Neuromodulation to restore motor function

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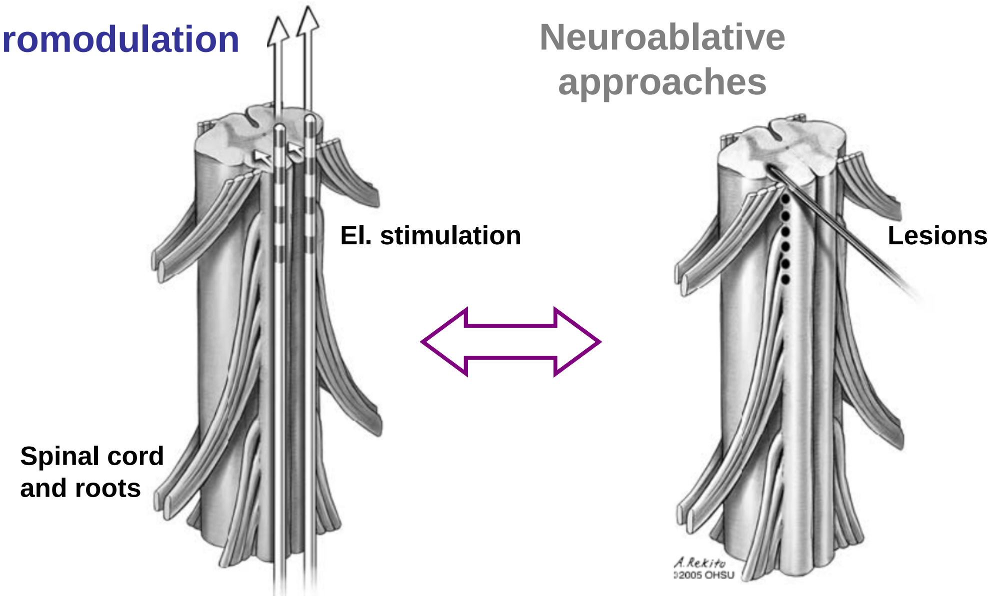
Neuromodulation

The therapeutic paradigm is the modulation of CNS activity

Neuromodulation is non-destructive, reversible, and adjustable

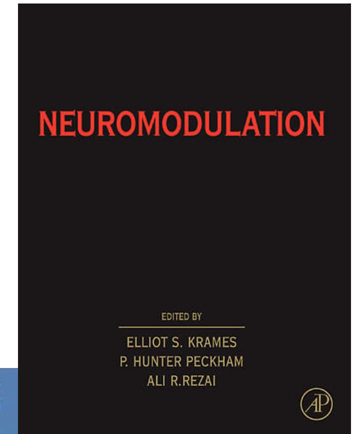
Neuromodulation **Neuroablative approaches**



Modification of function ⇔ Modification of structure

Illsutrations from: Raslan et al. Acta Neurochir Suppl 2007; 97: 33–41

The field of neuromodulation



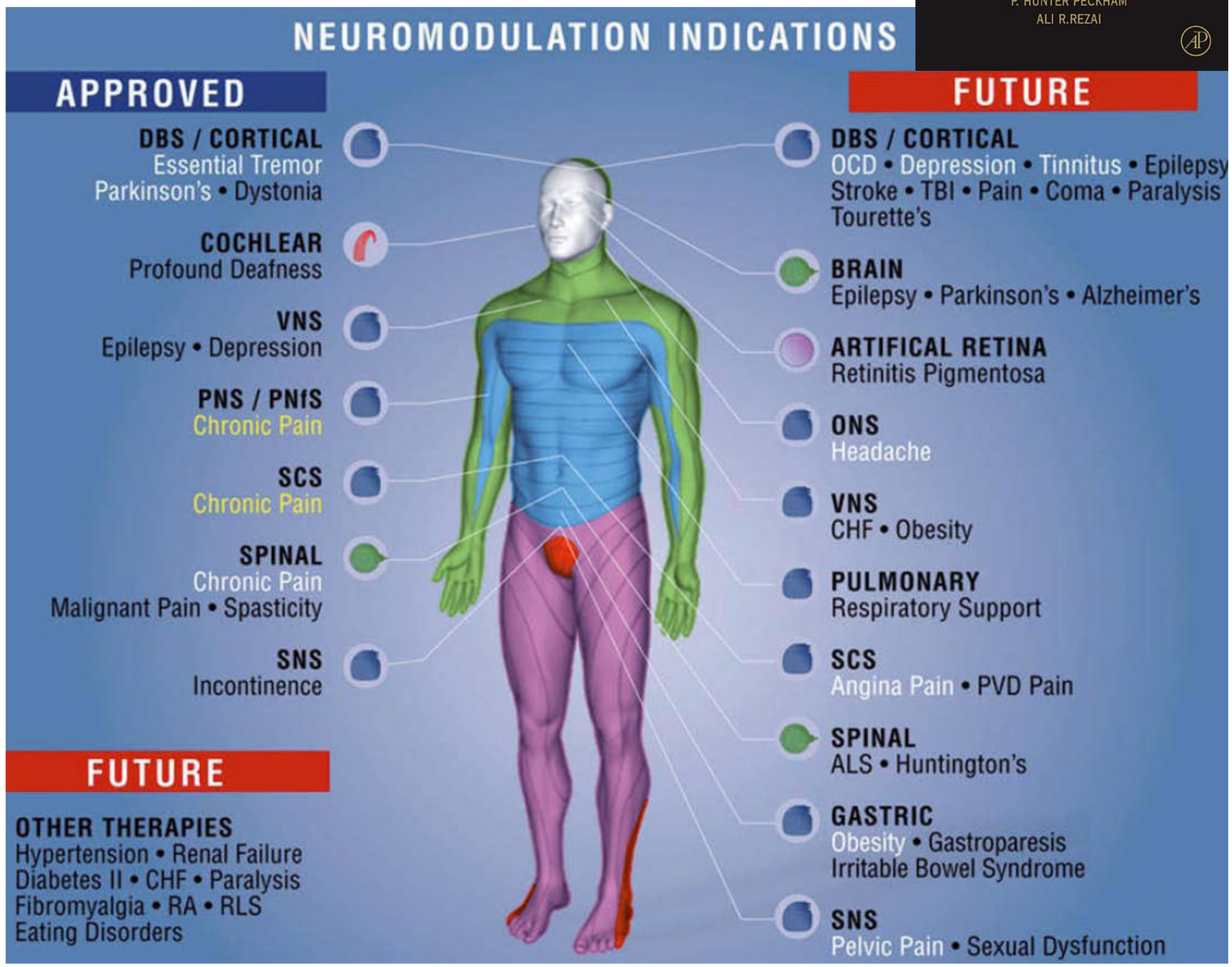
Brain
- Deep brain stimulation (DBS)

Cranial nerves
- Vagus nerve stimulation (VNS)

Spinal cord
- el. spinal cord stimulation (SCS)
- Implantable drug pumps

Spinal nerves
- Sacral nerve stimulation (SN)

Peripheral nerves
- Peripheral nerve stimulation (PNS)



From: Krames et al. Neuromodulation. London: Elsevier-Academic Press 2009:3-8.

Focus of the presentation

Spinal cord stimulation for

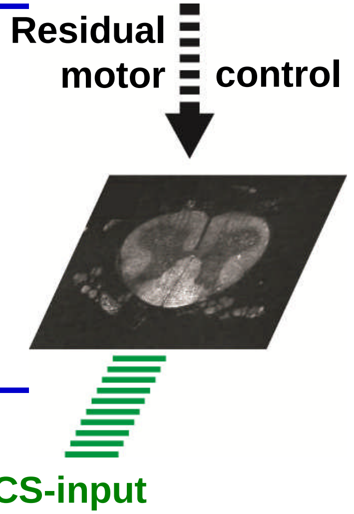
the treatment of spinal spasticity and
modification of altered motor control due to

multiple sclerosis and
spinal cord injury

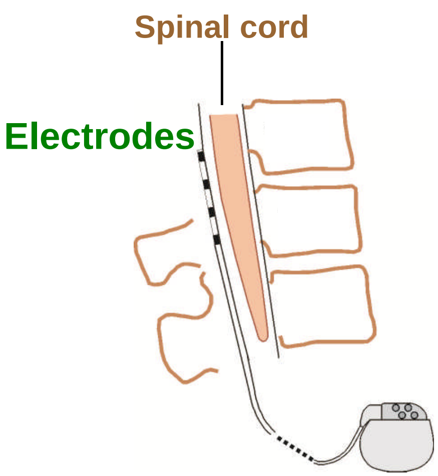
Dependence of the stimulation-induced effects on

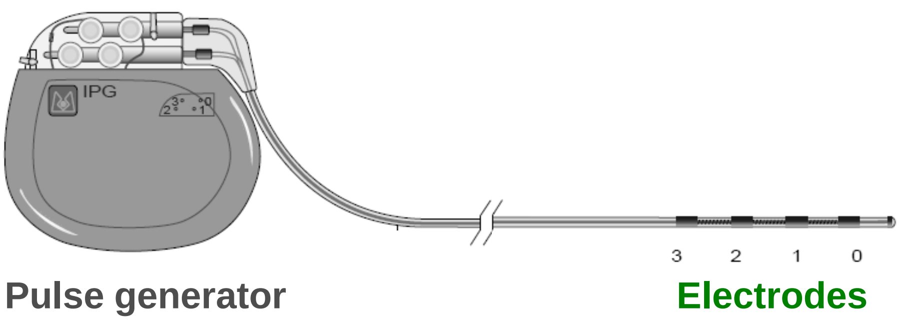
Stimulation site, stimulation frequency

Profile of the spinal cord physiology as a result of the lesion

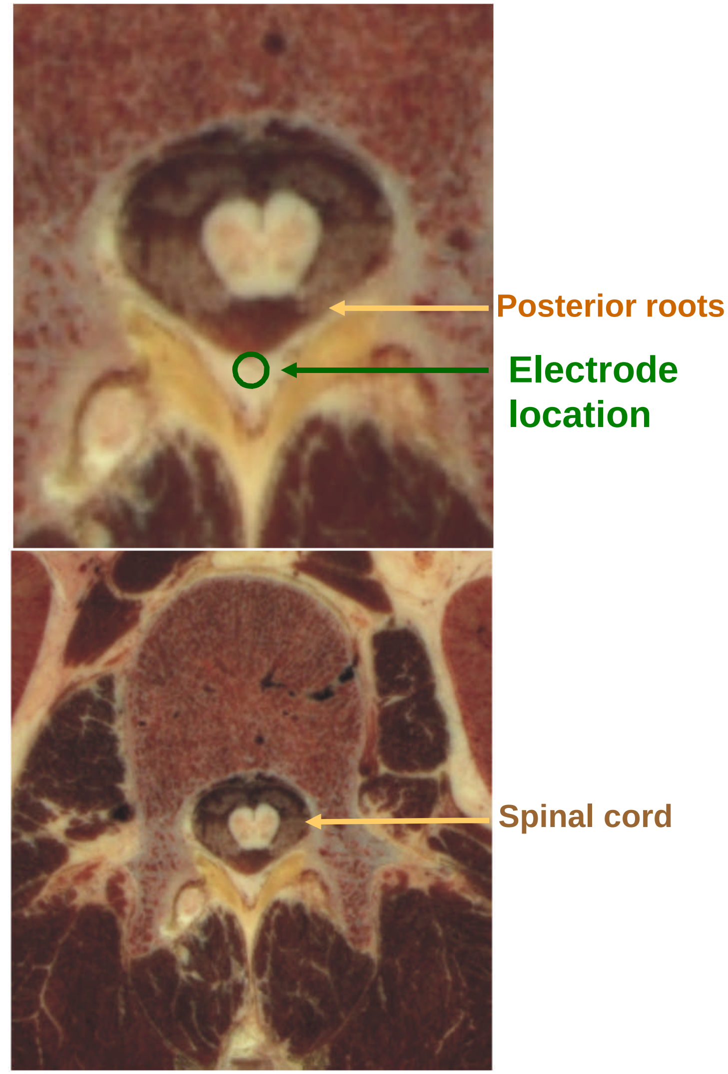


Epidural spinal cord stimulation





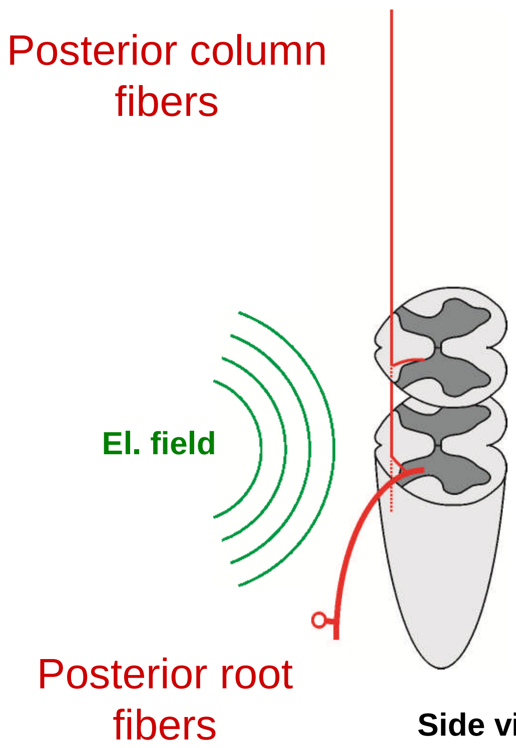
continuous stimulation



Cross-section at T12 vertebral level

Epidural spinal cord stimulation

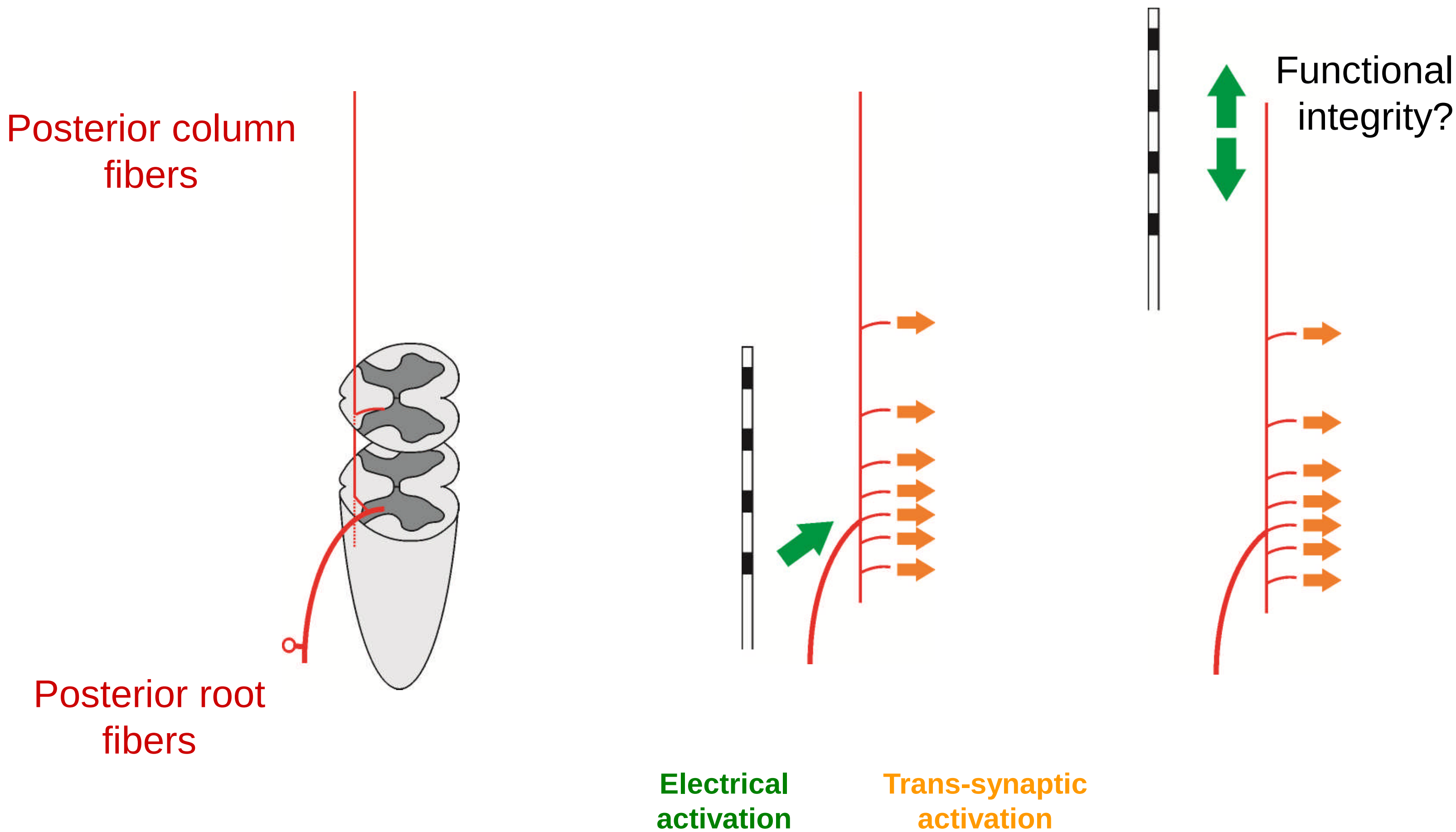
Immediate effects(1)



Side view of the terminal spinal cord and afferent structures

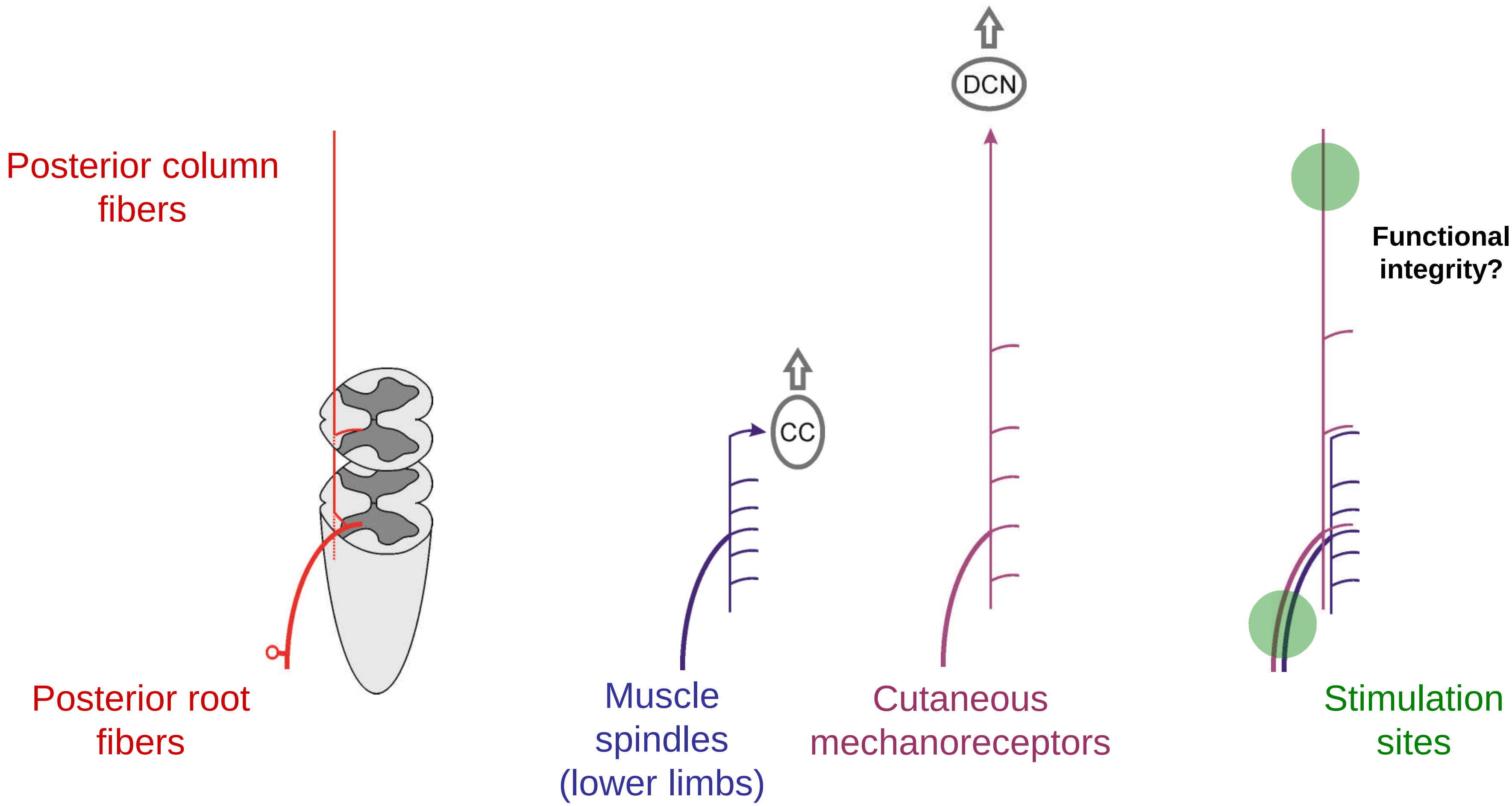
Epidural spinal cord stimulation

Immediate effects(2)



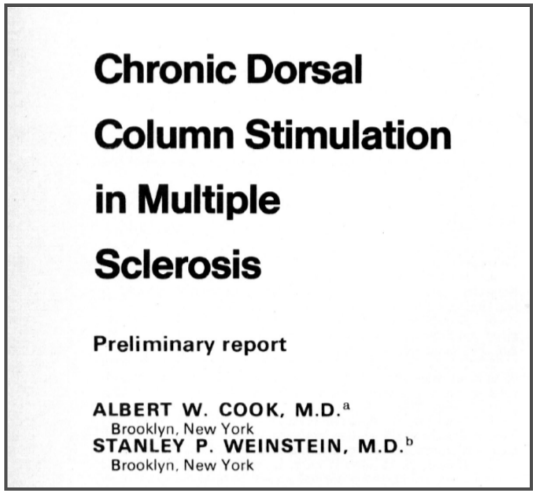
Epidural spinal cord stimulation

Immediate effects(3)



CC… Clarke's column; DCN… Dorsal column nuclei

Epidural SCS in multiple sclerosis


Chronic Dorsal Column Stimulation in Multiple Sclerosis

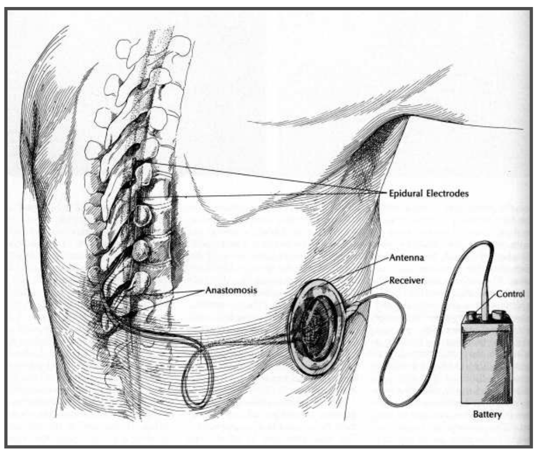
Preliminary report

ALBERT W. COOK, M.D.[a]
Brooklyn, New York
STANLEY P. WEINSTEIN, M.D.[b]
Brooklyn, New York

- 5 subjects with MS
- subdural, extra-arachnoid space over mid-thoracic spinal cord
- stimulation frequency: 150 – 200 Hz

Cook AW, Weinstein SP. N Y State J Med 1973;73:2868–72.

- ‘Lightness’ of the legs, less fatigue, more endurance
- Improvement of limb spasticity
- Regain of voluntary control
- Facilitation of sitting, standing and ambulation
- Increased functional activities of daily living



- more than other 70 with MS
- epidural space over mid- thoracic cord
- stimulation frequency: 30 – 50 Hz

Cook AW. Hosp Pract 1976;11:51–8.

Epidural SCS in multiple sclerosis

Selected reports

Study	# of subjects	Improvements of lower limb function	Stim. site (vertebral)	Stimulation frequency
Illis et al. 1980	18	feeling of lightness of the legs increased endurance stand and walk more easily regained unaided walking capability	C6-T10	33 Hz
Siegfried et al. 1981	111	improvement of walking capabilities regained unaided walking reduced spasticity	low cerv. to mid-thoracic	100-120 Hz
Waltz, 1998	130	improved weakness with positive impact on gait spasticity was abolished or significantly decreased	C2-C4	100-1500 Hz

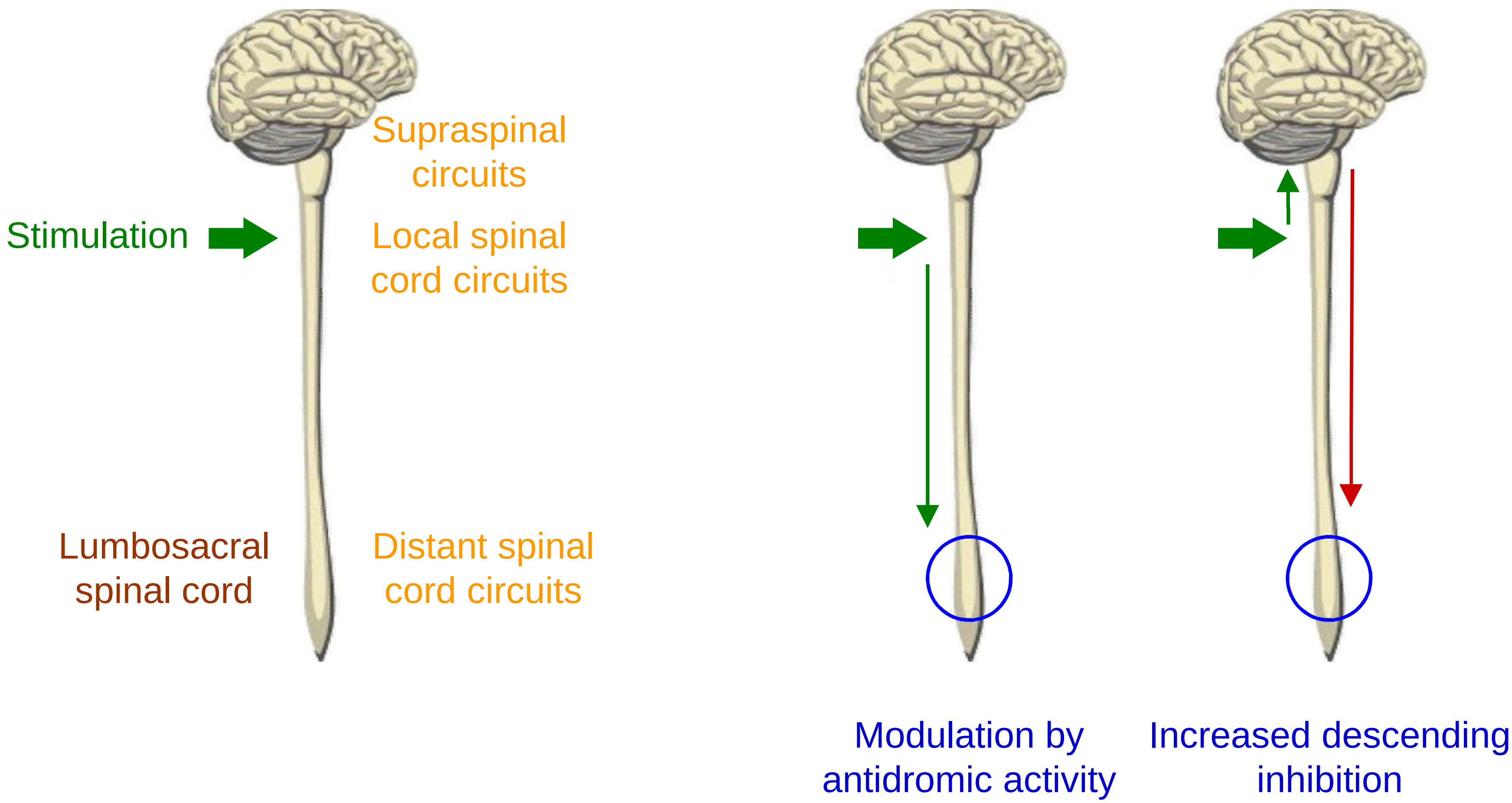
Epidural SCS in multiple sclerosis

Selected reports

Study	# of subjects	Improvements of lower limb function	Stim. site (vertebral)	Stimulation frequency	Benefit in % of subjects
Illis et al. 1980	18	feeling of lightness of the legs increased endurance stand and walk more easily regained unaided walking capability	C6-T10	33 Hz	28%
Siegfried et al. 1981	111	improvement of walking capabilities regained unaided walking reduced spasticity	low cerv. to mid-thoracic	100-120 Hz	33%
Waltz, 1998	130	improved weakness with positive impact on gait spasticity was abolished or significantly decreased	C2-C4	100-1500 Hz	33% 58%

Epidural SCS in multiple sclerosis

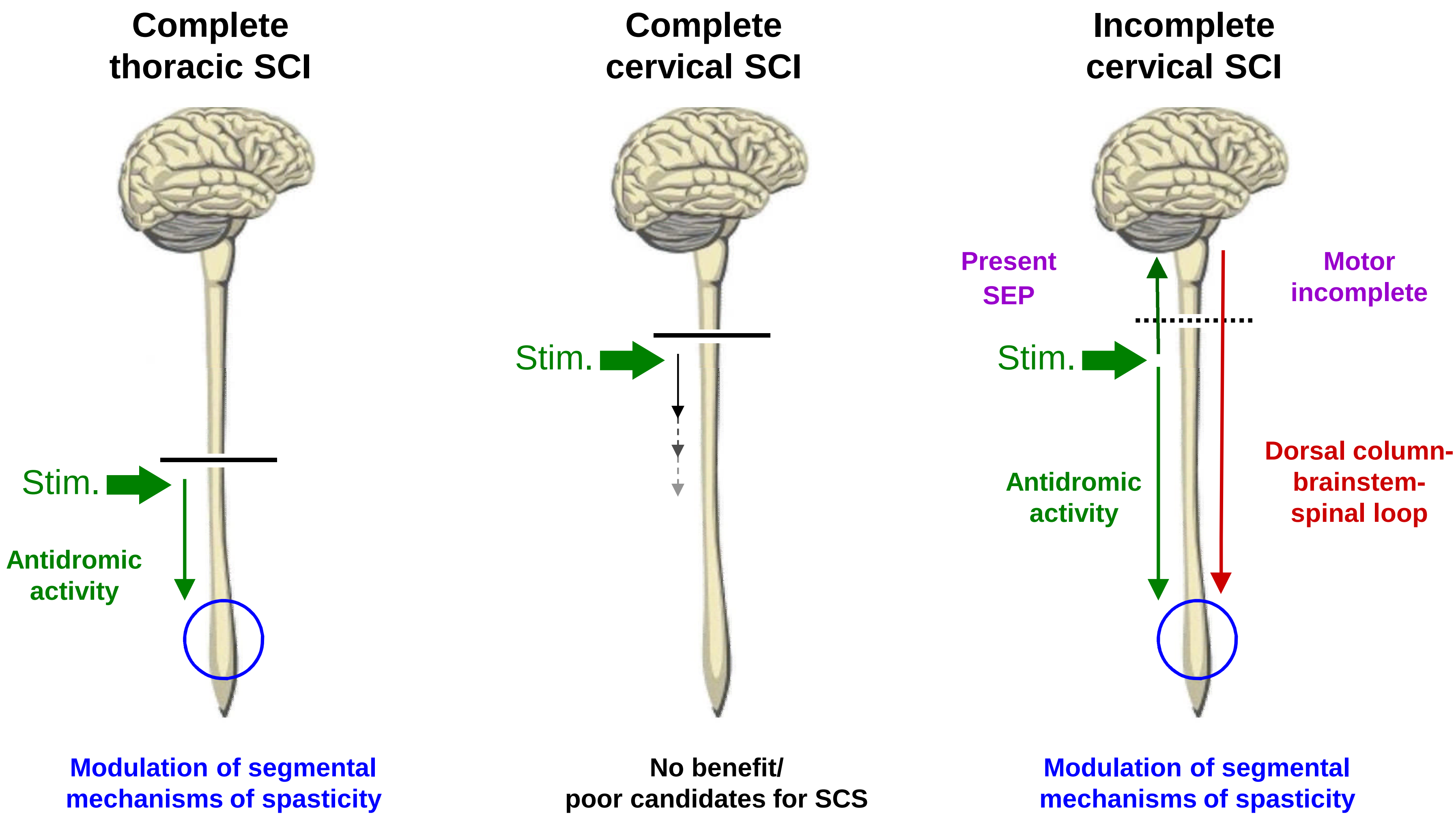
Physiological mechanisms of SCS in MS (lower limb function)



Epidural SCS for spasticity control after SCI

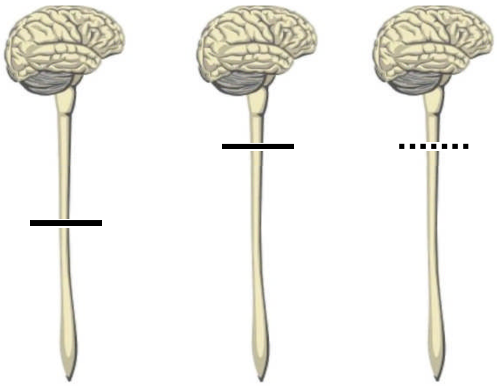
Profile of injury and efficacy of SCS

Dimitrijevic et al. Cent Nerv Syst Trauma. 1986;3:129-44



Epidural SCS for spasticity control after SCI

Profile of injury and efficacy of SCS



"…The great variety of pathologic conditions in chronic spinal cord lesions will determine whether or not SCS is effective. …"

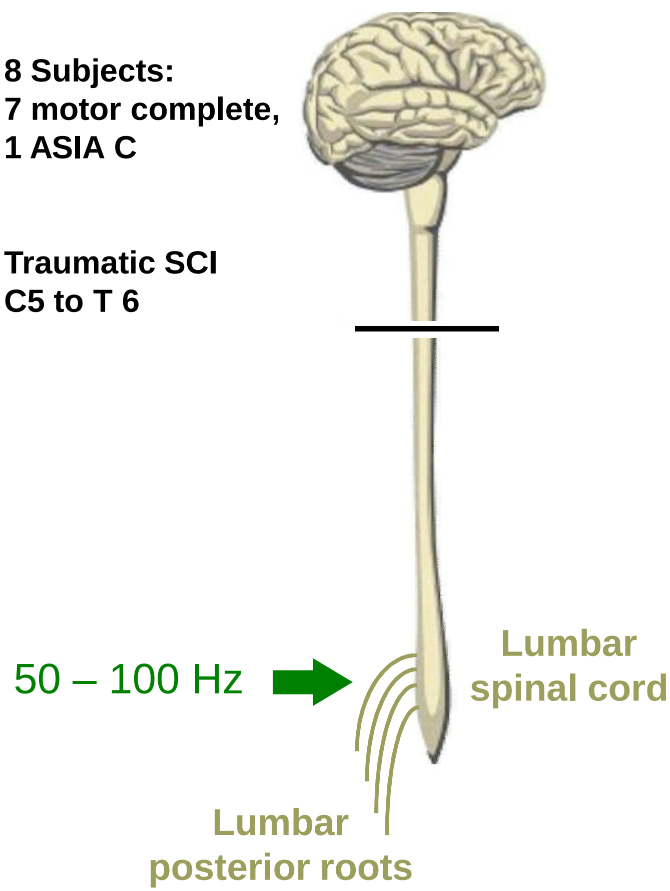
" … Placement of the electrode is the most critical part of the procedure …"

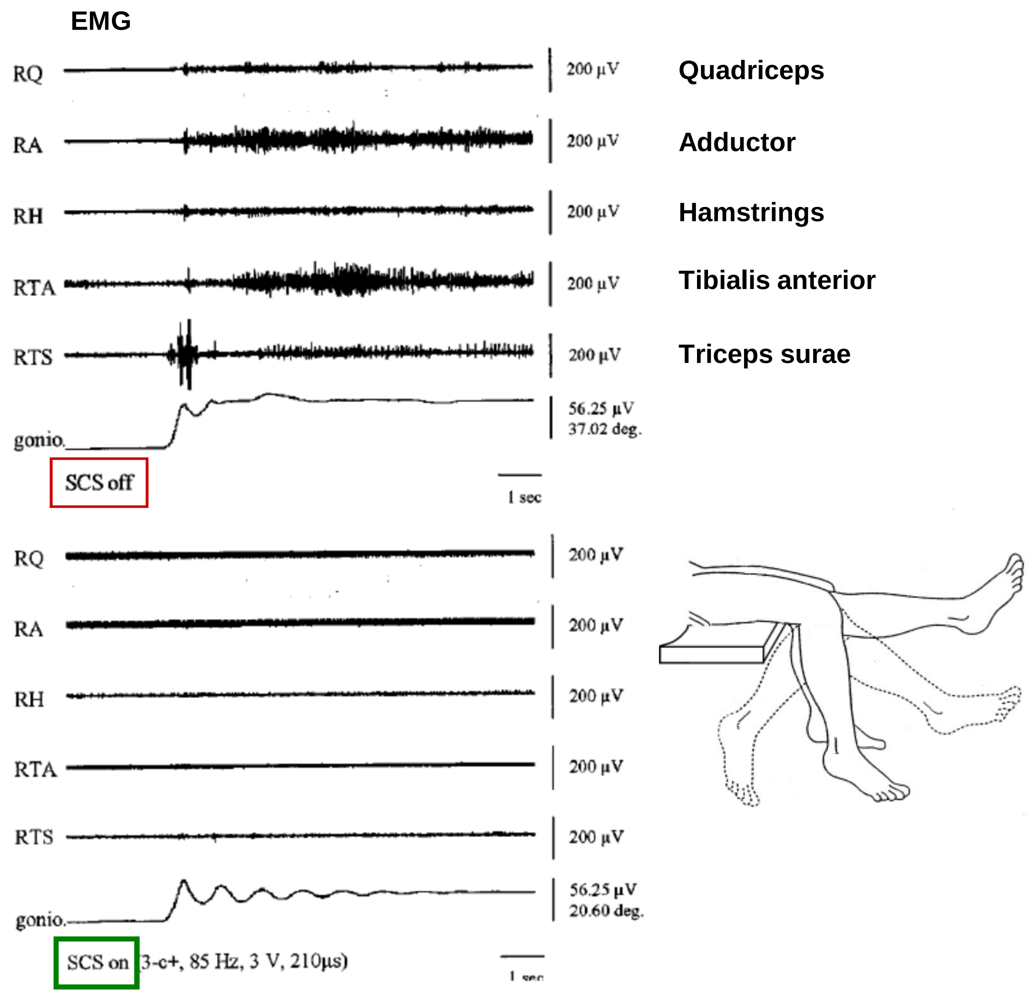
Dimitrijevic et al. Cent Nerv Syst Trauma. 1986;3:129-44.

Epidural stimulation of lumbar cord circuits for spasticity control after SCI (1)

8 Subjects:
7 motor complete,
1 ASIA C

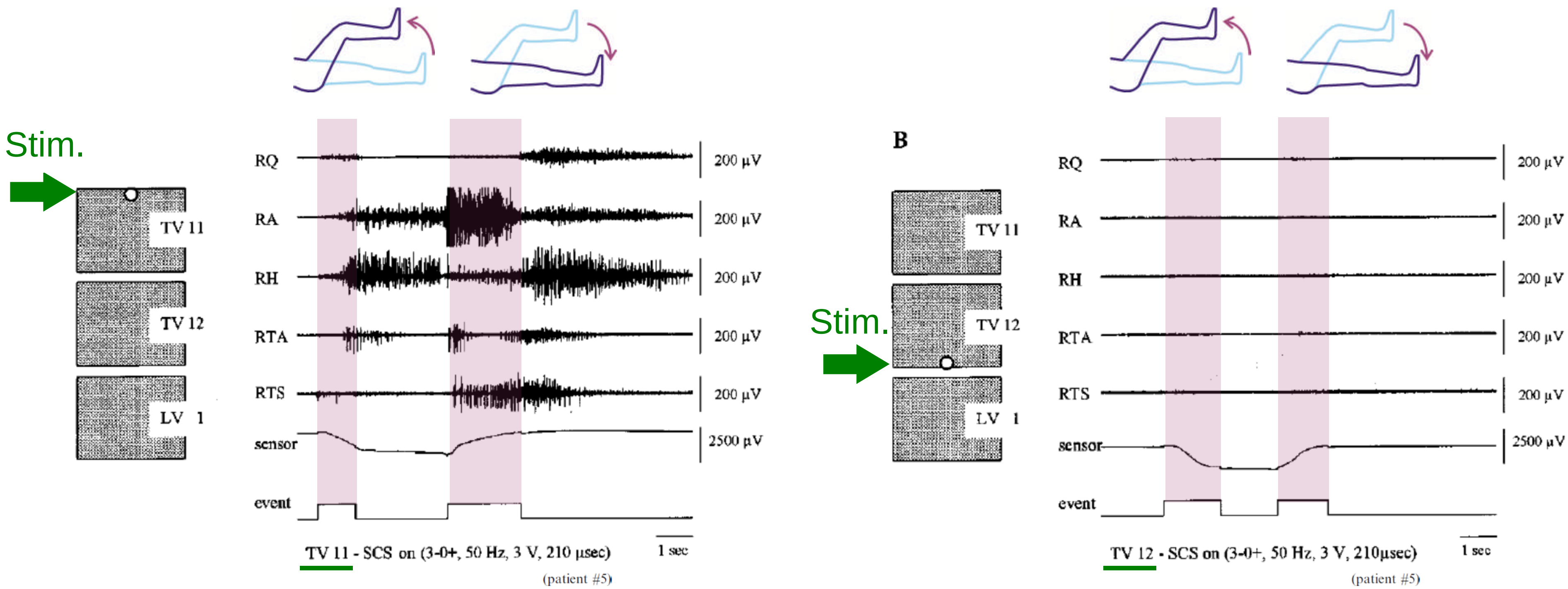
Traumatic SCI
C5 to T 6





Pinter, Gerstenbrand, Dimitrijevic. Spinal Cord. 2000;38:524-31.

Epidural stimulation of lumbar cord circuits for spasticity control after SCI (2)



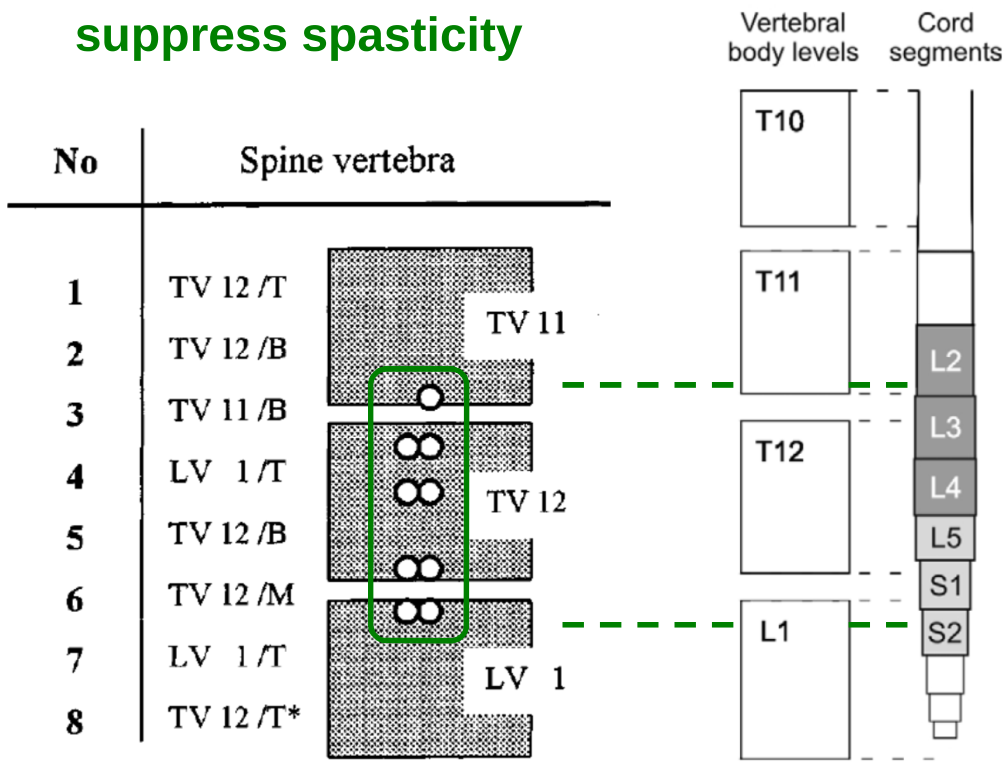
Q, Quadriceps; A, Adductor; H, Hamstrings;

TA, Tibialis anterior; TS, Triceps surae

Pinter, Gerstenbrand, Dimitrijevic. Spinal Cord. 2000;38:524-31.

<u>Epidural stimulation of lumbar cord circuits for spasticity control after SCI</u> (3)

Electrode sites effective to suppress spasticity

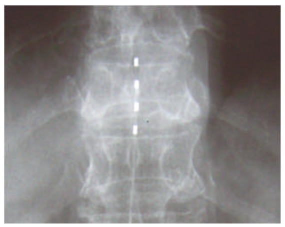


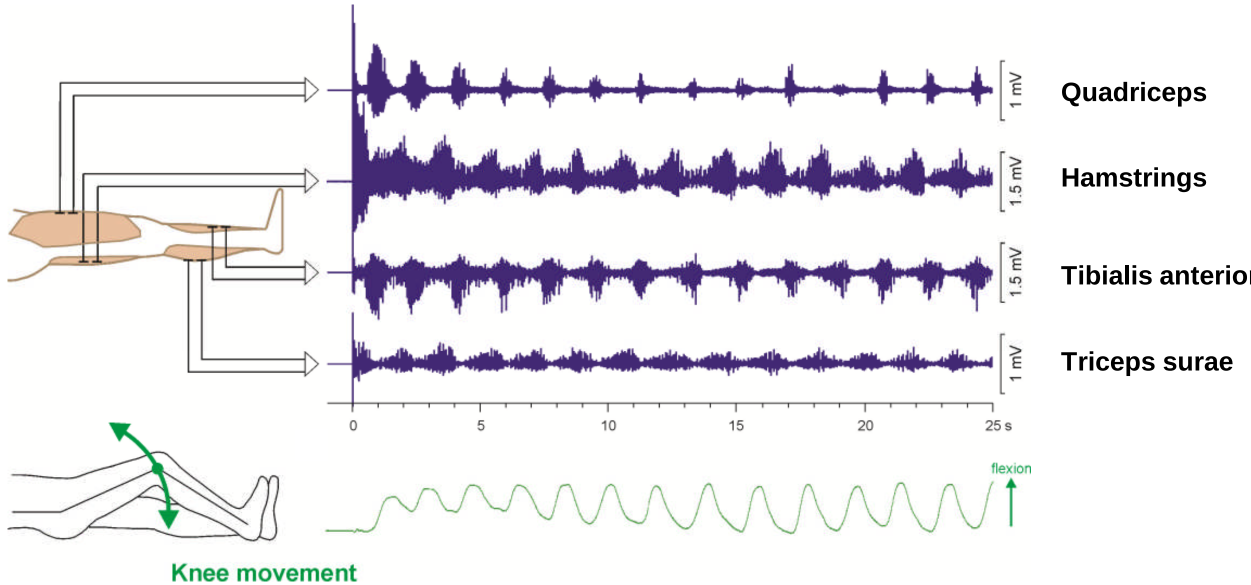
From: Pinter et al. Spinal Cord. 2000;38:524-31. **Minassian et al. Hum Mov Sci. 2007; 26:275-95**

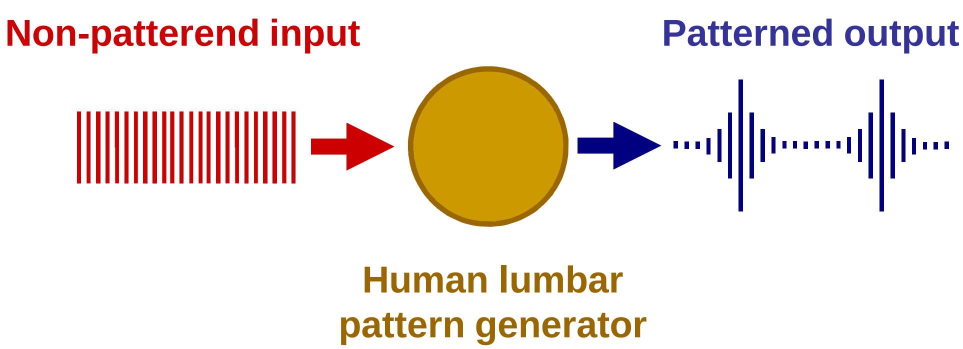
Epidural lumbar SCS generates rhythmic activity

Continuous stimulation at 25 – 50 Hz

Complete SCI subject

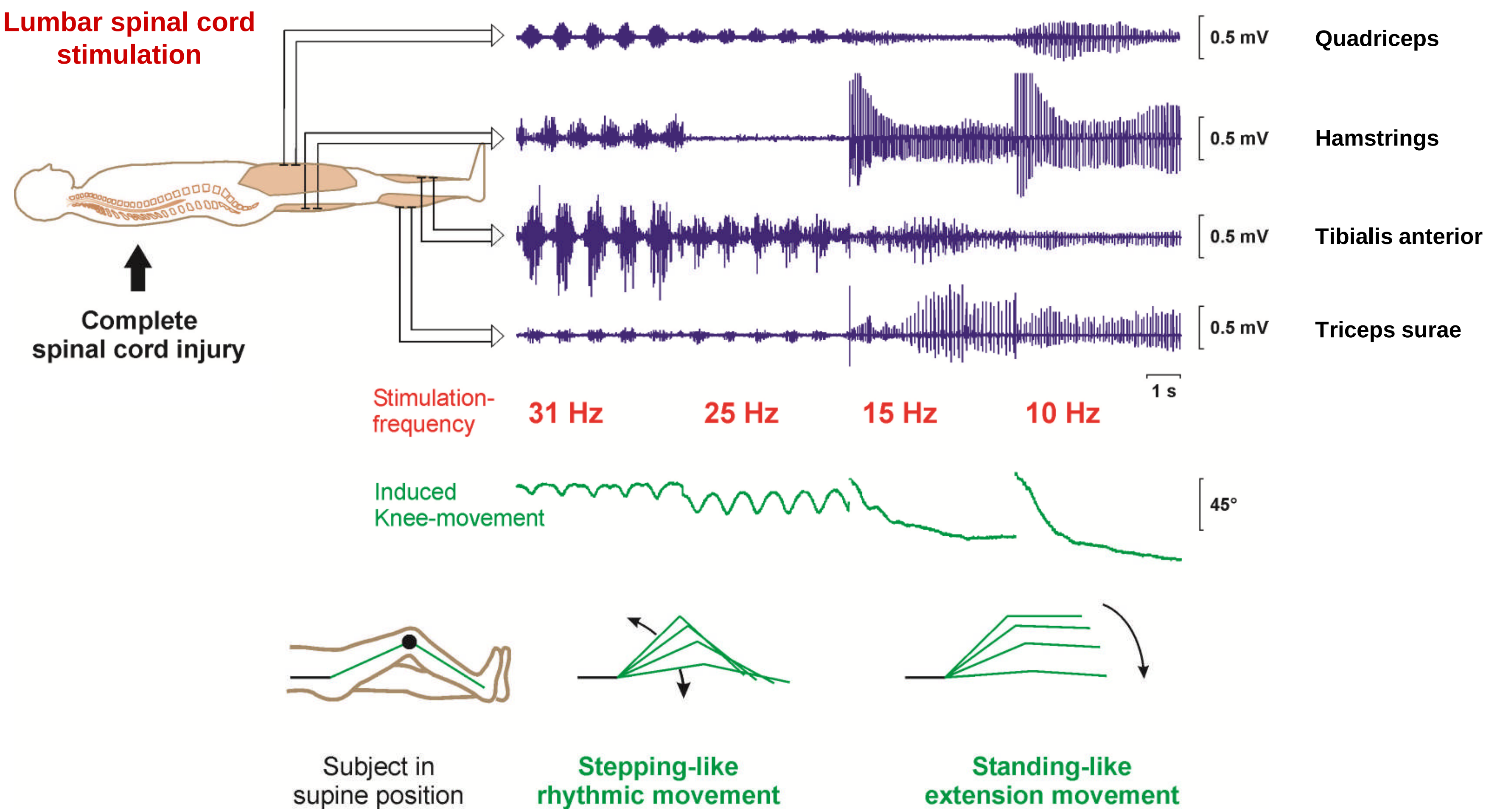






Dimitrijevic et al. Ann N Y Acad Sci. 1998; 860: 360-376.

SCS-frequency dependence of generated motor patterns



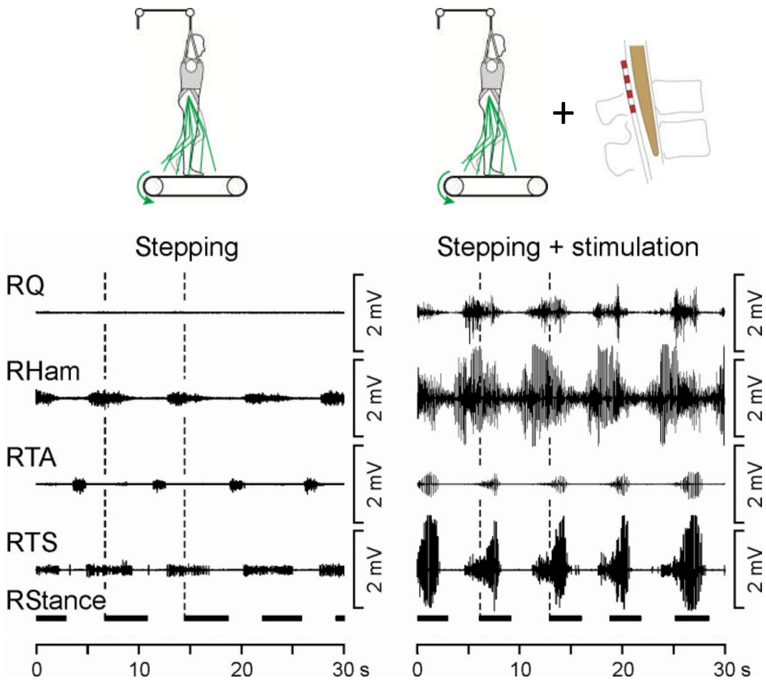
Jilge et al., Exp Brain Res, 2004; 154:308-26.

Potential for clinical applications

V. Reggie Edgerton

Susan Harkema

Vienna



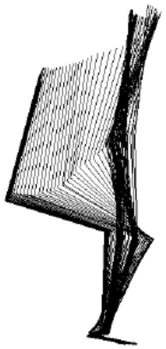
Increased step-cycle synchronized rhythmic activities

30-Hz SCS

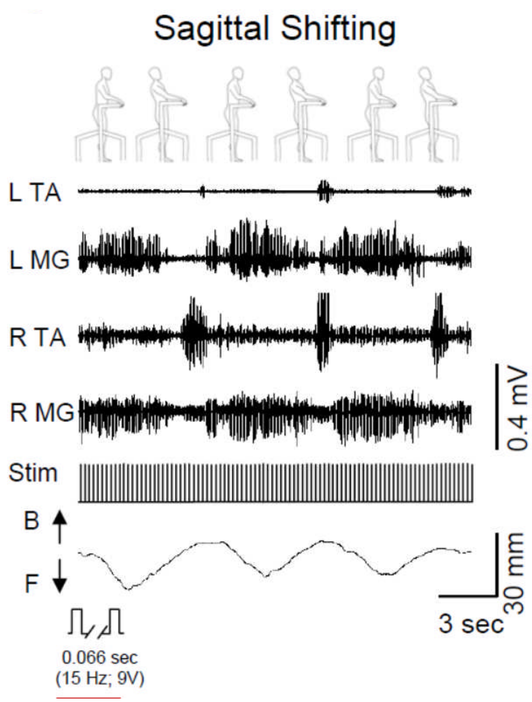
Q…quadriceps, Ham…hamstrings, TA…tibialis anterior, TS…triceps surae

Minassian et al. Biocyber Biomed Eng 2005;25:11–29.

Los Angeles, Louisville



Standing up and full weight-bearing standing



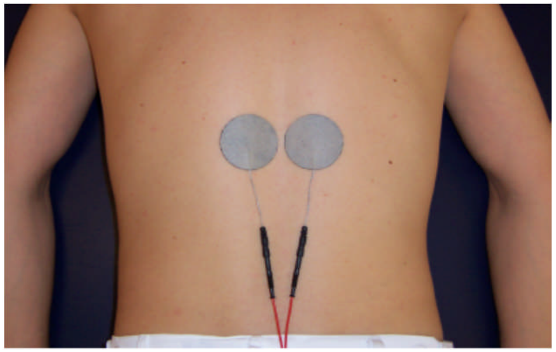
'Compensations' of shifted centre of gravity

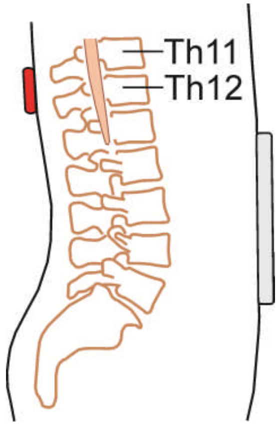
15-Hz SCS

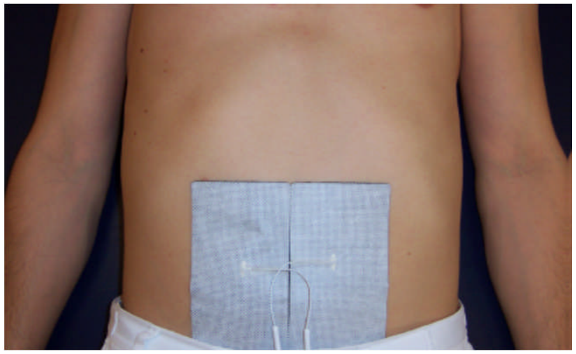
TA…tibialis anterior, MG…medial gastrocnemius

Harkema et al. Lancet 2011;377:1938–47.

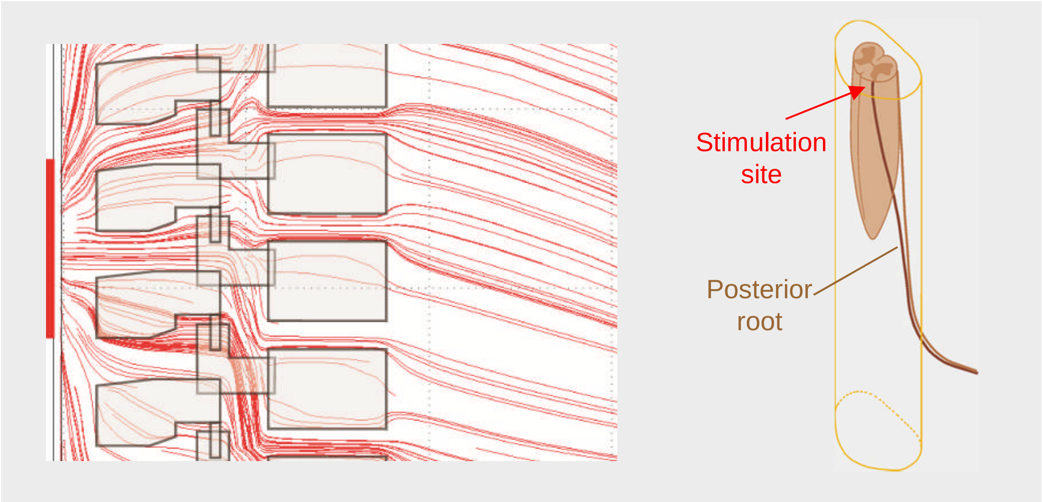
Transcutaneous lumbar spinal cord stimulation





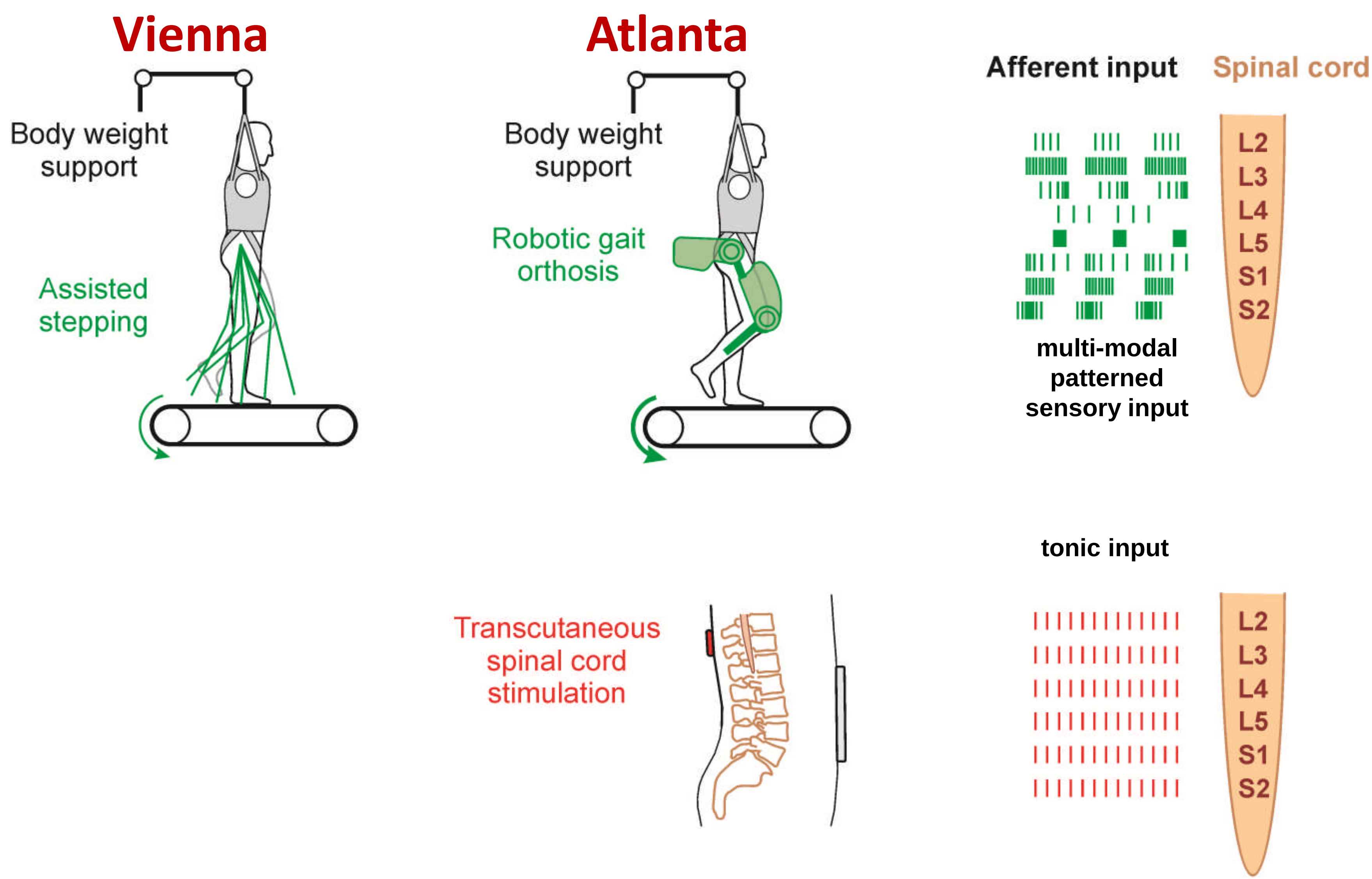


Minassian et al. Muscle Nerve. 2007;35:327-36.
Hofstoetter et al. Artif Organs. 2008;32:644-8.

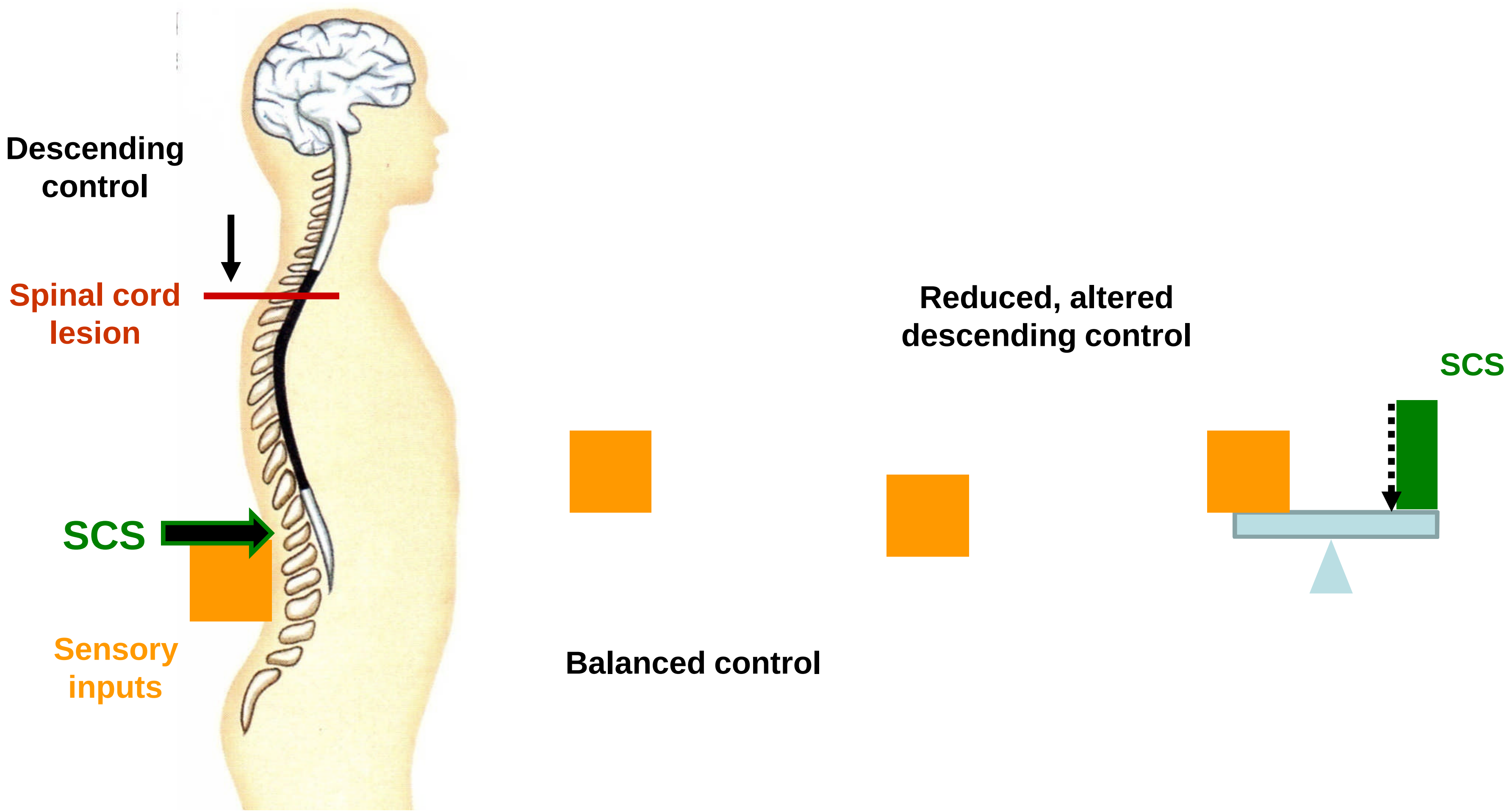


Ladenbauer et al. IEEE Trans Neural Syst Rehabil Eng. 2010;18:637-45; Danner et al. Artif Organs. 2011;35:257-62.

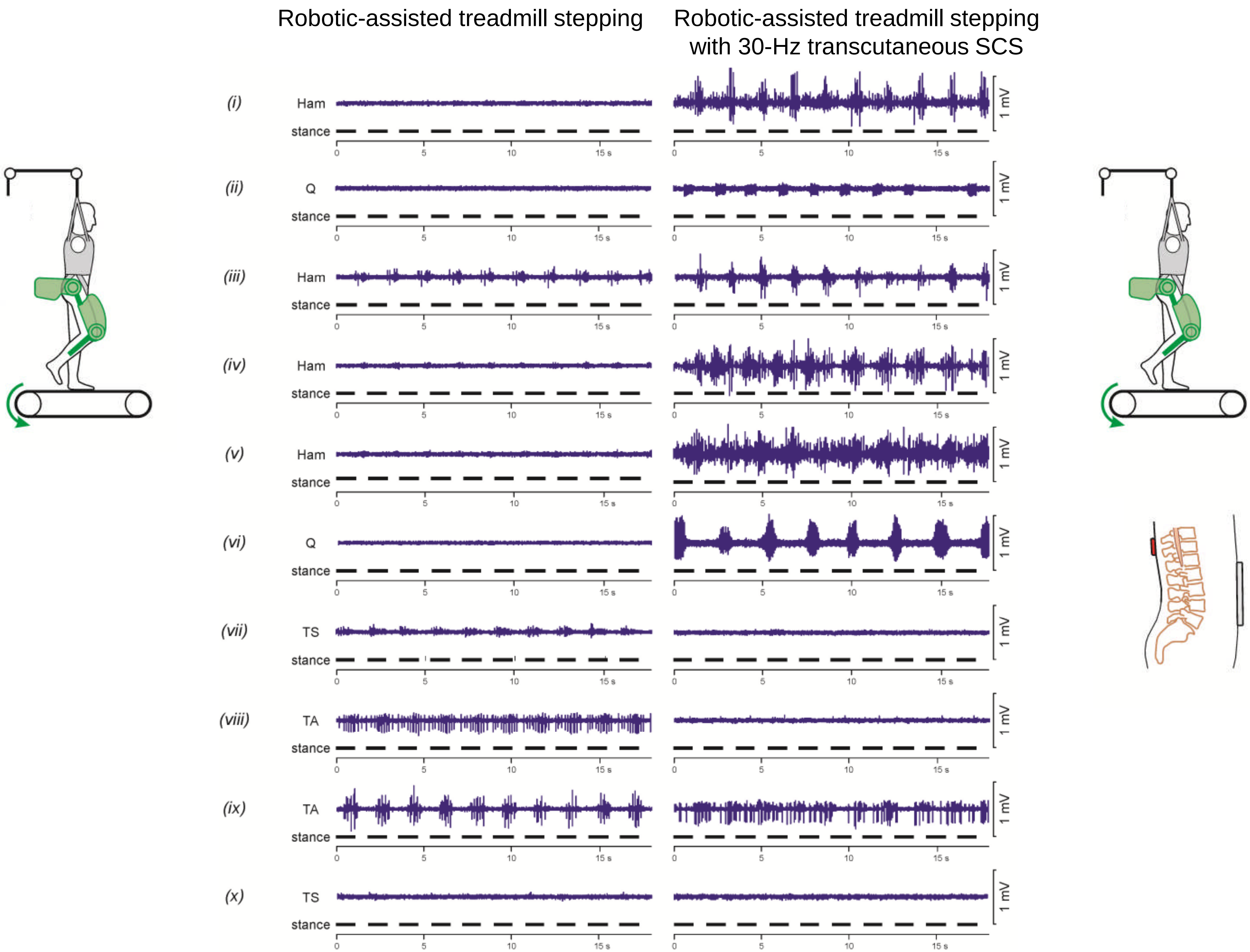
Assisted treadmill stepping + transcutaneous SCS



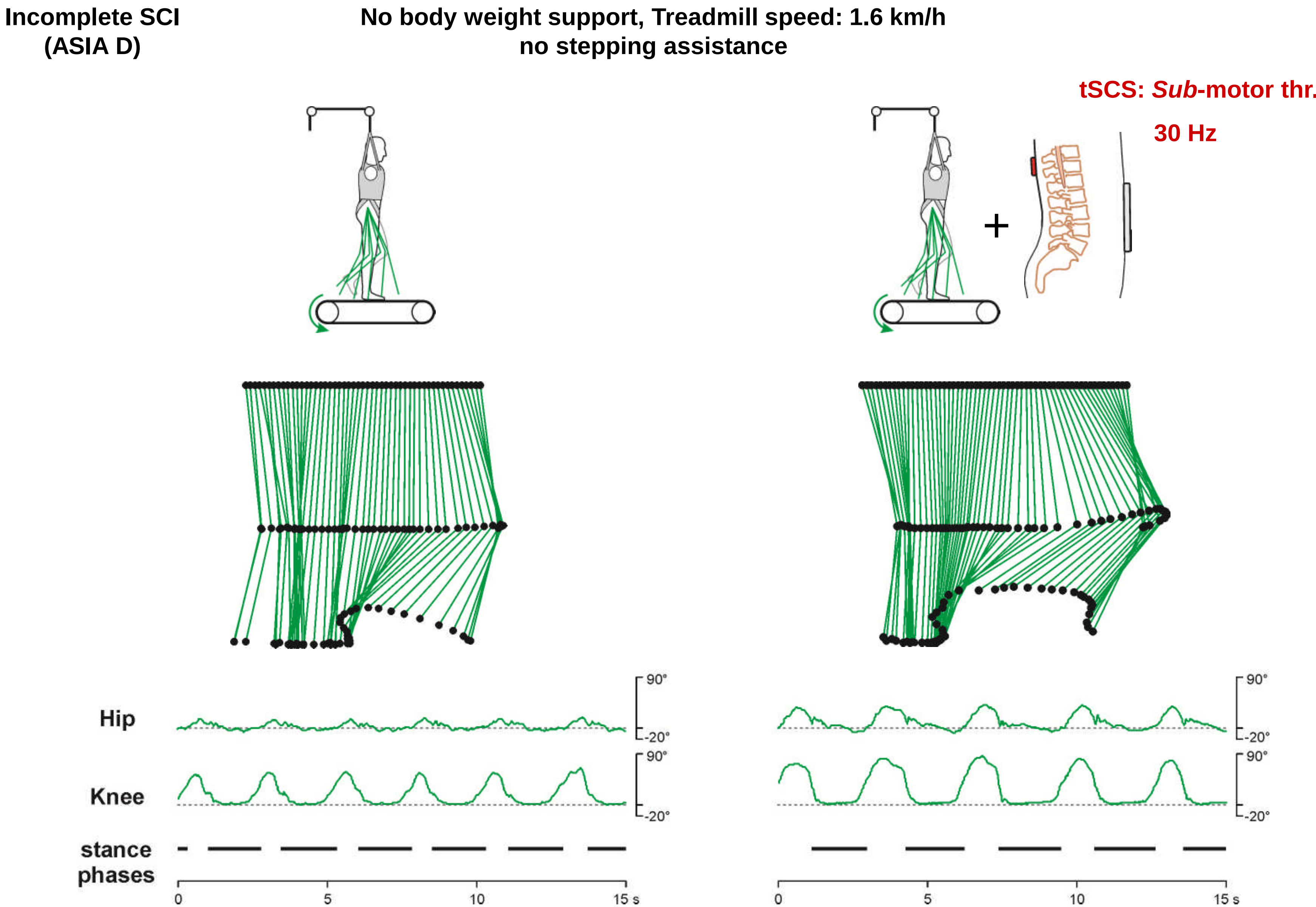
Concept of Restorative Neurology –
to augment surviving CNS capabilities

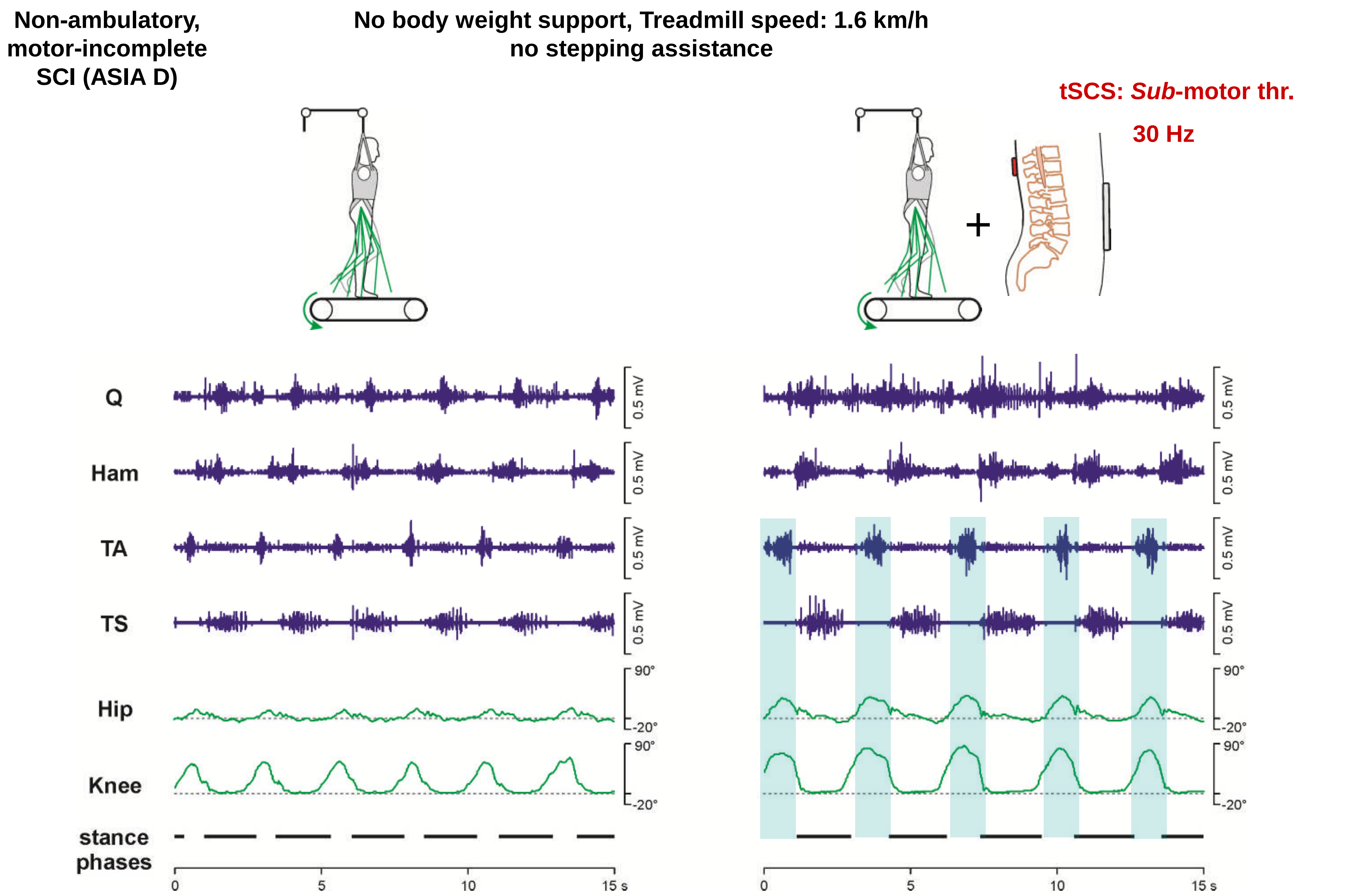


Adapted from Dimitrijevic, Textbook for stereotactic and functional neurosurgery, 1998.



Robotic-assisted treadmill stepping
Robotic-assisted treadmill stepping with 30-Hz transcutaneous SCS
(i)
Ham
stance
(ii)
Q
stance
(iii)
Ham
stance
(iv)
Ham
stance
(v)
Ham
stance
(vi)
Q
stance
(vii)
TS
stance
(viii)
TA
stance
(ix)
TA
stance
(x)
TS
stance
0
5
10
15 s
1 mV


Incomplete SCI
(ASIA D)
No body weight support, Treadmill speed: 1.6 km/h
no stepping assistance
tSCS: Sub-motor thr.
30 Hz
Hip
Knee
stance
phases
90°
-20°
0
5
10
15 s

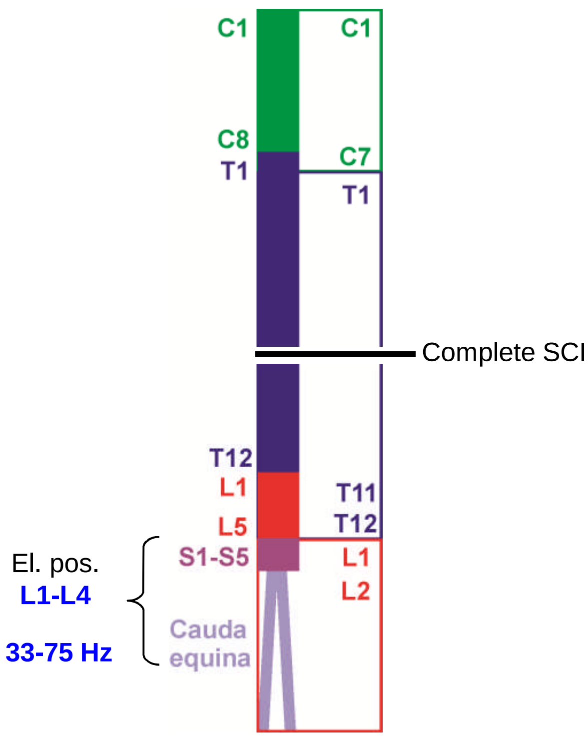


Non-ambulatory,
motor-incomplete
SCI (ASIA D)
No body weight support, Treadmill speed: 1.6 km/h
no stepping assistance
tSCS: *Sub*-motor thr.
30 Hz
+
Q
Ham
TA
TS
Hip
Knee
stance
phases
0.5 mV
90°
-20°
0
5
10
15 s

Epidural SCS for spasticity control after SCI

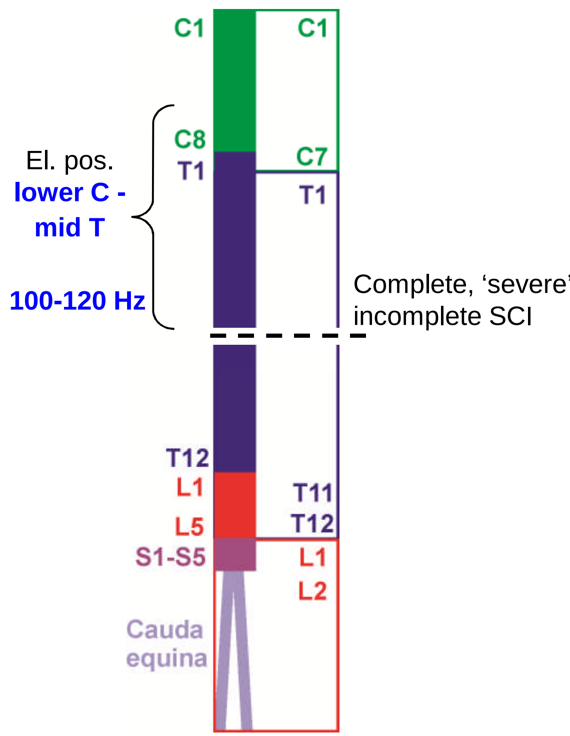
With regard to lower extremities

Richardson et al., 1978;1979



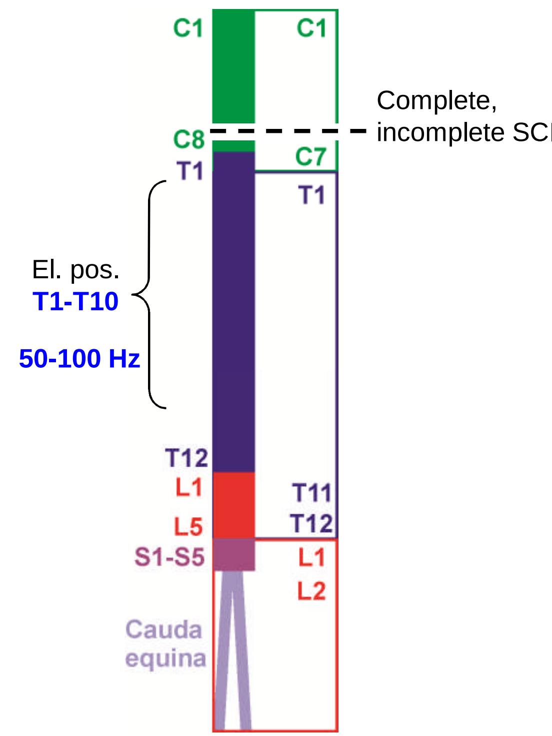
6 subjects,
All had significant therapeutic effects:
Complete control of spasticity
(hypertonia and spasms)

Siegfried et al., 1981



15 subjects,
No convincing therapeutic effects

Barolat et al., 1988



16 subjects,
14 with significant therapeutic effects:
Marked reduction of spasms, reduced clonus, improved motor function

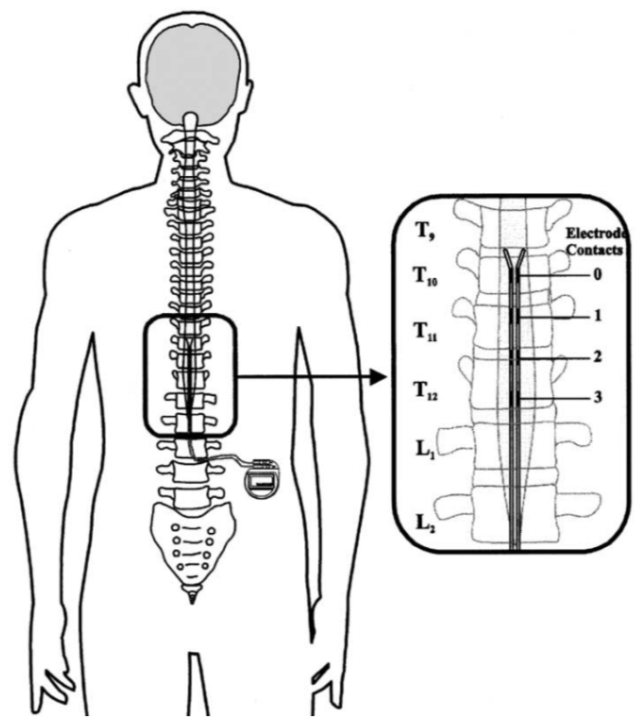
Spinal cord stimulation facilitates functional walking in a chronic, incomplete spinal cord injured.

Richard Herman
Phoenix, Arizona

2 subjects, ‘low‘- ASIA C

Ambulatory function was improved by combining treadmill training and epidural SCS

Improved over-ground walking, reduction in time and energy cost of walking, sense of effort



Herman et al.
Spinal Cord. 2002;40:65-8.

Carhart et al.
IEEE Trans Neural Syst Rehabil Eng. 2004;12:32-42.

Huang H et al.
IEEE Trans Neural Syst Rehabil Eng. 2006;14:14-23.