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Corresponding author(s):	DBPR NPJPARKD-00537R
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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 our <u>Editorial Policies</u> and the <u>Editorial Policy Checklist</u>.

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For all statistical analyses, confirm that the following items are present in the figure legend, table legend, main text, or Methods section.					
n/a	a Confirmed				
	The exact	sample size (n) for each experimental group/condition, given as a discrete number and unit of measurement			
	A stateme	ent 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. <i>F</i> , <i>t</i> , <i>r</i>) with confidence intervals, effect sizes, degrees of freedom and <i>P</i> value noted Give <i>P</i> values as exact values whenever suitable.				
\boxtimes	For Bayes	ian analysis, information on the choice of priors and Markov chain Monte Carlo settings			
\times	For hierar	chical and complex designs, identification of the appropriate level for tests and full reporting of outcomes			
\times	Estimates	of effect sizes (e.g. Cohen's d , Pearson's r), indicating how they were calculated			
Our web collection on <u>statistics for biologists</u> contains articles on many of the points above.					
Software and code					
Policy information about <u>availability of computer code</u>					
Da	ata collection	NO SOFTWARE WAS USED			
Da	ata analysis	SPSS VERSION 20			
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 Research guidelines for submitting code & software for further information.					

Data

Policy information about <u>availability of data</u>

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

The experimental data are available from the corresponding author, given reasonable requests.

· ·	ecific reporting ne 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 <u>nature.com/documents/nr-reporting-summary-flat.pdf</u>		
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All studies must di	sclose on these points even when the disclosure is negative. A formal sample size calculation was not performed because we had no prior information regarding the expected treatment effect (and	
All studies must di Sample size	A formal sample size calculation was not performed because we had no prior information regarding the expected treatment effect (and variability) of one month of treatment with nVNS. We recruited patients over a 36-month period.	

Randomization

The devices were dispensed in a randomised and blinded manner. Simple randomisation was performed using a computer-generated list of random numbers to assign either nVNS or sham devices in addition to standard treatment in a 1:1 ratio (Random Allocation version 2.0). Other than the device serial number, nVNS and sham devices were indistinguishable. A complete list of serial numbers and the stimulation mode of each device (sham or active and its serial number) was provided to the unblinded trial oversight committee (not involved in patient recruitment or assessment) by the commercial sponsor (electroCore, Inc.). Investigators, site coordinators and participants were blind to the allocation of devices until the trial had been completed.

Blinding

Investigators, site coordinators and participants were blind to the allocation of devices until the trial had been completed.

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		Methods	
n/a	Involved in the study	n/a	Involved in the study
\boxtimes	Antibodies	\boxtimes	ChIP-seq
\boxtimes	Eukaryotic cell lines	\boxtimes	Flow cytometry
\boxtimes	Palaeontology and archaeology	\boxtimes	MRI-based neuroimaging
\boxtimes	Animals and other organisms		
	Human research participants		
	☑ Clinical data		
\boxtimes	Dual use research of concern		

Human research participants

Policy information about studies involving human research participants

Population characteristics

PD patients of both sexes with freezing of gait, aged 30-80 years, were recruited consecutively from the movement disorders outpatient clinic at a tertiary care hospital in Eastern India. Only patients who could walk independently and continuously for at least 30 metres without support, and with the ability to turn 180° on the spot, were included in the study. Patients were diagnosed according to UK Brain Bank Criteria and those with baseline scores ≥2 on both items 2.13 and 3.11 (specific to freezing of gait on the MDS-UPDRS rating scale) were included. We were careful to exclude patients with early signs of atypical Parkinsonism e.g. supranuclear gaze palsy.

Patients with significant visual impairment or coexisting local or systemic diseases (e.g. osteoarthritis or other neurological conditions) likely to affect gait were excluded from our study. Patients who underwent deep brain stimulation surgery or those with an implanted cardiac pacemaker were also excluded to ensure the safe use of nVNS, as were patients with metallic implants near the stimulation site (e.g. fusion of cervical vertebrae). Finally, patients with known or suspected cardiovascular disease, uncontrolled hypertension or recent myocardial infarction were also excluded from the study.

Recruitment

PD patients were recruited consecutively from the movement disorders outpatient clinic at a tertiary care hospital in Eastern India. Only patients who could walk independently and continuously for at least 30 metres without support, and with the ability to turn 180° on the spot, were included in the study.

Ethics oversight

Protocols and procedures were approved by the Institutional Institute of Neurosciences Kolkata Ethics Committee (reference number I-NK/EComm/44/2016), dated 2nd April 2016

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

Clinical data

Policy information about <u>clinical studies</u>

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

ISRCTN14797144.

Study protocol

International Standard Registered Clinical/soCial sTudy Number

Data collection

 $PD\ patients\ were\ recruited\ from\ the\ movement\ disorders\ outpatient\ clinic\ of\ Institute\ of\ Neurosciences\ Kolkata\ India.$

Recruitment start date

01/11/2016

Recruitment end date

31/12/2019

Outcomes

Primary outcome measure

Measured at baseline and one month

- 1. Two dimensional spatio-temporal gait parameters derived from GAITRite walkway
- 2. Motor function using UPDRS III scrore
- 3. Extent of freezing of gait estimated from post hoc video analysis and FOGQ score

Secondary outcome measures

Measured at baseline and one month

- 1. Cognitive parameters assessed by MMSE, Mattis DRS scores
- 2. Severity of REM sleep behavior disorder from REM sleep behavior disorder screening questionnaire RBDSQ $\,$
- 3. Fear of fall by Fall Efficacy Scale
- 4. Peripheral biomarkers from serum sample (TNF- Alpha, IL-6, IL 10, reduced glutathione,

superoxide dismutase)