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MEETING ABSTRACT

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Presynaptic dopamine autoreceptors account for individual differences in the dopamine baseline: theory meets experiment in freely moving rats

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Dopamine (DA) release is maintained within a desired working range by pre-synaptic and somatodendritic dendritic D_2-like autoreceptors that provide negative feedback on DA release, synthesis and firing rate. The complex concerted action of these somatodendritic and presynaptic feedback systems has previously been studied computationally [1]. However, individual differences DA autoregulation have been related to numerable psychiatric traits, including novelty seeking and propensity for drug abuse [2,3], but the functional effect of such differences on the real time functional DA signal in behaving animals is unknown. We therefore extended our previous mathematical models to infer the real time DA signal in freely moving animals from experimental data obtained using fast-scan cyclic voltammetry [4]. The models were tailored to match DA cell firing with recorded spontaneous fluctuations in extracellular DA concentrations in individual animals. The output of the model includes direct estimates of the pre-synaptic D_2 autoreceptor action and a measure of the individual efficacy of the presynaptic autoreceptor system in each animal.

We applied the model to recordings from 36 freely moving rats, 19 hereof were recorded in nucleus accumbens shell and 17 in nucleus accumbens core. We tested the ability of the model to estimate the spontaneous real-time DA signal in freely moving conditions and tested predicted individual differences in DA release under raclopride and intravenous cocaine. We found that the DA level was negatively correlated with autoreceptor efficacy. In other words, low average DA levels observed in some animals were the result of strong autoreceptor control, while other animals had high DA levels and correspondingly low autoreceptor feedback. Our analysis suggests that individual differences in efficacy of presynaptic autoreceptor account for most of the between subject variability in DA signaling.

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