# New Frontiers in Research to Improve Motor Functioning in Individuals with CP


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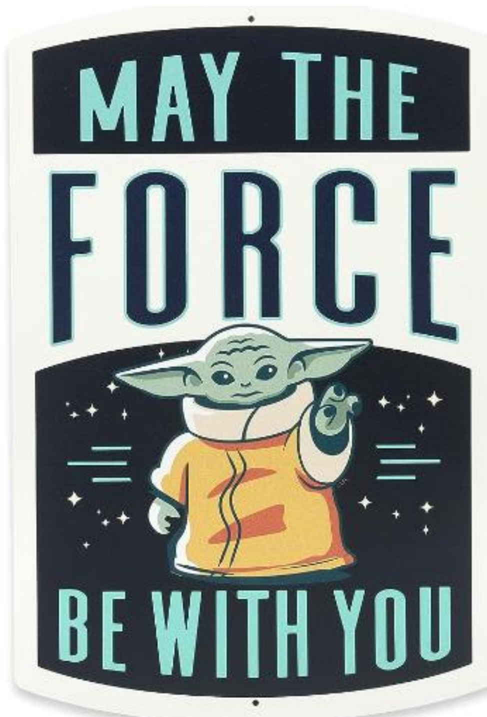
# Background

- Pediatric physical therapist; direct a laboratory that combines biomechanics, neuroscience and neuroengineering with primary goal of improving mobility in children with cerebral palsy

- **Old frontiers:** prior research on strengthening & activity-based training

- **Emerging technologies:**
  - Rehabilitation robotics
  - EEG neurofeedback

# Starting with strength training….

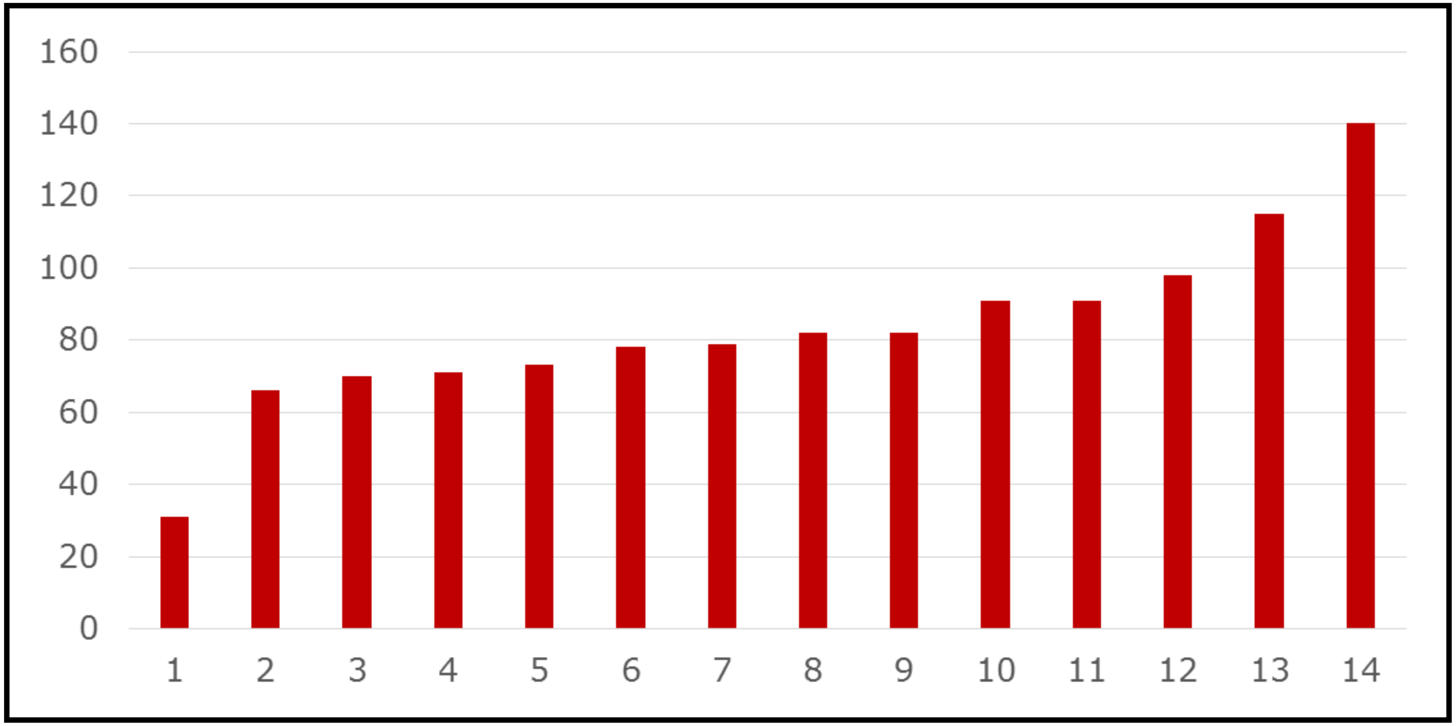



Dr. Luigi Puccinini

# 1st Strengthening Studies in CP

- Crouch gait common in CP, increases energy costs, makes walking progressively more difficult
- Are children with CP similar to typical teenagers?
- PhD thesis (1993): **“Effects of quadriceps strengthening on crouch gait”**
- Strengthening in CP was contraindicated
- 14 children with CP performed quadriceps PRE 3X/wk for 6 weeks using free weights in home
- *Outcomes:* quadriceps and hamstring strength, crouch (knee kinematics)

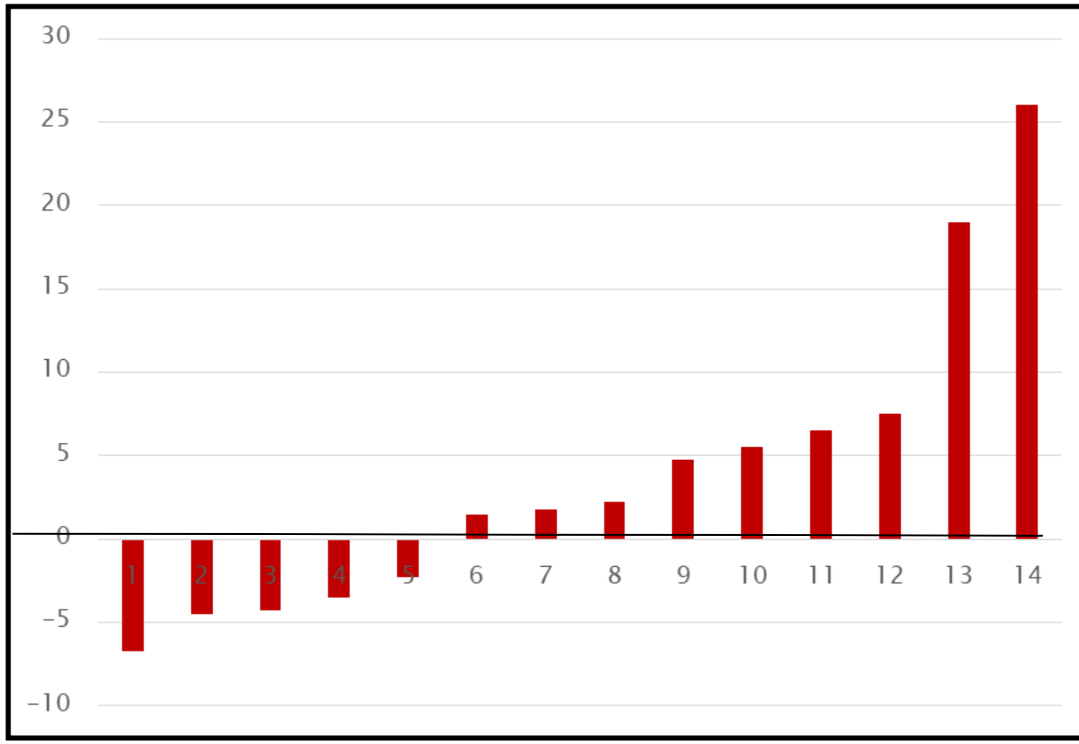
# Quadriceps Strength Gains (%)




Consistent effect, significant at group level

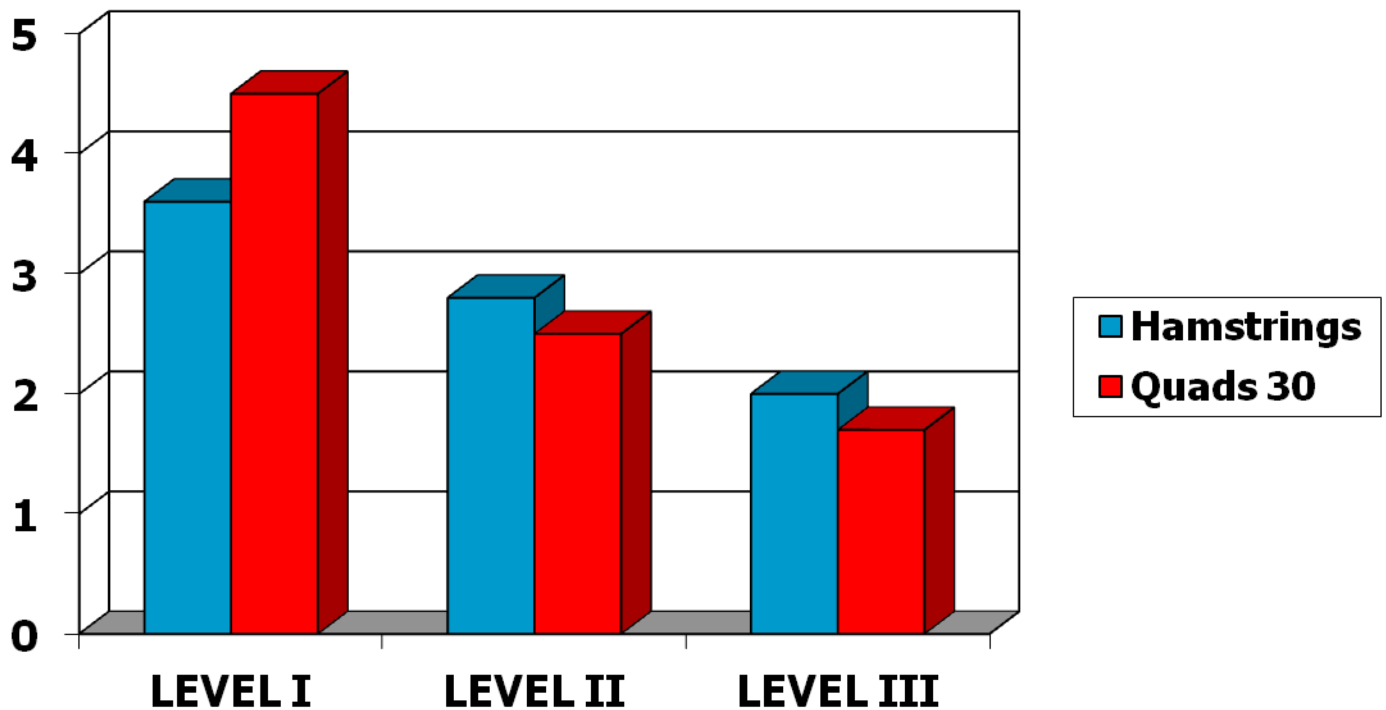
# Change in Knee Extension (Did this decrease crouch?)

Change in knee extension (degrees)




Significant at group level, but response variable

# Strength & Mobility in CP* (1990s)




Level I already 40% weaker than peers
Hams/Quad ratios distorted in CP
Leg strength related to walking speed (r=0.70)

# 2022 Review of RCTs: Strengthening works if you do it correctly!

Clinical Rehabilitation
Volume 36, Issue 1, January 2022, Pages 4-14

https://doi.org/10.1177/02692155211040199

SAGE journals

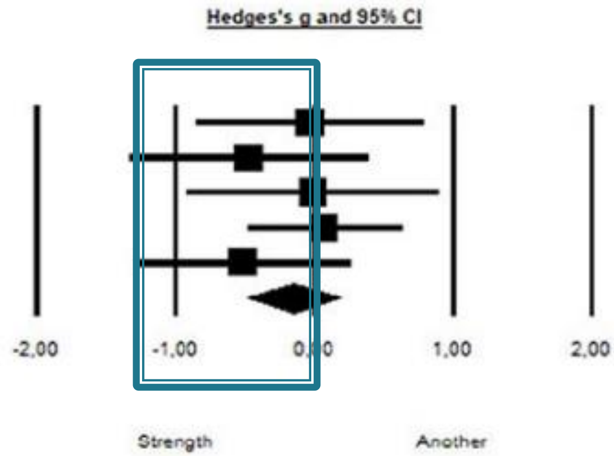
*Evaluative studies*

**Effect of muscle strength training in children and adolescents with spastic cerebral palsy: A systematic review and meta-analysis**

**Javier Merino-Andrés [1,2,3], Agustín García de Mateos-López [4], Diane L Damiano [5], and Alberto Sánchez-Sierra [2,3,6,7]**

# Forest Plot for GMFM Effect Size

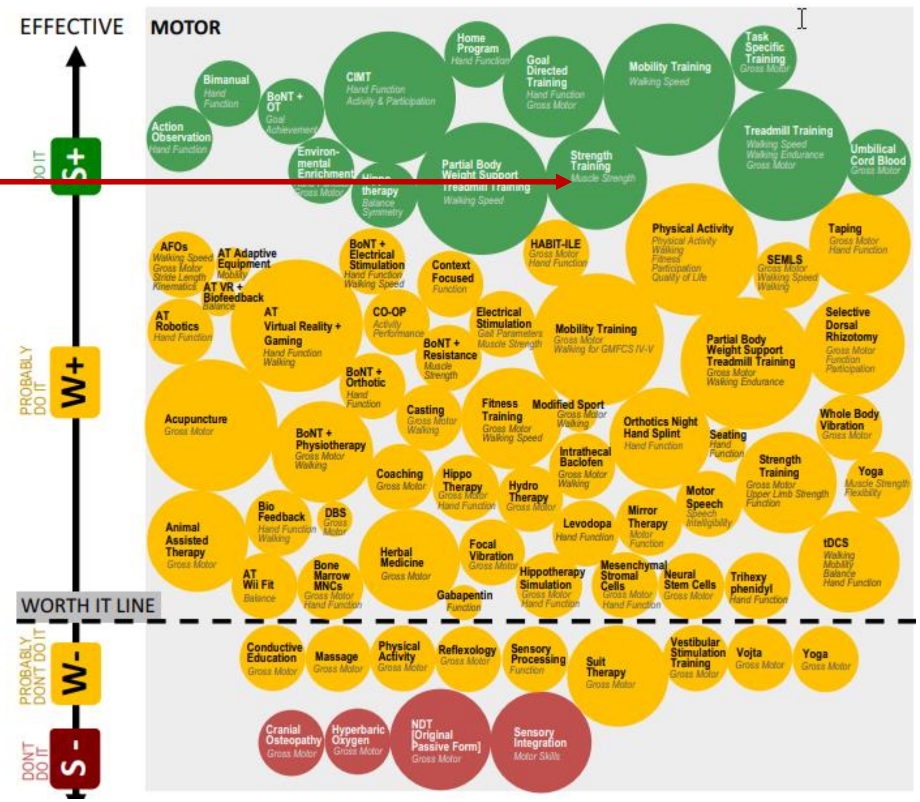
| Study name | Hedges's g | Variance | Lower limit | Upper limit | Z-Value | p-Value | Strength | Control | Relative weight |
|---|---|---|---|---|---|---|---|---|---|
| | Statistics for each study | | | | | | Sample size | | |
| Dodd et al. 2003 (15) | -0,034 | 0,176 | -0,856 | 0,788 | -0,081 | 0,936 | 11 | 10 | 16,49 |
| Senioru et al. 2007 (25) | -0,473 | 0,191 | -1,330 | 0,383 | -1,084 | 0,279 | 11 | 9 | 15,20 |
| Lee et al. 2008 (27) | -0,010 | 0,213 | -0,914 | 0,894 | -0,022 | 0,983 | 9 | 8 | 13,64 |
| Scholtes et al. 2010 (30) | 0,073 | 0,081 | -0,484 | 0,630 | 0,257 | 0,797 | 24 | 24 | 35,96 |
| Cho et al. 2020 (23) | -0,512 | 0,155 | -1,284 | 0,260 | -1,300 | 0,194 | 13 | 12 | 18,71 |
| | -0,148 | 0,029 | -0,482 | 0,185 | -0,871 | 0,384 | | | |




**Heterogeneity: I-squared = 0 (p=0.703)**

# Evidence for Strength Training in CP

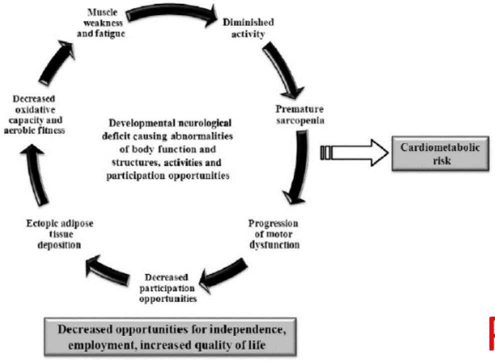
We made it to **GREEN** on traffic lights for improving motor function!




(Novak 2020)

# Cerebral palsy

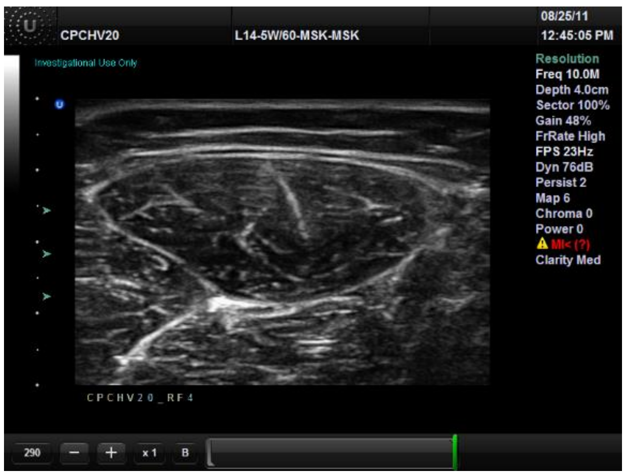
- Is weakness originating from the brain
- From birth, those with CP do not much as much or as vigorously as those w/out CP
- Muscle cells are immature at birth and never develop normally
- Vicious cycle of weakness-inactivity-greater weakness



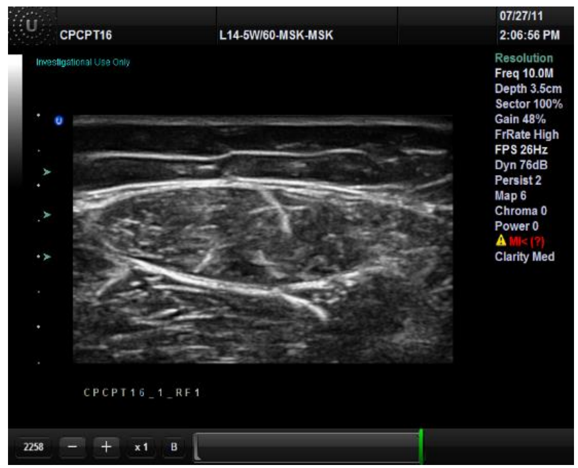

Peterson et al. 2012

# Muscle size matters in CP (Damiano 2009)

Rectus femoris mm ultrasound images in 3 children matched by body weight




Child without CP



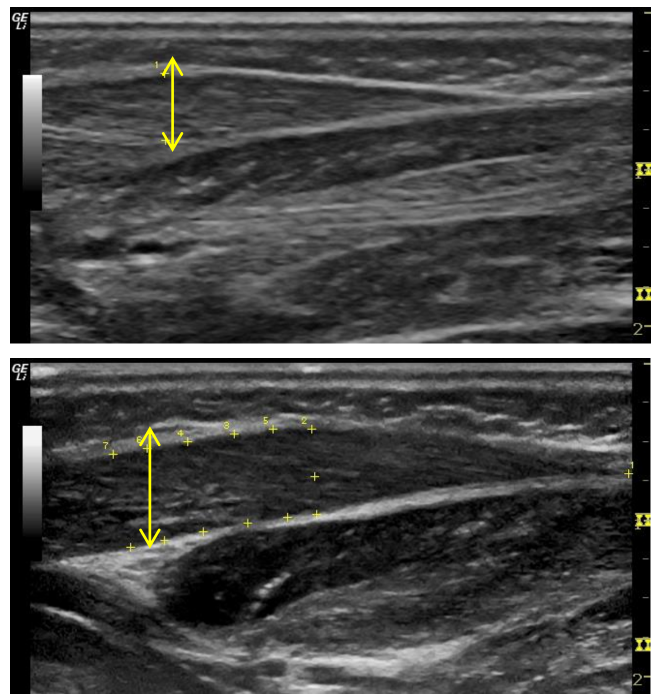

CP GMFCS II


CP GMFCS III

To what extent is this preventable/reversible?

# Muscle plasticity in infants

- Infants have most adult fibers; little antigravity control
- When do abnormal changes in muscle start?
  - Differences found in medial gastrocnemius muscle thickness between (high &) low risk preterm and full term infants



50% smaller in healthy preterm vs. full term at 6 weeks

Moreau et al, 2012

# How Do Muscles Adapt?
## (Harridge, *Exp Physiol*, Review 2007)

Two basic mechanisms at the muscle fiber (cell) level:

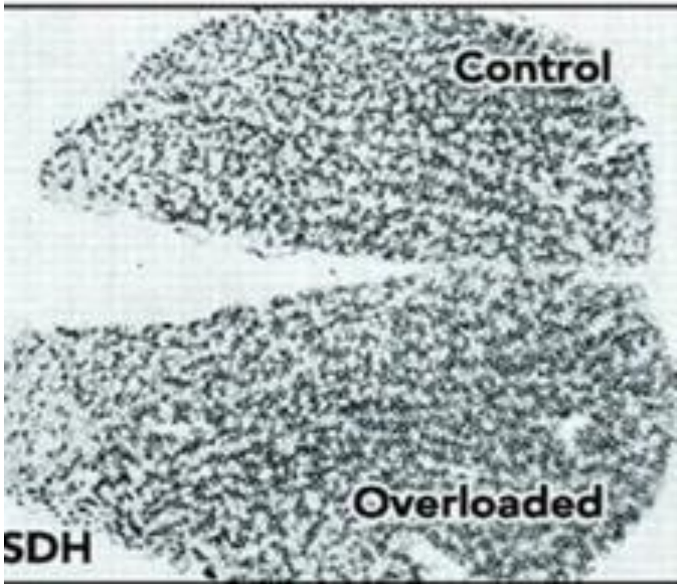
1. Increase/decrease muscle size based on load or inactivity
   - Loading breaks down muscle and starts increased protein synthesis for 72 hr
   - **Progressive resistance training best method**

2. Change in protein isoform (MHC) composition
   - Relates to maximal shortening velocity (Type II faster)
   - Denervation, **Electrical stimulation, high velocity (power) training** >Type II

# Muscle Plasticity and CP (Schiaffino 2007)

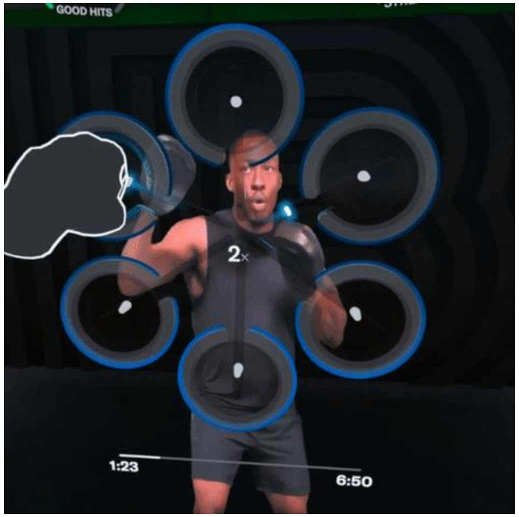
- Muscles are the most plastic tissue in body!
  - Set amount of activity needed to maintain size: differs by muscle with anti-gravity ones at greatest risk
  - Muscle more malleable when younger


AT BIRTH




IN ADULTHOOD

# Muscle Strengthening Methods



# Basic principles

- Strength training recommended at least 2X/wk for everyone (WHO); 3X to *increase* strength
- Muscles must be allowed to rest & recover (every other day for same muscle)
- Dose-response relationship important; under/over-dosing reduces effectiveness

| Goal | Reps/ Sets | LOAD | TEMPO |
|---|---|---|---|
| Strengthening | 3-8/3-5 | 80-100% | Slow w/ control & rest between |
| Endurance | 8-20/5+ | 60-80% | Moderate & sustained |
| Power | 1-3/10+ | 90-100%* | Fast; with rest |

# Resistance Training Guidelines in CP

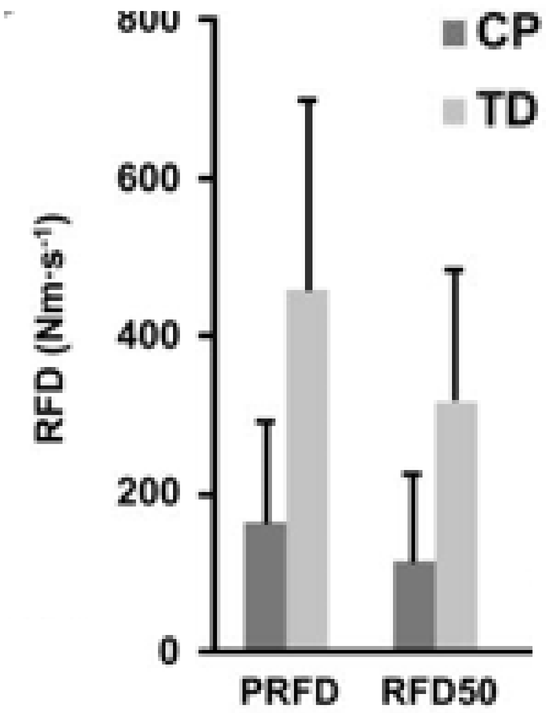
- Review on strength & power training in athletes with CP – effects on muscles and performance
- Load is the stimulus for strengthening (80% MAX)
- Recommended to progress from:
  - Lower to higher load intensity; e.g. 60–70% 1RM to 80–90% 1RM
  - More reps in fewer sets to fewer reps in more sets
- Individualized starting points may vary based on age, training experience, degree of weakness, motor control, training goals, etc.

Fleeton et al. 2020

# Rate of Force Development (RFD) in CP

(Moreau, Falvo, Damiano, 2012)

- Impulse & RFD even more impaired than strength in CP
- More correlated to function
- Must train at fast speed to increase RFD (power)
- Power training *may* increase gait speed in CP more than strength training



DISABILITY AND REHABILITATION
https://doi.org/10.1080/09638288.2022.2138575

Taylor & Francis
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REVIEW ARTICLE

# The effects of power exercises on body structure and function, activity and participation in children with cerebral palsy: an ICF-based systematic review

Ozgun Kaya Kara[a], Ceren Gursen[b], Sebahat Yaprak Cetin[a], Elif Nur Tascioglu[a], Seda Muftuoglu[a] and Diane L. Damiano[c]

- Power training showed superior outcomes in strength, gait speed and gross motor function compared to standard or no therapy, but was not consistently better than strength training.

- Should be more task-specific for gait speed, but results depend on protocol or capabilities

Kaya Kara et al. 2022

# Electrical Stimulation vs. Weight Training

- Preferential to Type II fibers; may > movement speed & power
- Stimulation intensity needed only tolerable in small or weak muscles (30–50% of MAX)
- Helpful if muscle not/barely contracting (sensory + motor stimulation)
- Best in combination with weight or task-specific training

# Functional (or whole leg) Strengthening

- 2 RCTS comparing functional strengthening w/ legs loaded during functional tasks to controls
  - increased strength only 11-27%
  - Little or no improvement in function
  - 1 study reported > mm tightness
  - Explanation: targeted already stronger muscles dominating task
- Verschuren 2011; Damiano 2013 recommend single joint approach instead in CP

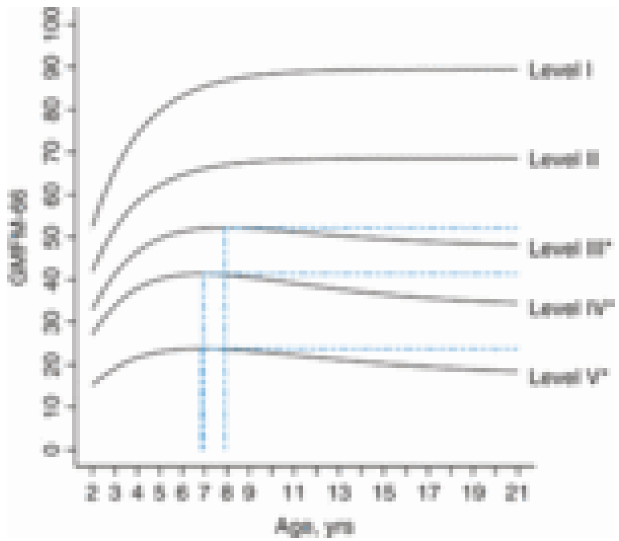

Nicholas Defrank
D.O.B: 5/8/89
Date: 2/24/03


Nicolas Defrank
D.O.B: 5/8/89
D.O.V: 2/26/04

# Summary on Strengthening in CP
## (after multiple studies & 4 clinical trials)

- Weakness is a major addressable impairment with large impact on function across lifespan
- Should be done "early" and "often"
- Benefits accumulate slowly over time
- Must be part of lifestyle (not constant therapy)
- Essential for maintaining long term health and functioning but they still have poor motor control (need to also address brain pathways)

# *Fast Forward* to Adulthood

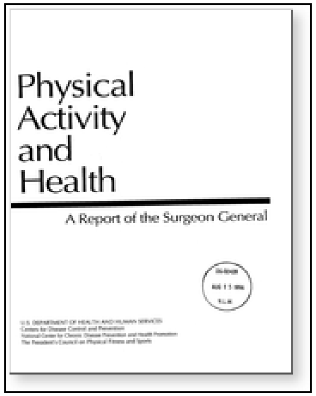



- Lifespan in CP more related to **inactivity** than diagnosis!
- 50% lose ability to walk in early-mid adulthood or walk less & fatigue more (Bottos 2003). Those who do not walk are at greater risk. Outliers were those who exercised regularly (Ando & Ueda 2000)

# Statement of the Problem

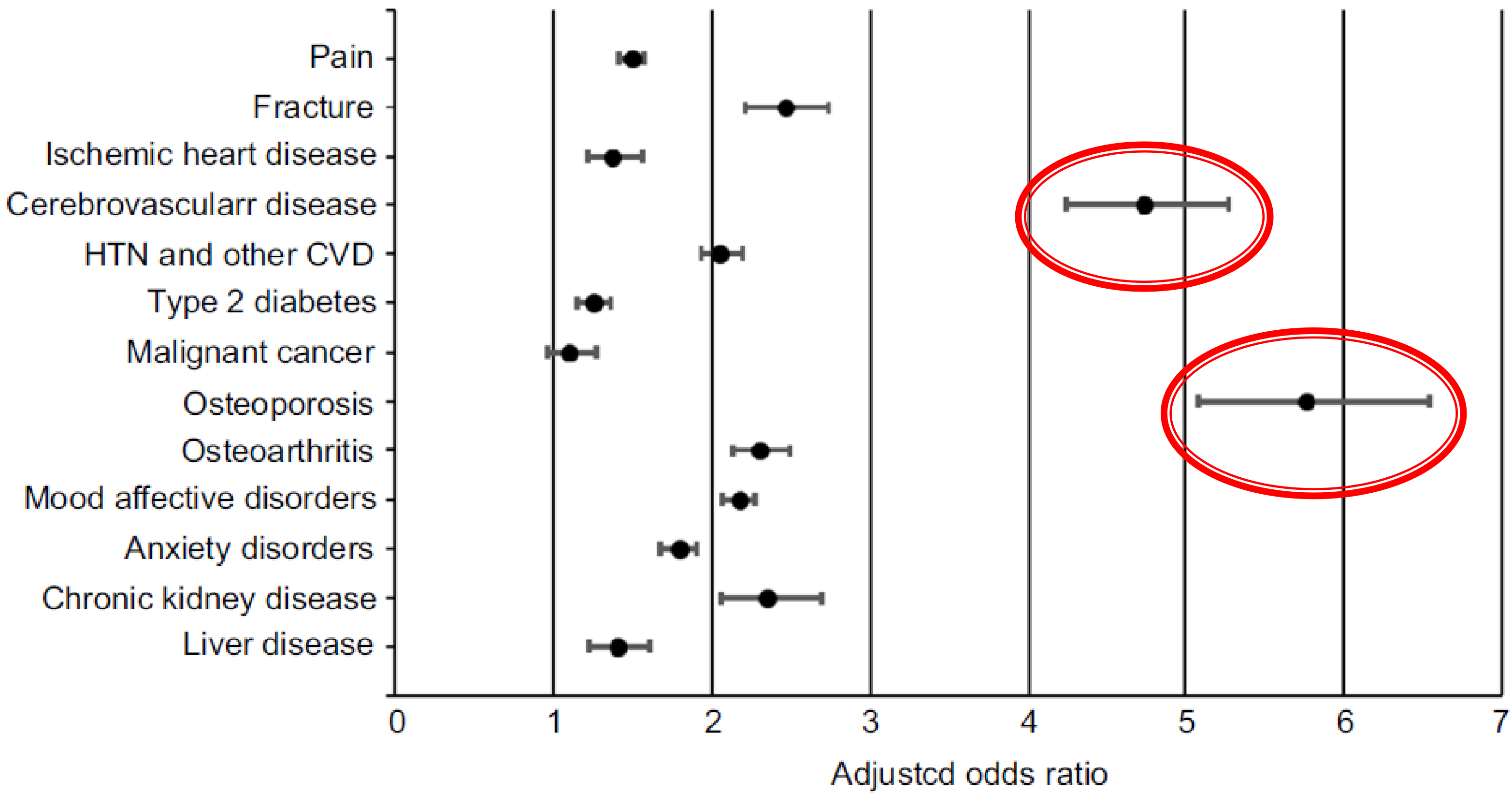
- **THEN**: "People with disabilities are less likely to engage in regular moderate physical activity than people without disabilities, yet they have similar needs to promote their health and prevent unnecessary disease"

Surgeon General's Report - 1996




- **NOW**: Those with disabilities are at greater risk for poor health consequences from inactivity; therefore have greater needs

# Health Risk in Adults with CP




Mean age = 42.5 years in CP & comparison groups; all significantly greater except cancer

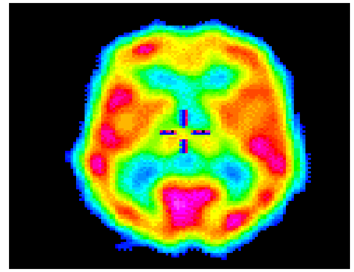
# Activity, Activity, Activity: Rethinking Our Physical Therapy Approach to Cerebral Palsy

This perspective outlines the theoretical basis for the presentation with the same name as the second part of this title, which was given at the III STEP conference in July 2005. It elaborates on the take-home message from that talk, which was to promote activity in children and adults with cerebral palsy and other central nervous system disorders. The author proposes that the paradigm for physical therapist management of cerebral palsy needs to shift from traditional or "packaged" approaches to a more focused and proactive approach of promoting activity through more intense active training protocols, lifestyle modifications, and mobility-enhancing devices. Increased motor activity has been shown to lead to better physical and mental health and to augment other aspects of functioning such as cognitive performance, and more recently has been shown to promote neural and functional recovery in people with damaged nervous systems. Although the benefits of fairly intense physical exercise programs such as strength training are becoming increasingly well recognized, few studies on the positive effects of generalized activity programs have been conducted in individuals with cerebral palsy. More research is needed and is currently under way to design and test the efficacy of activity-based strategies in cerebral palsy. [Damiano DL. Activity, activity, activity: rethinking our physical therapy approach to cerebral palsy. *Phys Ther.* 2006;86:1534–1540.]

**Key Words:** *Activity, Central nervous system, Cerebral palsy, Plasticity, Recovery, Strength.*

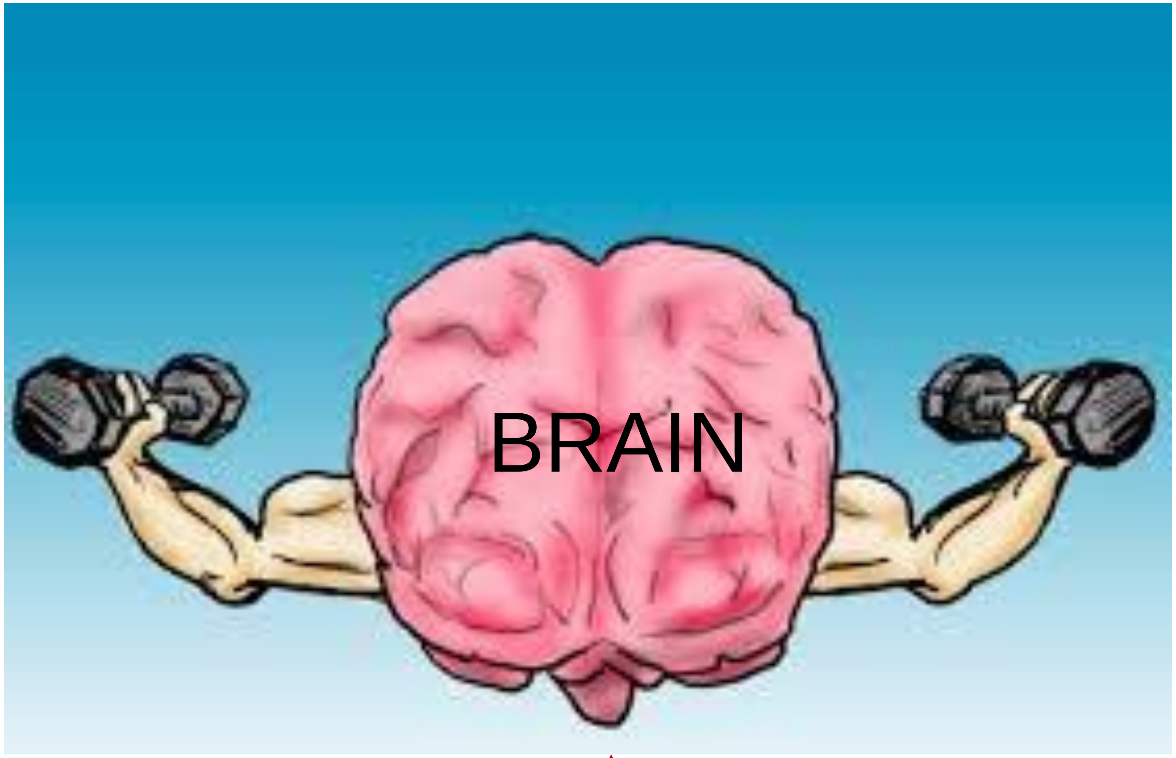
*Diane L Damiano*

# Neurobiology of Physical Activity



- Health benefits of exercise known for decades
- Exercise can also have major effects on the brain:
  - Strength training upregulates growth factors that signal brain to **grow** or **decay**
  - Muscle (electrical) activation via skill (coordination) training or inactivity (e.g. amputation) alters brain pathways
  - Improves cognition, memory, depression & anxiety, sleep
  - Increasing social engagement fosters health & wellness

# Two Major Targets Organs for Motor (Re)habilitation




MUSCLES

# Barriers to physical activity in CP

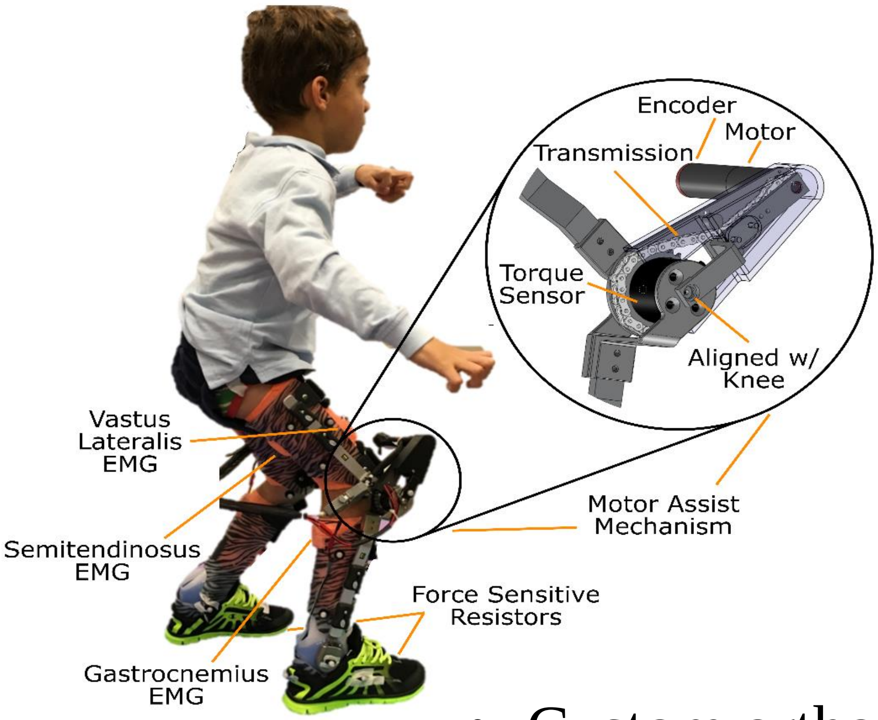
- Poorer physical capabilities only one limitation
- Self-perceived physical competence an issue (Chen 2013)
- Lack of appropriate accessible facilities nearby
- Lack of available sports & recreation opportunities
- Attitudes of public & those involved in sports and fitness towards those with disabilities
- Lack of safe or adapted equipment
- Transportation & financial concerns

# THE ROBOTS ARE COMING!

# Wearable Rehabilitation Device Goals

- **Substitute for lost function:** control or assist those with little or no strength & function to enable them to walk or move (SCI; GMFCS IV-V)
- **Enhance Functionality: if** already walking but with difficulty, can improve independence or decrease effort (military; factory workers). Under-utilized in rehabilitation
- **Provide rehabilitation:** train function & strengthen muscles while in device so user will walk better without device

# 1st Pediatric "Strengthening" Exoskeleton for Crouch Gait (Lerner, Damiano & Bulea 2017)





- Custom orthotics with motor at knee
- FES to facilitate strengthening
- Has assistive and assist/resist mode
- Separate exercise mode

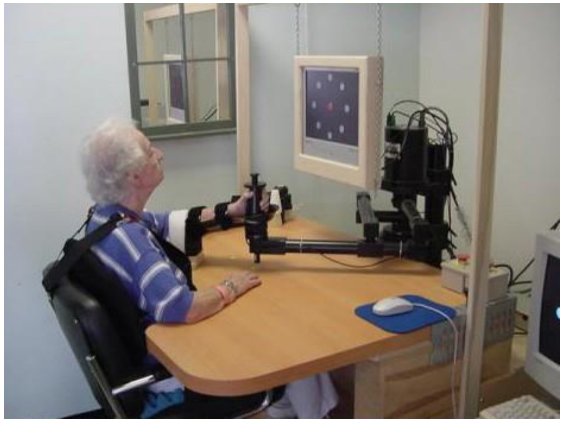
# Can robot(ic)s improve the outcomes of rehabilitation?

- **POSITIVES:**
- Can increase dose
- Reduce therapist effort
- Can give patients abilities they do not yet have
- Can individualize challenge & progression
- Can bring training into home (more affordable)?
- Can increase motivation

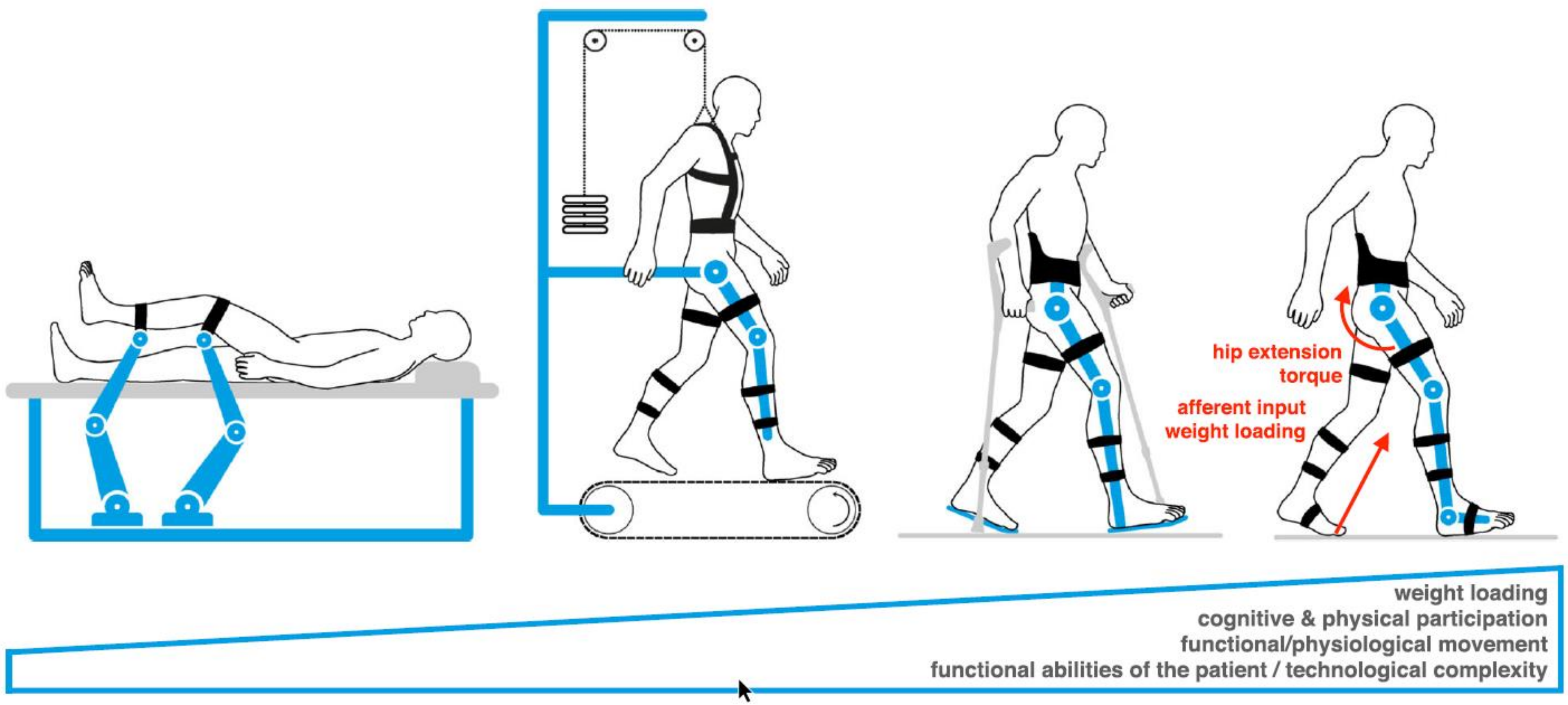
- **NEGATIVES:**
- May help too much (decrease effort & strength)
- May alter motor learning strategies (< errors, exploration)
- High costs; not broad accessibility, not user friendly

# History of Rehabilitation Robotics (Gassert & Dietz, 2018)

- Relatively "young" field (even younger for CP!)
  - 1989:  MIT Manus (upper extremity)
  - 1994: Lokomat (lower extremity)
- Upper extremity prognosis largely dependent on CST integrity; more flexible neural system for gait



# Evolution of Lower Limb Robotics



Gassert and Dietz *Journal of NeuroEngineering and Rehabilitation* (2018) 15:46
https://doi.org/10.1186/s12984-018-0383-x

Journal of NeuroEngineering and Rehabilitation

REVIEW **Open Access**

# Rehabilitation robots for the treatment of sensorimotor deficits: a neurophysiological perspective

Roger Gassert[1*] and Volker Dietz[2]

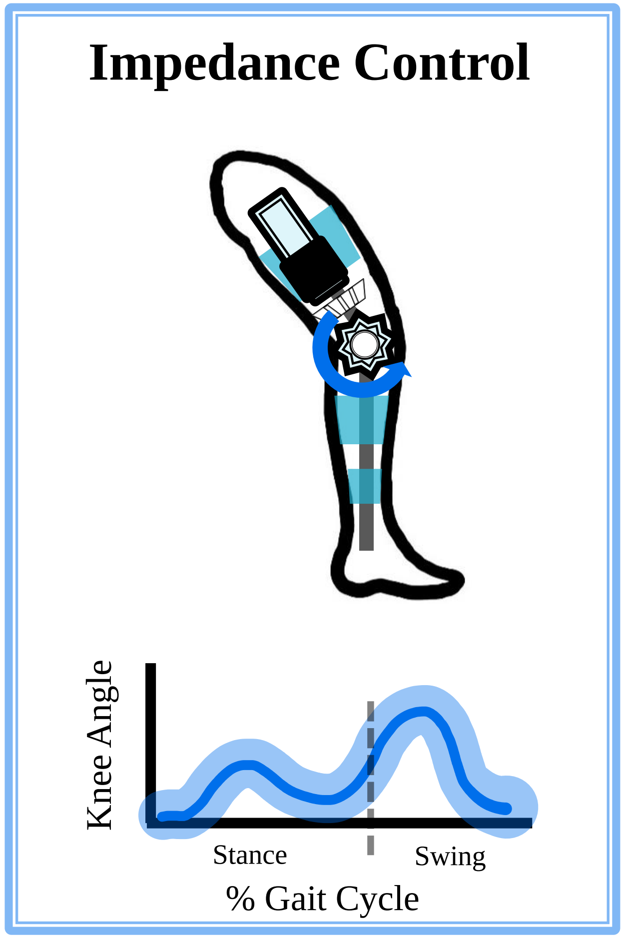
"Many of these innovations were technology-driven, limiting their clinical application and impact. Yet, **rehabilitation robots** should be designed on the basis of neurophysiological insights underlying normal and impaired sensorimotor functions, which requires interdisciplinary collaboration and knowledge".

# Key Principles in Neurorehabilitation

- **EFFORT**: most effort exerted by the person, not the device or the therapist
- **ERROR:** person needs to be aware of and actively correct their movement errors
- **ENGAGEMENT:** person should be cognitively involved in and motivated to do the task

# EFFORT, ERROR, ENGAGEMENT?

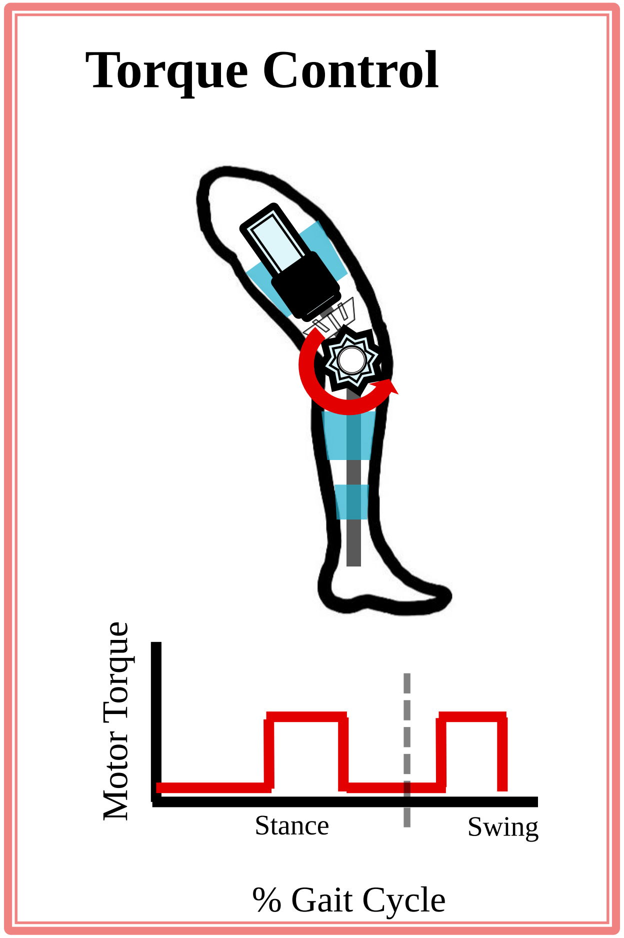
# Most robotic devices use assist-as-needed (impedance) control

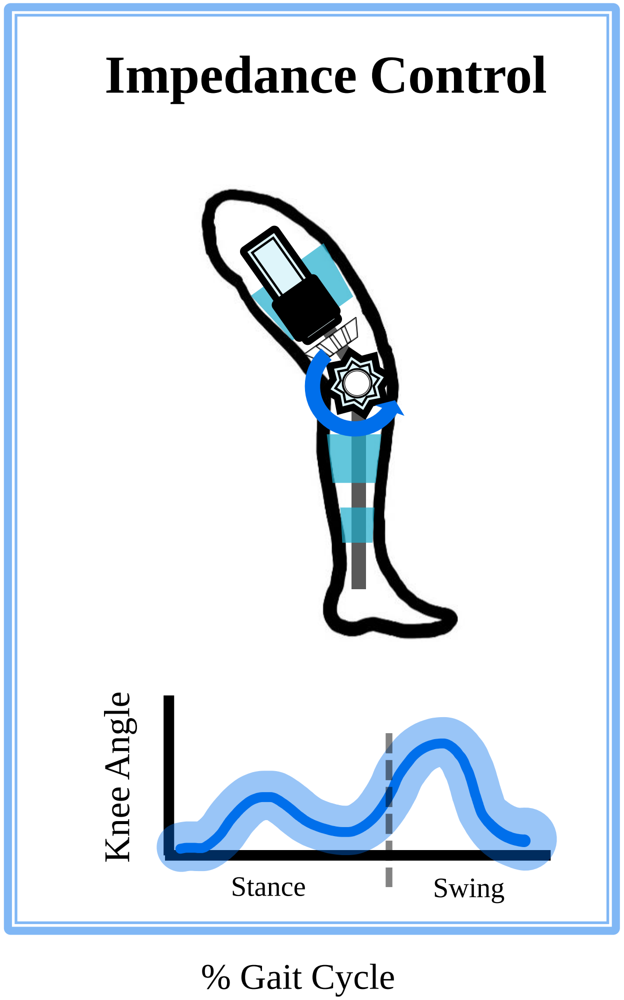


# EFFORT & the "Slacking" Hypothesis (Reinkensmeyer)

- With impedance control, user is "nudged" when they deviate from the target trajectory.
- Unconsciously, instead of fighting the device, users will just let the device move them
- SOLUTION: provide slightly less assistance than needed
- If you can prevent slacking, outcomes from assist-as-needed were superior in stroke
- ERRORS: His group also showed you need to introduce errors (challenge trials) so people learn more flexible and adaptable strategies

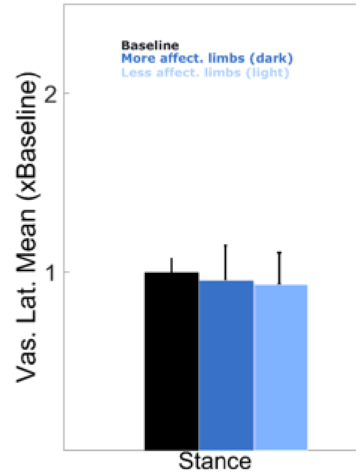
# Comparing Exoskeleton Controllers



# Effectiveness and EFFORT

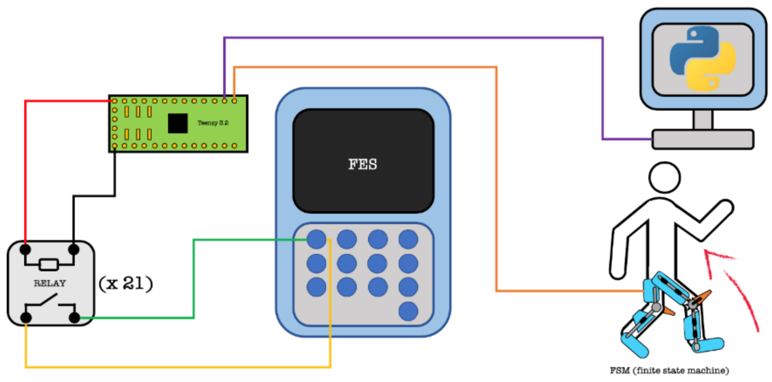
- N=7; independent ambulators; GMFCS I (1), II (6); 6–19yrs
- **Mean crouch reduction of 13.3° and 5.8° in more affected and less affected limbs, respectively ($p<0.05$); (similar to surgery)**
- **Knee extensors remained active**

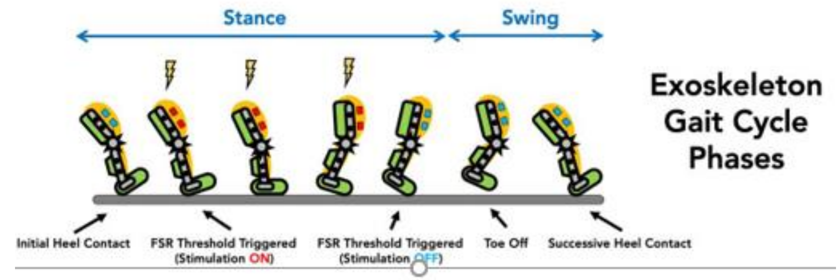



Knee Extensors without (dark) and with exoskeleton on More & Less Affected Legs (Medium & light blue)

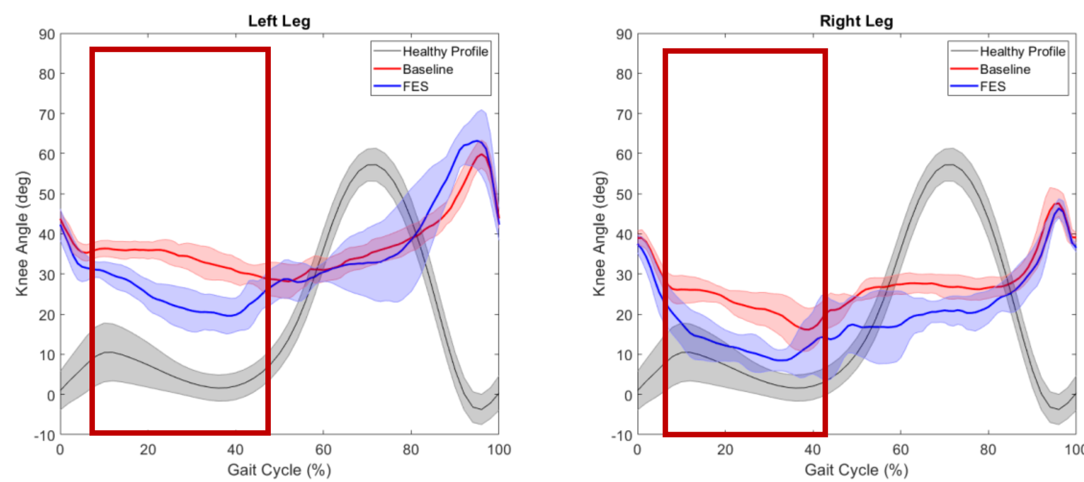

Baseline Walking

# Quadriceps FES With Exoskeleton




- 15 yo M GMFCS I
- FES at twitch level
- LEFT Peak KE > 3°
- RIGHT Peak KE > 6°
  (20 strides)




**Goal to combine w/ motor**

Shideler et al. 2020

# Resistance Mode

- For children who are stronger (GMFCS I & II) resistance can be provided during stance
- For those who are weaker, this may make it impossible to remain upright, so we *assist* during stance and *resist* at the end of swing (interleaved mode).
- Immediate response to resistance is to increase crouch, but when removed, the child is briefly less crouched – hopefully persists with training.

# Increasing ENGAGEMENT in training

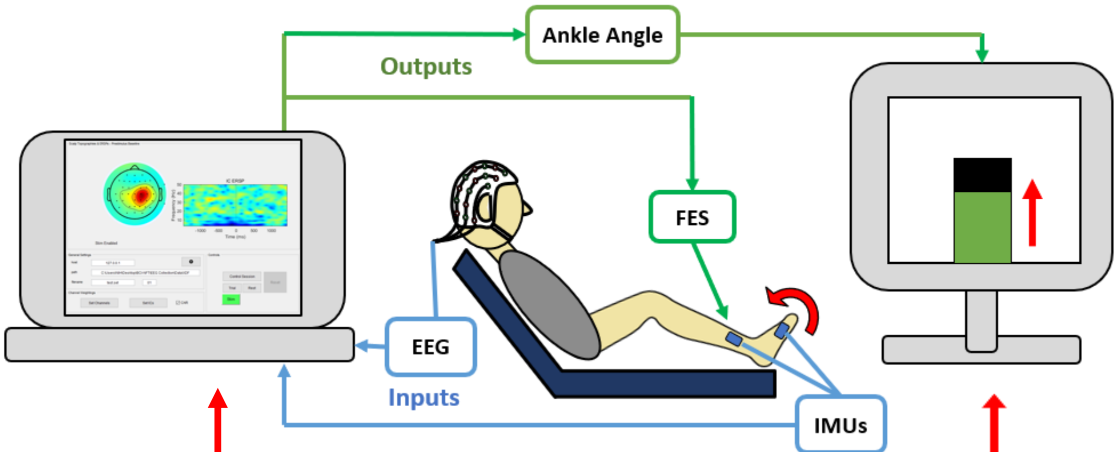
Exergaming with a Pediatric Exoskeleton

Functional & Applied Biomechanics Section
Rehabilitation Medicine Department
National Institutes of Health

# Motor control vs. weakness

- 21 children with unilateral CP used WalkAide to stimulate ankle dorsiflexors during gait
- Wore this 6 hours/day X 6 months
- All walked better with device
- Muscle size increased over time
- Selective control did not improve; even worsened in some because they no longer had to think about flexing their ankle

# EEG BCI-neurofeedback system to train ankle dorsiflexion in CP




Target ankle angle

What experimenter sees

What participant sees

# Goal of our neurofeedback system

- Enhance motor training (ankle dorsiflexion) & plasticity through EEG detection of movement intention that then activates FES to assist ankle movement and increase sensory input to cortex.
- Participant performs target movement "as far and fast" as possible while receiving real-time visual feedback of joint excursion.
- *Dose*: 20 5-trial blocks for each of 10 sessions
- *Outcomes:* Pre and post EEG, active ankle movement, and ankle gait kinematics assessment

# First participant with CP

PARTICIPANT

- 10 yo boy with Right unilateral CP, GMFCS I
- **Goal**: be able to run bases faster without catching his toes
- He had more than 10° of active dorsiflexion at baseline, so he trained mainly to increase ankle joint angular velocity

RESULTS:

- DF angular velocity increased from 482 °/s to 600 °/s. (Normal in swing phase of gait = 540°/s)
- Walking speed increased from 1.19 to 1.34 m/s
- Right step length increased from 0.56 to 0.61 meters
- EEG showed increased Beta ERD during both rest and task

# Three young athletes with CP who have educated and inspired me

- *Cathryn Gray and mom Cynthia Frisina*:
  - Mom started *Reaching for the Stars* parent advocacy group (now part of Cerebral Palsy Foundation); lobbied US Congress to increase research visibility and funding for CP; AACPDM lecture on no CP is "mild"
  - Cathryn is an internationally ranked paralympic track and field athlete now at University of Michigan & Women's Sports Foundation National Ambassador and grant recipient. ***" I want to be the role model that was not there for me".***

# Nils and Lars Bjork & Frame Running

- Nils is now a young adult with dystonic CP; GMFCS IV
- Dad & Nils discovered (race) framerunning as a young child. He began training & competing.
- Shattered perceptions: people with CP can be elite athletes!
- "I am glad I have CP because I get to be the best in the world at something"
- Now a young adult who still competes but more interested in music and wanting a girlfriend
- Both are a major force in promoting uptake of framerunning in Sweden and elsewhere and in research

# Matthew (and Janet) Paintin

- Mom knows best: when Matt was young, mom kept him very active- even invented a dynamic brace to preserve PFs
- Matt excelled as a distance runner in high school; won a track scholarship to Division III college
- Realized he could not compete on a national level
- 2019 USA Record Holder in the 800m and 1500m; competed in Paralympic World Junior Championships
- 2023 Para Athletic Championship, forced to shift to shorter distance (assumption that those with CP cannot run so far?)
- Placed 5th in 200m (26.97);8th in100m (13.75) in T35 category
- Works with and is a role model for other young athletes with CP


# Conclusions

- Brain injury in CP affects ability to move which then alters the muscles and makes it harder to move. Need to address both muscle strength and brain pathways (motor control)
- Therapist's role is to promote lifespan physical activity so people can pursue own life, fitness and recreation goals
- Robotics (assistive or rehabilitative) and other technologies can potentially transform one's capabilities & participation
- Physical activity is essential to long term health
- For people with CP, activity has many other benefits: increase participation, self-concept, mental health, sleep, ROM, modulate spasticity and decrease pain.

JUST DO IT

# Grazie per l'attenzione!

Neurorehabilitation & Biomechanics Research Section