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(Article begins on next page)

SEX DIFFERENCES IN RESPONSE TO UNPREDICTABLE CHRONIC MILD STRESS MODEL OF DEPRESSION IN MICE

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Many social factors and various aversive situations may induce affective disorders, like depression and anxiety-related disorders, suggesting complex relationships among stressful situations and the onset of clinical depression.

The unpredictable chronic mild stress (UCMS) protocol is a valid, reliable and sensitive model for studying depressive disorders in rodents: it involves a period of mild socio-environmental stressors and this procedure replicates several depression-related behavioral and physiological impairments [1].

The aim of our study was to investigate the impact of a six weeks UCMS paradigm (random pattern of mild stressors twice a day) on the development of a depressive and anxiogenic phenotype in CD1 mice.

Overall, at the end of the experiment, the measured parameters indicated a sexually dimorphic effect.

For assessing the anxiety-like behavior, we used the Elevated Plus Maze (EPM) and Open Field (OF): the analysis of mice activity on EPM revealed an anxiolytic effect of UCMS exposure in female (increased number of entries into the open arms) and an anxiogenic effect (decrease in the number of entries) in male. For OF, Two-way ANOVA indicated a significant interaction gender-treatment [$p < 0,05$] about the time spent in centre of the arena and a significant effect of the gender [$p < 0,001$] about the total distance travelled in the central zone.

To evaluate the depressive profile we used the Forced Swimming Test: the analysis of the time with animal spent in immobile posture (floating) during a five min trial revealed no differences of both gender and treatment.

For the hedonic behavior, we performed the sucrose preference test (SPT) calculating the consumption of sucrose solution and water. The results show that UCMS treatment causes a reduction in the fluids intake (sucrose, water and total), in particular UCMS male, suggesting a less anhedonic state. No effect of UCMS were observed about the sucrose preference.

Present results indicate that UCMS treatment may represent a good model to test the sexually dimorphic onset of affective disorders.

We are currently investigating the vasopressin systems in sexually dimorphic circuits and in future studies we will analyze other circuits involved on anxiety behaviour (i.e. nNOS system) and on regulation of stress response (i.e. serotonin system).

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Reference List

[1] Isingrini E, Surget A., Belzung C., Freslon J-L., Frisbee J., O'Donnell J., Camus V., d'Audiffret A., Altered aortic vascular reactivity in the unpredictable chronic mild stress model of depression in mice UCMS causes relaxation impairment to Ach; *Physiology & Behavior* 2011 103:540–4