

Effect of GABAergic precursor transplantation in a murine model of Syntaxin Binding Protein 1 (STXBP1) syndrome

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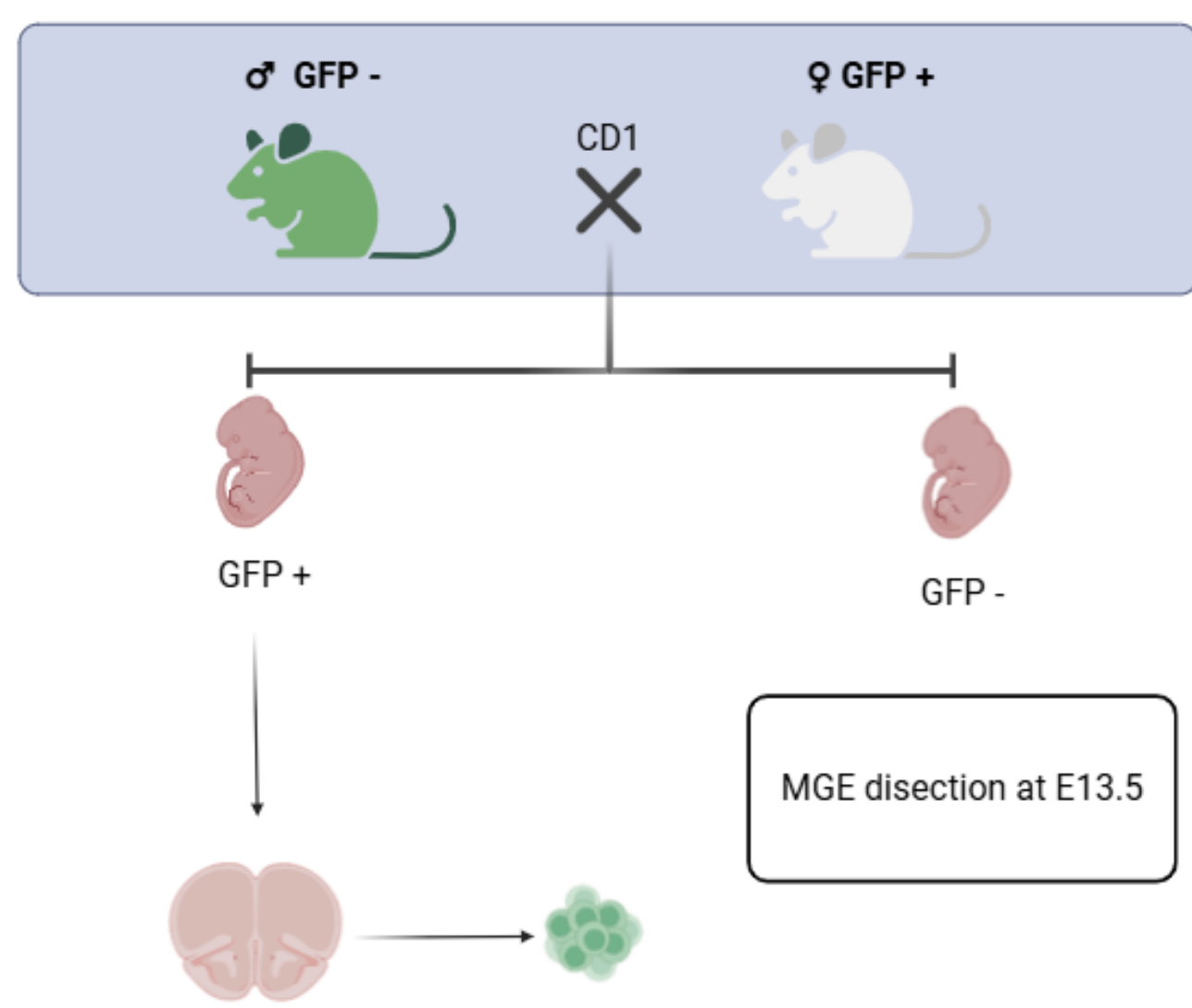
ABSTRACT

STXBP1 syndrome is considered an early infantile epileptic encephalopathy. It has a high mortality rate in childhood and presents with a variety of symptoms including severe seizures, cognitive impairment and autistic-like behaviour. The aetiology of this syndrome is caused by a mutation in the gene STXBP1, which encodes for Munc18-1 and is related to synaptic vesicle release. This dysfunction can affect all GABAergic interneurons, leading to a disruption of the excitatory/inhibitory balance, provoking hyperexcitability that leads to crisis and seizures. Our aim is to restore this balance and improve all associated symptoms by transplanting GABAergic precursors from the medial ganglionic eminence (MGE) at different ages. We are using a knock-out haploinsufficient mouse model for Munc18-1, which has symptoms similar to those described in patients. Our results show that transplantation improves the survival of the mice, reduces the frequency of seizures, and induces total or partial improvement in cognitive function and behavioural deficits. Taken together, our results suggest that GABAergic precursor cell transplantation is a potential therapy that may have future application in the treatment of STXBP1 syndrome.

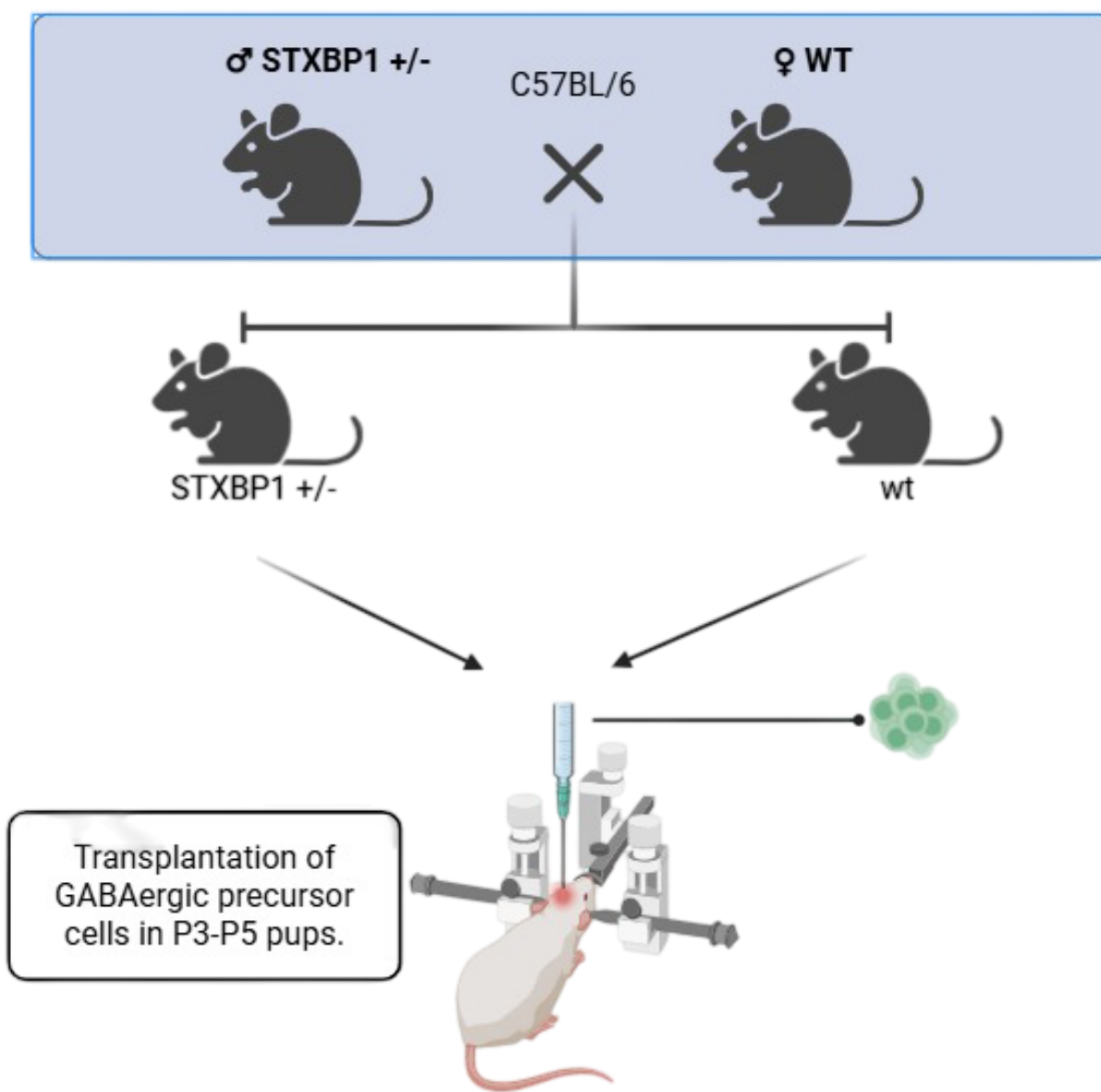
METHODS

1. GABAergic precursor cells transplant in neonates

1. MGE extraction



2. MGE transplantation



2. Behavioural test

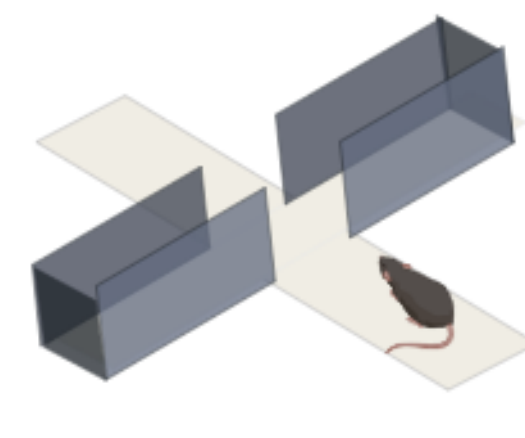
I. Open field



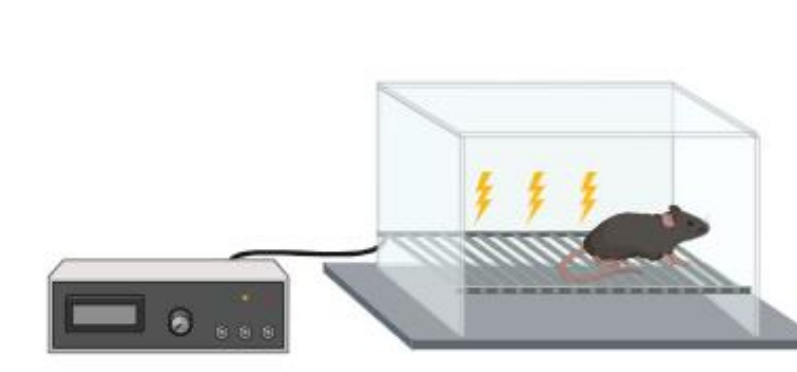
III. Nesting



II. Elevated plus maze

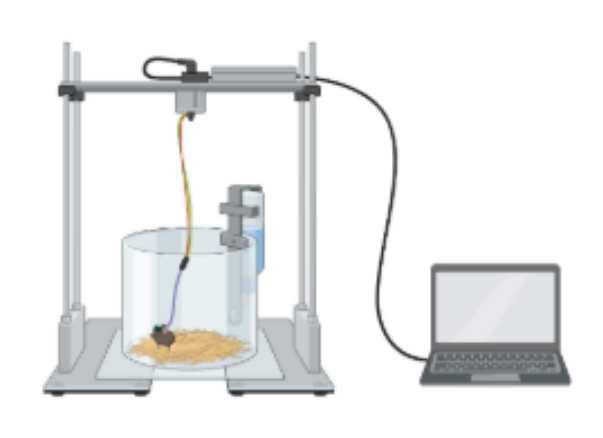


IV. Fear conditioning



3. EEG registration

EEG registration



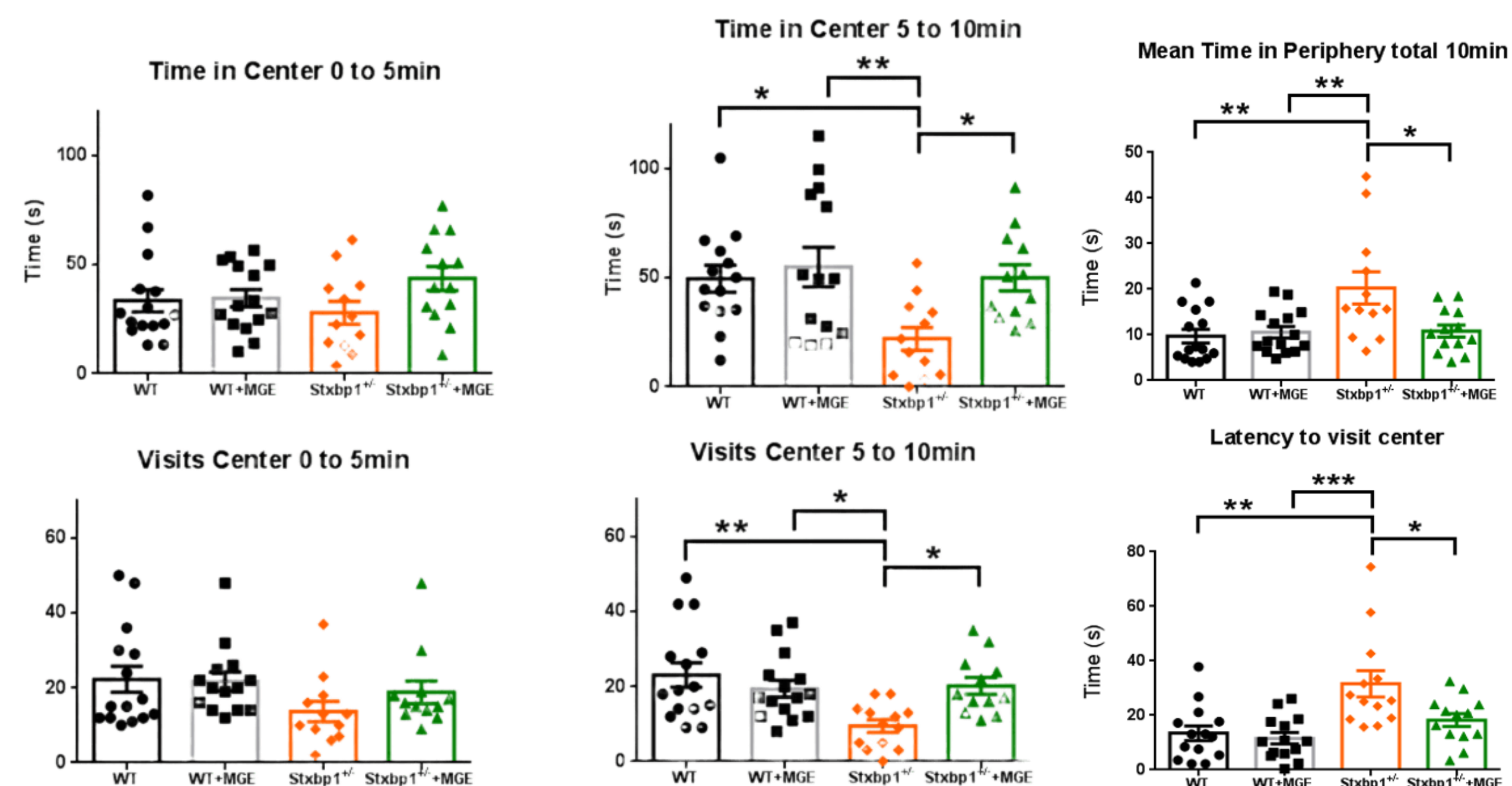
4. Survival

5. Histology

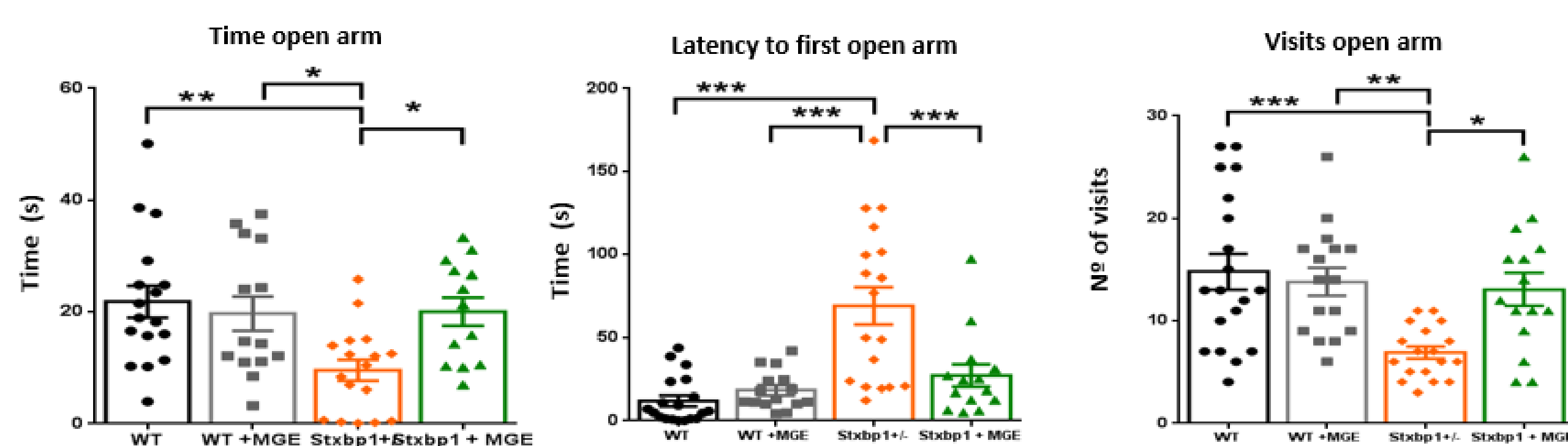
RESULTS

2. Behavioural test

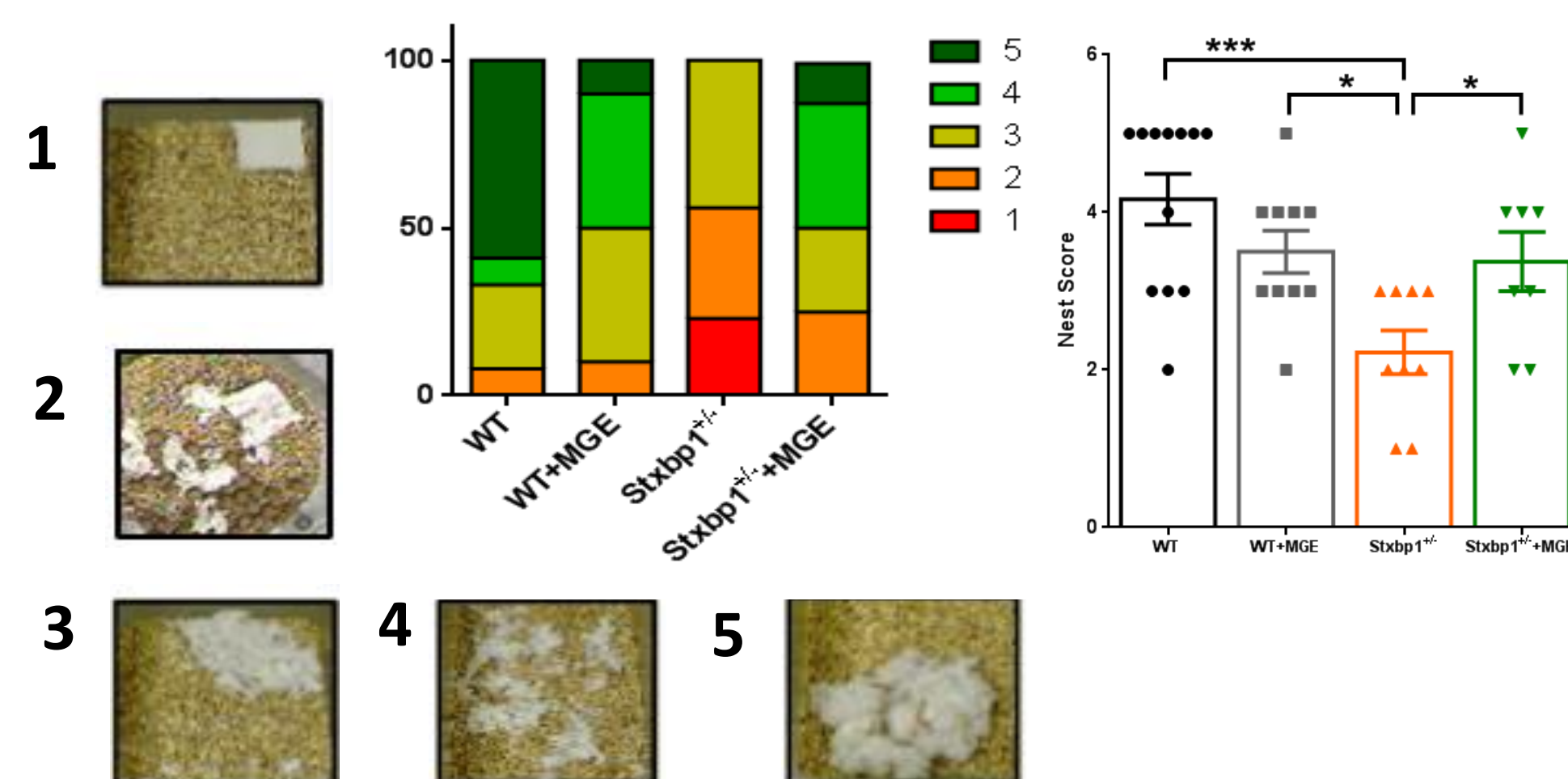
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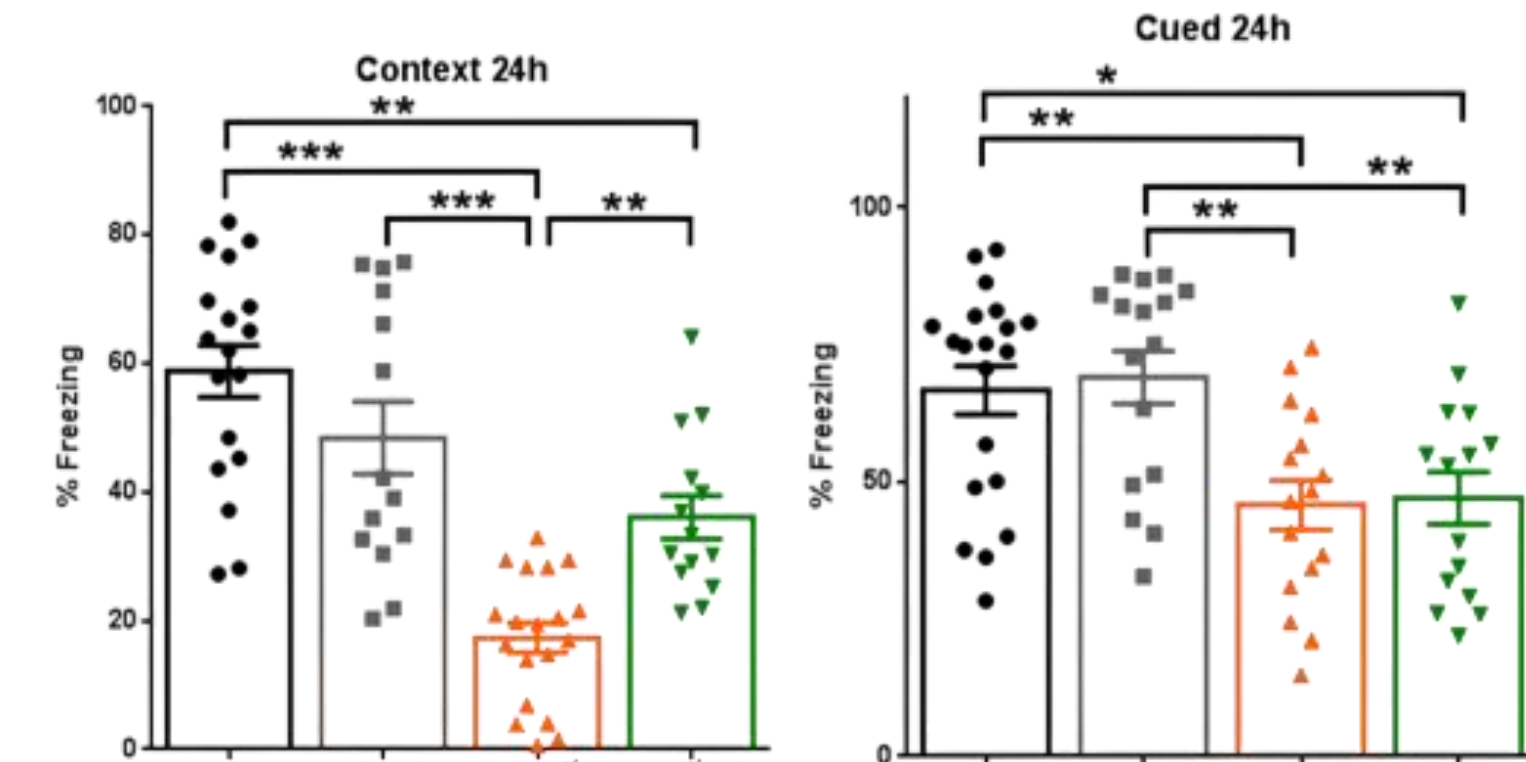
II. Elevated plus maze



III. Nesting

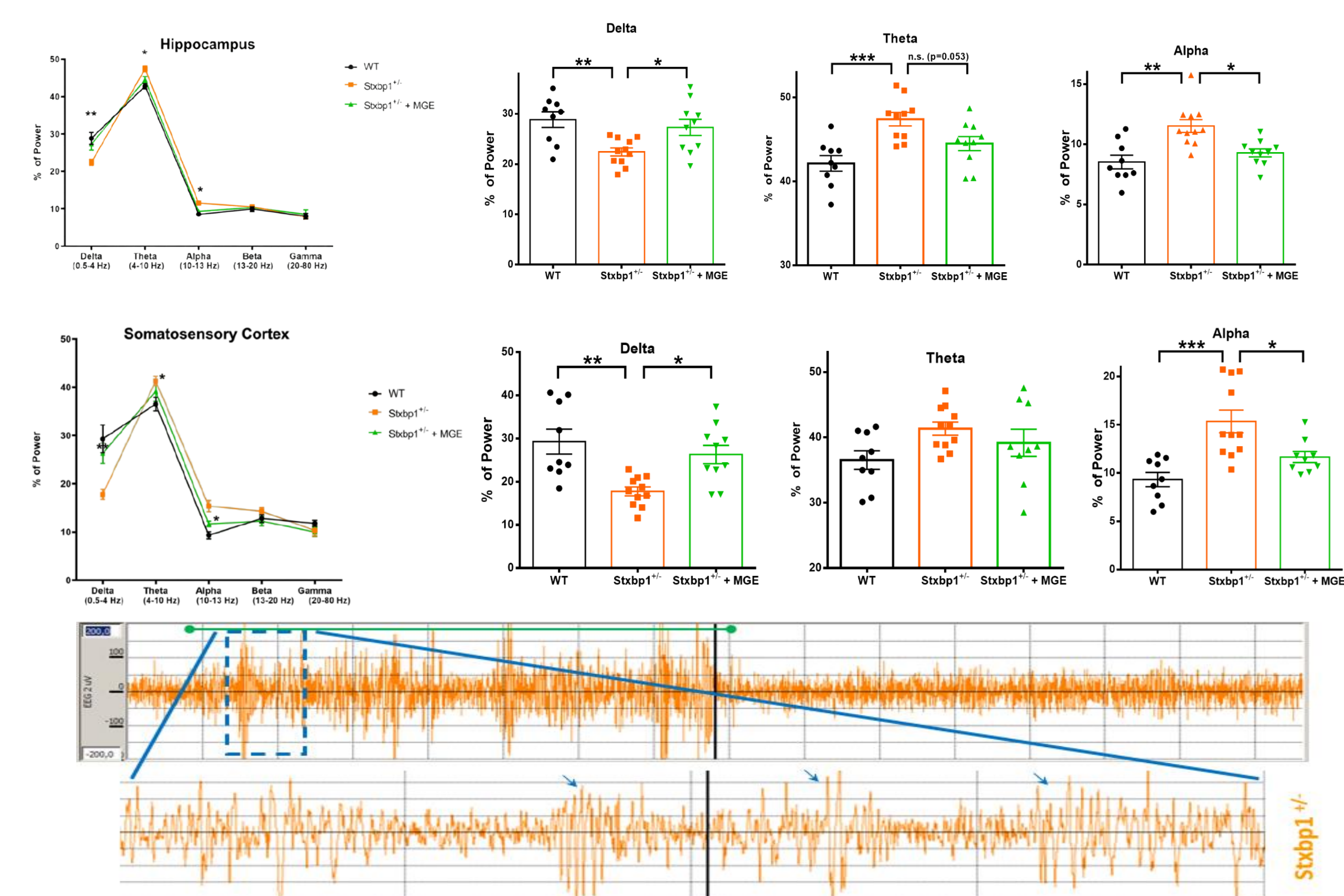


IV. Fear conditioning test



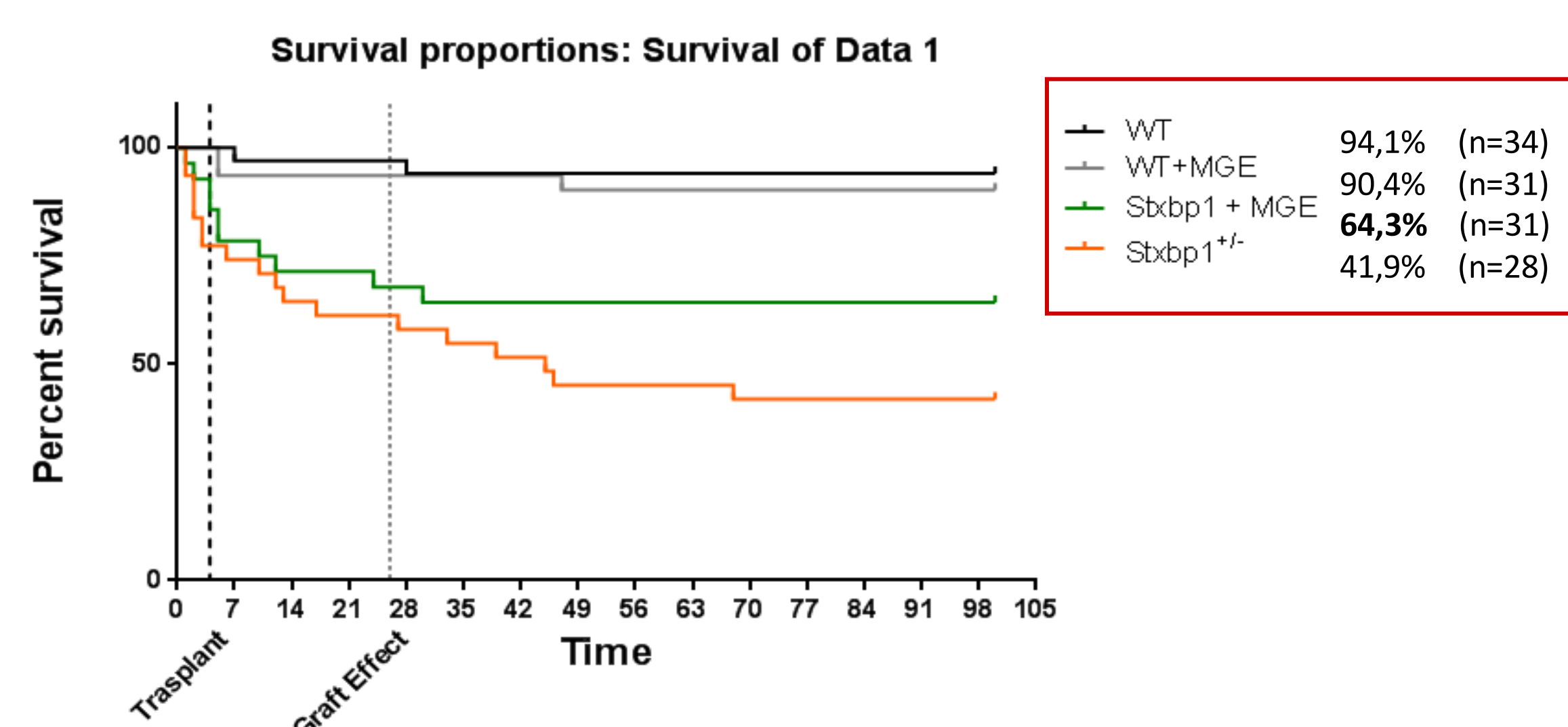
3. EEG registration

Waves spectrum resynchronization

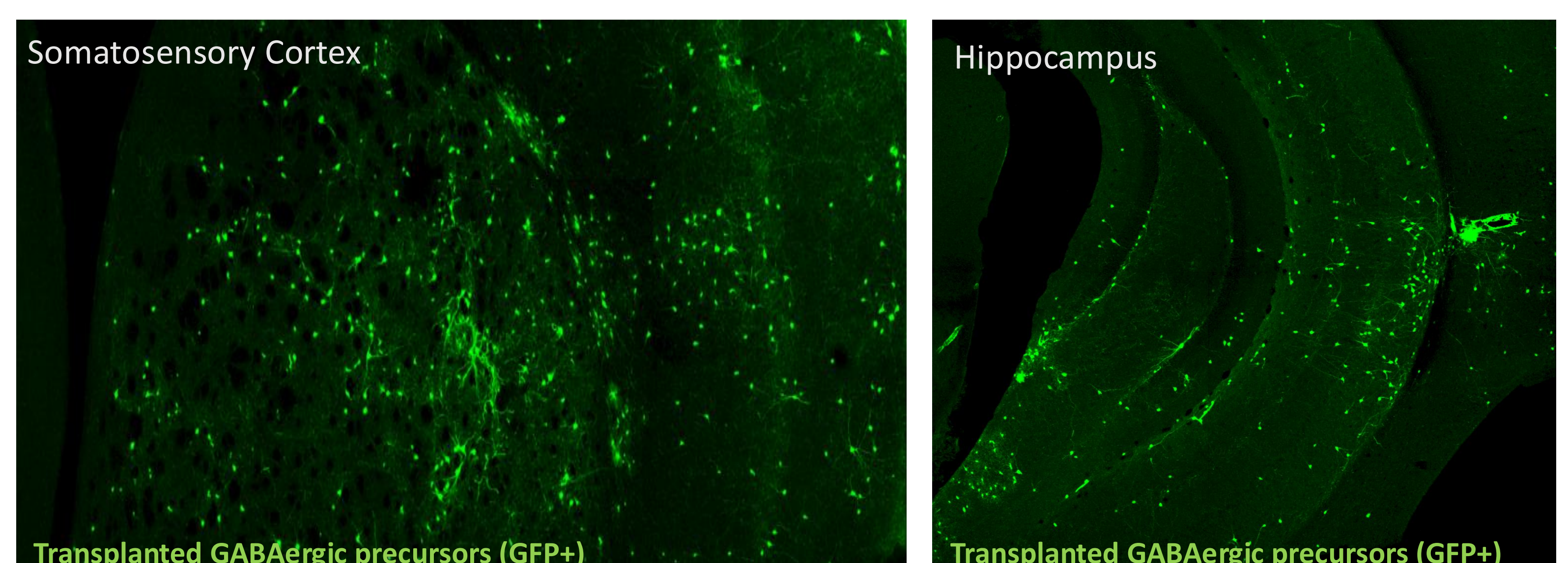


Brain activity

4. Survival rate: transplanted vs sham controls



5. Histology



Acknowledgments

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