

**Supplemental Figure 1:** Spatiotemporal gait parameters as relative deviations from respective measures obtained from patients with ET and no subjective gait disorder. (ET CONTROLS, black dotted line). Three stimulation conditions are depicted: ON bilateral deep brain stimulation (red line and area), instantly after unilateral deactivation of the DBS lead corresponding to the non-dominant hand (INSTANT – blue dashed line and area) and after prolonged deactivation over night (OVERNIGHT – green dashed line and area).

\* Indicates significant differences of gait parameters ON DBS compared with ET CONTROLs. p-values were adjusted for multiple comparisons using false discovery rate.

**Supplementary Table 1 – Spatial and temporal gait parameters**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Parameter**  **± 1 SD** | **Controls** | **ET ON** | **ET INSTANT** | **ET OVERNIGHT** | **p ANOVA**  **(Friedmann)** | **p ET Control vs. ET ON**  **(Mann-Whitney-U)**  *FDR-adjusted* |
| Stride length  [% stature] | 83,19  ±5,81 | 73,16  ±13,65 | 72,95  ±13,22 | 72,96  ±10,12 | 0,74 | 0,21 |
| Stride length  [m] | 1,45  ±0,17 | 1,22  ±0,24 | 1,21  ±0,24 | 1,21  ±0,18 | 0,74# | 0,14# |
| Stride velocity [%stature/s] | 75,98  ±5,07 | 66,66  ±14,46 | 63,38  ±14,78 | 64,78  ±9,29 | 0,20 | 0,29 |
| Stride velocity [m/s] | 1,32  ±0,12 | 1,11  ±0,25 | 1,05  ±0,25 | 1,07  ±0,16 | 0,20# | 0,14# |
| Stride time  [s] | 1,10  ±0,06 | 1,11  ±0,08 | 1,17  ±0,09 | 1,13  ±0,05 | 0,03 | 0,85 |
| Cadence  [steps/min] | 109,82  ±5,95 | 108,95  ±7,49 | 103,51  ±7,74 | 106,55  ±4,46 | 0,03 | 0,85 |
| Double support % gait cycle | 19,58  ±3,40 | 24,41  ±5,98 | 25,52  ±4,45 | 23,88  ±4,53 | 0,045 | 0,28 |
| Swing  % gait cycle | 40,21  ±1,70 | 37,80  ±2,99 | 37,24  ±2,23 | 38,06  ±2,27 | 0,045 | 0,28 |
| Stance  % gait cycle | 59,79  ±1,70 | 62,20  ±2,99 | 62,76  ±2,23 | 61,94  ±2,27 | 0,045 | 0,28 |
| RoM Shank [degrees] | 78,33  ±6,15 | 68,60  ±12,57 | 67,96  ±12,64 | 68,05  ±9,71 | 0,67 | 0,21 |
| RoM Knee [degrees] | 54,47  ±4,31 | 51,57  ±7,30 | 51,29  ±7,77 | 51,22  ±5,63 | 0,16 | 0,28 |
| RoM Trunk  Horizontal [degrees] | 4,96  ±1,77 | 8,21  ±2,91 | 7,70  ±2,80 | 7,60  ±2,34 | 0,49 | 0,21 |
| RoM Trunk  Sagittal [degrees] | 3,07  ±0,59 | 5,13  ±1,69 | 5,00  ±1,44 | 5,28  ±1,40 | 0,49 | **0,02** |
| RoM Trunk Frontal  [degrees] | 6,34  ±2,02 | 11,18  ±6,26 | 11,45  ±4,48 | 11,97  ±4,41 | 0,27 | 0,21 |

**Supplementary Table 1** – Variability of gait parameters of patients with essential tremor undergoing unilateral withdrawal of deep brain stimulation (ET) and controls with unaffected gait (Controls). Values in % ± 1 SD.

**ET ON** – assessment with initial stimulation parameter setting, **ET DBS INSTANT** – instant assessment after deactivation of unilateral deep brain stimulation contacts corresponding to the non-dominant hand, **ET OVERNIGHT** - assessment after overnight deactivation of unilateral deep brain stimulation contacts corresponding to the non-dominant hand **RoM** – Range of motion, **SD** – standard deviation. # only one p-value of stride length and stride velocity (SI or relative to stature) was included in FDR adjustment.

**Supplementary Table 2 – Coefficient of Variability of spatial and temporal gait parameters**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **CoV Parameter [%]**  **± 1 SD** | **Controls** | **ET ON** | **ET INSTANT** | **ET OVERNIGHT** | **p ANOVA**  **(Friedmann)** | **p ET Control vs. ET ON**  **(Mann-Whitney-U)**  *FDR-adjusted* |
| Stride length  [% stature] | 2,06  ±0,83 | 4,39  ±2,11 | 4,03  ±2,98 | 3,06  ±1,55 | **0,007** | **0,021** |
| Stride length  [m] | 2,06  ±0,83 | 4,39  ±2,11 | 4,03  ±2,98 | 3,06  ±1,55 | **0,007#** | **0,021#** |
| Stride velocity [%stature/s] | 2,90  ±1,16 | 5,27  ±2,88 | 5,60  ±3,85 | 4,81  ±2,00 | 0,50 | 0,077 |
| Stride velocity [m/s] | 2,90  ±1,16 | 5,27  ±2,88 | 5,60  ±3,85 | 4,81  ±2,00 | 0,50 | 0,077**#** |
| Stride time [s] | 1,91  ±0,85 | 3,28  ±1,56 | 3,71  ±1,85 | 3,39  ±0,96 | 0,50 | 0,075 |
| Cadence [steps/min] | 1,90  ±0,86 | 3,26  ±1,51 | 3,70  ±1,79 | 3,38  ±0,96 | 0,74 | 0,075 |
| Double support | 11,34  ±3,59 | 10,73  ±4,05 | 12,31  ±7,82 | 9,83  ±4,93 | 0,74 | 0,739 |
| Swing % | 2,78  ±1,15 | 3,44  ±1,42 | 4,18  ±2,45 | 3,11  ±1,74 | 0,67 | 0,739 |
| Stance % | 1,84  ±0,68 | 2,05  ±0,73 | 2,46  ±1,48 | 1,88  ±1,00 | 0,90 | 0,791 |
| RoM Shank [degrees] | 1,54  ±1,09 | 2,98  ±1,04 | 2,76  ±2,01 | 2,40  ±0,96 | 0,14 | **0,021** |
| RoM Knee [degrees] | 2,76  ±0,96 | 4,08  ±1,35 | 4,35  ±1,98 | 3,99  ±1,19 | 0,90 | 0,077 |
| RoM Trunk  Horizontal [degrees] | 17,34  ±8,16 | 20,58  ±13,28 | 22,58  ±8,48 | 19,77  ±6,97 | 0,14 | 0,739 |
| RoM Trunk  Sagittal [degrees] | 18,70  ±2,85 | 22,65  ±3,69 | 22,04  ±4,38 | 18,99  ±5,30 | 0,08 | 0,075 |
| RoM Trunk Frontal  [degrees] | 18,46  ±7,76 | 23,06  ±10,75 | 19,97  ±6,09 | 19,29  ±5,53 | 0,40 | 0,279 |

**Supplementary Table 2** – Variability of gait parameters of patients with essential tremor undergoing unilateral withdrawal of deep brain stimulation (ET) and controls with unaffected gait (Controls). Values in % ± 1 SD.

**CoV** – Coefficient of Variation, **ET ON** – assessment with initial stimulation parameter setting, **ET DBS INSTANT** – instant assessment after deactivation of unilateral deep brain stimulation contacts corresponding to the non-dominant hand, **ET OVERNIGHT** - assessment after overnight deactivation of unilateral deep brain stimulation contacts corresponding to the non-dominant hand **RoM** – Range of motion, **SD** – standard deviation

# only one p-value of stride length and stride velocity (SI or relative to stature) was included in FDR adjustment.

**Supplemental Table 3 – Clinical details of control cohort**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Control** | **Sex** | **Age** | **Disease duration in years** | **Months since DBS surgery** | **TRS** | **SARA axial subscore** | **Medication relevant for tremor** |
| **Patient 1** | M | 67 | 25 | 15 | 29 | 1 | - |
| **Patient 2** | M | 72 | 60 | 19 | 31 | 3 | Metoprolol 47,5mg 1-0-0 |
| **Patient 3** | F | 72 | 57 | 69 | 15 | 0 | Metoprolol 47,5mg 1-0-0,  Gabapentin 400mg 1-1-1-1 |
| **Patient 4** | M | 64 | 54 | 60 | 30 | 2 | Propanolol 100mg 1-0-0,  Primidon 250mg 1-0-0 |
| **Patient 5** | M | 57 | 44 | 117 | 25 | 0 | Gabapentin 600mg 1-0-1 |
| **Patient 6** | M | 48 | 18 | 67 | 38 | 0 | Primidon 125mg 1-1-0,  Propanolol 25mg 1-1-0 |
| **Patient 7** | M | 47 | 33 | 48 | 13 | 2 | Primidon 250mg 0-0-1/4 |
| **Patient 8** | F | 82 | 57 | 61 | 40 | 1 | Gabapentin 300mg 1-1-1-1 |
| **Patient 9** | F | 66 | 46 | 13 | 33 | 2 | Propanolol 40mg 1-0-1 |
| **Patient 10** | M | 59 | 39 | 109 | 19 | 0 | Gabapentin 300mg 1-0-1  Doxepin 25mg 0-0-1 |
| **average** |  | **63,4±10.4** | **43.3±13.7** | **57.8±34.3** | **27.3±8.7** | **1.1±1.0** |  |

**Clinical details of control cohort**

**DBS** – deep brain stimulation, **TRS** – Tremor rating scale, **SARA** - Scale for the assessment and rating of ataxia, **F**- female; **M** – male

**Supplement 1 – Visualization of fiber tracts**

Discriminative fiber tracts for modulation of behavioral scores and gait characteristics were determined using the built-in pipeline of Lead DBS V2.3 (Horn et al., 2019b) based on an approach described previously in Irmen et al.(Irmen et al., 2020) . In short, the electric field (E-field) describing gradient of electrical charge surrounding each active stimulation contact were estimated using the finite element method on a four-compartment (gray & white matter, insulating and metal parts) tetraedral mesh (Horn et al., 2017). E-Fields were estimated in native patient space and warped into MNI space using aforementioned deformation fields. An atlas of the basal ganglia pathways that had been manually curated by expert anatomists based on histological ground data and a holographic interaction system(Petersen et al., 2019) was ported into the same space using Lead-DBS. The analysis was calculated iteratively for a total of 28,600 tracts represented in the atlas (which compose a total of 28 bilateral anatomical bundles). For each tract, the average E-field vector magnitude overlaps were denoted while passing through each patient’s stimulation field (termed *tract modulation strength* in the following). For instance, if a tract traversed through the center of one patient’s E-Field and through the periphery of a second one, the average values during this passage (in V/mm) were denoted for each tract. Tracts that did not pass at least one E-Field with an average value above 100V/mm were automatically discarded. For each tract, the modulation strengths across patients were rank-correlated with relative changes in outcomes (see below). As a result, each tract could be assigned a Spearman’s rank correlation coefficient which was used to tag and color-code tracts that were positively or negatively associated with outcomes. This was done for only the stimulation electrodes that were *deactivated* during withdrawal, assuming the deactivation would drive the change in modulation. As all subjects were right-handed, in all subject the right-hemispherical electrodes were deactivated. The procedure was then repeated in a leave-one-patient out design to crossvalidate results. Here, sum overlaps with the left-out E-Fields and the tract model (tracts weighted with positive or negative correlation coefficients) were used to cross-predict variance in clinical and behavioral changes.