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## Treatment strategy targeting 5-HT6R in an innovative animal model of Schizophrenia

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## INTRODUCTION

### Schizophrenia

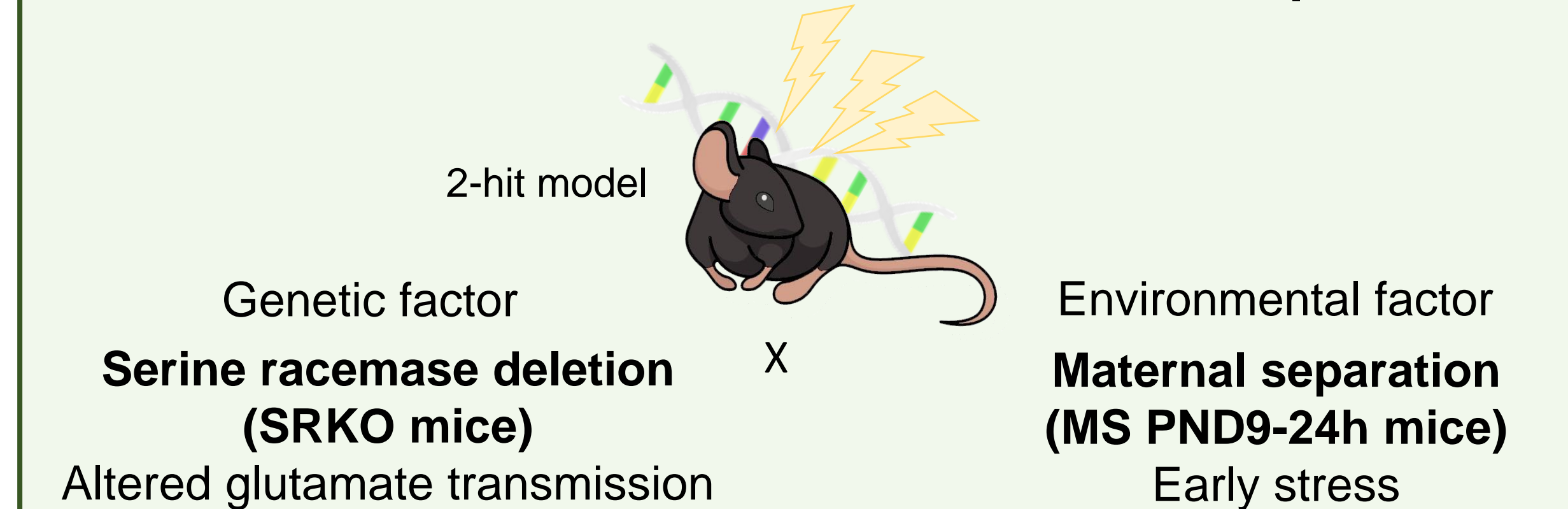
- Etiology: still unknown based on **genetic x environmental factors**
- Antipsychotic drugs improve positive symptoms (delirium, hallucination) but not **negative symptoms** (avolition, anhedonia, social withdrawal...) and **cognitive deficits** (memory impairment...)
- **New therapeutic targets need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

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

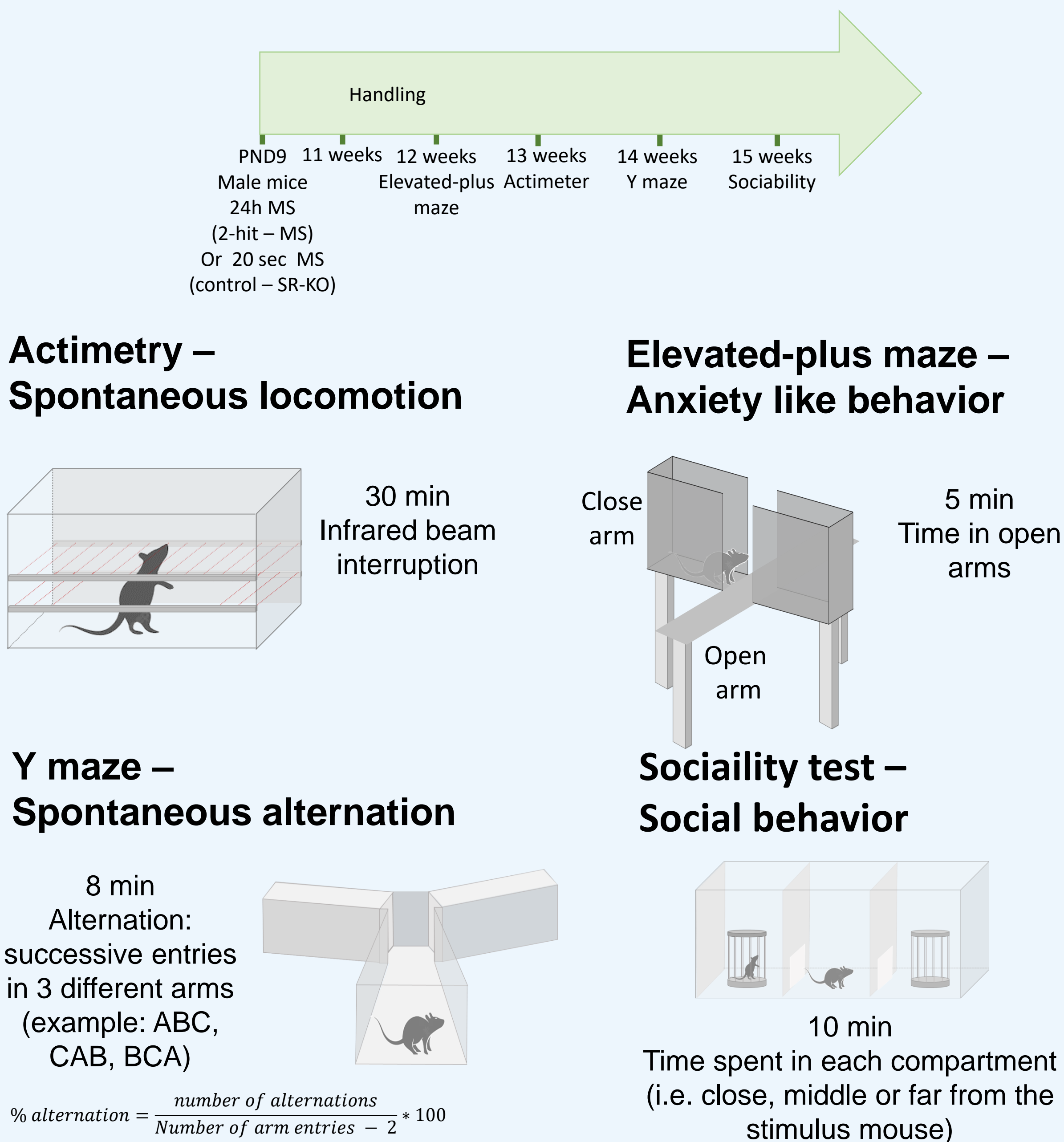
- 5-HT6R expressed in the brain regions involved in schizophrenia such as hippocampus
- Blockade of 5-HT6Rs (SB-271046) improves short- and long-term memory in rodents (*Da Silva Costa-Aze et al., 2011, 2012*)
- SB-271046** is a selective 5-HT6R antagonist
- **Blockade of 5-HT6 receptors is a promising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

## AIM

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

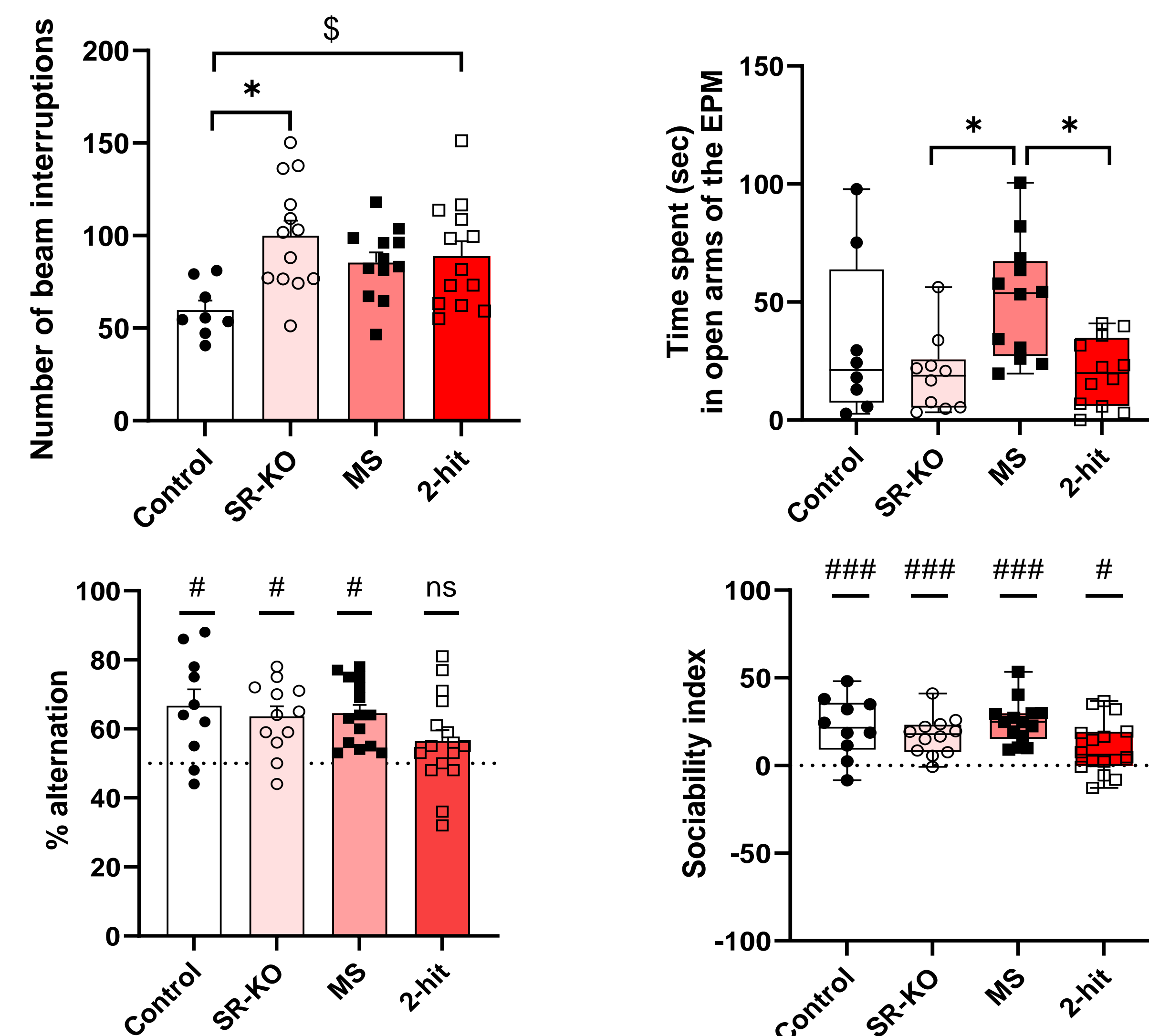


## MATERIALS & METHODS



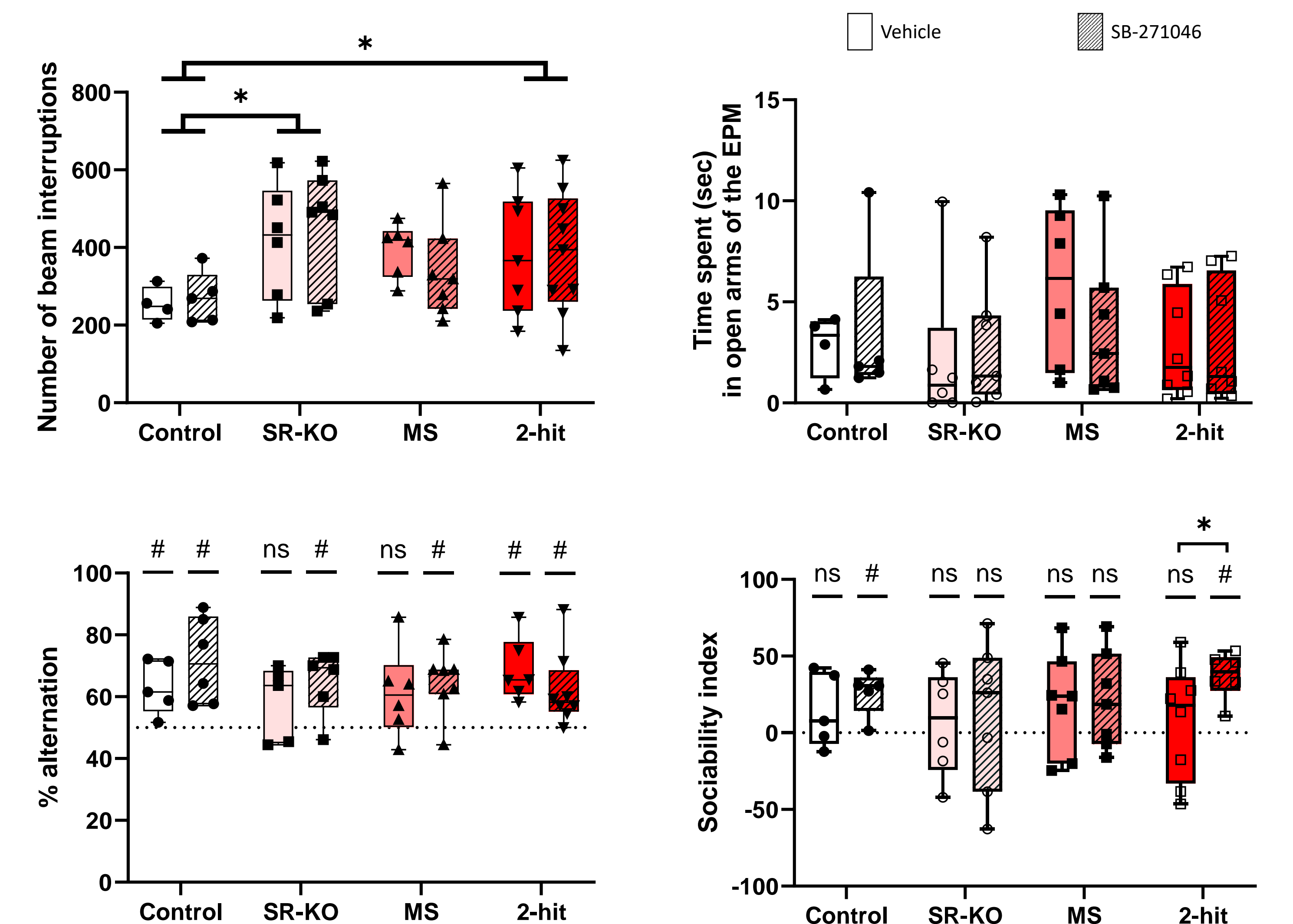
## CHARACTERIZATION OF 2-HIT MODEL

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

## 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 beneficial 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.**

