Neuromodulation to restore motor function

Karen Minassian
Ursula Hofstoetter, Keith Tansey, Winfried Mayr

Center for Medical Physics and Biomedical Engineering, Medical University Vienna, Vienna, Austria
Institute of Analysis and Scientific Computing, Vienna University of Technology, Vienna, Austria
Spinal Cord Injury Lab, Crawford Research Institute, Shepherd Center, Atlanta, GA, USA
Neuromodulation

The therapeutic paradigm is the modulation of CNS activity

Neuromodulation is non-destructive, reversible, and adjustable

![Diagram showing Neuromodulation and Neuroablative approaches](Illustrations 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)

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

Pulse generator

Electrodes

Spinal cord

Cross-section at T12 vertebral level

Posterior roots

Electrode location

Spinal cord

Continuous stimulation
Epidural spinal cord stimulation
Immediate effects(1)
Epidural spinal cord stimulation

Immediate effects(2)

Posterior column fibers

Posterior root fibers

Electrical activation

Trans-synaptic activation

Functional integrity?
Epidural spinal cord stimulation

Immediate effects (3)

Posterior column fibers

Muscle spindles (lower limbs)

Cutaneous mechanoreceptors

Stimulation sites

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

Stimulation of different mixtures of fiber types

Functional integrity?
Epidural SCS in multiple sclerosis

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

• ‘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
  
## Epidural SCS in multiple sclerosis

### Selected reports

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

### Selected reports

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

Physiological mechanisms of SCS in MS (lower limb function)
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)

El. pos. L1-L4
33-75 Hz

Spinal cord
Complete SCI
Epidural SCS for spasticity control after SCI

With regard to lower extremities

Richardson et al., 1978;1979
- Complete, incomplete SCI
- El. pos. T1-T10
- 50-100 Hz

Siegfried et al., 1981
- Complete, ‘severe’ incomplete SCI
- El. pos. lower C - mid T
- 100-120 Hz
- 15 subjects,
  6 subjects,
  All had significant therapeutic effects:
  Complete control of spasticity (hypertonia and spasms)
  14 with significant therapeutic effects:
  Marked reduction of spasms, reduced clonus, improved motor function

Barolat et al., 1988
- Complete, incomplete SCI
- El. pos. T1-T10
- 50-100 Hz
- 16 subjects,
  6 subjects,
  All had significant therapeutic effects:
  Complete control of spasticity (hypertonia and spasms)
Epidural SCS for spasticity control after SCI

Profile of injury and efficacy of SCS

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 …”

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

8 Subjects: 7 motor complete, 1 ASIA C

Traumatic SCI C5 to T6

50 – 100 Hz

Lumbar spinal cord

Lumbar posterior roots

EMG

<table>
<thead>
<tr>
<th>EMG</th>
<th>Quadriiceps</th>
<th>Adductor</th>
<th>Hamstrings</th>
<th>Tibialis anterior</th>
<th>Triceps surae</th>
</tr>
</thead>
<tbody>
<tr>
<td>RQ</td>
<td>200 µV</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RA</td>
<td>200 µV</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RH</td>
<td>200 µV</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RTA</td>
<td>200 µV</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RTS</td>
<td>200 µV</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>gonio</td>
<td>56.25 µV</td>
<td>57.02 deg.</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

SCS off

SCS on (3-cs, 85 Hz, 3 V, 210µs)

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

Q, Quadriceps; A, Adductor; H, Hamstrings; TA, Tibialis anterior; TS, Triceps surae

Epidural stimulation of lumbar cord circuits for spasticity control after SCI (3)

Electrode sites effective to suppress spasticity

<table>
<thead>
<tr>
<th>No</th>
<th>Spine vertebra</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>TV 12 / T</td>
</tr>
<tr>
<td>2</td>
<td>TV 12 / B</td>
</tr>
<tr>
<td>3</td>
<td>TV 11 / B</td>
</tr>
<tr>
<td>4</td>
<td>LV 1 / T</td>
</tr>
<tr>
<td>5</td>
<td>TV 12 / B</td>
</tr>
<tr>
<td>6</td>
<td>TV 12 / M</td>
</tr>
<tr>
<td>7</td>
<td>LV 1 / T</td>
</tr>
<tr>
<td>8</td>
<td>TV 12 / T*</td>
</tr>
</tbody>
</table>

Vertebral body levels:
- T10
- T11
- T12

Cord segments:
- L1
- L2
- L3
- L4
- L5
- S1
- S2

Epidural lumbar SCS generates rhythmic activity

Continuous stimulation at 25 – 50 Hz

Complete SCI subject

Patterned output

Non-patterend input

Human lumbar pattern generator

SCS-frequency dependence of generated motor patterns

Lumbar spinal cord stimulation

Complete spinal cord injury

Stimulation-frequency

31 Hz 25 Hz 15 Hz 10 Hz

Quadriceps Hamstrings Tibialis anterior Triceps surae

Induced Knee-movement

Subject in supine position

Stepping-like rhythmic movement

Standing-like extension movement

Potential for clinical applications

Vienna

Los Angeles, Louisville

Increased step-cycle synchronized rhythmic activities

30-Hz SCS

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


15-Hz SCS

TA...tibialis anterior, MG...medial gastrocnemius


Standing up and full weight-bearing standing

‘Compensations’ of shifted centre of gravity

V. Reggie Edgerton

Susan Harkema
Spinal cord stimulation facilitates functional walking in chronic, incomplete spinal cord injured

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

Richard Herman
Phoenix, Arizona


Transcutaneous lumbar spinal cord stimulation


Assisted treadmill stepping + transcutaneous SCS

Vienna
- Body weight support
- Assisted stepping

Atlanta
- Body weight support
- Robotic gait orthosis

Afferent input
- Multi-modal patterned sensory input

Spinal cord
- Tonic input
- L2, L3, L4, L5, S1, S2

Transcutaneous spinal cord stimulation
Effect-groups representing characteristic modifications of the EMG activities related to the application of tonic transcutaneous SCS during robotic-assisted treadmill stepping.
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 10 15 s
0 5 10 15 s
Incomplete SCI (ASIA D)

No body weight support, Treadmill speed: 1.6 km/h
no stepping assistance

tSCS: Sub-motor thr. 30 Hz
Concept of Restorative Neurology –
to augment surviving CNS capabilities

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