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Spinal cord epidural stimulation for lower limb motor function recovery in individuals with chronic motor complete spinal cord injury

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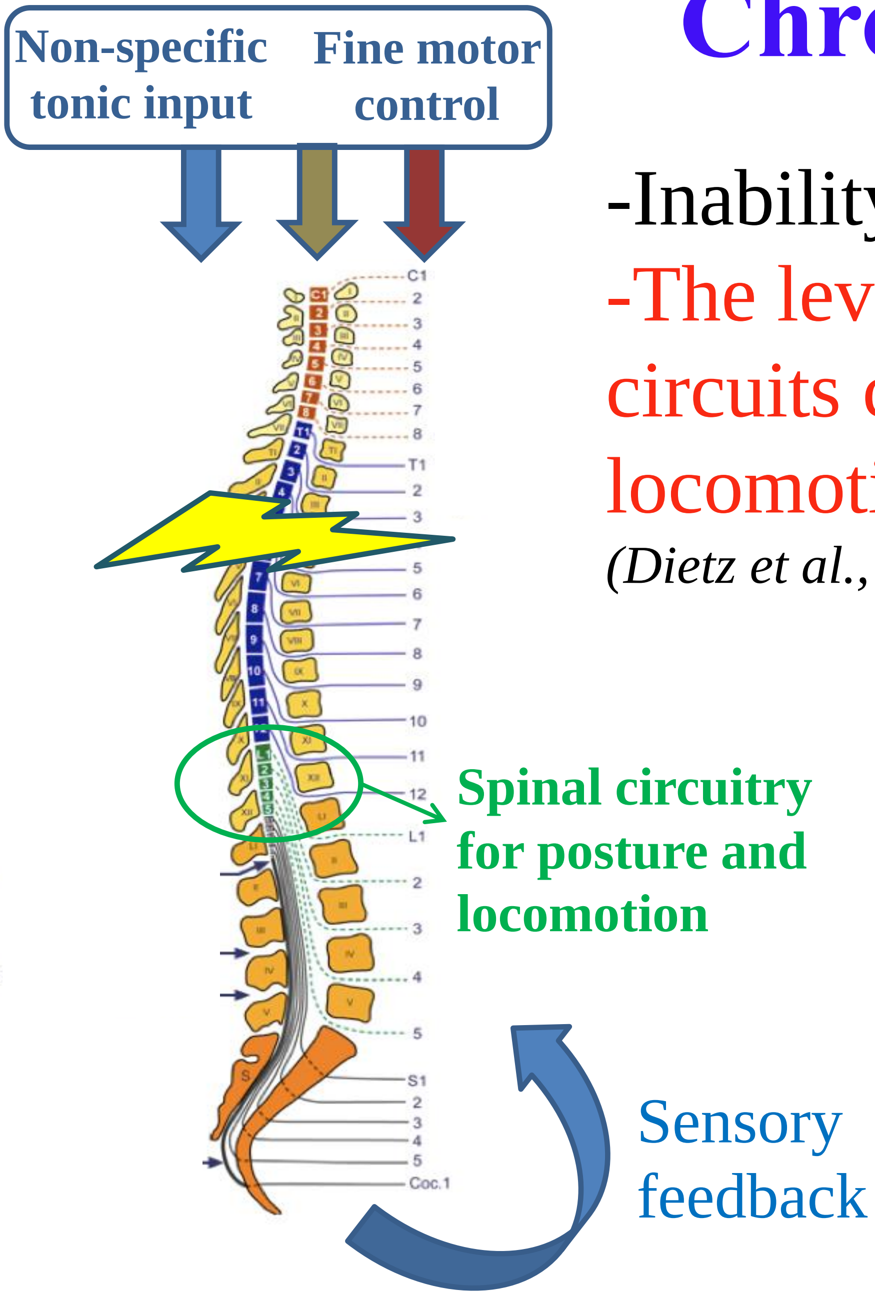
Chronic "complete" SCI



-Inability to stand and walk.

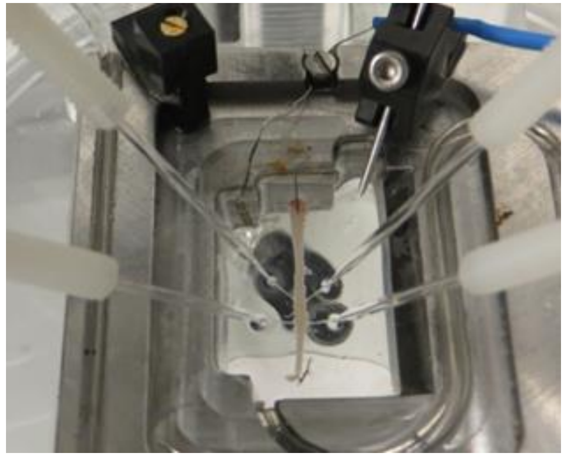
-The level of excitability of spinal circuits controlling posture and locomotion is compromised.

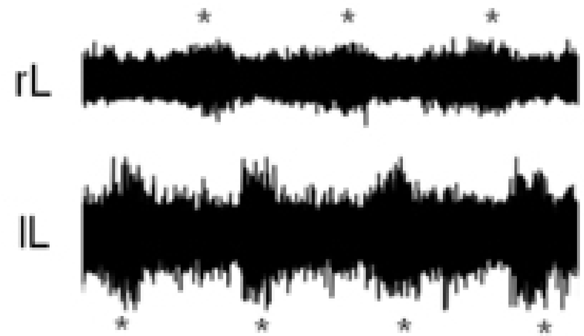
(Dietz et al., 1995; Harkema 2008; Cote et al., 2017)

<u>Spinal stimulation</u> for motor recovery <u>capitalizes on</u> the human spinal cord sensory-motor <u>potential that still persists</u> after SCI.

“The spinal cord is smart” – 1. Automaticity

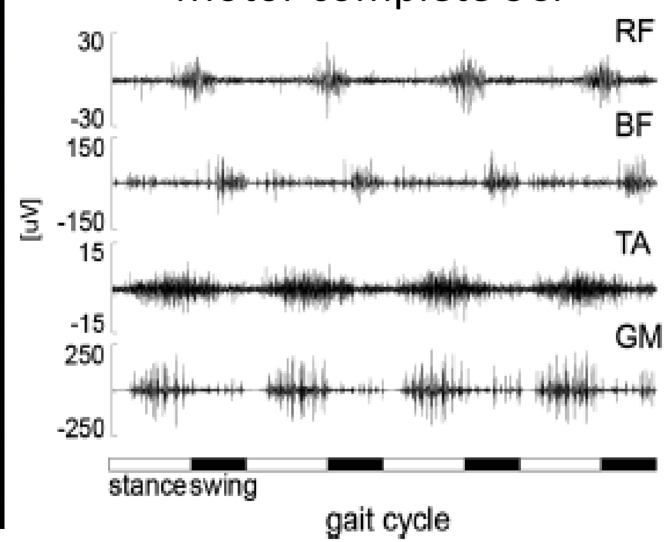
Pharmacological, Electric or Tactile stimulation can generate oscillating activation patterns,





which can be modulated by peripheral sensory information

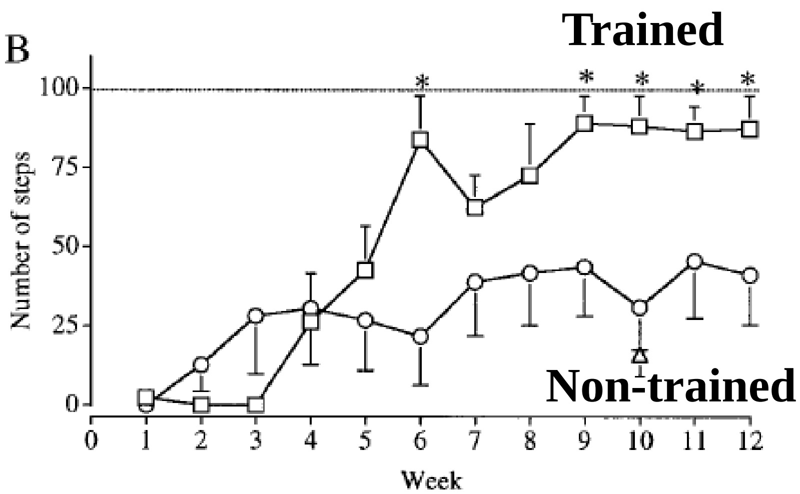
Motor complete SCI

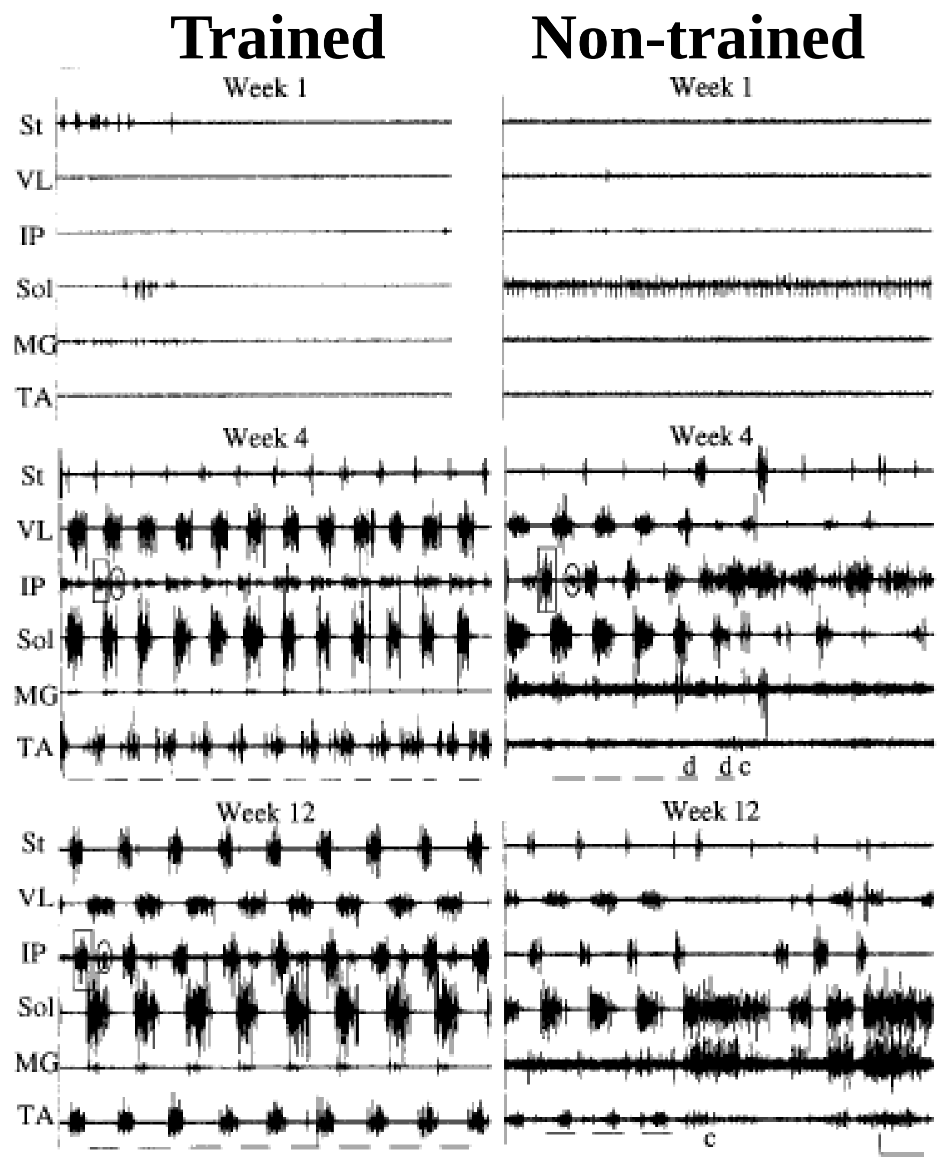


Hubli & Dietz, 2013

"The spinal cord is smart" – 2. Plasticity

After a complete transaction, <u>the spinal cord can learn to perform a motor task</u>





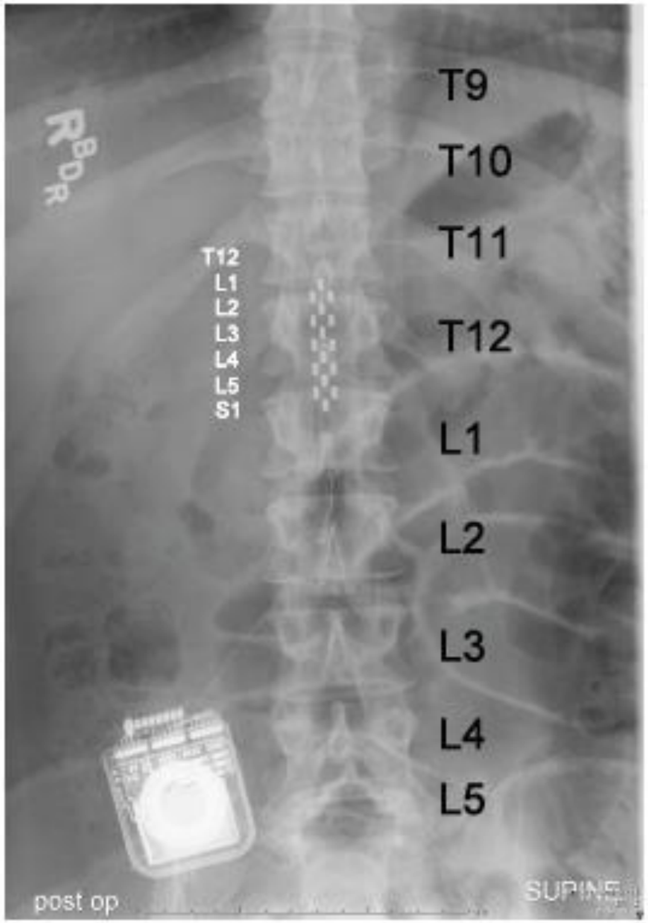
De Leon et al., 1998

3. Residual Supraspinal Connectivity to the Spinal Circuitry after Motor Complete Spinal Cord Injury

Most (~ 80%) of clinically motor complete SCI (AIS A and B) are not anatomically complete.

Non-detectable and/or non-functional descending input can play a crucial role with spinal stimulation.

Spinal cord epidural stimulator

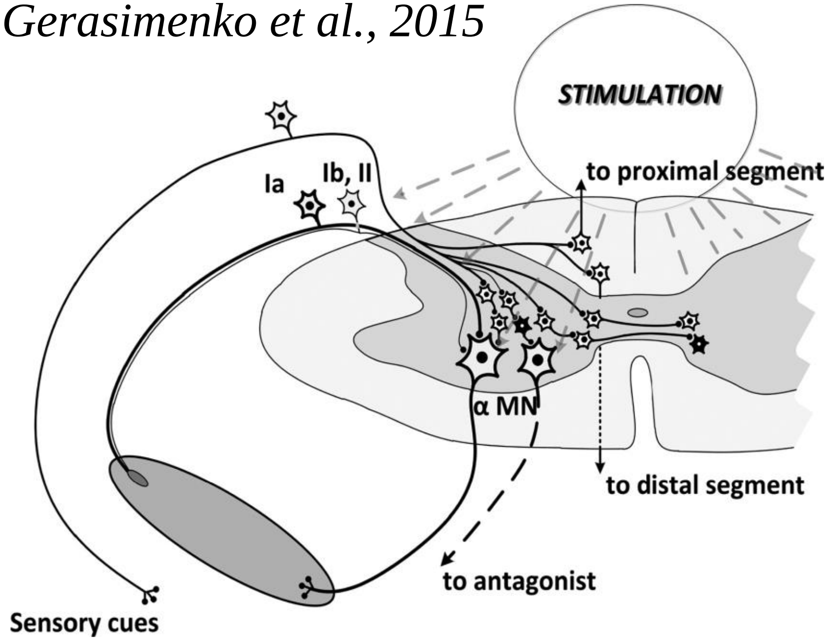


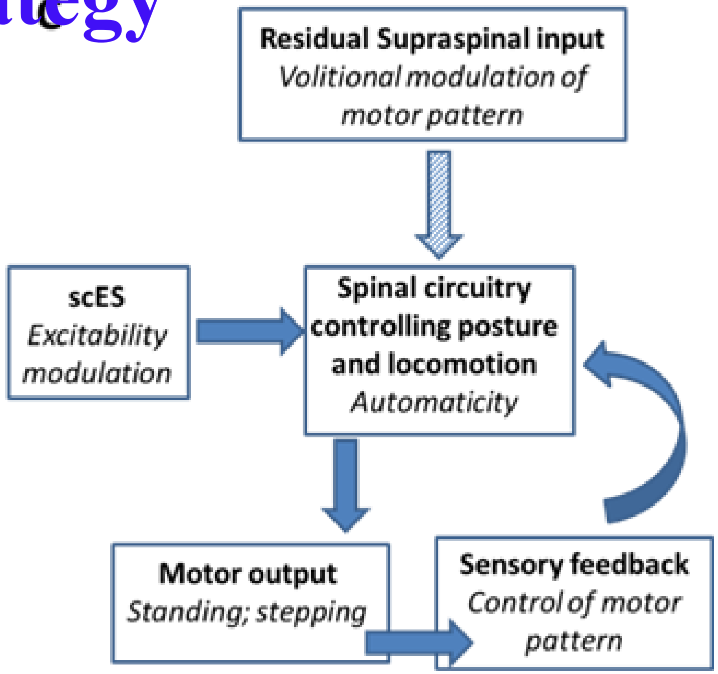
Arnold et al., 2019 → surgical placement and infections.
Boakye et al., *under review* → technical notes of surgical procedures

An epidural spinal cord **stimulation unit** (Medtronics, Restore ADVANCED or INTELLIS) and a **16-electrode array**, implanted at T11-L1 over spinal cord segments L1-S1.

Mechanisms and structures involved in scES - “enabling” strategy

Gerasimenko et al., 2015

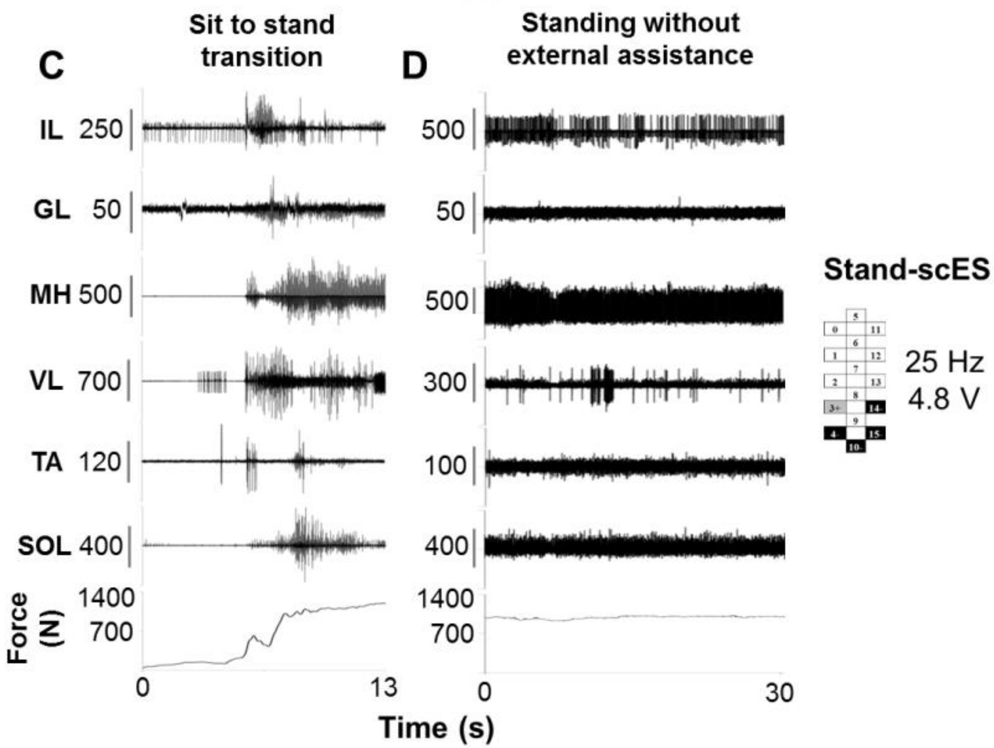




-Primary recruitment of large myelinated fibers associated with somatosensory information, altering the excitability of spinal circuits involved in motor pattern generation.

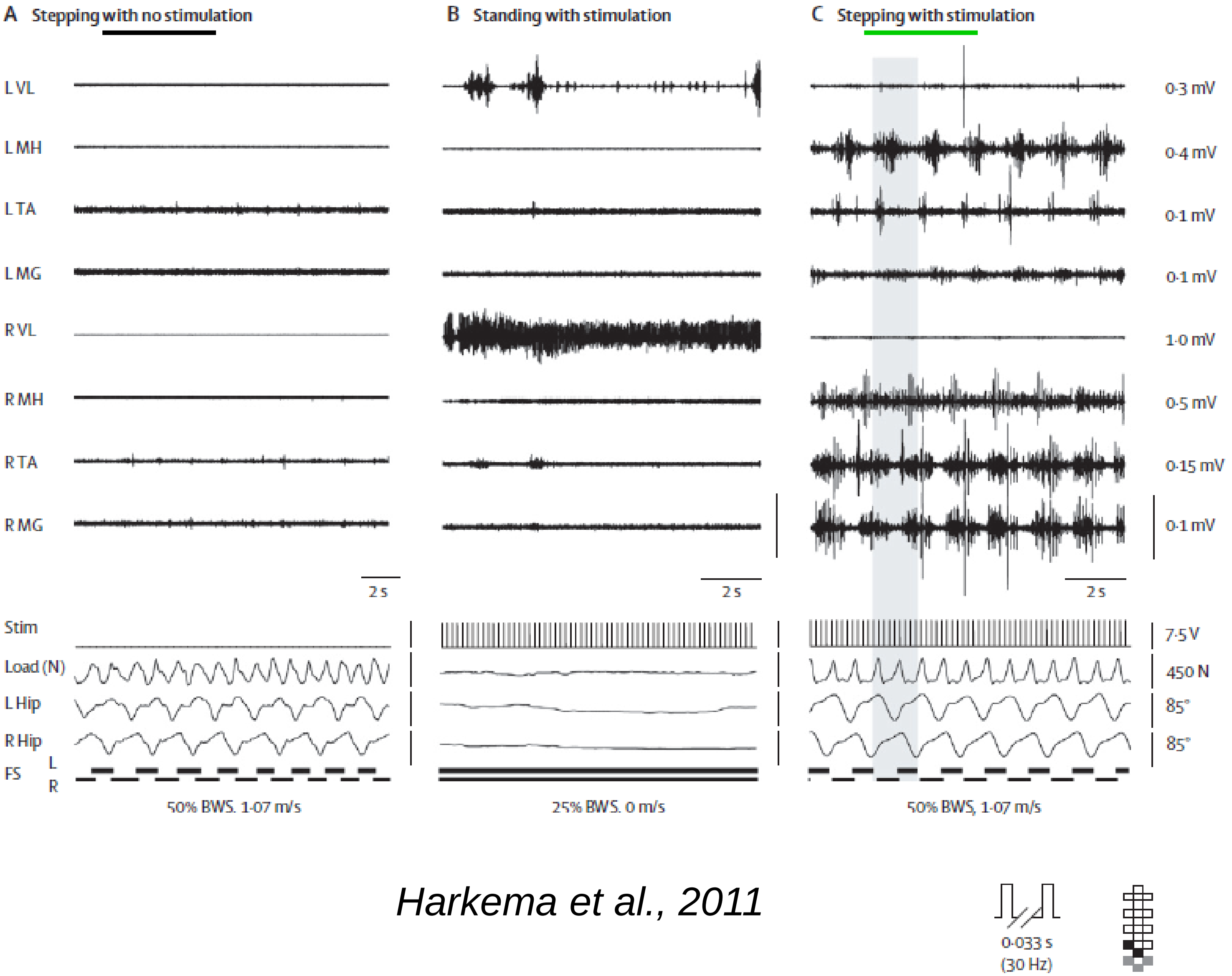
Capogrosso et al., 2013; Moraud et al., 2016)

Spinal cord Epidural Stimulation (scES) - "enabling" stimulation strategy



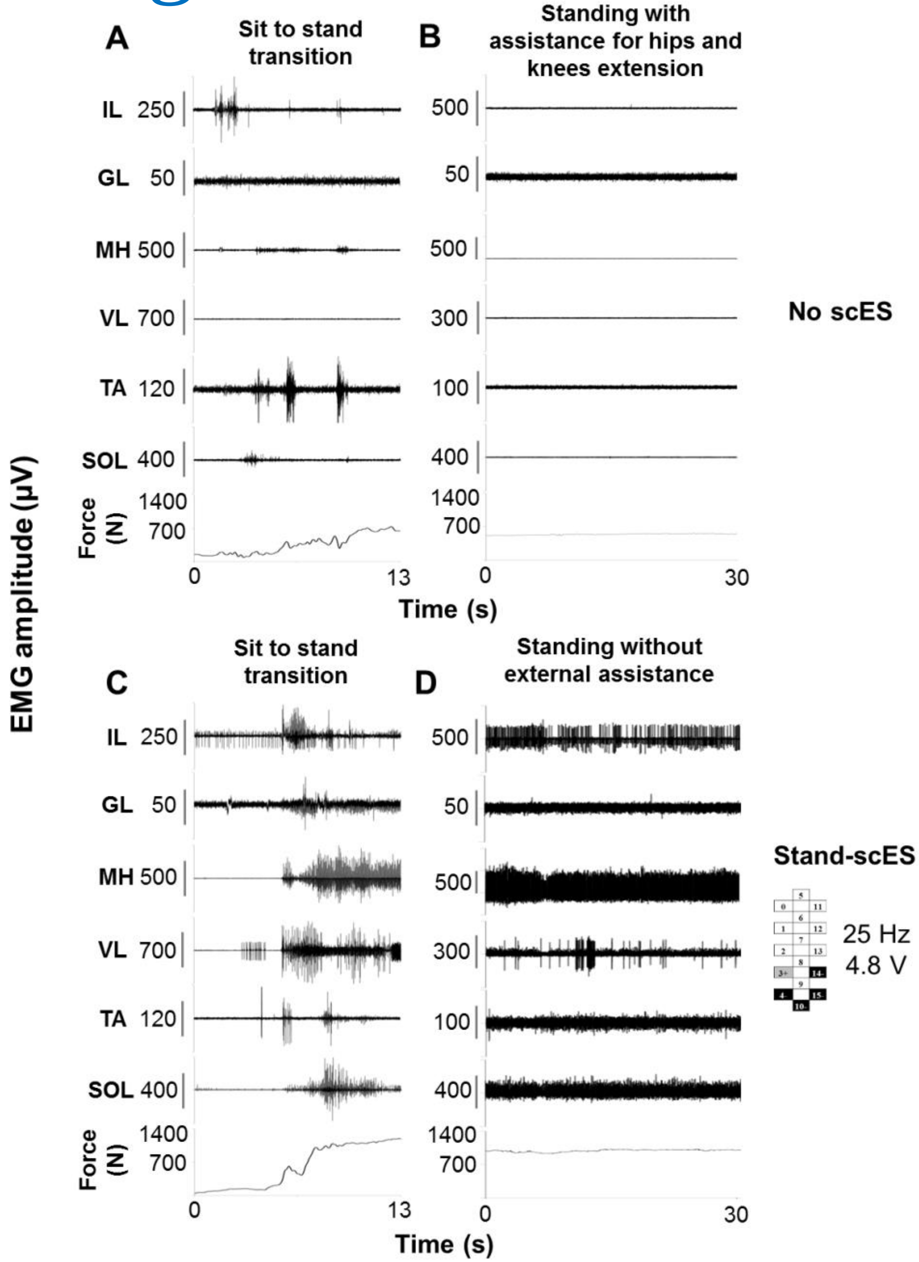
(1) Near-motor threshold stimulation amplitudes and (2) relatively high frequencies, which induce little EMG and no movement during sitting, allow sensory information to serve as a source of control. *(Rejc et al., 2015)*

scES and assisted stepping



Harkema et al., 2011

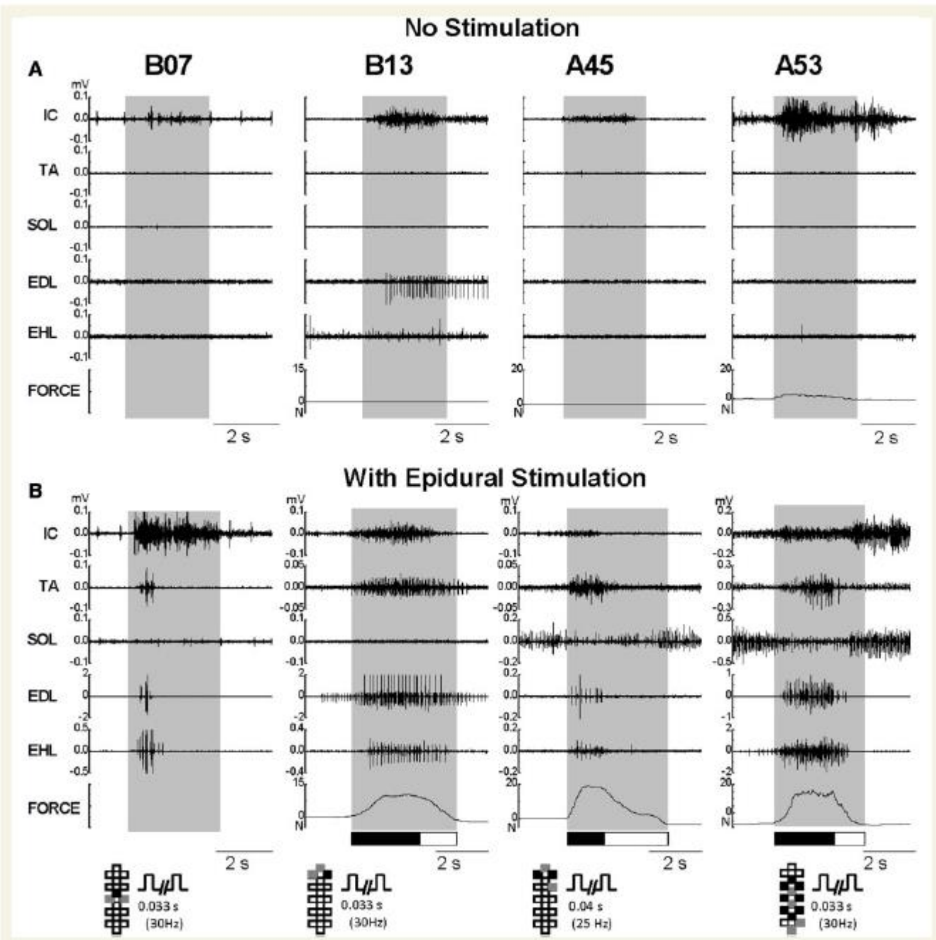
scES and training for standing



Rejc et al., 2015 & 2017

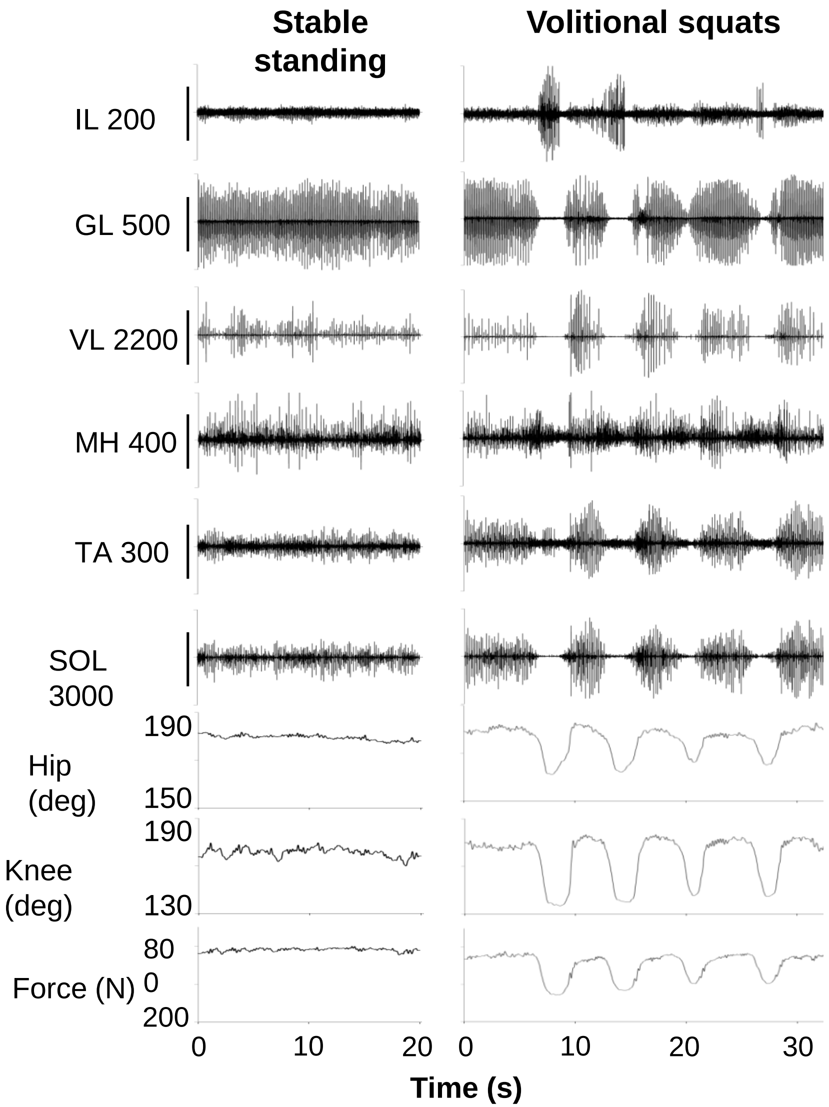
scES and training for volitional leg movements

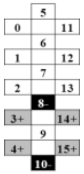
Sub-threshold scES can re-enable volitional motor control after paralysis through non-functional and /or non-detectable connectivity



Angeli et al., 2014

Volitional contribution during standing with scES

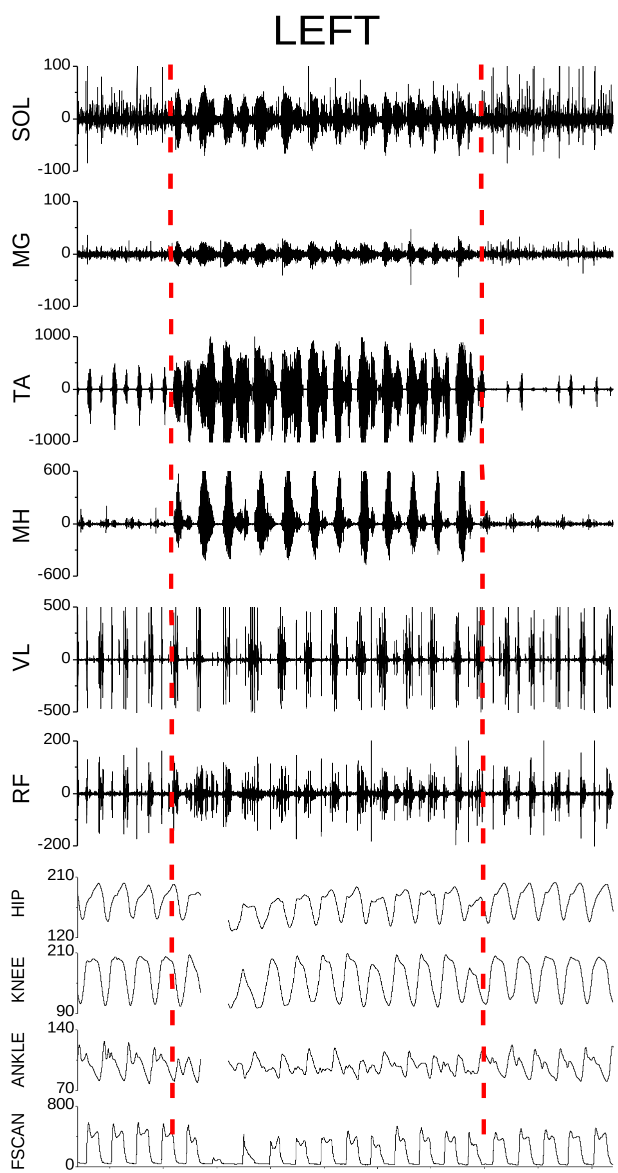




7.0 V
25 Hz

Rejc and Angeli, 2019

Volitional contribution during assisted stepping with scES

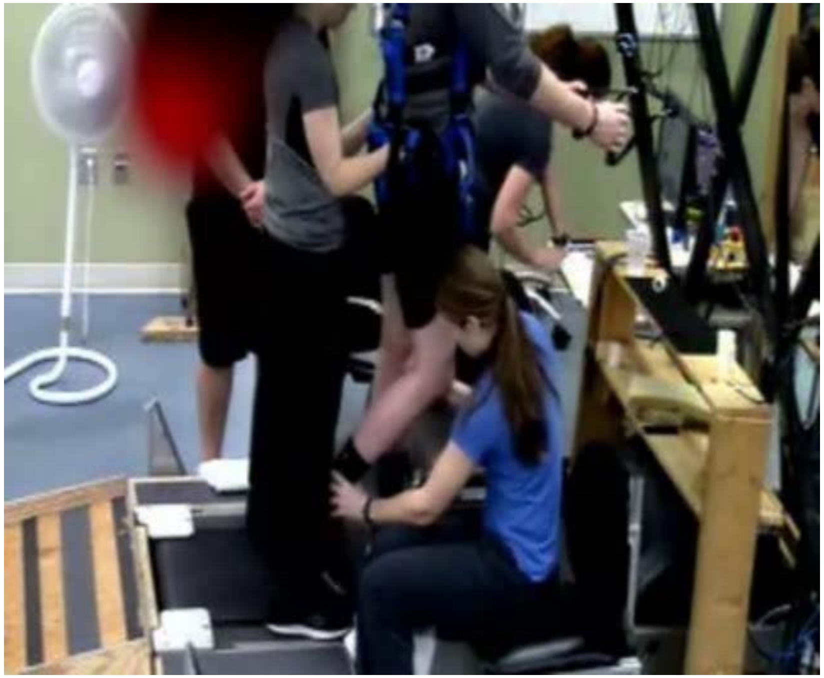


Help

Active involvement of the participant substantially modulates EMG

Angeli et al., 2014

scES, training and volitional contribution for stepping



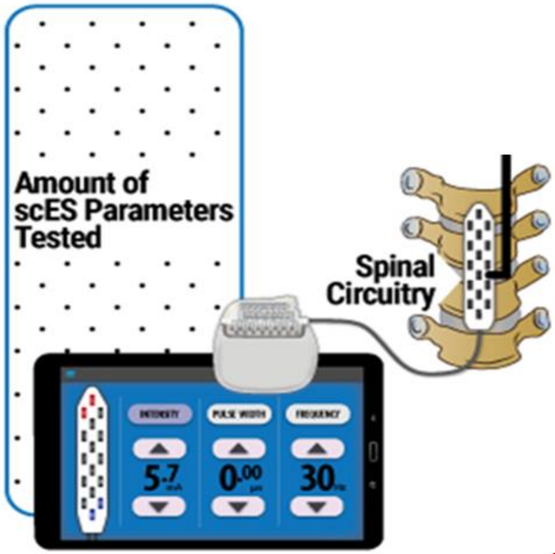
Independent step cycle components during stepping on a treadmill

scES, training and volitional contribution for walking overground

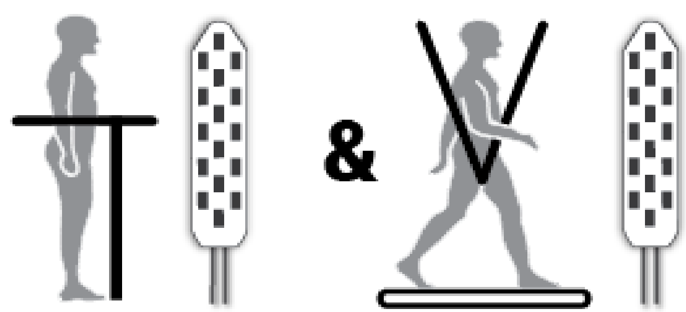
Angeli et al., 2018

Key factors for the recovery of motor function after motor “complete” using scES

1) scES parameters

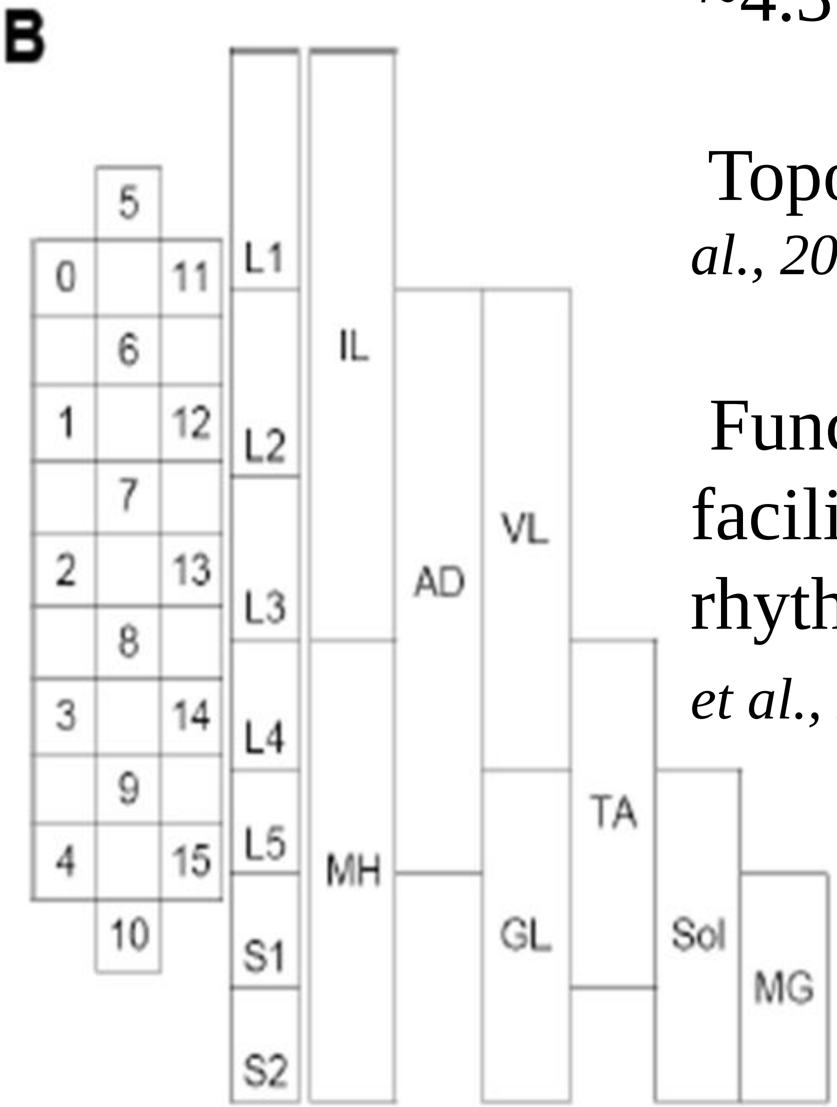


2) Characteristics of activity-based training



?) Characteristics of SCI and subsequent neural adaptations

scES parameters – electrode configuration 1

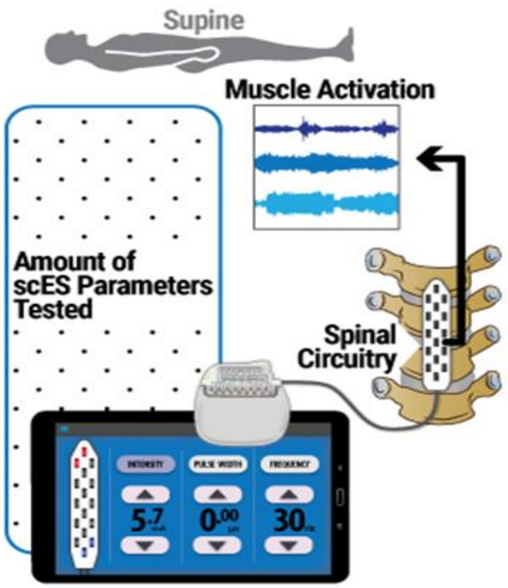


~4.3*10^7 combinations of electrodes.

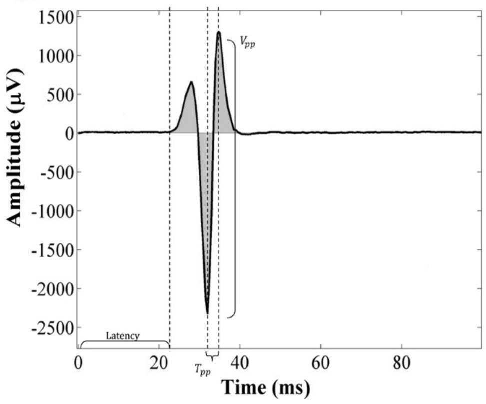
Topographical recruitment *(Sayenko et al., 2014)*

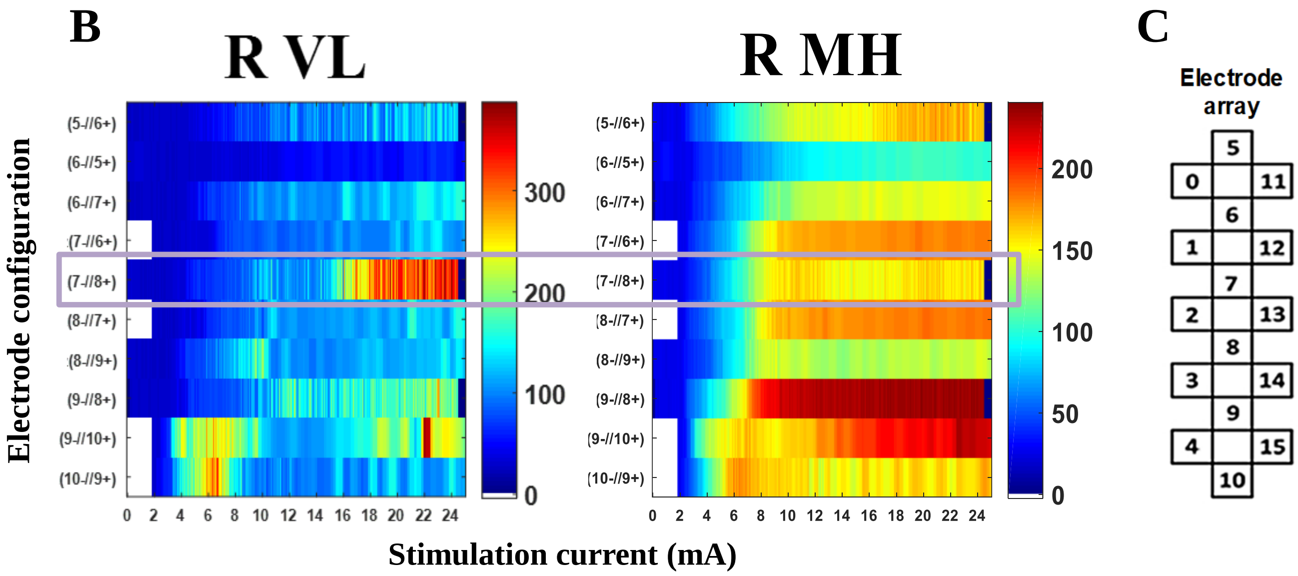
Functional characteristics of the facilitated pattern generation (i.e. rhythmic vs tonic activity, *Gerasimenko et al., 2008*)

scES parameters – electrode configuration 2



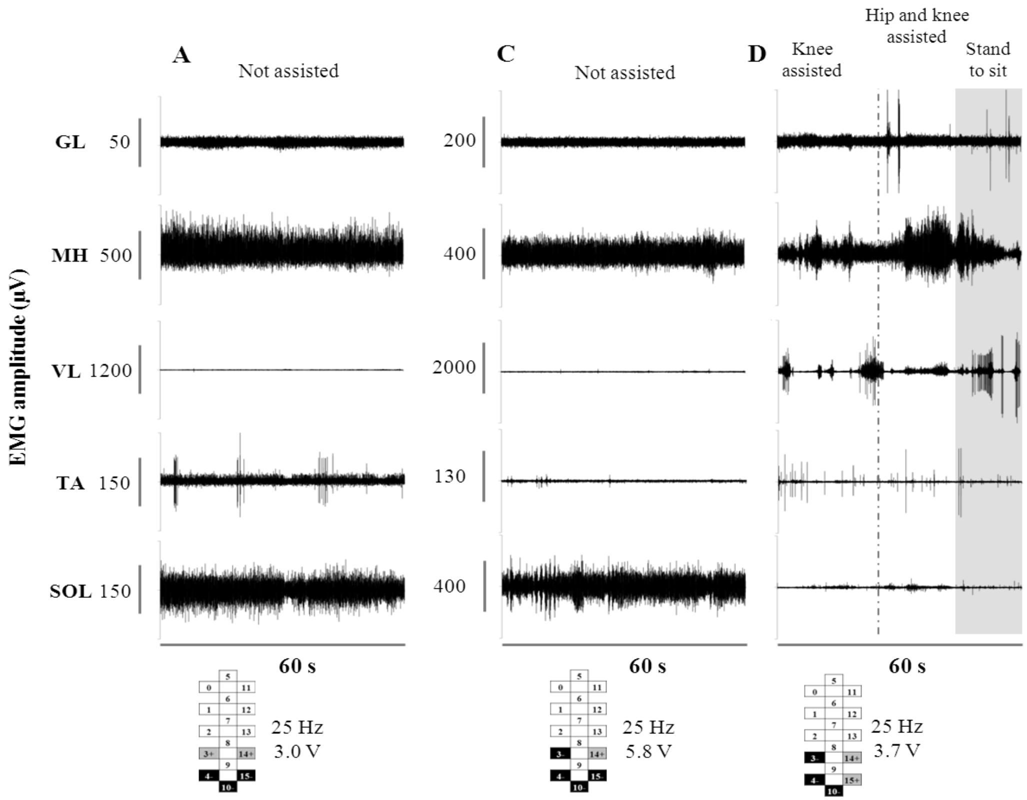
Individualized maps of motor pools activation – supine position





Mesbah et al, 2017

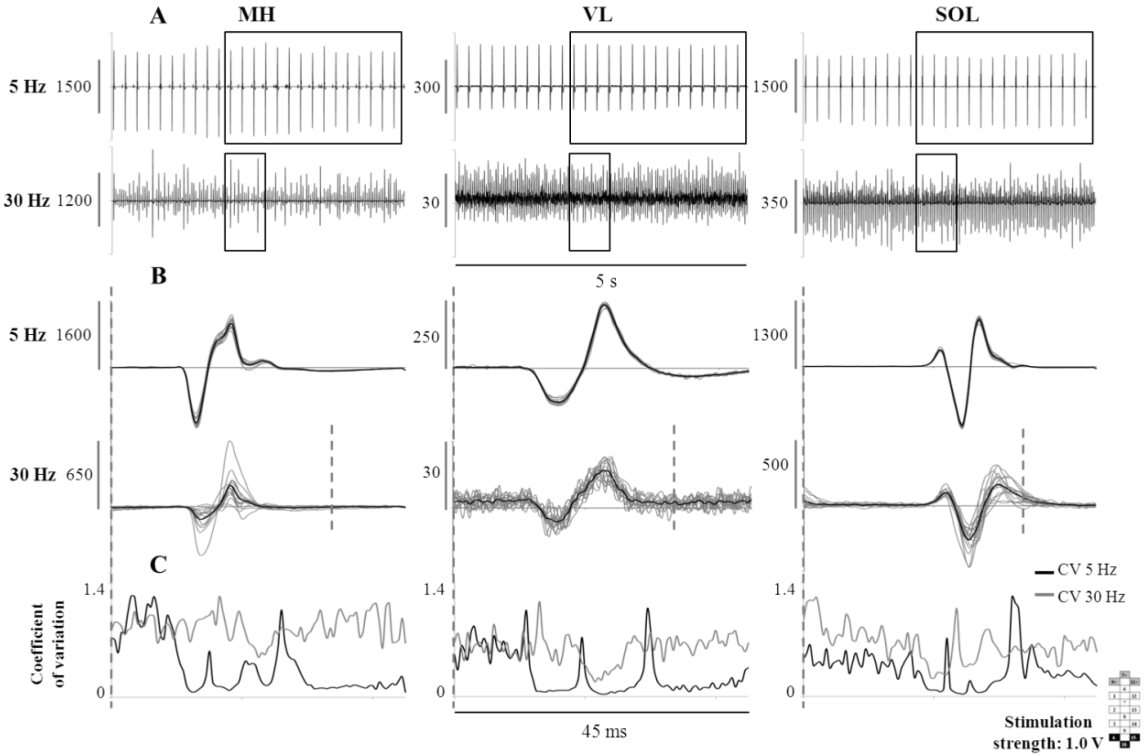
Minor electrode configuration adjustments may or may not result in a drastic change in motor output



Rejc et al., 2015

Selection of stimulation parameters – frequency

Higher stimulation frequency (i.e. > 25 Hz) facilitate: (1) rhythmic activity; (2) the progressive contribution of afferent inputs to shape the evoked responses through the activation of interneurons.



Low frequency (i.e. < 15 Hz): (1) favors extension pattern generation; (2) induce pulsatile muscle contraction

Jilge B, 2004; Minassian, 2004; Rejc et al., 2015

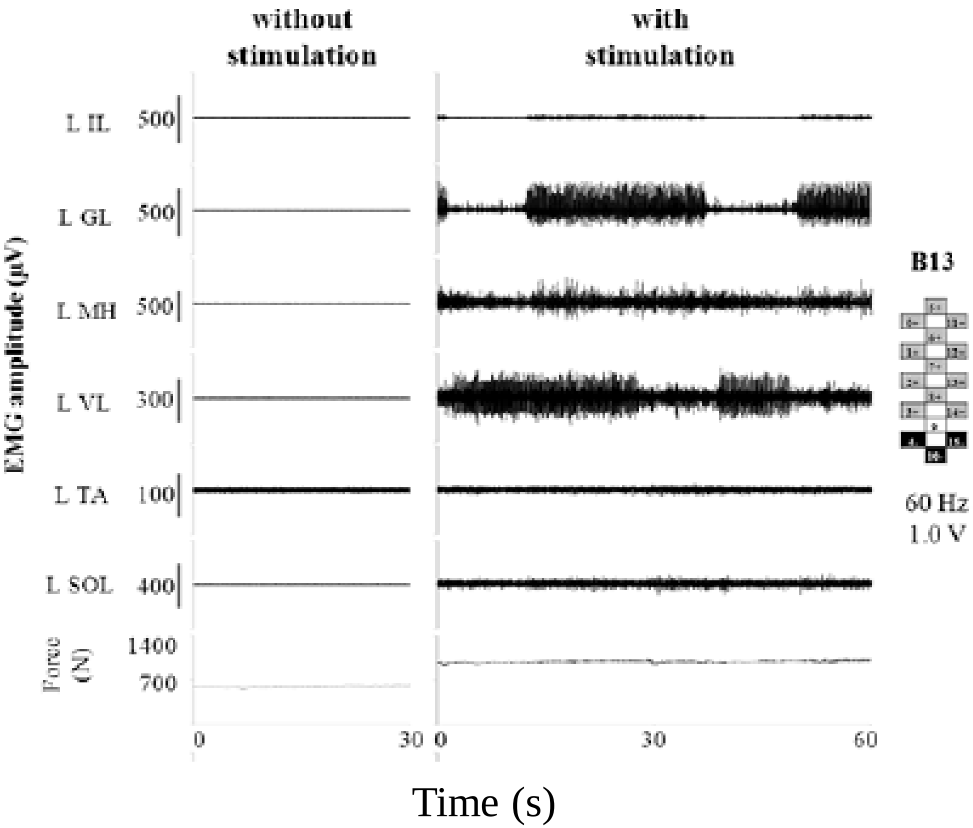
Selection of stimulation parameters – amplitude

Lower amplitude: initial recruitment of the lower threshold afferent structures

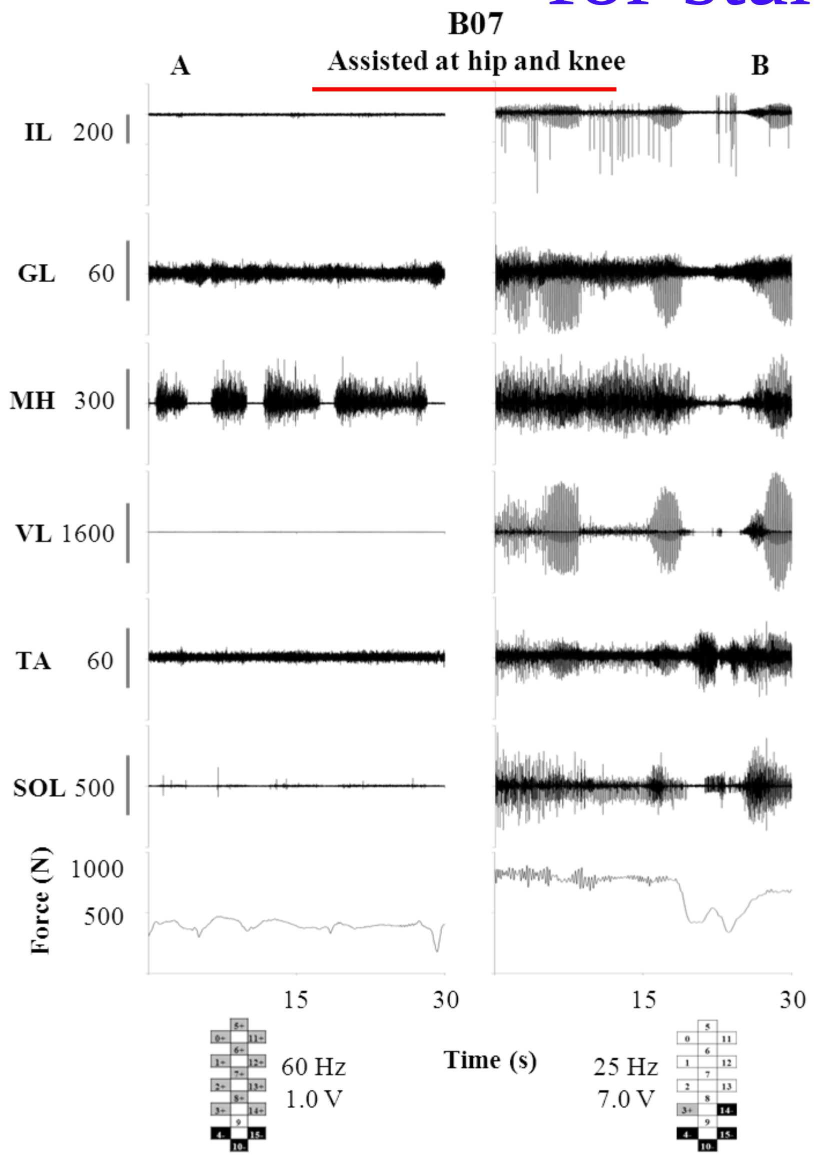
Higher amplitudes: more efferent volleys; possibly activating motorneurons and/or anterior roots.

Sayenko et al., 2014

Individual-specificity of stimulation parameters – 1



Individual-specificity of stimulation parameters for standing - 2



<u>-Difference in:</u>

1) spinal cord <u>anatomy</u>

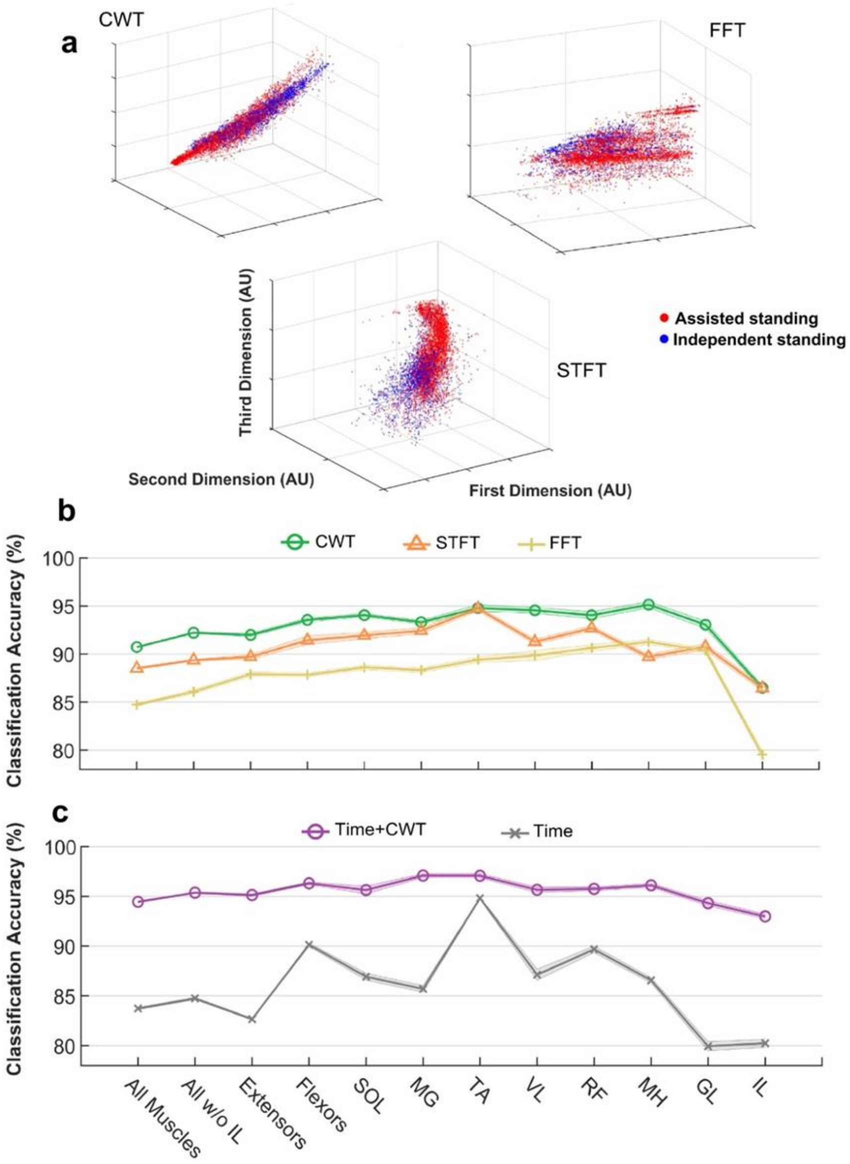
2) <u>position</u> of the electrode array with respect to the spinal cord.

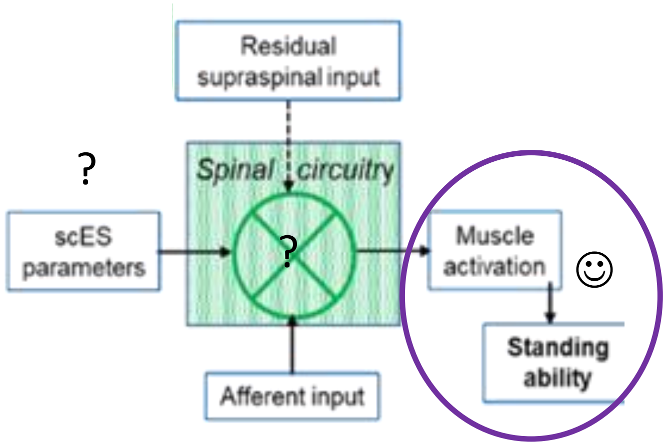
3) characteristics of the <u>lesion</u> and following <u>plasticity</u>

influence the reorganization of the spinal circuitry, including interneurons function.

(Ivanenko 2005; Arber 2012; Beauparlant 2013)

A step forward toward facilitating the selection of scES parameters - 1



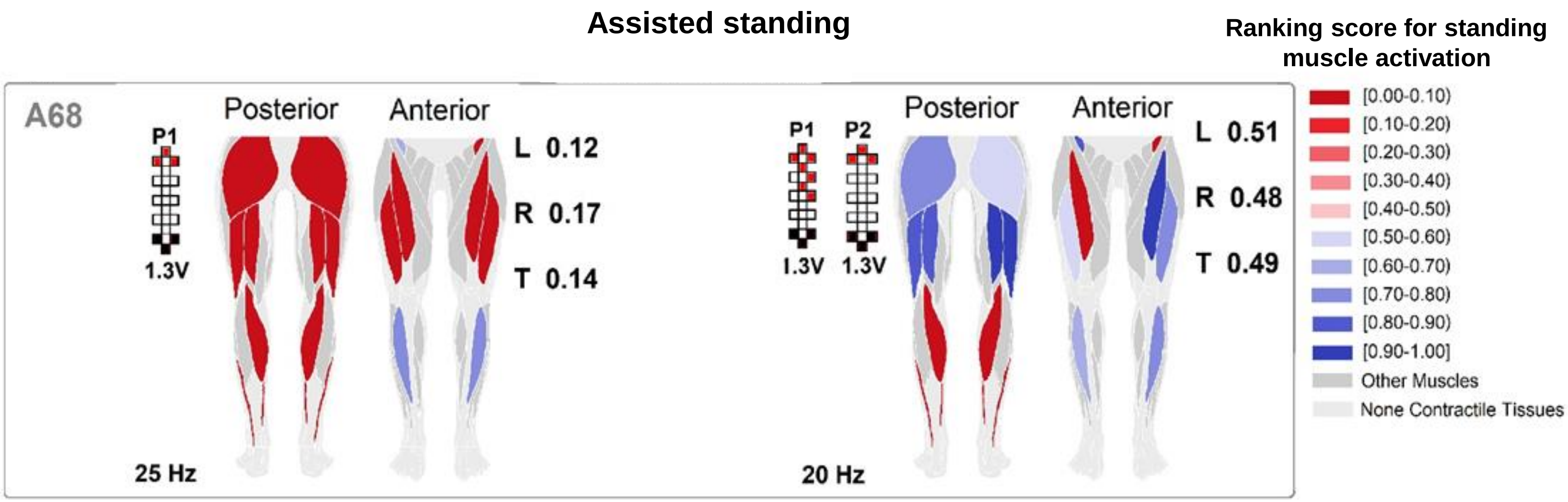


Machine learning can <u>classify</u> with high accuracy <u>standing ability</u> based on EMG-time and –frequency domain features.

Mesbah et al, 2019

A step forward toward facilitating the selection of scES parameters - 2

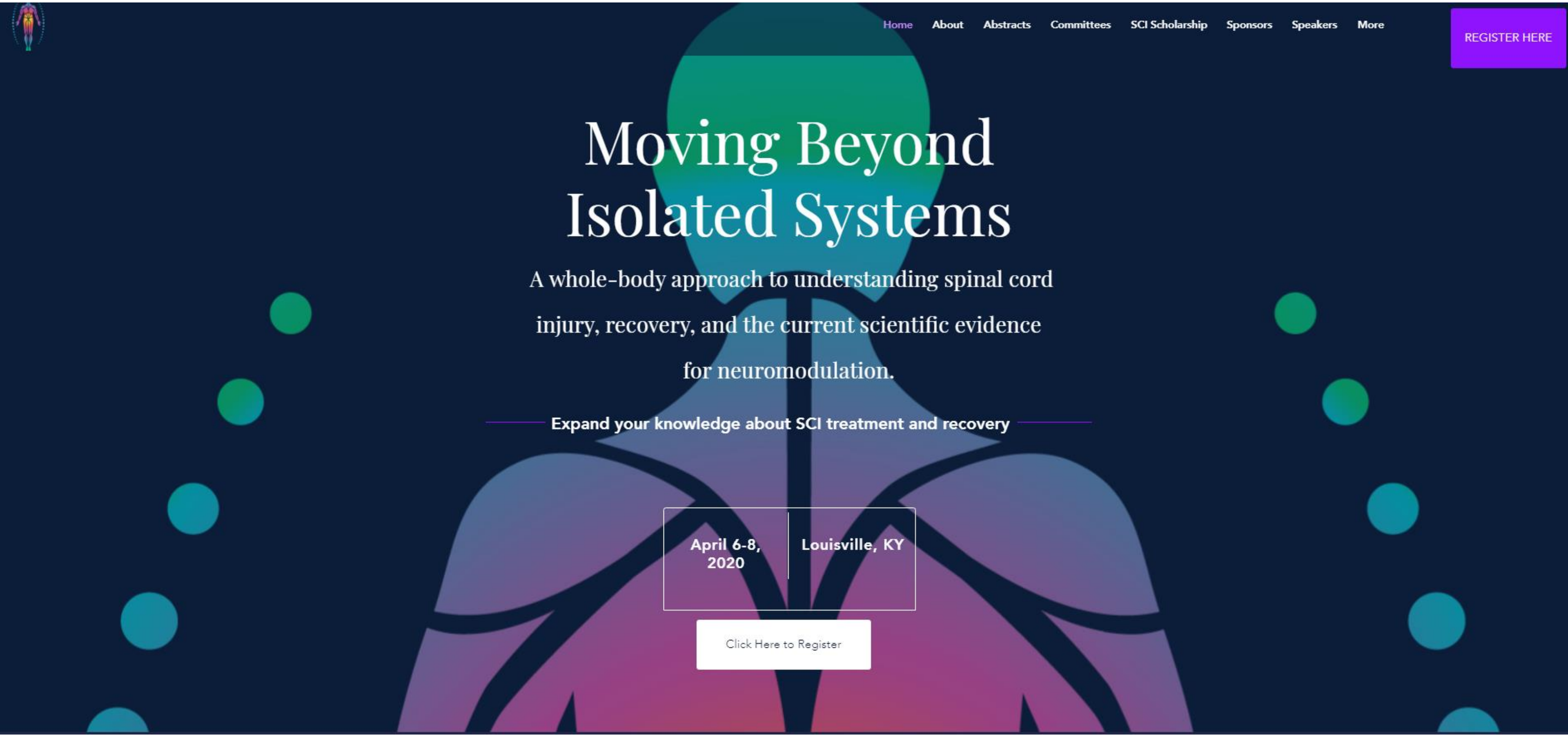
Machine learning prediction algorithm can rank the effectiveness of EMG activity for standing.



Mesbah et al, 2019

Severe Spinal Cord Injury

Impacts sensory-motor and autonomic functions



Epidural Stimulation Program

Susan Harkema

Back Row: Brittany Logsdon, Katelyn Smith, Katie Pfost, Kristen Benton
Front Row: Justin Vogt, Rebekah Morton, Ricky Seither, Dylan Pfost

Claudia Angeli

Steven Gruneisen, AJ Walden, Natasha Stoneking, Basia Szaflarski