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Mimicking schizophrenia symptoms in mice by combining factors: genetic, early environmental stress and late pharmacological conditioning

Valentine Bouet, Solenn Percelay, Nicole Turnbull, Thomas Freret, Michel Boulouard
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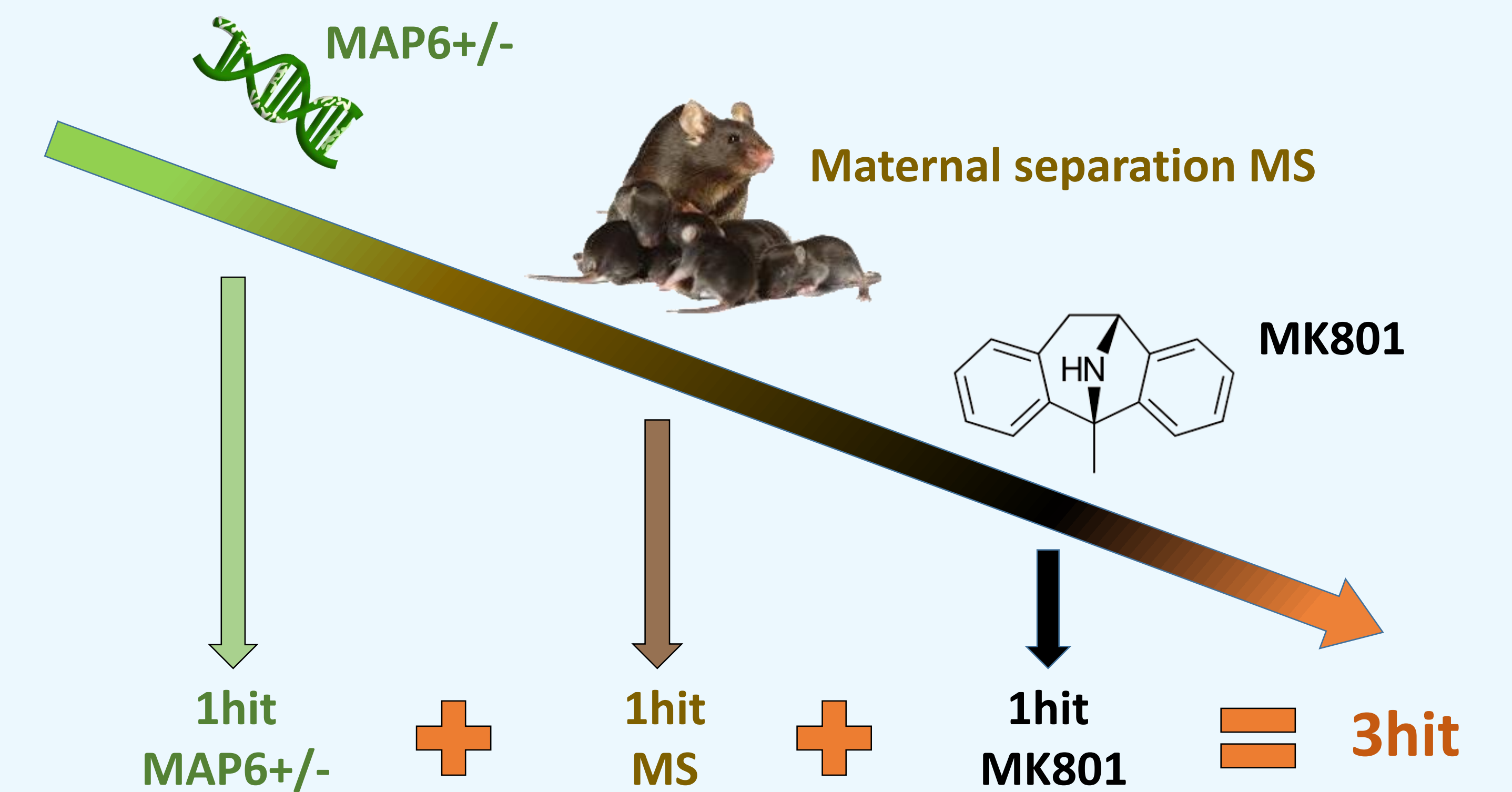
1. Schizophrenia

- Frequent psychiatric disease 1%
- Multifactorial etiology
- Unsatisfactory treatments

Crucial need to refine animal models of schizophrenia

2. Our model

- Partial genetic deletion **MAP6** *Microtubule-Associated Protein 6*
- Maternal Separation 24h in PND9 pups
- Subchronic MK801 0,05 mg/kg, ip, 5 days from PND60



3. Behavior

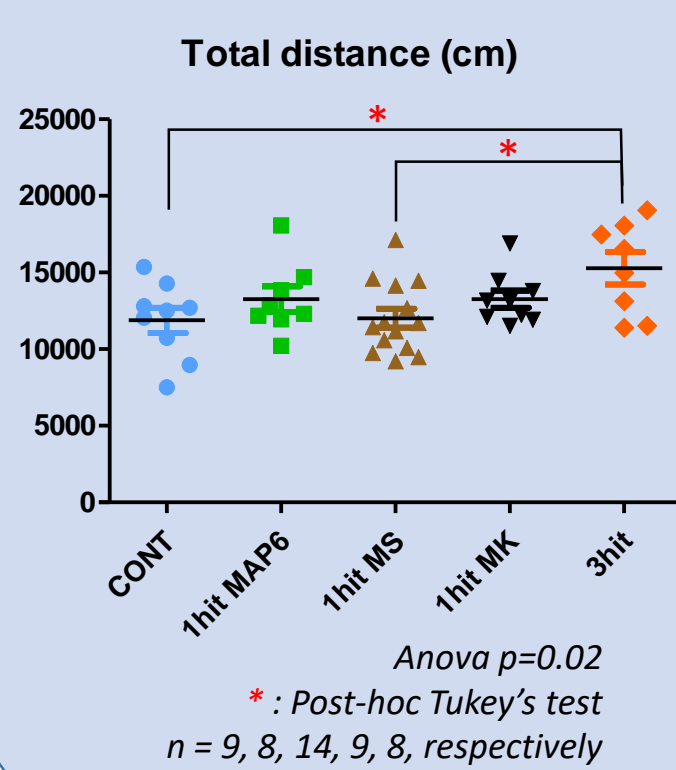
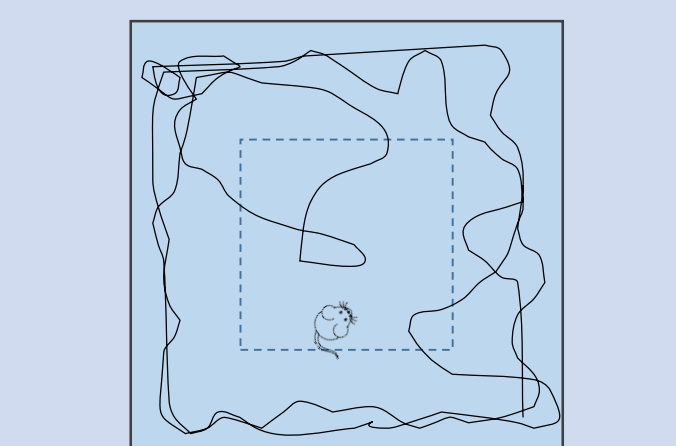
Openfield

Traveled distance increased in 3hit

MAP6 and MK : intermediate profiles

No difference in time in the center

Hyperactivity : positive-like symptom?

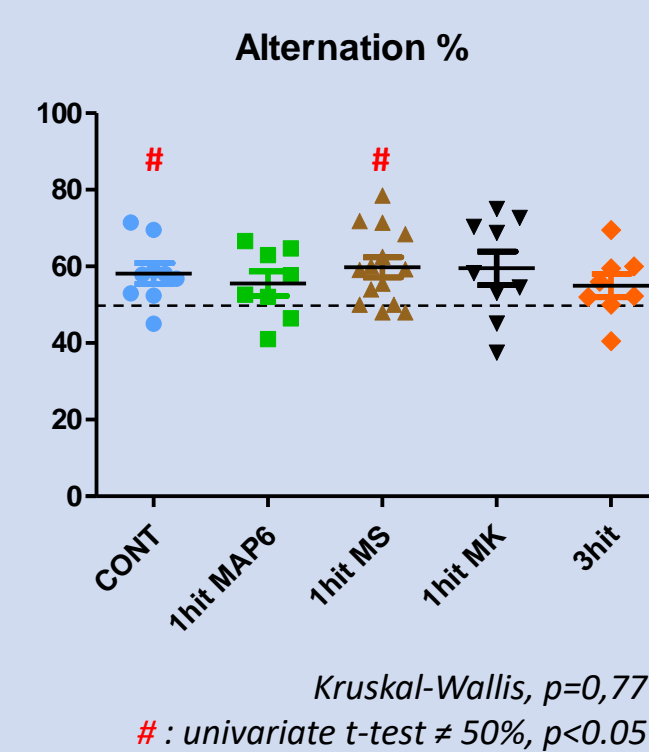
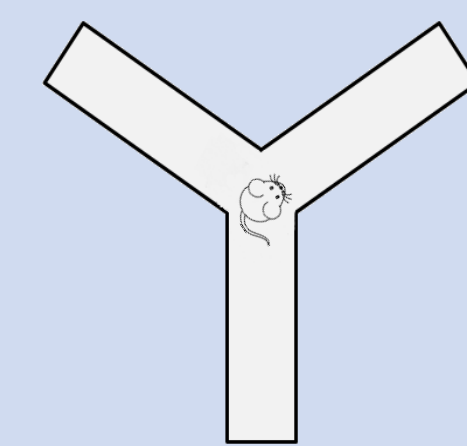


Working memory

Impaired performances in MAP6, MK and 3hit

Increased activity (number or arm entries) in MAP6 and 3hit

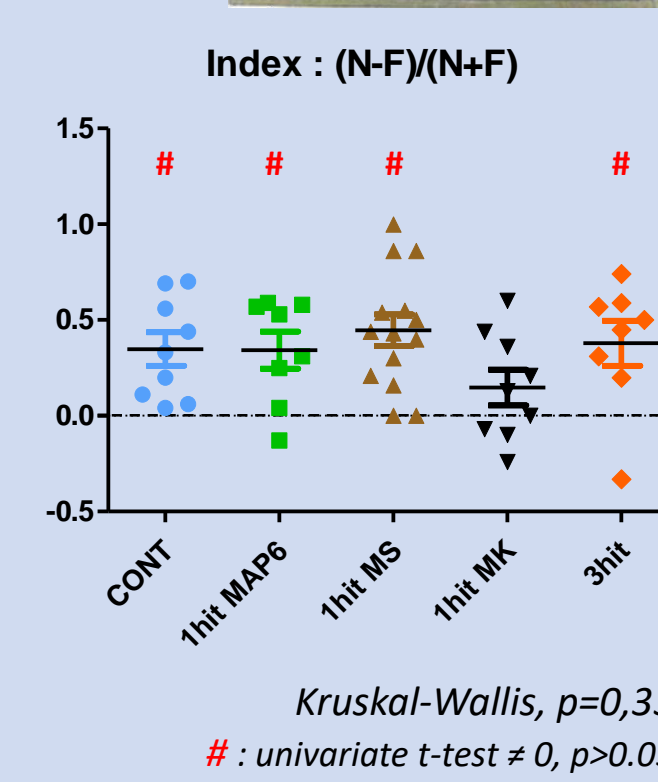
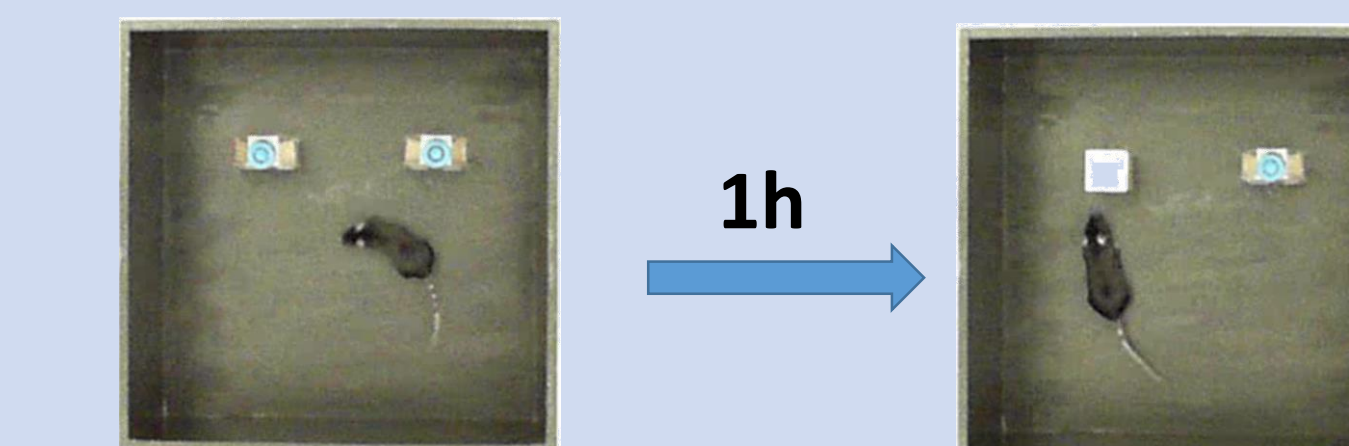
Deficit in working memory : Cognitive deficit



Object recognition

Impaired performances in MK But not evidenced in 3hit

No deficit in recognition memory

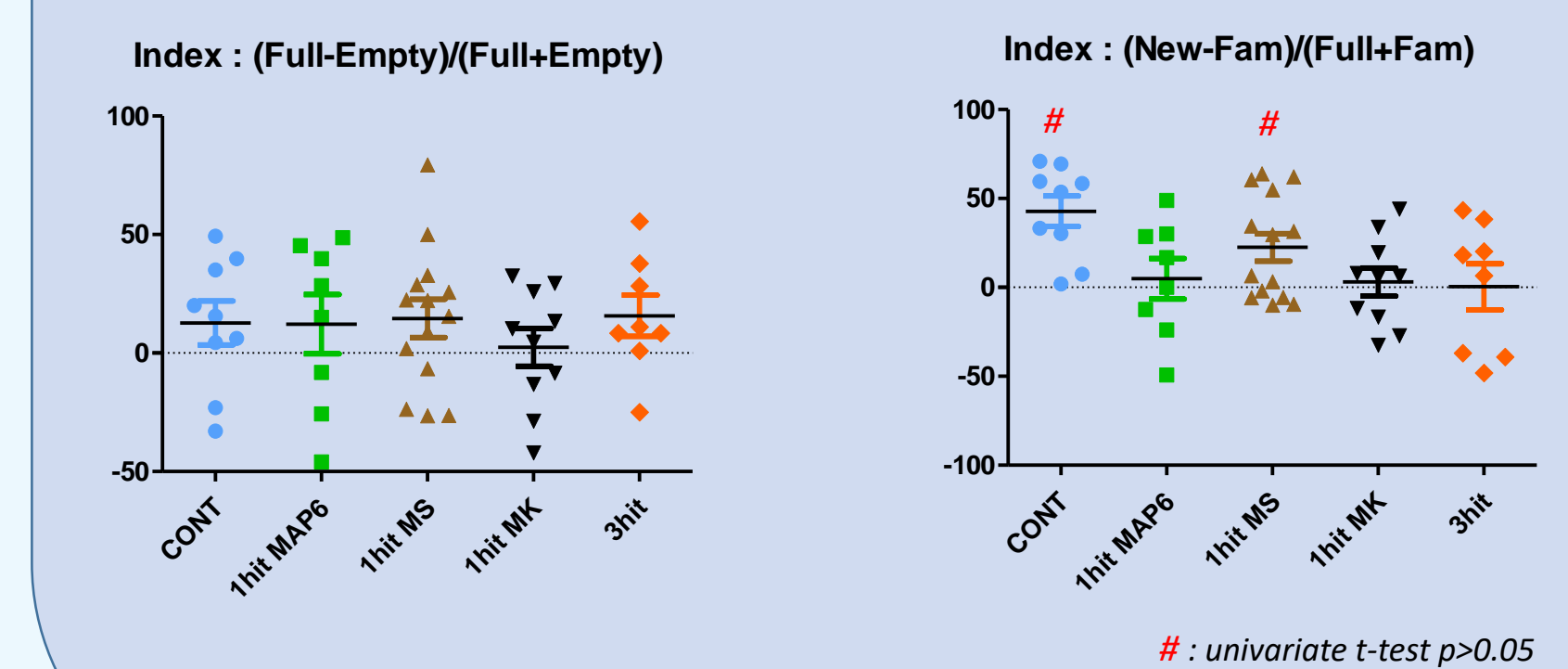
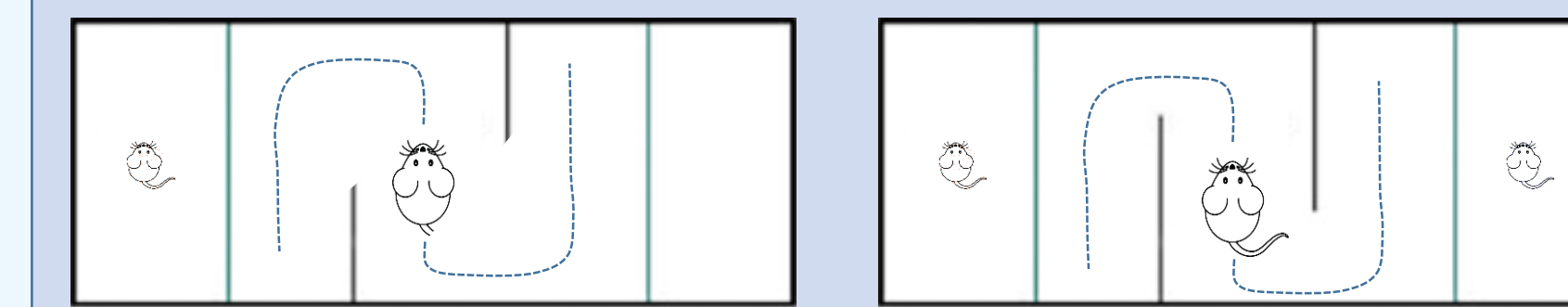


Social behavior

Social preference not observed in all groups

Social recognition altered in 1hit MAP6, 1hit MK and 3hit

Deficit in social recognition : Negative-like symptoms?



3hit model of schizophrenia mimics :
Positive like symptoms (increased spontaneous activity)
Negative like symptoms (decreased social recognition)
Cognitive-like symptoms (decreased working memory performances)

Construct validity ✓
Face validity ✓
Ongoing : parvalbumin+ neurons
To do : predictive validity

