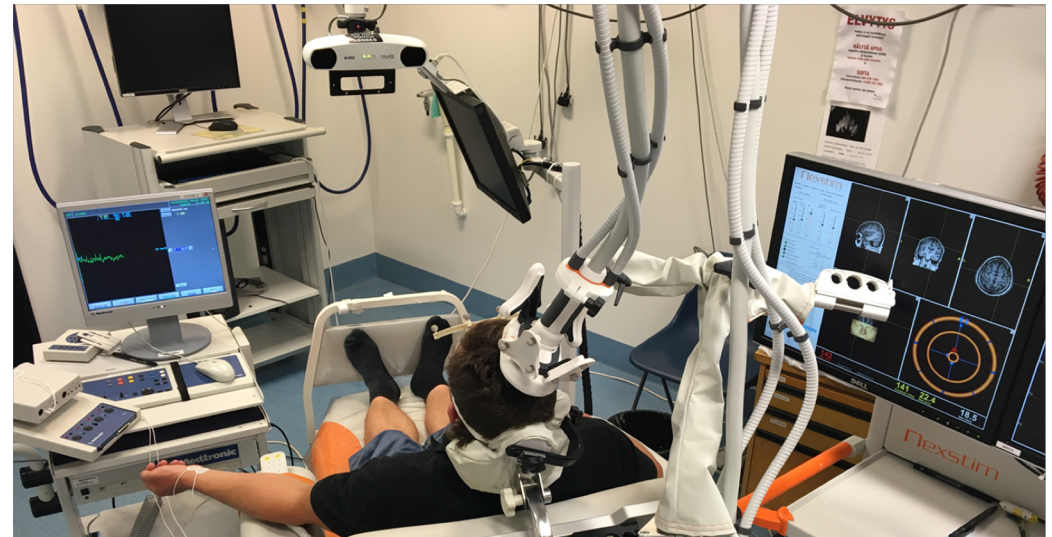


Long-term paired associative stimulation for incomplete chronic spinal cord injury: physiotherapist perspective

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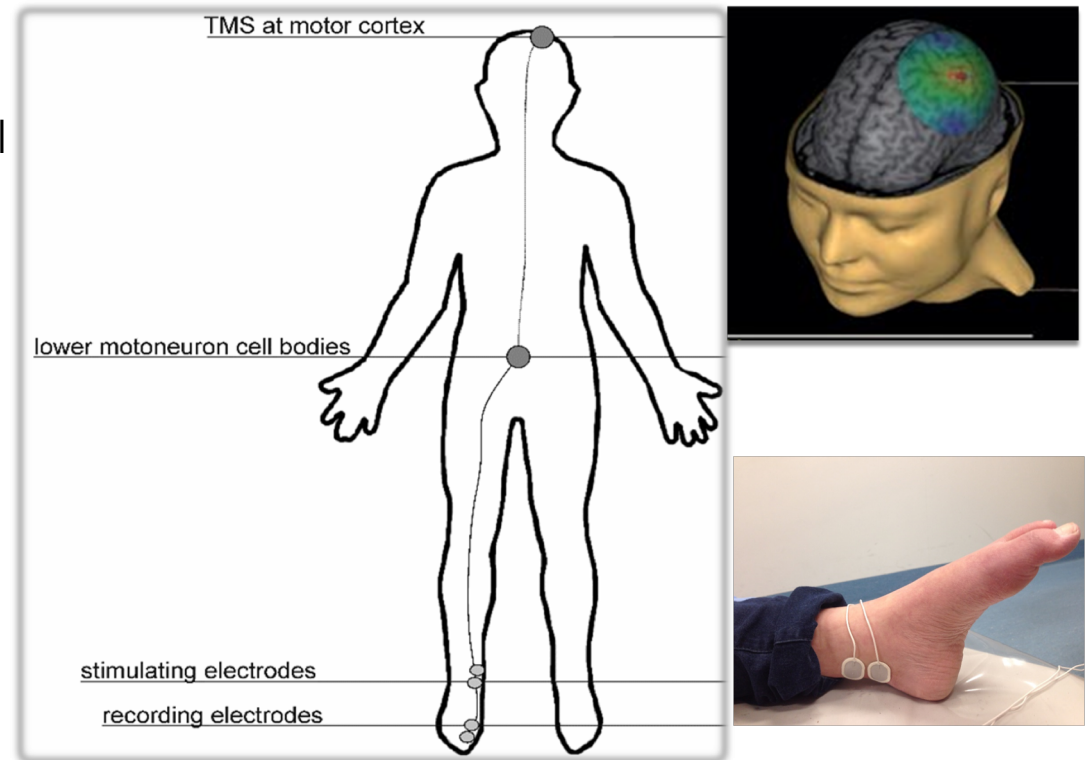
Long-term paired associative stimulation (PAS)

- Long-term paired associative stimulation (PAS) is a novel treatment under investigation for patients with incomplete spinal cord injury (SCI).
- PAS-SCI project conducted in Helsinki University Hospital and Validia Rehabilitation Centre before.
- I will present a summary of all patient data obtained by manual muscle testing in this project so far.



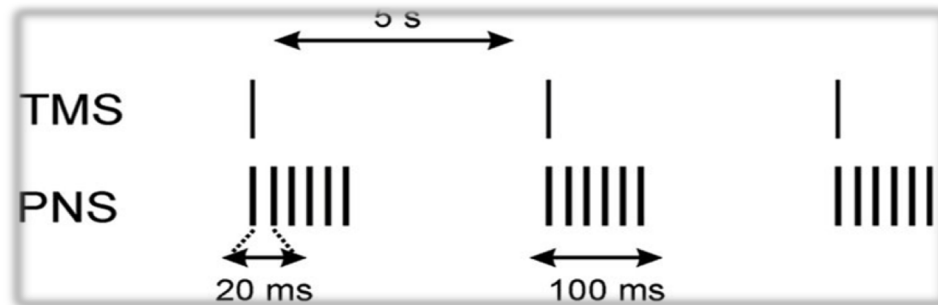
Introduction

- Long-term paired associative stimulation (PAS) comprises transcranial magnetic stimulation (TMS) and peripheral electrical nerve stimulation (PNS) given in a synchronous manner.
- We hypothesized that delivering this stimulation in a long-term manner after chronic incomplete spinal cord injury (SCI) would induce strengthening of weakened connections in the corticospinal tract.



Method

- We have developed a robust stimulation protocol with novel settings (below) which is effective (as indicated by the robust growth of motor-evoked potential amplitudes in healthy subjects after the stimulation) even if performing some neurophysiological measurements is not possible.
- We applied this novel protocol for the first time to incomplete SCI patients in a long-term manner (3-5 times per week, from 4 weeks to 1 year).



Measurement

- Patients were evaluated by Daniels and Worthingham's Manual Muscle Testing (MMT) on 0-5 scale and functional tests.
- Average of change in MMT score for each muscle was calculated.
- Muscles scored 5 at first evaluation were not taken into account.



0	No visible or palpable contraction.
1	Visible or palpable contraction.
2	Full ROM gravity eliminated.
3	Full ROM against gravity.
4	Full ROM against gravity, moderate resistance.
5	Full ROM against gravity, maximum resistance.

Results

- 17 patients in total
- In all studies, PAS was conducted in parallel with continuous conventional rehabilitation, which was individual, kept the same as before stimulation and not influenced by the researchers



1) Two pilot SCI patients

(Shulga et al 2016a Spinal Cord Ser Cases)

Patient A

Paraplegic (L1), 2 years after SCI, AIS C, full paralysis below knee level

- PAS for peroneal and tibial nerves for 12 weeks
- Regained plantarflexion and dorsiflexion of both ankles

Patient B

Tetraplegic (C3), 2 years after SCI, AIS C, no grasping ability

- PAS for median, ulnar and radial nerves for 12 weeks
- Regained grasping ability, average increase in MMT 1.1 point in each muscle

2) Five patients with tetraplegia of traumatic origin – upper limb stimulation, blinded evaluation

(Tolmacheva et al 2017 J Neurotrauma)

AIS B-D, 1-6 years after SCI, C3-C7

- PAS for median, ulnar and radial nerves for 4 weeks
- MMT increased in each muscle by 1 point (average across all patients)
- MMT increase was significantly higher in randomly selected hand treated with PAS as compared to contralateral hand treated with peripheral stimulation and sham TMS
- Motor scores in treated hand kept increasing during follow-up period of 1 month

3) Five patients with tetraplegia due to neurological disease upper limb stimulation, blinded evaluation

(Tolmacheva et al, manuscript in preparation)

AIS D, C1-C5, time since symptoms onset 2-15 years

- Causes: abscess, intervertebral disc protrusion and spinal stenosis, hemangioma, arteriovenous malformation
- PAS for median, ulnar and radial nerves for 6 weeks
- Average increase in MMT: 1.4 points after stimulation, 1.6 points at 1 month follow-up, 2 points at 6 month (3 first patients) follow-up - significant improvements in palmar, key and index finger pinch and Box and blocks test

4) Tetraplegic patient – stimulation applied for as long as improvement is observed

(Rodionov et al, manuscript in preparation)

AIS B (C7), traumatic tetraplegia, time since injury 5.5 years

- PAS to median, ulnar and radial nerves of both hands for over 1 year
- Stimulation of each nerve stopped when muscles innervated by it reached the score of at least 4 - 84 % of muscles reached score 5 and the rest score 4 at the end of the follow-up period (4 months after last session), average increase in each muscle being 2.7 points
- SCIM: self-care increased from 3 to 13 points, mobility (room) increased from 6 to 10 points, mobility (indoors and outdoors) increased from 5 to 7 points
- Increase in dynamometer, pinch, 9-hole peg test and Box and blocks test results

5) Three tetraplegic patients, lower limb stimulation, (Rodionov et al, ongoing study)

AIS C-D, C1-C5, time since injury 3-4 years

- Blinded evaluation
- PAS for femoral, gluteal, tibial and peroneal nerves for both limbs for 8 weeks (only 4-6 weakest nerves selected)
- MMT increased by 1.4 in muscles innervated by stimulated nerves across all patients
- In two ambulatory patients, walking distance increased 2-3 – fold under test conditions.
 - Both patients reported even greater increase in walking distance in daily life (up to 10-fold; distance in test conditions was restricted by lower back pain).
- Third patient was non-ambulatory before stimulation and could take several steps with Eva Support Walker without weight support after stimulation.

6) Pilot patient with paraplegia – lower limb stimulation, case study

(unpublished data)

- **Patient A - paraplegic AIS D, T7, one year after SCI**
- Non-ambulatory without weight support (conventional walking rehabilitation could not be started)
- PAS for peroneal, tibial, femoral and gluteal nerves for 2 months
- After stimulation was able to stand without weight support for 3 minutes and walk several meters in parallel bars without weight support.
- Conventional walking rehabilitation could be initiated without continuation of stimulation.

DISCUSSION

- Para- and tetraplegic, traumatic and non-traumatic incomplete SCI patients are responsive to PAS.
- Majority of incomplete injuries are asymmetric
- PAS enables specifically strengthening the weakest connections in upper and lower limbs.
- Reinforcing the connectivity of precisely defined motor cortex areas with corresponding nerves can be beneficial especially in hand rehabilitation where highly specific movements of small muscles are desirable.
- Obtained improvement in MMT increases during follow-up period without stimulation at least up to 6 months.
- Patients with more recent and milder injuries are more responsive than patients with more chronic and more severe injuries.
- PAS requires equipment that is already available in many hospitals and laboratories worldwide.
- PAS is effective at the chronic stage for at least up to 15 years after injury.
- It is plausible that starting PAS at subacute stage before irreversible changes in muscle tissue have occurred will result in even better outcomes.

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