



Effect of 5-HT₆-R blockade on NMDA activation in an innovative animal model of schizophrenia

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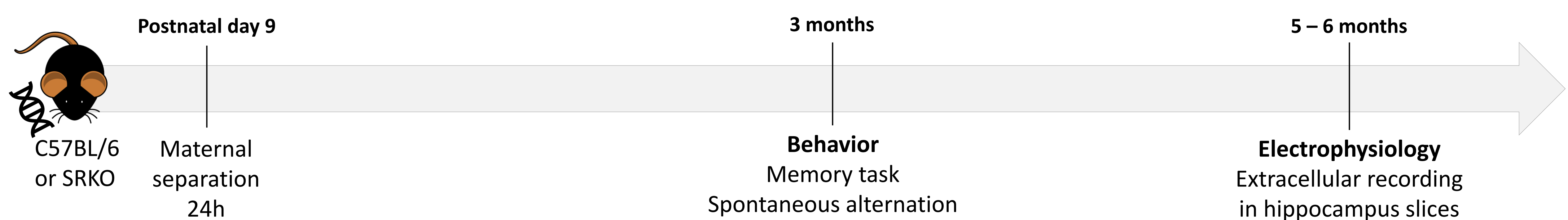
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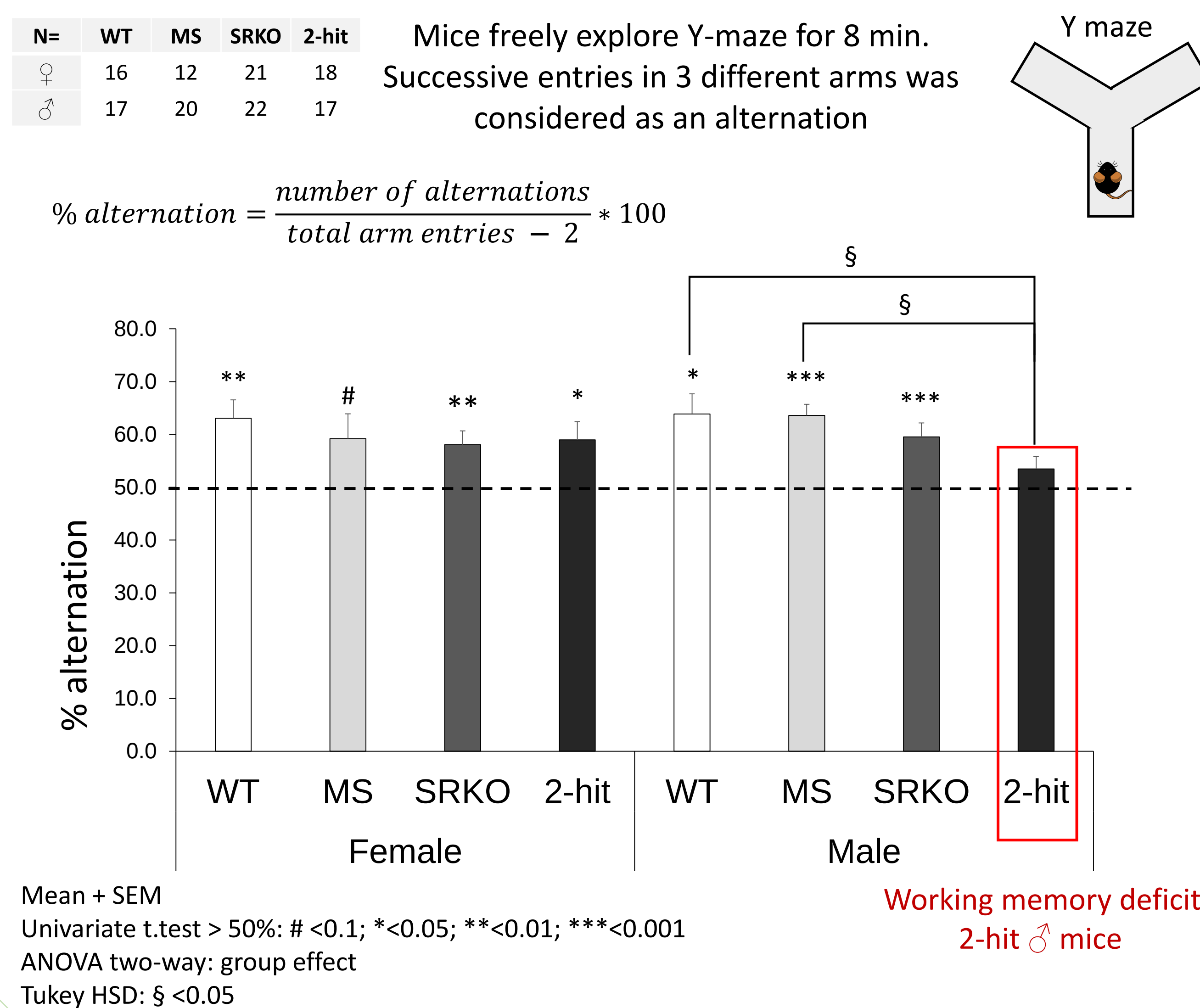
Assess **memory deficit** in a 2-hit model and investigate the effect of a 5-HT₆-R antagonist (SB-271046) on **basal NMDA-R activation**

2-hit mouse model

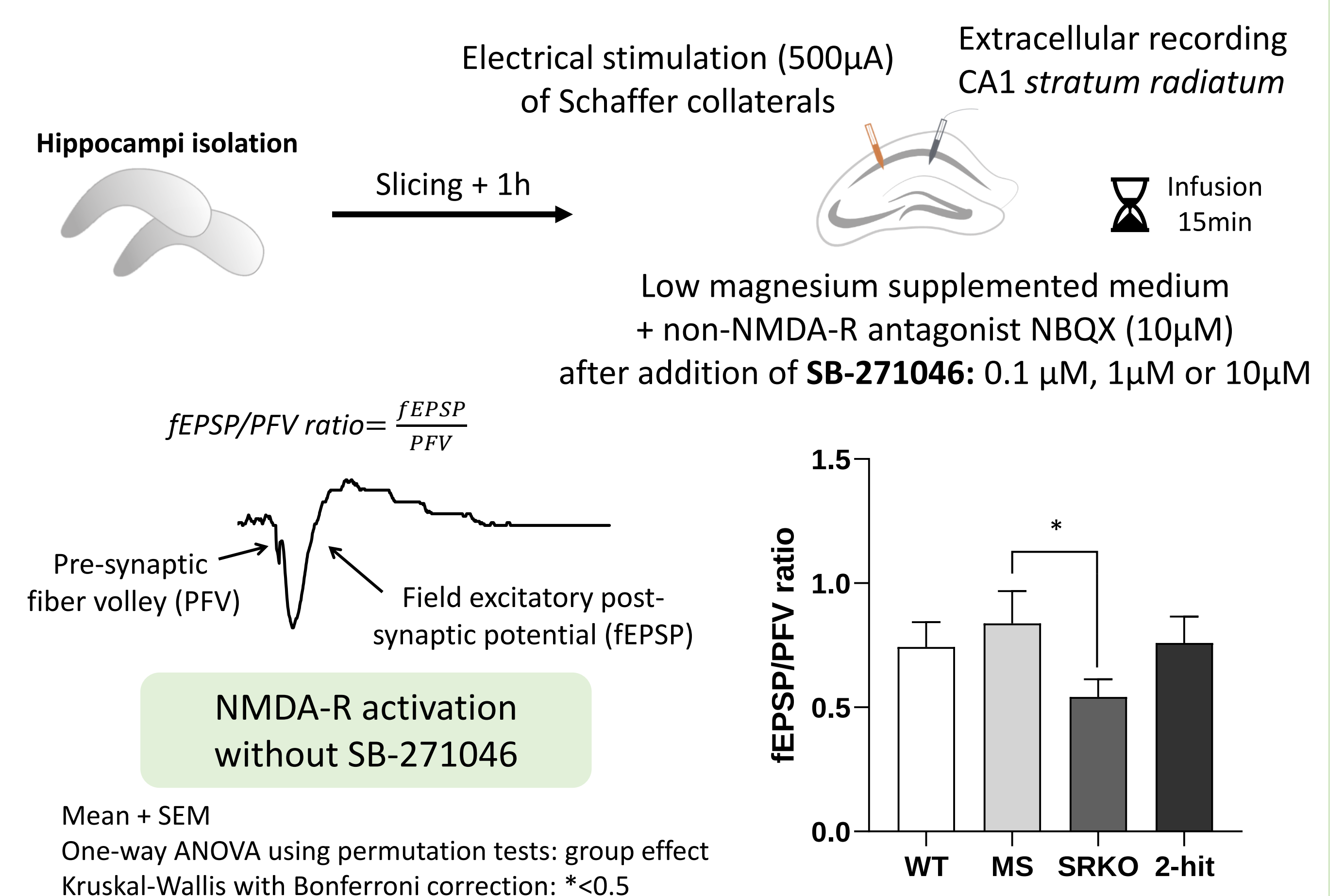
Serine racemase deletion (SRKO) [3] X Maternal separation (MS) PND9-24h [4]
Altered glutamate transmission Early stress



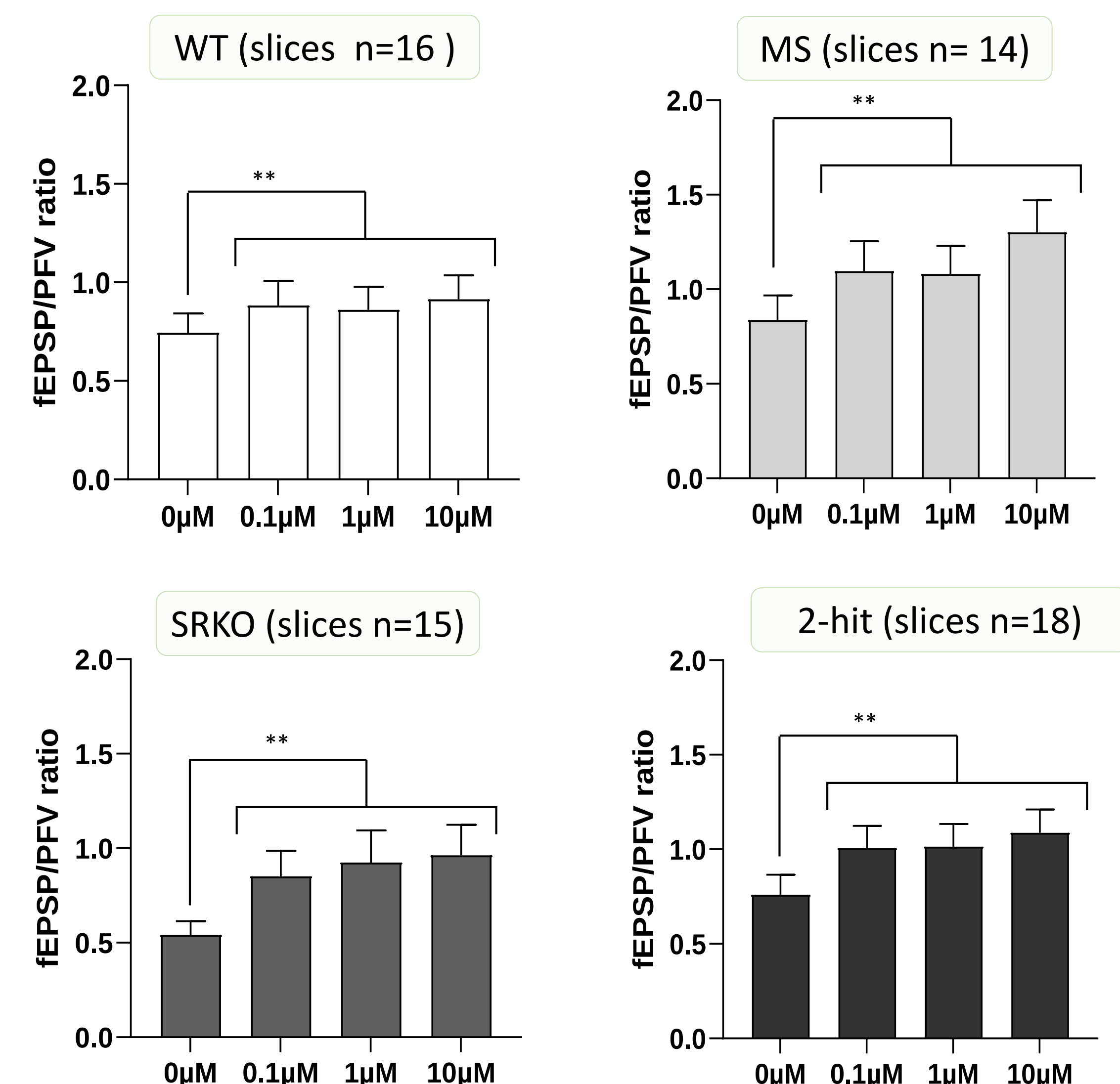
Spontaneous alternation Working memory



Extracellular recording Isolated NMDA-R activation



NMDA-R activation with SB-271046



Mean + SEM
t.test paired: ** <0.01

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The combination between genetic x environmental factor induces **working memory deficit** in 2-hit male mice. This is not accompanied with **deficit in basal NMDA-R activation** in 2-hit male mice.

We are now investigating the expression of synaptic plasticity (long term potentiation, LTP) which requires more intense NMDA-R activation, along with other memory functions (object/place discrimination).

5-HT₆-R antagonist SB-271046 whatever the dose **increases NMDA-R activation in all groups**. This increase could prevent working memory deficits and possible LTP dysregulation in 2-hit mice.

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[3] Coyle JT, Balu DT. Adv Pharmacol. 2018. DOI: 10.1016/bs.apha.2017.10.002

[4] Ellenbroek BA et al. Schizophr Res. 1998. DOI/ 10.1016/s0920-9964(97)00149-7