Mechanisms of Spinal Neuromodulation And Plasticity Post Paralysis

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Kessler Foundation
July 21, 2017
Disclosure

I hold shareholder interest in NeuroRecovery Technologies. I hold certain inventorship rights on intellectual property licensed by The Regents of the University of California to NeuroRecovery Technologies and its subsidiaries.
Specificity of Connectivity

From: Scheibel, M.E. and Scheibel, A.B., A Structural Analysis of Spinal Interneurons and Renshaw Cells, The Interneuron,
Principles Underlying Recovery of Function

- Sensory Input
- CPG Rhythmic Flex-Ext
- Automaticity
- Spinal Learning
- Neuromodulation
- *Regaining Voluntary & Autonomic Function
- *Enabling vs. Inducing Movement
- Recognition of Magnitude of Importance of Sensory Control

*Regaining Voluntary & Autonomic Function

**Enabling vs. Inducing Movement**
Plasticity

Recruitment

Motor Threshold
Resting Potential

Coordination

Torque / Metabostasis

eEmc + Training + Pharma

INJURY

Atrophy

Hypertrophy
4 Remodeling of lumbosacral circuits through use-dependent mechanisms

**c-fos**

NO REHABILITATION

REHABILITATION

<table>
<thead>
<tr>
<th>Locomotor performance PCA score (a.u.)</th>
<th># of c-fos positive neurons</th>
</tr>
</thead>
<tbody>
<tr>
<td>-12</td>
<td>0</td>
</tr>
<tr>
<td>-6</td>
<td>2000</td>
</tr>
<tr>
<td>0</td>
<td>4000</td>
</tr>
</tbody>
</table>

\[ r = 0.82 \]
Automaticity in Movement

(You don’t have to think about the details)
Spinal Learning
And
Sensory Control
Direction-dependent afferent input
Determines the features of locomotor patterns

0 deg ← ▶

STANCE
M
G
TA
VL
ST

SWING

180 deg ← ▶

90 deg ← ▶

Straight to Sideways

1s
1s
1s
Figure 5–7. Schematic illustration of a cord segment with its dorsal root, ganglion cells, and sensory organs. 1: Pacinian corpuscle; 2: muscle spindle; 3: Golgi tendon organ; 4: encapsulated ending; 5: free nerve endings.
Spontaneous EMG after Spinal Transection

![Graph showing EMG amplitudes and potentials with different postures.]
"Hearing Aid"
Epidural Stimulation in humans (N=4)
AIS-A: Motor and sensory complete
Neurological Level: T4

Fast Oscillations of Left Leg
(with non compliant cable measuring force generation)

Standing while throwing and catching a ball
(left hand on elastic band to challenge posture)
Network Excitability Amplification

![Graph showing peak force vs. stimulation strength.]

- **X-axis**: Stimulation Strength (V)
- **Y-axis**: Peak Force (N)

The graph illustrates the relationship between stimulation strength and peak force, with a clear upward trend as the stimulation strength increases.
electroEnabling motor control (eEmc)
Lumbosacral Neuromodulation after Chronic SCI (N=5)
Experimental design for percutaneous electrical spinal cord stimulation (PTES) in normal individual

Гурфинкель и др. 1998; Selionov et al. 2009

“A Russian” current

A 10kHz biphasic stimulation is delivered in 0.3 to 1ms bursts. These pulses are delivered at 1-40 Hz.
Non-invasive Neuromodulation to regain voluntary leg movements after complete paralysis
Combining pcEmc and Exoskeletal Assistive Devices (Ekso)
Cervical Spinal Neuromodulation
Before Injury

Post-Injury (1 week)

Left Paw Dominant

Same Representative Animal & Scale (amplitude, time)
Post-Injury (6 weeks)  Sham Treatment

Right Paw Dominant

Buspirone Treatment

Left Paw Dominant

Same Representative Animals as Previous Slide
Non-Invasive Neuromodulation to regain hand grip function after paralysis
CONTROL ANIMAL

Pre-injury

Post Injury

Session 1

Session 2

Session 3
STIM ON/OFF
Neuromodulation of Bladder Function
Principles Underlying Recovery of Function

You don’t have to think about the details the spinal cord knows what to do

Automaticity (Central Pattern Generation)

Activity Dependent Plasticity

Supra-spinal Input (Brain)

NEUROMODULATION Targeting Interneurons

Sensory (Proprioceptive Input & Control)

Learning

Voluntary Movement

Involuntary Movement

Spinal Cord

Recovery
To **relearn** there must be re-engagement of the circuits

This can be accomplished **pharmacologically** and via **electrical** neuromodulation when combined with **training**
Previously unrecognized potential levels of recovery of motor function via neuromodulation and neural plasticity

New clinical horizons
No Stimulation
Acknowledgments

National Institute of Biomedical Imaging and Bioengineering

National Institute of Neurological Disorders and Stroke

NASA

US Congress
Dana and Albert R. Broccoli Charitable Foundation

Al Mann Foundation

CRAIG H. NEILSEN FOUNDATION

Jonathan & Marilyn Palo Family