Deep brain stimulation improves gait velocity acutely in patients with Parkinson's disease

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Background

• Deep brain stimulation (DBS) in patients with Parkinson's disease (PD) is highly effective for appendicular symptoms (tremor, rigidity, bradykinesia, dyskinesia), but gait response is less predictable. Here we hypothesize that subthalamic nucleus (STN) and globus pallidus internus (GPi) DBS treatment exerts acute and chronic effects on gait and that the effects are related to the location of the active contact in the targeted nucleus.

• Our long-term goal is to develop a comprehensive DBS programming algorithm for improvement of gait in PD patients that is based on DBS lead location and its effects on stimulated neuronal tissue.

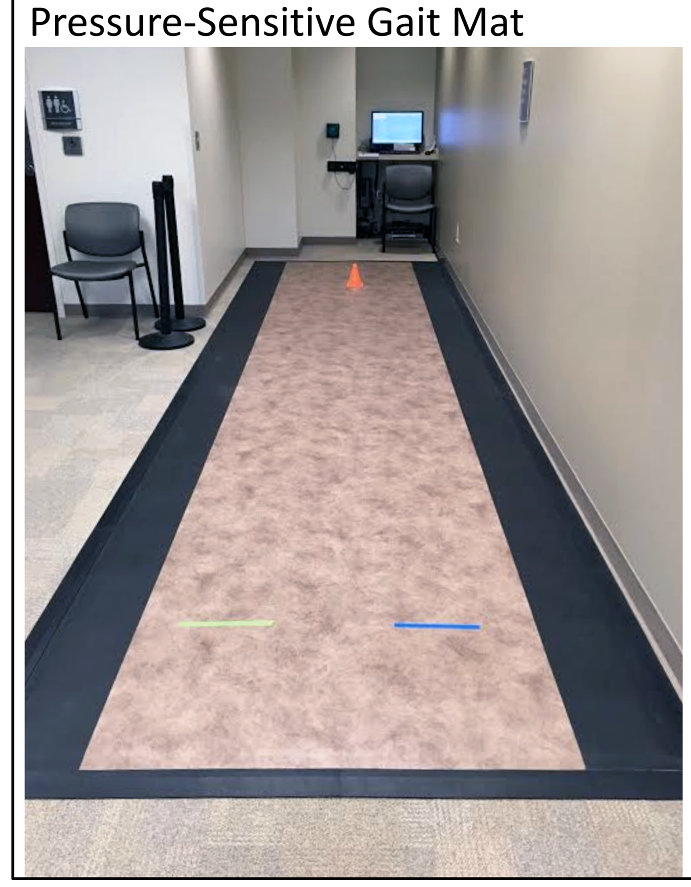
Objectives: To systematically investigate the acute (5 minutes) and chronic (1 month) effects of DBS of STN and GPi on gait velocity in patients with PD.

METHODS – Gait Mat measurements

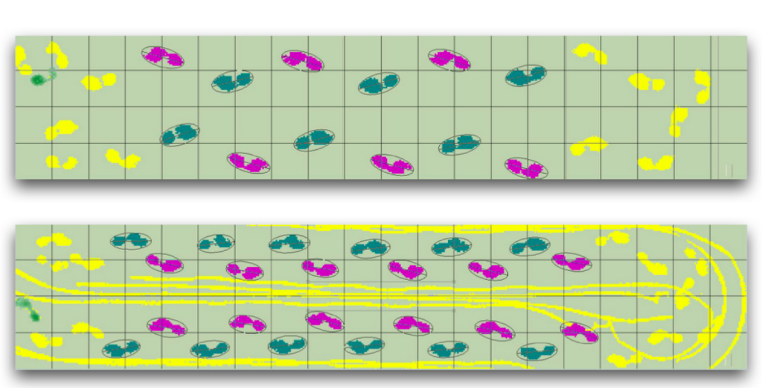
• Quantitative gait metrics were collected at initial DBS programming visit and at 1-month follow up using a pressure sensitive walkway (Protokinetics Zeno, Fig. 1).
• Measurements were obtained before device activation, after monopolar mapping and device off, after 5 minutes of DBS and after 1 month of DBS (same settings; off dopaminergic medications at all time points).
• Patients performed 2-4 walks with left and right turns. Gait velocity during straight walking was the primary outcome (Fig. 1).
• If patients could not walk without assistance of a person, they were classified as non-ambulatory and excluded from quantitative analyses for that time point.
• Linear mixed model was applied for statistical analysis of gait velocity data

Fig. 1

Pressure-Sensitive Gait Mat



Computer-guided processing to convert pressure maps into footfalls/ gait outcomes



Custom R / REDCap software for data management

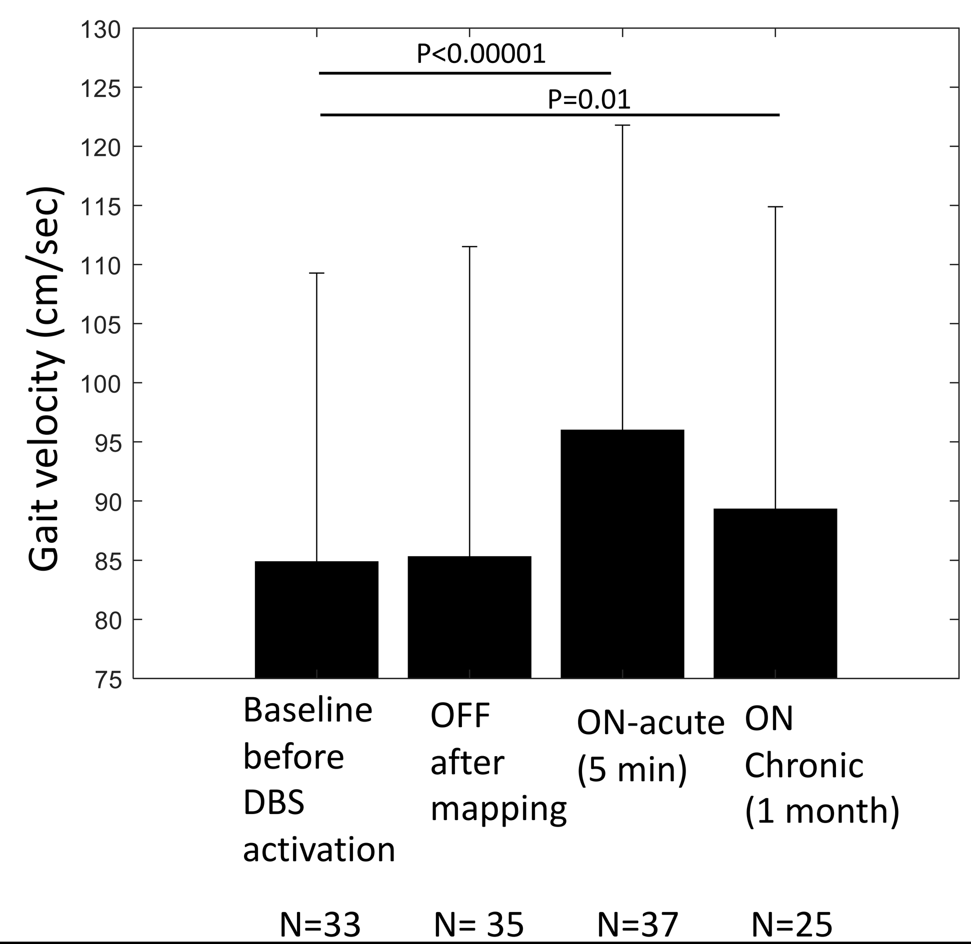
RESULTS – Gait Velocity

	All	STN	GPi
N*	40	19	21
Age	65.2±8.7	60.5±9.5	69.4±5.3
Gender	10W/30M	3W/16M	7W/14M
Dx durat (yrs)	12.6±8.0	12.0±10.6	13.1±4.6
Bilateral	23	11	12
Unilateral	14	8	6
Second side	3	0	3

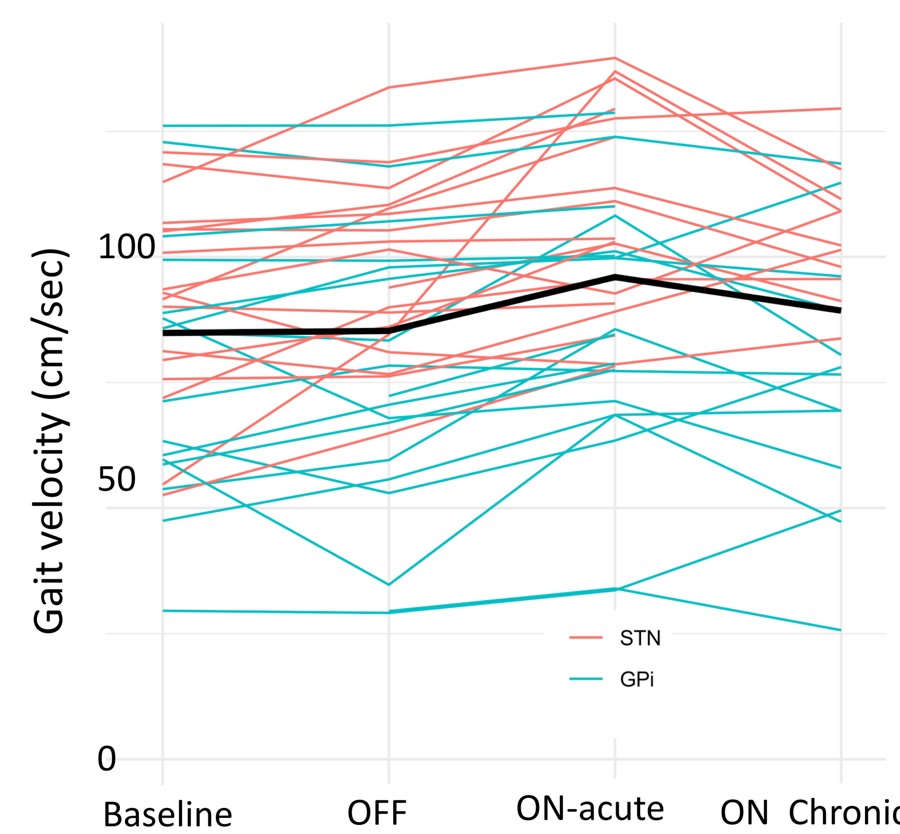
* 2 patients were non-ambulatory at all timepoints

• DBS activation resulted in statistically significant improvement at the acute and chronic time point (Fig.2).
• Acute clinically meaningful improvement (>5 cm/sec) was seen in 23/33 patients (69%). For 27 patients who had chronic follow up data, 14 (52%) improved, 9 (33%) had no change, and 4/27 (15%) worsened compared to baseline (Fig.2).
• 5 cm/sec is considered a clinically meaningful difference in gait velocity
• Listed clinical variables did not correlate with gait velocity change

Fig. 2

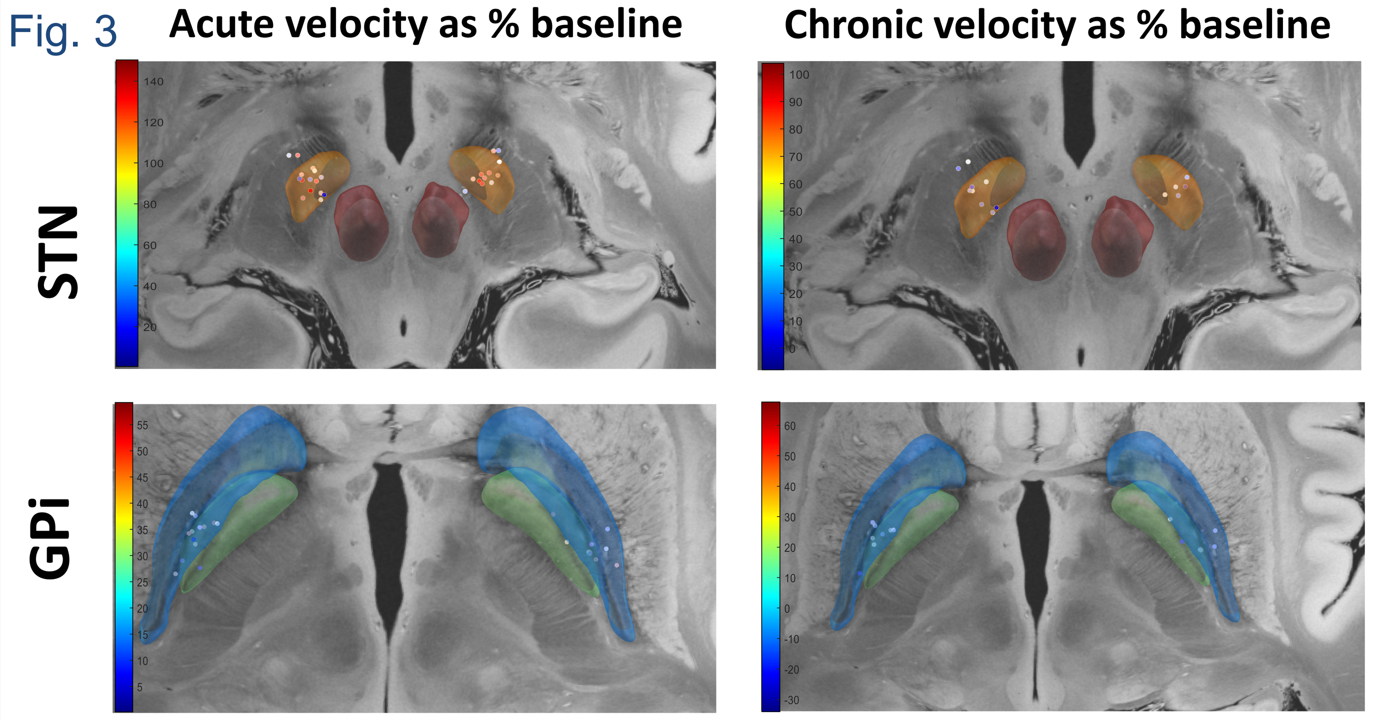


Single subject data by target. Mean is plotted in bold.



RESULTS – Active contact localization

Fig. 3

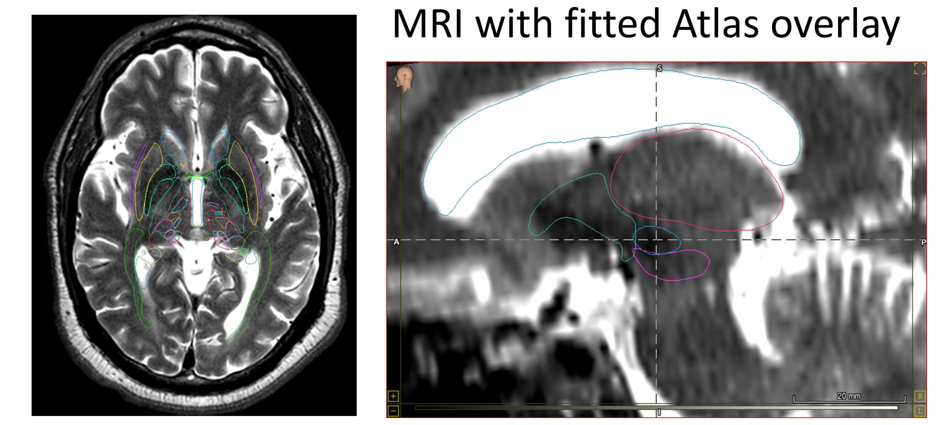


Each dot represents patient's active contact location in normalized brain space (STN: orange, top; Gpi: green, bottom). The color of the dot represents percent change from baseline for acute (left) and chronic (right).

• Chi-square analysis of active contact quadrant (DL, DM, VL, VM) and velocity change was not significant for either left or right brain hemispheres in either STN or GPi.

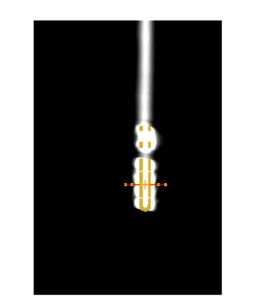
METHODS – DBS lead contact localization

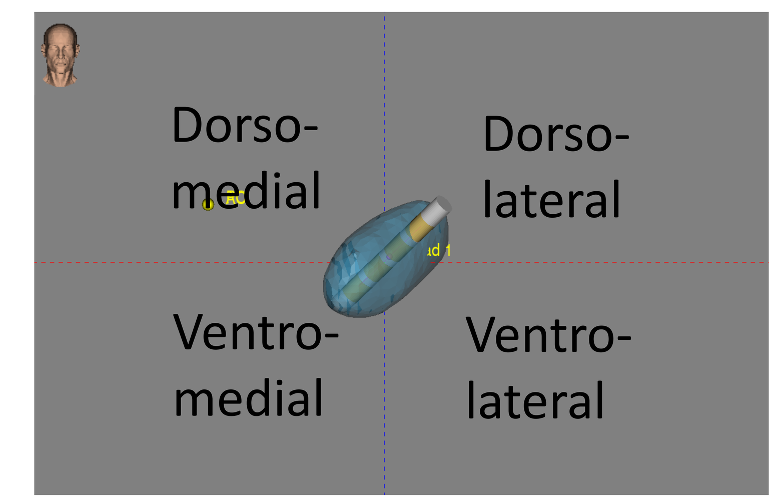
MRI with fitted Atlas overlay



• Each patient's pre-operative MRI was nonlinearly co-registered to an atlas in CranialVault software.
• Postoperative CT was used to semi-automatically localize the DBS lead in the brain, after CT to MRI co-registration.

CT lead artifact





• The active contacts were categorized in reference to the center of gravity of the nucleus of interest and divided into dorso-lateral (DL), ventro-lateral (VL), dorso-medial (DM) and ventro-medial quadrants for the left and right hemispheres.
• This division was chosen because DM quadrant corresponds to somatotopic leg area in the STN and GPi.

• Lead-DBS software was used to visualize all active contacts in a normalized brain space (MNI).
• Heat map indicates percent velocity change from baseline, calculated as:
100* (Velocity_ON-Velocity_Baseline) / Velocity_Baseline
• Chi-square was applied for statistical analysis of quadrant location (4 quadrants) with patients divided into tertiles (top, medium, bottom) based on percent velocity change.

CONCLUSIONS

• On a group level, gait velocity increased statistically significantly within minutes of DBS initiation. This effect was reduced but still significant at 1 month follow up.
• Very few patients demonstrated deterioration (4/27) with acute and/or chronic stimulation.
• The rapid improvement is consistent with immediate reduction of pathologic beta-band neural activity. The lack of significant change between baseline and OFF would argue against a practice effect but a placebo effect cannot be excluded.
• Sustained improvement may require reorganization of underlying neuronal networks which was not observed in all patients. This could be due to suboptimal stimulation settings (lower amplitude) at the initial programming. Longer follow with optimization of the DBS settings is necessary to determine the effect of chronic DBS therapy.
• There was no effect of target nucleus or active contact location (nucleus quadrant) on gait velocity.

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