slower (≈70 Hz) ones in D2 medium spiny neurons. While GPe-TI gamma oscillations were prominent in healthy and pathological states, D2 oscillations emerged under dopamine-depleted conditions. Both rhythms required self-inhibition within the corresponding nuclei to be generated. However, this mechanism alone could not account for all gamma dynamics. Beta oscillations, generated by the model under pathological conditions, affected GPe-TI gamma frequency via phase-frequency coupling and amplified D2 gamma activity through phase-amplitude coupling. Both interactions were mediated by beta-induced modulation of spiking activity.

Discussion

By employing a computational model of the BG, we offered a comprehensive explanation of gamma rhythmogenesis in these structures, identifying two sources: D2 and GPe-TI. Our results were consistent with experimental findings from both rat [3] and human local field potentials [4] and aligned with the results of other computational models [5]. We also clarified how these rhythms were generated through self-inhibition within these nuclei and how they interacted with pathological beta synchronization. Our insights into the mechanism behind gamma generation in BG represent a crucial step toward advancing our understanding of PD and improving their potential as biomarkers for adaptive deep brain stimulation.

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References

[1] Oehrn, C., Cernera, S., Hammer, L., Shcherbakova, M., Yao, J., Hahn, A., Wang, S., Ostrem, J., Little, S., & Starr, P. (2024). Chronic adaptive deep brain stimulation versus conventional stimulation in Parkinson's disease: a blinded randomized feasibility trial. *Nature Medicine, 30*(11), 3345-3356. doi: 10.1038/s41591-024-03196-z

[2] Ortone, A., Vergani, A., Ahmadipour, M., Mannella, R., & Mazzoni, A. (2023). Dopamine depletion leads to pathological synchronization of distinct basal ganglia loops in the beta band. *PLOS Computational Biology, 19*(4), e1010645. doi: 10.1371/journal.pcbi.1010645

[3] Bi, Y., Wang, P., Yu, J., Wang, Z., Yang, H., Deng, Y., Guan, J., & Zhang, W. (2023). Eltoprazine modulated gamma oscillations on ameliorating L-dopa-induced dyskinesia in rats. *CNS Neuroscience & Therapeutics, 29*(10), 2998-3013. doi: 10.1111/cns.14241

[4] Jenkinson, N., Kühn, A., & Brown, P. (2013). Gamma oscillations in the human basal ganglia. *Experimental Neurology, 245*, 72-76. doi: 10.1016/j.expneurol.2012.07.005

[5] Lindi, S., Mallet, N., & Leblois, A. (2023). Synaptic changes in pallidostriatal circuits observed in parkinsonian model triggers abnormal beta synchrony with accurate spatio-temporal properties across the basal ganglia. *The Journal of Neuroscience,* JN-RM-0419-23. doi: 10.1523/JNEUROSCI.0419-23.2023

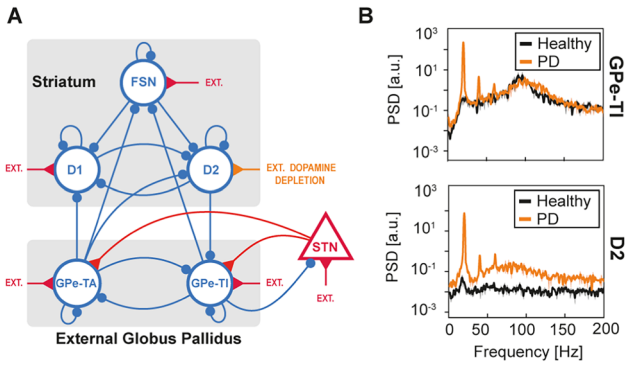

Figure 1: A) Computational model of the basal ganglia: FSN (striatal spiking interneurons), D1/D2 (medium spiny neurons with D1 and D2 dopamine receptors), GPe-TA/TI (arkypallidal/prototypic populations of the globus pallidus externa), and STN (subthalamic nucleus). B) Power spectral densities (PSDs) of GPe-TI (top) and D2 (bottom) activities under healthy and Parkinsonian (PD) conditions.

P085 Biological validation of a computational model of nitric oxide dynamics by emulating the nitric oxide diffusion experiment in the endothelium

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Introduction

Understanding how the brain works, how it is structured and how it computes is one of the goals of computational neuroscience. An essential step in this direction is to understand the cellular communication that enables the transition from nerve cells to cognition. It is now accepted that the links between neurons are not only established by synaptic connection, but also by the confluence of different cellular signals that affect global brain activity, with the underlying mechanism being the diffusion of neuroactive substances into the extracellular space (ECS). One of these substances is the free radical gas nitric oxide (NO), which, in turn, determines a new type of information transmission: the volume transmission (VT). VT is a non-simple form of short- and long-distance communication that acts not only as a microenvironment to separate nerve cells, but also as an information channel [1, 2]. NO is a signaling molecule that is synthesized in a number of tissues by NO synthases and has the ability to regulate its own production. It is lipid soluble, membrane permeable and has a high diffusivity in both aqueous and lipid environments.

Method

In the absence of definitive experimental data to understand how NO functions as a neuronal signalling molecule, we have developed a computational model of NO diffusion based on non-negative and compartmental dynamical systems and transport phenomena [3]. The proposed model has been validated in the biological environment, specifically in the endothelium. In this work, the biological validation is approached by reproducing the experiment performed by Tadeuzs et al, 1993 [4] on NO diffusion in the aorta. A fitting procedure to the observed NO dynamics was executed, and hypothesis related to the different processes in the NO dynamics were provided.

Results

We implement our model with two compartments, using real measurements of NO synthesis and diffusion processes in the endothelial cell and in the smooth muscle cells of the aorta at a distance of 100 ± 2 μm between them. Our results provide evidence that the compartmental model of NO diffusion has allowed the design of a computational framework [5] to study and determine the dynamics of synthesis, diffusion and self-regulation of NO in the brain and in artificial environments.

Discussion

We have also shown that this model is very powerful because it allows to incorporate all the biological features and existing constraints in NO release and diffusion and in the environment where NO diffusion processes take place. Finally, it has been shown that our model is an important tool for designing and interpreting biological experiments on the underlying processes of NO dynamics, NO behaviour and its impact on both brain structure and function and artificial neural systems.

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References

[1] Syková, E. (1997). The Extracellular Space in the CNS: Its Regulation, Volume and Geometry in Normal and Pathological Neuronal Function. *The Neuroscientist, 3*(1), 28-41. doi: 10.1177/107385849700300113

[2] Syková, E. (2004). Extrasynaptic volume transmission and diffusion parameters of the extracellular space. *Neuroscience, 129*(4), 861-876. doi: 10.1016/j.neuroscience.2004.06.077

[3] Fernández López, P., García Báez, P., & Suárez Araujo, C. (2015). Nitric Oxide Diffusion and Multi-compartmental Systems: Modeling and Implications. *Lecture Notes in Computer Science,* 523-531. doi: 10.1007/978-3-319-26555-1_59

[4] Malinski, T., Radomski, M., Taha, Z., & Moncada, S. (1993). Direct Electrochemical Measurement of Nitric Oxide Released from Human Platelets. *Biochemical and Biophysical Research Communications, 194*(2), 960-965. doi: 10.1006/bbrc.1993.1914

[5] Suárez Araujo, C. (2000). Study and reflections on the functional and organizational role of neuromessenger nitric oxide in learning: An artificial and biological approach. *AIP Conference Proceedings, 517*, 296-307. doi: 10.1063/1.1291268

P086 Synergistic short-term synaptic plasticity mechanisms for working memory

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