Activity Based Neuroplastic Interventions Individuals with Spinal Cord Related Paralysis

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Disclosures

- No conflicts of interest
- No other disclosures

Neuroplasticity

- the ability of the nervous system to change its activity in response to intrinsic or extrinsic stimuli by reorganizing its structure, functions, or connections after injuries

Activity Promotes Spinal Learning

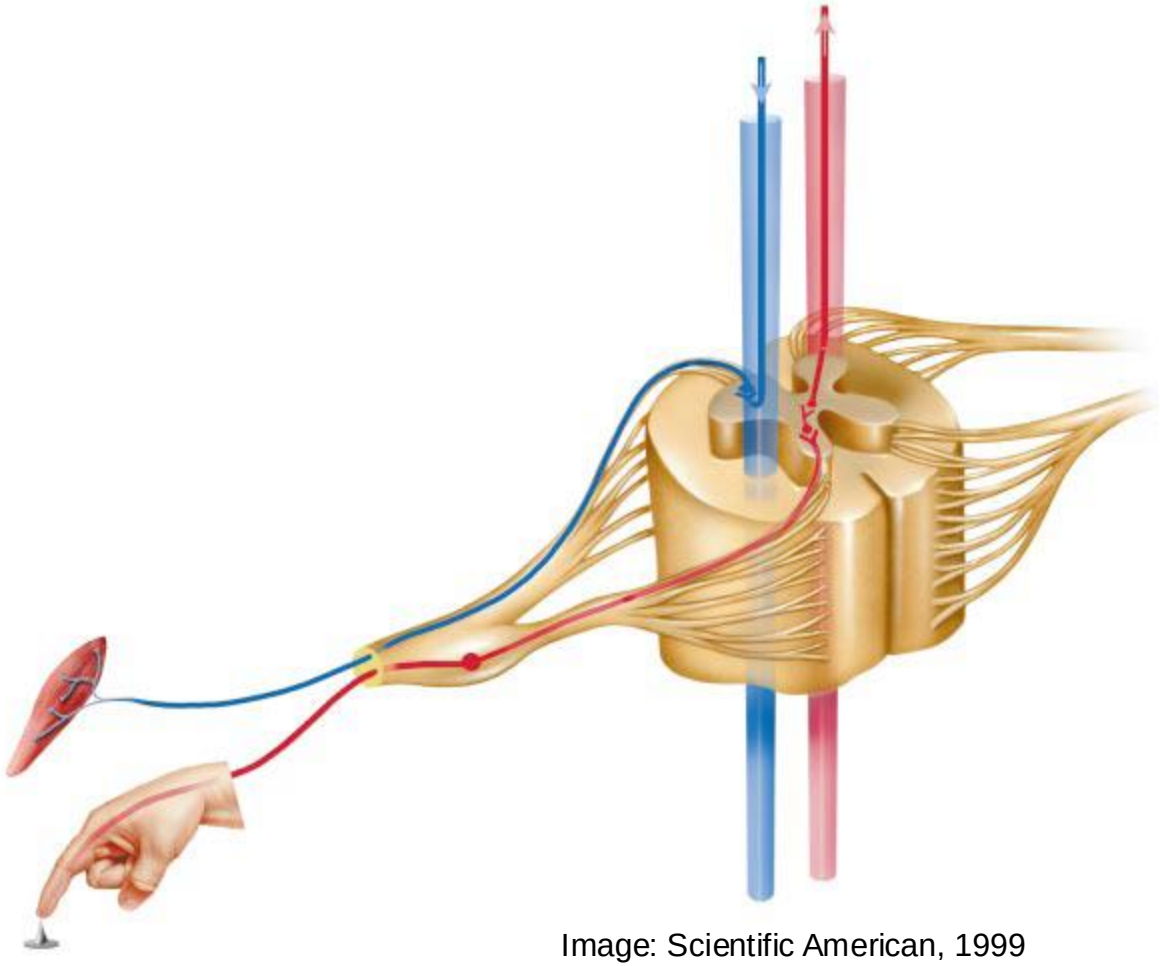
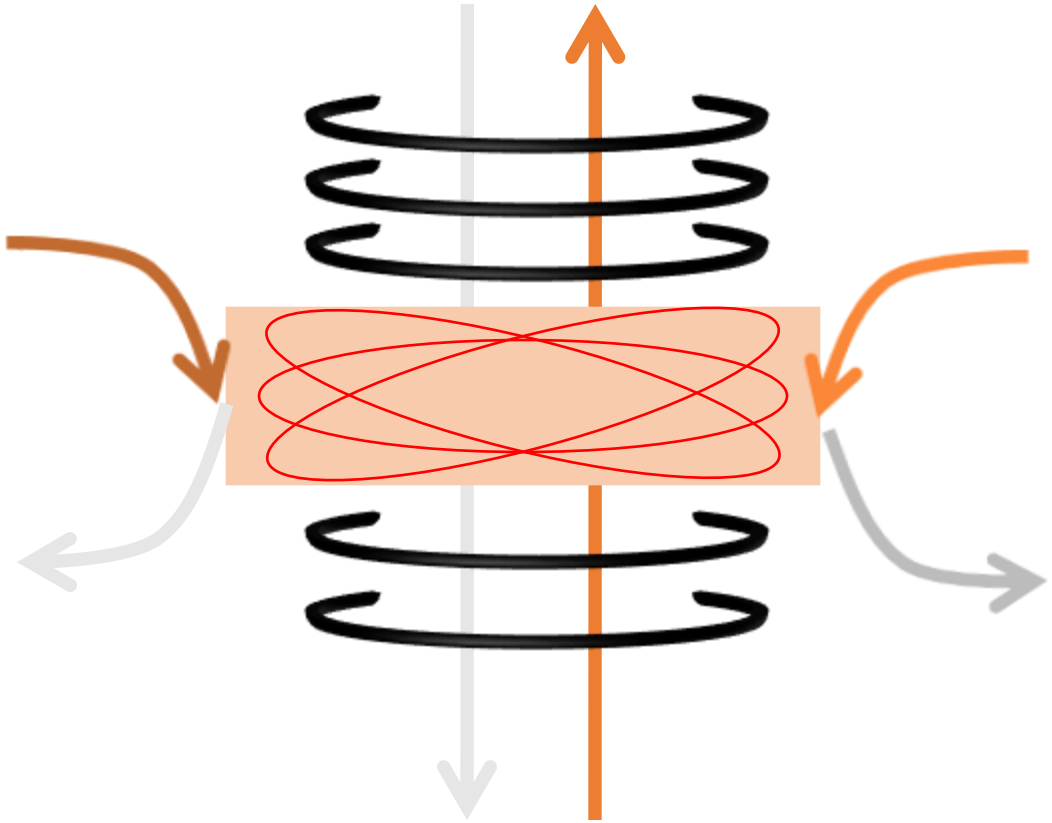
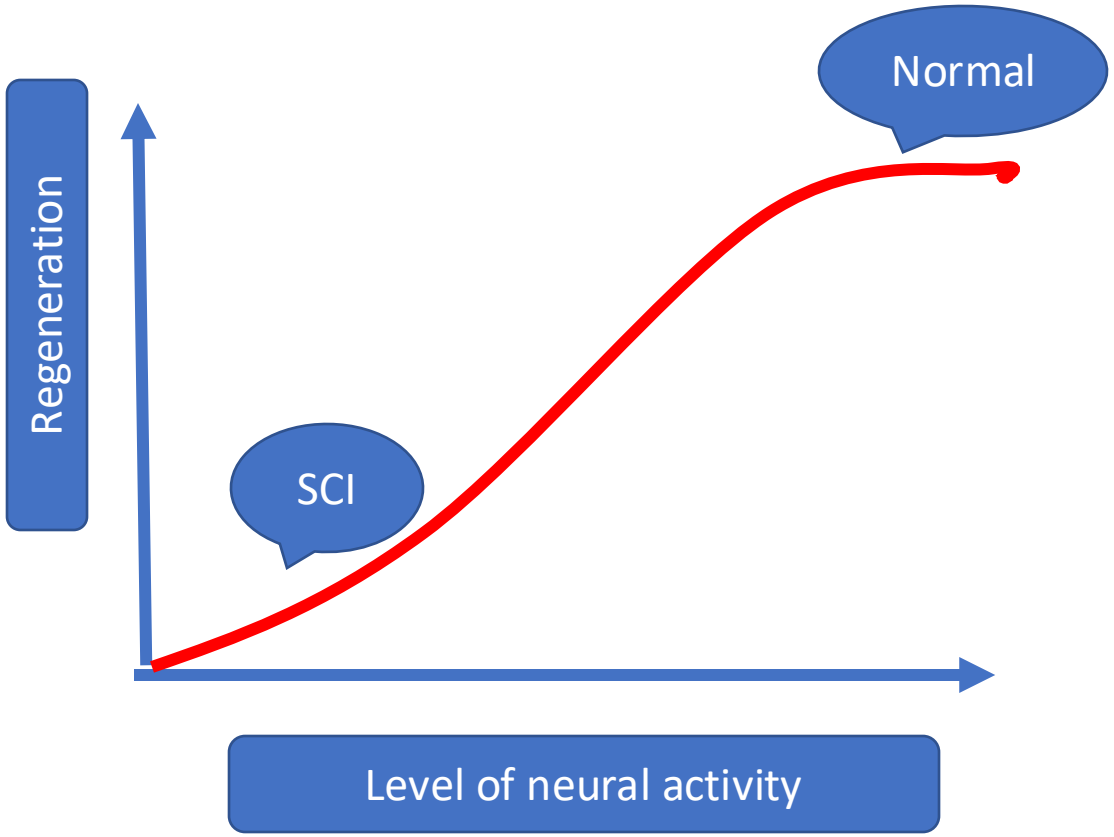


Image: Scientific American, 1999



Central pattern generator CPG

Activity


Normal
Regeneration
SCI
Level of neural activity

Activity Based Restorative Therapy (ABRT) framework

- Higher intensity and frequency
- Stimulation above *and* below the level of the injury
- Optimizing the nervous system for recovery
- Enhancing the physical integrity of the body

Not all rehabilitation is created equal

Traditional - Compensation

- Activate nervous system above the level of the lesion
- Low intensity practice (1 hour per day)
- Non-patterned movements
- Compensates for loss function
- Uses compensatory devices

Activity Based - Restoration

- Activate nervous system above and below the level of the lesion
- Massed/High intensity practice (2-5 hours per day)
- Non-patterned and patterned movements/task specificity
- Restores lost function

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ABRT Premises

- Optimizing spontaneous regeneration & functional recovery; goal is partial repair, as ‘micro’ repair produces disproportionate return of function and improvement in quality of life
- Maximizing physical integrity
- Sustained (“maintenance”) intervention is required

ABRT: Key Therapeutic Components

1. (Functional) Electrical Stimulation FES/Transcutaneous spinal cord stimulation TCSS

2. Locomotor Training (+/- Acute intermittent hypoxia AIH)

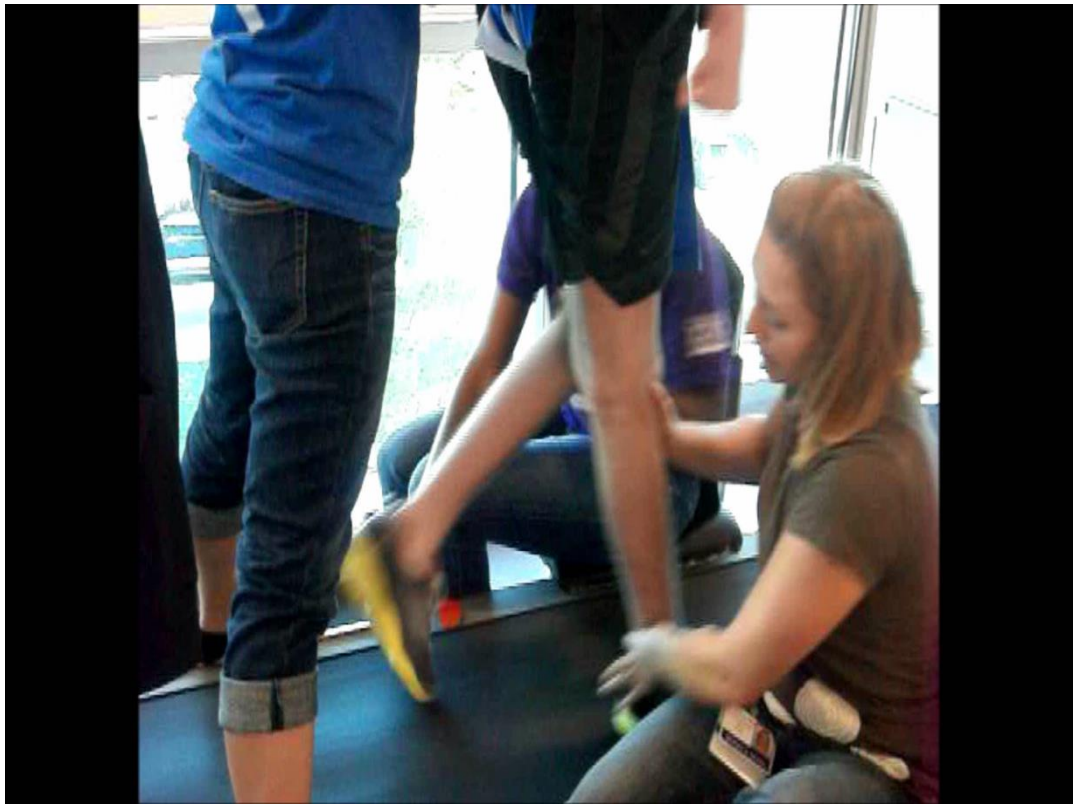
3. Weight Bearing/Loading

4. Massed and 5. task specific practice (+/- Acute intermittent hypoxia AIH)

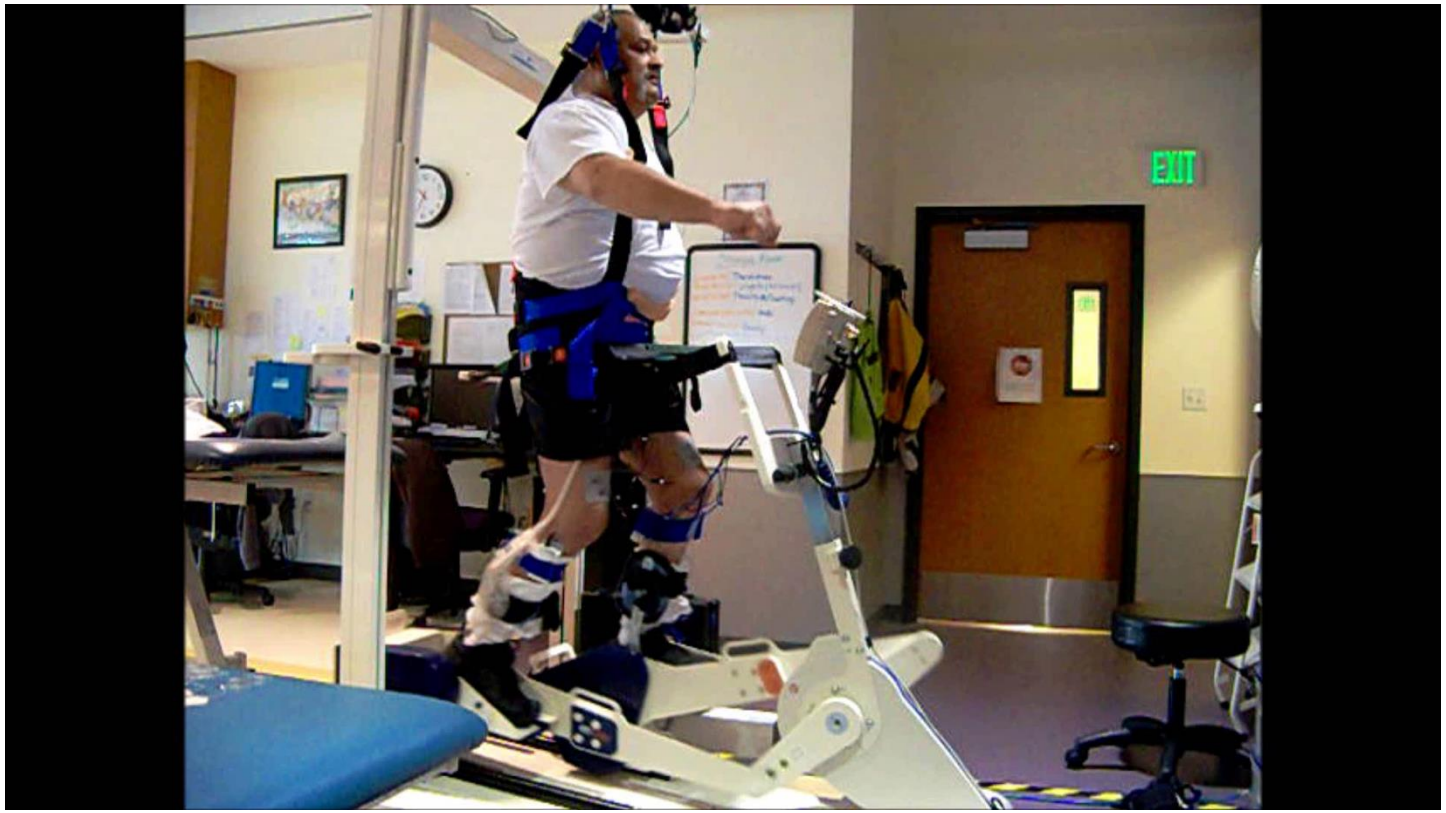
+ Others (aquatic therapy; vibration)

1. FES

2. LOCOMOTOR TRAINING

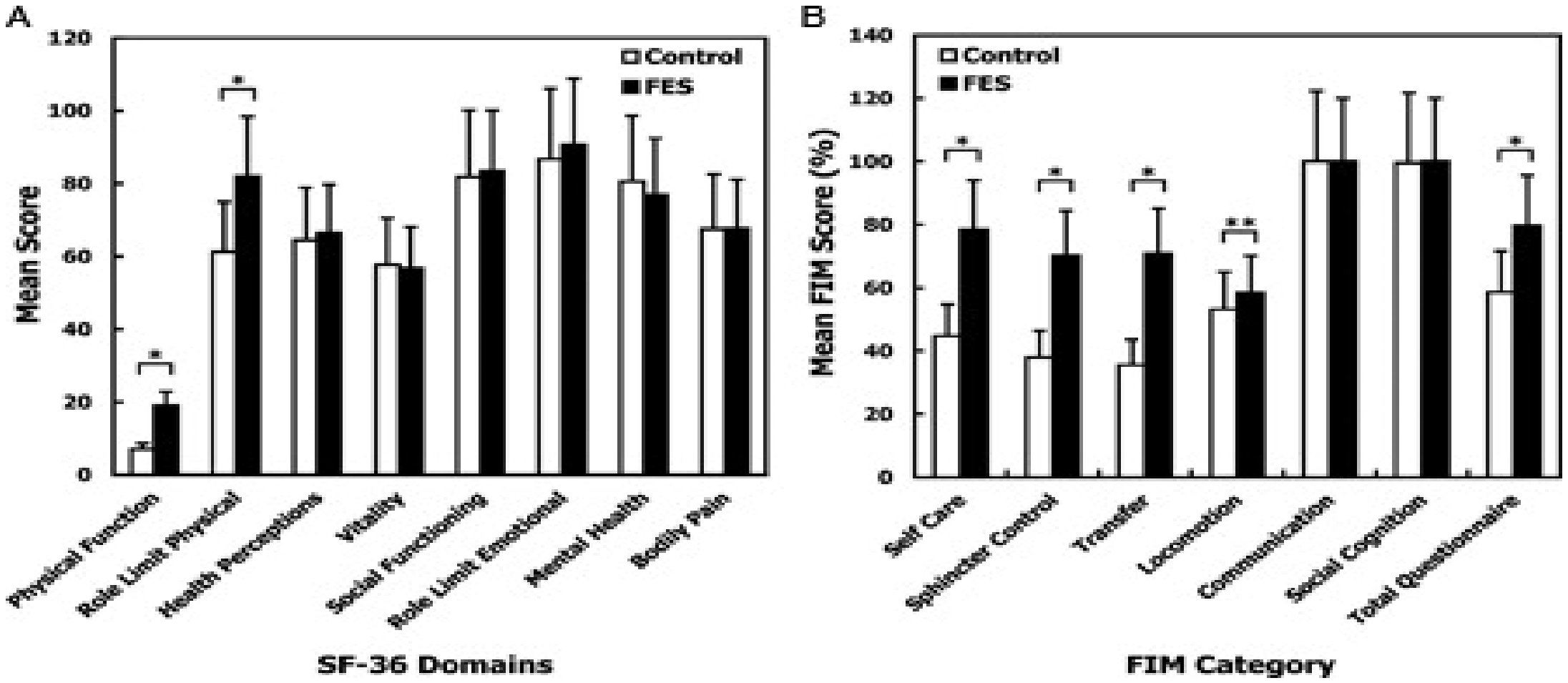


3. WEIGHT LOADING

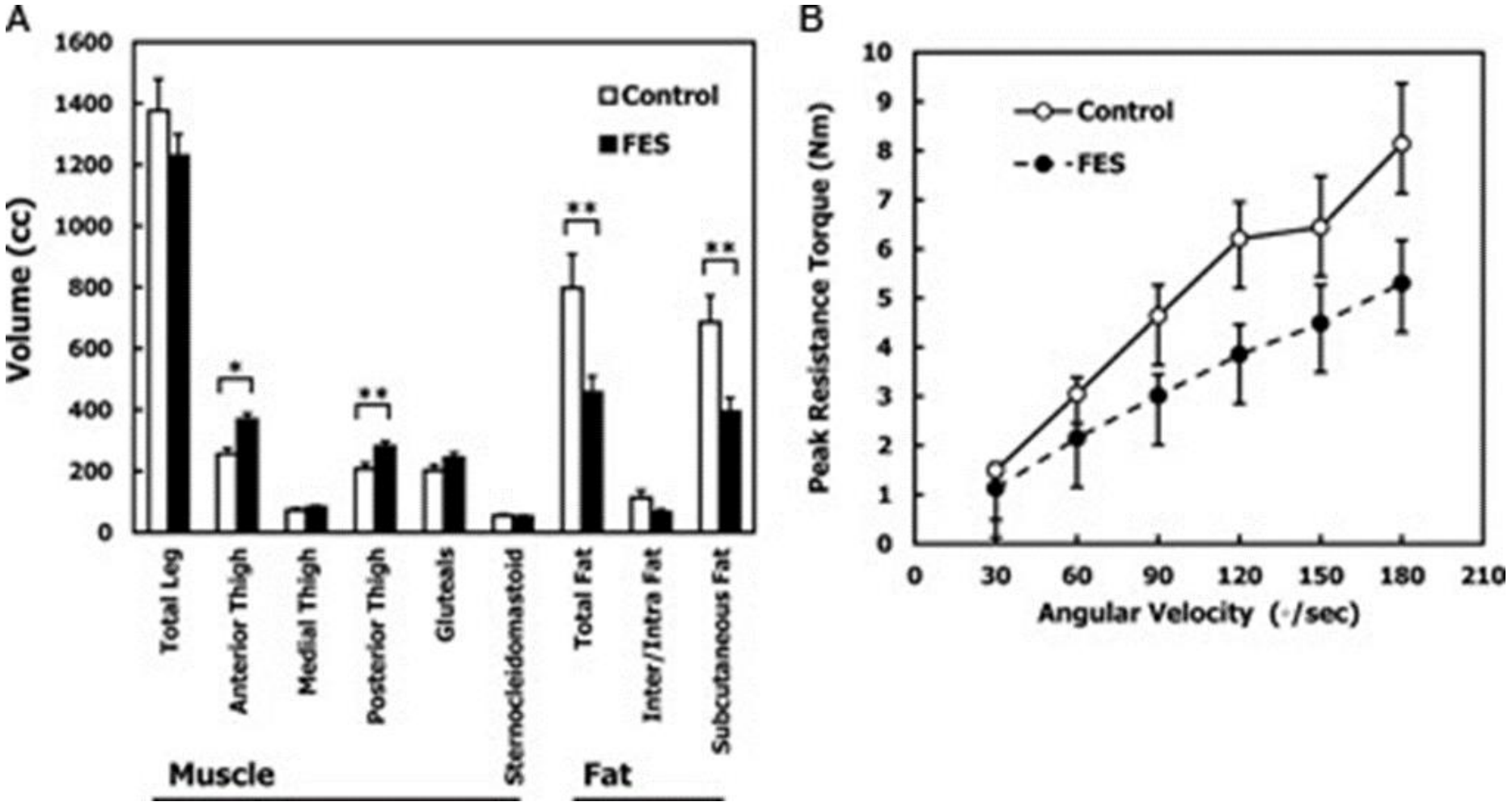


4. MASSED AND 5. TASK SPECIFIC PRACTICE

FES

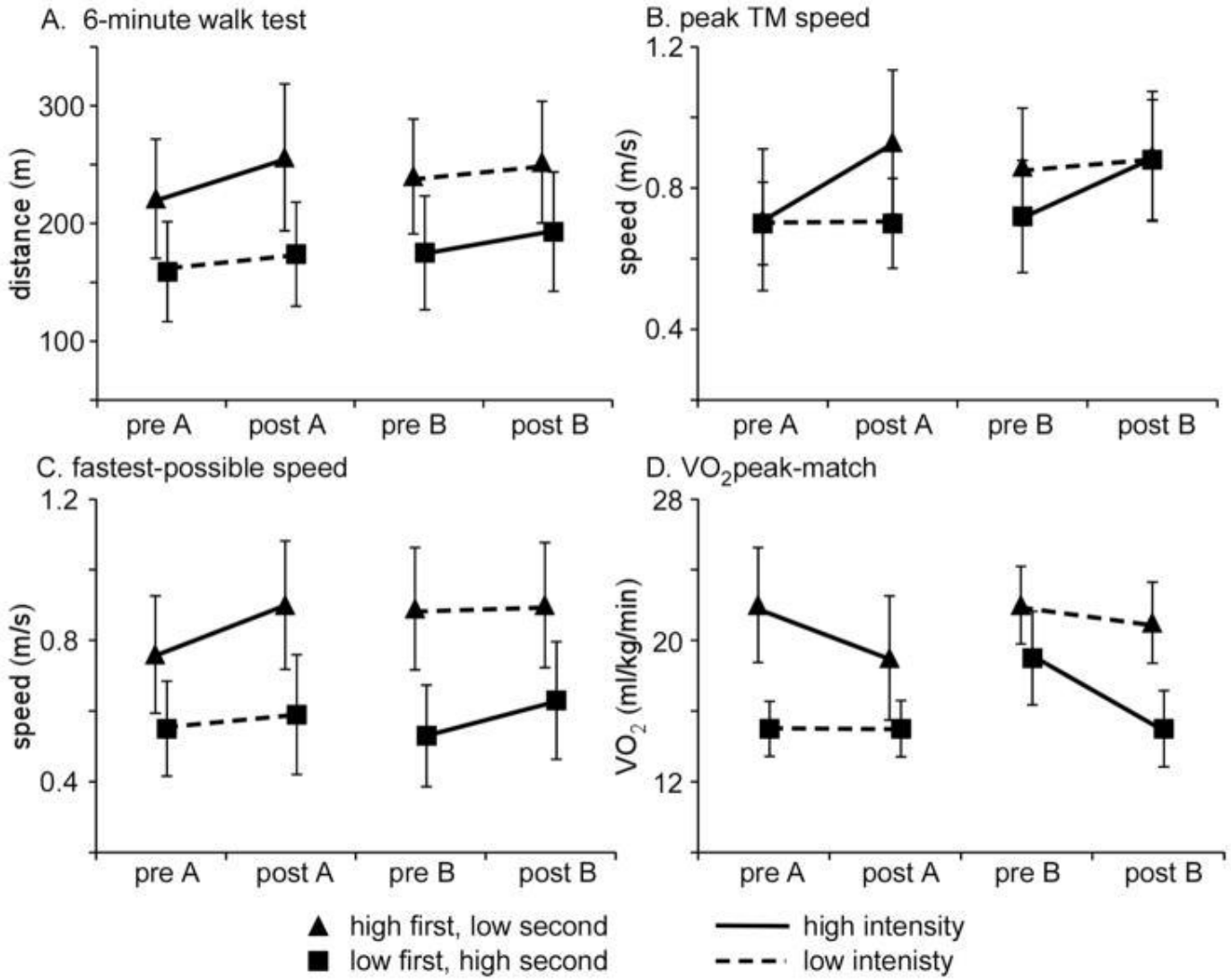


Sadowsky et al. (2013)



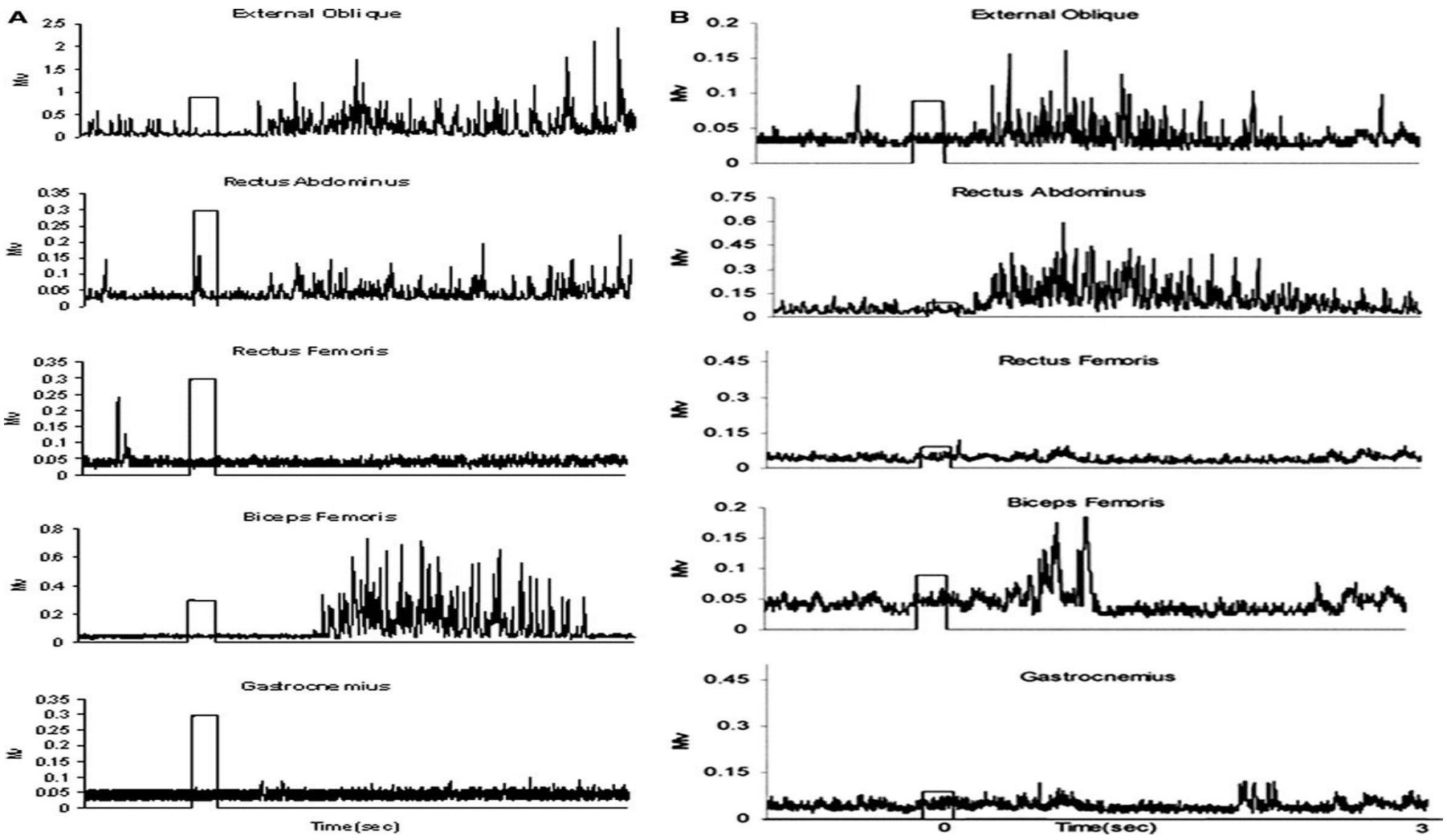
Sadowsky et al. (2013)

Locomotor gait training



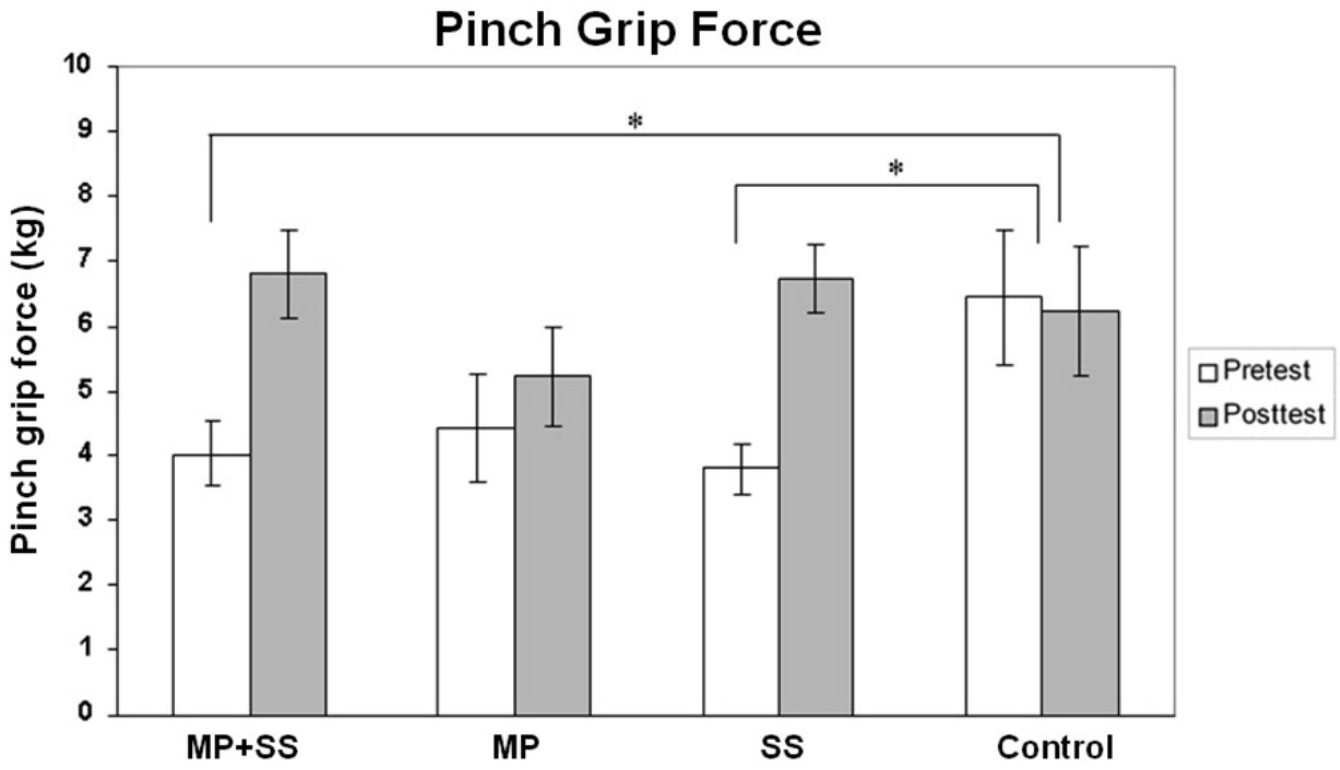
Brazg G (2017).

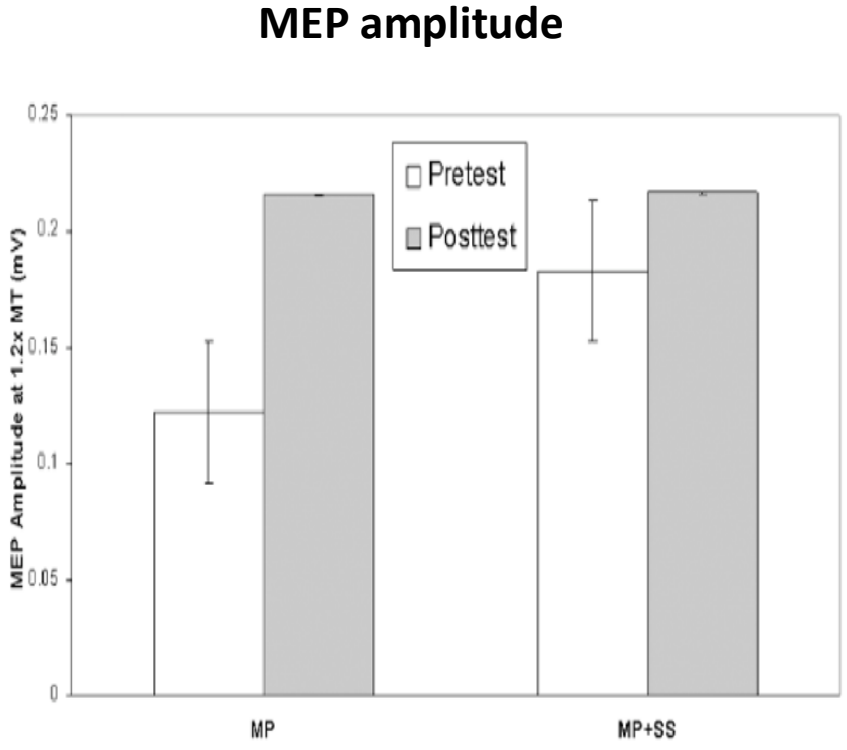
Weight loading



Edwards, et al (2007)

Massed practice





Beekhuizen et al (2008)

Acute Intermittent Hypoxia (AIH)

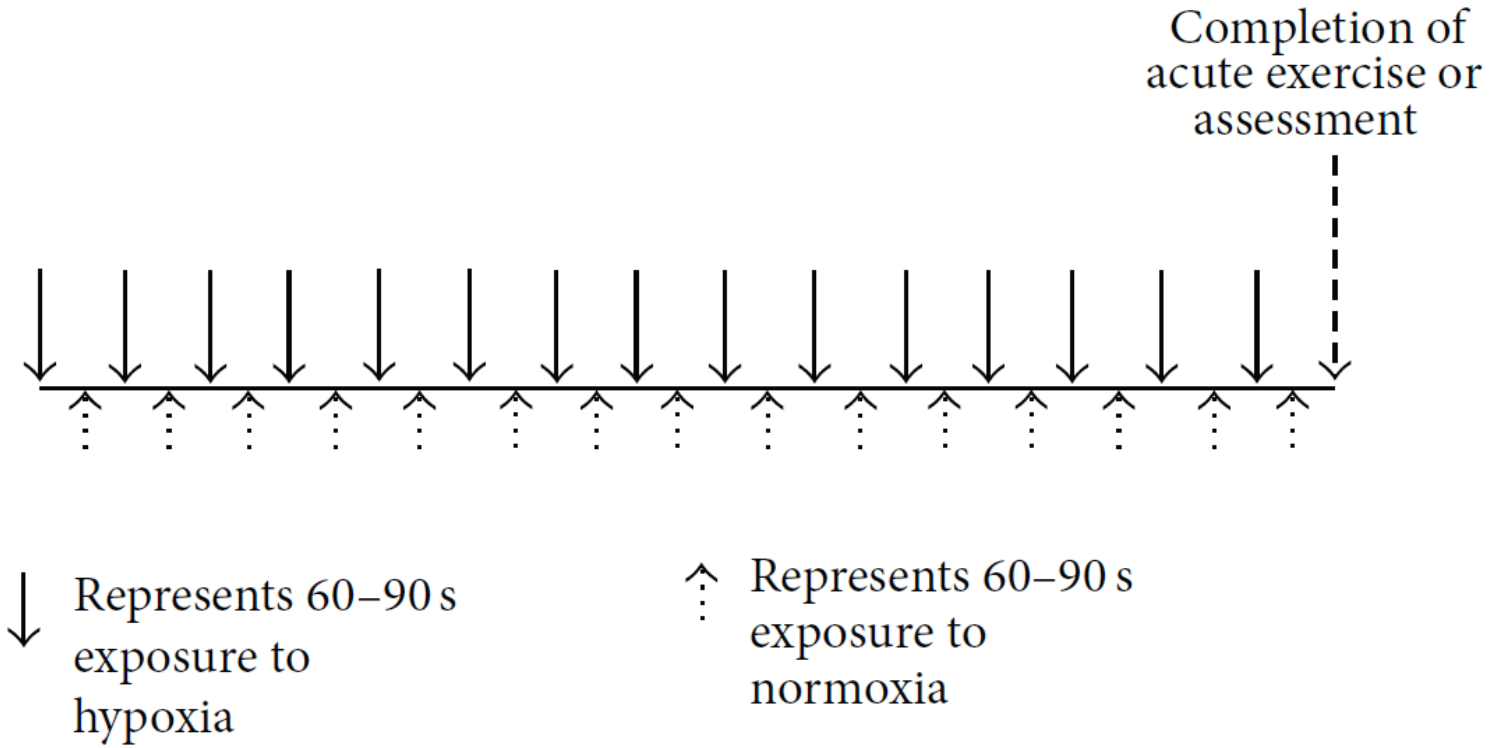
AIH

- Exposure to short, repeated bouts of moderate FiO_2 percentages (9-16% FiO_2)
- Interspersed with bouts

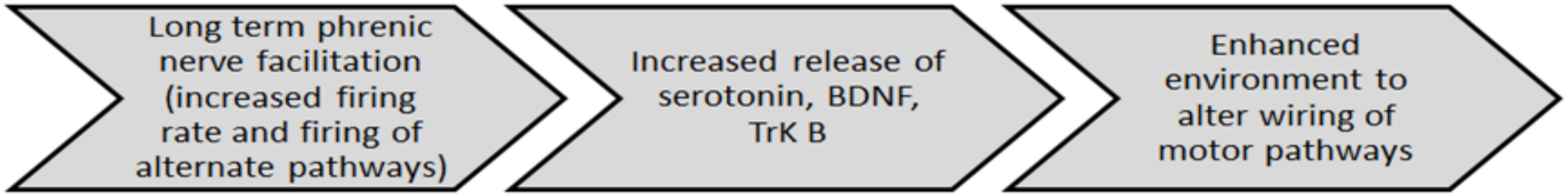
of normoxia (21% FiO_2)

- Performed for 3-15 cycles

of 60-90 seconds

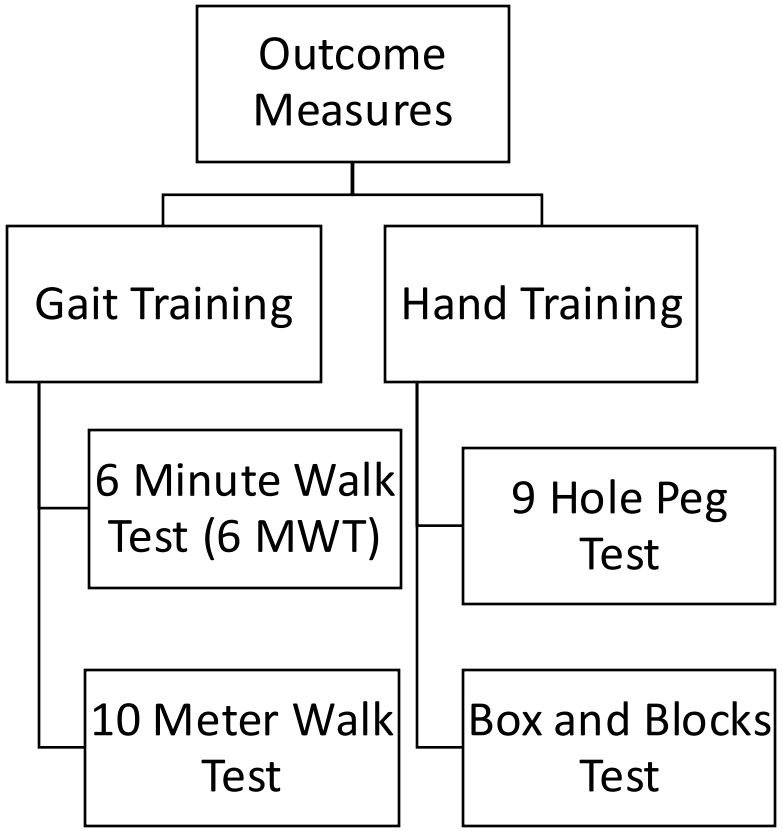


AIH: Proposed Mechanism of Neuroplasticity



ICSCI Clinical Protocol: AIH Training

- 60 seconds with mask on at 9-12% FiO2, 60 seconds with mask off at room air
- 15 rounds (total of 30 minutes)
- Following all 15 rounds, 30-45 minutes of task specific training (pre-gait or gait activities, repetitive hand opening tasks, Amadeo)



Outcomes

- 12 patients provided informed consent to participate in AIH
- 1 patient did not complete the protocol due to attendance and scheduling difficulties

MDC and MCID were utilized to assess effectiveness of intervention

6 Minute Walk Test: MDC = 150 feet; MCID = 0.10 m/s

10 Meter Walk Test: MDC = 0.13 m/s; MCID = 0.06 m/s

9 Hole Peg Test: MDC = 4.38 s (dominant hand); MDC = 7.46 s (non-dominant hand)

Box and Blocks Test: MDC = 4 blocks/minute

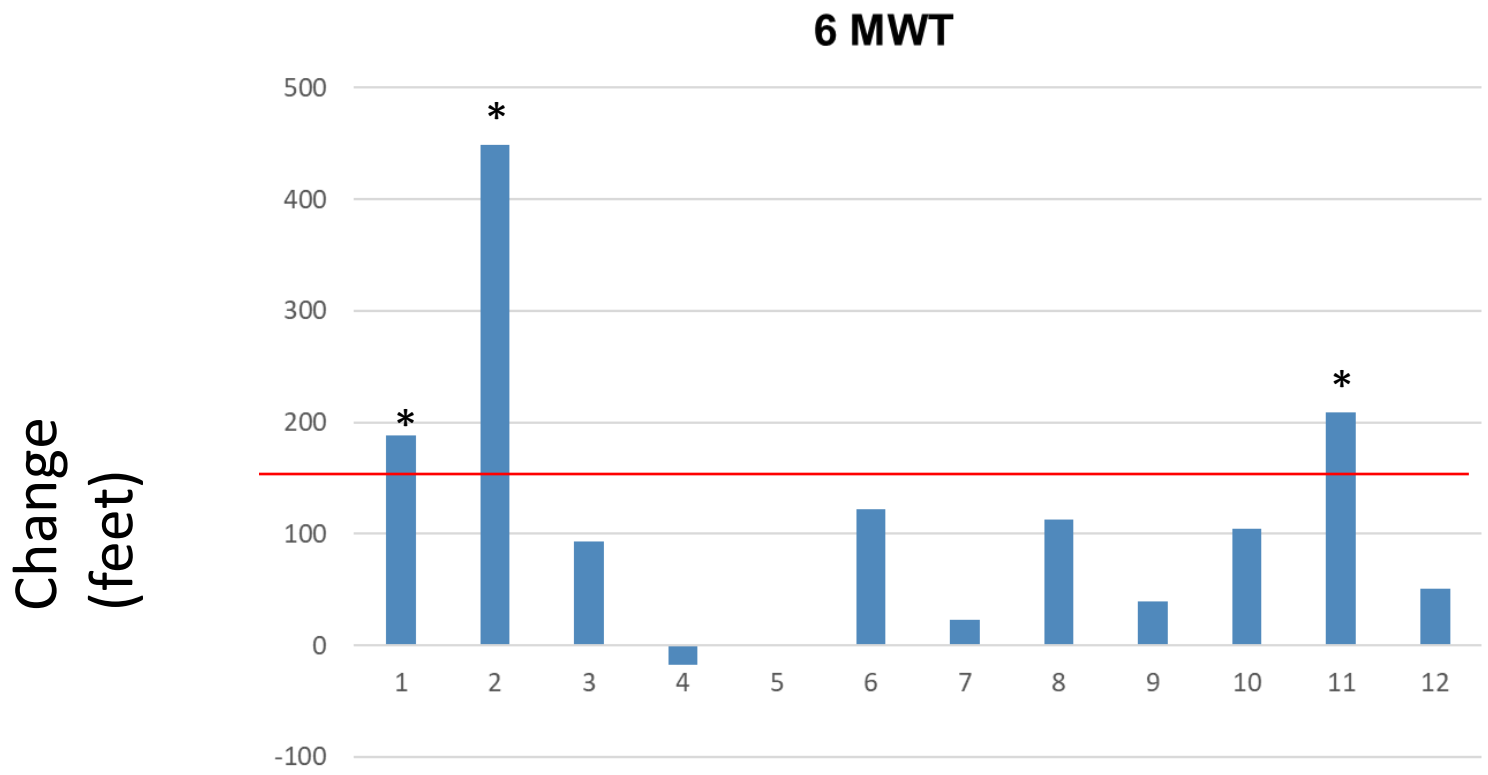
Participants

	Neurological level	AIS	Time from injury	Numbers of sessions	FiO2 %	Activities during AIH	Activities following AIH
1	C5	C	4	8	9-15 %	EKSO	OT
2	T6	D	2	5	9-10 %	None (seated)	Andago
3	C6	D	5	7	12 %	Andago	None
4	C4	D	9	6	10.5 %	Prone stretching	Pre-gait/gait
5	C5	D	14	0	NA	NA	NA
6	C4	D	1	6	10.5-11.5 %	LE FES	Amadeo
7	C4	C	7	5	10.5-11 %	Standing balance	Pre-gait/gait
8	T10	C	14	5	10-11 %	None (seated)	Gait training
9	C5	C	3	4	10.5 %	Seated/standing balance	Gait training
10	T2	D	5	6	10-11 %	None (seated)	(delayed) Gait training
11	L2	C	3	5	11-12 %	Static sitting/standing	Gait training
12	C7	C	5	5	12 %	None (seated)	Gait training

Outcome Measure Data

- 3 participants met the MDC for 6 minute walk test (endurance) (3 participants within 45 feet of MCID)
- 4 participants met the MCID for 6 minute walk (3 participants within 0.02 m/s of MDC)
- 4 participants met the MCID for 10 meter walk test (speed) (1 participant within 0.007 of MCID)

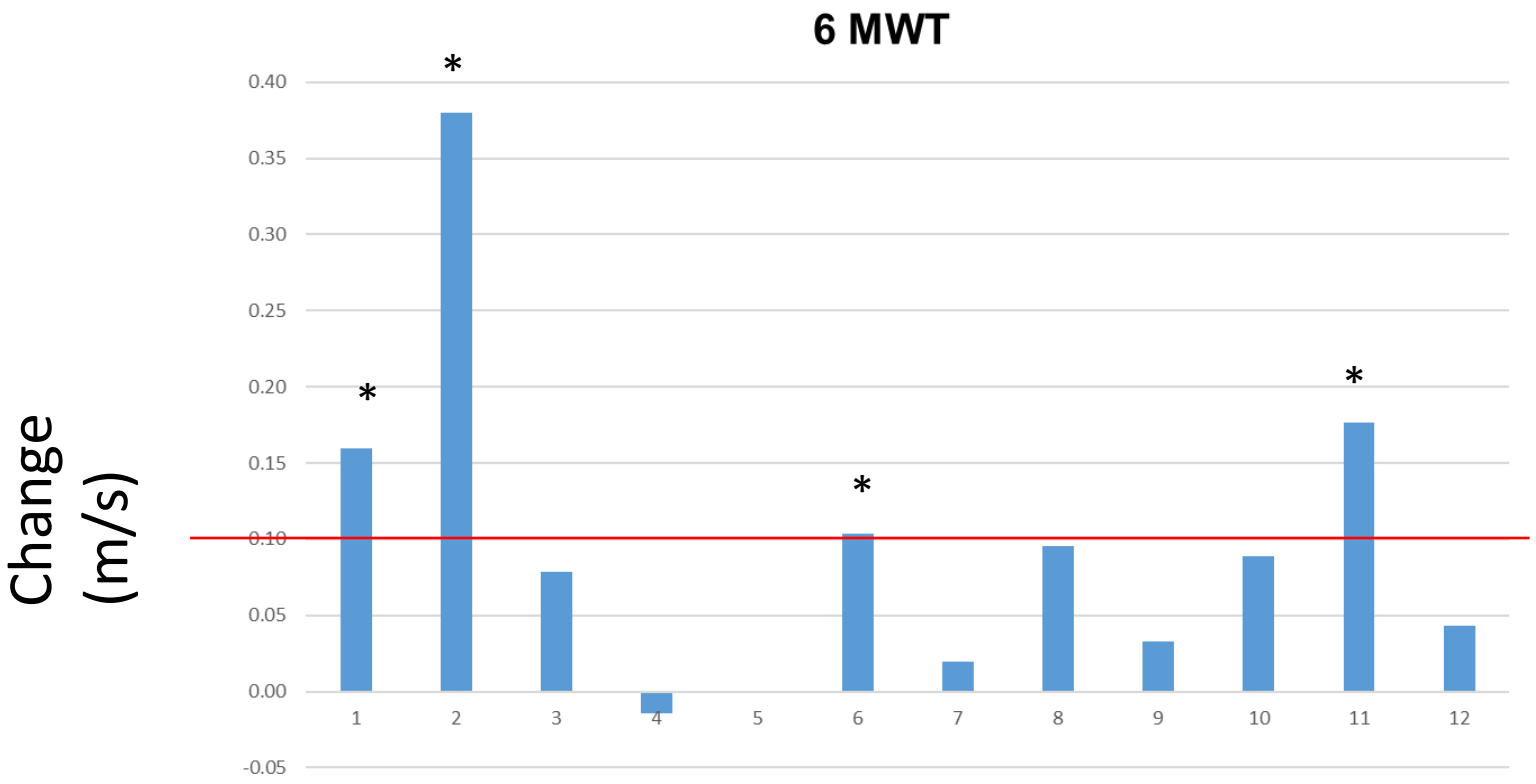
Outcome Measure Data



-- MDC = 150 feet

* = met MDC

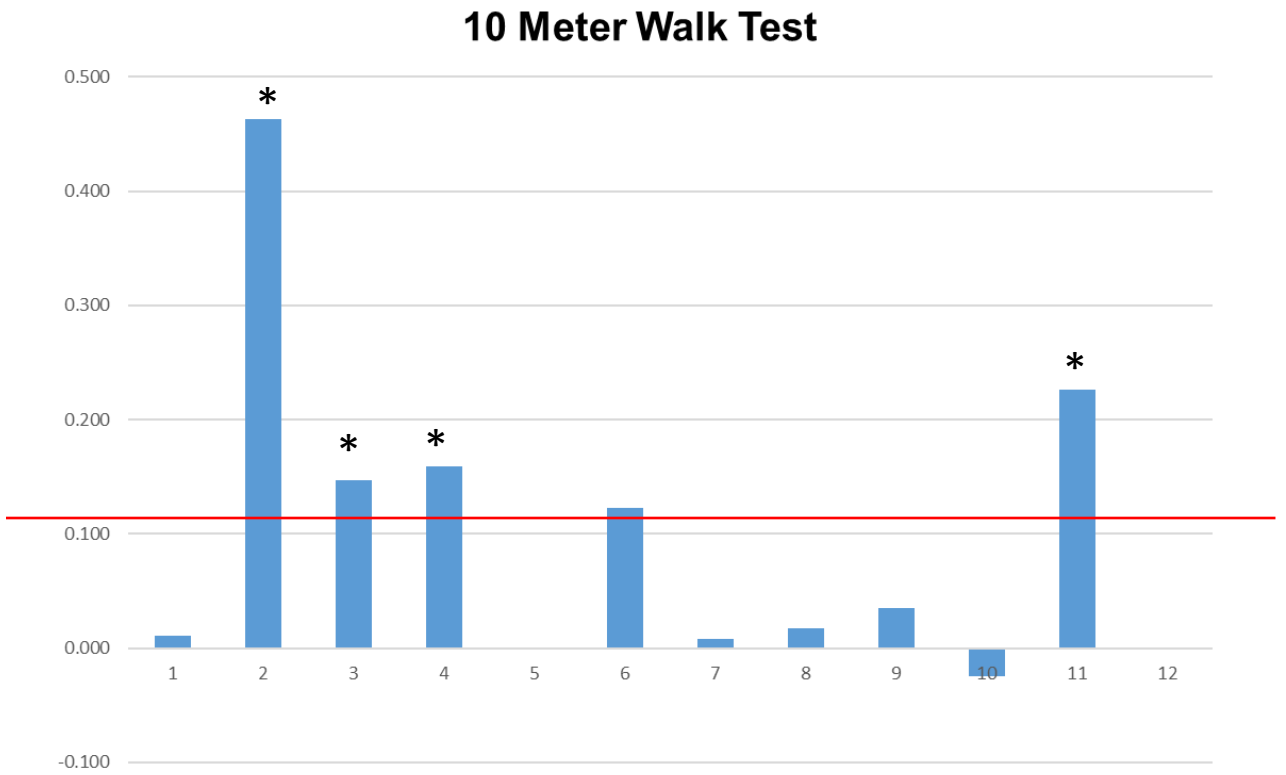
Outcome Measure Data



-- MCID = 0.10 m/s

* = met MCID

Outcome Measure Data



-- MCID = 0.13 m/s

* = met MCID

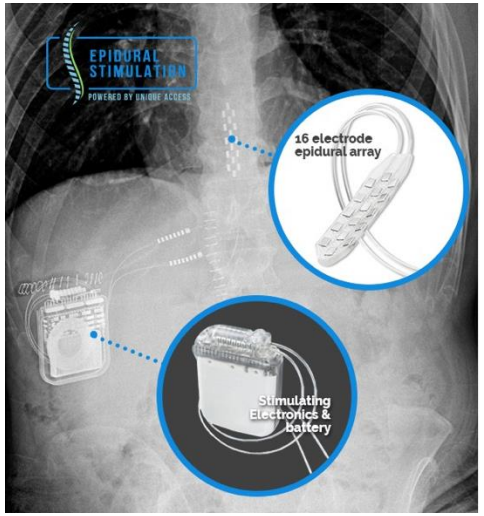
Some Discussion Points

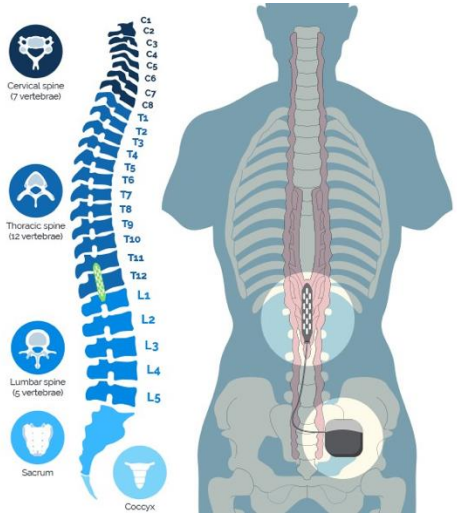
Fatigue levels

- Individuals (5) who participated in a higher frequency of ABRT (5 days/week) generally reported increased fatigue at the conclusion of their bout of care (this finding was consistent with their previous bouts of care without AIH at the same frequency and intensity)

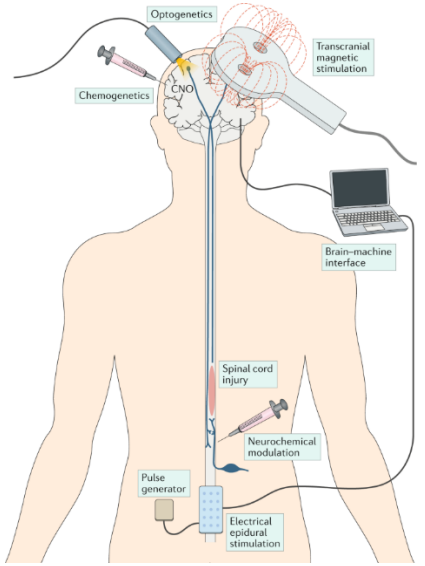
CNS stimulation

1. Transcutaneous spinal stimulation (TCSS)
2. Spinal epidural





3. Paired associated stimulation (TCSS + TMS/tDCS)

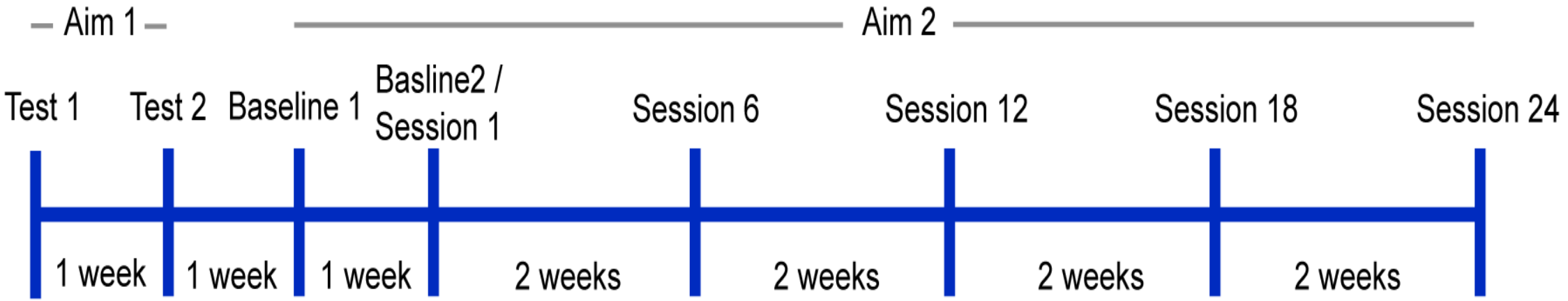


Transcutaneous Spinal Stimulation (TCSS)

- TCSS delivers modest stimulation (at/below motor threshold, activating large-to-medium diameter afferent fibers projecting to motor neurons resulting in increased spinal networks excitability
- appears to have a retrograde effect by enabling bi-directional communication between spinal and supraspinal centers rostral to the site of injury
- In people with incomplete injuries, TCSS **increases the size of motor evoked potentials** elicited by electrical stimulation + **amplitude of voluntary movements** without TCSS
- Immediate clinical results: decreased spasticity and initiation of involuntary step-like movement utilizing a non invasive intervention
- TCSS applied during functional tasks **improves performance**
- TCSS can lead to significant **improvements in autonomic functions** after SCI, such as cardiovascular and lower urinary tract function

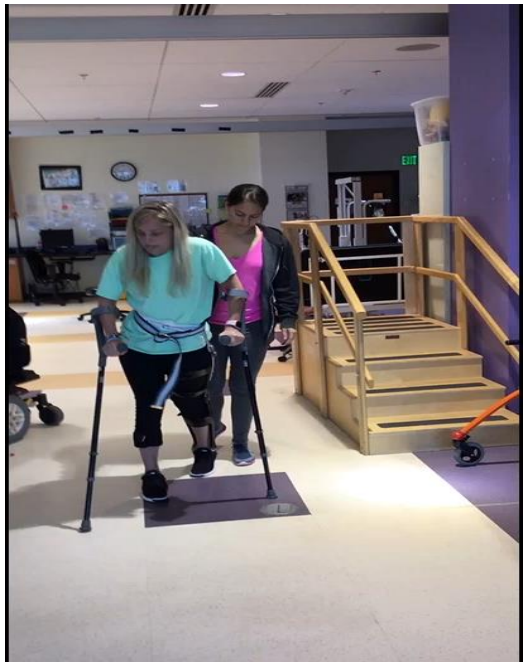
Methods

- 8 weeks of training: 30 min of TCSS inside a 2 hour therapy session, 3x/week
- 10 meter walk test 10MWT, timed up and go (TUG), 6 minute walk test 6MinWT, Walking Index for Spinal Cord Injury WISCI II



Intervention

Without TCSS



With TCSS

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Demographics and Clinical Characteristics

	M/F	Age	TSI (years)	COI	NL	AIS
01	M	64	3	Non	T3	D
02	F	22	2	Non	T8	C
03	M	52	11	Trauma	C6	D
04	M	63	57	Trauma	T1	D
05	M	55	18	Non	T4	D
06	F	28	2	Trauma	C4	D
07	F	22	6	Non	C5	C
08	M	40	20	Trauma	C5	D
09	F	60	12	Non	T9	C
10	M	24	3	Non	C7	C

TSI: time since injury, COI: cause of injury, NL: neurological level

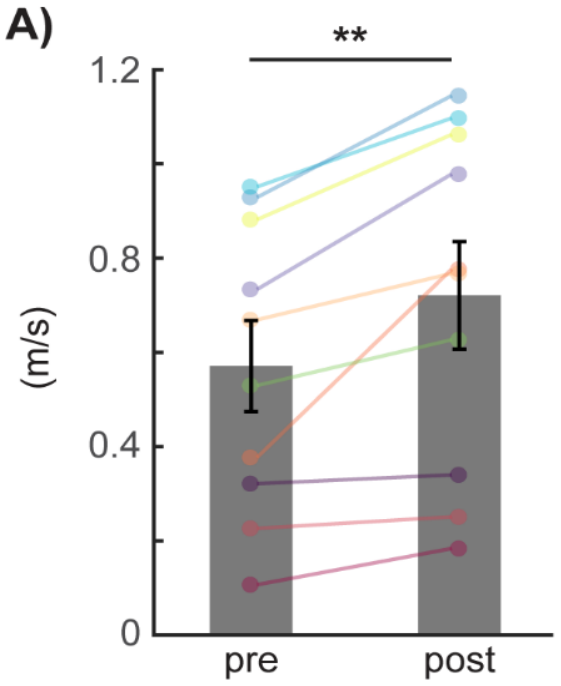
Feasibility Outcomes

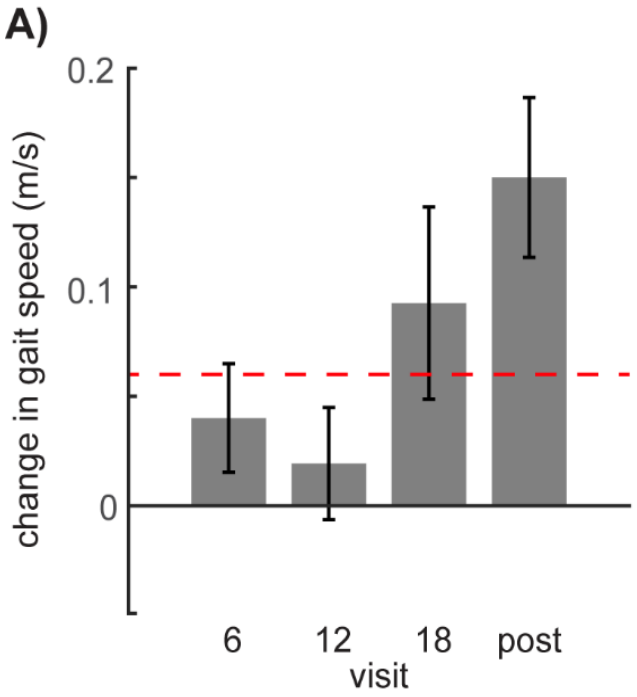
- No significant or recurrent pain was reported. Reported pain levels ranged from 0-4 on the Numeric Rating Scale NRS for Pain with an average of 0.12 ± 0.27 across all subjects and sessions.

- No significant adverse events, including but not limited to falls, injury, autonomic dysreflexia, or related illness, were reported or observed.

- All subjects completed the 8 week intervention.

Walking Speed Improves (10MWT)





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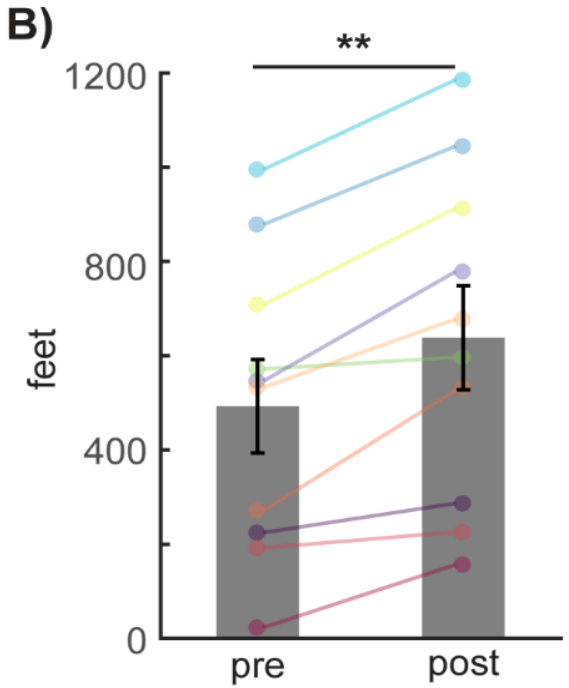
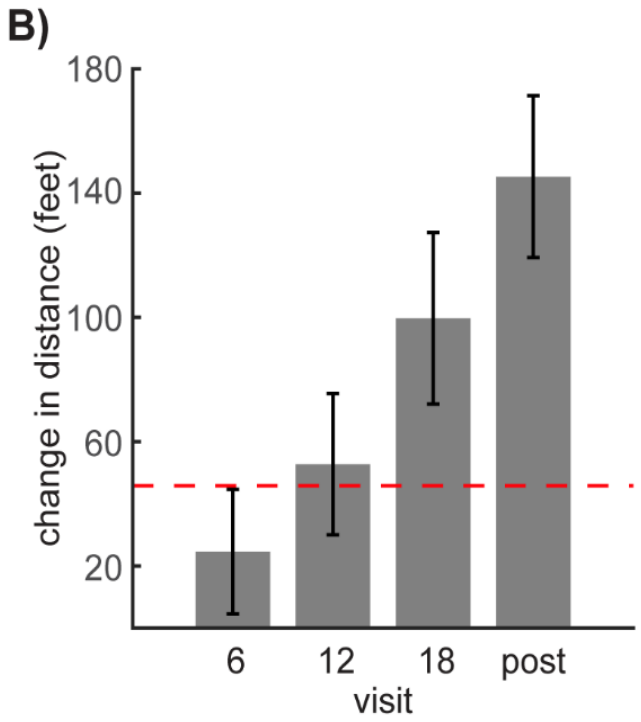
Walking Endurance Improves (6MinWT)





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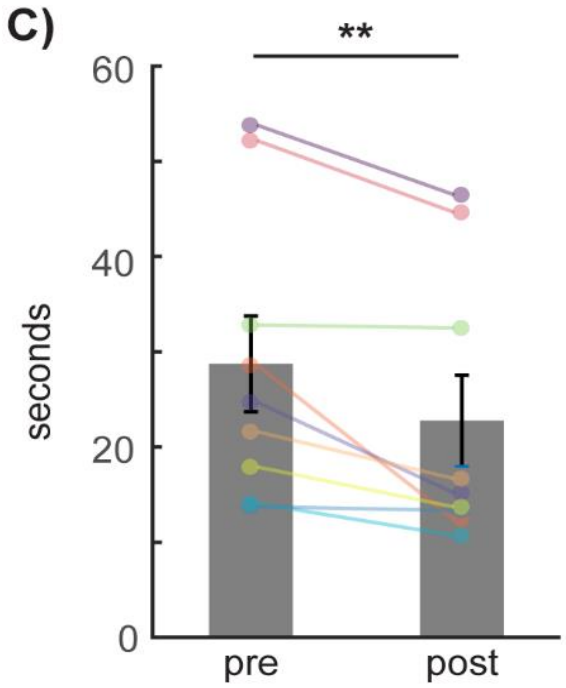
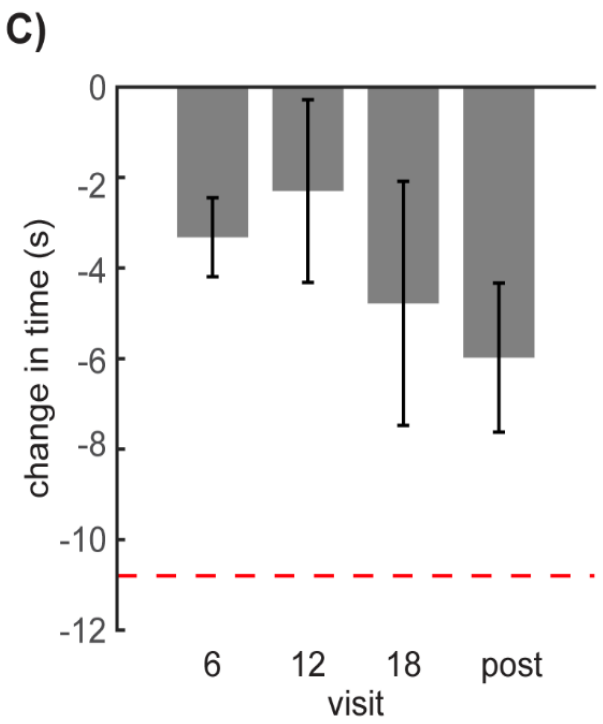
Improvements in Timed Up and Go (TUG)





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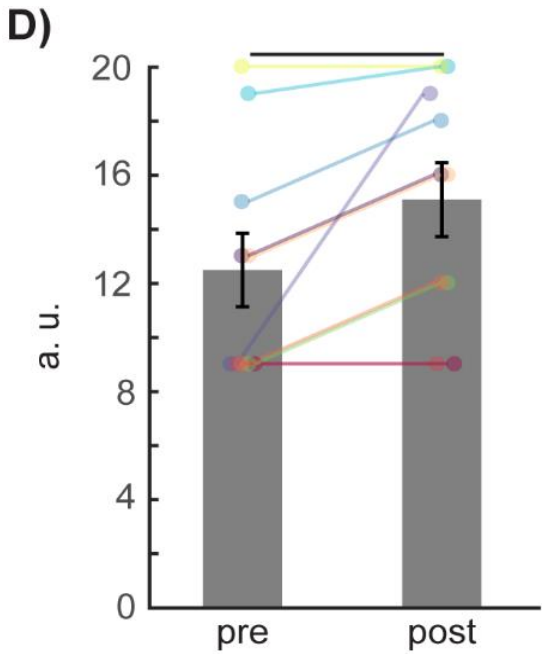
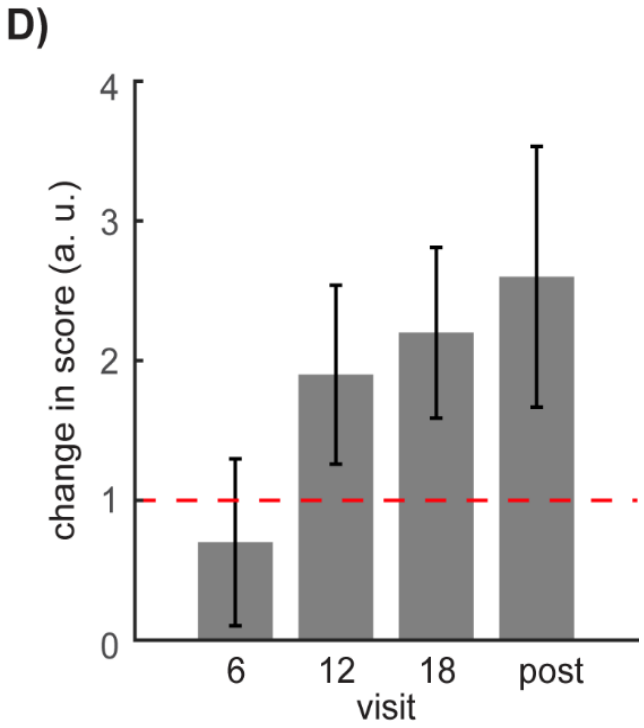
Walking Quality Improves (WISCII)





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Additional Findings

- Half the subjects reported recovery of or improvement in voluntary voiding
- Two thirds report improvement in pain, both musculo-skeletal and neuropathic
- Few subjects report improvement in sensory function (light touch, pinprick, vibration)

Conclusions

- Safe and feasible delivery in outpatient clinical setting
- Improvements in all outcome measures
- Lasting improvements in voluntary function

What About Downstream?

Therapeutic electrical stimulation (TES): Use of electricity to drive a desired nerve response for therapy.

MOTOR

- NMES (Neuromuscular electrical stimulation): Electricity applied across the surface of the skin over intact peripheral nerve evokes an action potential in the nerve fiber which causes an exchange of ions to drive the muscle to contract. Low frequency (20-60Hz), longer pulse duration (100 µsec-1millisec), amplitude to tolerance
- FES (Functional electrical stimulation): Application of electrical stimulus to a paralyzed nerve or muscle to restore or achieve function (also refers to orthotic substitution).

SENSORY

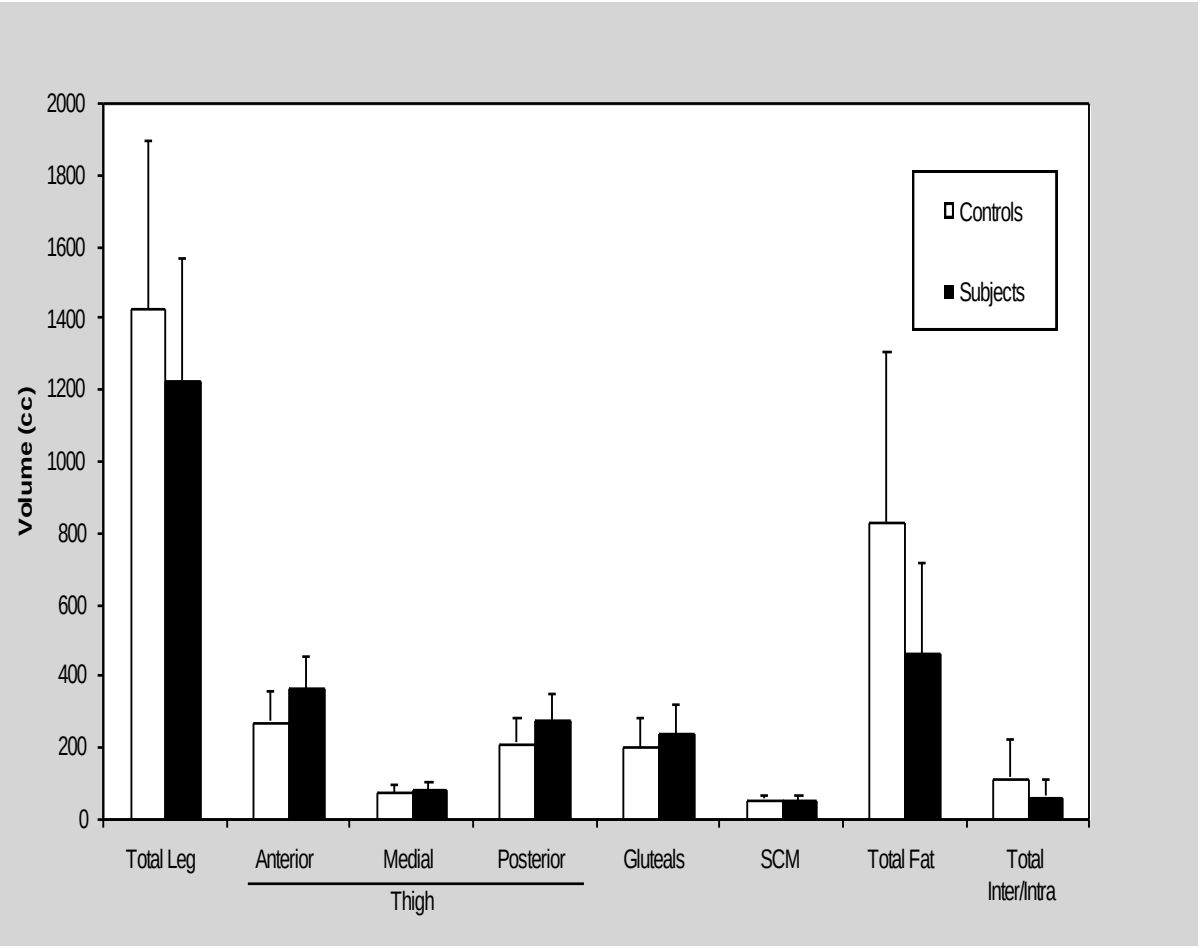
- TENS (Transcutaneous electrical stimulation): Pain modulation by exciting peripheral nerves. High frequency (80-100Hz), low pulse duration (80-100µsec), amplitude sub-motor

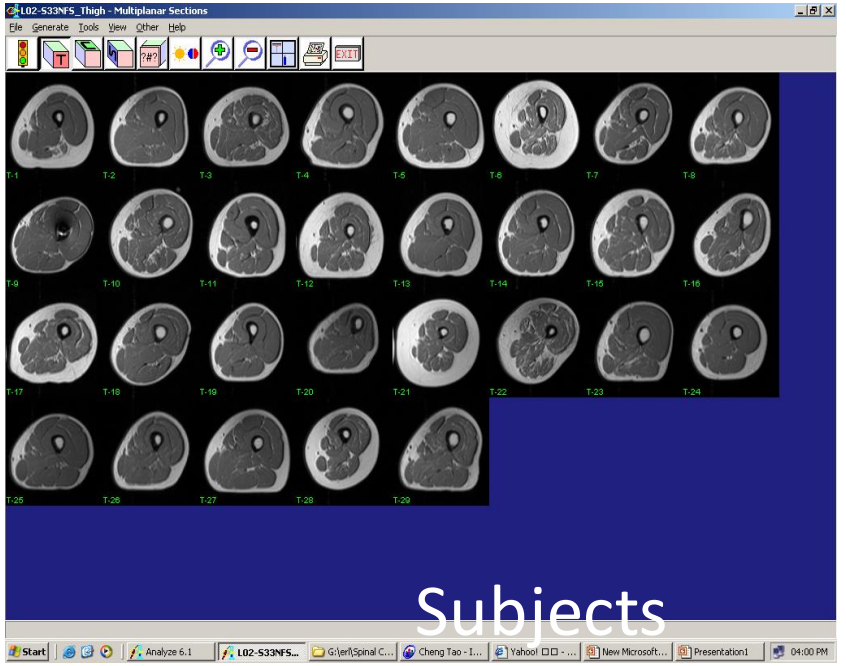
Effector - muscle

E-stim strengthening: there is a difference between e-stim driven and regular strengthening

- recruitment: regular – small, fatigue resistant red fibers first; e-stim – large, fatigable white fibers first
- Time: regular: 2 weeks, e-stim: 4 weeks (need conversion of fast twitch to slow twitch fibers)

Volume measurements of muscle and fat.
Data represent the mean ± SD, (n=22 and 26 controls and RT subjects respectively).





Mid-thigh fat/muscle distribution by MRI

Blood flow restricted (BFR) strengthening

- low-load (training to muscular failure) BFR training is more effective than low-load training without BFR (and less effective than high load training - 70% of an individual's one repetition maximum (1RM)

	Age	Sex	Neurological level	AIS classification	Time since injury	Limb	Pre Strength (ft·lb)	Post Strength	Pre timed Walk	Post Timed Walk	Pre Circumference	Post Circumference	Pre Quad Skinfold (mm)	Post Quad Skinfold
A	67	Male	C3	D	5 years									
						Right Leg	81.4	99.5	7.62	6.5	53.5	54	10	7
						Left leg	74.9	86.3			53	54.5	9	9
B	19	Male	C5	C	3 years									
						Right Leg	27.5	49.6	7	7	52	52.5	7	5.5
						Left leg	66.2	71.2			53	53	5	4.5
C	73	Male	C4	D	4 years									
						Right Leg	67.1	73.3	7.31	9.81	59	57.5	17	18
						Left leg	67.8	89.3			61	59	17	18

Computers/Robotics/Technology


WITHOUT
ELECTRICAL STIMULATION
after 5 months of treatment

Myomo

Amadeo

Armeo

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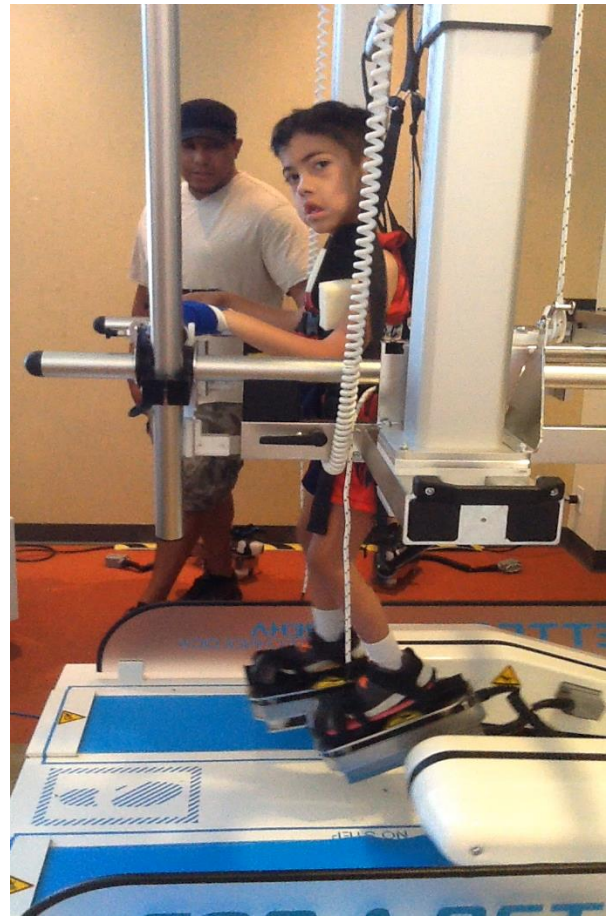
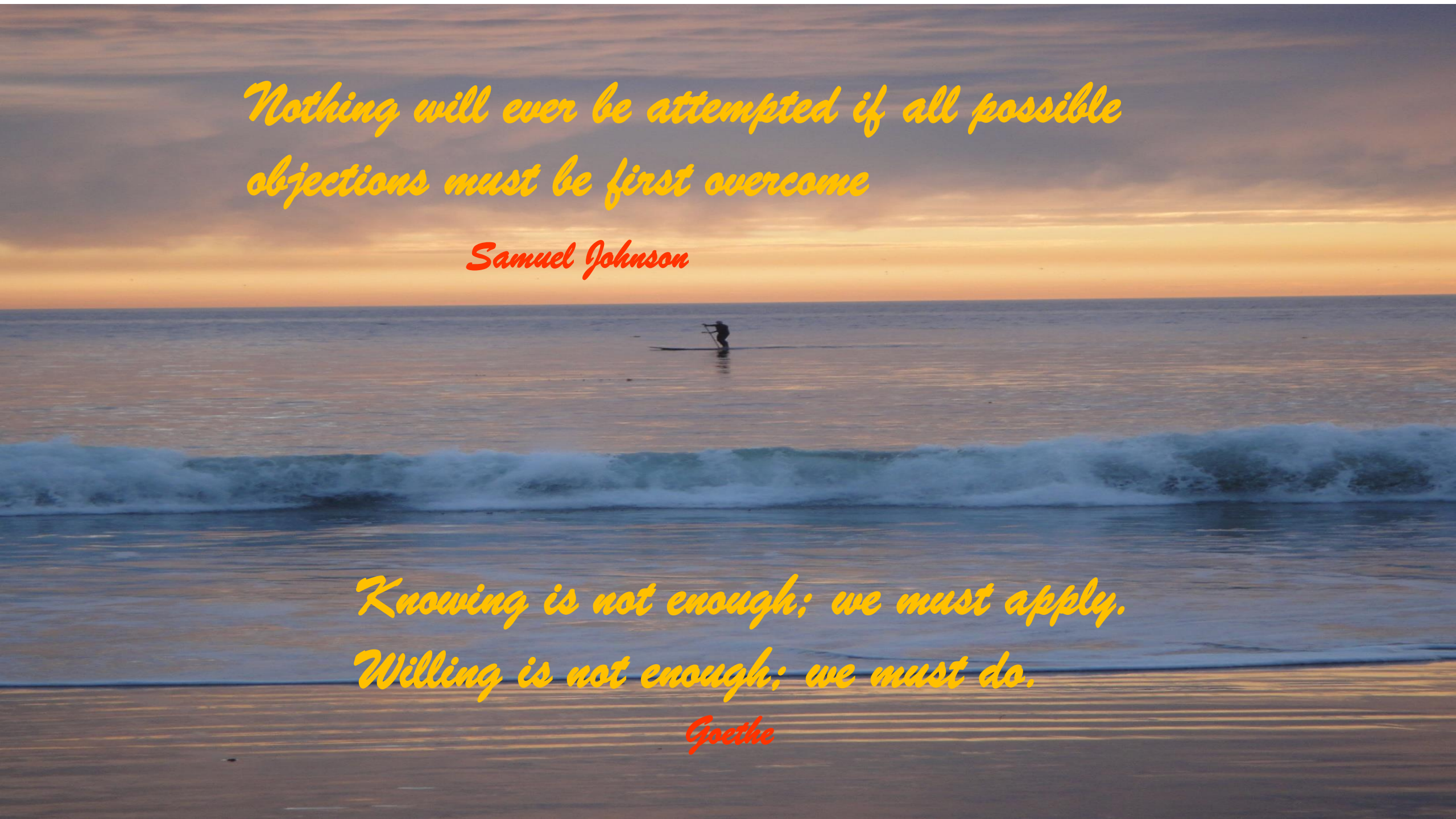
Exoskeletons- EKSO



Brain Computer Interface


Nothing will ever be attempted if all possible objections must be first overcome
Samuel Johnson
Knowing is not enough; we must apply.
Willing is not enough; we must do.
Goethe