Learning and memory impairments in a neuroendocrine mouse model of anxiety/depression

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Introduction
Patients suffering from major depressive disorders (MDD) present significant neurocognitive deficits, including lack in attention, executive function failures and spatial learning and memory impairments compared to healthy volunteers [1]. Compelling works, using animal models based on environmental stress, have demonstrated that anxiety/depression-like phenotype is associated with learning and memory alterations [2,3]. We developed a mouse model of anxiety/depression based on a chronic exposure to exogenous corticosterone (CORT model), a stress hormone implicated in the dysregulation of the hypothalamo-pituitary-adrenal axis, known to be part of MDD aetiology [4]. If anxiety/depression-like phenotype is now well described in the CORT model, cognitive aspects remain to be examined.

Our aim was to characterize cognitive functions through episodic, associative and spatial learning/memory tasks in a neuroendocrine mouse model of anxiety/depression.

Materials and Methods
• Animals: Male C57BL/6J (Janvier Labs, France) mice, 8 to 10 weeks old.
• Anxiety/depression model: Anxiety/depression-like state was induced by a chronic corticosterone administration (CORT, 35 µg/ml for 4 weeks in the drinking water) [4].

Results
1. CORT-treated mice display an anxiety/depression-like phenotype

2. Chronic corticosterone induces discrimination impairment in the novel object recognition test

3. Chronic corticosterone induces associative memory deficit in the One-trial contextual fear conditioning

4. Chronic corticosterone induces learning and mental flexibility alterations in the Morris water maze

5. Chronic corticosterone induces learning, short- and long-term memory deficits in the Barnes maze

Conclusion
• Chronic corticosterone-treated mice displayed cognitive deficits in all aspects of memory tested.
• To further investigate the link between cognitive states and emotional disorders, we will focus our work on monoaminergic antidepressants and 5HT1 receptor agonists to determine whether these molecules are able to reverse cognitive performances in CORT-treated mice.

References