Control/Tracking Number: 2009-S-13245-SfN
Activity: Scientific Abstract
Current Date/Time: 6/23/2009 5:14:46 AM

Spike patterns and dopamine release in ventral midbrain by computational analysis

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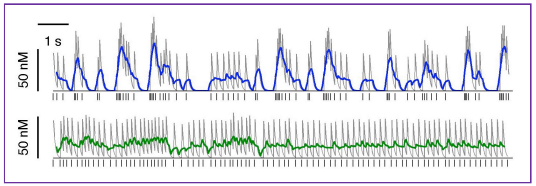
Abstract: Dopamine neurons in the ventral midbrain are spontaneously active in firing patterns ranging from highly regular (tonic) to burst firing (phasic). It has been debated whether spontaneous asynchronous burst firing of dopamine neurons results in higher extracellular concentrations of dopamine compared to tonic firing. Alternatively, the dopamine released by a burst may be able to reach receptors located further away from the release site. To quantitatively test these hypotheses we investigated different computational models of dopamine release. We ask: 1) What is the extracellular dopamine concentration for different firing patterns, 2) what is the concurrent differential binding of D1 and D2 receptors, and 3) what is the role of diffusion from the release site in activation of these.
An example of the dopamine output from two typical spike trains is shown below. The spikes are shown below each trace. We find the average dopamine level from asynchronous firing to be mainly dependent on the mean firing rate and only weakly dependent on the spike pattern, i.e. tonic versus phasic. Nevertheless, the balance between the activation of postsynaptic D1 or D2 type dopamine receptors is highly dependent on the firing pattern. The model predicts that phasic firing favours D1 receptor activation, whereas tonic firing favours D2 receptor activation at comparable levels of average dopamine release.
Further, we apply our dopamine release model to experimentally recorded single unit spike patterns of spontaneously active dopamine neurons from the substantia nigra of urethane-anesthetized C57BL/6 mice. Using the predicted levels of receptor activation from our model, we find that compounds that modulate firing rate and spike pattern by regulation of SK channels (Apamin, NS309, NS8593) significantly change the ratio of activation of D1 and D2 receptors.
Our model translates spike trains into dopamine release and binding of D1 and D2 receptors and we suggest it as an important new tool in the interpretation of experimental data from dopaminergic neurons.



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Presentation Preference (Complete): Poster Only
Linking Group (Complete): None selected
Nanosymposium Information (Complete):
Newsworthy : False
Suspicious : False
Sensitive : False
Mapped Theme : Neuroinformatics

Theme and Topic (Complete): G.06. Computation, Modeling, and Simulation
Keyword (Complete): DOPAMINE ; DIFFUSION ; STRIATUM
Support (Complete):
Support: No

Special Requests (Complete):
Religious Conflict?: No Religious Conflict
Additional Conflict?: No
Mapped Theme One : Neuroinformatics
Mapped Theme Two : Computational Neurobiology/Neural Networks
Newsworthy: : False
Sensitive: : False
Suspicious : False

Status: Finalized