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Combining adverse factors to build a new 3-hit model of schizophrenia

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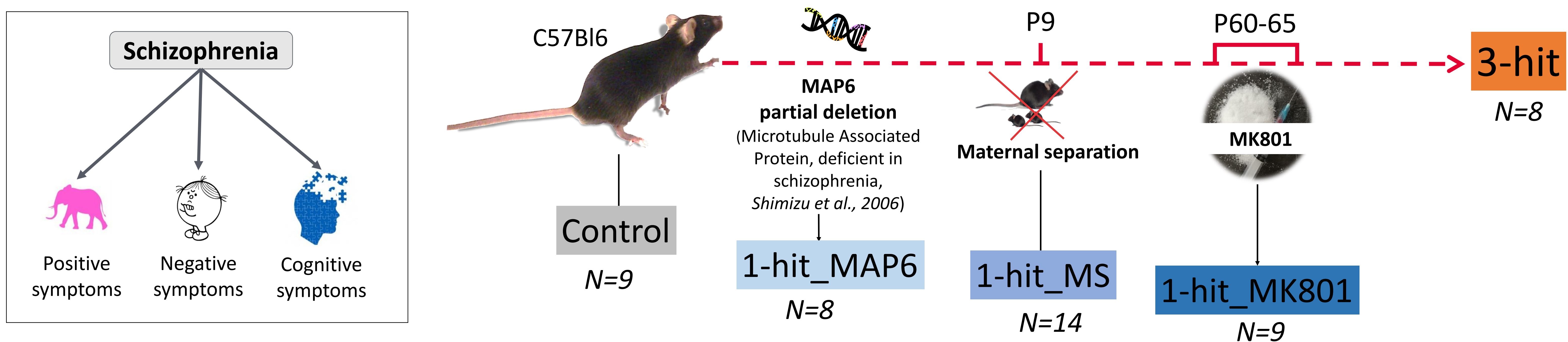
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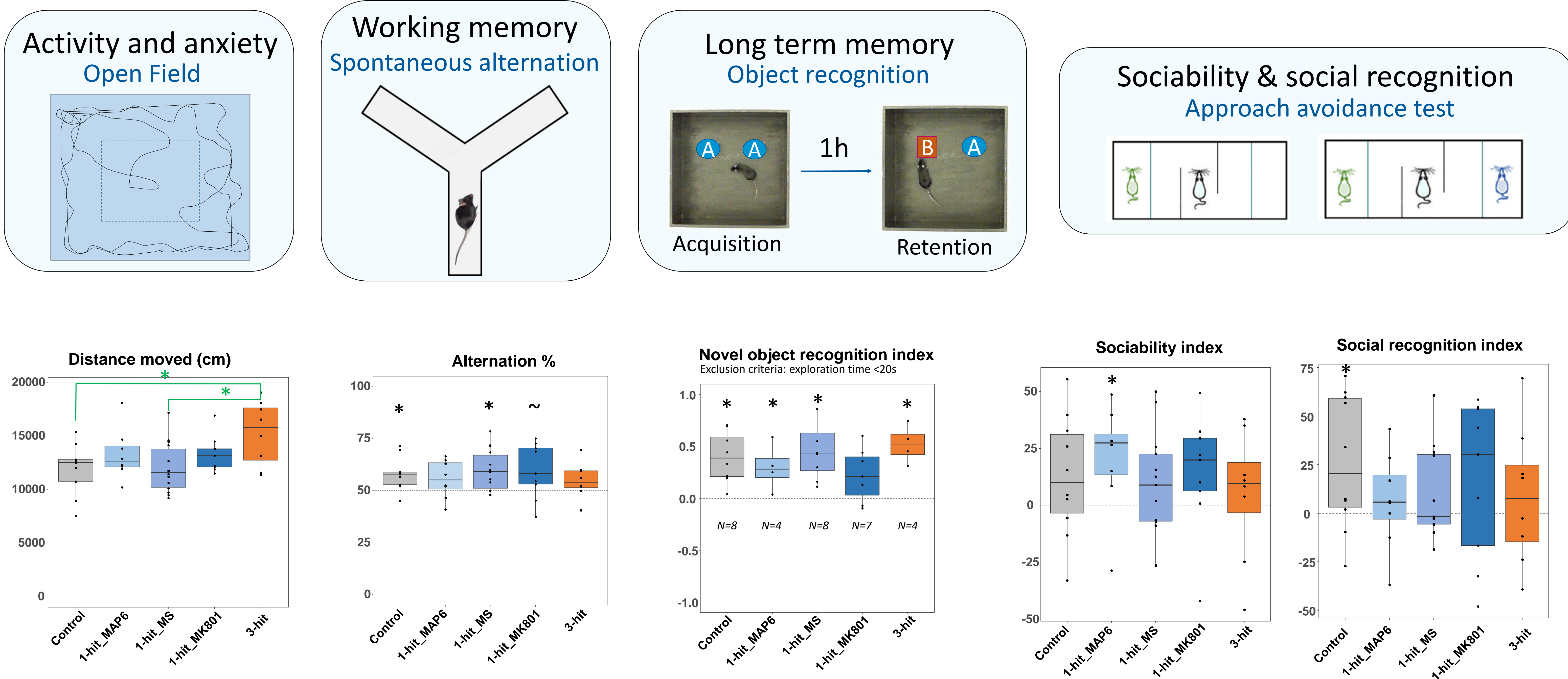
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Introduction

Schizophrenia is a disabling psychiatric disease found in approximately 1% of the population, with an unknown etiology. Currently patients are treated with antipsychotic drugs, which are only symptomatic and not curative. Unfortunately, these treatments do not cover the entirety of symptoms and are inefficient in 30 % of patients (Millan *et al.*, 2016). Moreover, antipsychotics treatments can even worsen cognitive symptoms. In this context, we are developing a mouse model of schizophrenia based on three factors (3-hit), which take into account the multifactorial nature of this pathology (Ellenbroek *et al.*, 2003). A behavioral exploration was performed, then, density of parvalbumin-positive neurons was measured via immunohistochemistry (Lewis *et al.*, 2012).



Results



Anova *: $p < 0,05$

T test with comparison to reference value *: $p < 0,05$; ~: $0,05 < p < 0,1$

Discussion and conclusion

Our first results showed that each factor, taken separately (1-hit), induced behavioral impairments: MAP6 partial deletion impairs working memory; maternal separation impairs social recognition, and MK801 induces deficits in all tests. The 3-hit group showed an increase of locomotor activity (positive-like symptoms), alteration of working memory and of social recognition performances. These behavioral results are encouraging for the development of a new schizophrenia model. Indeed, construct validity is relevant, taken into account the multifactorial nature of this pathology. Face validity is interesting, notably given alteration of cognitive functions. Ongoing immunochemistry study will give possible mechanisms involved.