The patchwork of dopamine domains in the rat nucleus accumbens core

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Introduction

Evoked dopamine overflow within the rat striatum (dorsal and ventral) is heterogeneous [1]. Evoked dopamine overflow depends on the location of the carbon fiber electrode. So the striatum is thought to contain active DA “hot spots” and “non-DAergic cold spots.” However, this view is inconsistent with the structure of the striatum, which contains a homogeneous array of DA terminals. Thus, the striatum does not contain “non-DAergic cold spots.” Recently, we reported that the dorsal striatum contains a patchwork of DA kinetic domains, fast and slow, which exhibit significantly different DA concentrations and kinetics [2, 3]. DA terminals in the slow domains are autoinhibited by DA itself, so the slow domains are DAergic. The objective of the present study was to test the hypothesis that DA kinetic domains exist also in the nucleus accumbens.

Methods

Male Sprague-Dawley rats (250-300 g) were anesthetized with isoflurane and placed in a stereotax. First carbon fiber microelectrodes (200 μm in length and 7 μm in diameter) were placed in the striatum to help locate the medial forebrain bundle (MFB). A twisted, bipolar, stainless steel stimulating electrode was aimed at MFB. The placement of the stimulating electrode will be fixed when there was evoked DA overflow detected in striatum. Then the microelectrode was lowered down into the NAc core. Standard fast scan cyclic voltammetry parameters (400 V/s, 0 to 1 to -0.5 V vs. Ag/AgCl) were applied at 10Hz. Evoked DA overflow was monitored during MFB stimulation with a constant-current, biphasic waveform (frequency 60 Hz, amplitude 250 μA, pulse width 2 ms). Two stimulus protocols were used: single trains lasted 200 ms or 1.0 s. Evoked responses were recorded before and after the administration of the D2 antagonist, raclopride (2 mg/kg i.p.).

Results and Discussion

In NAc core, we applied 200 ms stimulus at 60 Hz (12 pulses) on MFB to evoke dopamine overflow. In 8 out of 17 rats, the microelectrode detected about 1 μM of dopamine release (“Fast” in Figure 1). However, we were unable to find any observable dopamine signal in other 9 rats in response to 200 ms stimulus. In order to verify that there were active dopamine terminals in those sites, we extended electrical stimulations to 1.0 s, and plotted recordings as ‘Slow’ in Figure 1.
Electrical stimulation of DAergic fibers in MFB evoked two types of responses, fast and slow, in NAc core. All the recordings can be grouped into either fast or slow type, based on the responses towards 200 ms stimulus.

There are distinct kinetic differences between these two types. First, the rate of evoked DA overflow is much faster in the fast responses than in the slow responses: the amplitudes of fast and slow responses are similar (~1 μM) despite the fivefold difference in stimulus duration. Second, the clearance rate of fast responses is much faster than that of slow responses: in Figure 1, fast sites and slow sites needed 0.8 s and 2.8 s to clear 1 μM DA 0.3 μM, respectively. Third, there was evoked DA overflow at the very beginning of the stimulus in the fast responses. But in the case of slow responses, under the first 12 pulses of electrical stimulation, there was no detectable DA signal on the microelectrode.

Although differences in the fast and slow responses are evident, as just summarized, similarities also exit. For example, both responses exhibit short-term facilitation: slow at first and increases as the stimulus proceeds. And, both fast and slow responses continue to increase for 200 ms (overshoot) after the stimulus ends.

Fast and slow responses in NAc core show different features comparing with fast and slow in striatum: fast responses in NAc core exhibit short-term facilitation whereas fast responses in striatum show short-term inhibition [2]: note that in Figure 1 the dopamine concentration after 100 ms stimulus is less than half that after 200 ms (triangle). Cragg has also reported this difference between dorsal and ventral striatum in a study on primate striatal slices [4]. Raclopride (2 mg/kg i.p.) did very little effect on the initial release rate in fast responses in NAc core.
This carries two meanings. First, autoinhibition of fast responses in NAc core begins only after the stimulus itself delivers dopamine into the extracellular space. Second, the low DA release after 100 ms stimulus in NAc core was not caused by autoinhibition. Another difference is that overshoot is prevalent in NAc core, whereas overshoot in striatum can so far only be observed after the treatment with DAT inhibitor nomifensine (20 mg/kg I.p.) [5]. It implies that there is less DAT uptake in NAc core than in dorsal striatum.

In summary, the results presented in this study suggest that a patchwork of DA kinetic domains, fast and slow, exist in rat NAc core. Fast and slow domains in NAc core show different features comparing with domains in striatum.

References