**Cognitive performances 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 [3]. Compelling works, using animal models based on environmental stress, have demonstrated that anxiety/depressive-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 hypothalamic-pituitary-adrenal axis, known to be part of MDD aetiology [4]. If anxiety/depressive-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 and visuo-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/depressive-like state was induced by a chronic corticosterone administration (CORT, 35 µg/ml/day for 4 weeks in the drinking water) as previously described [4].

**Results**

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

   - **During the learning phase, CORT-treated mice show**:
     - a decrease in exploratory behaviour
     - no change in locomotor activity
   - **During the test phase, CORT-treated mice display**:
     - a lower ability to discriminate between the novel and the familiar one (40% decrease)
     - a lower discrimination index

2. **Corticosterone induces discrimination impairment in the Novel Object Recognition Test**

3. **Learning and mental flexibility alterations in CORT-treated mice in the Morris Water Maze**

   - **During the acquisition phase, CORT-treated mice show**:
     - severe learning impairments, reflecting their loss of mental flexibility
     - mild memory difficulties (decrease in crossing the initial platform zone)
   - **During the reversals phase, CORT-treated mice demonstrate**:
     - memory abnormalities (decrease in swimming duration in the new target quadrant, decrease in entries in the platform zone)

4. **Learning and memory deficits in CORT-treated mice in the Barnes maze**

   - **CORT-treated mice show learning alterations** indicated by the absence of a decrease in the time and number of errors before the first contact with the target hole and the number of total errors compared to control mice.

**Conclusion**

This study reveals that mice chronically exposed to corticosterone displayed cognitive deficits such as:

- episodic memory alterations in the Novel Object Recognition Test
- visuo-spatial learning and mental flexibility impairments in the Morris Water Maze
- visuo-spatial learning and memory abnormalities in the Barnes Maze

To further investigate the link between cognitive states and emotional disorders, we will focus our work on monoaminergic antidepressants activity to determine whether these molecules are able to reverse cognitive performances in CORT-treated mice.

**References**