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Supplementary information

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Deep brain stimulation induces white matter remodeling and functional changes to brain-wide networks

In the format provided by the authors and unedited

Supplementary Methods

1. DWI data preprocessing

A DWI data preprocessing pipeline was established by adapting standard human DWI analysis pipelines[1] and implementing them with AFNI (version 21.0.8)[2], FMRIB Software Library (FSL, version 6.0.4)[3-5], Advanced Normalization Tools (ANTs, version 2.4.1)[6-8], ITK-SNAP (version 3.6.0)[9] and MRtrix3 (version 3.0.3)[10-14]. Raw DWI DICOM data were first converted into the MRtrix format (.mif). The data were then denoised using a principal component analysis-based approach (Marchenko–Pastur principal component analysis, MP-PCA) to improve the signal-to-noise ratio. Next, data acquired with both phase encoding directions (AP and PA) were merged and susceptibility-induced distortions, eddy-current–related artifacts and intensity inhomogeneity were corrected. Non-diffusion-weighted images (b=0 volumes) were extracted, averaged, and converted into NIfTI format. After brain extraction, images were aligned with session specific average T1w linearly. Then, diffusion tensors were fitted to each voxel using DTIFIT[15]. Finally, voxel-wise crossing-fiber model fitting of diffusion orientations was performed using FSL's BedpostX[16].

2. White matter tract mask definitions

Cingulum bundle (CB) seed mask: CB seed mask was manually delineated on a coronal plane at the level of the genu of the corpus callosum by encompassing the white matter dorsal and medial to the corpus callosum. The seed was selected to capture the characteristic curve of the CB connecting the subcallosal anterior cingulate cortex to the parahippocampal region[17]. For monkey N, an additional seed mask for the subcallosal CB was drawn separately on a sagittal plane to better visualize the subcallosal segment of CB.

Uncinate fasciculus (UF) seed mask: UF seed mask was manually made on axial slices in the anterior temporal lobe white matter. The final seed mask was chosen to accommodate the strong curve of the UF fibers as they enter the frontal lobe, transitioning from dorsal-ventral to anterior-posterior orientation[18].

Forceps Minor (FM) seed mask: FM seed mask was manually drawn in the frontal lobe of one hemisphere on a coronal plane near the frontal pole, with the target mask placed in the contralateral hemisphere on the same coronal plane[19].

We used a coronal waypoint mask at the level of the rostral genu of the corpus callosum to ensure that the fibers emanating from each seed projected to the frontal cortex for the CB and UF[18]. For the FM, we used a waypoint mask drawn in the posterior part of the FM. To reduce false-positive streamlines, we applied exclusion masks including (1) basal ganglia and internal capsule masks to prevent leakage into the anterior limb of the internal capsule, (2) a posterior exclusion mask for the UF and FM to avoid false-positive streamlines projecting posteriorly (3) an interhemispheric mask separating the left and right hemispheres (not applied to the FM), (4) an FM-specific frontal interhemispheric mask, consisting of the anterior part of the interhemispheric mask limited to the frontal lobe anterior to the corpus callosum, and (5) mutual exclusion masks derived from the other tract seeds to ensure non-overlapping tract reconstructions for the CB, UF and FM (for example, UF, FM, and the internal capsule seeds were used as exclusion masks for the CB).

3. Surgical approach for SCC-DBS implantation

DBS was implanted in the confluence of three white matter tracts (the CB, UF and FM) identified from pre-DBS DWI. First, alignment between image space and surgical space was ensured using toothmarker registration of the subjects' head relative to the stereotactic frame[20].

In a dedicated operating suite, aseptic technique was used throughout. Anesthesia was induced using ketamine (5 m/kg) and dexmedetomidine (0.0125 mg/kg) and maintained with isoflurane (2-3%). The skin, fascia and muscles were opened and retracted. A small craniotomy was made over the target location and the dura was opened. A 22-gaude stylet needle within 18-gaude sheath was stereotaxically inserted to a point just above the target to make an insertion tract. The stylet was then removed, and a custom-made mini-DBS lead (NuMed Inc., Hopkinton, NY, USA) was inserted under stereotactic guidance through the sheath and placed at the target. The sheath was then removed. The DBS lead was secured by filling the craniotomy with adhesive silicone (KWIK-SIL, low toxicity silicone adhesive, World Precision Instruments, Sarasota, FL, USA). For safety, the DBS generator (Activa SC for Monkey N, Percept PC for monkey T, Medtronic, Minneapolis, MN, USA) was housed in a 3D printed case (Designed in Autodesk Fusion (Fusion version 2604.1.25, Autodesk Inc., San Francisco, CA, USA) and Formlabs software (PreForm version 3.57.2.624, Formlabs Inc., Someville, MA, USA), printed on Form2 printer (Formlabs Inc., Someville, MA, USA) using Dental LT clear VC Biocompatible Resin (Formlabs Inc., Someville, MA, USA)). This case was fixed on the skull using acrylic cement (Lang Dental, IL, USA), with ceramic screws serving as anchors (Thomas recording GmbH, Germany). The mini-DBS lead and DBS generator were connected via a human DBS extension (37086, Medtronic). In monkey N, the DBS generator was grounded to a titanium screw (Veterinary orthopedic implants, Augustine, USA) implanted in the contralateral parietal skull connected by a silver wire (0.004" diameter, Surepure Chemicals, Florham Park, NJ, USA). In monkey T, a second small craniotomy was made over the contralateral parietal skull, and a second DBS lead was placed epidurally as a grounding wire connected to the generator. The 3D printed case containing the DBS generator was filled with conductive gel (New Bio Technology Ltd., Israel). Finally, the muscles, fascia, and skin were sutured closed.

4. ROI definitions for fMRI seed analysis

For seed-based functional connectivity analysis, the target ROI were defined as follows: area 25 on the unstimulated side, area 32, dorsal ACC (dACC, area 24abc), middle cingulate cortex (MCC, area 24a'b'c'), posterior cingulate cortex (PCC, area 23, area 31), dorsal insula, hippocampus (HIP), amygdala (AMY), dorsolateral prefrontal cortex (DLPFC, area 8, area 9, area 46), ventromedial prefrontal cortex (vmFC, area 10mr, area 10o, area 10mc), superior temporal gyrus (STG), posterior parietal cortex (PPC, inferior parietal part of area 7), primary motor cortex (area 4), somatosensory cortex (area 1, 2, 3ab), supplementary motor area (SMA, area 6), primary visual cortex (V1), middle temporal lobe (MT, another visual network hub).

5. Histological processing

Animals were deeply anesthetized with a sodium pentobarbital solution and perfused transcardially with 0.1 M phosphate buffered saline (PBS) and 1% paraformaldehyde (PFA), followed by 0.1 M PBS, 4% PFA solution and 0.125% glutaraldehyde. Brains were removed and immersed in 4% PFA solution overnight. Following post-fixation, brains were transferred to a solution of 2% DMSO and 10% glycerol in 0.1 M PBS for 24-48 hrs, until the tissue sank, then transferred to a solution of 2% DMSO and 20% glycerol in 0.1 M PBS for at least 24 hours, until the tissue sank. Cryoprotected brains were flash frozen in isopentane at -80°C. After freezing, brains were dried and stored at -80°C until sectioning. Tissue was cut serially in 30 µm steps for immunofluorescence staining and 120 µm (monkey N) or 200 µm (monkey T and monkey D) for electron microscopy analysis in coronal sections on a sliding microtome equipped with a freezing stage (Leica SM

2010R, Leica Biosystems, Deer Park, IL, USA). Slices for immunofluorescence staining were stored at -20°C in antifreeze solution (20% glycerol, 30% ethylene glycol, 50% PBS). Slices for electron microscopy analysis were stored at 4°C in fixation solution (2% PFA, 2.5% glutaraldehyde, 0.1M sodium cacodylate buffer (SCB) pH 7.4, Electron Microscopy Sciences (EMS), Hatfield PA, USA).

6. Electron microscopy sample preparation

Tissue blocks were washed in sodium cacodylate buffer, and then placed in 0.1% tannic acid/SCB for 30 minutes. After washing with SCB, the tissue blocks were incubated with 2% osmium tetroxide and 1.5% potassium ferricyanide diluted in SCB for 30 minutes in a dark setting. Then tissue blocks were washed with filtered distilled water and incubated with 1% thiocarbohydrazide in distilled water for 30 minutes. After washing with distilled water, the tissue blocks were immersed in 1% uranyl acetate in distilled water for 1 hour in the dark followed by a washing step with distilled water. Lastly, tissue blocks were incubated in lead aspartate staining solution (0.0066g lead nitrate/ 1ml aspartic acid solution) for 30 minutes at 60°C and washed with distilled water again.

Tissue blocks were dehydrated in ascending ethanol concentrations and washed with 100% ethanol three times (10 to 15 minutes incubation for each dehydration step) at room temperature. Tissue blocks were rinsed in 100% ethanol mixed 1:1 with propylene oxide for 10 minutes, followed by 100% propylene oxide for 10 min. The tissue was then infiltrated with EMbed-812 resin (EMS) mixed 2:1 with propylene oxide for 1 hour, followed by 1:1 EMbed-812: propylene oxide for 1 hour and then 1:2 EMbed-812: propylene oxide for 1 hour at room temperature. The tissue blocks were next placed into EMbed-812 for 2 hours, then placed into flat molds in the coronal orientation, filled with fresh resin, and placed into a 65°C oven for 72 hours. Ultra thin sections (80 nm) were taken on a Leica UltracutEM UCT (Leica, Wetzlar, Germany) were mounted on Formvar/carbon coated slot grids (EMS, FCF2010-Cu) or 100 mesh Cu grids (EMS, FCF100-Cu).

7. Effect size

Effect sizes were quantified for each statistical test and are reported in the corresponding figure legends. For analysis of variance (ANOVA), effect sizes were calculated as partial eta squared (ηp^2), defined as ηp^2 = SS_effect / (SS_effect + SS_error). For paired t-tests, effect sizes were calculated as Cohen's dz, defined as the mean paired difference divided by the standard deviation of the paired differences. For nonparametric comparisons, effect sizes were estimated using rank-biserial correlation (r_rb).

Supplementary Method References

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Supplementary Table 1

P value for Fig. 4B, DBS group

DBS group	
Area	**p value**
area_25	3.7 ×10^-14
PCC	2.2 ×10^-06
RSC	6.8 ×10^-07
area_10	7.0 ×10^-06
STGr	2.2 ×10^-13
STGc	3.3 ×10^-09
area_32	1.5 ×10^-04
area_24	1.4 ×10^-08
paraHipp	5.8 ×10^-05
ERh	1.7 ×10^-10
area_8A	7.0 ×10^-06
area_8B	2.2 ×10^-06
rostral_dlPFC	2.1 ×10^-05
rostral_vlPFC	2.1 ×10^-05
SI	1.5 ×10^-04
MT	8.8 ×10^-16
V4	2.2 ×10^-13
V3	2.1 ×10^-05
TGa	6.8 ×10^-07
TEO	5.3 ×10^-08
gyral_TE	1.5 ×10^-04
TE_in_STSv	1.3 ×10^-12
STSf	6.8 ×10^-07
STSd	2.2 ×10^-13
lat_belt	3.3 ×10^-09
med_belt	6.8 ×10^-07
RTp	2.2 ×10^-06
core	3.5 ×10^-11
area_14	5.3 ×10^-08
areas_11/13	2.1 ×10^-05
OLF	2.2 ×10^-06
cl_OFC	5.3 ×10^-08
caudal_vlPFC	1.9 ×10^-07
V6	1.6 ×10^-17
V6A	7.7 ×10^-10
area_5	2.1 ×10^-05
vm_IPS	2.2 ×10^-13
lat_IPS	2.2 ×10^-13
MST	8.8 ×10^-16
area_7_in_IPL	6.9 ×10^-12
area_7m	5.9 ×10^-15
Cl	3.9 ×10^-04
Pir	1.9 ×10^-07
HF	2.1 ×10^-05
stAmy	7.0 ×10^-06
mAmy	1.2 ×10^-16
pdAmy	1.9 ×10^-07
VStr	1.9 ×10^-07
Pd	5.3 ×10^-08
BR	2.1 ×10^-05
opt	1.2 ×10^-16
VTHy	7.0 ×10^-06
DTHy	7.7 ×10^-10
ZI-H	2.1 ×10^-05
Rt	5.3 ×10^-08
A+	2.2 ×10^-06
MLThal	7.0 ×10^-06
SpThal	2.2 ×10^-13
DLG	1.4 ×10^-08
MG	7.7 ×10^-10
Pi	3.3 ×10^-09
Hb	6.8 ×10^-07
OC+	3.9 ×10^-04
R+	1.4 ×10^-11
Pn+	3.9 ×10^-04
DCb	1.9 ×10^-07
VCC	3.3 ×10^-09
MedRaphe	1.5 ×10^-04
PreCbMed	1.9 ×10^-07

Supplementary Table 2

P value for Fig. 4B, Non-surgical control group

Non-surgical Control group	
Area	**p value**
STGr	6.8 ×10^-07
STGc	2.2 ×10^-06
ERh	2.2 ×10^-06
PRh	5.8 ×10^-05
area_8B	2.1 ×10^-05
Ri	6.8 ×10^-07
SI	3.8 ×10^-06
PM	2.2 ×10^-06
MT	5.3 ×10^-08
V1	3.3 ×10^-09
gyral_TE	7.0 ×10^-06
TE_in_STSv	1.9 ×10^-07
STSd	5.8 ×10^-05
lat_belt	3.9 ×10^-04
med_belt	3.9 ×10^-04
area_14	1.3 ×10^-12
area_12m/o	5.9 ×10^-15
V6	6.8 ×10^-07
En	3.0 ×10^-21
Pir	1.4 ×10^-08
stAmy	3.3 ×10^-09
mAmy	3.0 ×10^-21
DStr	2.1 ×10^-05
opt	7.7 ×10^-10
POR	6.5 ×10^-06
MTHy	1.5 ×10^-04
VTHy	2.2 ×10^-06
DTHy	3.7 ×10^-14
VPHy	1.9 ×10^-07
A+	2.2 ×10^-06
MD	3.9 ×10^-04
MLThal	2.1 ×10^-05
CbThal	3.9 ×10^-04
LD	3.7 ×10^-14
Pul	1.5 ×10^-04
DLG	2.1 ×10^-05
PrT	2.2 ×10^-06
Co	1.4 ×10^-08
raphe_Mid	3.9 ×10^-04
wmCB	1.5 ×10^-04
Fl-PFl	2.1 ×10^-05
ICbCx	7.0 ×10^-06
LCbCx	2.1 ×10^-05
MedMC	1.9 ×10^-07

Supplementary Table 3

Effect size (rank-biserial correlation, r_rb) for Fig. 4B, DBS group

DBS group	
ROI	r_rb
area_25	-0.16393
PCC	-0.14754
RSC	-0.47541
area_10	-0.40984
STGr	0.016393
STGc	-0.36066
area_32	0.114754
area_24	0.213115
MCC	0.295082
paraHipp	-0.04098
ERh	-0.2541
PRh	0.032787
area_8A	-0.06557
area_8B	-0.27869
rostral_dlP	-0.08197
rostral_vlP	0.131148
Ins/Pi	0.081967
Ri	0.245902
SI	0.442623
SII	0.319672
SMA/preSMA	0.491803
M1	0.590164
PM	0.131148
MT	0.295082
V4	-0.04918
V3	-0.09836
V2	-0.16393
V1	-0.31148
TGa	-0.2459
TGg/TGd	0
TEO	-0.2459
gyral_TE	-0.03279
TE_in_STSv	-0.29508
STSf	-0.29508
STSd	-0.29508
lat_belt	-0.01639
med_belt	0.065574
RTp	0
core	0.098361
area_14	-0.36066
areas_11/13	-0.21311

DBS group	
ROI	r_rb
area_12m/o	-0.10656
OFa-p	-0.19672
OLF	-0.2623
cl_OFC	0.065574
caudal_vlPF	-0.04098
V6	-0.18852
V6A	-0.29508
area_5	0.377049
vm_IPS	0.278689
lat_IPS	0.278689
MST	0.229508
area_7_in_I	0.327869
area_7m	0.098361
Cl	0.081967
En	-0.09836
Pir	-0.11475
HF	-0.35246
f	-0.19672
vpAmy	-0.52459
lpAmy	0.016393
stAmy	-0.16393
mAmy	-0.42623
pdAmy	-0.36066
DStr	0.122951
VStr	-0.11475
Pd	0.04918
BR	-0.14754
ST	-0.16393
SDBR	-0.16393
opt	-0.57377
POR	-0.09836
MTHy	-0.02459
VTHy	-0.44262
DTHy	-0.40984
DPHy	-0.21311
VPHy	-0.57377
ZI-H	-0.13934
Rt	-0.2459
A+	-0.44262
ILThal	-0.52459
MD	-0.5082

DBS group	
ROI	r_rb
MLThal	-0.2623
PNThal	-0.39344
CbThal	-0.44262
SpThal	-0.42623
LP	-0.2459
LD	-0.22951
Pul	-0.72131
DLG	-0.52459
MG	-0.77049
Pi	0.081967
Hb	-0.2459
PrT	-0.18033
Co	-0.70492
PAGR	-0.22951
TgMid	-0.45082
RtMid	-0.4918
OC+	-0.19672
raphe_Mid	-0.62295
R+	-0.22951
DA_Mid	-0.62295
PBC	-0.42623
LGR	-0.40984
tgPons	-0.63934
ll+	-0.36066
retPons	-0.52459
SO/ml	-0.0082
Pn+	-0.34426
wmCB	-0.2623
DCb	-0.04918
Fl-PFl	-0.2459
VCbCx	-0.77049
ICbCx	-0.34426
LCbCx	-0.31148
VCC	-0.36066
C5	-0.27869
SVC	-0.40164
MedMC	-0.42623
MedRet	-0.04918
MedRaphe	0.467213
PreCbMed	-0.39344
vmt	0.459016

Supplementary Table 4

Effect size (rank-biserial correlation, r_rb) for Fig. 4B, Non-surgical control group

Non-surgical Control	
ROI	r_rb
area_25	-0.16393
PCC	-0.14754
RSC	-0.47541
area_10	-0.40984
STGr	0.016393
STGc	-0.36066
area_32	0.114754
area_24	0.213115
MCC	0.295082
paraHipp	-0.04098
ERh	-0.2541
PRh	0.032787
area_8A	-0.06557
area_8B	-0.27869
rostral_dlP	-0.08197
rostral_vlP	0.131148
Ins/Pi	0.081967
Ri	0.245902
SI	0.442623
SII	0.319672
SMA/preSMA	0.491803
M1	0.590164
PM	0.131148
MT	0.295082
V4	-0.04918
V3	-0.09836
V2	-0.16393
V1	-0.31148
TGa	-0.2459
TGg/TGd	0
TEO	-0.2459
gyral_TE	-0.03279
TE_in_STSv	-0.29508
STSf	-0.29508
STSd	-0.29508
lat_belt	-0.01639
med_belt	0.065574
RTp	0
core	0.098361
area_14	-0.36066
areas_11/13	-0.21311

Non-surgical Control	
ROI	r_rb
area_12m/o	-0.10656
OFa-p	-0.19672
OLF	-0.2623
cl_OFC	0.065574
caudal_vlPF	-0.04098
V6	-0.18852
V6A	-0.29508
area_5	0.377049
vm_IPS	0.278689
lat_IPS	0.278689
MST	0.229508
area_7_in_I	0.327869
area_7m	0.098361
Cl	0.081967
En	-0.09836
Pir	-0.11475
HF	-0.35246
f	-0.19672
vpAmy	-0.52459
lpAmy	0.016393
stAmy	-0.16393
mAmy	-0.42623
pdAmy	-0.36066
DStr	0.122951
VStr	-0.11475
Pd	0.04918
BR	-0.14754
ST	-0.16393
SDBR	-0.16393
opt	-0.57377
POR	-0.09836
MTHy	-0.02459
VTHy	-0.44262
DTHy	-0.40984
DPHy	-0.21311
VPHy	-0.57377
ZI-H	-0.13934
Rt	-0.2459
A+	-0.44262
ILThal	-0.52459
MD	-0.5082

Non-surgical Control	
ROI	r_rb
MLThal	-0.2623
PNThal	-0.39344
CbThal	-0.44262
SpThal	-0.42623
LP	-0.2459
LD	-0.22951
Pul	-0.72131
DLG	-0.52459
MG	-0.77049
Pi	0.081967
Hb	-0.2459
PrT	-0.18033
Co	-0.70492
PAGR	-0.22951
TgMid	-0.45082
RtMid	-0.4918
OC+	-0.19672
raphe_Mid	-0.62295
R+	-0.22951
DA_Mid	-0.62295
PBC	-0.42623
LGR	-0.40984
tgPons	-0.63934
ll+	-0.36066
retPons	-0.52459
SO/ml	-0.0082
Pn+	-0.34426
wmCB	-0.2623
DCb	-0.04918
Fl-PFl	-0.2459
VCbCx	-0.77049
ICbCx	-0.34426
LCbCx	-0.31148
VCC	-0.36066
C5	-0.27869
SVC	-0.40164
MedMC	-0.42623
MedRet	-0.04918
MedRaphe	0.467213
PreCbMed	-0.39344
vmt	0.459016

Supplementary Table 5

Sample size for Fig. E4A (CB)

mkN	Zaxis_s	sample size (n)
stim side	-3.603	7
SCC	-2.103	6
	-0.603	5
	0.897	6
	2.397	8
	3.897	8
	5.397	5
	6.897	3

mkN	Zaxis_c_s	sample size (n)
ctrl side	-3.603	8
SCC	-2.103	8
	-0.603	6
	0.897	10
	2.397	12
	3.897	14
	5.397	5
	6.897	3

mkT	Zaxis3_s	sample size (n)
stim side	0.0215	4
SCC	1.5215	2
	3.0215	1
	4.5215	2

mkT	Zaxis3_c_s	sample size (n)
ctrl side	1.5215	2
SCC	3.0215	2
	4.5215	11

mkN	Yaxis	sample size (n)
stim side	-41.477	3
dACC-PCC	-39.977	7
	-38.477	17
	-36.977	18
	-35.477	17
	-33.977	16
	-32.477	6
	-30.977	4
	-29.477	3
	-27.977	4
	-26.477	3
	-24.977	2
	-23.477	3
	-21.977	4
	-20.477	4
	-18.977	4
	-17.477	4
	-15.977	4
	-14.477	3
	-12.977	3
	-11.477	2
	-9.977	2
	-8.477	2
	-6.977	3
	-5.477	3
	-3.977	4
	-2.477	3
	-0.977	3
	0.523	4
	2.023	3

mkN	Yaxis_c	sample size (n)
ctrl side	-39.977	2
dACC-PCC	-38.477	9
	-36.977	14
	-35.477	13
	-33.977	7
	-32.477	5
	-30.977	2
	-29.477	1
	-27.977	2
	-26.477	1
	-24.977	2
	-23.477	2
	-21.977	2
	-20.477	1
	-18.977	1
	-17.477	2
	-15.977	2
	-14.477	1
	-12.977	2
	-11.477	4
	-9.977	4
	-8.477	3
	-6.977	1
	-5.477	1

mkT	Yaxis3	sample size (n)
stim side	-39.2537	1
dACC-PCC	-37.7537	3
	-36.2537	9
	-34.7537	12
	-33.2537	7
	-31.7537	4
	-30.2537	4
	-28.7537	4
	-27.2537	4
	-25.7537	3
	-24.2537	2
	-22.7537	2
	-21.2537	2
	-19.7537	2
	-18.2537	3
	-16.7537	3
	-15.2537	3
	-13.7537	3
	-12.2537	4
	-10.7537	4
	-9.2537	4
	-7.7537	3
	-6.2537	2
	-4.7537	3
	-3.2537	2
	-1.7537	2
	-0.2537	3
	1.2463	5
	2.7463	8
	4.2463	3

mkT	Yaxis3_c	sample size (n)
ctrl side	-43.7537	2
dACC-PCC	-42.2537	6
	-40.7537	4
	-39.2537	9
	-37.7537	9
	-36.2537	7
	-34.7537	15
	-33.2537	15
	-31.7537	16
	-30.2537	7
	-28.7537	6
	-27.2537	4
	-25.7537	3
	-24.2537	4
	-22.7537	4
	-21.2537	4
	-19.7537	4
	-18.2537	4
	-16.7537	4
	-15.2537	4
	-13.7537	4
	-12.2537	4
	-10.7537	4
	-9.2537	5
	-7.7537	5
	-6.2537	5
	-4.7537	5
	-3.2537	4
	-1.7537	4
	-0.2537	4
	1.2463	6
	2.7463	4
	4.2463	4

Supplementary Table 6

Sample size for Fig. E4B (UF)

mkN	Yaxis	sample size (n)	mkN	Yaxis	sample size (n)	mkT	Yaxis	sample size (n)	mkT	Yaxis	sample size (n)
stim side	-47.477	2	ctrl side	-48.977	2	stim side	-37.7537	1	ctrl side	-43.7537	4
UF sup	-45.977	4	UF sup	-47.477	2	UF sup	-36.2537	1	UF sup	-42.2537	8
	-44.477	6		-45.977	2		-34.7537	1		-40.7537	4
	-42.977	4		-44.477	4		-33.2537	2		-39.2537	7
	-41.477	6		-42.977	7		-31.7537	7		-37.7537	4
	-39.977	5		-41.477	9		-30.2537	7		-36.2537	4
	-38.477	6		-39.977	12		-28.7537	8		-34.7537	4
	-36.977	5		-38.477	11		-27.2537	8		-33.2537	5
	-35.477	6		-36.977	11		-25.7537	10		-31.7537	6
	-33.977	11		-35.477	13		-24.2537	6		-30.2537	9
	-32.477	15		-33.977	15		-22.7537	2		-28.7537	10
	-30.977	18		-32.477	18		-21.2537	2		-27.2537	12
	-29.477	19		-30.977	19		-19.7537	1		-25.7537	10
	-27.977	18		-29.477	22	mkT	Zaxis	sample size (n)		-24.2537	8
	-26.477	14		-27.977	21	stim side	-13.4785	2		-22.7537	4
	-24.977	11		-26.477	19	UF inf	-11.9785	2		-21.2537	1
	-23.477	12		-24.977	13		-10.4785	1	mkT	Zaxis	sample size (n)
	-21.977	8		-23.477	6		-8.9785	2	ctrl side	-11.9785	3
	-20.477	1		-21.977	5		-7.4785	5	UF inf	-10.4785	3
mkN	Zaxis	sample size (n)	mkN	Zaxis	sample size (n)		-5.9785	10		-8.9785	4
stim side	-8.103	5	ctrl side	-12.603	4					-7.4785	6
UF inf	-6.603	4	UF inf	-11.103	6					-5.9785	9
				-9.603	5						
				-8.103	6						
				-6.603	10						

Supplementary Table 7

Sample size for Fig. E4C (FM)

mk N	Yaxis	sample size (n)	mk N	Yaxis	sample size (n)	mk T	Yaxis	sample size (n)	mk T	Yaxis	sample size (n)
stim side	-47.477	4	ctrl side	-50.477	3	stim side	-45.2537	6	ctrl side	-46.7537	1
FM	-45.977	6	FM	-48.977	5	FM	-43.7537	6	FM	-45.2537	2
	-44.477	3		-47.477	7		-42.2537	7		-43.7537	5
	-42.977	2		-45.977	4		-40.7537	6		-42.2537	6
	-41.477	4		-44.477	3		-39.2537	5		-40.7537	4
	-39.977	4		-42.977	3		-37.7537	4		-39.2537	5
	-38.477	5		-41.477	5		-36.2537	3		-37.7537	4
	-36.977	7		-39.977	5		-34.7537	5		-36.2537	5
	-35.477	5		-38.477	5		-33.2537	4		-34.7537	5
	-33.977	7		-36.977	5		-31.7537	5		-33.2537	4
	-32.477	5		-35.477	4		-30.2537	3		-31.7537	5
	-30.977	1		-33.977	5		-28.7537	2		-30.2537	11
				-32.477	8					-28.7537	7
				-30.977	5					-27.2537	2

Supplementary Table 8
Sample size for Fig. E9A

ROI	Pre-DBS Sim side	Post-DBS Sim side	Pre-DBS Ctrl side	Pre-DBS Ctrl side
PCC	249	249	249	249
vmFC	109	109	109	109
STG	499	499	499	499
Anterior-dorsal Insula	100	100	100	100
dACC	162	162	162	162
DLPFC	766	766	766	766
PPC	336	336	336	336
Area 25	18	18	18	18
Area 32	48	48	48	48
MCC	101	101	101	101
HIP	132	132	132	132
AMY	111	111	111	111
Sensory Cx	692	692	692	692
Motor Cx	446	446	446	446
SMA	101	101	101	101
Visual Cx	1161	1161	1161	1161
MT	56	56	56	56

Supplementary Table 9

P value for Fig. E9

ROI	Stimulation side	Control side
PCC	8.22E-12	4.03E-07
vmFC	0	0
STG	0	0
Anterior-dorsal Insula	4.42E-08	0.029284354
dACC	4.75E-04	0
DLPFC	0	0
PPC	0.999983327	0.11576317
Area 25	0	0
Area 32	2.44E-13	0
MCC	0.991825378	0.999989453
HIP	1.19E-05	0.01848539
AMY	7.70E-06	0.999989453
Sensory Cx	0	0
Motor Cx	0.999909913	0.999125683
SMA	0.999989453	0.999989453
Visual Cx	0.999989453	0.999984425
MT	0.998895555	7.85E-07

Supplementary Table 10

P value for Fig. E10 C

Non-stimulation Control animal	
Area	**p value**
area_25	1.4 ×10^-08
PCC	2.1 ×10^-05
RSC	7.0 ×10^-06
area_10	1.9 ×10^-07
STGr	2.1 ×10^-18
STGc	1.3 ×10^-12
ERh	1.4 ×10^-08
PRh	1.3 ×10^-12
area_8B	7.0 ×10^-06
rostral_dlPFC	6.8 ×10^-07
SII	3.3 ×10^-09
V3	1.5 ×10^-04
TGa	1.2 ×10^-06
TGg/TGd	5.9 ×10^-15
gyral_TE	7.7 ×10^-10
TE_in_STSv	1.3 ×10^-12
STSf	7.0 ×10^-06
STSd	1.3 ×10^-12
lat_belt	3.5 ×10^-11
med_belt	5.3 ×10^-08
RTp	1.2 ×10^-16
core	6.8 ×10^-07
area_14	2.4 ×10^-04
areas_11/13	7.7 ×10^-10
OLF	1.7 ×10^-10
cl_OFC	6.9 ×10^-12
V6	5.3 ×10^-08
MST	1.7 ×10^-10
area_7m	1.5 ×10^-04
Cl	1.4 ×10^-08
HF	5.8 ×10^-05
mAmy	7.7 ×10^-10
DStr	1.9 ×10^-07
ST	5.3 ×10^-08
SDBR	7.7 ×10^-10
opt	2.2 ×10^-13
POR	2.1 ×10^-05
MTHy	3.3 ×10^-09
DTHy	7.0 ×10^-06
Rt	1.5 ×10^-04
A+	7.0 ×10^-06
ILThal	1.5 ×10^-09
MLThal	1.5 ×10^-04
PNThal	7.0 ×10^-06
LD	7.0 ×10^-06
Hb	5.8 ×10^-05
OC+	6.8 ×10^-07
DA_Mid	3.3 ×10^-09
Pn+	1.5 ×10^-04
Fl-PFl	6.8 ×10^-07
ICbCx	5.9 ×10^-15
LCbCx	2.1 ×10^-05
VCC	3.9 ×10^-04

Supplementary Table 11

Effect size (rank-biserial correlation, r_rb) for Fig. E10 C

Non stimulation control	
ROI	r_rb
area_25	-0.16393
PCC	-0.14754
RSC	-0.47541
area_10	-0.40984
STGr	0.016393
STGc	-0.36066
area_32	0.114754
area_24	0.213115
MCC	0.295082
paraHipp	-0.04098
ERh	-0.2541
PRh	0.032787
area_8A	-0.06557
area_8B	-0.27869
rostral_dlP	-0.08197
rostral_vlP	0.131148
Ins/Pi	0.081967
Ri	0.245902
SI	0.442623
SII	0.319672
SMA/preSMA	0.491803
M1	0.590164
PM	0.131148
MT	0.295082
V4	-0.04918
V3	-0.09836
V2	-0.16393
V1	-0.31148
TGa	-0.2459
TGg/TGd	0
TEO	-0.2459
gyral_TE	-0.03279
TE_in_STSv	-0.29508
STSf	-0.29508
STSd	-0.29508
lat_belt	-0.01639
med_belt	0.065574
RTp	0
core	0.098361
area_14	-0.36066
areas_11/13	-0.21311

Non stimulation control	
ROI	r_rb
area_12m/o	-0.10656
OFa-p	-0.19672
OLF	-0.2623
cl_OFC	0.065574
caudal_vlPF	-0.04098
V6	-0.18852
V6A	-0.29508
area_5	0.377049
vm_IPS	0.278689
lat_IPS	0.278689
MST	0.229508
area_7_in_I	0.327869
area_7m	0.098361
Cl	0.081967
En	-0.09836
Pir	-0.11475
HF	-0.35246
f	-0.19672
vpAmy	-0.52459
lpAmy	0.016393
stAmy	-0.16393
mAmy	-0.42623
pdAmy	-0.36066
DStr	0.122951
VStr	-0.11475
Pd	0.04918
BR	-0.14754
ST	-0.16393
SDBR	-0.16393
opt	-0.57377
POR	-0.09836
MTHy	-0.02459
VTHy	-0.44262
DTHy	-0.40984
DPHy	-0.21311
VPHy	-0.57377
ZI-H	-0.13934
Rt	-0.2459
A+	-0.44262
ILThal	-0.52459
MD	-0.5082

Non stimulation control	
ROI	r_rb
MLThal	-0.2623
PNThal	-0.39344
CbThal	-0.44262
SpThal	-0.42623
LP	-0.2459
LD	-0.22951
Pul	-0.72131
DLG	-0.52459
MG	-0.77049
Pi	0.081967
Hb	-0.2459
PrT	-0.18033
Co	-0.70492
PAGR	-0.22951
TgMid	-0.45082
RtMid	-0.4918
OC+	-0.19672
raphe_Mid	-0.62295
R+	-0.22951
DA_Mid	-0.62295
PBC	-0.42623
LGR	-0.40984
tgPons	-0.63934
ll+	-0.36066
retPons	-0.52459
SO/ml	-0.0082
Pn+	-0.34426
wmCB	-0.2623
DCb	-0.04918
Fl-PFl	-0.2459
VCbCx	-0.77049
ICbCx	-0.34426
LCbCx	-0.31148
VCC	-0.36066
C5	-0.27869
SVC	-0.40164
MedMC	-0.42623
MedRet	-0.04918
MedRaphe	0.467213
PreCbMed	-0.39344
vmt	0.459016