

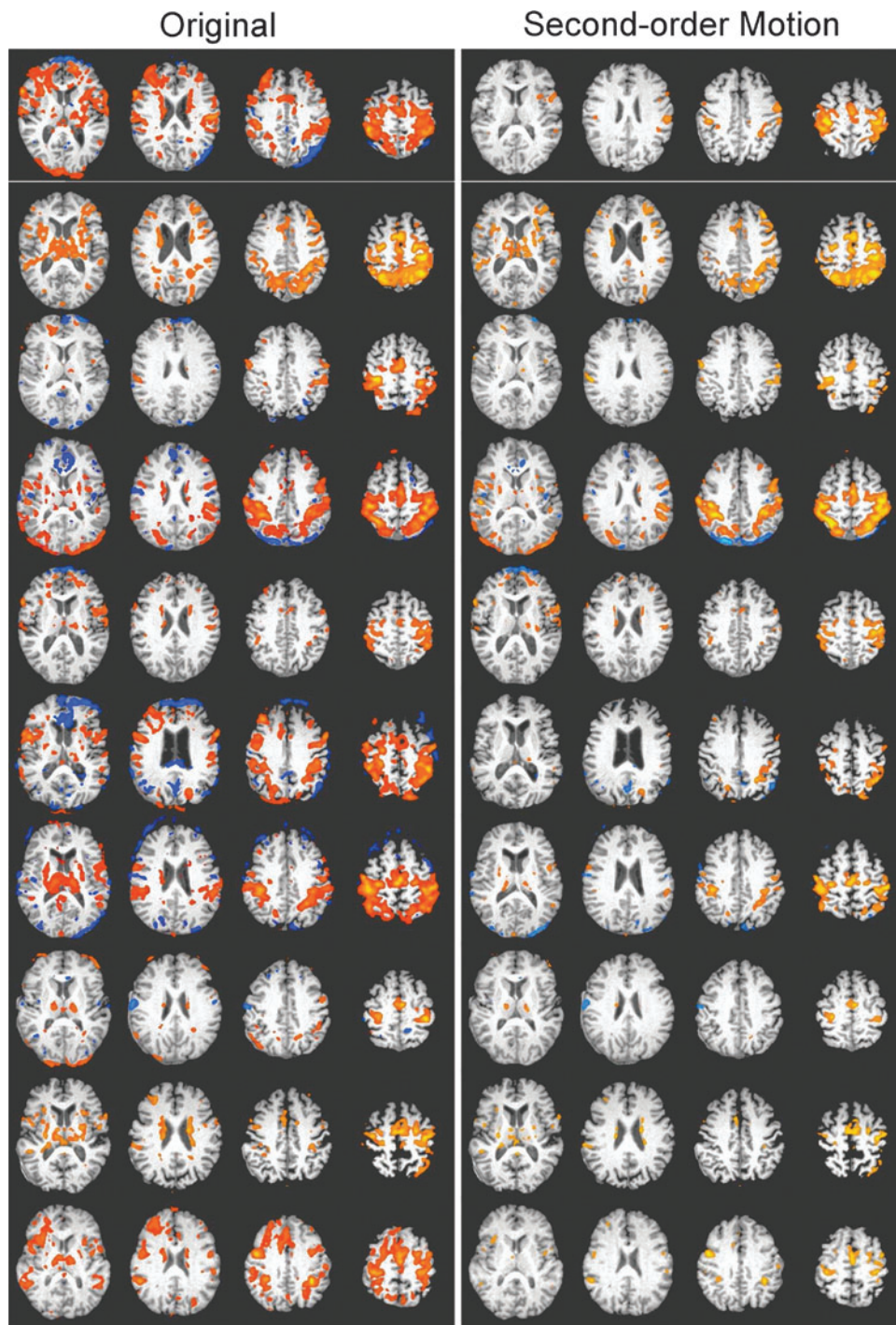
Supplementary Data

Second-Order Motion Correction

A second-order motion correction is a regression and subtraction of various parameterizations of voxel-level motion. This is done using a trigonometric conversion of the volumetric rigid-body six degree of freedom motion parameters into voxel level translations for x , y , and z motion and for the vector sum of those displacements, denoted by td (e.g., every voxel has a different set of volumetric motion-based regressors based on their position with respect to the origin of the retrospective motion correction as in Bullmore et al. (1999). An exploratory analysis in separate datasets identified the following 15 parameterizations of the voxel-level motion as reliably identifying motion: the four voxel-wise displacement measures (x , y , z , and td), the four measures squared, the measures lagged by one volume (delayed in time by one repetition), and the first derivative of y , z , and td .

These regressors are identical to those commonly stated as used in other second-order motion correction procedures.

The effect of this process on the data was observed in a larger set of human Parkinson's disease data to dramatically reduce the false positive rate. If we were concerned with activation volume or mean activation determination (which we are not—we are instead only concerned with an accurate localization by the maximum activation), it would be necessary to estimate the measurement uncertainty due to motion on each subject's activation volume or mean activation (e.g., using the difference between data corrected and uncorrected for second-order motion). For connectivity localization, however, it is necessary to compare the locations of the most activated voxel in the second-order corrected and uncorrected data to determine whether localization has been compromised by the motion. If this distance is greater than 1 voxel, then localization is compromised by motion. The information in the Supplementary Table S3 and Supplementary Figure S1 shows that in several subjects, localization was compromised by motion without the second-order motion correction procedure.



SUPPLEMENTARY FIG. S1. Functional magnetic resonance imaging activation to a complex finger tapping task, without and with the second-order motion correction procedure applied before spatial filtering. The threshold for significance was set to 2.5σ greater than the mean for a fitted Gaussian distribution to nonzero t-statistics in the original scan space.

SUPPLEMENTARY TABLE S1. MEAN CONNECTIVITY CHANGES, CORRELATIONS BETWEEN THERAPEUTIC EFFECT ON CONNECTIVITY, AND FITTED SLOPE BETWEEN CHANGES IN CONNECTIVITY BETWEEN THERAPIES, AFTER SECOND-ORDER MOTION CORRECTION (SEE TABLE 3 IN MAIN TEXT FOR SAME WITHOUT SECOND-ORDER MOTION CORRECTION) APPLIED TO CONNECTIVITY DATA (AS WELL AS ACTIVATION SEEDING DATA)

	$\Delta Conn_{med}$	$\Delta Conn_{ex}$	<i>Correlation</i>	<i>p-Value (x100)</i>	<i>Fitted slope</i>
LM1-RM1	-0.63	0.33	0.47	4.3297	0.41
LSMA-RSMA	-0.31	2.38	0.03	89.583	0.04
LM1-LSMA	0.36	0.52	0.57	1.124	0.55
RM1-RSMA	-0.95	-0.19	0.53	1.9931	0.52
LM1-LPUT	-0.37	-0.26	0.72	0.0572	0.62
LM1-LGP	0.31	0.11	0.61	0.603	0.49
LM1-LTHAL	-0.48	0.09	0.63	0.3557	0.70
RM1-RPUT	-0.19	-0.18	0.53	1.9379	0.87
RM1-RGP	0.42	0.33	0.43	6.9375	0.40
RM1-RTHAL	-0.42	-0.50	0.57	1.0026	0.83
LSMA-LPUT	-0.72	-0.11	0.52	2.1122	0.55
LSMA-LGP	-0.28	-0.32	0.45	5.0628	0.25
LSMA-LTHAL	-0.54	-0.70	0.67	0.1648	0.65
RSMA-RPUT	-0.12	0.50	0.70	0.0846	0.73
RSMA-RGP	-0.62	-0.62	0.34	15.54	0.32
RSMA-RTHAL	-0.62	-0.73	0.65	0.2658	1.18

PUT, putamen; THAL, thalamus; GP, globus pallidus; SMA, supplementary motor area.

SUPPLEMENTARY TABLE S2. SUBJECT DEMOGRAPHICS (PARTIAL, SEE TABLE 3 IN MAIN ARTICLE) AND MEAN CORTICAL AND SUBCORTICAL CONNECTIVITY CHANGES, AFTER SECOND-ORDER MOTION CORRECTION APPLIED TO CONNECTIVITY DATA

<i>Subject</i>	<i>MAH/DH</i>	<i>Cort</i> Δf_c^{med}	<i>Cort</i> Δf_c^{FE}	<i>Subcort</i> Δf_c^{med}	<i>Subcort</i> Δf_c^{FE}
1	L/R	0.24	3.76	-0.22	0.16
2	L/R	-0.51	-1.49	-0.92	-1.11
3	L/R	2.27	-1.80	-0.38	-0.39
4	L/R	-1.05	0.36	-1.22	-0.40
5	L/R	0.09	0.42	-0.90	-0.48
6	R/R	-1.51	1.08	0.37	0.18
7	R/L	-1.71	-0.06	-0.18	0.06
8	R/R	-0.80	0.15	-0.06	0.22
9	R/R	0.32	1.65	0.15	-0.14
10	R/L	-0.98	3.16	0.48	-0.01

FE, forced exercise; MAH, most affected hand; DH, dominant hand.

SUPPLEMENTARY TABLE S3. LOCATION SHIFT IN MILLIMETERS FOR EACH REGION OF INTEREST, FOR EACH SUBJECT, BETWEEN DATA ANALYZED WITH AND WITHOUT SECOND-ORDER MOTION CORRECTION

<i>Subject</i>	<i>Rmot</i>	<i>Rsma</i>	<i>Rthal</i>	<i>Rput</i>	<i>Rgp</i>	<i>Lmot</i>	<i>Lsma</i>	<i>Lthal</i>	<i>Lput</i>	<i>Lgp</i>
1	0	2	10	11	10	0	0	2	3	3
2	10	0	4	0	5	0	5	0	0	7
3	12	0	0	3	0	6	0	0	11	7
4	7	0	4	4	11	7	0	0	26	6
5	0	4	13	2	13	0	2	19	4	5
6	6	2	0	3	6	14	14	0	9	0
7	0	2	25	0	4	0	6	15	15	2
8	17	2	10	4	13	6	4	2	0	0
9	6	3	3	4	3	14	0	0	8	3
10	17	2	4	3	0	0	7	0	4	0

SUPPLEMENTARY TABLE S4. OFF MEDICATION,
ON MEDICATION, AND FORCED EXERCISE UNIFIED
PARKINSON'S DISEASE RATING MOTOR SCALE
AND LEVODOPA-EQUIVALENT DAILY DOSAGE

<i>Patient</i>	<i>UPDRS total</i>			<i>Medication</i>
	<i>Off</i>	<i>Meds</i>	<i>Off+FE</i>	<i>LEDD (mg)</i>
1	49	31	33	900
2	58	26	27	225
3	50	INC	31	300
4	46	23	22	550
5	49	27	24	550
6	51	21	25	650
7	37	50	21	160
8	43	24	18	1864
9	47	30	19	532
10	23	22	7	500
Mean	45.30	28.22	22.70	623.10
SD	9.53	8.86	7.35	486.34

SD, standard deviation; UPDRS, Unified Parkinson's Disease Rating Motor Scale; LEDD, levodopa-equivalent daily dosage.