The role of glutamate receptor-dependent signaling in the dopamine system in reinforcement learning and adaptive decision-making

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Two-armed bandit problem

LEFT choice

20%

RIGHT choice

80%

Choice: L L R R R R L L L R R R R L L L R R R

Outcome:

Learned expected value:

$\text{Value}_{\textit{LeftChoice}} < \text{Value}_{\textit{RightChoice}}$

Two-armed bandit problem

LEFT choice

80% $

RIGHT choice

20% $

Negative

!? prediction error

Positive

!? prediction error

Choice:	R	R	R	R	R	R	R	R	L	L	L	L	L	L	L	L
Outcome:	✗	✗	✗	$	✗	✗	✗	✗	$	$	$	$	✗	$	$	$

Updated expected value:

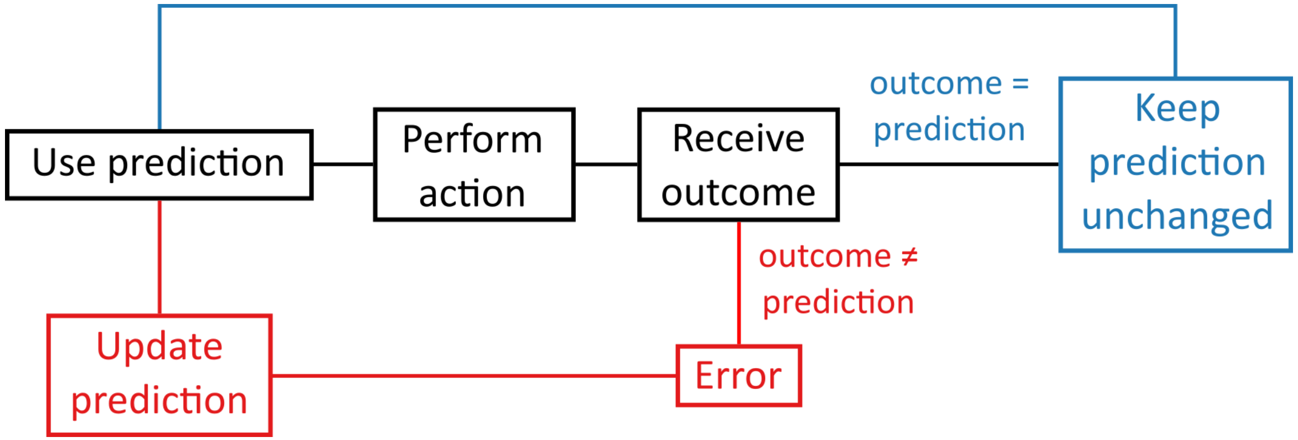
$\text{Value}_{LeftChoice} > \text{Value}_{RightChoice}$

What is reinforcement learning?

Reinforcement learning (RL):

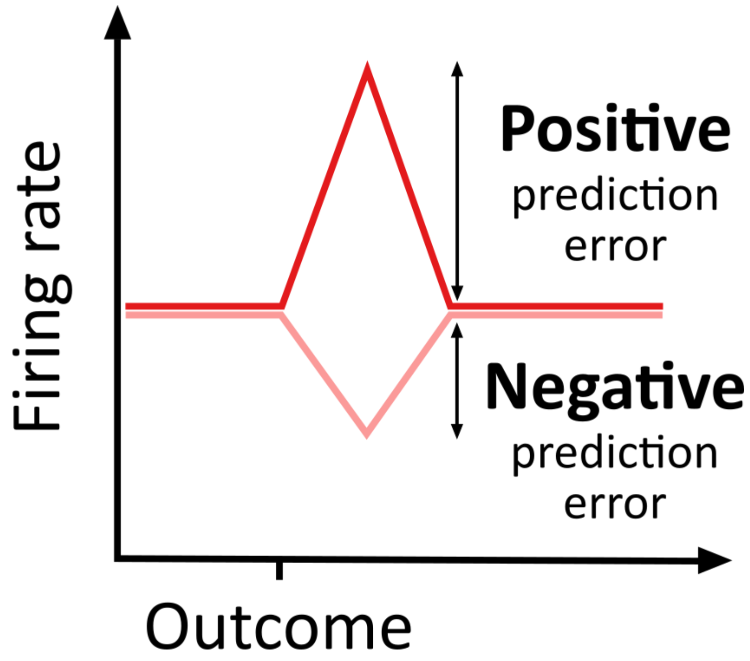
- Learning from the consequences of actions
- Actions are performed in the expectation of a predicted outcomes (expected value)
- Learning to select actions that maximize the accumulated reward over time (with higher value)
- The errors that occurs when the actual outcome differs from what had been predicted are used for updating predictions

- Framework for studying value-based decision-making

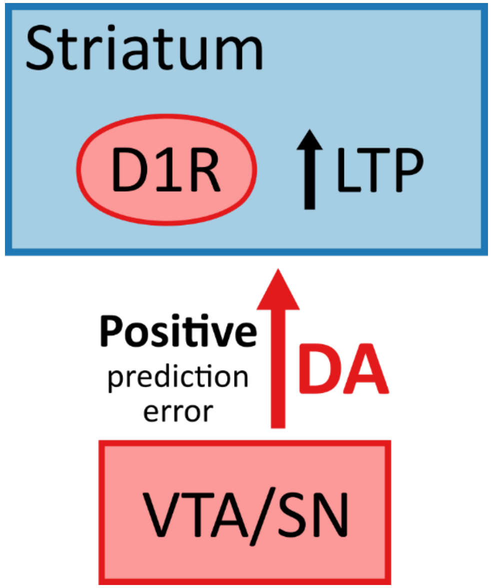


Dopamine system and reinforcement learning

- DA neurons code the discrepancy between the reward and its prediction

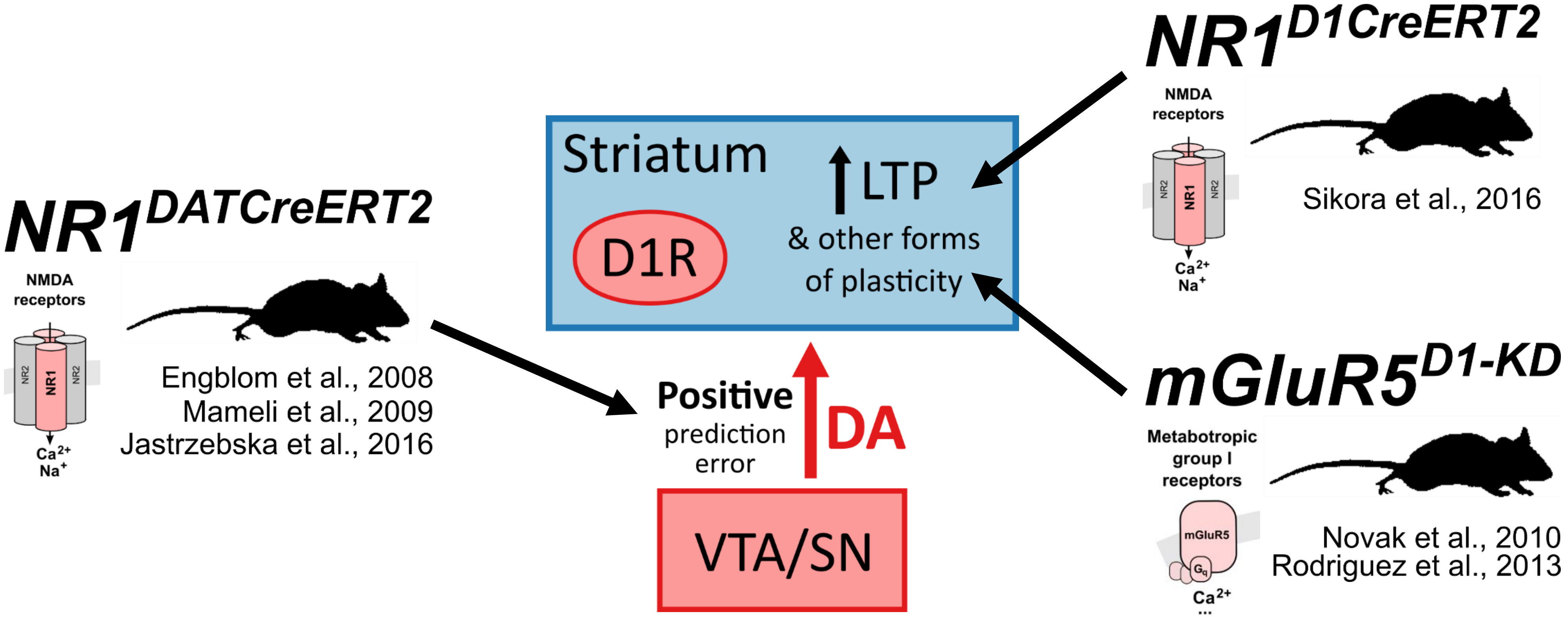


- The **RPE signal** is used for updating the action values stored by striatal neurons
- DA bursts associated with **Positive PEs** potentiate corticostriatal synapses that are active at the time of DA release via D1R

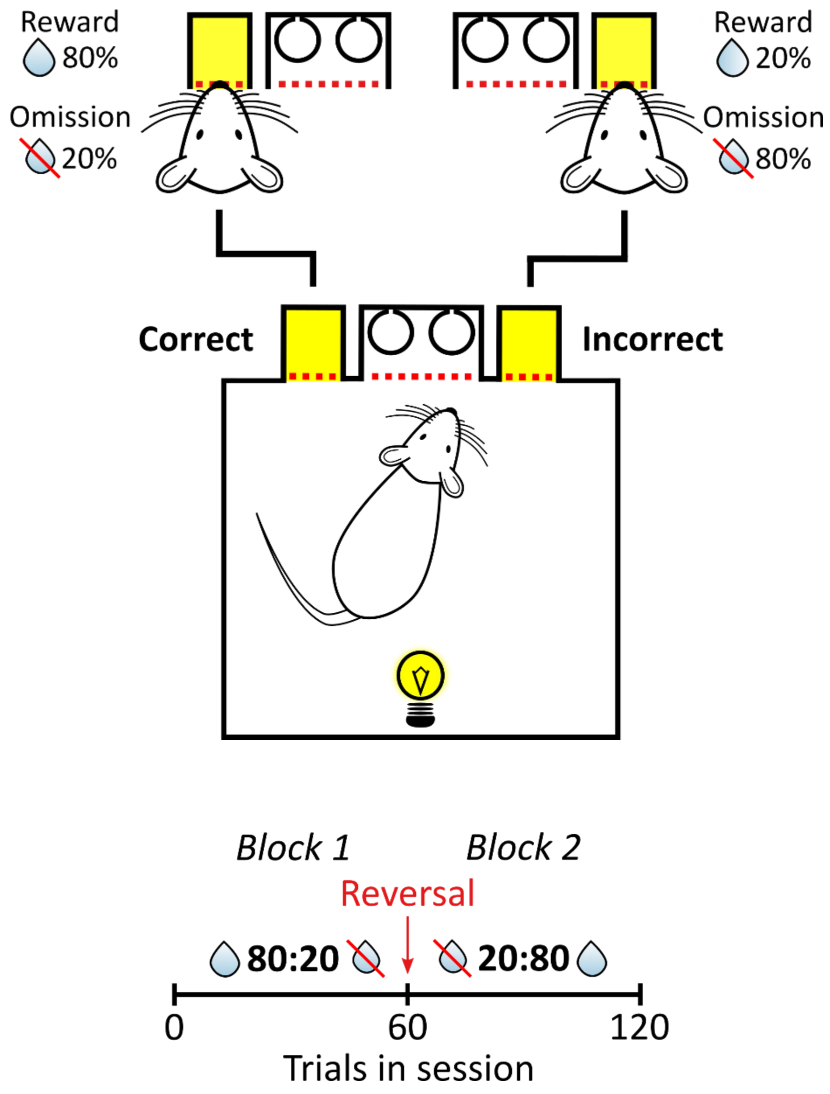


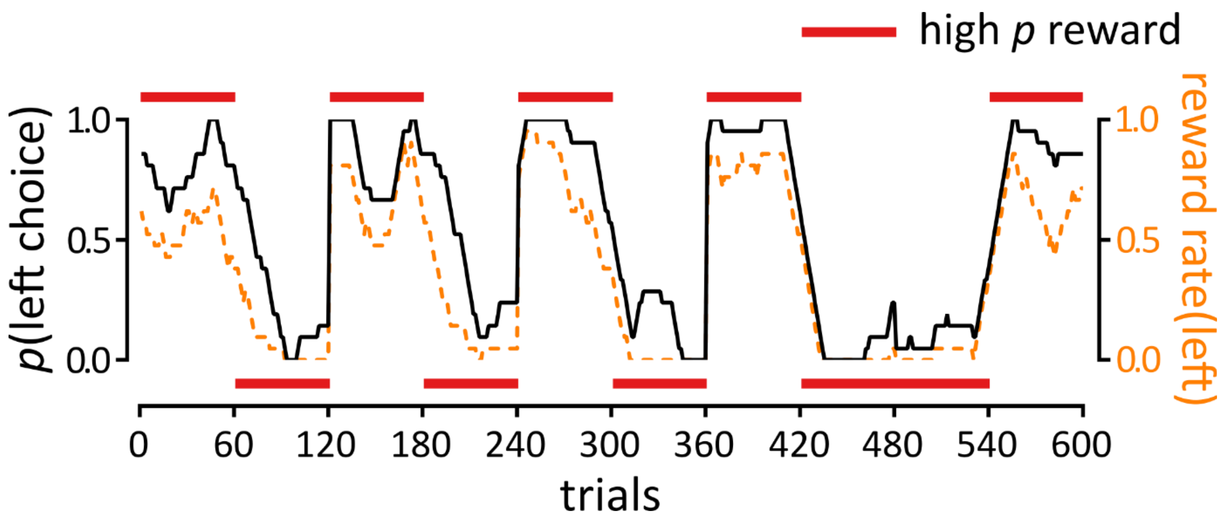
Aim

Use transgenic animals with ablation of Glu receptors in DA and D1R-expressing neurons to investigate the specific role of DA in reward-based learning



Rodent ‚two-armed bandit' task

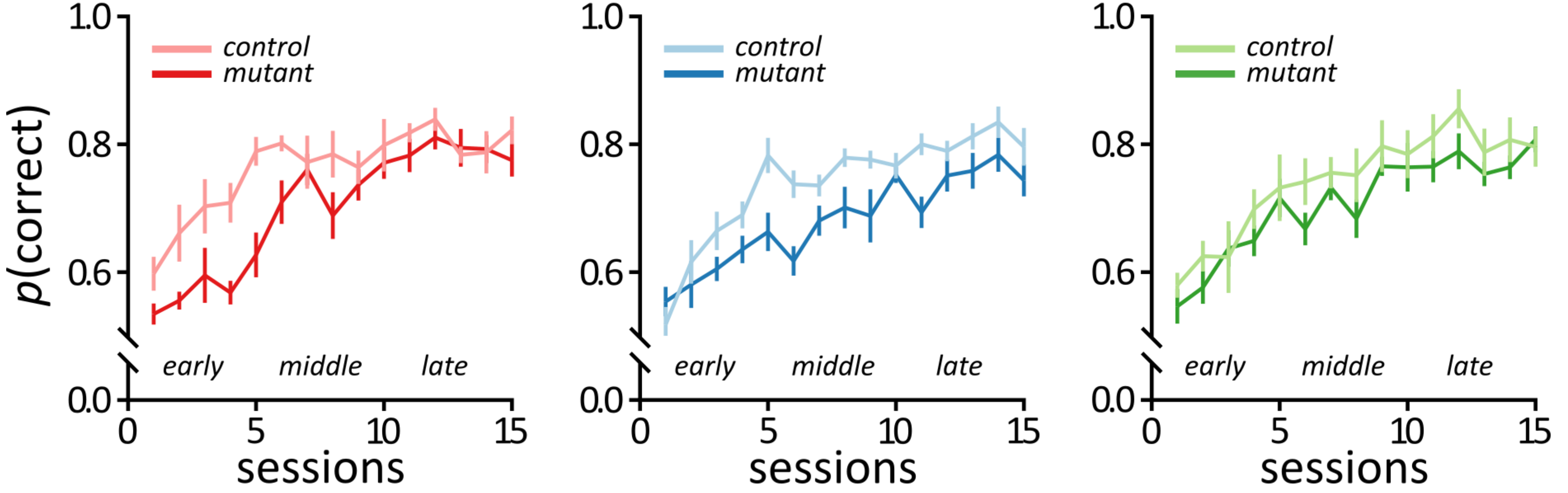




Representative example of one mouse's performance in the ‚TAB' task

General performance

$NR1^{DATCreERT2}$ **$mGluR5^{D1\text{-}KD}$** **$NR1^{D1CreERT2}$**



genotype $F_{1,12} = 11.5$, $p < 0.01$
session $F_{14,168} = 17.15$, $p < 0.001$
interaction $\mathbf{F_{14,168} = 1.90}$, $\boldsymbol{p < 0.05}$

genotype $\mathbf{F_{1,15} = 12.62}$, $\boldsymbol{p < 0.01}$
session $F_{14,210} = 20.69$, $p < 0.001$
interaction $F_{14,210} = 1.49$, *ns*

genotype $F_{1,13} = 1.80$, *ns*
session $F_{14,182} = 19.17$, $p < 0.001$
interaction $F_{14,182} = 0.53$, *ns*

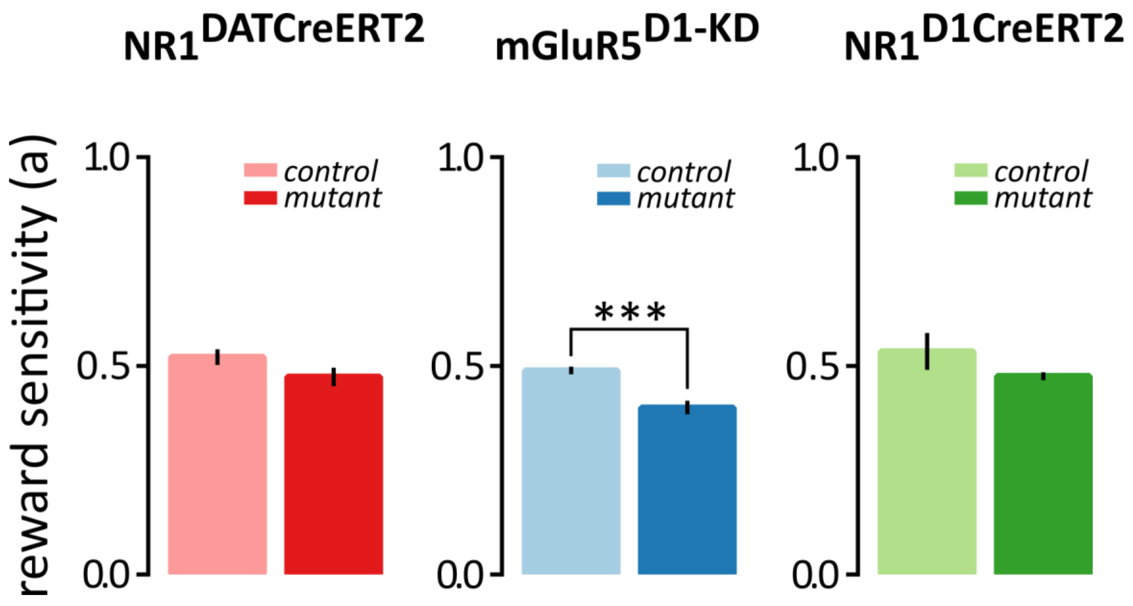
Influence of reward ratio on choice (reward sensitivity)

Generalized Matching Law

$$\log_2\left(\frac{C_L}{C_R}\right) = a \cdot \log_2\left(\frac{R_L}{R_R}\right) + \log_2 b$$

Choice ratio — Reward sensitivity — Reward ratio

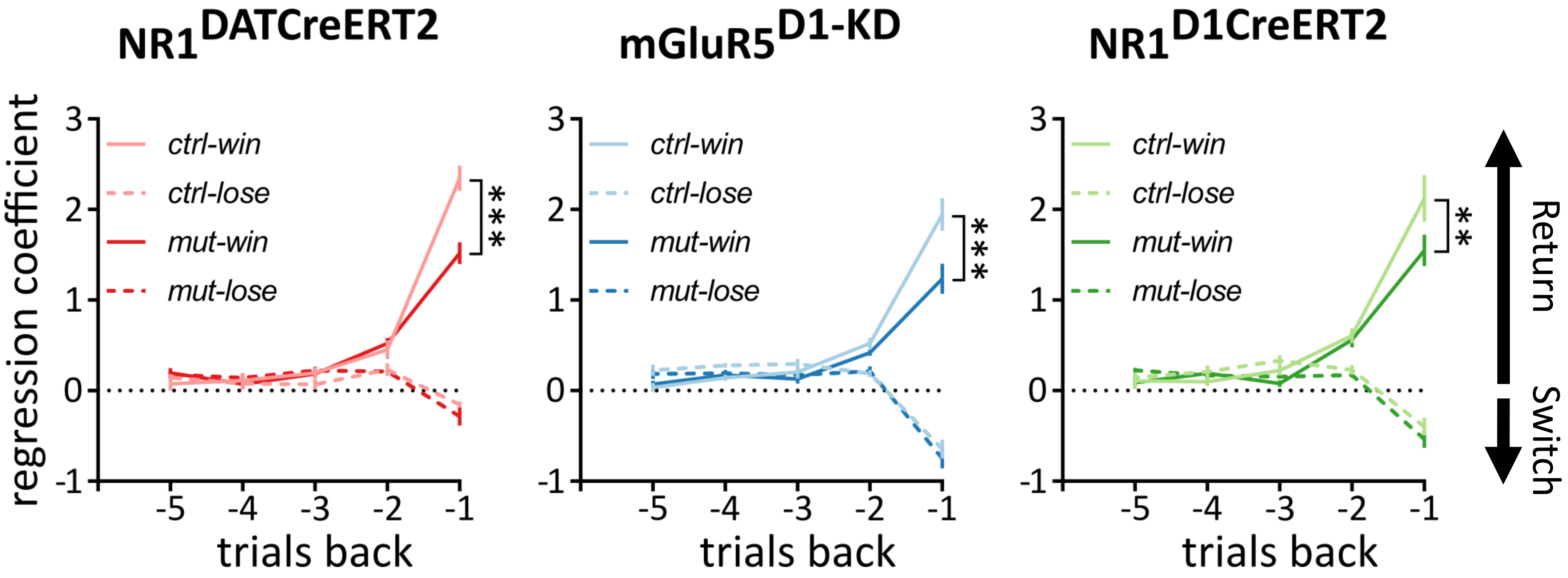
Reward sensitivity – reflects the degree to which the reward ratio actually impacts the choice ratio



Model fits

	NR1DATCreERT2	mGluR5D1-KD	NR1D1CreERT2
control	R^2 = 0,90	R^2 = 0,87	R^2 = 0,85
mutant	R^2 = 0,82	R^2 = 0,84	R^2 = 0,84

Influence of previous choices & outcomes on subsequent choice



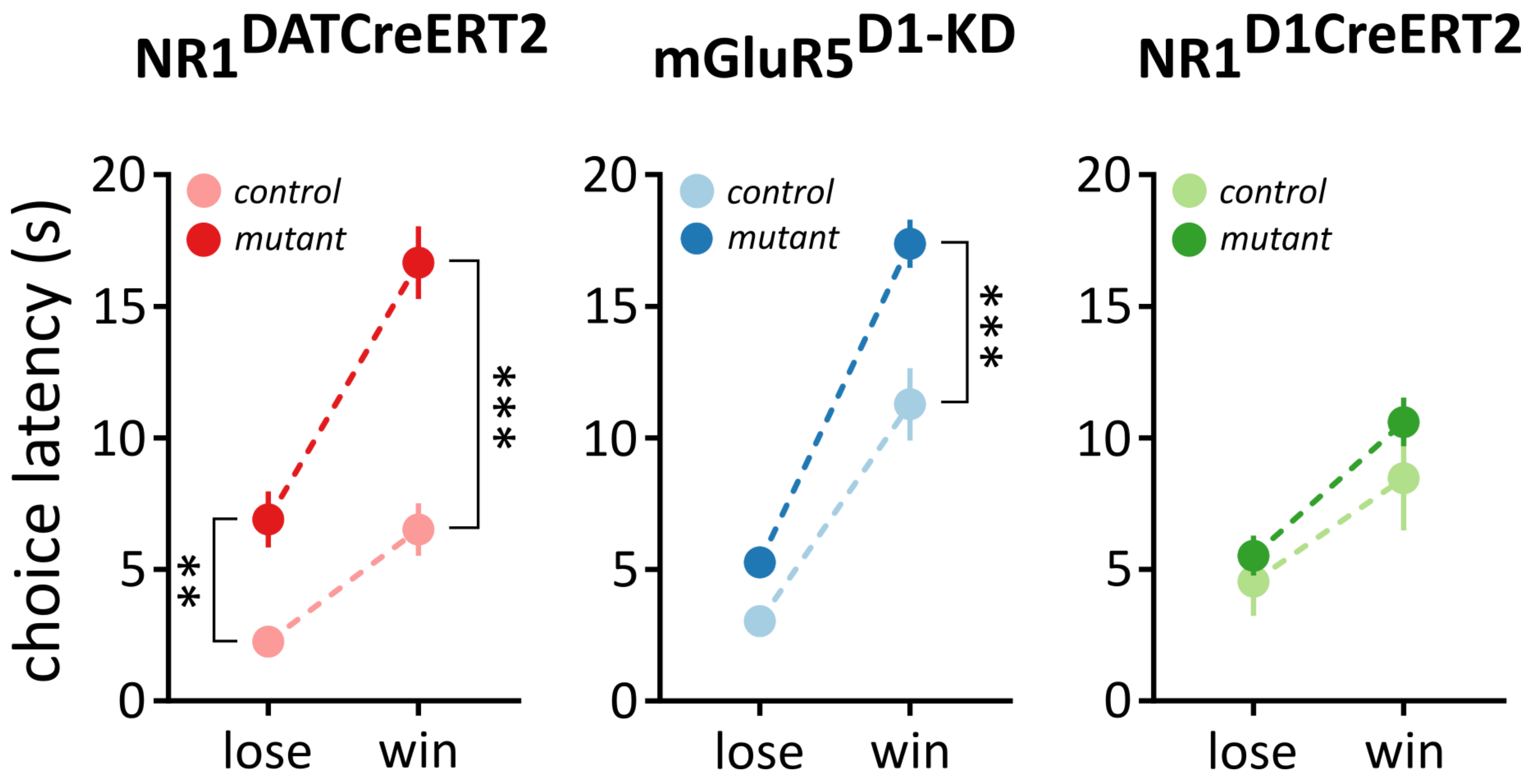
Model fits

ps-R^2 = 0,47	ps-R^2 = 0,41	ps-R^2 = 0,45
ps-R^2 = 0,32	ps-R^2 = 0,25	ps-R^2 = 0,32

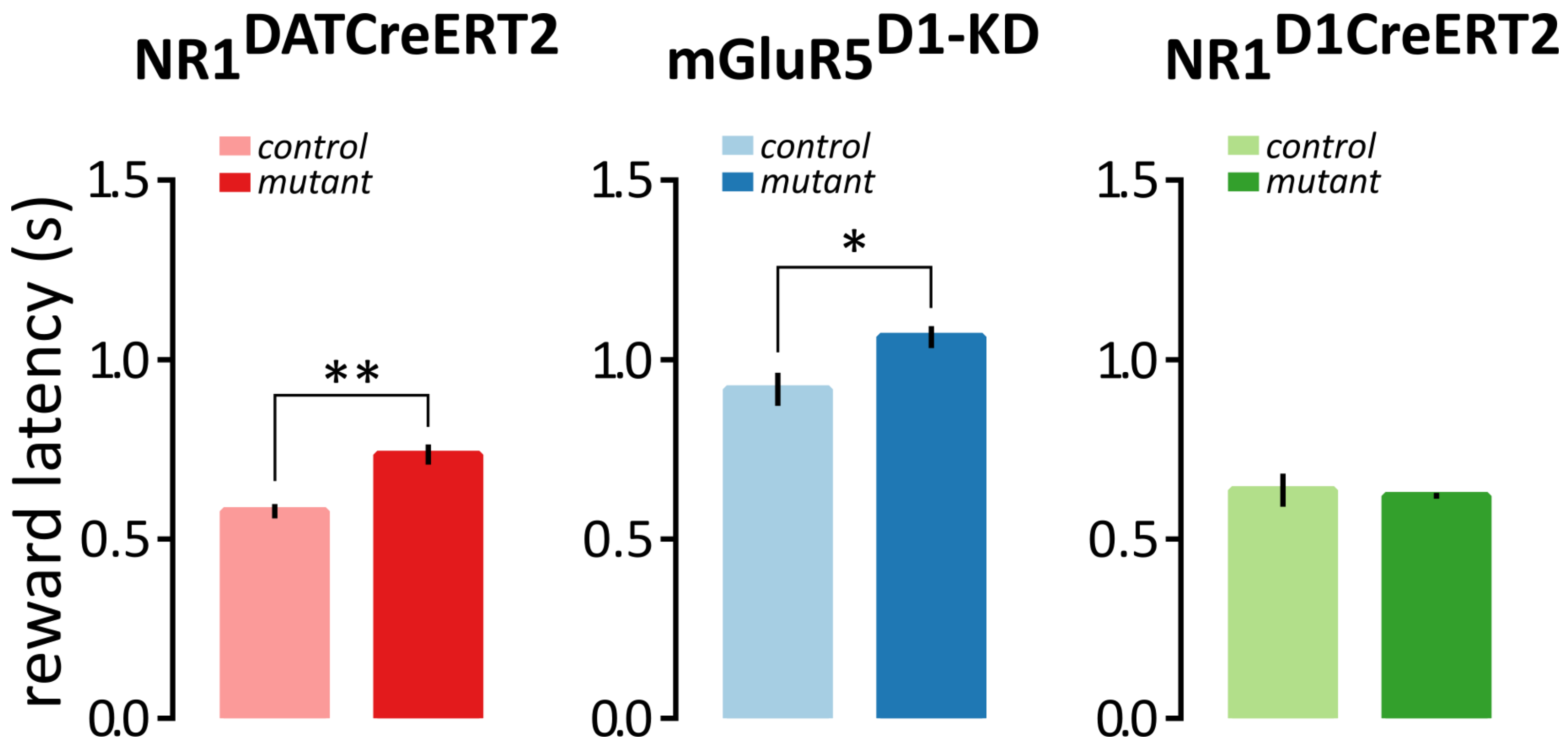
Logistic regression model

Parker et al., 2016 *Nat Neurosci*

Reaction time (choice)



Reaction time (reward)



Learning the value of actions & value-based action selection

(1) Value updating rule:

$$V_L \leftarrow V_L + \alpha \cdot RPE$$
$$RPE = R_L - V_L$$

where: V_L – expected value of ‚Left' option

R_L – outcome received from ‚Left' option

$\boldsymbol{\alpha}$ – **learning rate**, determines how rapidly the estimate of expected value is updated

(2) Action selection rule (softmax):

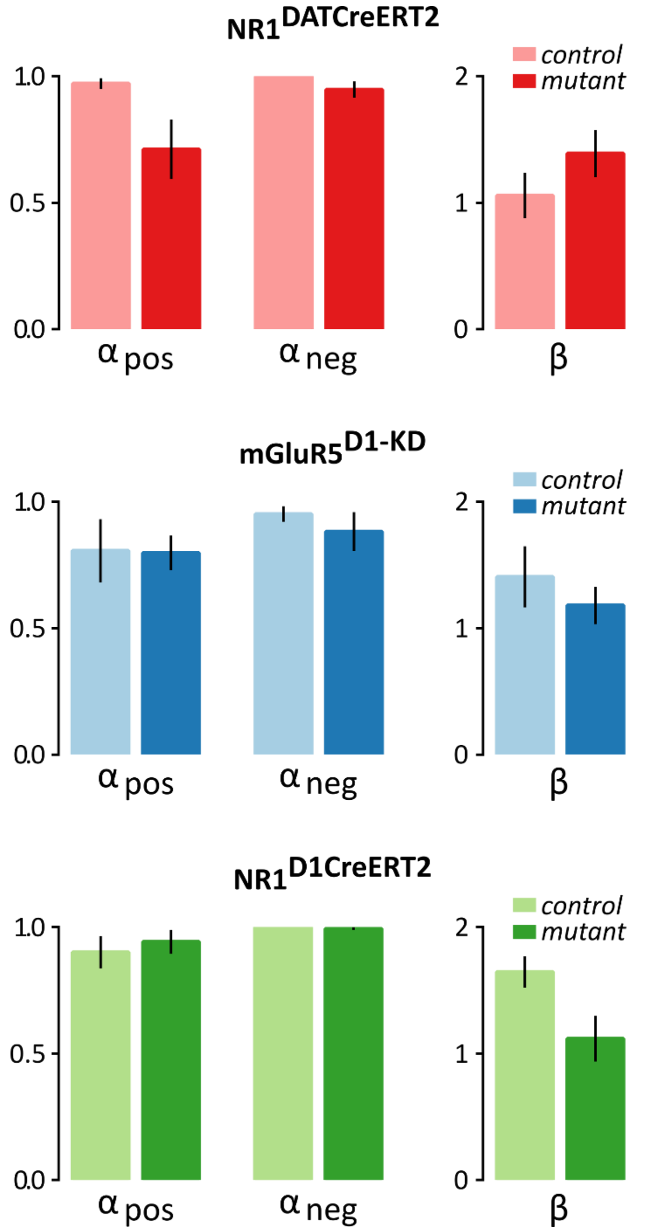
$$P_L = \frac{e^{\beta V_L}}{e^{\beta V_L} + e^{\beta V_R}}$$

where: P_L – probability of choosing ‚Left' option

$\boldsymbol{\beta}$ – **randomness in action selection:**

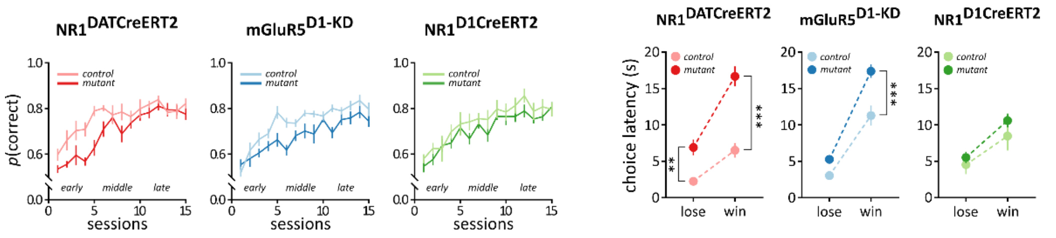
With β = 0, action selection is totally random,

As β is increased, the model is more likely to choose the action believed to have the maximum value

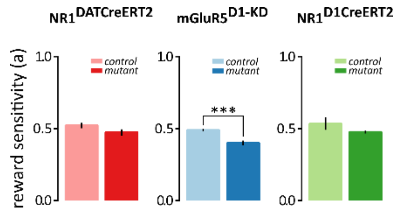


Summary & conclusion

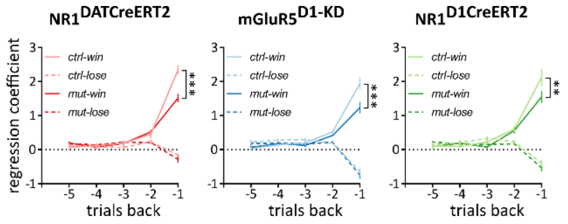
- Ablation of NMDA receptors in DA neurons and mGluR5 receptors in D1R-expressing neurons decreased the likelihood of choosing alternative with higher probability of reward and increased response latency



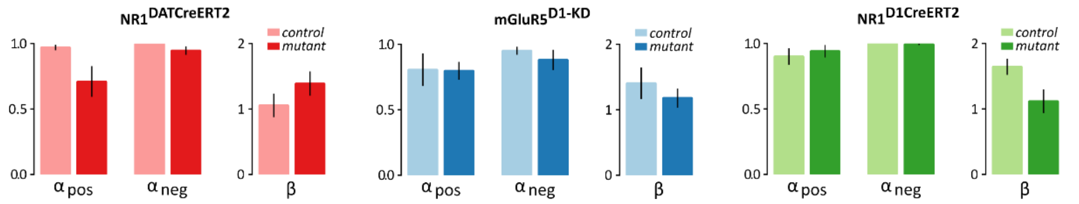
- Ablation of mGluR5 receptors in D1 neurons reduced sensitivity of mutant animals to changes in reward ratios



- Mutant animals were less likely to return to a choice which was previously rewarded



- Loss of NMDA receptors in DA neurons decreased the learning rate from positive outcomes, while ablation of Glu receptors in D1 neurons increased randomness in action selection



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Jan Rodriguez Parkitna

Thank You!

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