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Background

What is Parkinson's Disease?

- Is a degenerative disease of the brain.
- The death of dopaminergic neurons in the substantia nigra results in altered activity patterns within the basal-ganglia-thalamo-cortical network.
- The basal ganglia is a group of nuclei in the brain that are involved in the modulation of voluntary movement.
- The cause of cell death in the substantia nigra and how this cell death leads to symptoms is still unknown.

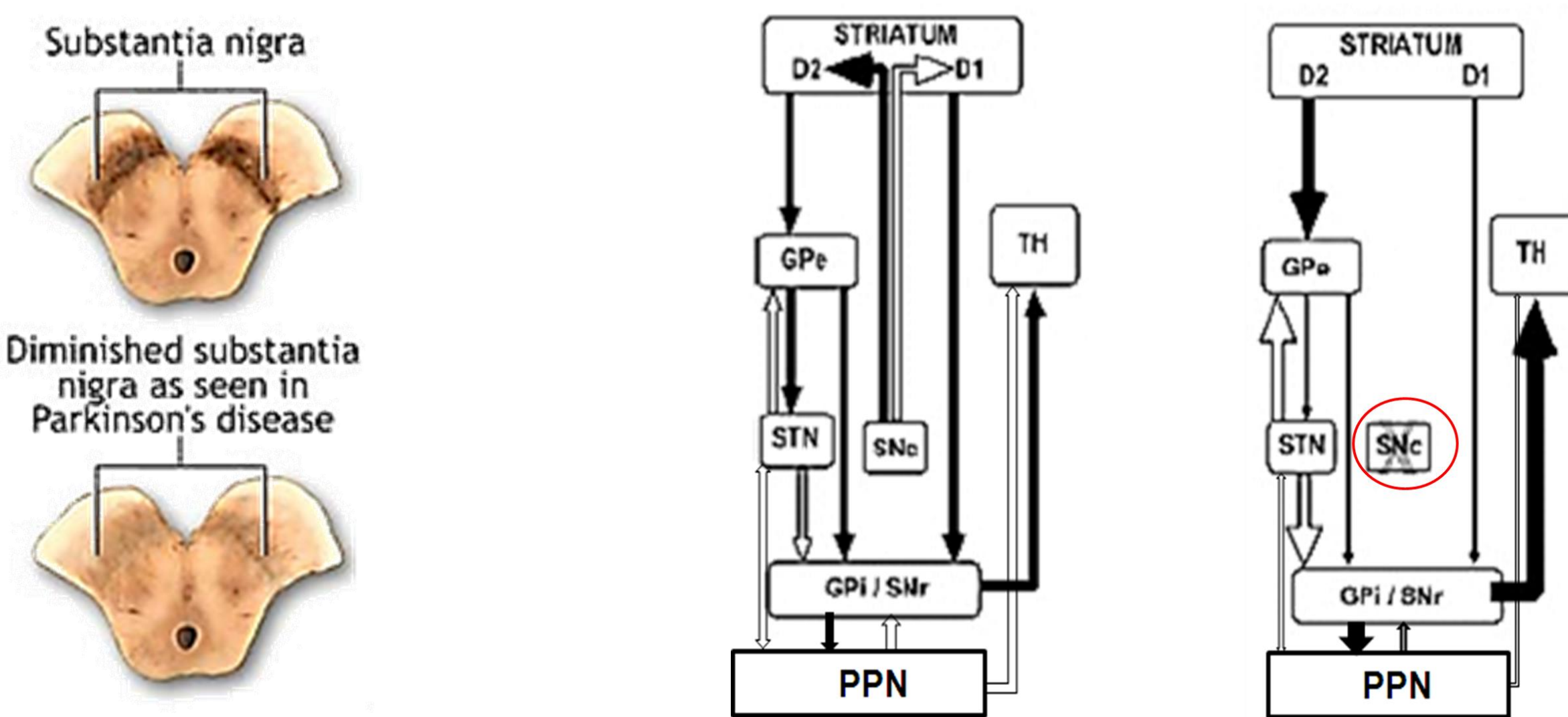


Figure 1: (left) An image of normal vs. PD substantia nigra. (right) Schematic diagram of the basal-ganglia-thalamo-cortical network in the normal and parkinsonian state.

Phenotypes

- People with Parkinson's Disease can present a range of symptoms including: involuntary tremors in the extremities, rigidity of major joints, slow movement, abnormal posture and balance issues.
- The combination of symptoms, severity and progression of the disease is different for every patient.
- Based on the predominant symptoms expressed by a patient, PD can be categorized as Tremor dominant (TD), akinetic-rigid (AR) or combination.
- Gait and balance disorders as well as cognitive impairments can develop as the disease progresses.

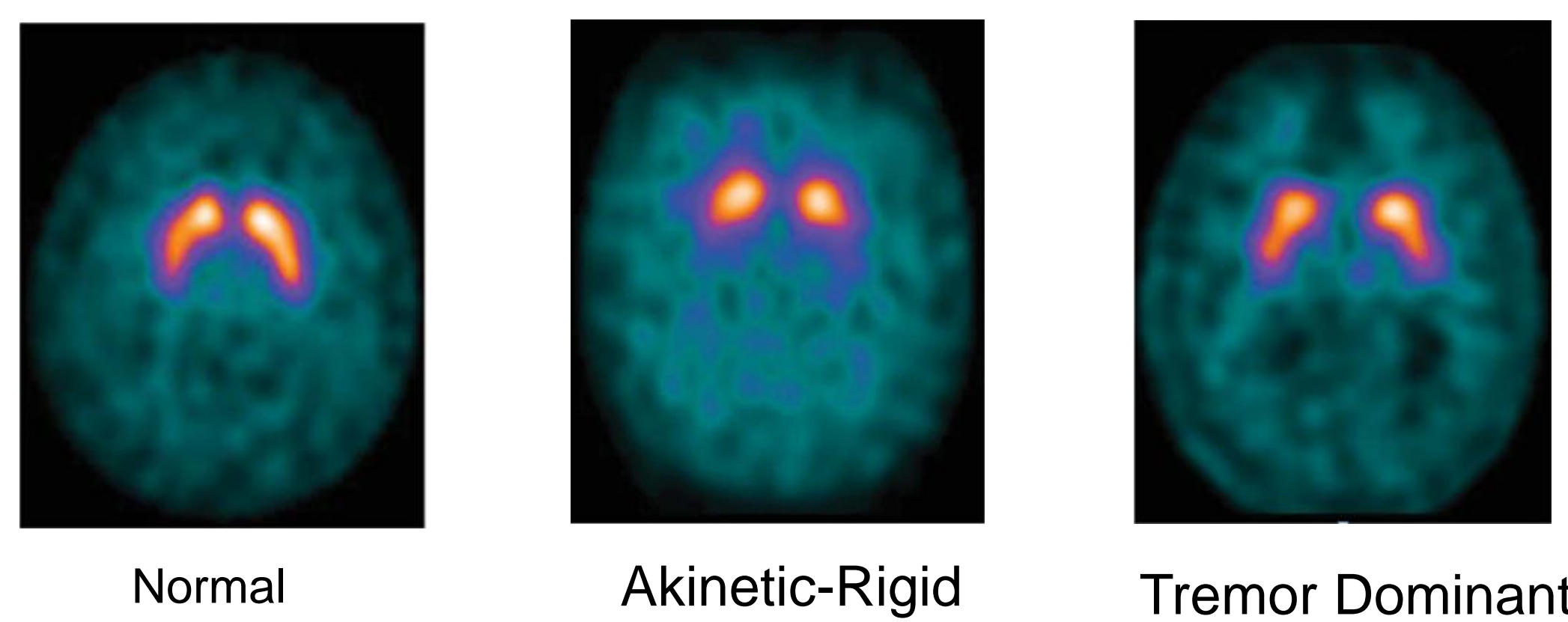


Figure 2: Dopamine uptake patterns in the caudate and putamen showing anatomical differences between the two PD subtypes¹.

Objective

To quantify the differences in the neuronal firing patterns of akinetic rigid and tremor dominant types of Parkinson's disease.

Methods

- Patients enrolled to receive either a lesion or deep brain stimulation lead implant in the pallidum or sub-thalamic nucleus, to alleviate parkinsonian symptoms, were identified from a clinical database.
- They were categorized as tremor dominant or akinetic rigid based on their unified PD rating score.
- Activity of single neurons was isolated from electrophysiology signals recorded during surgical targeting of the nuclei.
- Discharge rate, presence and nature of bursting activity and power spectrum was computed for each neuron.

Table 1: The number of patients and cells analyzed from each nuclei for the two groups.

	Number of Patients	External Globus Pallidus (GPe)	Internal Globus Pallidus (GPi)	Sub-thalamic Nucleus (STN)
Akinetic-rigid	53	203	163	202
Tremor dominant	21	83	49	113

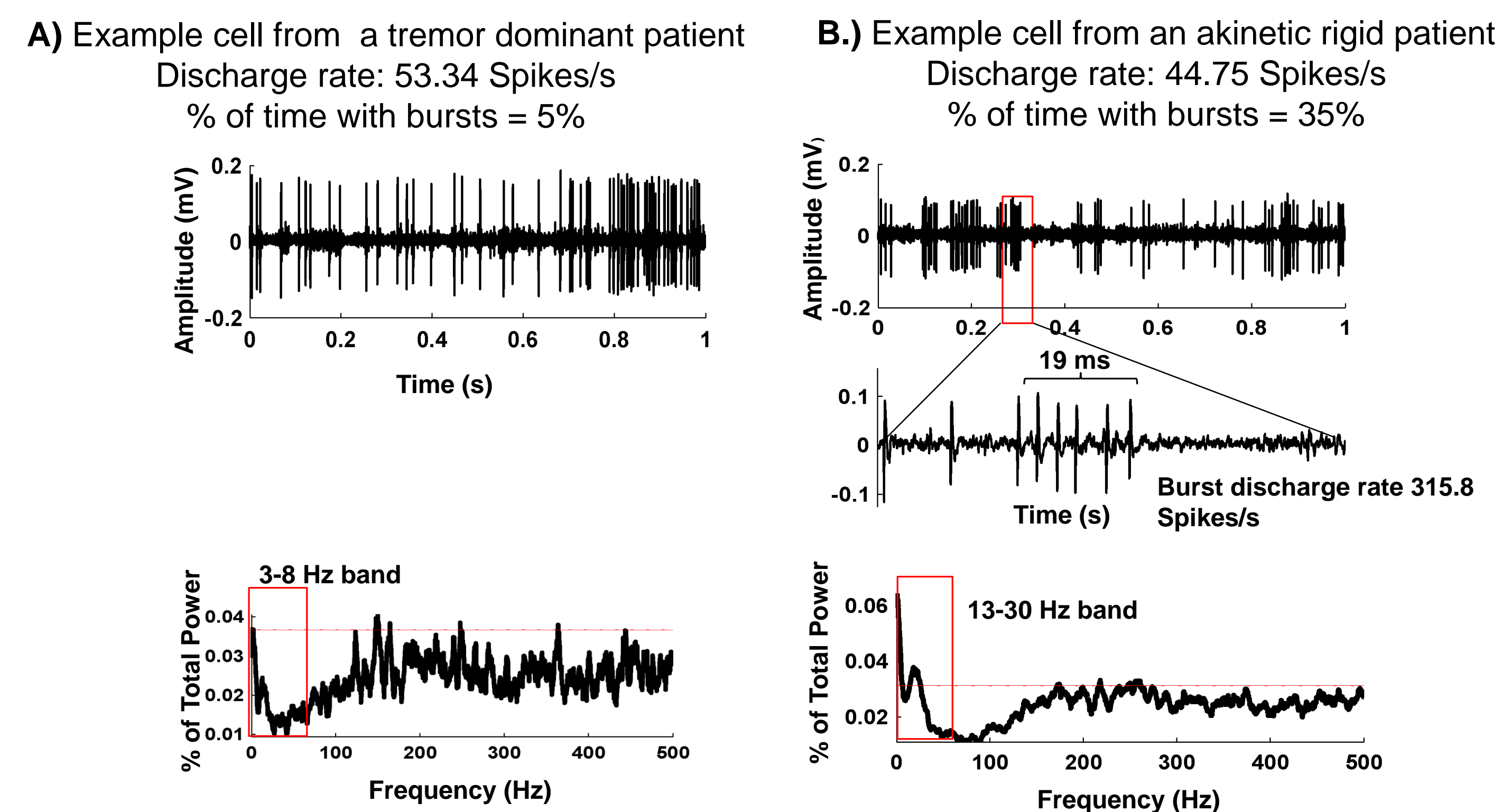


Figure 3: Two neural recordings with firing rate, burst analysis and power spectral density analysis. (A) is a neuron from a tremor-dominant patient showing oscillations at the tremor frequency (3-8 Hz). (B) is an example neuronal activity from an akinetic-rigid patient showing oscillations 13-30 Hz band, which is known to be pathological in PD.

Results

Firing Rate

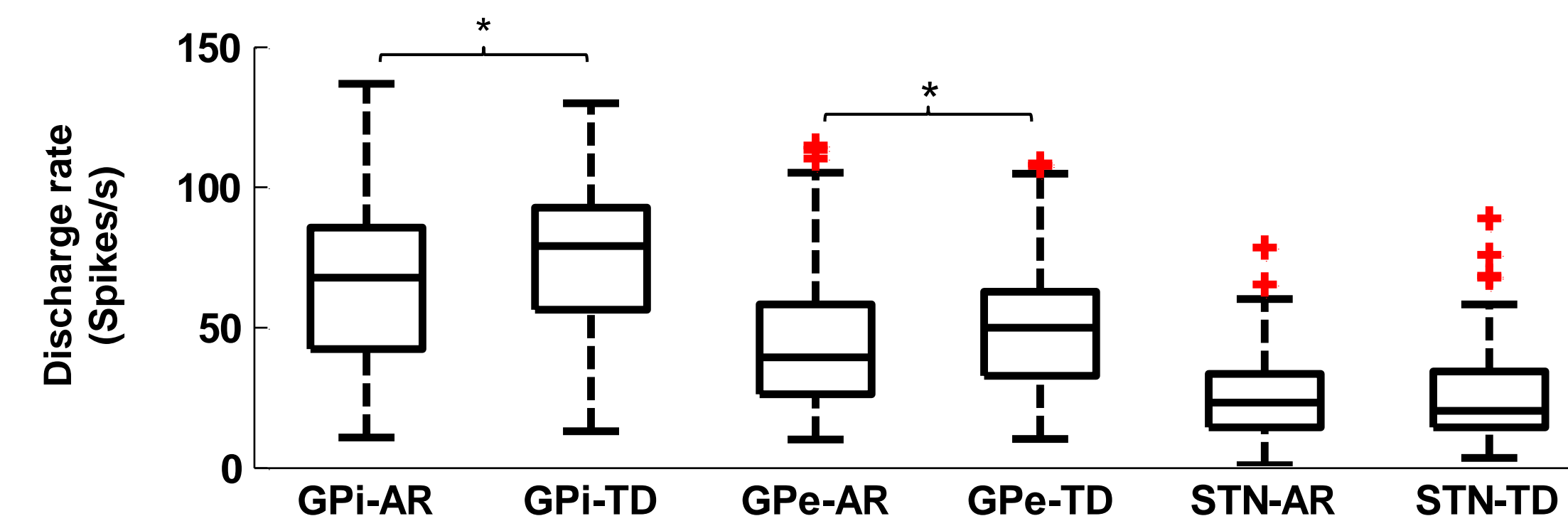


Figure 4: Discharge rates of the cells from each nuclei for both PD subsets. Comparison of discharge rates between tremor-dominant and akinetic-rigid groups was done using the non-parametric Wilcoxon rank sum test. (*p<0.05)

References

1.) Eggers, C., Kahraman, D., Fink, G. R., Schmidt, M. and Timmermann, L. (2011), Akinetic-rigid and tremor-dominant Parkinson's disease patients show different patterns of FP-CIT Single photon emission computed tomography. *Mov. Disord.*, 26: 416-423. doi: 10.1002/mds.23468

Burst Analysis

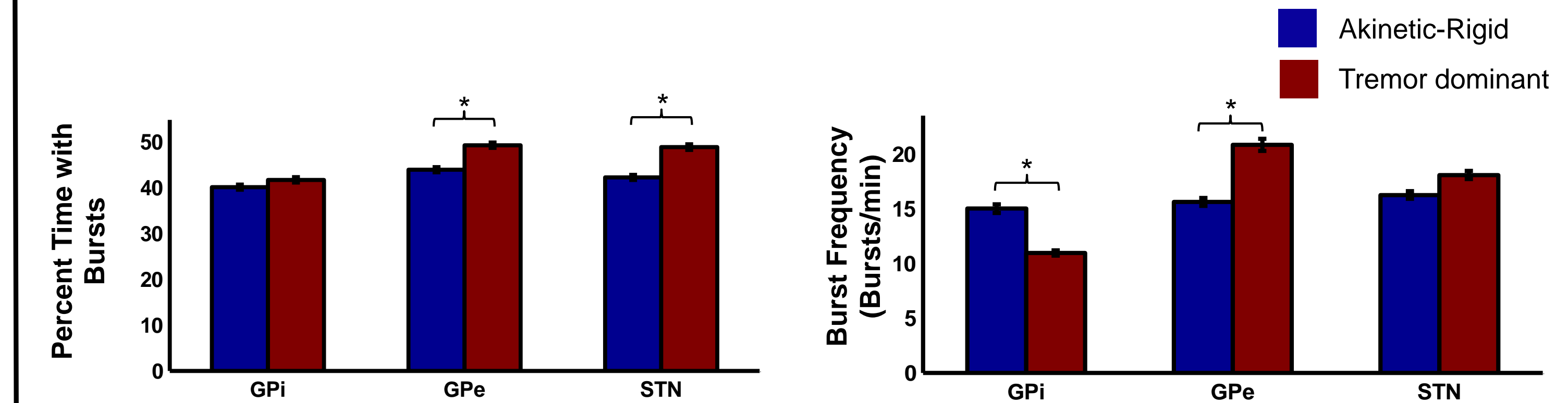


Figure 5: (Left) Percent of time that cells had with burst activity in each nuclei. (Right) Burst frequency of cells in bursts/min. Comparison of burst parameters between TD and AR groups was done using the non-parametric Wilcoxon rank sum test. (*p<0.05)

Power Spectral Density

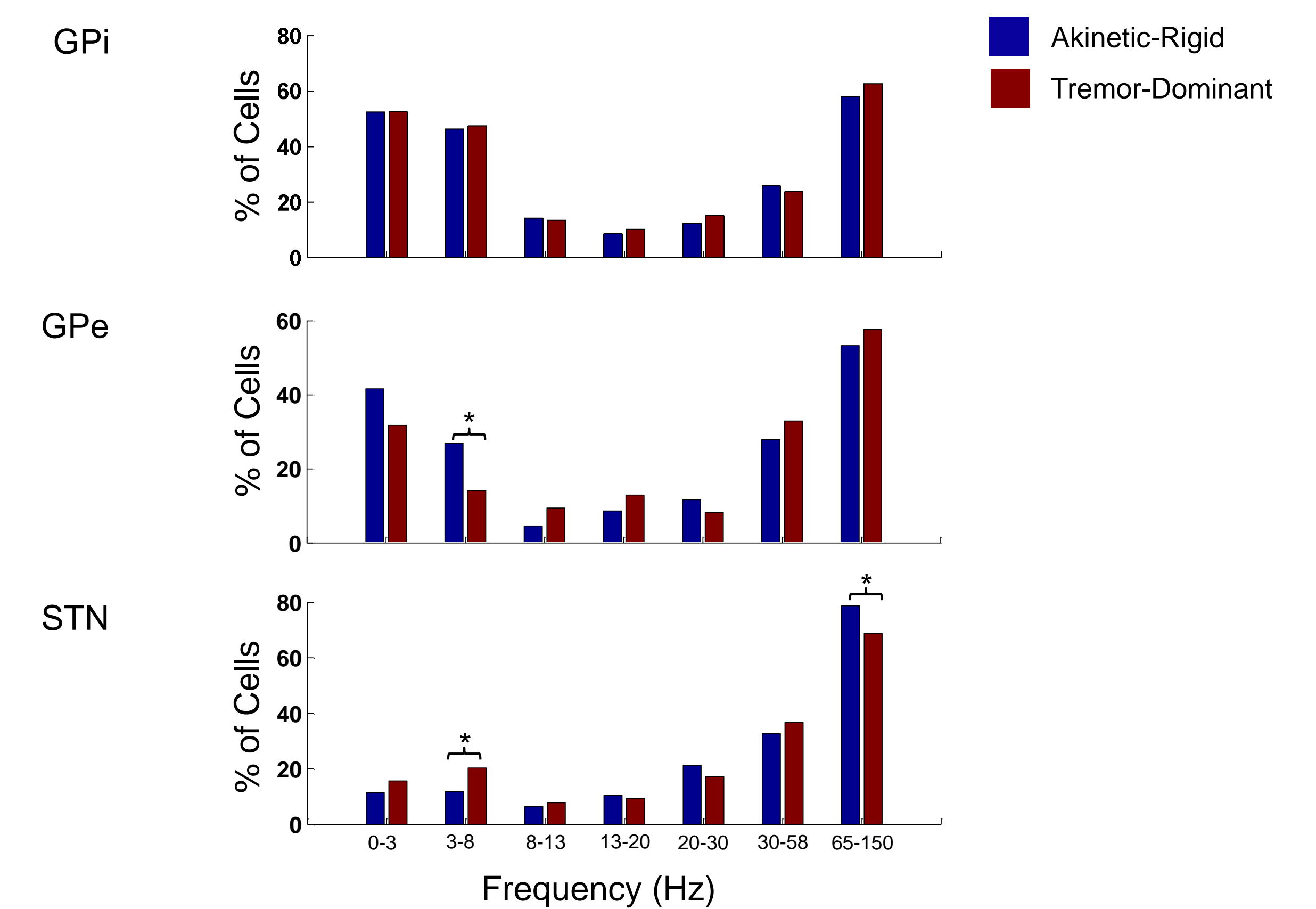


Figure 6: Percent of cells with significant power in various frequency bands. % of cells with significant activity in the tremor band was higher for the TD group in the STN and for the AR group in the GPe. The AR group also had more cells with 65-150 Hz activity. Comparison of % of cells with significant power in the different bands was done using the likelihood ratio test. (*p<0.05)

Conclusions

1. The discharge rate showed a slight change between PD phenotypes in the GPi and GPe.
2. There was a difference in the percent of time with bursting activity and the frequency of the bursts.
3. Different patterns of relative power were seen in the STN and GPe.
4. The trends seen in this study suggest that patterns of neuronal activity are likely to be more correlated with disease phenotypes than differences in cell discharge rates.
5. The data will be analyzed further to assess the impact of disease severity, type of cell, presence of sensorimotor response and location within the nucleus and interaction of the above with PD phenotype.

Acknowledgements

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