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Reporting Summary

Nature Portfolio 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 Portfolio policies, see our Editorial Policies and the Editorial Policy Checklist.

Statistics

For all statistical analyses, confirm that the following items are present in the 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
☐	☒ A statement on 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 statistical parameters 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

Our web collection on statistics for biologists contains articles on many of the points above.

Software and code

Policy information about availability of computer code

Data collection

We collected data from 11 macaque monkeys, 34 human participants of the PREDI-STIM clinical study, two participants of the "Motor Network in Parkinson's Disease and Dystonia: Mechanisms of Therapy" clinical trial, and one participant of the STIMO-PARK clinical trial,as follows: 1) Non-human primate data: behavioral, motion tracking, electromyographic, intracortical neurophysiological and histological data. 2) Human data: self-reported and observational behavioral, motion tracking, electromyographic, epicortical neurophysiological and medical imaging data, as well as data from clinically-established questionnaires on motor capacity and quality of life.

All softwares and software versions used to acquire data: G-Drive Plus software suite by EPFL, DecodingGate software application by EPFL, Neural Research Programmer v5.2.999 and later by Medtronic, NEUWalk Research Programmer Application 09103 by Medtronic, Research Development Kit 4NR013 by Medtronic, Cerebus Central Suite v6 and later by Blackrock Neurotech, Simi Motion software v8 and later by Simi Reality Motion Systems, Nexus 1.8.5 by Vicon, and ISIS XPress by inomed

The methods, procedures and devices to to collect data are described in the man text of the manuscript and in the Method section of the relevant paragraphs.

Data analysis	All softwares and software versions used to analyze data : Matlab v2018a and later by Mathworks, Sim4Life v7.0 by ZMT, Cerebus Central Suite v6 and later by Blackrock Neurotech, Simi Motion software v8 and later by Simi Reality Motion Systems, Nexus 1.8.5 by Vicon, OpenSim software suite v4.2 and later by SimTK, SCONE software v2.0.0 and later, ISIS XPress by inomed, Neurolucida image analysis software v2019.1.1 and later by MBF Bioscience, Spinal Cord Toolbox v5.4 These are described in the Method section at the relevant paragraphs.

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 and reviewers. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Portfolio 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 description of any restrictions on data availability
- For clinical datasets or third party data, please ensure that the statement adheres to our policy

Data that supports the findings and software routines developed for the data analysis will be made available upon reasonable request to the corresponding authors. Third party datasets used in our study are available under the Creative Commons Public License: VerSe 2019 (https://osf.io/nqjyw/) and VerSe 2020 (https://osf.io/t98fz/).

Human research participants

Policy information about studies involving human research participants and Sex and Gender in Research.

Reporting on sex and gender	We comply with the sex and gender guidelines.
Population characteristics	PREDI-STIM clinical study The study involved 25 participants with PD (12 female, 13 male, mean age 60 +/- std 7.8) and 9 participants without PD as controls (4 female, 5 male, mean age 58.8 +/- std 4.5). Sex was self-reported. Sex was considered in the study design – the participants were enrolled to ensure a balanced sex distribution. Informed consent was obtained for all participants. The participants received no compensation for the study. Key inclusion criteria for people with Parkinson's disease: o Diagnosed with Parkinson's disease o Receiving a pre-therapeutic assessment and monitoring for one, three and five years as part of the regular monitoring of the subthalamic nucleus deep brain stimulation. Motor Network in Parkinson's Disease and Dystonia: Mechanisms of Therapy clinical trial Key inclusion criteria for people with Parkinson's disease: o Ability to give informed consent for the study. o Movement disorder symptoms that are sufficiently severe, in spite of best medical therapy, to warrant surgical implantation of deep brain stimulators according to standard clinical criteria. o Patient has requested surgical intervention with deep brain stimulation for their disorder. o No MR abnormalities that suggest an alternative diagnosis or contraindicate surgery. o Absence of significant cognitive impairment (score of 20 or greater on the Montreal Cognitive Assessment - MoCA). o Signed informed consent. o Ability to comply with study follow-up visits for brain recording, testing of adaptive stimulation, and clinical assessment. o Age 21-75 (for STN patients, minimum age is 25). o Diagnosis of idiopathic PD with duration of motor symptoms for 4 years or greater. o Patient has undergone appropriate therapy with oral medications with inadequate relief as determined by a movement disorders neurologist, and has had stable doses of antiparkinsonian medications for 30 days prior to baseline assessment. o UPDRS-III score off medication between 20 and 80 and an improvement of at least 30% in the baseline UPDRS-III on medication score, compared to the baseline off-medication score, and motor fluctuations with at least 2 hours per day of on time without dyskinesia or with non-bothersome dyskinesia, or Patients with tremor-dominant PD (a tremor score of at least 2 on a UPDRS-III sub-score for tremor), treatment resistant, with significant functional disability despite maximal medical management. Key exclusion criteria: o Coagulopathy, anticoagulant medications, uncontrolled hypertension, history of seizures, heart disease, or other medical conditions considered to place the patient at elevated risk for surgical complications. o Evidence of a psychogenic movement disorder: Motor symptoms that remit with suggestion or "while unobserved", symptoms that are inconsistent over time or incongruent with clinical condition, plus other manifestation such as "false" signs, multiple somatizations, or obvious psychiatric disturbance. o Pregnancy: all women of child bearing potential will have a negative urine pregnancy test prior to undergoing their surgical procedure. o Significant untreated depression (BDI-II score >20) History of suicidal attempt or active suicidal ideation (Yes to #2-5 on C-SSRS). o Any personality or mood symptoms that study personnel believe will interfere with study requirements. o Subjects who require ECT, rTMS or diathermy.

o Implanted stimulation systems such as; cochlear implant, pacemaker, defibrillator, neurostimulator or metallic implant.
o Previous cranial surgery.
o Drug or alcohol abuse.
o Meets criteria for Parkinson's disease with mild cognitive impairment (PD-MCI). These criteria are: performance of more than two standard deviations below appropriate norms, for tests from two or more of these five cognitive domains: attention, executive function, language, memory, and visuospatial tests.

STIMO-PARK clinical trial
STIMO-PARK is an ongoing clinical feasibility study (clinicaltrials.gov ID: NCT04956770) that investigates the effects of lumbosacral EES to improve mobility in people with Parkinson's disease. Study participation was not compensated, but all the study-related costs incurred on the participants were reimbursed. The sex of participants was not considered in the clinical trial design as not a relevant criterium to evaluate in this feasibility case study. The inclusion criteria include idiopathic Parkinson's disease with III-IV Hoehn-Yahr stage, exhibiting severe gait difficulties and postural instability, use of the Medtronic DBS implant and receiving medication for Parkinson's disease. The study involves assessments before the implantation surgery for the spinal EES neurostimulation system, the surgical implantation of the neurostimulation system, a 1-month period for configuration of EES protocols and sequences, and a 3-month period of physiotherapist-assisted rehabilitation during 1–3-hour sessions taking place 2 to 3 times per week. The rehabilitation program is personalized based on the participants' needs and improvements.

Key inclusion criteria:
o Diagnosed with idiopathic Parkinson's disease with III-IV Hoehn-Yahr stage, exhibiting severe gait difficulties and postural instability.
o Implanted with Medtronic DBS implant and receiving medication for Parkinson's disease.
o Aged 18 to 80 years.
o Stable medical, physical and psychological condition as considered by the Investigators in accordance with treating physician and treating neurologist.
o Must agree to comply in good faith with all conditions of the study and to attend all required study training and visit
o Must provide and sign the study's Informed Consent prior to any study-related procedures.

Key exclusion criteria:
o Severe or chronic medical disorder pre-existing PD diagnosis affecting rehabilitation.
o Active oncological disease requiring heavy treatments and frequent MRI controls.
o Having an implanted device that is active (e.g., pacemaker, implantable cardiac defibrillator) whose interference with the investigational system's neurostimulator (Activa RC) is not confirmed safe by the CE-mark of the device, or having an indication that might lead to implantation of such device.
o Inability to follow study procedures, e.g. due to language problems, psychological disorders, dementia as considered by the Investigators in accordance with treating physician and treating neurologist.
o Hematological disorders with an increased risk of hemorrhagic event during surgical interventions.
o Life expectancy of less than 12 months.
o Pregnant or breast feeding.
o Participation in another interventional study.

Recruitment

PREDI-STIM clinical study
This article describes the analysis of data collected from 25 people with Parkinson's disease and 9 age-matched healthy controls that were enrolled in the PREDI-STIM clinical study, conducted at the Bordeaux University Hospital. People with Parkinson's disease were recruited among all the pool of patients being followed within the Neurology Dpt. Participation in the study was proposed to all patients as they were being followed in the clinic, until filling the sex / gender distribution. The controls were recruited by adds.

Motor Network in Parkinson's Disease and Dystonia: Mechanisms of Therapy clinical trial
This article described the analysis of data collected from two people with Parkinson's disease that were enrolled in the clinical trial. They were recruited from a population referred for implantation of deep brain stimulators for PD. Before recruitment, they were evaluated by a movement disorders neurologist and met diagnostic criteria for PD and by a neuropsychologist to exclude major cognitive impairment or untreated mood disorder. Inclusion criteria included motor fluctuations with prominent rigidity and bradykinesia in the off-medication state, baseline off-medication MDS-UPDRS-III scores between 20 and 80, greater than 30% improvement in MDS-UPDRS-III on medication than off of medication and absence of significant cognitive impairment (score of 20 or above on the Montreal Cognitive Assessment). The full IDE application (G180097) and study protocol have been shared with other researchers via the Open Mind initiative (https://openmind-consortium.github.io). After enrollment, participants underwent bilateral placement of cylindrical quadripolar deep brain stimulator leads into the STN (Medtronic model 3389; 1.5-mm contact length and 2.0-mm intercontact spacing), bilateral placement of quadripolar cortical paddles into the subdural space over the cortical area that included the motor cortex (Medtronic model 0913025; 4-mm contact diameter and 10-mm intercontact spacing) and bilateral placement of investigational sensing IPGs in a pocket over the pectoralis muscle (Medtronic Summit RC+S model B35300R). The IPG on each side was connected to two leads by 60-cm lead extenders (Medtronic model 37087). The Summit RC+S IPG is a 16-channel device that, through the use of its application programming interface, allows researchers to record four bipolar time domain channels (250/500 Hz) or two channels at 1,000 Hz62,63. For all research functions, including configuring and initiating sensing and developing embedded or distributed adaptive DBS, investigators controlled the device by writing software in C# within the device API, accessed using a 'research development kit' (RDK; Medtronic model 4NR013) provided by the manufacturer. We wrote a software application to configure and initiate streaming data from two RC+S devices simultaneously (available at https://openmind-consortium.github.io).

STIMO-PARK clinical trial
This article describes the analysis of data collected from P1, the first and only participant enrolled in the STIMO-PARK study by February 2022. Recruitment was performed through referral from Neurology clinics in the consortium. P1 was a 61-year-old male at time of enrollment. He has been diagnosed with Parkinson's Disease at the age of 36 and implanted with DBS at the age of 44. He is currently in stage 3 of the Hoen-Yahr scale. He experiences fluctuations in his gait pattern and lower limb

symptoms typical of later stages of PD, including slowness, asymmetry, rigidity, small steps, flexed posture. Before being implanted with the EES system, during the 6-minute walk test P1 was able to cover 433 meters with DBS turned on and during his regular levodopa intake, and 224 meters with DBS turned off and with the last levodopa intake the evening before. His MDS-UPDRS motor examination scores (part III) in these two states were 20 and 47, respectively. He started to experience freezing-of-gait over the last decade, which greatly impacted his independence and quality of life. Before participation in the study, he reported 4 falls per day on average due to freezing-of-gait. Following the enrolment, we performed a CT scan of his torso and a structural MRI scan of his spine to generate a personalized anatomical model of his spine. Following the pre-surgical assessments, P1 was implanted with the spinal EES neurostimulation system. After the surgery, P1 was transferred to the neurosurgery ward for recovery. P1 then went back to the hotel for a one-week recovery period. After recovery, we successfully configured the EES protocols and sequences for P1 during the study configuration period.

Ethics oversight

PREDI-STIM clinical study
The study was approved by the Nord Ouest-IV Ethical Committee, France (2013- A00193-42) and was conducted in accordance with the Declaration of Helsinki (clinicaltrials.gov ID: NCT02360683).

Motor Network in Parkinson's Disease and Dystonia: Mechanisms of Therapy clinical trial
The study was approved by the University of California, San Francisco IRB and was conducted in accordance with the Declaration of Helsinki (clinicaltrials.gov ID: NCT03582891).

STIMO-PARK clinical trial
The study was approved by the Swiss ethical authorities (Swissethics protocol number 2021-0047) and is conducted following the Declaration of Helsinki (clinicaltrials.gov ID: NCT04956770).

Note that full information on the approval of the study protocol must also be provided in the manuscript.

Field-specific reporting

Please select the one below that is 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/documents/nr-reporting-summary-flat.pdf

Life sciences study design

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

Sample size

No power calculation was used to determine the sample size.
- Data from 9 non-human primates was used to characterize gait deficits developed by the MPTP-treated macaque model. This sample size is larger than most studies that study locomotor deficits in nonhuman primate models of PD.
- Data from 25 people with Parkinson's disease and 9 healthy age-matched controlled was used to characterize gait deficits of Parkinson's disease. This sample size is in line with most studies that study motor deficits in people with PD in a clinical settings, as this sample size is enough for statistical power, while ensuring feasibility and maximizing adherence (due to the difficulty of inviting patients of an advanced age to the hospital)
- Data from 5 rhesus macaques was used to count the dopaminergic fiber density in Caudate and Putamen after the use of our MPTP-treatment protocol. This sample size is larger than most studies that study histology in nonhuman primate models of PD.
- Data from 4 rhesus macaques was used to count dopaminergic cells in substantia nigra. This sample size is larger than most studies that study histology in nonhuman primate models of PD.
- Data from 4 rhesus macaques was used to evaluate the impact of the MPTP treatment on the spatiotemporal maps of spinal cord motor neuron activity. This sample size is larger than most studies that study locomotor deficits in nonhuman primate models of PD.
- Data from 3 rhesus macaques was used to characterize the spinal motor neuron activity evoked by epidural electrical stimulation of the lumbar spinal cord. This sample size is larger than most studies that study locomotor deficits in nonhuman primate models of PD.
- Data from 3 rhesus macaques was used to longitudinally quantify the accuracy of detecting gait events from the activity of motor cortical neural ensembles after the MPTP treatment. This sample size is larger than most studies that study neural correlates of locomotor deficits in nonhuman primate models of PD.
- Data from two people with Parkinson's disease was used to quantify the accuracy of detecting gait events from the epicortical brain signals collected over the motor cortex. This sample size is in line with studies that report on epicortical neural correlates of locomotor deficits in people with PD.
- Data from 3 macaques was used to evaluate the efficacy of spinal cord neuroprosthesis to alleviate parkinsonian locomotor deficits after the MPTP treatment. This sample size is larger than most studies that report on the efficacy of a neuroprosthesis in nonhuman primates.
- Data from 3 rhesus macaques was used to quantify the accuracy of detecting gait events from the activity of motor cortical neural ensembles after the MPTP treatment during the use of spinal cord neuroprosthesis.
- Data from 3 rhesus macaques was used to characterize the motor responses to electrical epidural stimulation of the lumbar spinal cord at different frequencies. This sample size is larger than most studies that report the efficacy of a neuroprosthesis in nonhuman primates.
- Data from 2 macaques was used to demonstrate that lack of synchrony between the spinal cord stimulation and the motor intention causes the loss of efficacy of the spinal cord neuroprosthesis in alleviating parkinsonian locomotor impairments. This sample size is in line with most studies that report on the efficacy of a neuroprosthesis in nonhuman primates.
- Data from 1 macaque was used to evaluate the efficacy of spinal cord neuroprosthesis to alleviate parkinsonian locomotor impairments synergistically with the deep brain stimulation of the substantia nigra after the MPTP treatment. This sample size is in line with studies that report on the efficacy of a neuroprosthesis in nonhuman primates.
- Data from one person with Parkinson's disease was used to evaluate the efficacy of spinal cord neuroprosthesis to alleviate parkinsonian

	locomotor deficits synergistically with the deep brain stimulation of the substantia nigra and the levedopa treatment. This N=1 sample size corresponds to a feasibility case study and is in line with studies that report on the use of neuroprosthesis in people with neurological disorders.
Data exclusions	None.
Replication	The analysis of kinematic, electromyography and neurophisiological datasets of non-human primates was performed on multiple sessions, each recorded on a different day. Detailed list is provided in Supplementary Table 2. Replication numbers for analysis of human data are provided in detail in figure captions.
Randomization	Different trials during the non-human primate experimental sessions and trial sets during the P1 sessions were randomly interleaved. PREDI-STIM data and data from P2 and P3 were collected in only one conditions, therefore randomization was not applicable.
Blinding	The investigators operating the stimulation could not blinded to allocation during experiments and outcome assessment. However: 1) In NHP: Experienced technicians working at the non-human primate facility and not part of the study were blinded during their assessments of PD scores. They were unaware of the MPTP administration protocol or any of the details related to our experiments. 2) In P1: all evaluations from physiotherapists and clinicians were performed blinded to the therapy being delivered. All data analyses, except for the semi-automatic kinematic reconstruction in the Simi Motion software, Vicon software and marking of gait events from video recordings were performed "blindly" using automatic computer routines. 3) In PREDI-STIM: data were collected in only one conditions, therefore blinding was not applicable. 4) In Motor Network in Parkinson's Disease and Dystonia: Mechanisms of Therapy clinical trial: data were collected in only one conditions, therefore blinding was not applicable.

Reporting for specific materials, systems and methods

We require information from authors about some types of materials, experimental systems and methods used in many studies. Here, indicate whether each material, system or method listed is relevant to your study. If you are not sure if a list item applies to your research, read the appropriate section before selecting a response.

Materials & experimental systems

n/a	Involved in the study
☐	☒ Antibodies
☒	☐ Eukaryotic cell lines
☒	☐ Palaeontology and archaeology
☐	☒ Animals and other organisms
☐	☒ Clinical data
☒	☐ Dual use research of concern

Methods

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

Antibodies

Antibodies used	Tyrosine hydroxylase (TH) immunochemistry was performed using mouse anti-TH primary antibody (1:1000; clone LNC1; catalog MAB318, Millipore/Chemicon International, Technology, Billerica, MA, USA). Unbiased stereological counting of nigral THON neurons as well as striatal optical density measurement were performed using Exploranova Mercator (Explora Nova, La Rochelle, France).
Validation	We used commercial antibodies. All of them were quality controlled by the manufacturer. They are extensively validated in the NHP as referenced already in the mansucript (refs 62-65) Merck website reports more than 85 papers reporting its use.

Animals and other research organisms

Policy information about studies involving animals; ARRIVE guidelines recommended for reporting animal research, and Sex and Gender in Research

Laboratory animals	Data from 10 rhesus macaques and one fascicularis macaque (aged 4-6 yo)
Wild animals	None.
Reporting on sex	All the animals were males.
Field-collected samples	No field collected samples were used in the study
Ethics oversight	Experiments were approved by the Institutional Animal Care and Use Committee of Bordeaux (CE50, France) under the license number 50120102-A and performed in accordance with the European Union directive of 22 September 2010 (2010/63/EU) on the protection of animals used for scientific purposes in an AAALAC-accredited facility.

Note that full information on the approval of the study protocol must also be provided in the manuscript.

Clinical data

Policy information about clinical studies

All manuscripts should comply with the ICMJE guidelines for publication of clinical research and a completed CONSORT checklist must be included with all submissions.

Clinical trial registration	PREDI-STIM clinical study: clinicaltrials.gov ID NCT02360683 Motor Network in Parkinson's Disease and Dystonia: Mechanisms of Therapy clinical trial: clinicaltrials.gov ID NCT03582891 STIMO-PARK clinical trial: clinicaltrials.gov ID NCT04956770
Study protocol	PREDI-STIM clinical study: clinicaltrials.gov/ct2/show/NCT02360683 Motor Network in Parkinson's Disease and Dystonia: Mechanisms of Therapy clinical trial: clinicaltrials.gov/ct2/show/NCT03582891 STIMO-PARK clinical trial: clinicaltrials.gov/ct2/show/NCT04956770
Data collection	PREDI-STIM clinical study Patient recruitment and data collection took place between Sept 2015 and January 2019 at the Neurology Dpt of the Bordeaux University Hospital. We recorded whole-body kinematics using a Vicon motion-capture system (Vicon, Oxford, UK). We attached 34 reflective markers (26 on the legs, arms and trunk, and 8 on the head and wrists) on the surface of the skin of the participants to cover all key body joints (foot, ankle, knee, hip, shoulder, elbow, hand, neck and head, as well as spinal vertebrae T10 and C7). Motor Network in Parkinson's Disease and Dystonia: Mechanisms of Therapy clinical trial The period of recruitment and data collection for the two patients were from June 2019 – December 2019. The data were collected at the Human Performance Center at Mission Bay Campus at the University of California San Francisco. Data was collected from two people with Parkinson's disease that were enrolled in the clinical trial. They were recruited from a population referred for implantation of deep brain stimulators for PD. Before recruitment, they were evaluated by a movement disorders neurologist and met diagnostic criteria for PD and by a neuropsychologist to exclude major cognitive impairment or untreated mood disorder. Inclusion criteria included motor fluctuations with prominent rigidity and bradykinesia in the off-medication state, baseline off-medication MDS-UPDRS-III scores between 20 and 80, greater than 30% improvement in MDS-UPDRS-III on medication than off of medication and absence of significant cognitive impairment (score of 20 or above on the Montreal Cognitive Assessment). The full IDE application (G180097) and study protocol have been shared with other researchers via the Open Mind initiative (https://openmind-consortium.github.io). After enrollment, participants underwent bilateral placement of cylindrical quadripolar deep brain stimulator leads into the STN (Medtronic model 3389; 1.5-mm contact length and 2.0-mm intercontact spacing), bilateral placement of quadripolar cortical paddles into the subdural space over the cortical area that included the motor cortex (Medtronic model 0913025; 4-mm contact diameter and 10-mm intercontact spacing) and bilateral placement of investigational sensing IPGs in a pocket over the pectoralis muscle (Medtronic Summit RC+S model B35300R). The IPG on each side was connected to two leads by 60-cm lead extenders (Medtronic model 37087). The Summit RC+S IPG is a 16-channel device that, through the use of its application programming interface, allows researchers to record four bipolar time domain channels (250/500 Hz) or two channels at 1,000 Hz62,63. For all research functions, including configuring and initiating sensing and developing embedded or distributed adaptive DBS, investigators controlled the device by writing software in C# within the device API, accessed using a 'research development kit' (RDK; Medtronic model 4NR013) provided by the manufacturer. We wrote a software application to configure and initiate streaming data from two RC+S devices simultaneously (available at https://openmind-consortium.github.io). We have analysed recordings collected with P2 and P3 during one session of overground walking in a corridor, and with P2 during one session of walking on a treadmill. In those sessions, the participants were on their regular levodopa therapy and their DBS was kept off. Cortical field potentials were sampled at 500 Hz. We simultaneously recorded video using a camera and full body kinematics using a set of IMU sensors distributed across major anatomical landmarks. STIMO-PARK clinical trial Recruitment and data analyses ranged between August 2021 and Dec 2022. Data collected from P1, the first and only participant, was enrolled in the study by October 2021. He was a 61-year-old male at time of enrollment. He has been diagnosed with Parkinson's Disease at the age of 36 and implanted with DBS at the age of 44. He is currently in stage 3 of the Hoen-Yahr scale. He experiences fluctuations in his gait pattern and lower limb symptoms typical of later stages of PD, including slowness, asymmetry, rigidity, small steps, flexed posture. Before being implanted with the EES system, during the 6-minute walk test P1 was able to cover 433 meters with DBS turned on and during his regular levodopa intake, and 224 meters with DBS turned off and with the last levodopa intake the evening before. His MDS-UPDRS motor examination scores (part III) in these two states were 20 and 47, respectively. He started to experience freezing-of-gait over the last decade, which greatly impacted his independence and quality of life. Before participation in the study, he reported 4 falls per day on average due to freezing-of-gait. Following the enrolment, we performed a CT scan of his torso and a structural MRI scan of his spine to generate a personalized anatomical model of his spine. Following the pre-surgical assessments, P1 was implanted with the spinal EES neurostimulation system. After the surgery, P1 was transferred to the neurosurgery ward for recovery. P1 then went back to the hotel for a one-week recovery period. After recovery, the study protocol continued with a 1-month period for configuration of EES protocols and sequences, and a 3-month period of physiotherapist-assisted rehabilitation during 1–3-hour sessions taking place 2 to 3 times per week. The rehabilitation program is personalized based on the participants' needs and improvements. We collected data from P1 through the entire duration of the study protocol.
Outcomes	PREDI-STIM clinical study Primary Outcome Measures : - Improve of quality of life on PDQ39>20% [Time Frame: 1 year] Secondary Outcome Measures : - Percentage of motor score MDS-UPDRS III improve under stimulation [Time Frame: 1 year] - Socio-familial evolution (institutionalization) [Time Frame: 1, 3 and 5 years] - Clinical Global Impression of Patient by 7-point scale with the CGI-scale [Time Frame: 1, 3 and 5 years]

- Clinical Global Impression of doctor by 7-point scale with the CGI-scale [Time Frame: 1, 3 and 5 years]
- Death [Time Frame: 1, 3 and 5 years]
- Cognitive function with a neuropsychological examination with Mattis scale, Wisconsin Card Sorting test, Stroop test, , verbal episodic memory test with 16 items, phonemic and semantic verbal fluency, Boston naming test (15 items), clock drawing and Benton line orientation task [Time Frame: 1, 3 and 5 years]
- Behavior test [Time Frame: 1, 3 and 5 years]
- ECMP scale of Ardouin 2009, Hamilton depression scale, Anxiety Hamilton scale, Lille Apathy Rating Scale, QUIP questionnaire, Billieux Impulsivity Scale, Hallucination questionnaire of Miami
- Motor response rates to Levodopa with the difference of the motor handicap measured by MDS UPDRS part III before and after an acute L-dopa challenge [Time Frame: 1, 3 and 5 years]
- Non-motor functions evaluated by a numerical evaluation scale [Time Frame: screening and at 1, 3 and 5 years]

Motor Network in Parkinson's Disease and Dystonia: Mechanisms of Therapy clinical trial
Primary Outcome Measures :
- Duration of 'on' stimulation time without dyskinesia from motor diaries in adaptive compared to standard open loop stimulation. (Parkinson's disease patients) [Time Frame: Comparison will use data from the testing of open and closed-loop stimulation during chronic adaptive DBS testing at home.]
- Karolinska Sleepiness Scale [Time Frame: Through study completion, up to 4 years]
- Psychomotor vigilance task (PVT) [Time Frame: Through study completion, up to 4 years]
- Positive and Negative Affect Schedule (PANAS-SF) [Time Frame: Through study completion, up to 4 years]

Secondary Outcome Measures :
- The Unified Parkinsons Disease Rating Scale (UPDRS) III scores off of medication in adaptive compared to standard open-loop stimulation. [Time Frame: Comparison will use data from the testing of open and closed-loop stimulation during chronic adaptive DBS testing at home.]
- Schwab England scale in adaptive compared to standard open loop stimulation. [Time Frame: Comparison will use data from the testing of open and closed-loop stimulation during chronic adaptive DBS testing at home.]
- Hoehn and Yahr Staging in the medication 'on' state in adaptive compared to standard open loop stimulation.
[Time Frame: Comparison will use data from the testing of open and closed-loop stimulation during chronic adaptive DBS testing at home.]
- The patient' quality of life report (PDQ-39) in adaptive compared to standard open loop stimulation. The PDQ39 yields a score between 0 to 100, where a higher score indicates more health problems. [Time Frame: Comparison will use data from the testing of open and closed-loop stimulation during chronic adaptive DBS testing at home.]
- Patient's Global Impression of Change (PGIC) in adaptive compared to standard open loop stimulation. [Time Frame: Comparison will use data from the testing of open and closed-loop stimulation during chronic adaptive DBS testing at home.]
- Total Electric Energy Delivered (TEED) by the pulse generator in adaptive compared to standard open loop stimulation.
[Time Frame: Comparison will use data from the testing of open and closed-loop stimulation during chronic adaptive DBS testing at home.]
- Resting state EEG Recording [Time Frame: Through study completion, up to 4 years]

STIMO-PARK clinical trial
Primary Outcome Measures :
- Occurence of all SAEs and AEs deemed or related to study procedure or to the study investigational system [Time Frame: Through study completion, an average of 6 months]

Secondary Outcome Measures :
- EMG measurements of muscle recruitment in response to stimulation of increasing amplitudes for different contact configurations [Time Frame: At baseline and during the 5-month TESS-supported rehabilitation phase]
- Maximum voluntary contraction (MVC) of single joints [Time Frame: At baseline and during the 5-month TESS-supported rehabilitation phase]
- Muscle Fatigue Test [Time Frame: At baseline and during the 5-month TESS-supported rehabilitation phase]
- 10-meter walk test [Time Frame: At baseline and during the 5-month TESS-supported rehabilitation phase]
- 6 minute walk test [Time Frame: At baseline and during the 5-month TESS-supported rehabilitation phase]
- Timed up and Go test and its cognitive version, as custom-made FOG circuit [Time Frame: At baseline and during the 5-month TESS-supported rehabilitation phase]
- Kinematic analysis [Time Frame: At baseline and during the 5-month TESS-supported rehabilitation phase]
- Mini Balance Evaluation Systems Test (mini-BESTest) [Time Frame: At baseline and during the 5-month TESS-supported rehabilitation phase]
- Movement Disorders Society Unified Parkinson's Disease Rating Scale (MDS-UPDRS) [Time Frame: At baseline and during the 5-month TESS-supported rehabilitation phase]

Magnetic resonance imaging

Experimental design

Design type	Participant P1 was positioned supine with arms at their side.
Design specifications	Resting state structural MRI.
Behavioral performance measures	The participant did not perform any behavioral experiment while being scanned (no fMRI was acquired on the human participant). The MRI scan was an anatomical structural volume image with participant at rest.

Acquisition

Imaging type(s)	Structural MRI
Field strength	1.5T
Sequence & imaging parameters	2D sagittal T2-weighted turbo spin-echo
Area of acquisition	Thoracolumbar spine

Diffusion MRI ☐ Used ☒ Not used

Preprocessing

Preprocessing software	MRI image acquisition did not require a preprocessing software. No preprocessing software was used.
Normalization	MRI image acquisition did not require normalization. Normalization was not used.
Normalization template	MRI image acquisition did not require a normalization template. Normalization template was not used.
Noise and artifact removal	MRI image acquisition did not require neither noise nor artifact removal. Neither noise nor artifact removal was used.
Volume censoring	MRI image acquisition did not require volume censoring. Volume censoring was not used.

Statistical modeling & inference

Model type and settings	We did not perform any functional MRI experiments. Therefore, neither statistical modeling nor inference was carried out.
Effect(s) tested	We did not perform any functional MRI experiments. Therefore, neither statistical modeling nor inference was carried out.

Specify type of analysis: ☐ Whole brain ☐ ROI-based ☐ Both

Statistic type for inference (See Eklund et al. 2016)	We did not perform any functional MRI experiments. Therefore, neither statistical modeling nor inference was carried out.
Correction	We did not perform any functional MRI experiments. Therefore, neither statistical modeling nor inference was carried out.

Models & analysis

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