WHO’S IN CHARGE?
NEURAL CONTRIBUTIONS TO
MOVEMENT AFTER SCI & STROKE

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OBJECTIVES

- Compare and contrast the sensorimotor impairments following brain versus spinal cord injury
- Appreciate the mechanisms underlying abnormal muscle activation/deactivation in persons with SCI & stroke
- Explain the implications of excessive brainstem contributions to loss of independent joint control following brain injuries; and the implications of loss of brainstem contributions to motor output after SCI
- Differentiate between contributions to spastic hypertonia in persons with stroke versus spinal cord injury
- Be able to implement effective interventions that address the motor impairments

WHAT ARE THE CHALLENGES TO RESTORING FUNCTION AFTER SCI?

Damage to descending tracts
Detrimental spinal reorganization
Damage to ascending tracts
Detrimental cortical reorganization
**Spinal Cord Anatomy -- Transverse**

At each level there are spinal neurons subserving various functions, as well as axons ascending and descending to other levels.

**Monoamines Mediate Communication Between Bulbospinal and Spinal Centers**

- Excite motoneurons and CPGs to activate movement
- Excite inhibitory interneurons to modulate reflex activity

**What about Brainstem Plasticity Role after SCI?**

Animals models of hemisection → relevance to typical human SCI unclear*

Early evidence of reticulospinal sparing in humans → relevance to function unclear**

**Stuart & Perez. Soc Neurosci Abstr, 2015 158.15

**Hand Function is Highly Dependent on Corticospinal Tract Function**

- Corticospinal function depends on corticomotor excitability
- Sensory input influences corticomotor excitability

The cortex reorganizes after SCI…

…does this contribute to functional deficits?

CONTROLS

SCI

Green et al. Neurology, 1998

Supraspinal input is needed for control of voluntary & involuntary movement


Supraspinal input is needed for control of voluntary & involuntary movement.

Like hand function, in humans after SCI walking is highly dependent on cortical input.

- N = 492
- Early test: 3-15 days post SCI
- Follow-up: 1 year post SCI
- Excellent discrimination between: Independent walkers vs non-walkers.
- Discriminative ability of AIS AUC = 0.898 95% CI = 0.867–0.928, p<0.0001

Spasticity after SCI

After 1 year post-SCI spasticity is reported by
- 78-93% of those with tetraplegia
- ~70% of those with paraplegia

Skold et al Arch Phys Med Rehabil, 1999

Fluren et al Spinal Cord 2009

Van der Linden et al. A clinical prediction rule for ambulation outcomes after SCI. Lancet (2011)
WHAT IS SPASTICITY?
THE CLASSIC DEFINITION...

- motor disorder characterized by a velocity-dependent increase in the tonic stretch reflex with exaggerated tendon jerks, resulting from hyper excitability of the stretch reflex, as one component of the upper motor neurone syndrome.

(Lance, 1980)

A Challenge from the SPASM Consortium
Pandyan et al 2005

The classic definition of spasticity is too narrow and not consistent with experimental and clinical observation...

- Cutaneous pathways have a role in triggering spasms
- Reflexes beyond the stretch reflex are also hyperactive
- Spasms may be triggered by both passive OR active movement
- Beyond reflexes, feedforward mechanisms are also disordered (eg, impaired phase-dependent modulation)

WHAT IS SPASTICITY?
AN UPDATED DEFINITION...

- “...disordered sensori-motor control, resulting from an upper motoneuron lesion, presenting as intermittent or sustained involuntary activation of muscles.”

(The SPASM Consortium Pandayan et al, 2005)

PERSISTENT INWARD CURRENTS (PICs)
sustain motoneuron firing following activation

Heckman CJ, 2004
SCI-related Synaptic Changes Result in Loss of Reflex Inhibition

- KCl co-transporter (KCC2) maintains low intracellular Cl- in adults
- KCC2 is downregulated after SCI
- Result: decreased inhibitory effects of glycine & GABA on spinal reflex excitability


In ND Subjects: Immobilization Induces Reflex Changes Similar to SCI


Biomechanical Quantification of Stretch Reflex Excitability

Pendulum Test
Low spasticity
High spasticity

Who’s In Charge? Neural Contributions to Movement after Stroke

Jules Dewald

WHO’S IN CHARGE?
Neural Contributions to Movement after Stroke

Jules Dewald

Northwestern University, Biomedical Engineering
Physical Therapy and Human Movement Sciences
Motor Impairments following stroke

• Functional deficits in the paretic upper/lower limb following adult or pediatric onset hemiparesis may be caused by:
  • Weakness
  • Spasticity
  • Abnormal muscle synergies resulting in a loss of independent joint control (IJC)

Neural Mechanisms

• Increased use of projections via ipsilateral descending pathways
• Comes at a penalty of a loss in independent joint control

Source: A. Stienen and A. Chen

SPASTICITY

• An enhanced stretch reflex behavior resulting in hypersensitivity of the muscle to elongation which results in increased resistance of the limb to imposed movements (Lance, 1980).

Evidence for Bistable Motoneuron Behavior following stroke: increased monoaminergic input to the spinal cord

• Use of TVR in chronic hemiparetic stroke subjects
  – Under relaxed conditions
  • Increased noradrenergic and serotonergic input to the spinal cord
  – Increase dependence on brainstem pathways especially the dorsal reticulospinal pathway
Following stroke or hemiparetic CP, increase of reticulospinal drive increases tonic vibration reflex

PICs and pathology: stroke
Repeated-stretch relaxed

Tonic vibration

McPherson, 2006

Single-stretch relaxed

Single-str preactivated

• 10 participants with stroke (mod-severe)
• 5 age-matched controls
• 5 young controls
• EF torque 15% MVT
• Stretch at 270°/s

Representative single-subject data


Elbow flexion torque [ % MVT ]
**Static mechanical measurements: Synergies**

- **Single task protocol** for measuring static (isometric) joint torque coupling during maximum voluntary contractions

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**Pilot results in pediatric subjects**

- Decreased elbow extension ability with shoulder abduction

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**Dual task results**

- Shoulder abduction control subjects

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**ACT 3D System video**

- Table Supported
Shoulder abduction effort affects work area

(Sukal et al, 2007)

Severe impairment (N=13, FMA=10–25/CMSAh=2–3) and Moderate impairment (N=13, FMA=26–40/CMSAh=4–5). (Pentagon area)

Lan, Yao and Dewald, 2011, 2013, 2017

Shoulder abduction at the end of a reach reduced hand opening

Shoulder abduction at the end of a reach reduced grasp force control

Dynamic EEG experimental setup

Surface EMG and kinematics/forces recorded during movements performed on the ACT3D robot
Joint kinematic trajectories

Angular excursions and velocities decrease significantly at the shoulder and elbow for stroke subjects as shoulder abduction drive is increased.

Sample cortical activity maps

Example for one of the stroke subjects (most impaired individual)

- When lifting 25% of his max abduction force with the left paretic limb, cortical activity appears over the left ipsilateral cortex.

Discussion

- Damage to corticofugal projections
- Increased use of projections via ipsilateral descending pathways
- Comes at a penalty of a loss in independent joint control

Stretch reflex activity during movement

Source: A. Stienen and A. Chen
Stretch reflex activity during movement

Lower Extremity Torque coupling

- Post-Stroke abnormal lower extremity (LE) coupling patterns (Brunnstrom, 1970)
  - Flexor Synergy
    (Hip Flexion + Hip Abduction + Knee Flexion + Ankle Dorsiflexion)
  - Extensor Synergy
    (Hip Extension + Hip Adduction + Knee Extension + Ankle Plantarflexion)
Loss of independent joint in the paretic leg: isometric setup

Robots for lower limb rehab
• Lokomat position controlled robot

Loss of independent joint in the paretic leg: Dual-task results

Who’s in Charge?
Science based interventions to regain function after SCI

Edelle Field-Fote
<Recap> SCI vs Stroke

Control of Voluntary Movement

SCI
- Impaired bilateral voluntary drive

Stroke
- Impaired contralateral drive
- Increased ipsilateral drive
- Increased brainstem (reticulospinal) drive

Control of Involuntary Movement

SCI
- Decreased monoamines (reduced brainstem input)

Stroke
- Increased monoamines (excessive brainstem input)

Accessible Approaches to Increasing Cortical Activation for Improved Hand Function

Clinically Accessible Interventions Increase Cortical Excitability & Hand Function

Dashed line = moderate effect size
Gomes-Osman & Field-Fote, J Neurol Phys Ther, 2015

Reorganization of the cortical map
Hoffman & Field-Fote, Phys Ther, 2007
**Change in Hand Function is Associated with Change in Cortical Excitability**

Sample thenar MEPs at 80% MSO (avg of 5 traces)


**Groupwise Changes in Walking Speed & Distance**


**Is There a “Best” Approach to Locomotor Practice?**

- Treadmill training with manual assistance (TM)
- Treadmill training with CPN stimulation assist (TS)
- Overground training with CPN stimulation assist (Walkaide II stimulator; OG)
- Treadmill training with robotic assistance (Lokomat robotic orthosis; LR)

N = 74 enrolled, 64 completed (across 4 groups)

Field-Fote & Reach. Phys Ther, 91:48-60, 2011

**Whole-body Vibration (WBV) Improves Walking and Decreases Spasticity in SCI**

- Subjects: 17 individuals with chronic SCI
- 50 Hz, low amplitude (2-4 mm)
- 3 days/week x 4 wks
- Outcomes:
  - increased walking speed
  - decreased quad spasticity

Spasticity: Ness & Field-Fote. Restor Neural Neurosci, 2009

**GROUPWISE CHANGES IN WALKING SPEED & DISTANCE**

Field-Fote & Reach. Phys Ther, 91:48-60, 2011

**WHOLE-BODY VIBRATION (WBV) IMPROVES WALKING AND DECREASES SPASTICITY IN SCI**

Walkaide II stimulator; OG

Spasticity: Ness & Field-Fote. Restor Neural Neurosci, 2009
IMPROVED WALKING FOLLOWING
12-SESSION COURSE OF WBV

WBV influences on spasticity in chronic SC

WHAT DOSE OF WBV IS HAS LARGEST EFFECT?
A single-session dose-response study

<table>
<thead>
<tr>
<th>WBV Frequency</th>
<th>0 Hz</th>
<th>35 Hz</th>
<th>50 Hz</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exposure duration</td>
<td>180 sec</td>
<td>Dose 2 (shlo)</td>
<td>Dose 4 (shhi)</td>
</tr>
<tr>
<td>360 sec</td>
<td>Dose 1 (placebo)</td>
<td>Dose 3 (l glo)</td>
<td>Dose 5 (lghi)</td>
</tr>
</tbody>
</table>

Is there a “BEST” physical therapeutic/electroceutic intervention for spasticity?
**Is there a “BEST” physical therapeutic/electrocutaneous intervention for spasticity?**

A. Immediate

B. Delayed

Changes in H-reflex, M-wave, Dorsiflexor, and TA/MVC amplitude.

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**Should we train to ↓ reflexes or to ↑ voluntary control?**

C. TA ↓

D. SOL ↓

Outcomes of training approaches.

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**Sample SOL ↓ Outcome**

A. Training Session 1

B. Testing Session 1

Changes in H-reflex and M-wave.

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**Outcomes Reflexes, Strength, Walking, EMG**

<table>
<thead>
<tr>
<th>Outcome</th>
<th>TA ↑</th>
<th>SOL ↓</th>
</tr>
</thead>
<tbody>
<tr>
<td>TA %MVC amplitude</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>Stretch reflex threshold</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>Active dorsifexor ROM</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>Dorsifexor strength</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>Step height in walking</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>2MinWT distance</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>TA/SOL co-activation</td>
<td>✔</td>
<td>✔</td>
</tr>
</tbody>
</table>

THE CAUDAL END

- In SCI, maladaptive plasticity of the cortex and spinal cord impairs voluntary and involuntary motor output.
- Training promotes adaptive neuroplasticity.
- Movement & stimulation influence the neural environment.
- Clinically accessible stimulation can be a valuable adjuvant to training & spasticity management.

WHO'S IN CHARGE?
SCIENCE BASED INTERVENTIONS TO REGAIN FUNCTION AFTER STROKE

Mike Ellis
Jun Yao
Ana Maria Acosta
Jules Dewald

Treating impaired reaching is safe and feasible

- Initial ACT intervention
- Reaching practice with progressive abduction loading
- Initiation and progression with quantitative markers
  - Load at level where reaching is 50%
  - Increase load when reaching is at 80%

Hand path traces pre (left) and post (right) training, with 9 support levels shown for comparison. Note the increase area and elbow extension capabilities particularly at the 150-200% support levels.
Randomized study results

- Work area gain scores greater in experimental group
- Up to 68% increase in work area at functionally-relevant loading levels
- Therapeutic element of reaching practice is abduction loading

Early Robotic Intervention Results: Single Subject Results

<table>
<thead>
<tr>
<th>Pre-SABD</th>
<th>Pre-EF</th>
<th>Post SABD &amp; EF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Session</td>
<td>SABD &amp; EF</td>
<td>SABD &amp; EF</td>
</tr>
<tr>
<td>FM Score</td>
<td>10/66 (pre)</td>
<td>19/66 (post)</td>
</tr>
<tr>
<td>Overlap Area</td>
<td>0.15</td>
<td>0.08</td>
</tr>
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Preliminary single subject cortical plasticity data
Novel Human Machine interfaces to Regain Hand Function Using Muscle Signals

Conclusions

- Proper quantification combined with hypothesis driven science will lead to a better understanding of mechanisms underlying movement impairments following neural injury.
- Once mechanisms of impairment are understood devices can be used to augment very specific science based interventions in addition to providing treatment intensity.
- The overall goal is to develop the best interventions that promote the use of remaining neural resources (e.g., CST) from the lesioned hemisphere or remaining spinal neural circuits (SCI).
- There are distinct differences in neural losses between unilateral brain injury due to stroke or CP and SCI and consequently there are differences in motor impairment and optimal treatment approaches.

Debate