



# Altering glutamate transmission in combination with an early post-natal stress to mimic schizophrenia in male and female mice

F Menager, Solenn Percelay, T. Freret, M. Boulouard, Jean-Marie Billard, V. Bouet

## ► To cite this version:

F Menager, Solenn Percelay, T. Freret, M. Boulouard, Jean-Marie Billard, et al.. Altering glutamate transmission in combination with an early post-natal stress to mimic schizophrenia in male and female mice. Journée Normande de Recherche Biomédicale, Nov 2019, Caen, France. hal-02363095

HAL Id: hal-02363095

<https://hal-normandie-univ.archives-ouvertes.fr/hal-02363095>

Submitted on 14 Nov 2019

**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.

# Altering glutamate transmission in combination with an early post-natal stress to mimic schizophrenia in male and female mice

F. Menager, S. Percelay, T. Freret, M. Boulouard, JM. Billard, V. Bouet  
Normandie Univ, UNICAEN, INSERM, COMETE, GIP CYCERON, 14000 Caen, France

## Schizophrenia

1% population, onset 15-25 years  
Multifactorial: genetic x environmental factors  
Symptoms: positive, negative, cognitive  
Debilitating disease → heavy costs

Treatments: not efficient on negative and cognitive symptoms, multiple side-effects

### Crucial need to refine treatments

- Improving validity of animal models of schizophrenia
- Combining genetic x environmental factors

Total Serine racemase deletion  
Coyle et al., 2018



X

Maternal separation  
PND9-24h

Ellenbroek et al., 1998; Bouet et al., 2011



C57Bl6 male and female mice

Altered glutamate transmission:

➤ Serine racemase KO mice **SRKO**

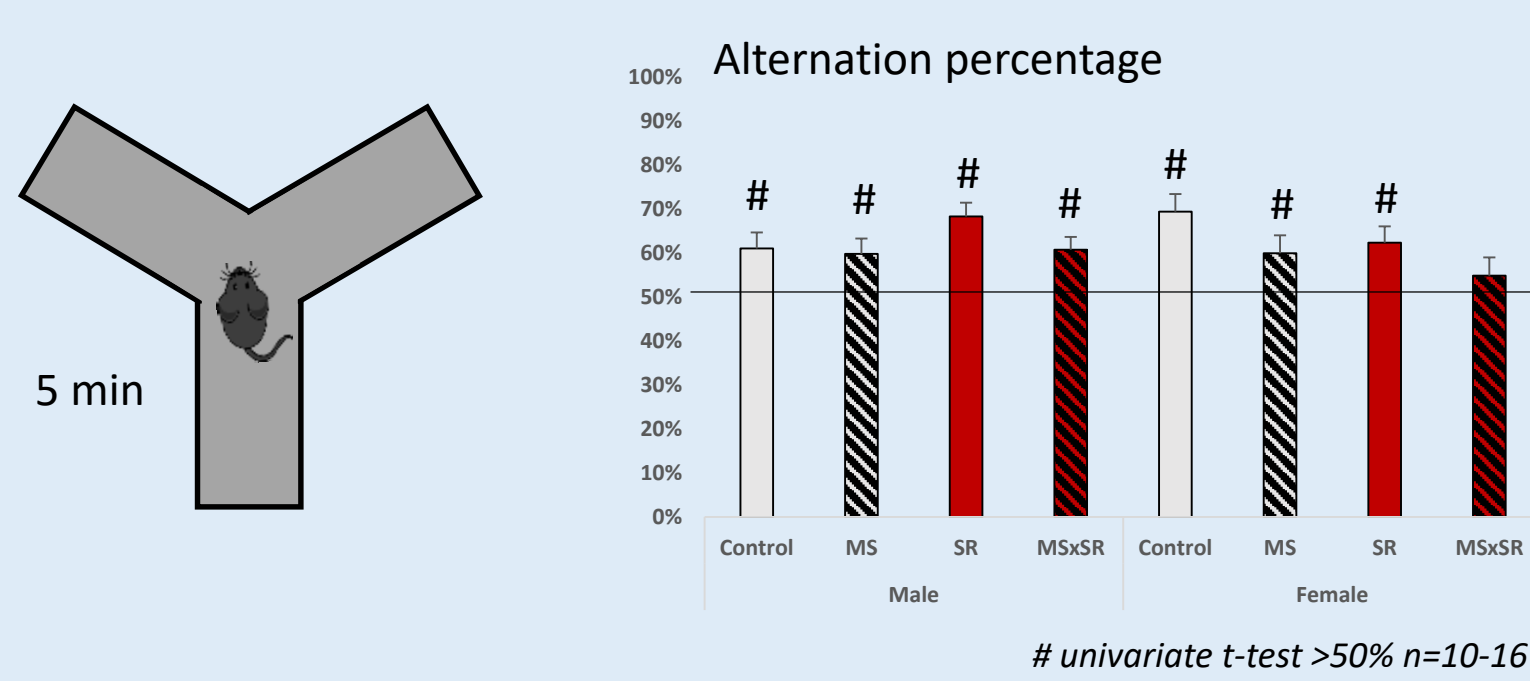
Early stress:

➤ Maternal separation **MS**

Behavioural testing

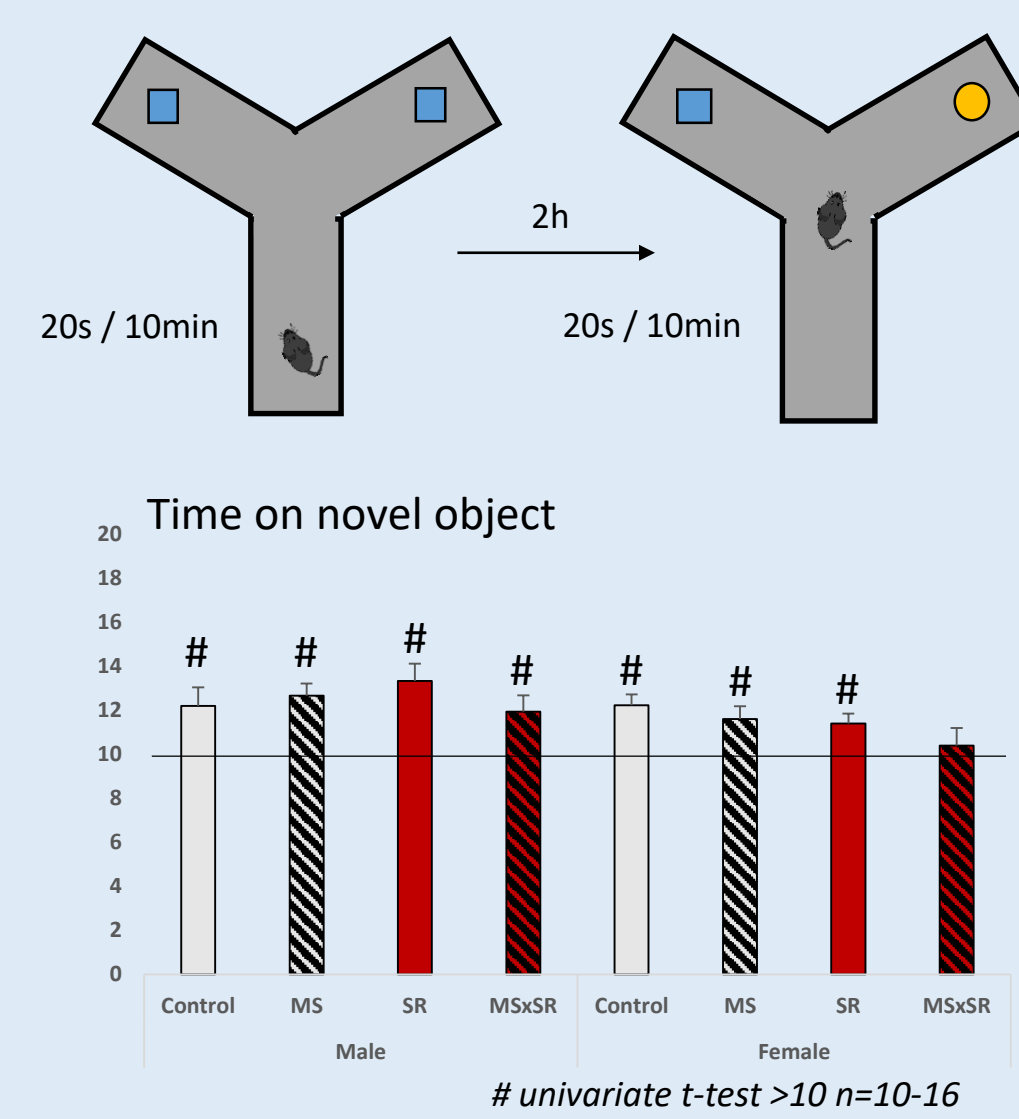
- Anxiety-like behavior
- Short and long-term memory
- Social behavior
- Sensory-motor gating

### Short-term memory Spontaneous alternation



MSxSR combination induced working memory deficit in female but not in male mice

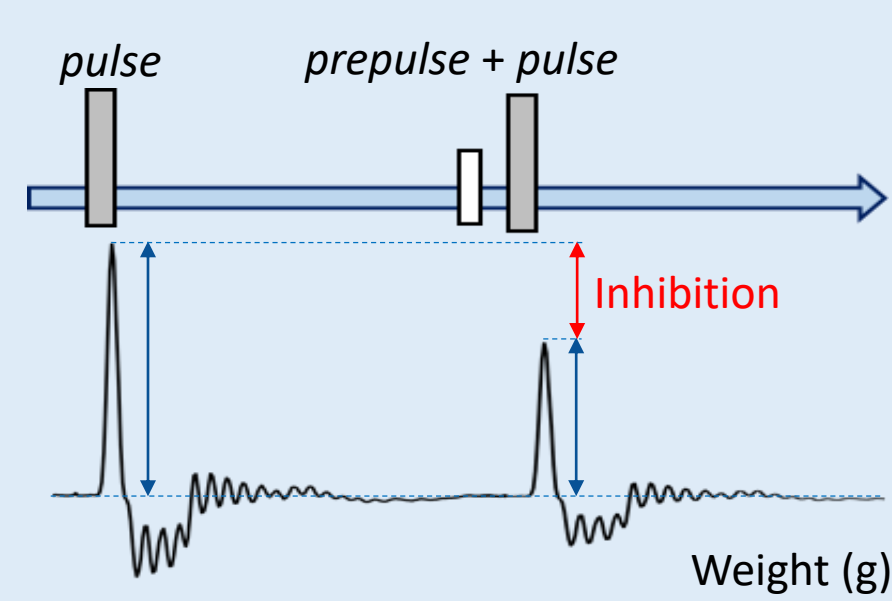
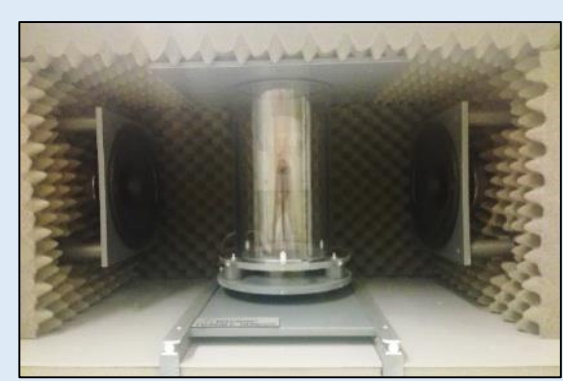
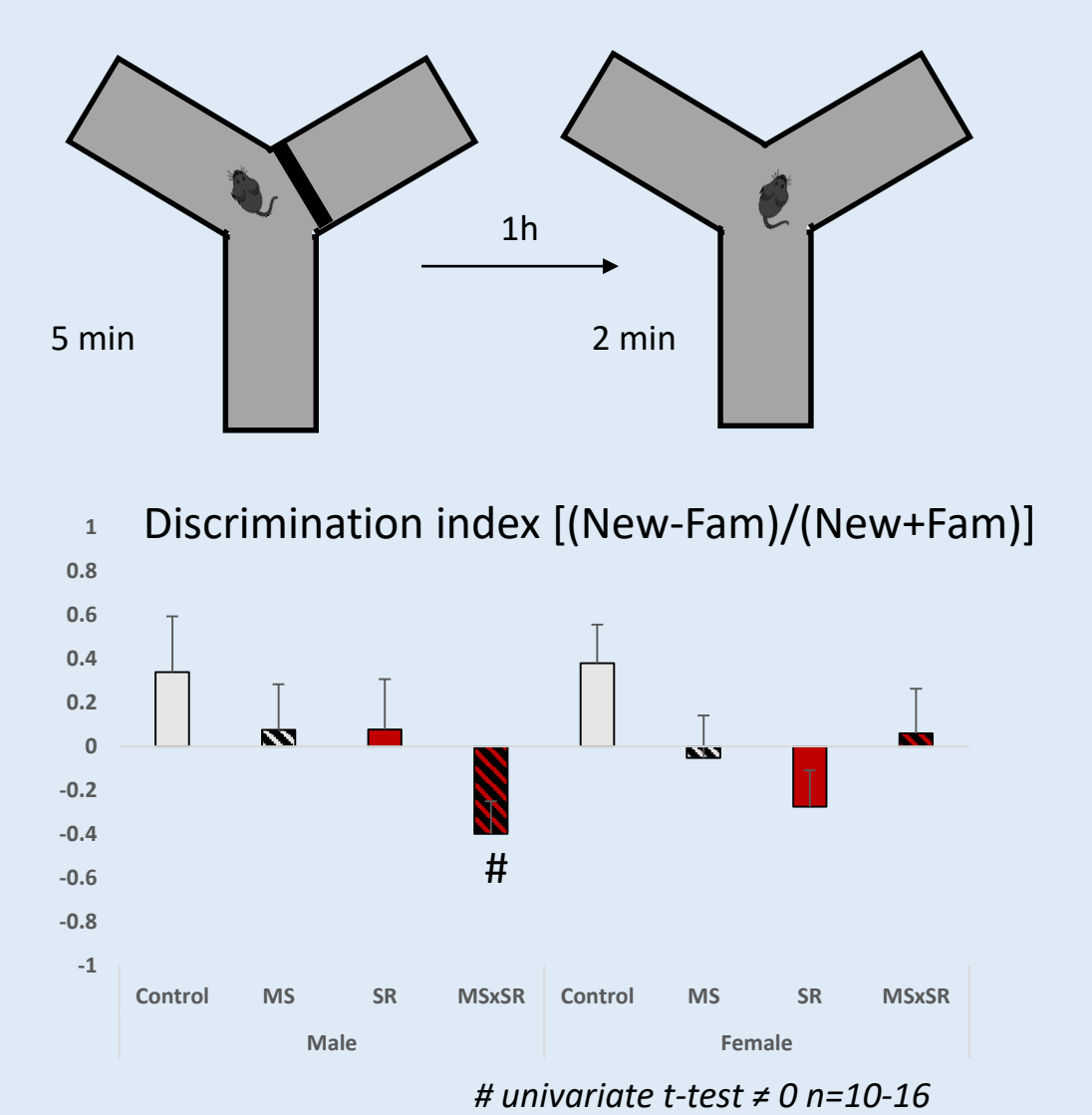
### Object recognition memory



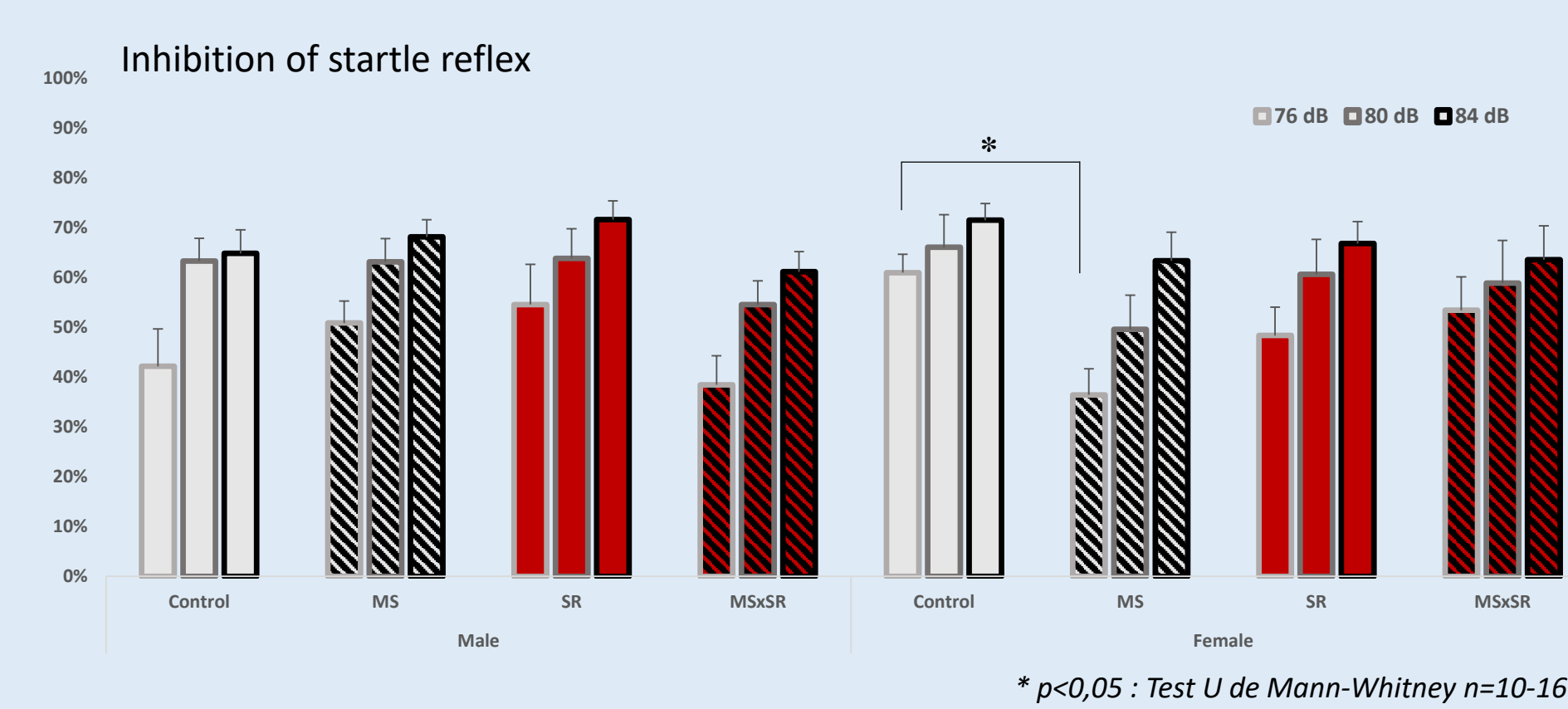
← Object recognition: MSxSR combination altered performances in female mice

→ Place recognition: MSxSR combination altered performances in male mice

### Place recognition memory

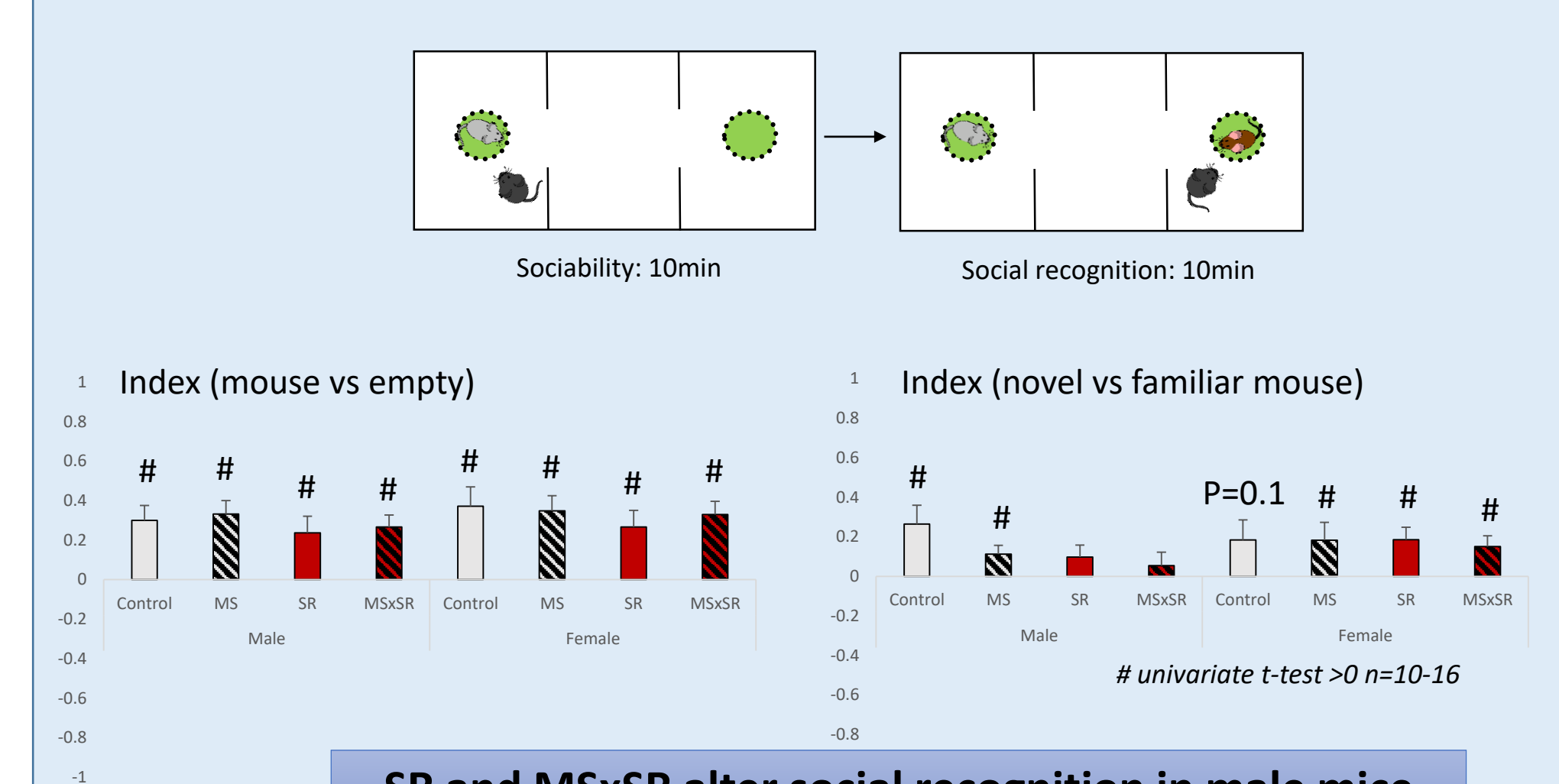


### Sensorimotor gating



MS decreased PPI in female mice

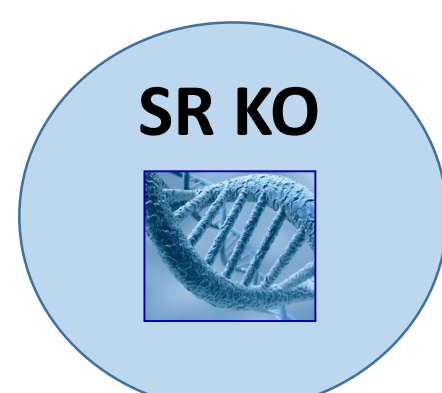
### Social behavior



SR and MSxSR alter social recognition in male mice

## Summary of the results

1-hit  
SR



- Locomotor activity in all experiments
- Place recognition
- Social recognition

1-hit  
MS



- Place recognition
- Prepulse Inhibition

SR KO



2-hit

X

Maternal separation



- Activity
- Social recognition in male mice
- Working memory in female mice
- PPI in female mice
- Anxiety-related behavior
- Place recognition performances
- Object recognition performances in female mice
- Neophobia in males

**2-hit animal models** gathers several deficits considered as hallmarks of schizophrenia.

**Serine racemase** deletion induces an **increase in activity**, promotes **social memory troubles**, and contributes to a **higher sensitivity** to maternal separation.

**Maternal separation** mostly contributes to **sensorimotor gating deficits**.

**2-hit model** differentially affect males and females.

Because some deficits (working memory, object recognition, social recognition) appears only in 2-hit mice, combining factors may help in improving validity of animal models of schizophrenia.

Moreover, combining factors reveals differences between males and females, probably accounting for gender vulnerability/resilience differences.