Activity patterns in the Globus Pallidus, and Sub-thalamic Nucleus in Akinetic-Rigid and Tremor Predominant Parkinsonian Patients

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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.

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.

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.

Results

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

<table>
<thead>
<tr>
<th>Phenotype</th>
<th>Number of Patients</th>
<th>External Globus Pallidus (GPe)</th>
<th>Internal Globus Pallidus (GPi)</th>
<th>Sub-thalamic Nucleus (STN)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Akinetic-rigid</td>
<td>53</td>
<td>203</td>
<td>163</td>
<td>202</td>
</tr>
<tr>
<td>Tremor dominant</td>
<td>21</td>
<td>83</td>
<td>49</td>
<td>113</td>
</tr>
</tbody>
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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.

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

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.

Figure 4: Burst Analysis

Power Spectral Density

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.

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