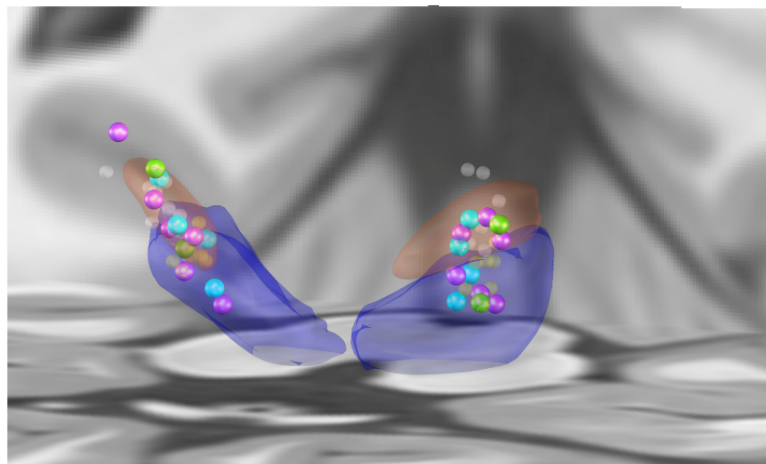
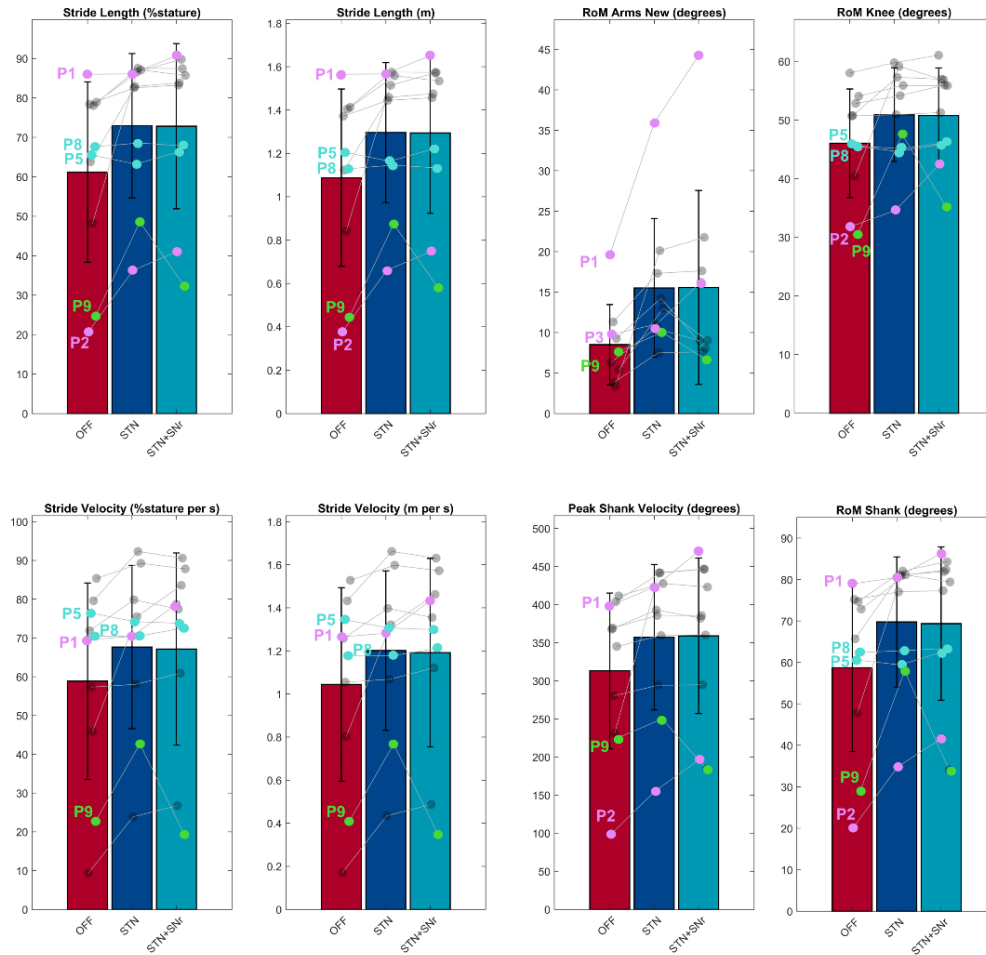
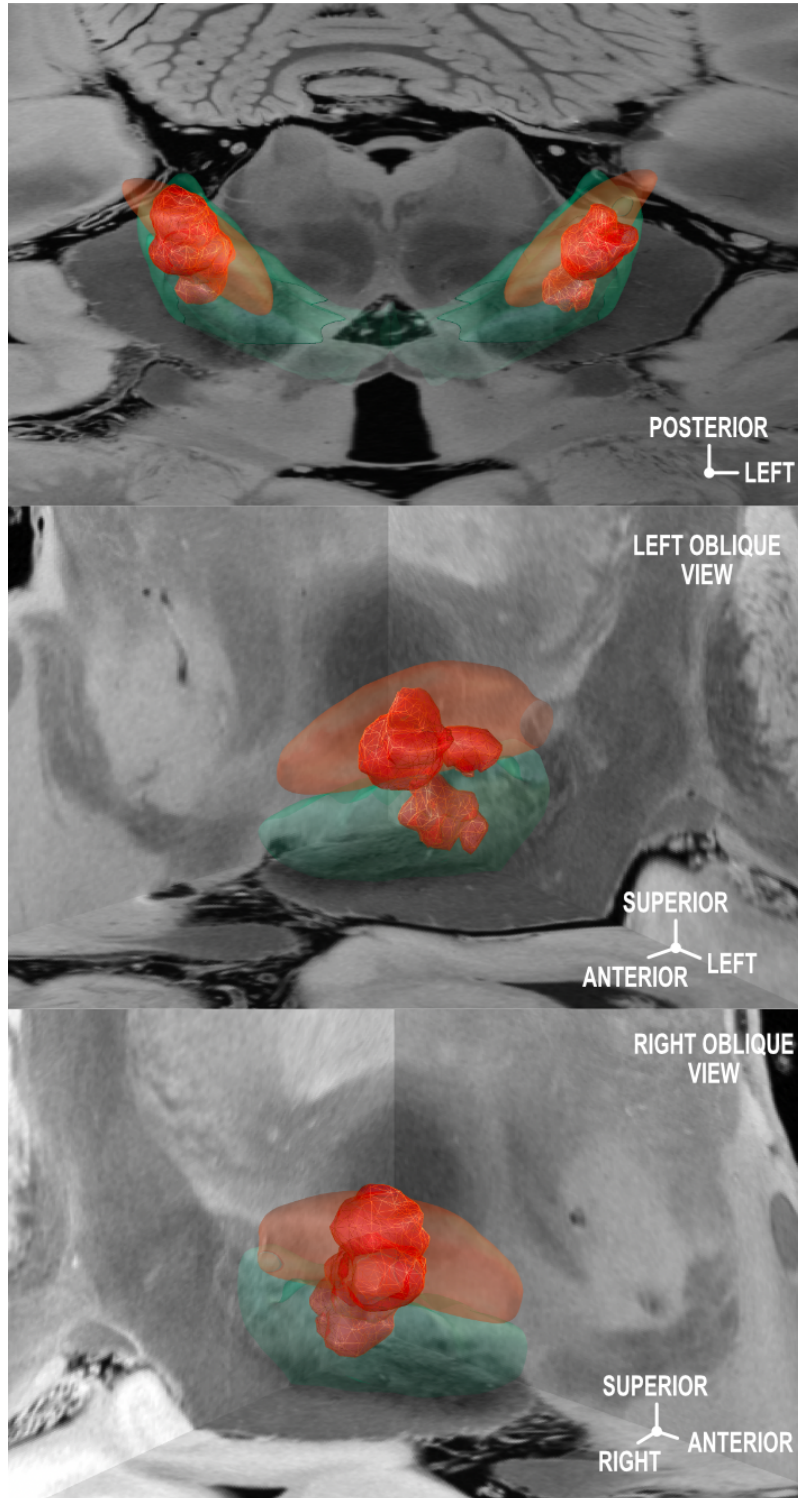


Supplementary Material

Kinematic Effects of Combined Subthalamic and Dorsolateral Nigral Deep Brain Stimulation in Parkinson's Disease



Supplementary Figure 1. Individual changes of all gait parameters that were significantly improved with STN-DBS (dots) superimposed on cohort averages for the three stimulation conditions OFF DBS, STN-DBS and combined STN+SNr DBS. Purple markers highlight individuals where an additional improvement of gait parameters was observed with combined STN+SNr DBS compared to STN DBS. Green markers highlight a patient with consistent deterioration of gait performance with combined STN+SNr DBS. Turquoise markers highlight two patients with almost no change of gait parameters with both STN and STN+SNr DBS. **Bottom panel** shows spatial distribution of active contact pairs corresponding to those individuals, superimposed on an atlas representation of the substantia nigra (DISTAL Atlas [1]).



Supplementary Figure 2. 3D-visualization of the spatial extent of clusters of stimulation volumes of both hemispheres. Upper panel displays coronal view, middle shows clusters of left hemisphere in oblique sagittal view, lower panel shows right hemisphere in oblique sagittal view. Clusters are superimposed on a slice of 7 Tesla MRI of ex vivo human brain at 200 micron resolution [2] and on atlas representations of subthalamic nucleus (orange) and substantia nigra (green) as defined by the DISTAL atlas [1]).

Supplementary Table 1. Gait parameters for walking performance

Gait Parameter ± STD	STN	STN+SNr	OFF	p Friedmann	p STN vs. OFF (Wilcoxon)	p STN vs. STN+SNr (Wilcoxon)
Stride Length (%stature)	72.93 ± 18.29	72.82 ± 20.92	61.18 ± 22.87	0.002	0.010	0.432
Stride Length SI (m)	1.30 ± 0.32	1.29 ± 0.37	1.09 ± 0.41	0.002	0.010	0.432
Stride Velocity (%stature/s)	67.66 ± 21.03	67.14 ± 24.77	58.85 ± 25.36	0.025	0.014	0.557
Stride Velocity SI (m/s)	1.20 ± 0.37	1.19 ± 0.44	1.04 ± 0.45	0.025	0.014	0.557
Cadence (steps/min)	109.54 ± 14.25	107.69 ± 17.11	111.66 ± 24.06	0.741	n.a.	n.a.
Gait Cycle Time (s)	1.12 ± 0.18	1.19 ± 0.30	1.16 ± 0.40	0.741	n.a.	n.a.
Double support (%)	22.66 ± 7.11	25.08 ± 12.66	25.69 ± 16.97	0.905	n.a.	n.a.
Swing (%)	38.67 ± 3.56	37.46 ± 6.33	37.15 ± 8.49	0.905	n.a.	n.a.
Stance (%)	61.33 ± 3.56	62.54 ± 6.33	62.85 ± 8.49	0.905	n.a.	n.a.
RoM Shank (degrees)	69.77 ± 15.68	69.36 ± 18.51	58.74 ± 20.25	0.001	0.006	0.232
RoM Knee (degrees)	50.89 ± 7.99	50.75 ± 8.13	46.03 ± 9.26	0.006	0.020	0.557
RoM Arm (degrees)	15.52 ± 8.1	15.57 ± 11.3	8.51 ± 4.67	0.016	0.004	0.99
RoM Trunk Horiz. (degrees)	5.06 ± 2.68	5.16 ± 2.82	4.61 ± 2.82	0.045	0.084	0.846
RoM Trunk Sagit. (degrees)	4.32 ± 2.05	4.73 ± 2.47	4.14 ± 1.63	0.497	n.a.	n.a.
RoM Trunk Frontal (degrees)	8.15 ± 2.32	8.30 ± 2.82	6.32 ± 2.37	0.273	n.a.	n.a.
Peak Shank Velocity (degrees/s)	357.20 ± 95.39	359.01 ± 102.13	313.08 ± 102.12	0.002	0.002	0.625
Peak Arm Swing Velocity (degrees/s)	143.95 ± 57.29	142.47 ± 77.82	162.20 ± 150.66	0.122	n.a.	n.a.
Peak Horiz. Trunk Velocity (degrees/s)	21.47 ± 10.12	21.64 ± 8.73	21.34 ± 11.88	0.670	n.a.	n.a.
Peak Sagit. Trunk Velocity (degrees/s)	24.48 ± 8.56	24.70 ± 8.32	24.21 ± 11.17	0.497	n.a.	n.a.
Peak Frontal Trunk Velocity (degrees/s)	33.48 ± 7.39	33.08 ± 9.54	29.05 ± 15.06	0.273	n.a.	n.a.

Supplementary Table 2. Gait parameters of turning and transitioning

	Gait Parameter ± STD	STN	STN+SNr	OFF	<i>p</i> Friedmann	<i>p</i> STN vs. OFF (Wilcoxon)	<i>p</i> STN vs. STN+SNr (Wilcoxon)
Turning	Duration (s)	2.76 ± 1.28	3.03 ± 1.21	3.56 ± 1.30	0.001	0.004	0.02
	Number of Steps	5.44 ± 2.92	5.59 ± 2.01	6.61 ± 2.64	0.139	n.a.	n.a.
	Peak Velocity (degrees/s)	153.22 ± 45.55	145.18 ± 45.32	120.42 ± 27.45	0.008	0.004	0.203
	Step Time (s)	0.66 ± 0.13	0.71 ± 0.10	0.63 ± 0.12	0.121	n.a.	n.a.
	Step Time before turn (s)	0.54 ± 0.05	0.51 ± 0.14	0.43 ± 0.06	0.117	n.a.	n.a.
Sit to stand	Peak Velocity (degrees/s)	91.18 ± 31.75	85.40 ± 25.60	64.23 ± 19.48	0.050	0.020	0.496
	Duration (s)	2.21 ± 0.26	2.59 ± 0.66	2.26 ± 0.34	0.460	n.a.	n.a.
	RoM Trunk (degrees)	36.81 ± 13.01	37.11 ± 9.95	28.16 ± 9.78	0.016	0.012	0.99
Turn to sit	Peak Velocity (degrees/s)	155.83 ± 55.25	163.76 ± 53.62	110.51 ± 37.38	0.038	0.016	0.652
	Duration (s)	23.43 ± 4.23	24.96 ± 6.11	32.81 ± 11.04	0.236	n.a.	n.a.
	RoM Trunk (degrees)	20.95 ± 7.34	21.65 ± 7.54	17.08 ± 4.63	0.150	n.a.	n.a.

Supplementary Table 3. Individual characteristics of gait disability

Characterization of clinical phenotype of gait disorder in MedOFF /StimOFF	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7	Patient 8	Patient 9	Patient 10
UPDRS III OFF / ON (%improvement)	30/16 (47%)	37/25 (32%)	23/6 (73%)	48/24 (50%)	32/23 (28%)	31/12 (61%)	41/18 (56%)	56/41 (27%)	40/31 (23%)	28/17 (39%)
Freezing of Gait during TUG	-	-	-	+	+	+	-	+	+	+
Imbalance (postural instability item from UPDRS III)	1	2	0	1	0	0	0	1	1	1
Gait Item from UPDRS III	2	3	1	2	2	2	1	3	3	2
Global hypokinesia item from UPDRS III	2	4	1	3	2	2	1	3	3	2
Decreased Stride Length (Normative: 85.97 % stature \pm 8.13)	o	+++	+	++	++	+++	+	+	+++	+
Decreased Stride velocity (Normative: 85.13 % stature/s \pm 10.11)	++	+++	++	+	+++	+++	+	++	+++	o

REFERENCES

- [1] Ewert S, Plettig P, Li N, Chakravarty MM, Collins DL, Herrington TM, Kühn AA, Horn A (2018) Toward defining deep brain stimulation targets in MNI space: A subcortical atlas based on multimodal MRI, histology and structural connectivity. *Neuroimage* **170**, 271-282.
- [2] Edlow BL, Mareyam A, Horn A, Polimeni JR, Witzel T, Tisdall MD, Augustinack JC, Stockmann JP, Diamond BR, Stevens A, Tirrell LS, Folkerth RD, Wald LL, Fischl B, van der Kouwe A (2019) 7 Tesla MRI of the ex vivo human brain at 100 micron resolution. *Sci Data* **6**, 244.