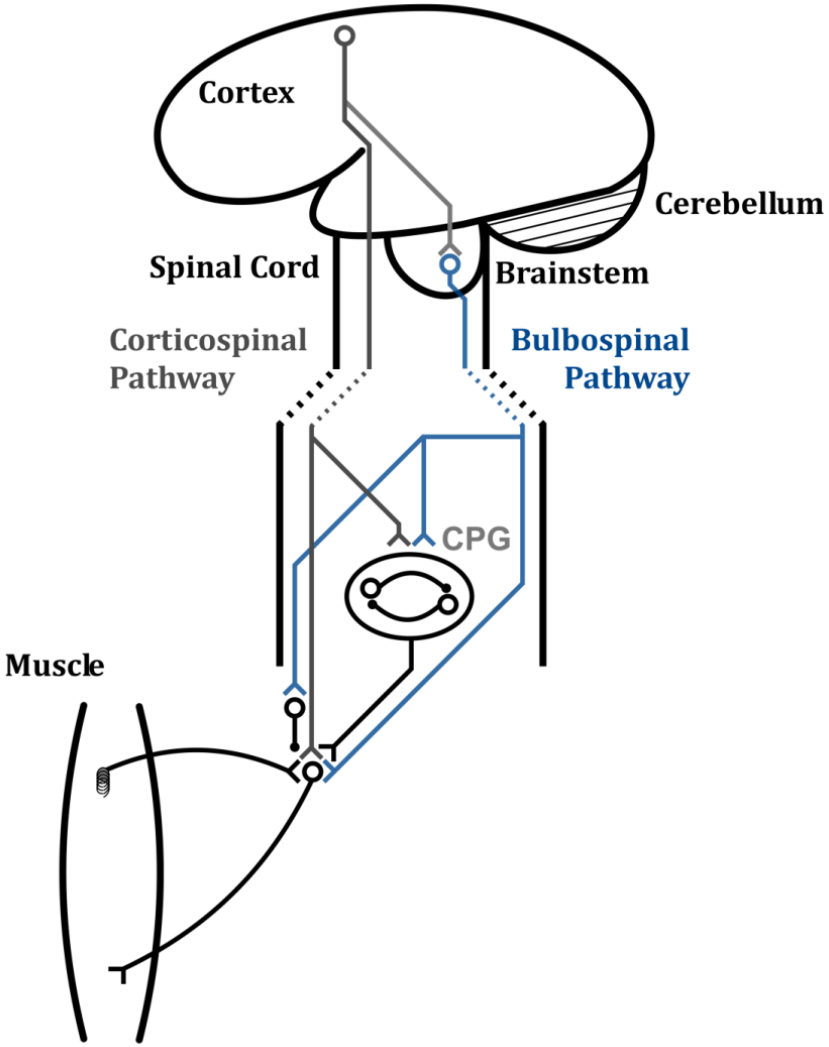
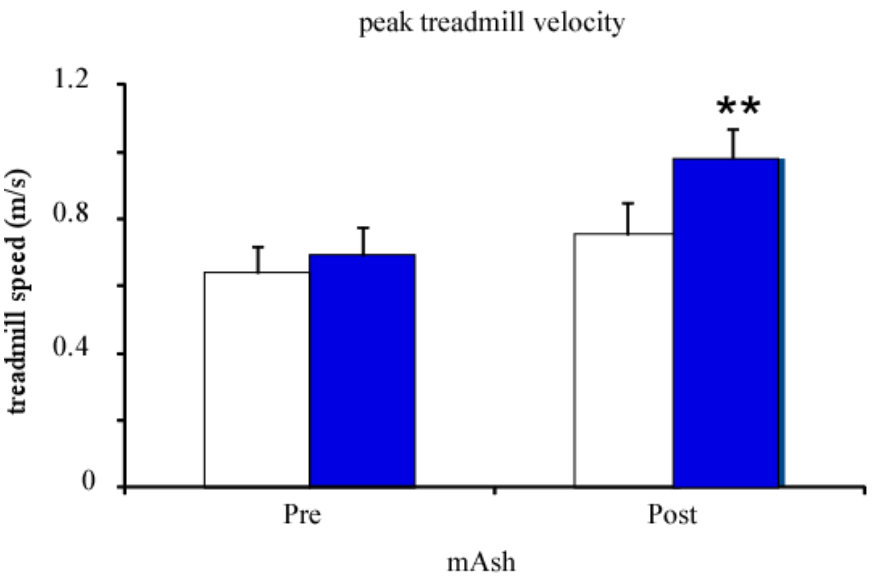
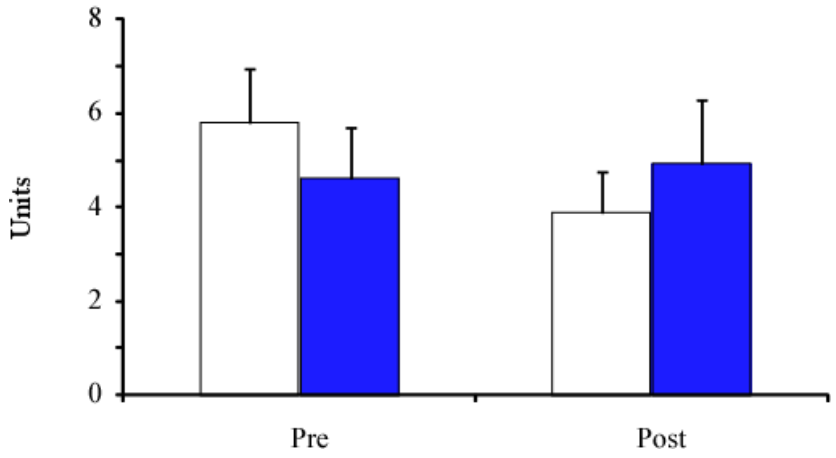


Chronic doses with training

- Randomized, blinded clinical trial
  - 8 weeks treadmill training with and without SSRI administration
  - SSRIs/placebo only on days of training
  - 34 ambulatory subjects > T10 incomplete SCI



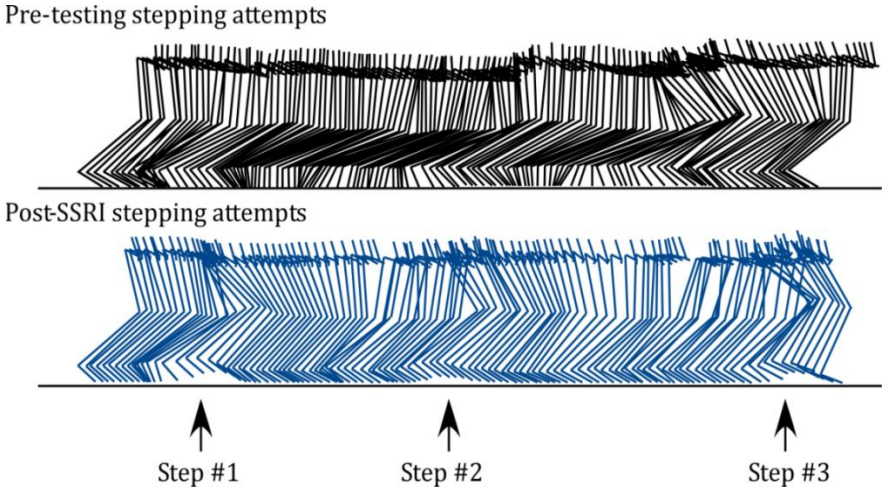
- Results
  - Significant difference in changes in peak treadmill speeds
  - Significant difference in modified Ashworth scores favoring control group
  - Spasticity may not matter



Current/future directions- single/chronic doses in subacute SCI

- Single dose responses – prior to following acute SSRI administration

Pre to Post-SSRI administration



Acknowledgements

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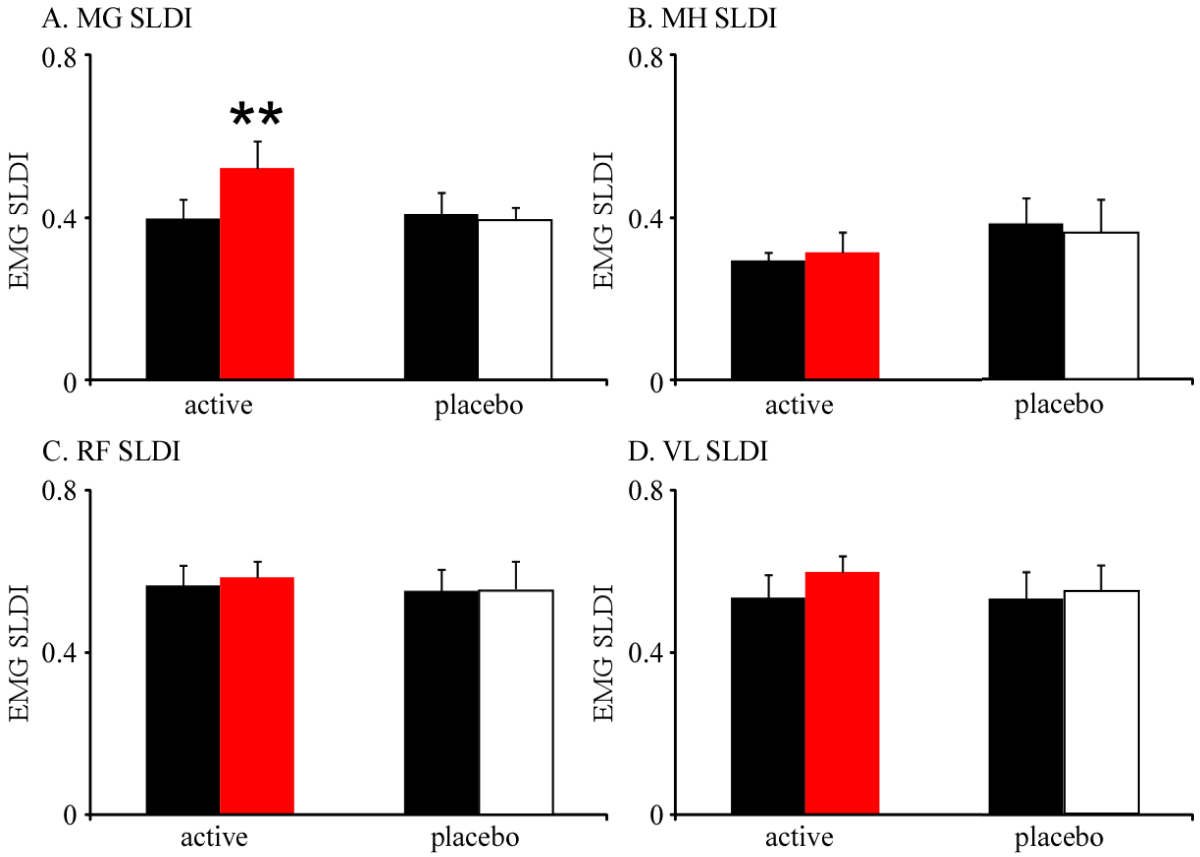
Results – Single dose study: muscle activity patterns

- Significantly worse MG timing (SLDI) with SSRI vs placebo (drug * test interaction)
- No other differences noted – trend towards worsening with SSRIs



Results – Repeated doses-LT study: spatiotemporal parameters

- *Significant* improves favoring SSRI vs placebo on treadmill only:
  - **D Peak speed** (0.17±0.17 vs 0.05±0.15 m/s p < 0.001)
  - **D paretic step length** (0.09±0.08 vs 0.03±0.07 m, p<0.01)
  - **D non-paretic step length** (0.10±0.10 vs 0.01±0.08 m; p=0.02)
  - No difference in cadence (p=0.25)