



**HAL**  
open science

## Effect of 5-HT<sub>6</sub>-R blockade on NMDA activation in an innovative animal model of schizophrenia

Caroline Lahogue, Jean-Marie Billard, Thomas Freret, Valentine Bouet

### ► To cite this version:

Caroline Lahogue, Jean-Marie Billard, Thomas Freret, Valentine Bouet. Effect of 5-HT<sub>6</sub>-R blockade on NMDA activation in an innovative animal model of schizophrenia. GDR Mémoire - 1er Colloque Interdisciplinaire du GDR mémoire, Oct 2021, Vers, France. . hal-04216528

**HAL Id: hal-04216528**

**<https://hal.science/hal-04216528>**

Submitted on 25 Sep 2023

**HAL** is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

Memory impairments belong to symptoms of schizophrenia which are not alleviated by antipsychotic drugs

→ Serotonergic subtype 6 receptors (5-HT<sub>6</sub>-R) are an interesting target to improve current treatment:

- localized in regions involved in schizophrenia such as hippocampus
- reverse memory deficit by selective blockade (SB-271046) [1]

→ N-methyl-D-aspartate subtype of glutamate receptors (NMDA-R):

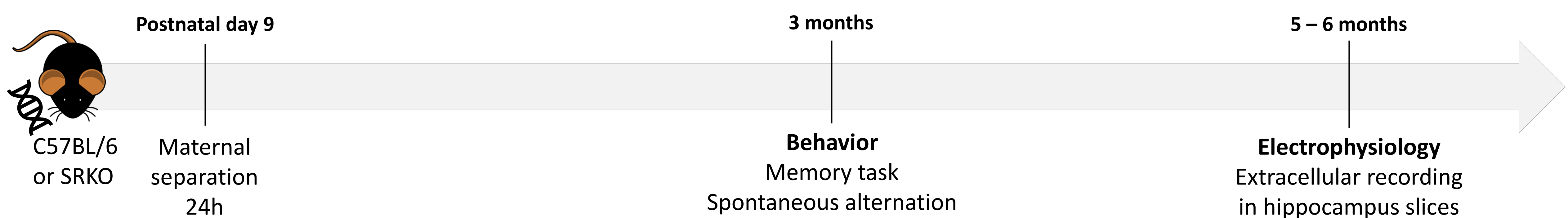
- are key regulators of memory processes
- have crucial role in the physiopathology of schizophrenia [2]

## AIMS

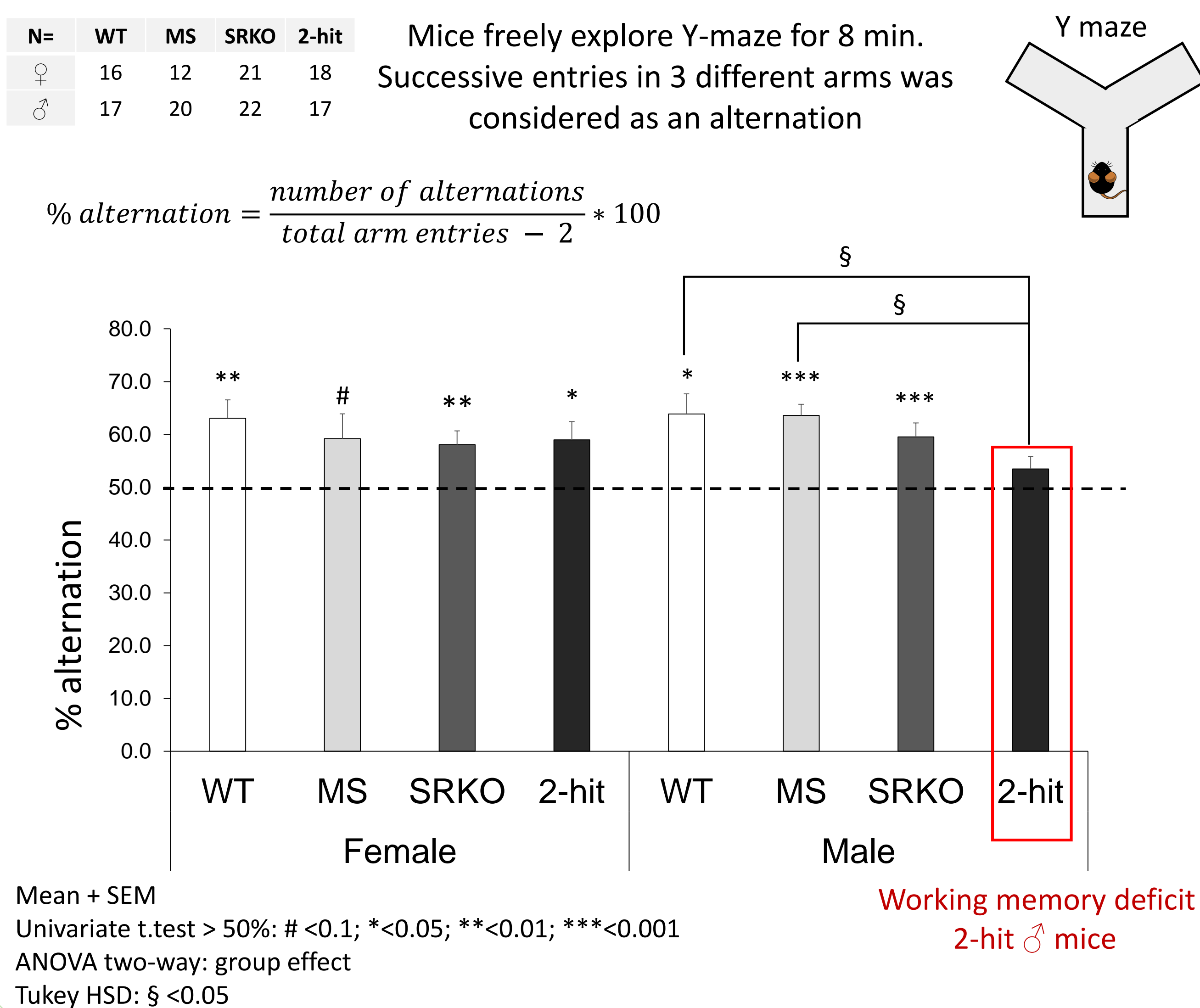
Assess memory deficit in a 2-hit model and investigate the effect of a 5-HT<sub>6</sub>-R antagonist (SB-271046) on basal NMDA-R activation

## 2-hit mouse model

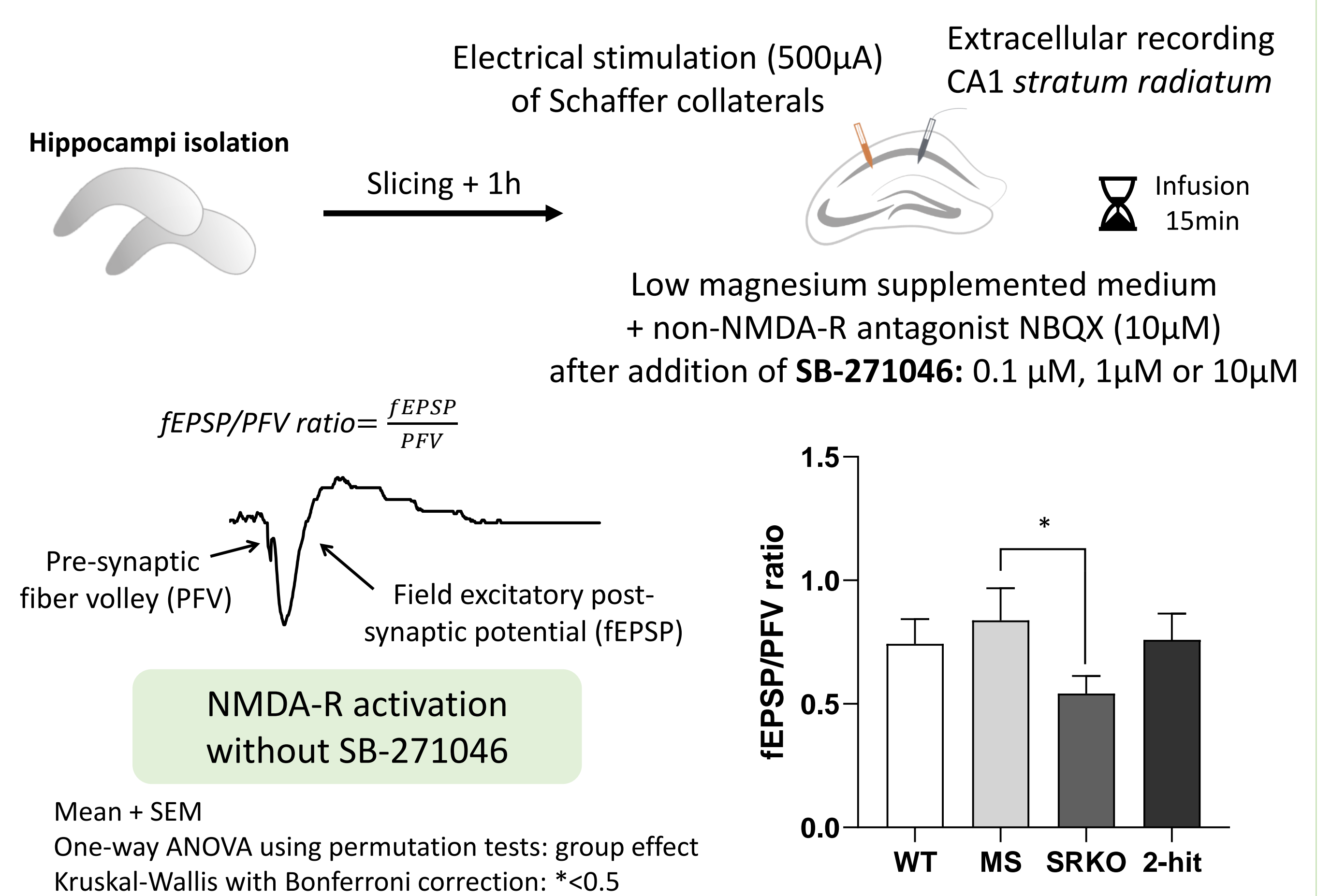
Serine racemase deletion (SRKO) [3] X Maternal separation (MS) PND9-24h [4]  
Altered glutamate transmission Early stress



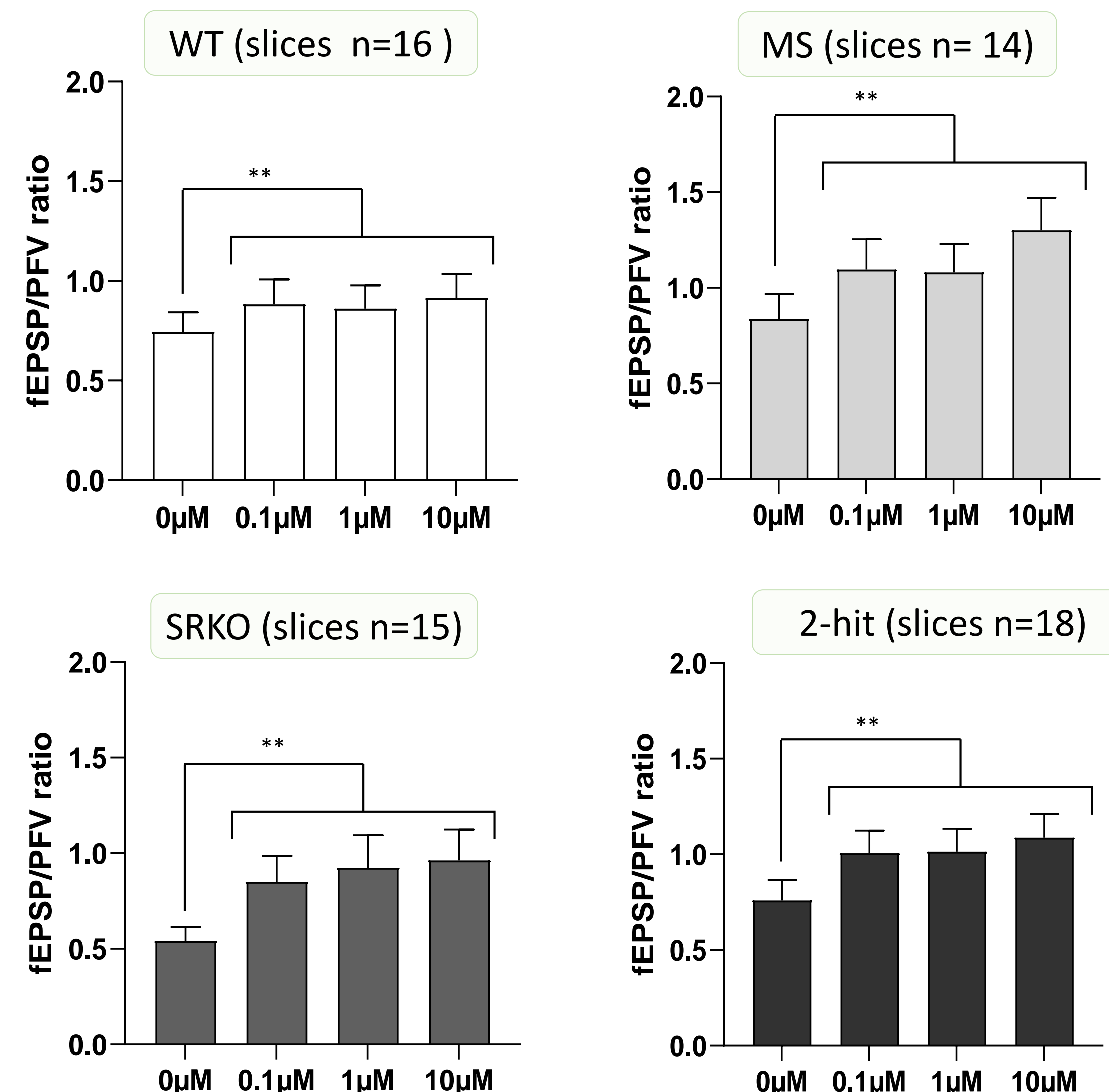
## Spontaneous alternation Working memory



## Extracellular recording Isolated NMDA-R activation



## NMDA-R activation with SB-271046



## TAKE HOME MESSAGE

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-HT<sub>6</sub>-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.

[1] Da Silva Costa-Aze V et al. Behav Brain Res. 2011. DOI: 10.1016/j.bbr.2011.03.046.

[2] Balu DT. Adv Pharmacol. 2013. DOI: 10.1016/bs.apha.2016.01.006.

[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