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Supplementary information

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Circuit response to neuromodulation characterized with simultaneous deep brain stimulation and precision neuroimaging in humans

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Supplementary Information

Supplementary Table 1. Demographics and clinical characteristics of patients

Patient ID	Age (yrs)	Sex	Edu (yrs)	MMSE	H-Y (yrs)	PD duration (yrs)	UPDRS-III	PDQ-39
DBS01	40	Male	9	26	3	8	22	75
DBS02	53	Male	12	25	3	13	34	34
DBS03	67	Male	12	27	3	8	21	78
DBS04	51	Male	12	27	4	20	20	40
DBS05	65	Male	12	28	3	6	21	14
DBS06	60	Female	9	28	3	7	29	71
DBS07	46	Male	15	29	4	7	47	60
DBS08	59	Male	6	28	4	10	40	51
DBS09	61	Female	6	28	4	8	29	51
DBS10	51	Male	15	28	1.5	6	8	75
DBS11	47	Female	9	28	5	12	38	68
DBS12	56	Female	15	26	4	15	51	61
DBS13	61	Female	9	30	4	8	41	127
DBS14	51	Male	12	30	4	8	54	39
Mean	54.9	5F/9M	10.9	27.7	3.5	9.7	32.3	60.3
Std	7.7		3.0	1.4	0.8	4.0	13.3	26.7

Edu: Education; H-Y, Hoehn and Yahr Staging Scale; UPDRS-III, Unified Parkinson's Disease Rating Scale Part 3; PDQ-39, The 39-item Parkinson's disease questionnaire;

Supplementary Table 2. Demographics of healthy controls

Control ID	Age (yrs)	Sex
SUB01	48	Female
SUB02	68	Male
SUB03	66	Male
SUB04	55	Male
SUB05	59	Male
SUB06	55	Male
SUB07	54	Female
SUB08	45	Male
SUB09	61	Male
SUB10	60	Female
SUB11	50	Male
SUB12	46	Female
SUB13	65	Male
SUB14	63	Female
SUB15	60	Female
SUB16	47	Male
SUB17	55	Male
SUB18	49	Female
SUB19	48	Female
SUB20	57	Male
SUB21	60	Female
SUB22	66	Female
SUB23	55	Female
SUB24	61	Female
SUB25	56	Male
SUB26	58	Female
SUB27	50	Female
SUB28	49	Male
Mean	55.9	14F/14M
Std	6.6	

*SUB25 was excluded in analyses due to incomplete imaging data.

Supplementary Table 3. LME results of therapeutic effects (UPDRS-III sub-scores)

ON vs OFF: lmer(UPDRS-III Score ~ Time * Stimulation + (1 | ID))				
Tremor	DOF	DOF.res	*F*	*P*
Time	3	164.59	1.4374	0.2338
Stimulation	1	163.90	32.5489	5.308e-08 ***
Time : Stimulation	3	163.90	0.4841	0.6938

Bradykinesia	DOF	DOF.res	F	P
Time	3	164.54	10.2523	3.171e-06 ***
Stimulation	1	163.87	88.5350	< 2.2e-16 ***
Time : Stimulation	3	163.87	1.4785	0.2223

Posture instability	DOF	DOF.res	F	P
Time	3	166.42	5.6657	0.001016 **
Stimulation	1	163.50	55.8700	4.446e-12 ***
Time : Stimulation	3	163.50	0.9354	0.425030

Gait difficulty	DOF	DOF.res	F	P
Time	3	165.28	6.2807	0.000462 ***
Stimulation	1	164.11	42.9494	6.943e-10 ***
Time : Stimulation	3	164.11	0.4909	0.689046

PIGD symptom	DOF	DOF.res	F	P
Time	3	166.01	6.0426	0.000626 ***
Stimulation	1	163.89	57.9723	1.995e-12 ***
Time : Stimulation	3	163.89	0.8218	0.483599

Rigidity	DOF	DOF.res	F	P
Time	3	164.32	9.2491	1.094e-05 ***
Stimulation	1	163.99	95.4536	< 2.2e-16 ***
Time : Stimulation	3	163.99	1.6225	0.1862

DOF, Degrees of freedom; DOF.res, residual degrees of freedom; F, F-statistic; P: P-value. ***$P < 0.001$, **$P < 0.01$, *$P < 0.05$.

Supplementary Table 4. LME results of therapeutic effects (UPDRS-III total score)

lmer(UPDRS-III Score ~ Time * Stimulation + (1 | ID))					
ON vs OFF	DOF	DOF.res	*F*	*P*	
Time	3	180.29	6.0706	0.0005855 ***	
Stimulation	1	179.13	134.9311	< 2.2e-16 ***	
Time : Stimulation	3	179.13	1.3507	0.2595064	
Post-hoc contrasts	B	SE	DOF	*t*	*P*
Time = 1m	-16.0	3.03	179	-5.261	<.0001 ***
Time = 3m	-14.0	3.03	179	-4.602	<.0001 ***
Time = 6m	-21.3	3.16	179	-6.760	<.0001 ***
Time = 12m	-20.7	3.16	179	-6.545	<.0001 ***

HFS vs OFF	DOF	DOF.res	*F*	*P*	
Time	3	80.559	3.4090	0.02142 *	
Stimulation	1	79.230	113.3319	< 2e-16 ***	
Time : Stimulation	3	79.230	0.8194	0.48695	
Post-hoc contrasts	B	SE	DOF	*t*	*P*
Time = 1m	-18.8	4.08	79.1	-4.610	<.0001 ***
Time = 3m	-19.0	4.08	79.1	-4.662	<.0001 ***
Time = 6m	-25.9	4.25	79.1	-6.088	<.0001 ***
Time = 12m	-25.0	4.25	79.1	-5.882	<.0001 ***

VFS vs OFF	DOF	DOF.res	*F*	*P*	
Time	3	80.205	3.4909	0.0194 *	
Stimulation	1	79.134	66.7562	4.014e-12 ***	
Time : Stimulation	3	79.134	0.8460	0.4728	
Post-hoc contrasts	B	SE	DOF	*t*	*P*
Time = 1m	-15.1	4.02	79	-3.752	0.0003 ***
Time = 3m	-12.3	4.02	79	-3.059	0.0030 **
Time = 6m	-20.5	4.19	79	-4.904	<.0001 ***
Time = 12m	-19.2	4.19	79	-4.576	<.0001 ***

LFS vs OFF	DOF	DOF.res	*F*	*P*	
Time	3	80.111	3.5503	0.01805 *	
Stimulation	1	79.151	54.7957	1.247e-10 ***	
Time : Stimulation	3	79.151	0.7346	0.53447	
Post-hoc contrasts	B	SE	DOF	*t*	*P*
Time = 1m	-14.0	3.97	79	-3.518	0.0007 ***
Time = 3m	-10.5	3.97	79	-2.656	0.0096 **

Time = 6m	-17.6	4.13	79	-4.267	0.0001 **
Time = 12m	-17.8	4.13	79	-4.318	<.0001 ***

HFS vs VFS	DOF	DOF.res	*F*	*P*	
Time	3	80.107	4.1431	0.0087832 **	
Stimulation	1	79.243	15.8133	0.0001535 ***	
Time : Stimulation	3	79.243	0.2223	0.8806384	
Post-hoc contrasts	B	SE	DOF	*t*	*P*
Time = 1m	-3.73	2.66	79	-1.400	0.1654
Time = 3m	-6.73	2.66	79	-2.526	0.0135 *
Time = 6m	-5.33	2.77	79	-1.923	0.0581
Time = 12m	-5.83	2.77	79	-2.103	0.0386 *

HFS vs LFS	DOF	DOF.res	*F*	*P*	
Time	3	80.331	2.7950	0.04551 *	
Stimulation	1	79.302	20.7313	1.884e-05 ***	
Time : Stimulation	3	79.302	0.2835	0.83716	
Post-hoc contrasts	B	SE	DOF	*t*	*P*
Time = 1m	-4.87	3.10	79	-1.571	0.1202
Time = 3m	-8.50	3.10	79	-2.745	0.0075 **
Time = 6m	-8.25	3.22	79	-2.560	0.0124 *
Time = 12m	-7.17	3.22	79	-2.223	0.0290 *

VFS vs LFS	DOF	DOF.res	*F*	*P*
Time	3	80.049	3.1334	0.03006 *
Stimulation	1	79.218	1.2528	0.26641
Time : Stimulation	3	79.218	0.0610	0.98015

DOF, Degrees of freedom; DOF.res, residual degrees of freedom; F, F-statistic; P: P-value; B, estimate; SE, standard error, t, t-statistic. ***$P < 0.001$, **$P < 0.01$, *$P < 0.05$.

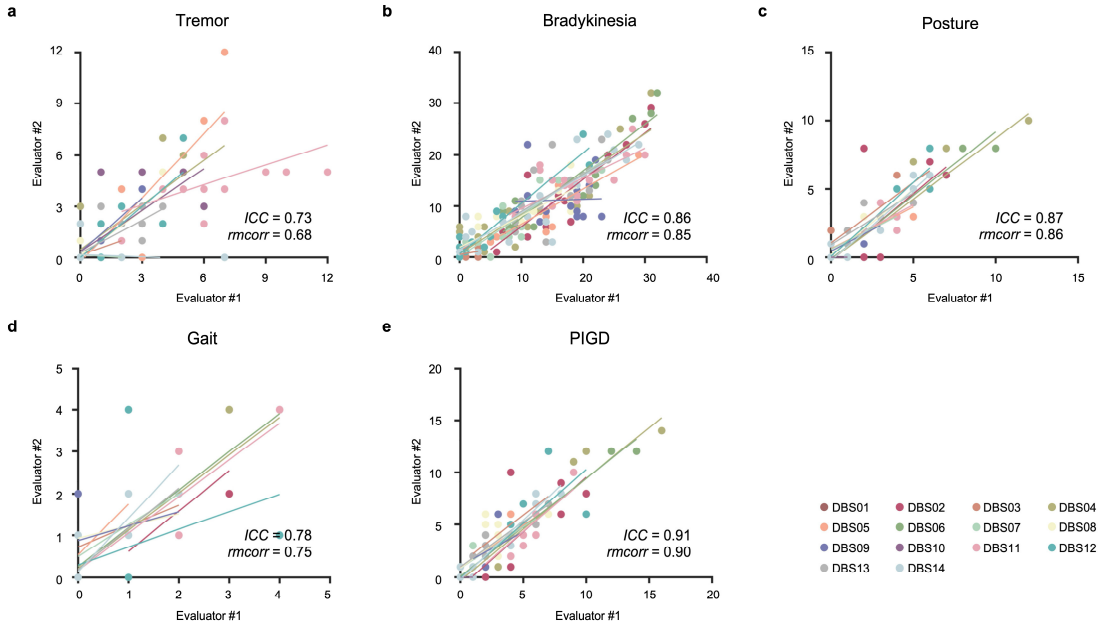
Supplementary Table 5. The peak coordinates in MNI space of DBS-induced BOLD signal change.

	GPi		Thalamus		Putamen		M1	
	Increased BOLD signal		Increased BOLD signal		Decreased BOLD signal		Decreased BOLD signal	
Patient ID	Left	Right	Left	Right	Left	Right	Left	Right
DBS01	(-15, -2, 1)	(18, -4, 3)	(-14, -4, 8)	(13, -3, 7)	(-27, 2, 15)	(28, -16, 10)	(-34, -25, 67)	(2, -12, 63)
DBS02	(-21, -6, 1)	(16, -4, -1)	(-18, -10, 6)	(18, -10, 6)	(-32, -20, 1)	(22, 4, 13)	(-22, -21, 65)	(2, -20, 66)
DBS03	(-24, -8, 0)	(15, 0, 1)	(-12, -5, 15)	(15, -7, 2)	(-33, -11, 3)	(30, -10, -10)	(-22, -21, 66)	(22, -22, 64)
DBS04	(-22, -5, 1),	(14, -2, -1)	(-18, -10, 9)	(11, -2, 5)	(-32, -12, 6)	(28, -15, 4)	(-3, -17, 64)	(0, -18, 64)
DBS05	(-15, -2, 1)	(16, -4, -1)	(-12, -7, 4),	(15, -7, 2)	(-32, -11, 9)	(26, -10, 8)	(-3, -26, 67)	(27, -23, 63)
DBS06	(-19, -3, -2)	(14, -2, -1)	(-16, -17, 9)	(11, -3, 0)	(-25, -2, 15)	(25, -8, 7)	(-21, -24, 62)	(3, -17, 67)
DBS07	(-24, -8, -2)	(18, -6, -1)	(-12, -2, 10)	(15, -5, 6)	(-32, -9, 6)	(18, 15, -5)	(-29, -23, 63)	(23, -22, 67)
DBS08	(-24, -11, -1)	(20, -8, -1)	(-20, -17, 17)	(11, -17, 8)	(-25, -4, 15)	(28, -14, 7)	(-1, -21, 65)	(3, -20, 64)
DBS09	(-22, -3, -1)	(15, -2, -1)	(-14, -4, 8)	(11, -3, 0)	(-32, -13, 8)	(28, -11, 3)	(-16, -25, 67)	(22, -24, 62)
DBS10	(-11, 0, -5)	(16, -4, -1)	(-14, -4, 9)	(15, -7, 2)	(-25, -8, 13)	(31, -10, -10)	(-3, -19, 65)	(20, -25, 67)
DBS11	(-21, -3, -1)	(18, -4, 3)	(-12, -2, 8)	(14, -7, 7)	(-30, -5, 13)	(28, -16, 11)	(-2, -20, 62)	(3, -20, 62)
DBS12	(-22, -5, 1)	(18, -4, 3)	(-12, -2, 8)	(17, -9, 3)	(-32, -11, 9)	(33, -10, -8)	(-6, -13, 62)	(2, -13, 62)
DBS13	(-20, -1, 1)	(14, 0, 1)	(-12, -4, 4)	(11, -1, 4)	(-32, 1, -2)	(26, -10, 11)	(-23, -24, 62)	(21, -24, 63)
DBS14	(-24, -9, 0)	(16, -2, 1)	(-22, -18, 4)	(13, -3, 7)	(-34, -9, 3)	(26, -10, 11)	(-27, -22, 62)	(0, -21, 67)
Group	(-22, -5, 1)	(16, -4, -1)	(-14, -4, 8)	(15, -7, 2)	(-32, -10, 8)	(26, -10, 10)	(-21, -24, 67)	(1, -21, 65)

Supplementary Table 6. Target locations and stimulation parameters of STN-DBS

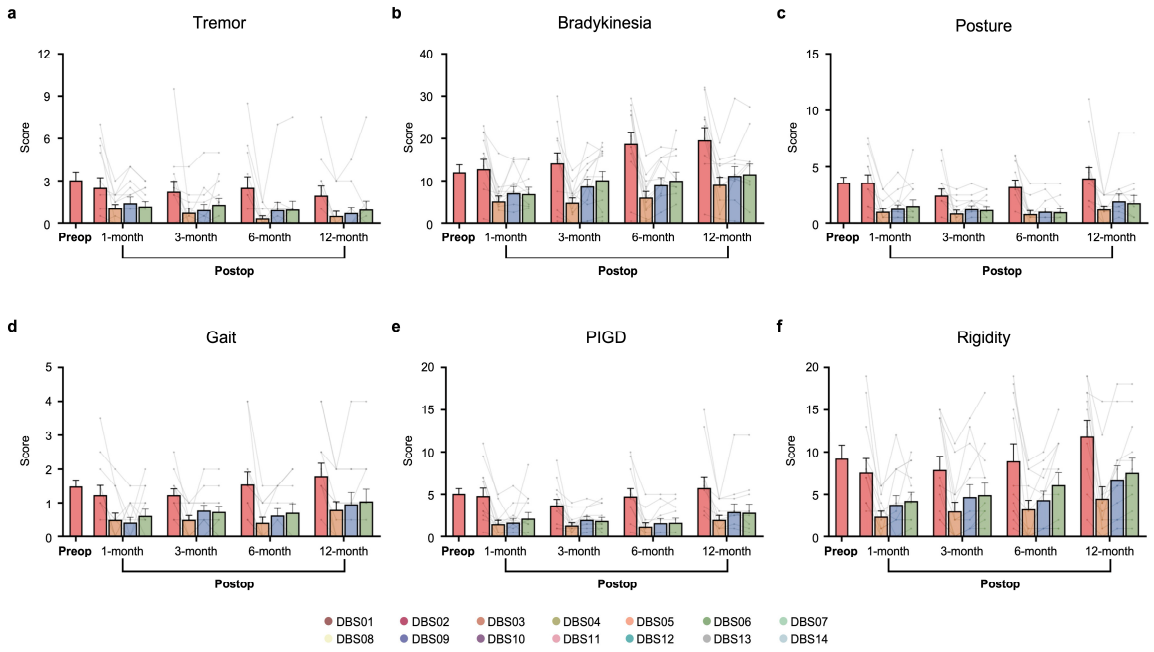
			Stimulation amplitudes (V)/pulse width (us) across post-surgical treatment visits							
	VTA centers MNI coordinates		1-month post-surgery		3-months post-surgery		6-months post-surgery		12-months post-surgery	
Patient ID	Left	Right	Left	Right	Left	Right	Left	Right	Left	Right
DBS01	-12 -12 -5	17 -12 -5	1.5/60	1.7/60	NA	NA	NA	NA	NA	NA
DBS02	-12 -14 -10	13 -13 -9	2.1/60	2.1/60	2.5/60	2.5/70	2.6/60	2.5/60	2.6/60	2.5/60
DBS03	-11 -14 -9	16 -14 -5	1.5/60	1.8/60	2.1/60	2.0/60	NA	NA	NA	NA
DBS04	-12 -15 -9	15 -11 -6	1.5/60	2.0/60	2.2/60	2.2/60	1.7/60	3.1/60	1.7/60	3.1/60
DBS05	-14 -10 -5	13 -11 -10	1.9/60	1.8/80	2.3/60	2.3/60	2.7/90	3.0/60	2.7/90	3.0/60
DBS06	-14 -10 -5	15 -10 -7	2.5/80	1.9/60	2.5/70	2.5/60	2.8/70	2.9/60	2.8/70	2.9/60
DBS07	-11 -13 -6	16 -13 -6	1.9/60	1.4/60	2.6/80	2.4/70	2.9/70	2.7/60	2.9/70	2.7/60
DBS08	-12 -18 -10	16 -14 -6	1.7/60	1.8/60	1.6/60	1.7/60	1.3/50	1.2/60	1.3/50	1.2/60
DBS09	-13 -12 -4	14 -13 -7	1.9/60	2.5/60	1.9/60	2.5/60	2.5/60	2.7/60	2.5/60	2.7/60
DBS10	-13 -14 -5	14 -15 -6	1.0/60	1.9/60	1.0/60	2.4/60	1.1/60	2.1/60	1.1/60	2.1/60
DBS11	-10 -18 -12	13 -15 -8	2.0/80	1.8/60	2.0/70	1.8/70	3.6/90	3.5/80	3.7/90	3.8/70
DBS12	-12 -17 -10	13 -16 -10	2.0/60	2.0/60	2.2/60	2.4/60	2.5/60	2.4/60	2.8/50	2.6/60
DBS13	-10 -14 -9	13 -16 -9	2.5/80	2.2/40	2.5/80	2.5/60	3.0/70	2.7/60	3.2/80	3.1/60
DBS14	-11 -15 -9	15 -14 -6	1.3/60	1.5/60	1.7/60	2.6/60	2.1/60	2.2/70	2.4/60	2.8/60
Mean	-11.9 -14 -7.7	14.5 -13.4 -7.1	1.8/64.3	1.9/60.0	2.1/64.6	2.3/62.3	2.4/66.7	2.6/62.5	2.5/66.7	2.7/60.8
Std			0.4/8.5	0.3/7.8	0.5/7.8	0.3/4.4	0.7/12.5	0.6/6.2	0.8/13.7	0.6/2.9

VTA: The volume of tissue activated

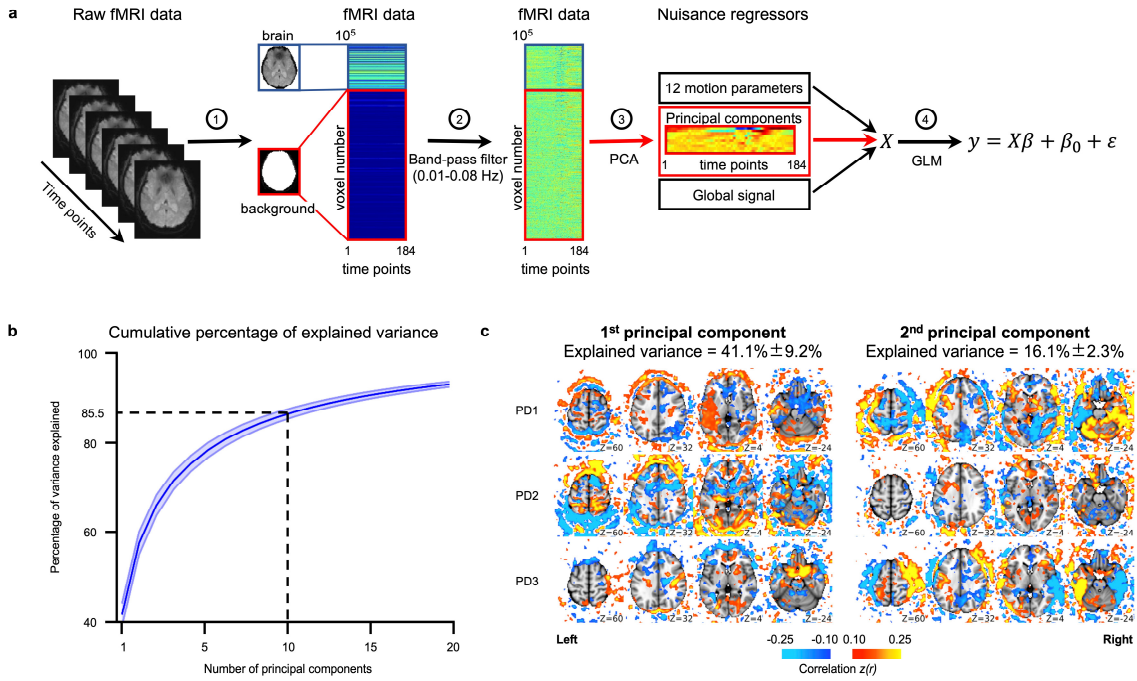


Supplementary Fig. 1. Inter-rater reliability for each symptom category of the UPDRS-III. Reproduction of Fig. 2a for the various UPDRS-III symptom categories. Scatter plots and linear fitting lines illustrate the inter-rater reliability for each UPDRS-III symptom category, except for rigidity since it was scored by a single neurologist. Patients (n = 14) are represented by different colors. Both ICC and *rmcorr* were calculated for tremor, bradykinesia, gait difficulty, posture instability, and PIGD scores.

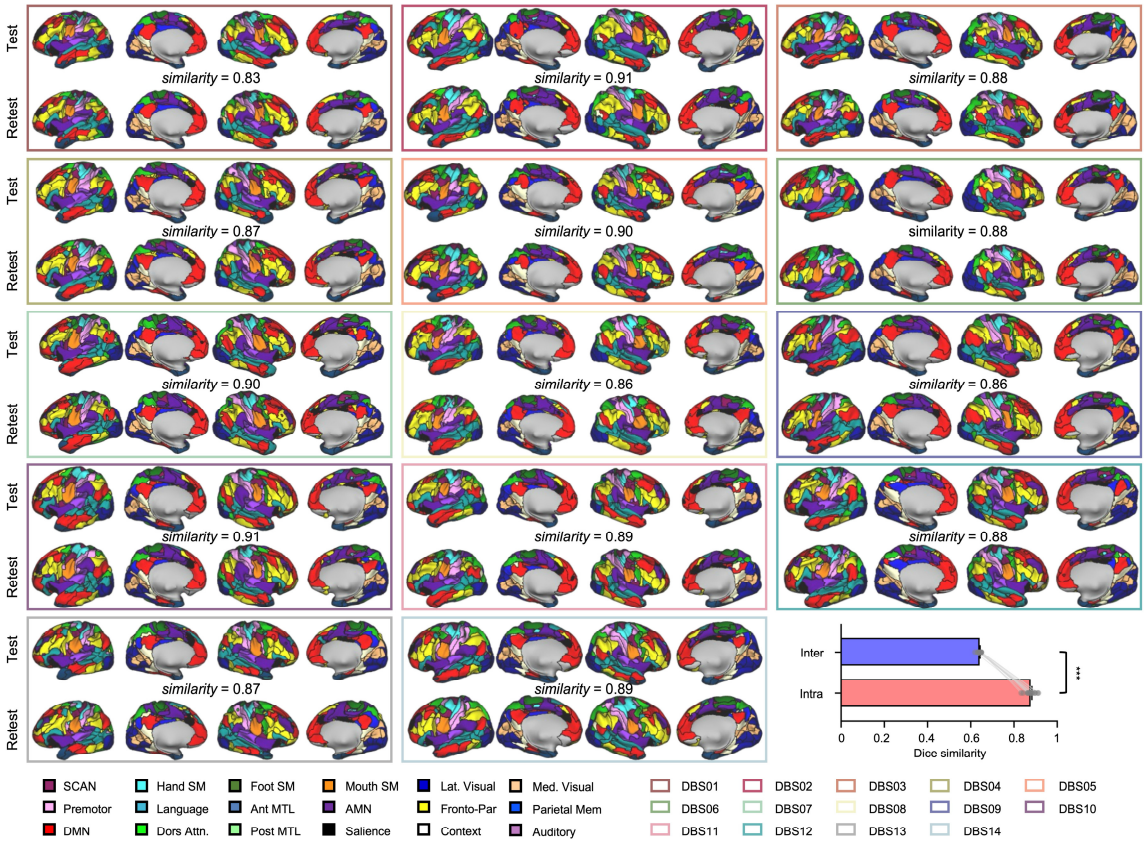
PIGD: postural instability/gait difficulty, UPDRS-III: Unified Parkinson's Disease Rating Scale.



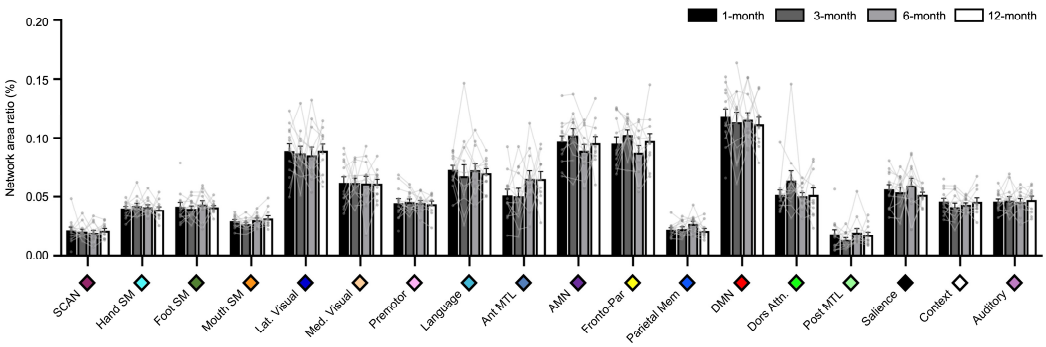
Supplementary Fig. 2. The therapeutic benefit of STN-DBS for each symptom category of the UPDRS-III. Reproduction of Fig. 2B of the article for the various UPDRS-III symptom categories. Bar graphs illustrate clinical outcomes for tremor, bradykinesia, posture instability, gait difficulty, PIGD symptom categories, and rigidity under no/HFS/LFS/VFS stimulation in patients (n = 14) with PD at all time points. Improvements were significant in all six motor symptom dimensions when DBS was ON compared to DBS OFF (see Supplementary Table 4 for statistics).



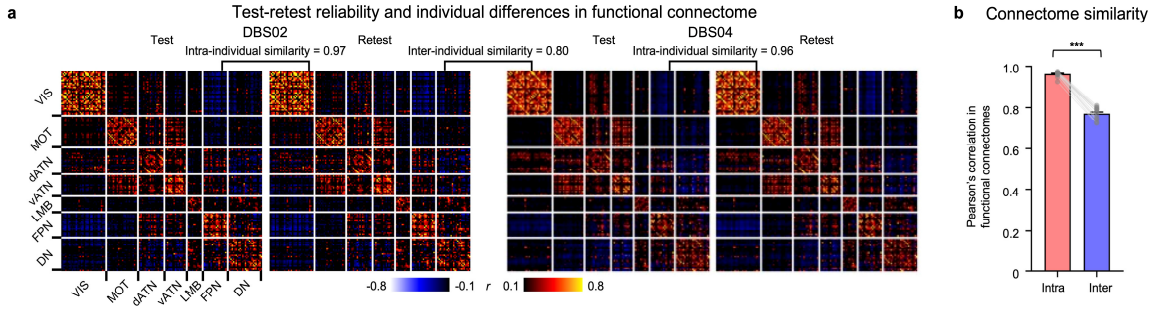
Supplementary Fig. 3. The bCompCor pipeline and background noise distribution. (a) A schematic representation of the four-step bCompCor pipeline used to extract and remove principal components of noise embedded within the background field of view (FOV) from functional images: 1. Identification of noise ROIs: Noise ROIs in the background FOV are indicated in white within the red box. The corresponding time series were displayed as a matrix (voxel numbers by time points) with scaled colors. 2. Bandpass temporal filtering: Time series were filtered in the range of 0.01–0.08 Hz. 3. Principal component analysis (PCA): PCA was performed on the time series within the noise ROI to identify principal components. 4. Noise removal: Identified noise components, along with other predefined confounds, are regressed out from functional data using general linear modeling (GLM). (b) The cumulative percentage of explained variance for the top principal components is presented. The top 10 components accounted for 85.5% of the cumulative variance in the background FOV. (c) Correlation maps of the first and second principal components with BOLD signals across the full FOV are shown for three DBS patients. These maps demonstrate that the principal components are highly correlated with noise both outside and within the brain, indicating that bCompCor effectively captures global structured noise in fMRI data from patients with DBS.



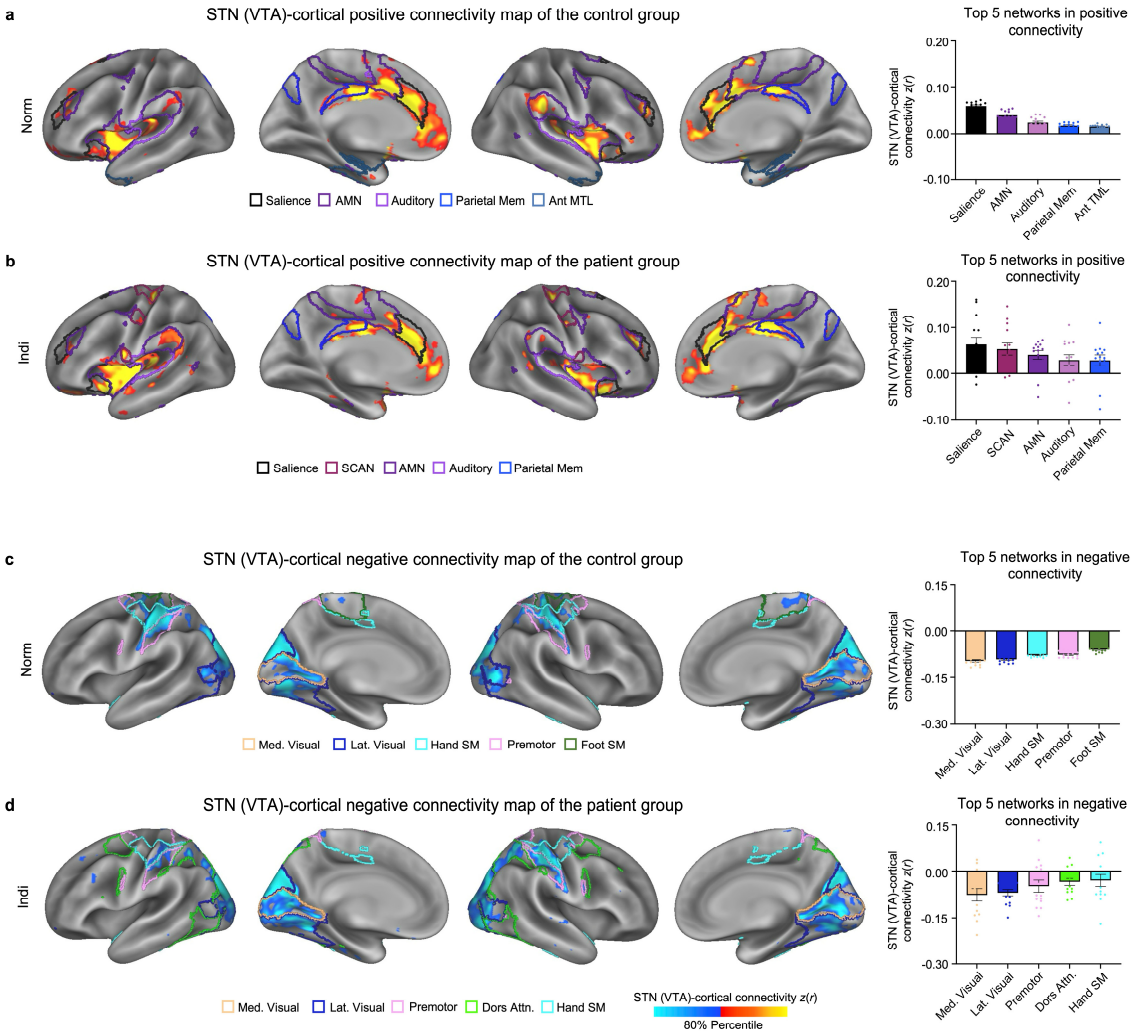
Supplementary Fig. 4. Test-retest reliability of individual functional parcellation for all 14 patients. Individual-level functional parcellations generated from the "test" half of data and the "retest" half of data are shown. The intra-patient test-retest similarity, measured using the Dice coefficient, is shown within each patient's panel. Test-retest reliability or intra-individual similarity is significantly higher than inter-individual similarity (two-tailed paired $t(13) = 38.19$, $P = 9.74\times10^{-15}$, $***P < 0.001$). Each dot/line represents a patient ($n = 14$).



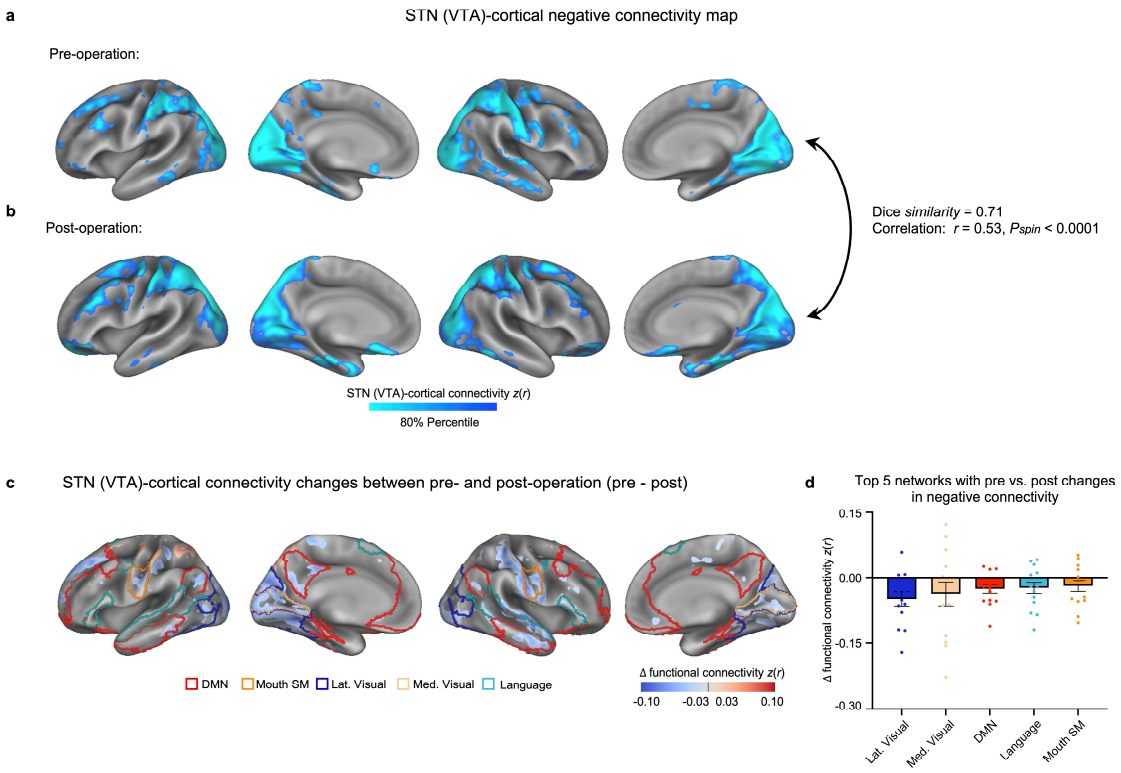
Supplementary Fig. 5. Longitudinal changes in cortical network size following DBS surgery. The proportional surface area of each of the 18 personalized functional networks at four post-operative time points (1-month, 3-month, 6-month and 12-month) of the 14 patients. The surface area occupied by each network remained highly stable over time, with no significant differences observed across time points (one-way repeated measures ANOVA, all $P > 0.05$).



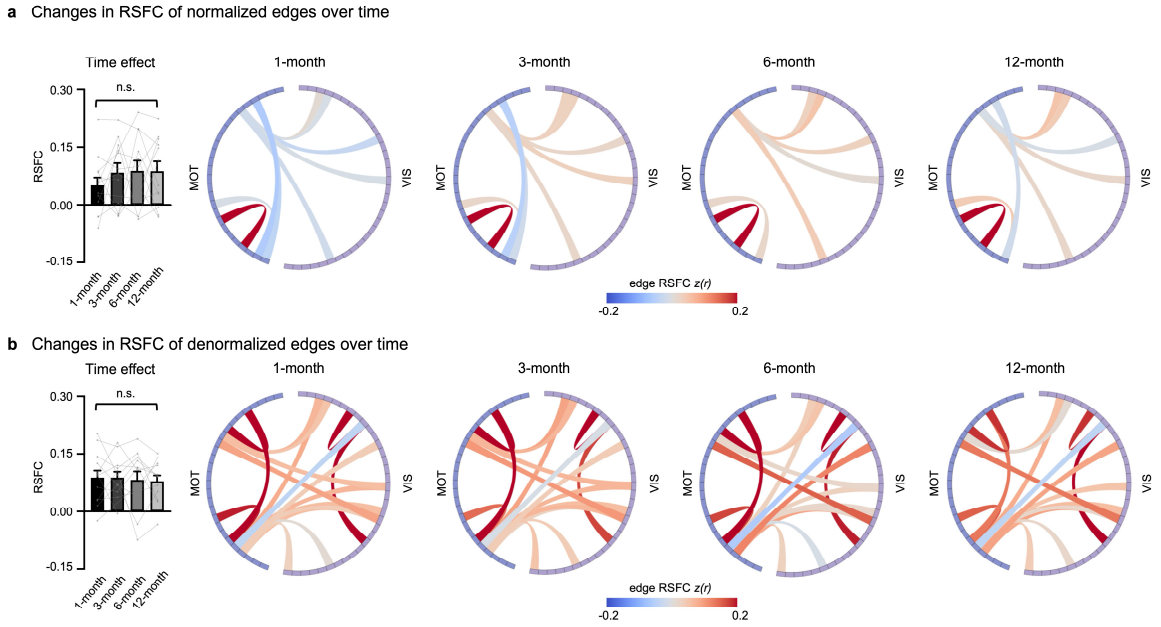
Supplementary Fig. 6. Intra-patient and between-patient similarity of the functional connectome. (a) Individual-specific functional connectome based on individual-specific functional parcellation from test data (left) and retest data (right) are shown for two patients (DBS02 and DBS04). (b) The bar plot illustrates that the intra-patient similarity in connectome (red) is significantly greater than between-patient similarity in connectome (blue, two-tailed paired $t(13) = 23.00$, $P = 6.46\times10^{-12}$, ***$P < 0.001$). Each dot/line represents a patient ($n = 14$).



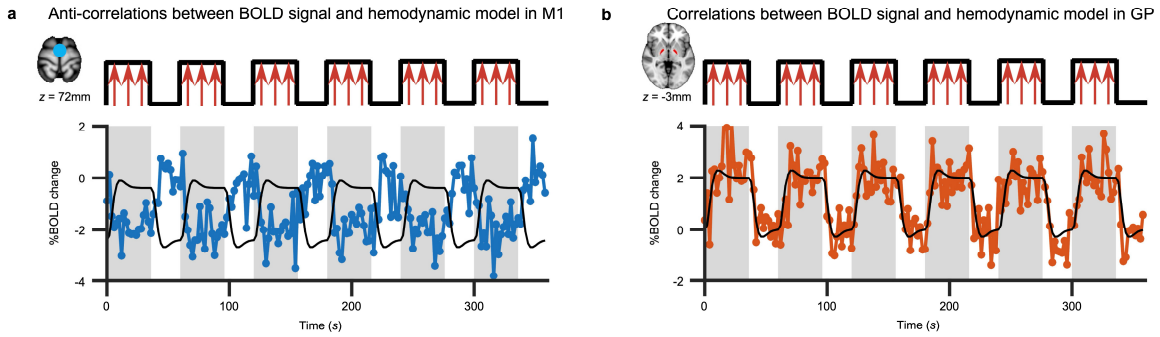
Supplementary Fig. 7. Cortical RSFC maps derived from the STN (VTA) seeds overlaid network boundaries. (a) The "Norm" panel indicates the STN (VTA)-cortical positive connectivity map generated using rsfMRI data from the healthy control group. In the normative map, the top five networks positive connected with the STN (VTA) are the salience network (black), action mode network (AMN, purple), auditory network (light purple), parietal memory network (Parietal Mem, blue), and anterior medial temporal network (Ant MTL, blue-gray). These networks are displayed in a bar plot with individual data points overlaid. (b) The "Indi" panel indicates the STN (VTA)-cortical positive connectivity based on patients' presurgical rsfMRI data. Network boundaries delineate the top five networks with the strongest positive connectivity to the STN (VTA) seeds. In addition to salience, AMN, Auditory, and Parietal Mem, the patient-derived maps revealed prominent connectivity with the somato-cognitive action network (SCAN, maroon). The top five networks by positive connectivity strength are shown in a bar plot, arranged according to their ranked strength. (c) The top five networks exhibiting negative connectivity in the normative dataset were the medial visual (Med. Visual, apricot), lateral visual (Lat. Visual, dark blue), hand sensorimotor (Hand SM, cyan), premotor (pink), and foot sensorimotor (Foot SM, green) networks. (d) In PD patients, the top networks included the Med. Visual, Lat. Visual, premotor, and Hand SM networks, with the addition of the dorsal attention (Dors. Attn, light green) network. Data are presented as mean ± s.e.m., and each dot represents a patient (n = 14).



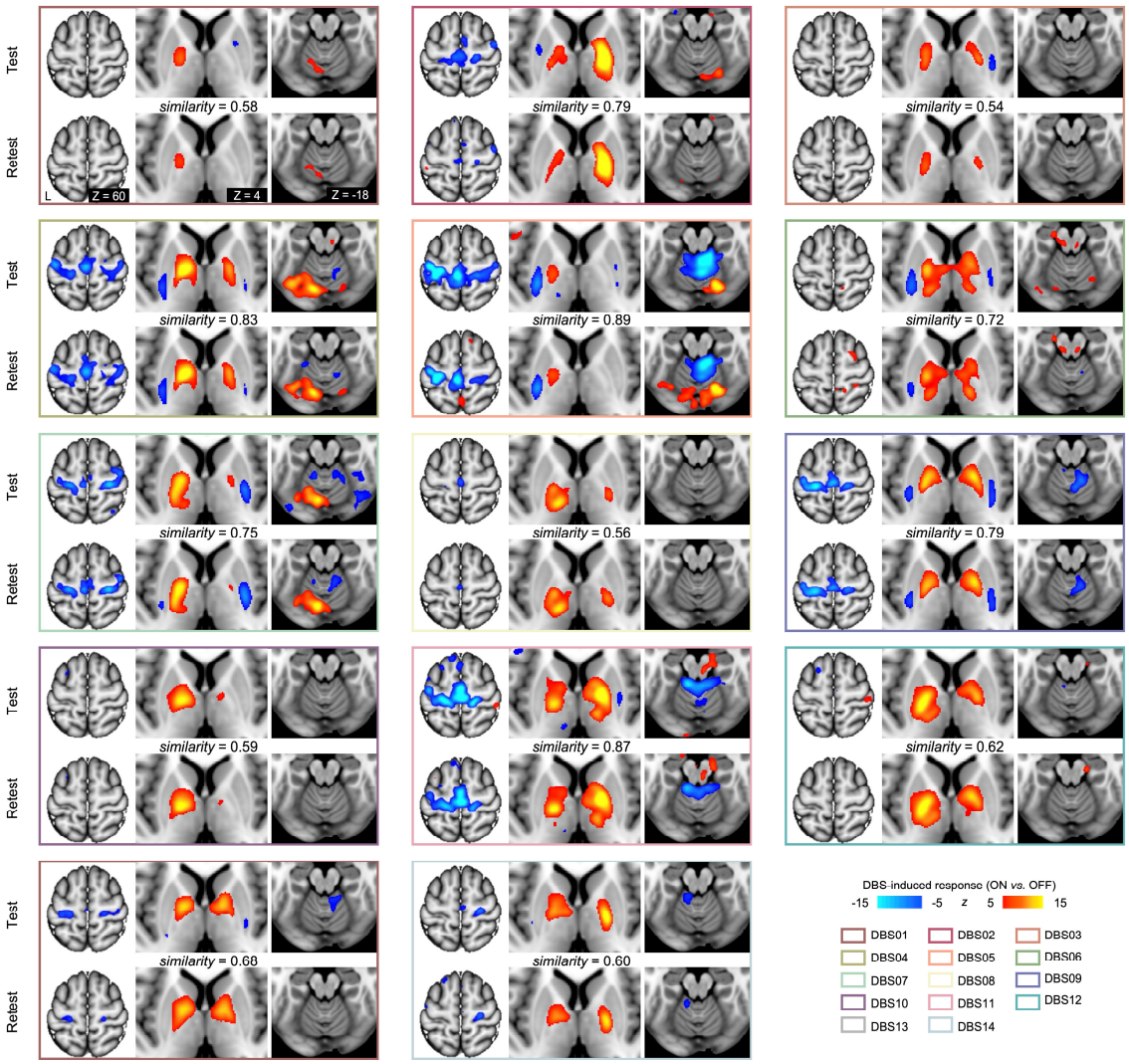
Supplementary Fig. 8. Comparison between pre- and post-surgical target-cortical negative connectivity maps. (a) Group-averaged cortical resting-state functional connectivity (RSFC) map seeded from the STN volume of tissue activated (VTA) across pre-surgical data, showing only negative correlations. (b) Group-averaged STN (VTA)-cortical negative RSFC map derived from post-surgical data. The two maps showed substantial similarity (*Dice coefficient* = 0.71; Pearson's $r = 0.53$, spin test, $P_{spin} < 0.0001$), particularly around the visual network. (c) Pre-minus-post subtraction map of negative connectivity, highlighting the top five networks with the greatest RSFC changes after DBS surgery, which include the lateral visual (Lat. Visual, dark blue), medial visual (Med. Visual, apricot), default mode network (DMN, red), language (azure), and mouth sensorimotor (Mouth SM, orange) network. Red/blue colors indicate decreased/increased functional connectivity, respectively, in the subtraction maps (pre – post). (d) Bar plot showing the magnitude of negative RSFC change (pre - post) for the top five networks. Data are presented as mean ± s.e.m., and each dot represents a patient ($n = 14$).



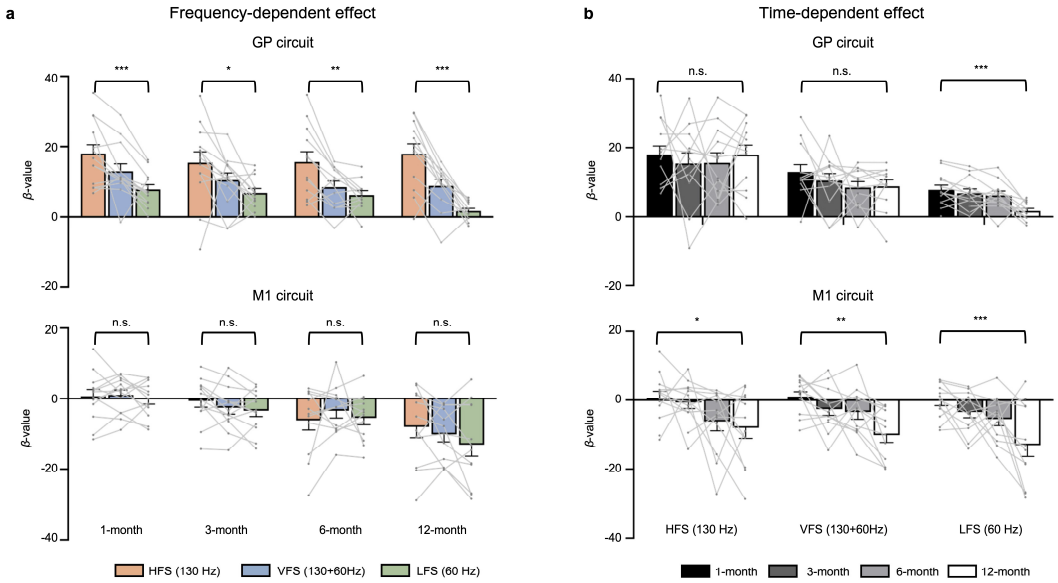
Supplementary Fig. 9. Time effects on resting-state functional connectivity. (a) The changes in resting-state functional connectivity (RSFC) of normalized edges across follow-up visits are shown in the bar plot (left) and Circos plot (right). While the 1-month visit showed modestly lower normalization effects compared with later visits, no significant time-dependent effect was observed in the RFSC of normalized edges (one-way ANOVA, $F(3, 45) = 0.56$, $P = 0.643$). (b) The changes in RSFC of denormalized edges are shown in the same way. Similarly, no significant time effect was detected ($F(3, 45) = 0.07$, $P = 0.978$). The bar plot data are presented as mean ± s.e.m., and each dot represents a patient ($n = 14$). n.s. = non-significant.



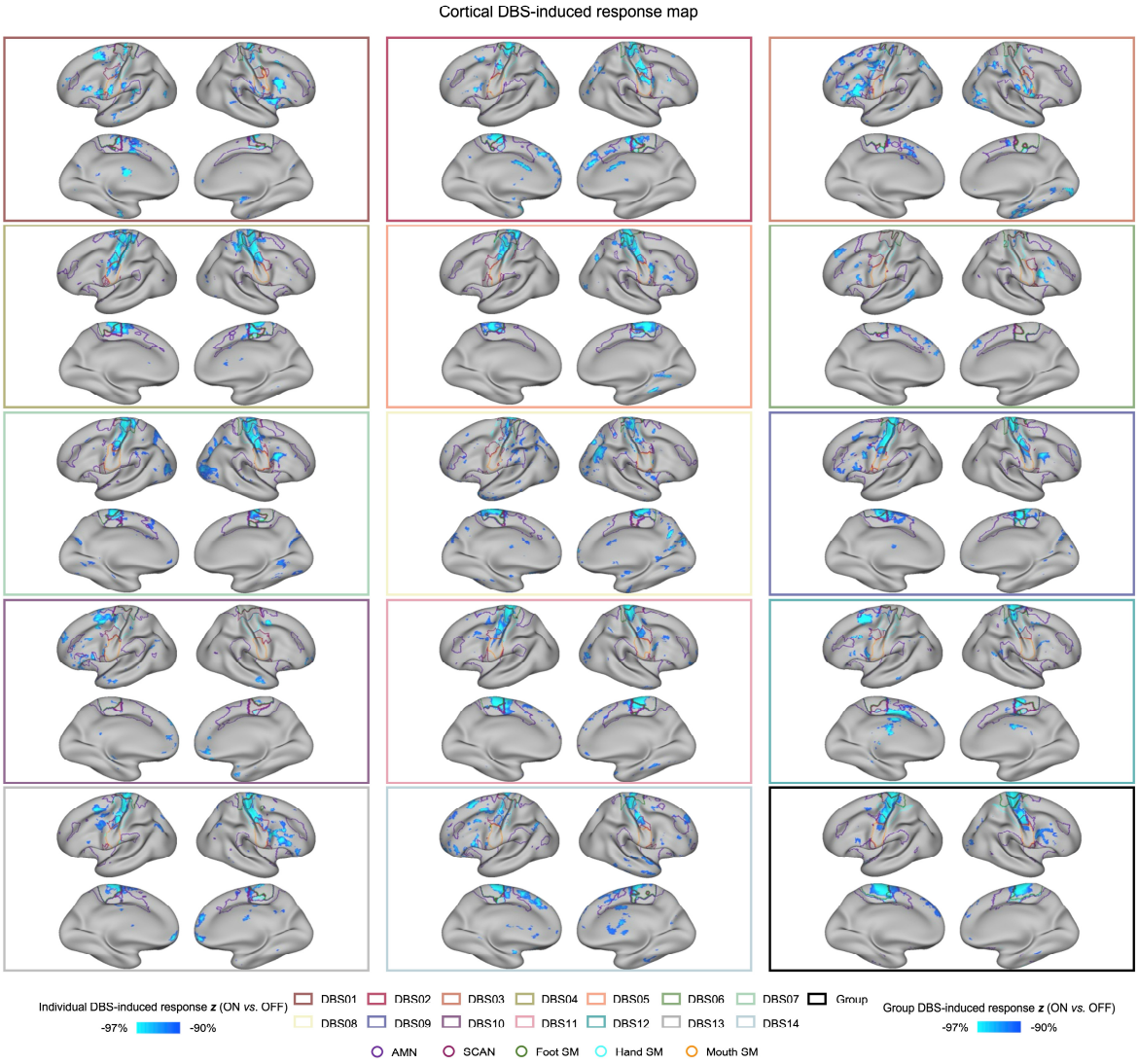
Supplementary Fig. 10. Correlation between BOLD signal responses and the expected BOLD signal change in M1 and GP. (a) BOLD signal responses were extracted from the primary motor cortex (M1) during a single patient's 12-month postsurgical high-frequency stimulation run. Stimulation paradigms are shown at the top. Black lines depict the expected percentage of BOLD signal change, calculated from the convolution of block design and hemodynamic response function. The observed percentage of BOLD signal changes in the M1 was anti-correlated with the expected signals (two-tailed Pearson's $r = -0.70$, $P < 10^{-37}$). (b) The same analysis was applied to the globus pallidus (GP), revealing that the observed percentage of BOLD signal changes was positively correlated with the expected signals (two-tailed Pearson's $r = 0.78$, $P < 10^{-53}$).



Supplementary Fig. 11. Reliable individual-specific DBS-induced responses mapping. For each patient, block-designed fMRI data were divided into two equivalent halves ("test" and "retest"), and DBS-induced responses were estimated separately for each half. Both the "test" and "retest" response maps and their similarity, measured by Pearson's correlation coefficient, are shown for each patient (n = 14).



Supplementary Fig. 12. Decoupled frequency-dependent and time-dependent effects on two circuits. (a) Timepoint-specific analysis of frequency-dependent effects. In the GP circuit, DBS-induced activations showed significant differences across stimulation frequencies at each postoperative time point (one-way repeated measures ANOVA: 1-month: $F(2, 24) = 14.45$, $^{***}P = 7.59\times10^{-5}$; 3-month: $F(2, 24) = 4.20$, $^{*}P = 0.027$; 6-month: $F(2, 22) = 9.45$, $^{**}P = 0.005$; 12-month: $F(2, 22) = 23.66$, $^{***}P = 3.29\times10^{-6}$; all FDR-corrected). In contrast, the M1 circuit showed no significant frequency-dependent changes at any timepoint (one-way repeated measures ANOVA: 1-month: $F(2, 24) = 0.36$, $P = 0.703$; 3-month: $F(2, 24) = 1.33$, $P = 0.282$; 6-month: $F(2, 22) = 0.58$, $P = 0.568$; 12-month: $F(2, 22) = 1.75$, $P = 0.211$; all FDR-corrected), consistent with our prior coupled analyses. (b) Frequency-specific analysis of longitudinal (time-dependent) effects. In the GP circuit, DBS-induced activations under HFS and VFS remained stable over time (one-way repeated measures ANOVA: HFS: $F(3, 30) = 0.41$, $P = 0.750$; VFS: $F(3, 30) = 1.04$, $P = 0.390$; both FDR-corrected), whereas LFS induced a significant time-dependent decrease in GP activation (one-way repeated measures ANOVA: $F(3, 30) = 11.54$, $^{***}P = 3.37\times10^{-5}$, FDR-corrected). In the M1 circuit, DBS-induced deactivations showed a significant increase over time across all stimulation frequencies, indicating a robust and progressive cortical suppression (one-way repeated measures ANOVA: HFS: $F(3, 30) = 4.48$, $^{*}P = 0.010$; VFS: $F(3, 30) = 7.01$, $^{**}P = 0.001$; LFS: $F(3, 30) = 7.53$, $^{***}P = 6.71\times10^{-4}$; all FDR-corrected). $^{*}P < 0.05$, $^{**}P < 0.01$, $^{***}P < 0.001$; n.s. = not significant. Data are presented as mean ± s.e.m., and each dot represents a patient ($n = 14$).



Supplementary Fig. 13. Cortical maps of DBS-induced responses in individuals. Block-design fMRI data from different stimulation conditions and follow-up timepoints were concatenated for this individual-level analysis. For visualization, we projected the responses onto the cortical surface and overlaid individualized network boundaries, including the action mode network (AMN, purple), and M1-related networks (SCAN: maroon; foot: green; hand: cyan; mouth: orange). The group-averaged cortical response map across all patients (n = 14) is shown in the bottom right corner.