

Antidepresszáns gyógyszerjelöltek viselkedéstani és szinaptológiai tesztelése
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Investigation of sex differences in major depression using the learned helplessness paradigm in rats

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Introduction

Major depressive disorder (MD) is a devastating disease with a high lifetime prevalence worldwide. Stressful life events, especially in western societies contribute to an increasing tendency. Human studies report greater susceptibility of females to stress related disorders, including depression. However, the underlying mechanisms of this obvious gender difference are still largely unknown. Researching of the mechanisms is essential to have a good animal model. We hypothesize that female rats are more sensitive to stress; therefore they are prone to develop depressive symptoms more frequently compared to males. To prove our hypothesis, the sensitivity to stress in CD(SD) intact male and ovariectomized female rats have been investigated in the learned helplessness paradigm (LH). The current optimization study serves an essential basis for future investigations for the learned helplessness model of depression.



The Med Associates shuttle box system used in the AE

Methods

Animals:

16 male and 16 female CD(SD) rats (200-250 g) were used. Animals were kept under normal laboratory conditions (12/12 h light/dark cycle, air-conditioned (21±2°C), humidity-controlled room), water and regular rat chow were available *ad libitum*. All animal experimental protocols were reviewed and approved by the Hungarian Health Committee (1998) and the European Communities Council Directives (86/609/EEC).

Ovariectomy:

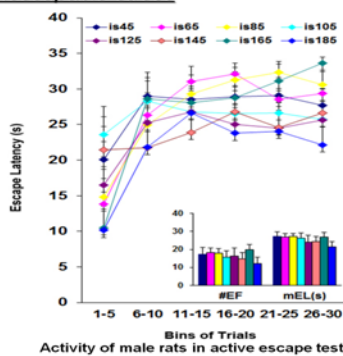
7 days prior to the behavioral experiments, female rats were bilaterally ovariectomized under deep anaesthesia with an intraperitoneal injection of chloral-hydrate (400 mg/kg).

Learned helplessness paradigm:

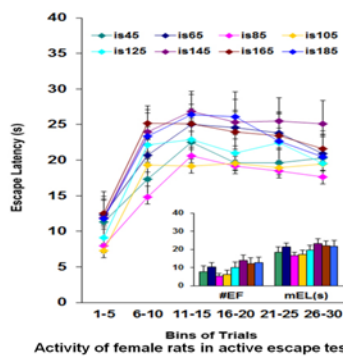
In the learned helplessness paradigm, animals are exposed to inescapable footshock stress, what was established an escape deficit. In performing an avoidance task was tested in active escape test. During the IS the guillotine door was closed, but while AE the guillotine door was opened and the animals were able to avoid the footshocks. The escape latency (time to accomplish the trial), and escape failure (unsuccessful trial) of the animals were measured and statistically analyzed.

Results

Inescapable stress

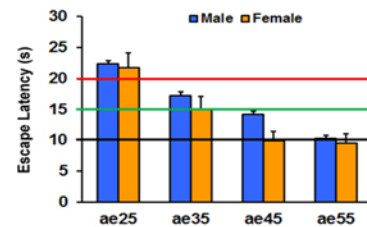


Activity of male rats in active escape test



Activity of female rats in active escape test

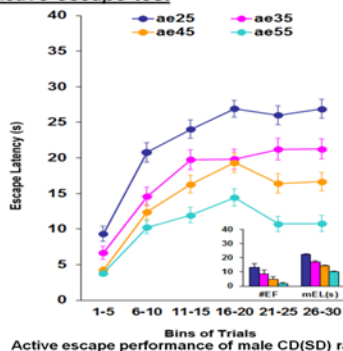
Summary



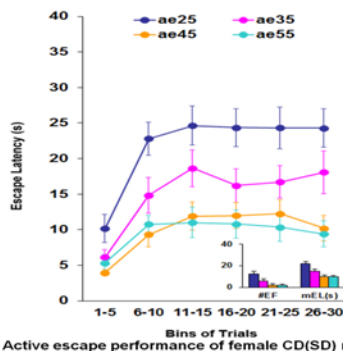
Gender differences in the performance of AE

Active escape tests showed clear differences in efficient footshock intensity. In the whole range of footshock intensity applied in our experimental protocol, female rats performed the task with less failures and their escape latency was shorter compared to males.

Active escape test



Active escape performance of male CD(SD) rats



Active escape performance of female CD(SD) rats

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Conclusions

our data:

- show clear gender differences in the active escape paradigm, in the sense of the sensitivity of footshock intensity
- indicate that CD(SD) ovariectomized females have reduced tolerance to footshock stress compared to males
- contribute to an encouraging basis for future studies on the mechanisms of sex differences in MD
- provide a new avenue for the unraveling of the mechanisms behind gender differences in MD

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