The role of glutamate receptor-dependent signaling in the dopamine system in reinforcement learning

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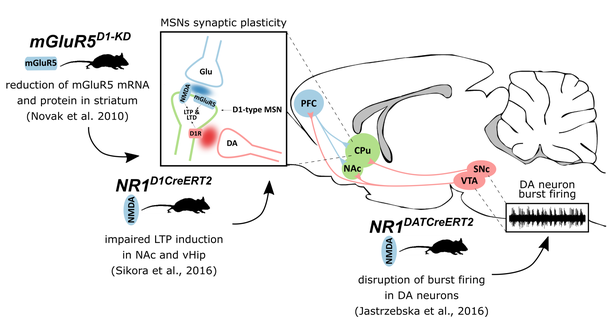
INTRODUCTION

The dopamine (DA) system plays a role in reinforcement learning and incentive motivation. The activity and plasticity in the DA system are largely dependent on excitatory glutamatergic transmission. Glutamatergic inputs activating N-methyl-D-aspartate (NMDA) receptors drive the burst firing in DA neurons and phasic DA release. Moreover, NMDA and metabotropic glutamate 5 (mGluR5) receptors are crucial for the induction of synaptic plasticity in dopaminoceptive striatal medium spiny neurons (MSNs).

Here, we used genetically modified mice with cell type-specific inactivation of **NMDA** or **mGluR5** receptors in dopamine transporter **DAT-expressing** and **D1 receptor-expressing** neurons to investigate the **consequences of disrupted glutamate receptor-dependent signaling in the DA system for adaptive behavior**.



Animals were tested in tasks that assess:

- reinforcement-driven learning and value-based decision-making
- stimulus-reward learning and conditioned reinforcement
- motivation to engage in reward-seeking behavior under conditions of increasing instrumental effort

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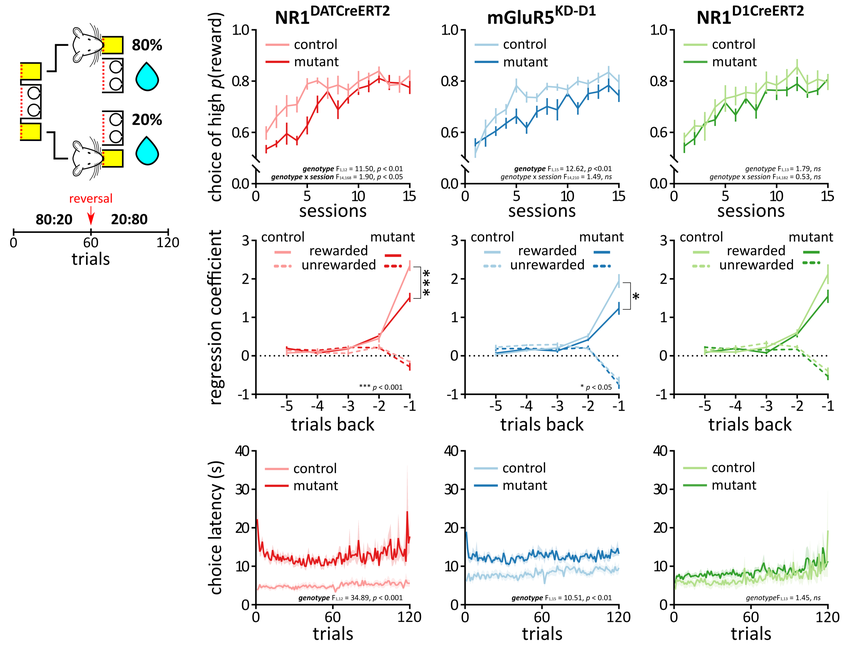
RESULTS

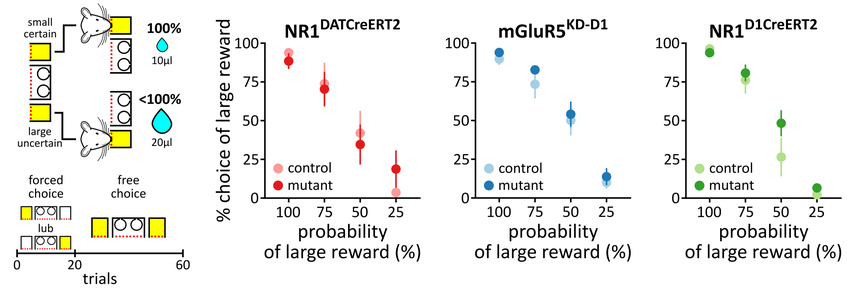
Probabilistic reversal learning

Inactivation of NMDA receptors in DA neurons and inactivation of mGluR5 receptors in D1R-expressing cells resulted in (1) fewer choices of more frequently rewarded alternative, (2) decreased likelihood of repeating previously rewarded choice, and (3) increased choice latency.



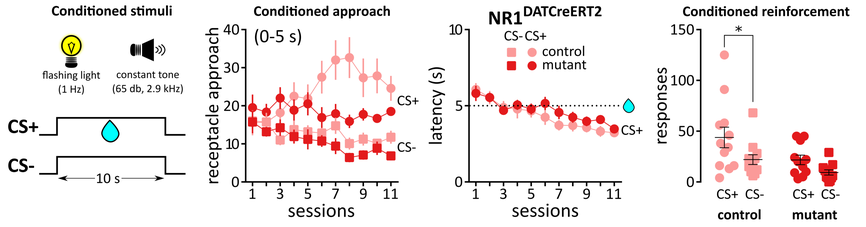
Magnitude discrimination and probability discounting

Disruption of glutamate receptor-dependent signaling in the DA system had no effect on the reward magnitude discrimination or discounting of the value of a large reward when its occurrence was uncertain.



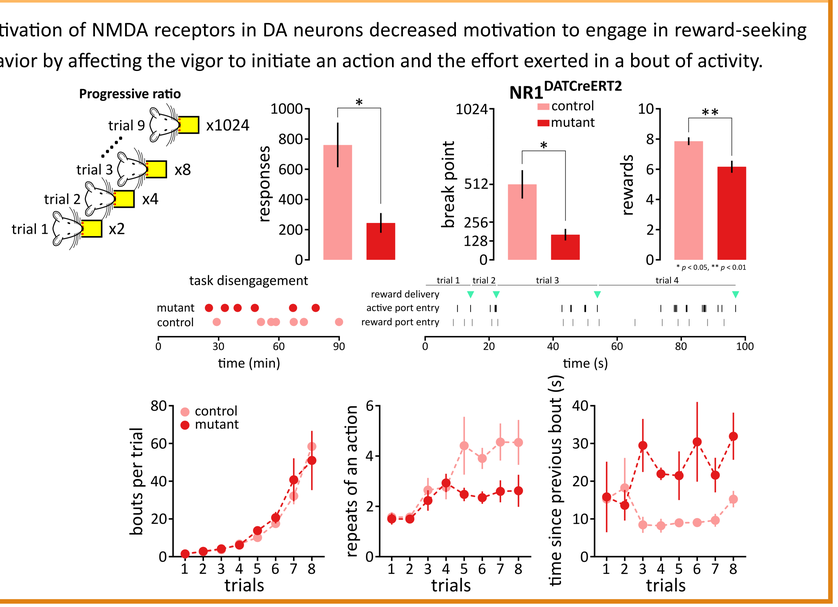
Stimulus-reward learning

Ablation of NMDA receptors in DA neurons disrupted attribution of motivational incentive value to reward-paired stimuli, but had no effect on learning its predictive value.



Motivation to engage in reward-seeking behavior

Inactivation of NMDA receptors in DA neurons decreased motivation to engage in reward-seeking behavior by affecting the vigor to initiate an action and the effort exerted in a bout of activity.



CONCLUSIONS

- NMDAR-dependent signaling in DA neurons and mGluR5-dependent signaling in D1R-expressing neurons play a role in reinforcement learning by affecting the likelihood of repeating of rewarded actions and the speed of decision-making
- NMDAR-dependent signaling in DA neurons is crucial for attribution of incentive motivational value to reward-paired stimuli and regulation of motivated behavior by controlling the initiation vigor and the amount of effort exerted