Exploring neurochemical alterations and cognitive deficits in the woozy mouse model

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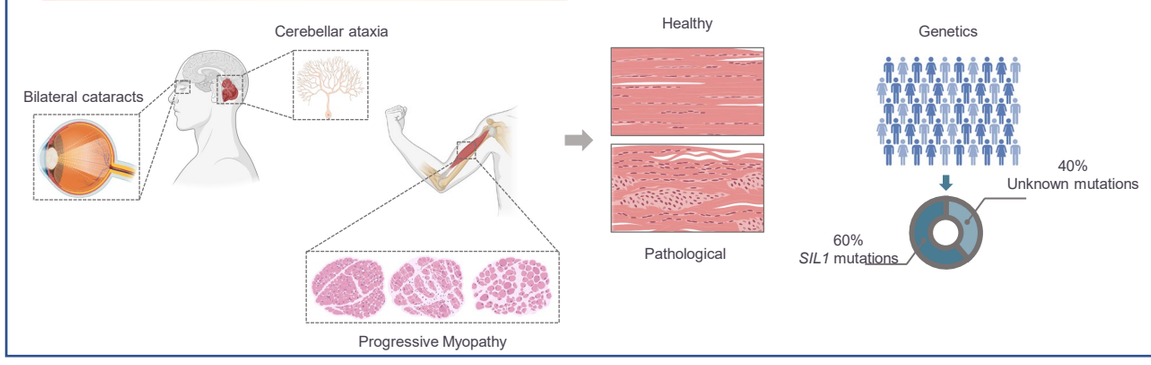
Introduction & Aims

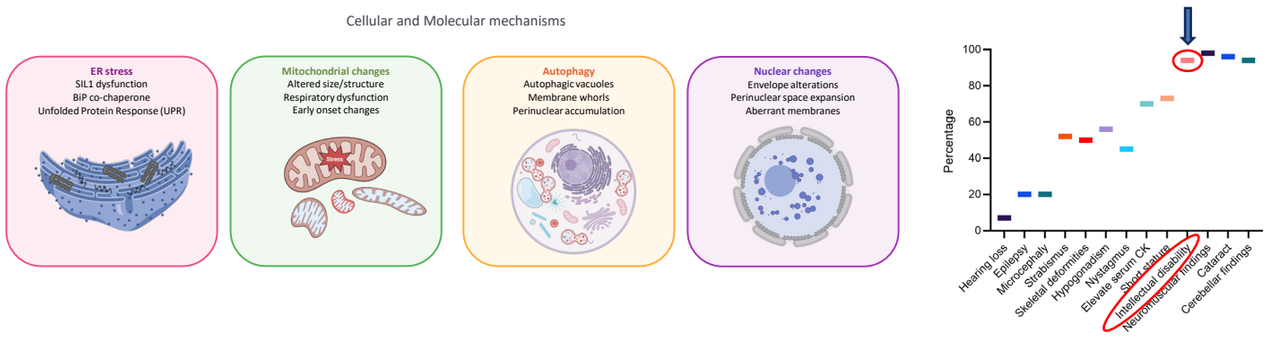
Marinesco-Sjögren Syndrome (MSS) is a rare autosomal recessive disorder characterized by cerebellar ataxia, cataracts, myopathy, and intellectual disability (Anttonen et al. 2005; Ichhaporia and Hendershot 2021; Senderek et al. 2005; Van Raamsdonk 2006). Although MSS patients do not show brain macroscopic alterations, the underlying neurobiological mechanisms that lead to cognitive impairments remain poorly understood. While previous research documented motor impairments in the woozy mouse model (*Sil1*^{wz}), a preclinical MSS model, our investigation focused on potential cognitive deficits and underlying neurobiological mechanisms. The woozy (*Sil1*^{wz}) mouse line is the most used preclinical model of MSS. The *Sil1*^{wz} mouse was selected by a natural mutation in the Sil1 gene, resulting in the phenotypical features of human patients, with complete PC loss until the fourth month of life and progressive muscular atrophy manifesting from young adulthood. Although these two animal models serve as invaluable tools for investigating the mechanisms involved in MSS and potentially identifying therapeutic targets, possible alterations in the brain were still not investigated.

Conclusions

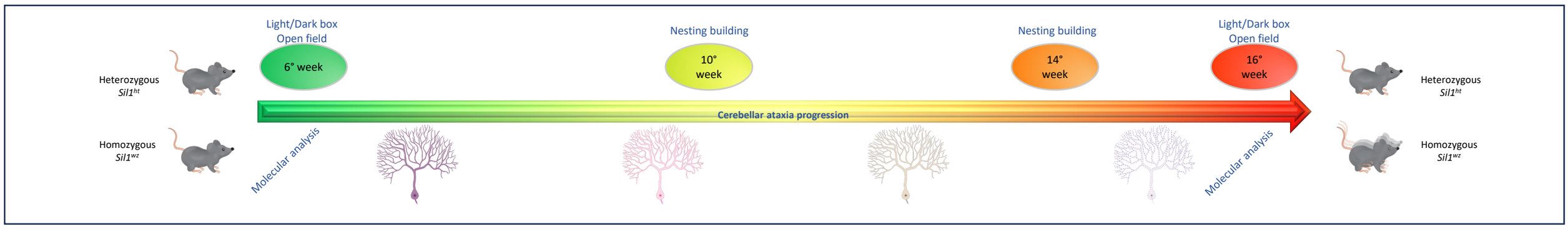
- ✓ *Sil1* deficiency affects cognitive mechanisms, resulting in atypical behaviour in the nesting building and open field tests;
- ✓ Woozy mice exhibited alterations in several pathways connecting the prefrontal cortex and the hippocampus;
- ✓ Investigating these mechanisms in Marinesco-Sjögren Syndrome preclinical models may help in identifying potential molecular targets and therapeutic approaches transferable to human patients.

Marinesco-Sjögren Syndrome's clinical picture





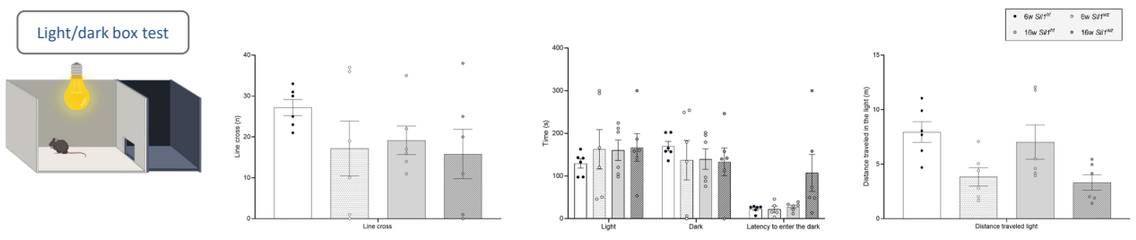
Methods



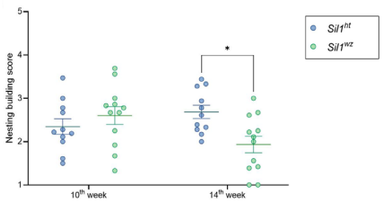
Results

Behavioural

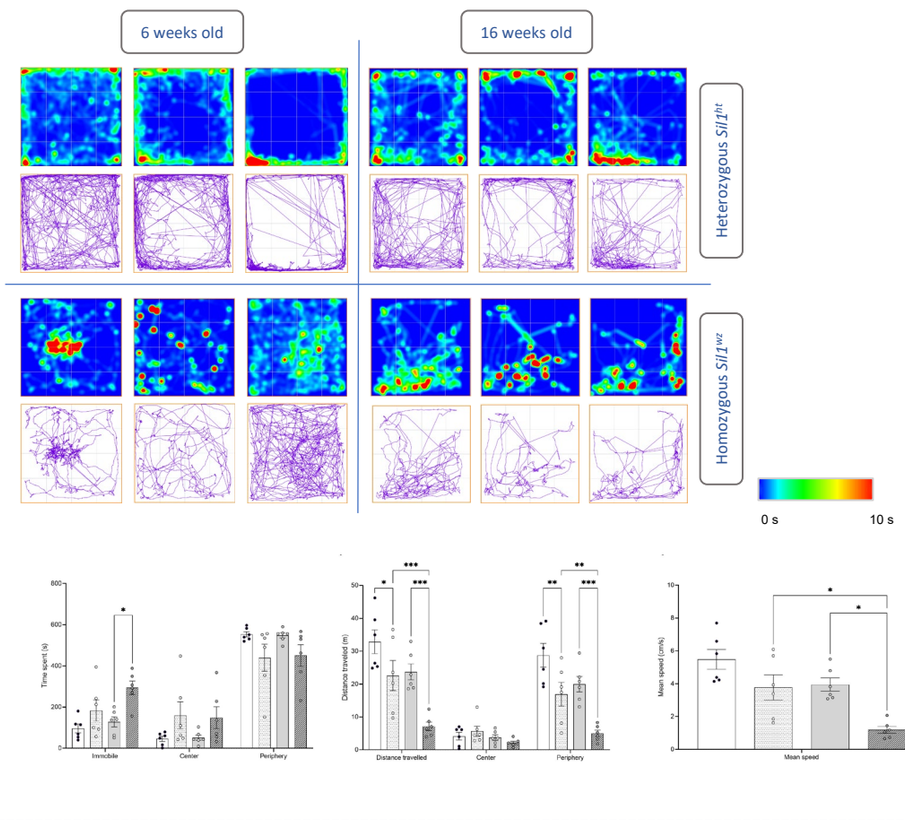
Light/dark box test



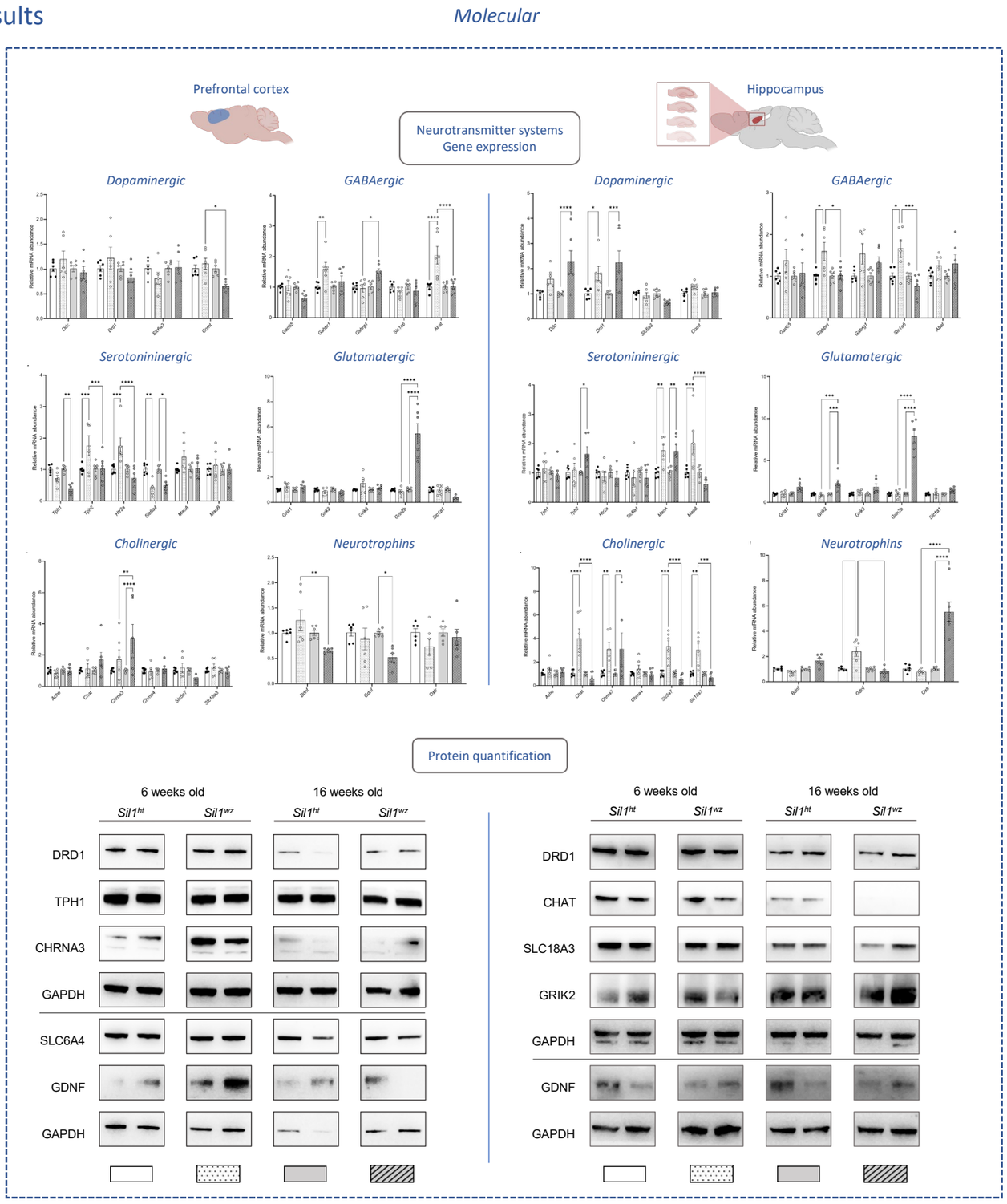
Nesting building test



Open field test



Molecular



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Disclosure

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