

Reporting Summary

Nature Research wishes to improve the reproducibility of the work that we publish. This form provides structure for consistency and transparency in reporting. For further information on Nature Research policies, see [Authors & Referees](#) and the [Editorial Policy Checklist](#).

Statistical parameters

When statistical analyses are reported, confirm that the following items are present in the relevant location (e.g. figure legend, table legend, main text, or Methods section).

n/a Confirmed

- ☐ ☒ The exact sample size (n) for each experimental group/condition, given as a discrete number and unit of measurement
- ☐ ☒ An indication of whether measurements were taken from distinct samples or whether the same sample was measured repeatedly
- ☐ ☒ The statistical test(s) used AND whether they are one- or two-sided
Only common tests should be described solely by name; describe more complex techniques in the Methods section.
- ☐ ☒ A description of all covariates tested
- ☒ ☐ A description of any assumptions or corrections, such as tests of normality and adjustment for multiple comparisons
- ☐ ☒ A full description of the statistics including central tendency (e.g. means) or other basic estimates (e.g. regression coefficient) AND variation (e.g. standard deviation) or associated estimates of uncertainty (e.g. confidence intervals)
- ☐ ☒ For null hypothesis testing, the test statistic (e.g. F , t , r) with confidence intervals, effect sizes, degrees of freedom and P value noted
Give P values as exact values whenever suitable.
- ☒ ☐ For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings
- ☒ ☐ For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes
- ☐ ☒ Estimates of effect sizes (e.g. Cohen's d , Pearson's r), indicating how they were calculated
- ☐ ☒ Clearly defined error bars
State explicitly what error bars represent (e.g. SD, SE, CI)

Our web collection on [statistics for biologists](#) may be useful.

Software and code

Policy information about [availability of computer code](#)

Data collection

EMG system: Myon 320, Myon AG, Schwarzenberg, Switzerland
Motion capture system: Vicon Nexus software v1.8.5, Vicon Motion Systems, Oxford, UK
Data acquisition system: Twincat 3.1, Beckhoff Automation GmbH & Co. KG, Huelshorstweg 20 33415 Verl Germany
Custom C++ code to control stimulation in real-time inside the laboratory environment
Custom C# code to control stimulation in real-time outside the laboratory environment
Microsoft Visual Studio Professional 2012 (for development in C++)
Microsoft Visual Studio Community 2017 (for development in C#)

Data analysis

Custom code in MATLAB R2018a used for all data analysis
Kinematic analysis performed using Vicon Nexus software v1.8.5, Vicon Motion Systems, Oxford, UK
Sim4Life v3.4
ImageJ 1.52

For manuscripts utilizing custom algorithms or software that are central to the research but not yet described in published literature, software must be made available to editors/reviewers upon request. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Research [guidelines for submitting code & software](#) for further information.

Data

Policy information about [availability of data](#)

All manuscripts must include a [data availability statement](#). This statement should provide the following information, where applicable:

- Accession codes, unique identifiers, or web links for publicly available datasets
- A list of figures that have associated raw data
- A description of any restrictions on data availability

Data that supports the findings and software routines developed for the data analysis will be made available upon reasonable request to the corresponding author at gregoire.courtine@epfl.ch.

Field-specific reporting

Please select the best fit for your research. If you are not sure, read the appropriate sections before making your selection.

☒ Life sciences ☐ Behavioural & social sciences ☐ Ecological, evolutionary & environmental sciences

For a reference copy of the document with all sections, see nature.com/authors/policies/ReportingSummary-flat.pdf

Life sciences study design

All studies must disclose on these points even when the disclosure is negative.

Sample size	We report proof-of-concept results in three patients who contributed to a First-in-Man study. No previous data existed to predetermine sample size. Previous studies employing spinal cord stimulation or novel implanted neurotechnologies (e.g. brain machine interface) in individuals with spinal cord injury reported their results in 1 to 4 participants.
Data exclusions	No data were excluded from the analyses.
Replication	Reproducibility of the experimental findings was verified across several steps, several recording sessions and between all 3 participants.
Randomization	Randomization was not sought in the present study. Each participant served as his own control (stimulation off vs. on conditions; evaluations at different points over time throughout the rehabilitation training period)
Blinding	Investigators were not blinded. Their expertise was required to optimize the intervention and to apply the intervention during evaluations. Furthermore, the effects of the intervention were obvious, acutely producing changes in the kinematics and muscle activities of the participants during walking.

Reporting for specific materials, systems and methods

Materials & experimental systems

n/a	Involved in the study
☒	☐ Unique biological materials
☒	☐ Antibodies
☒	☐ Eukaryotic cell lines
☒	☐ Palaeontology
☒	☐ Animals and other organisms
☐	☒ Human research participants

Methods

n/a	Involved in the study
☒	☐ ChIP-seq
☒	☐ Flow cytometry
☐	☒ MRI-based neuroimaging

Human research participants

Policy information about [studies involving human research participants](#)

Population characteristics	Three male individuals, aged 28-47 y, all with a traumatic cervical spinal cord injury participated in the study. All participants had completed standard of care rehabilitation following their injury and were in a chronic state, 4-6 y post-injury. All displayed low motor scores in the lower limbs or complete motor paralysis, which bound them to a wheelchair.
Recruitment	Participant recruitment was done via the clinicaltrial.gov website where the principal investigators' contact details were disclosed (NCT02936453). Patients and physicians contacted them directly to communicate their interest to participate or to

refer a patient to the STIMO study. The clinical study nurse communicated with the patients or the referring physician and reviewed the clinical status of the patient for compliance with the inclusion and exclusion criteria listed below. Patients meeting the inclusion criteria were given the study's flyer and the informed consent form to understand further their implications and involvement within this clinical study. The participants' selection was also based on their ability to live independently and their autonomy in their daily living activities.

Inclusion Criteria:

- Age 18-65 (women or men)
- Incomplete SCI graded as AIS C & D
- Level of lesion: T10 and above, based on AIS level determination by the PI, with preservation of conus function
- The intact distance between the cone and the lesion must be at least 60mm
- Focal spinal cord disorder caused by either trauma or epidural, subdural or intramedullary bleeding
- Minimum 12 months post-injury
- Completed in-patient rehabilitation program
- Able to stand with walker or 2 crutches
- Stable medical and physical condition as considered by Investigators
- Adequate care-giver support and access to appropriate medical care in patient's home community
- Agree to comply in good faith with all conditions of the study and to attend all required study training and visits
- Must participate in two training sessions before enrolment
- Must provide and sign Informed Consent prior to any study related procedures

Exclusion Criteria:

- Limitation of walking function based on accompanying (CNS) disorders (systemic malignant disorders, cardiovascular disorders restricting physical training, peripheral nerve disorders)
- History of significant autonomic dysreflexia
- Cognitive/brain damage
- Epilepsy
- Patient who uses an intrathecal Baclofen pump.
- Patient who has any active implanted cardiac device such as pacemaker or defibrillator.
- Patient who has any indication that would require diathermy.
- Patient who has any indication that would require MRI.
- Patient that have an increased risk for defibrillation
- Severe joint contractures disabling or restricting lower limb movements.
- Haematological disorders with increased risk for surgical interventions (increased risk of haemorrhagic events).
- Participation in another locomotor training study.
- Congenital or acquired lower limb abnormalities (affection of joints and bone).
- Women who are pregnant (pregnancy test obligatory for woman of childbearing potential) or breast feeding or not willing to take contraception.
- Known or suspected non-compliance, drug or alcohol abuse.
- Spinal cord lesion due to either a neurodegenerative disease or a tumour.
- Patient has other anatomic or co-morbid conditions that, in the investigator's opinion, could limit the patient's ability to participate in the study or to comply with follow-up requirements, or impact the scientific soundness of the study results.
- Patient is unlikely to survive the protocol follow-up period of 12 months.

Magnetic resonance imaging

Experimental design

Design type	clinical structural MRI
Design specifications	N/A
Behavioral performance measures	N/A

Acquisition

Imaging type(s)	structural
Field strength	3 Tesla
Sequence & imaging parameters	Scanning sequence: TSE (Turbo Spin Echo) SPACE (Sampling Perfection with Application optimized Contrasts using different flip angle Evolution), imaging type: Cartesian, field of view: 200 mm x 200 mm, matrix size: 320 pixels x 320 pixels, slice thickness: 1 mm, orientation: axial, TE: 133 ms, TR: 1500 ms, flip angle: 125 degrees
Area of acquisition	spine
Diffusion MRI	☐ Used ☒ Not used

Preprocessing

Preprocessing software	N/A
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Normalization	N/A
Normalization template	N/A
Noise and artifact removal	N/A
Volume censoring	N/A

Statistical modeling & inference

Model type and settings	N/A
Effect(s) tested	N/A
Specify type of analysis:	☐ Whole brain ☐ ROI-based ☐ Both
Statistic type for inference (See Eklund et al. 2016)	N/A
Correction	N/A

Models & analysis

n/a	Involved in the study
☒	☐ Functional and/or effective connectivity
☒	☐ Graph analysis
☒	☐ Multivariate modeling or predictive analysis