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Computational study of putative coupling between dopamine receptors and Ca2+ channels to investigate excitability properties in layer II stellate cells

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MOTIVATION
The firing patterns of stellate cells in layer II of medial entorhinal cortex are involved in memory, cognition and perception [1]. These patterns are largely modulated by the underlying subcellular calcium dynamics within the axon initial segment (AIS) [2]. Recent experimental data have suggested a putative coupling between dopamine D2 receptors (D2R) and T-type Ca2+ channels as another biophysical explanation for the firing pattern modulation [3]. This in silico study aims to enhance our understanding of the subcellular membrane mechanisms within AIS of the layer II stellate cells and their modulating effects on resting membrane potential (RMP) and action potential (AP) plasticity in pathological conditions.

METHODS
The biophysical parameters for various ion channels in the AIS region of layer II stellate cells were combined and adapted from previous models and experimental studies. We developed equations for restrained diffusion-based D2R activation to alter cAMP concentration, which was merged with the maximum conductance of T type Ca2+ channels in a modified Boltzmann equation. Using the NEURON software platform, RMP, APs and T-type Ca2+ channel currents were simulated under voltage clamp and current clamp protocols.

RESULTS AND DISCUSSION
In simulations, application of 10 μM of a dopamine agonist reduced the AP threshold voltage by 3 mV, changes of membrane potential with time (dV/dt) by1 mV/ms, and RMP by 2 mV. The frequency of the AP was reduced from 6 to 4 spikes/s with 400 pA current injection. The cAMP concentration was reduced and it shifted the half-activation potential of the T-type Ca2+ channel from –36 mV to –32 mV. The window current to maintain the RMP was reduced due to activation of D2R receptors and it was counter balanced by decreasing the A-type K+ channel conductance. This in silico study suggests that the application of cAMP antagonists and K+ channel agonists could be used to replace dopamine in certain pathological conditions and in studies of spatial memory performance.

Keywords: Layer II Stellate cells, Dopamine receptor, T-type Ca2+ channel, Computational model

REFERENCES

[1] Rowland, D. C., Obenhaus, H. A., Skytoen, E. R., Zhang, Q., Kentros, C. G., Moser, E. I., & Moser, M. B. (2018). Functional properties of stellate cells in medial entorhinal cortex layer II. eLife 7.
[2] Lipkin, A. M., Cunniff, M. M., Spratt, P. W., Lemke, S. M., & Bender, K. J. (2021). Functional microstructure of CaV-mediated calcium signaling in the axon initial segment. Journal of Neuroscience, 41(17), 3764-3776.
[3] Jin, X., Chen, Q., Song, Y., Zheng, J., Xiao, K., Shao, S., ... & Huang, Z. (2019). Dopamine D2 receptors regulate the action potential threshold by modulating T-type calcium channels in stellate cells of the medial entorhinal cortex. The Journal of Physiology, 597(13), 3363-3387.

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