



## Schizophrenia: validity of a 3-hit mouse model

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# Schizophrenia:

## validity of a 3-hit mouse model

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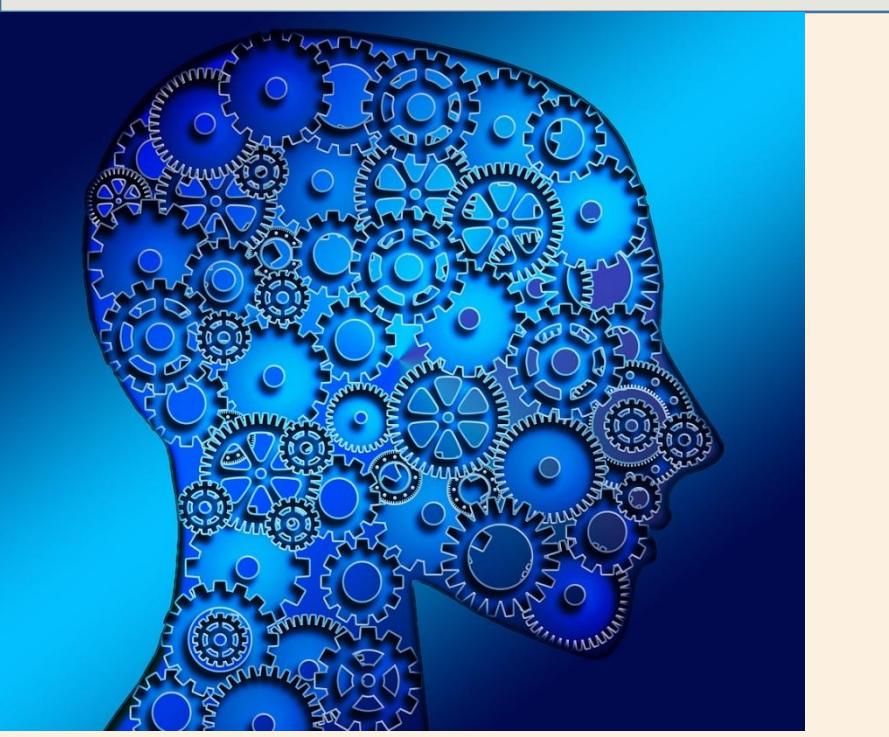
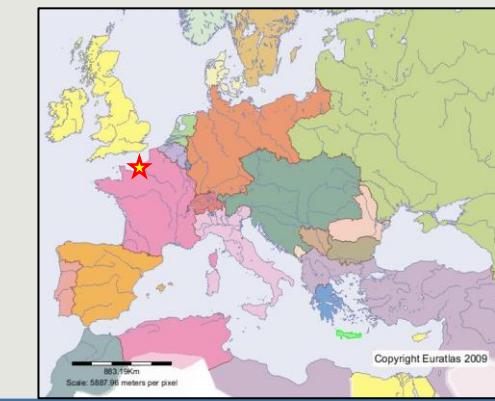
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### Schizophrenia

#### Disease

Prevalence: 1%  
Age onset: 15-25 years  
Symptoms: positive, negative, cognitive  
Debilitating  
→ Heavy costs

#### Causes

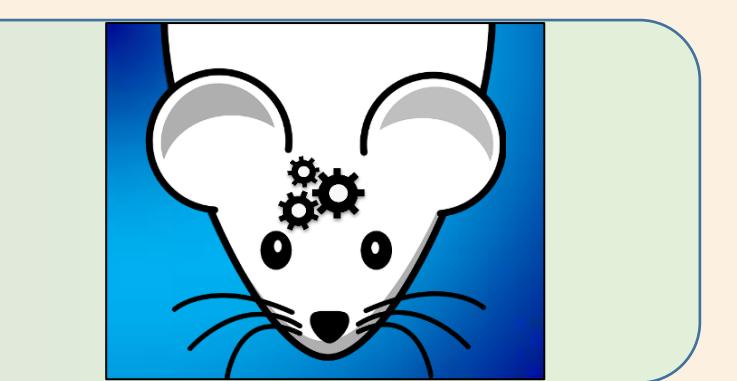
Unknown  
Genetic X Environment

#### Treatments

Worsen negative and cognitive deficits  
Inefficient in 30% patients

Absolute need to improve treatment  
→ improve animal models validity

### New 3-hit model



#### Genetic factors

#### Early environmental factors

#### Late environmental factors

Ellenbroek et al., 2003

#### 1. Partial MAP6 deletion

Andrieux et al., 2002



#### 2. Maternal separation PND9-24h

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

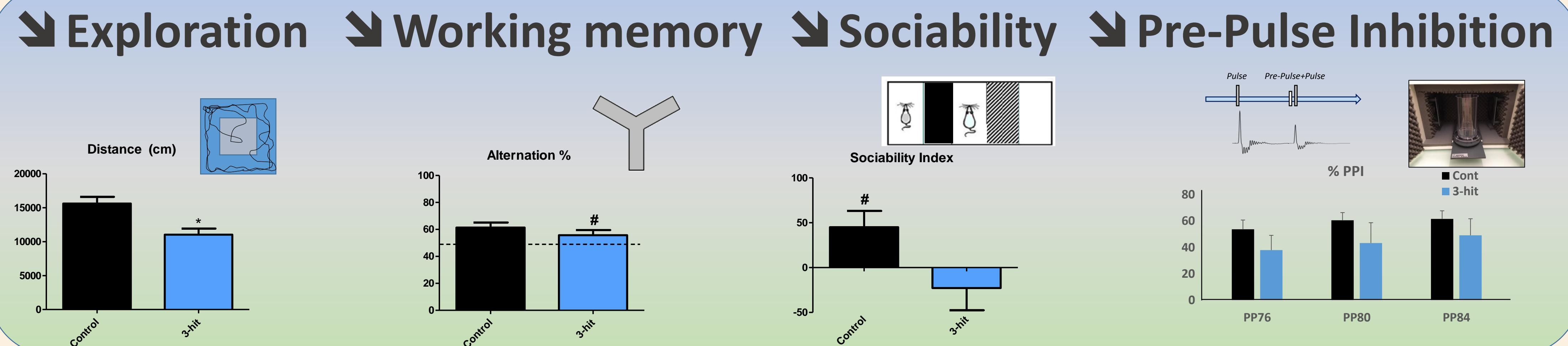


#### 3. THC during adolescence

Rubino et al., 2009  
O'Tuataigh et al., 2010

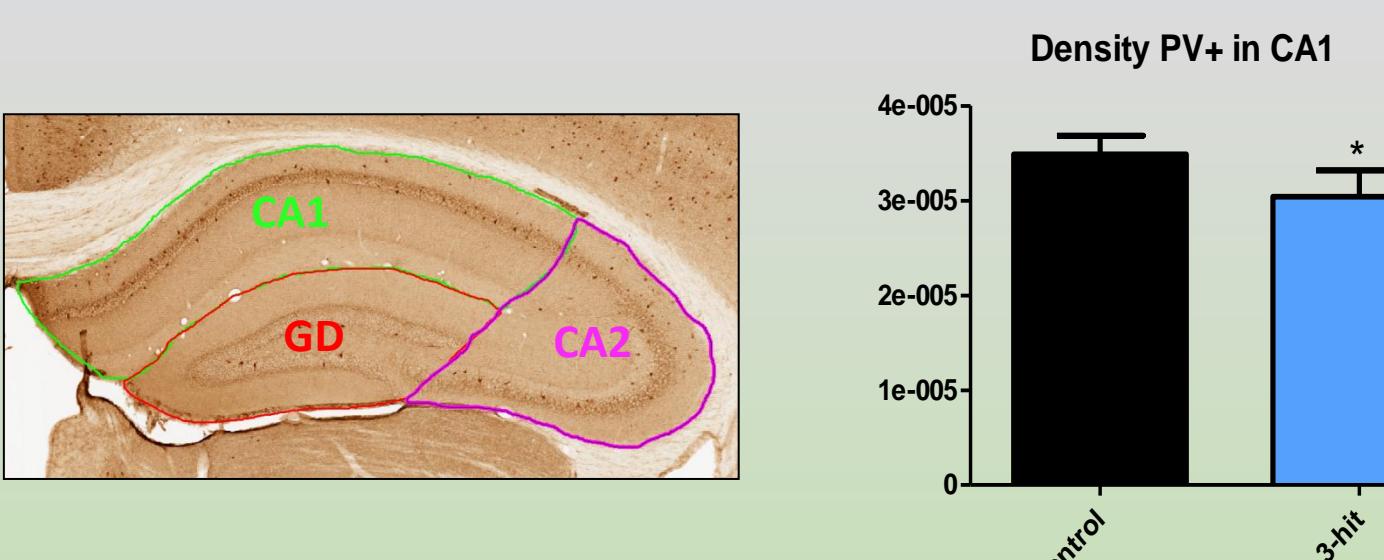


### Behavior



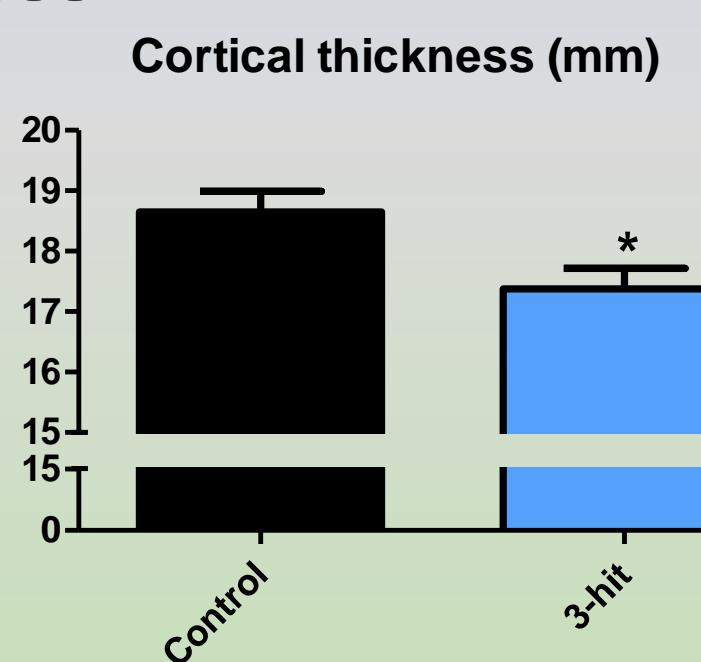
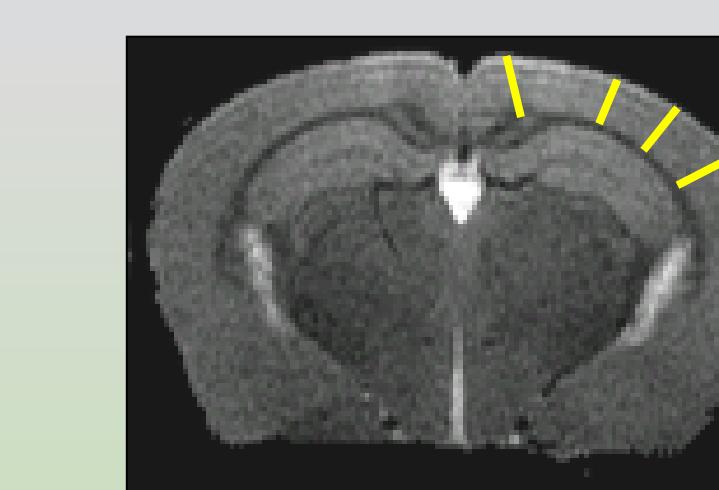
### Immunohistochemistry

➔ Density of parvalbumin-positive neurons in CA1 of hippocampus



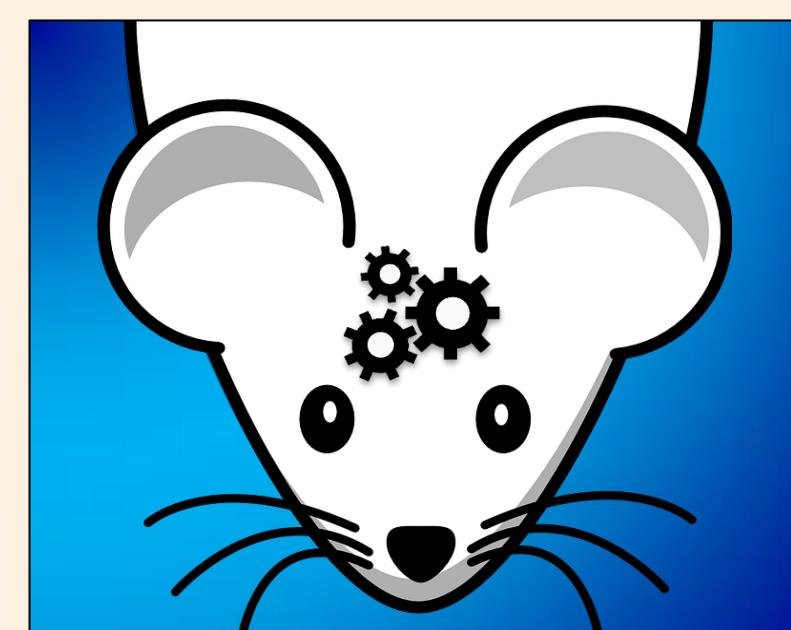
### MRI

➔ Cortical thickness  
➔ Less axons, less myelin in corpus callosum



### Pharmacology

➔ Antipsychotics (lurasidone) reduces variability and normalize behavioral performances (ongoing study)



The 3-hit combination causes negative- and cognitive-like symptoms together with brain alterations mimicking what is observed in schizophrenic patients

Construct validity ✓

Face validity ✓

Predictive validity ✓