Attenuation of dopamine release during intracranial self-stimulation *may be* mediated at the dopaminergic cell body

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Introduction

During intracranial self-stimulation of the mesencephalon, forebrain dopamine release is attenuated below that of non-contingent stimulation "playbacks" to untrained controls[1,2].

Potential mechanisms for this "failure" in dopamine release are those that reside in the presynaptic terminal and are responsible for transducing action potentials into neurotransmitter release, as well as dopaminergic cell body effects in the ventral tegmental area such as hyperpolarization, limiting the generation of action potentials and their propagation beyond the axon hillock.

To test the locus of the suppression we used fast-scan cyclic voltammetry to compare dopamine release in the nucleus accumbens during intracranial self-stimulation and non-contigent stimulation of dopaminergic cell bodies with that of their axons.

1. Garris PA, Kilpatrick M, Bunin MA, Michael D, Walker QD & Wightman RM (1999) Dissociation of dopamine release in the nucleus accumbens from intracranial self-stimulation. *Nature* **398**, 67-9.

2. Kilpatrick MR, Rooney MB, Michael DJ & Wightman RM (2000) Extracellular dopamine dynamics in rat caudate-putamen during experimenter-delivered and intracranial self-stimulation. *Neuroscience* **96**, 697-706.

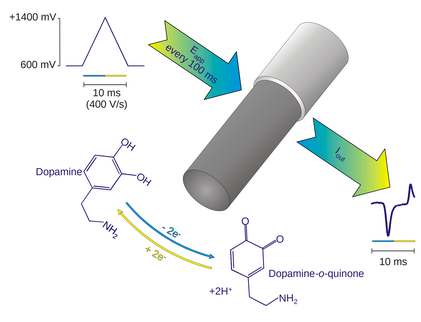
Key

▲ Electrical stimulation
24 pulses, 60 Hz, 120 µA

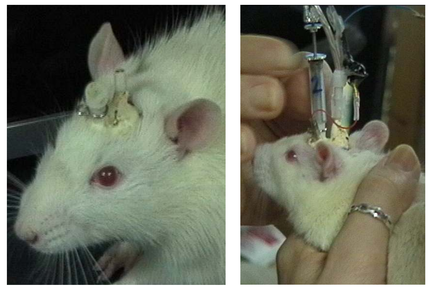
[Dopamine] in the nucleus accumbens following:

- ICS-VTA
  intracranial self-stimulation of the ventral tegmental area
- PB-VTA
  non-contingent stimulation of the ventral tegmental area
- ICS-MFB
  intracranial self-stimulation of the medial forebrain bundle
- PB-MFB
  non-contingent stimulation of the medial forebrain bundle

Detection of dopamine



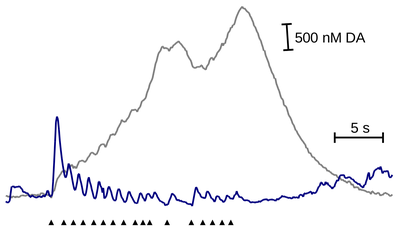
Using fast-scan cyclic voltammetry, dopamine is electro-oxidized by application of voltage. This liberates two electrons which are detected as current at a carbon-fiber microelectrode.



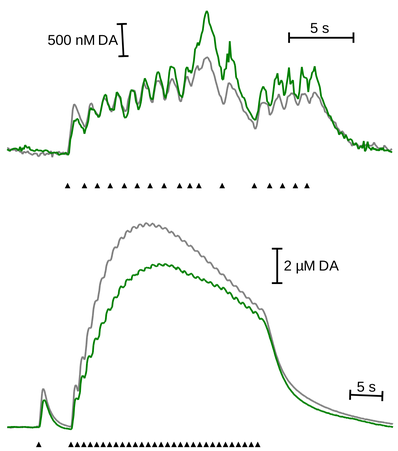
Electrical stimulation

Bipolar stimulating electrodes were chronically implanted in the ventral tegmental area (VTA; -5.6 mm AP, +1.0 mm ML, ~-8.6 mm DV vs bregma) or in the medial forebrain bundle (MFB; -4.0 mm AP, +1.4 mm ML, ~-8.6 mm DV vs bregma). Electrical stimulation trains (24 pulses, 60 Hz, 120 µA) were delivered either by intracranial self-stimulation on a fixed ratio-1 schedule or non-contigently by the experimenter ("playback").

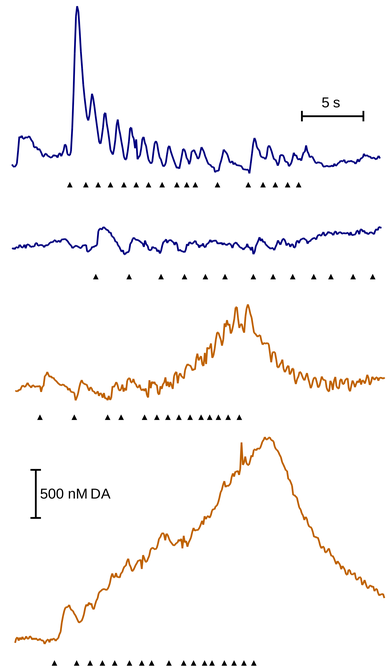
Dopamine changes during intracranial self-stimulation appear different to playbacks in untrained animals



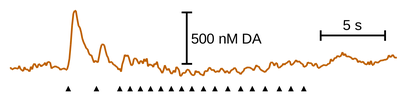
Dopamine changes during playback to the MFB in untrained rats appear similar to those to the VTA



Dopamine changes during intracranial self-stimulation of the MFB appear different to those of the VTA

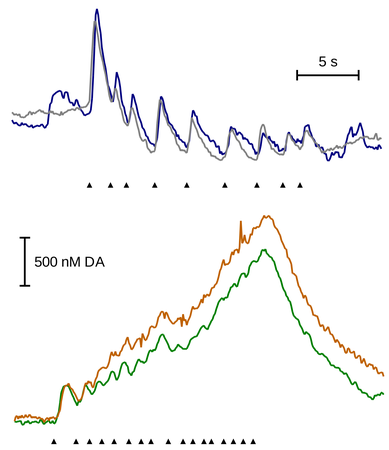


...or do they?



We have now also observed cases where the dopamine pattern following intracranial self-stimulation of the MFB resemble those of the VTA.

Dopamine changes for playbacks in trained animals appear similar to those for intracranial self-stimulation



Summary

As rats acquire intracranial self-stimulation behavior of the ventral tegmental area, there appears to be a change in dopamine dynamics, so that dopamine is suppressed during continued stimulation for *both* intracranial self-stimulation and non-contigent delivery of electrical stimulus trains.

This change is not so robust when trained with intracranial self-administration of the medial forebrain bundle, suggesting that either the suppression of dopamine is not implemented or it can be overcome with stimulation of the distal axons.

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