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Firing rate dynamics of striatal circuit in a Go and No-go tasks

Jyotika Bahuguna, Ad Aertsen, Arvind Kumar

To correctly govern the action-selection it is important that D1 and D2 neurons have differential firing rates such that either direct or indirect pathway can win. To understand how dopamine depletion in the striatum could affect the balance of firing rate in the D1 and D2 MSNs it is important to consider dichotomous integration properties [5] and connectivity [2]. Our preliminary results based on reduced firing rate model and numerical stimulations revealed several important insights: a.) D1 MSNs are massively inhibited by the D2 MSNs and require stronger cortical drive to overcome the recurrent inhibition from D2 MSNs. b.) Firing rates of D1 and D2 change in a non-monotonic fashion as a function of the strength of cortical inputs. For low input rates D1 MSNs have higher firing rate than D2 MSNs and vice versa.This is due to the preferential connection by FSI to D1, which at higher cortical input inhibits D1 more than D2. [3] c.) The cortical input rate at which D2 MSNs surpasses D1 MSNs, depends on the strength of cortico-striatal synapses and firing rates of fast-spiking interneurons (FSI). d.) The STN can control the activity of FSIs via the GPe neurons and thus can adjust the decision threshold.

The model suggest that under dopamine depletion conditions even for weak cortical inputs D2 MSNs activity is higher than D1 MSNs consistent with the fact that PD patients have difficulty in making voluntary decision. We also observed that dopamine depletion reduced the parameter regime supporting D1 MSNs activation, suggesting that under dopamine depleted state striatum would require arbitration by STN-GPe network even for low conflict task, providing a plausible explanation of increased reaction times in PD patients. Finally, reduced activity in STN and increased activity in GPe during DBS could also reduce the activity of FSIs in the striatum such that D1 MSNs fire at higher rates than D2 MSNs creating a situation similar to impulsivity.

References

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