



**HAL**  
open science

## Treatment strategy targeting 5-HT<sub>6</sub>R in an innovative animal model of Schizophrenia

Caroline Lahogue, Michel Boulouard, François Menager, Thomas Freret,  
Jean-Marie Billard, Valentine Bouet

► **To cite this version:**

Caroline Lahogue, Michel Boulouard, François Menager, Thomas Freret, Jean-Marie Billard, et al..  
Treatment strategy targeting 5-HT<sub>6</sub>R in an innovative animal model of Schizophrenia. FENS 2024,  
Jun 2024, Vienne, Austria. hal-04634813

**HAL Id: hal-04634813**

**<https://hal.science/hal-04634813v1>**

Submitted on 15 Jul 2024

**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.



Distributed under a Creative Commons Attribution - NonCommercial - ShareAlike 4.0 International License



Contact: caroline.lahogue@unicaen.fr

Lahogue C., Boulouard M., Menager F., Freret T., Billard J-M., Bouet V.

Normandie Univ, UNICAEN, INSERM, FHU A2M2P, COMETE, 14000 Caen, France

## INTRODUCTION

### Schizophrenia

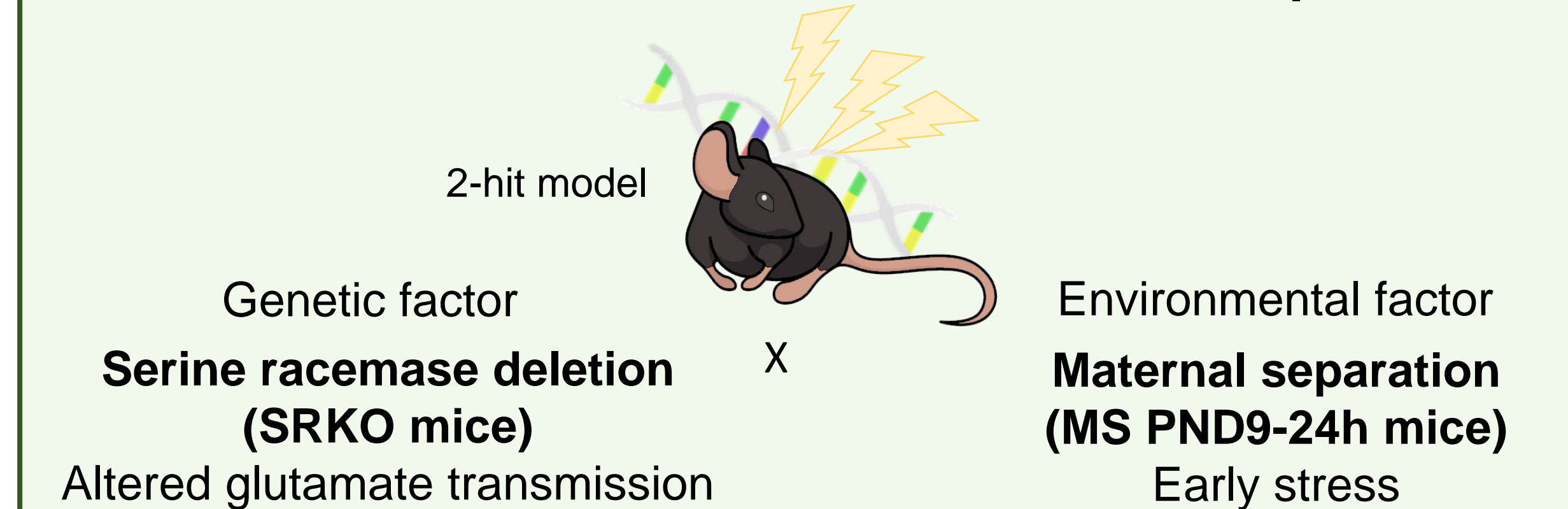
- Etiology: still unknown based on **genetic x environmental factors**
- Antipsychotic drugs improve positive symptoms (delirium, hallucination) but not **negative symptoms** (avolition, anhedonia, social withdrawal...) and **cognitive deficits** (memory impairment...)
- **New therapeutic targets need to be tested in multifactorial animal model to improve negative and cognitive symptoms**

### Serotonergic subtype 6 receptors (5-HT6R)

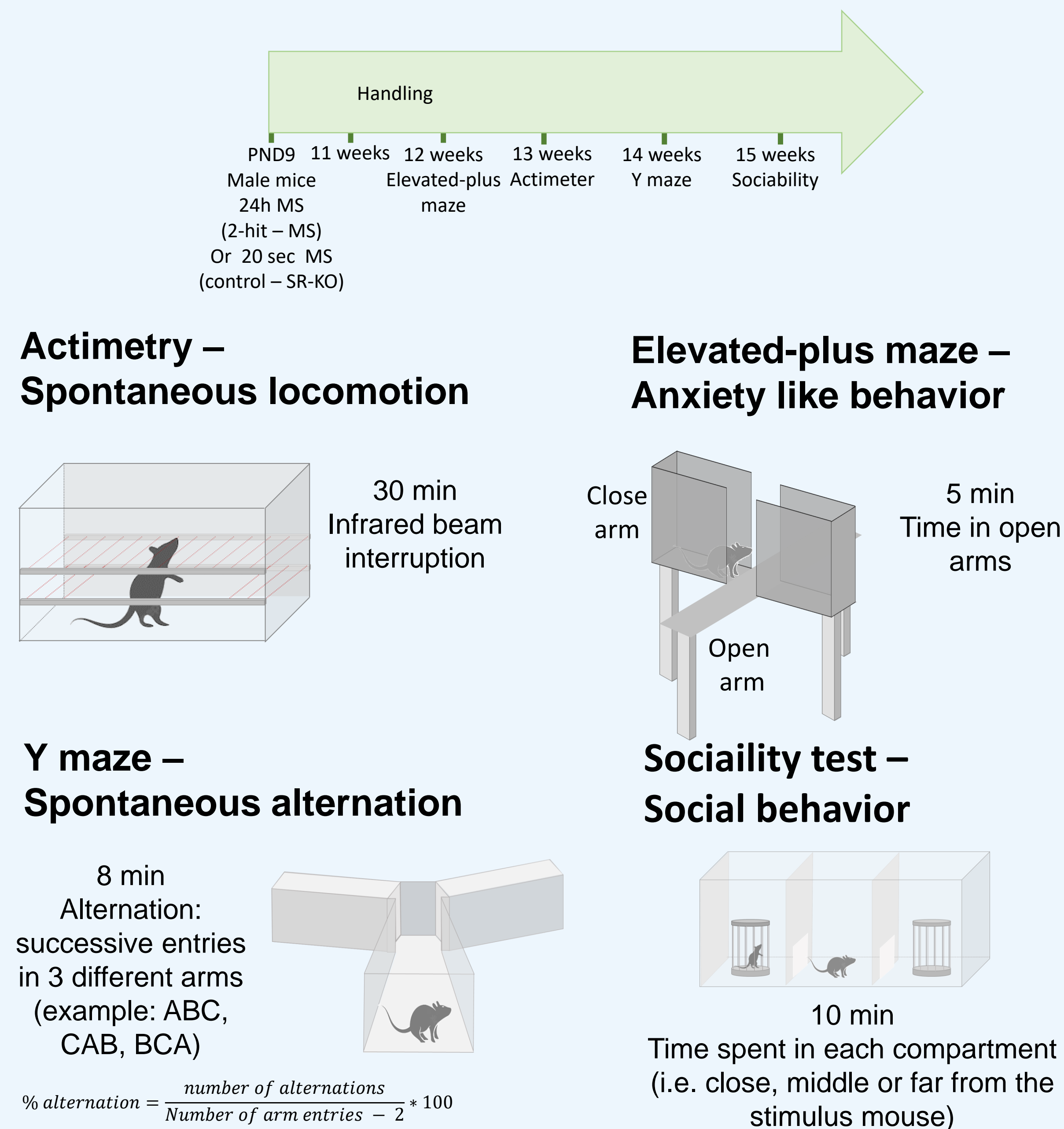
- 5-HT6R expressed in the brain regions involved in schizophrenia such as hippocampus
- Blockade of 5-HT6Rs (SB-271046) improves short- and long-term memory in rodents (*Da Silva Costa-Aze et al., 2011, 2012*)
- SB-271046** is a selective 5-HT6R antagonist
- **Blockade of 5-HT6 receptors is a promising strategy to improve memory deficits**

## AIM

Characterize the efficacy of pharmacological modulation of 5-HT6R in a new mouse model of schizophrenia

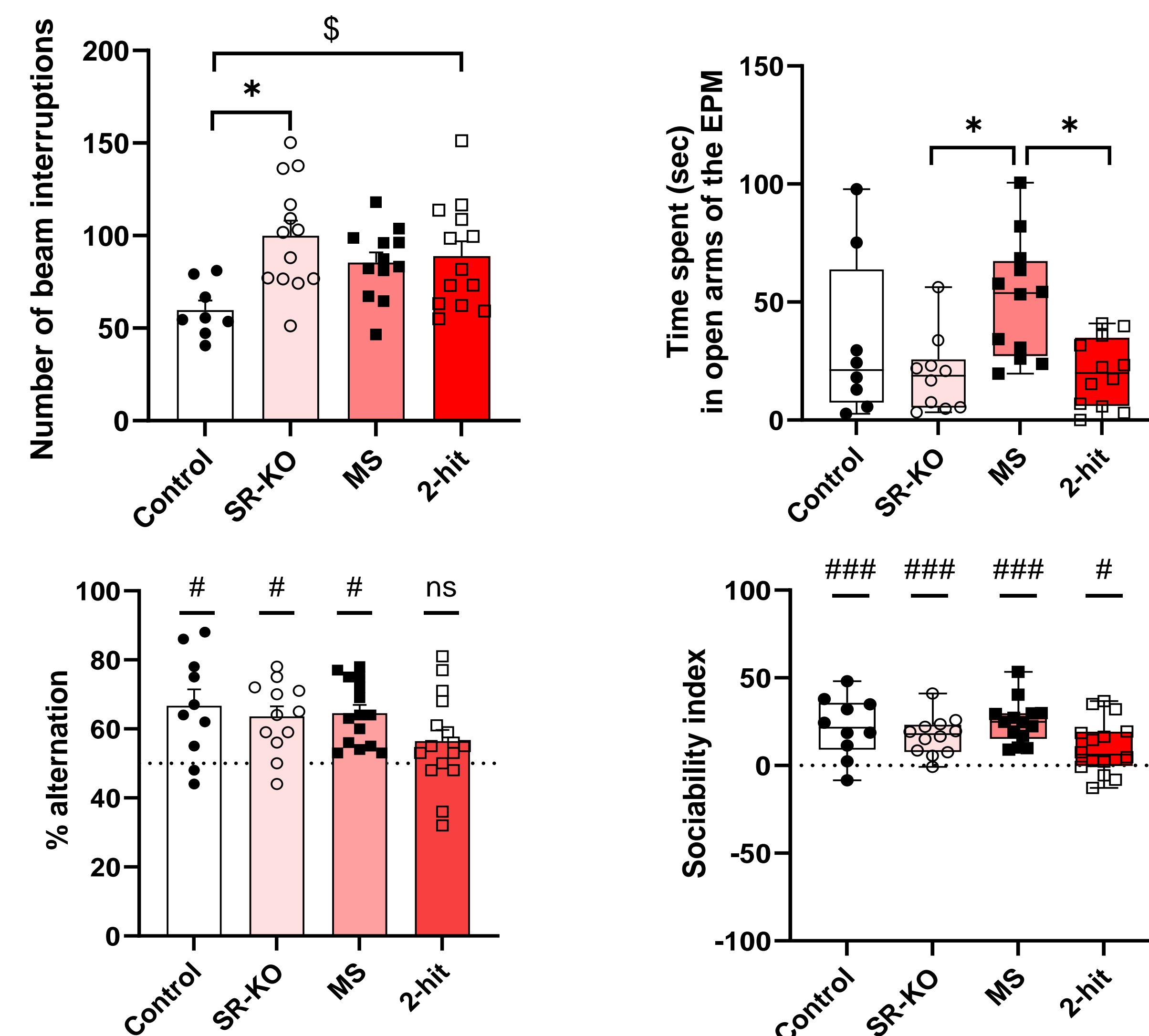


## MATERIALS & METHODS



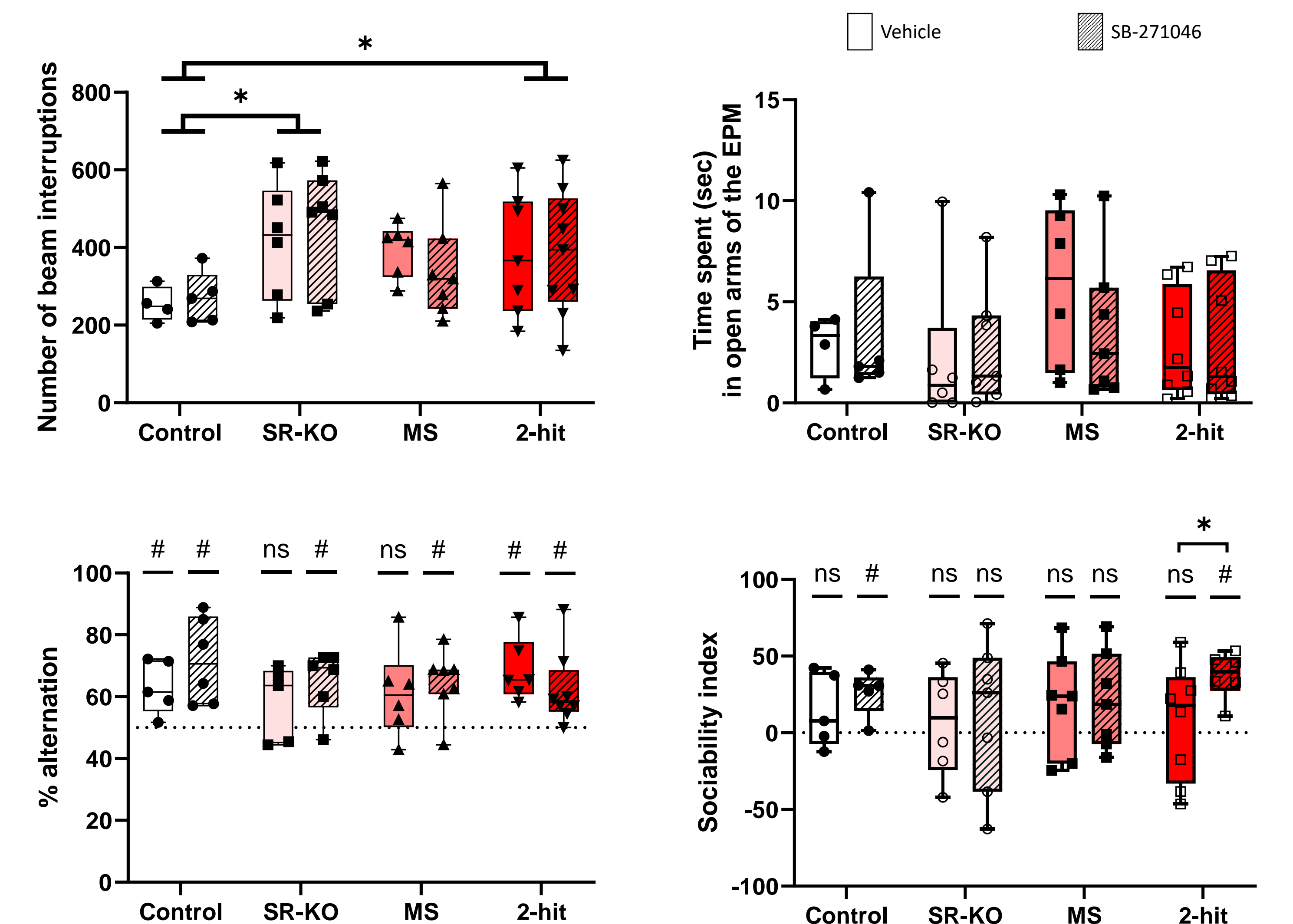
## CHARACTERIZATION OF 2-HIT MODEL

2-hit mice show an increase in locomotor activity and an impairment of working memory processes



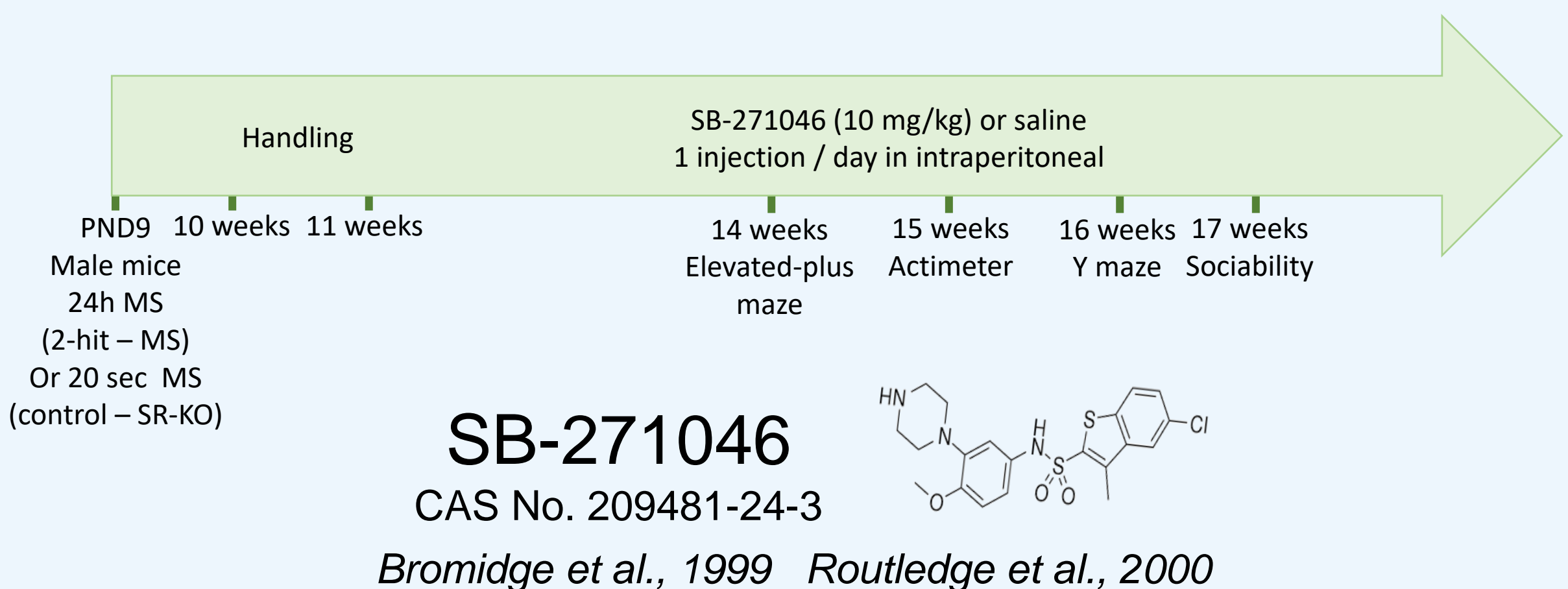
## CHARACTERIZATION OF 5-HT6R EFFICACY

SB-271046 treatment improves sociability in 2-hit mice, but has no effect on locomotion, anxiety-like behavior or working memory.



S < 0.1; \* < 0.05 2-way ANOVA or 2-way ANOVA using permutation  
# < 0.05; ### < 0.001 compared to reference value one-sample t-test or one-Sample Wilcoxon test

## PROTOCOL CHRONIC TREATMENT



## TAKE HOME MESSAGE

- Our combination between genetic x environmental factor induces working memory deficit and hyperlocomotion in 2-hit male mice.
- **The 2-hit mice mainly modelis an interesting phenotype the positive and cognitive symptoms of schizophrenia.**
- SB-271046 is benefical for on sociability in 2-hit group. SB-271046 does not improve cognitive deficits, maybe due to the insufficient dose or the duration of treatment. The combination of the 5-HT6R antagonist with an antipsychotic could be relevant to improve the effects.
- **SB-271046 could be an adjuvant treatment for negative symptoms.**