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Decrease in neuronal firing rate in the STN after microelectrode insertion during DBS surgery for Parkinson's disease

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Introduction

Background

Characterization of electrophysiological recordings during deep brain stimulation (DBS) surgery is critical for anatomical targeting and is extensively utilized to investigate physiologic markers of Parkinson's Disease (PD).[1,2] Transient improvement in clinical symptoms has been reported after microelectrode penetration, but the mechanism(s) underlying this improvement are not well understood.[3] DBS treatment leads to a suppression of the increased tonic firing rates of the Subthalamic Nucleus (STN) for PD.[4] Thus, we sought to determine the acute electrophysiologic effects of microelectrode penetration in the STN.

Methods

Patients

We obtained microelectrode recordings from six patients with advanced PD who underwent surgical implantation of bilateral DBS electrodes in the STN.

Microelectrode Recordings

Single- (SU) and multi-unit (MU) recordings were collected beginning at the entrance of the dorsal border of the STN as determined by electrophysiological criteria.[5,6] These recordings were 8 seconds in duration and were obtained at 0.3mm steps until the ventral border was reached (Figure 1). The microelectrode was then extracted in a step-wise fashion using 0.3mm-step increments to ensure repeat 8-second recordings obtained from the same anatomic positions.

Data Pre-processing and Analysis

Data was processed and analyzed in MATLAB 2020a using custom scripts and the Fieldtrip toolbox. Significance was determined using Wilcoxon signed-rank nonparametric tests. A p-value of <0.05 was deemed statistically significant.

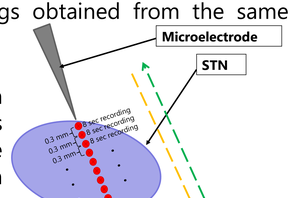

Figure 1 - Path of recordings (orange line representing direction of insertion; green line representing direction of extraction; red targets indicating recording locations; not to scale).

Hypothesis: Microelectrode penetration will cause decreased firing rates in single-/multi-unit recordings.

Patient Demographics

Patient	Age/Gender	Handedness	Sx Dominant Side	Disease duration/yrs	Awake/Asleep
STN 1	62M	RHD	Right (bilateral)	9	Awake
STN 2	46M	RHD	Right	9	Awake
STN 3	57F	LHD	Right	~20	Asleep
STN 4	65F	RHD	Right	5	Awake
STN 5	81M	RHD	Bilateral	8	Asleep
STN 6	53M	RHD	Right (bilateral)	9	Awake

Methods (Cont.)

Waveforms were filtered and thresholded to obtain timepoints for spikes processed by sliding rectangular window functions along the spike trains to determine firing rates for each 8-second recording. Waveform analysis performed to filter out noise causing artifacts prior to performing data analyses. The MU firing rates for each location were then normalized by converting raw rates to a % rate between extraction and insertion recordings. All patient data was then pooled for larger data analysis.

Results

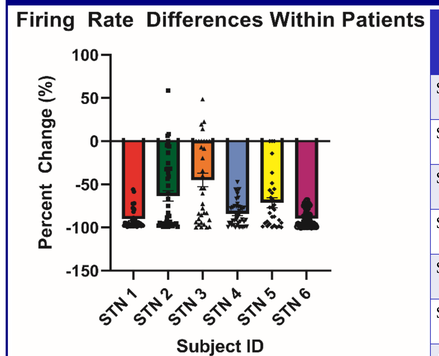

Figure 2 – Percent differences (bars) in firing rates during insertion of microelectrode compared to those during extraction of microelectrode for each patient's recordings (both hemispheres combined).

Patient	FR Median (Left)	FR Median (Right)	FR Median (Both)
STN 1	I : 107.1 E: 13.3	I: 83.3 E: 3.1	I: 91.8 E: 5.1
STN 2	I: 99.4 E: 10.1	I: 88.9 E: 7.6	I: 98.1 E: 9.3
STN 3	I: 3.6 E: 2.9	I: 8.6 E: 6	I: 6.3 E: 4.3
STN 4	I: 57.4 E: 6	I: 14.8 E: 0.9	I: 18.3 E: 2.6
STN 5	I: 7.3 E:1.9	I: 36.3 E: 5.7	I: 17.4 E: 3.1
STN 6	I: 134.8 E: 5.9	I: 138.3 E: 8.3	I: 138.3 E: 7.1
ALL DATA	**I: 59.4 E: 6.8**	**I: 49.6 E: 4.9**	**I: 55.9 E: 5.9**

Table 1 – Median firing rates (spikes per sec) of recordings during insertion (I) and during extraction (E) of the microelectrode.

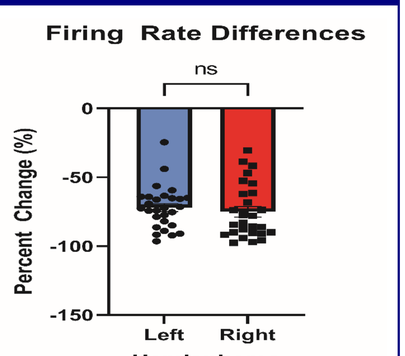

Figure 3 – Percent differences in firing rates within the left and right hemispheres of all patients combined (pooled data).

Summary of Results

Pooled Firing Rate Data

- Significant decrease in firing rate during extraction compared to insertion of microelectrode (5.9 vs. 55.9 spikes/second)
  - Data significant at $p<0.0001$ (One-sample Wilcoxon signed-rank test; n=242)

Left Hemisphere vs Right Hemisphere

- No significant difference between left and right hemisphere data ($p = 0.36$), thus combined for overall analysis

Conclusions & Future Directions

Conclusions

- There is an effect of microelectrode penetration on the single-/multi-unit activity in electrophysiologic recordings of the STN:
  - Could represent an electrophysiologic effect produced by a lesion from penetration
  - May be related to electrophysiologic changes from subthalamotomies
  - However, unable to determine if only a transient effect

Future Studies

- Larger sample size to verify results
- Longer recording times to determine transience vs permanence of effect
  - Long-term recordings from implantable electrode
- More brain locations to expand generalizability
- Correlate with clinical outcomes for potential predictive modeling
- Spike-field correlational analyses

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