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P139: Break-up and recovery of harmony between direct and indirect pathways in a spiking neural network of the basal ganglia; Huntington's disease and treatment

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Passi Perduti

P139 Break-up and recovery of harmony between direct and indirect pathways in a spiking neural network of the basal ganglia; Huntington's disease and treatment

Sang-Yoon Kim andWoochang Lim*
Institute for Computational Neuroscience and Department of Science Education, Daegu National University of Education, Daegu 42411, Korea
*Email: wclim@icn.re.kr

The basal ganglia (BG) in the brain exhibit diverse functions for motor, cognition, and emotion. Such BG functions could be made via competitive harmony between the two competing pathways, direct pathway (DP) (facilitating movement) and indirect pathway (IP) (suppressing movement). As a result of break-up of harmony between DP and IP, there appear pathological states with disorder for movement, cognition, and psychiatry. In this paper, we are concerned about the Huntington's disease (HD), which is a genetic neurodegenerative disorder causing involuntary movement and severe cognitive and psychiatric symptoms. For the HD, the number of D2 SPNs (ND2) is decreased due to degenerative loss, and hence, by decreasing xD2 (fraction of ND2), we investigate break-up of harmony between DP and IP in terms of their competition degree Cd, given by the ratio of strength of DP (SDP) to strength of IP (SIP) (i.e., Cd = SDP/SIP). In the case of HD, the IP is under-active, in contrast to the case of Parkinson's disease with over-active IP, which results in increase in Cd (from the normal value). Thus, hyperkinetic dyskinesia such as chorea (involuntary jerky movement) occurs. We also investigate treatment of HD, based on optogenetics and GP ablation, by increasing strength of IP, resulting in recovery of harmony between DP and IP. Finally, we study effect of loss of healthy synapses of all the BG cells on HD. Due to loss of healthy synapses, disharmony between DP and IP increases, leading to worsen symptoms of the HD.

Acknowledgements

References

[1]Kim,S.-Y., & Lim, W. (2024). Break-up and recovery of harmony between direct and indirect pathways in the basal ganglia; Huntington's disease and treatment. *Cognitive Neurodynamics,* 18, 2909-2924.https://doi.org/10.1007/s11571-024-10125-w