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MEETING ABSTRACT

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The effects of the neurosteroid dehydroepiandrosterone on rat behavior in the forced swim test

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Background: Neurosteroid dehydroepiandrosterone (DHEA) has been associated with various functions in the central nervous system, including modulation of memory and behavior. It has been suggested that the effects of DHEA are mediated through several neurotransmitter systems; however its mechanisms of action are not fully understood. This study aimed to investigate the behavioral profile of DHEA in the forced swim test (FST), and also its impact on locomotor activity.

Methods: FST was performed in a glass cylinder, 45 cm high, 20 cm diameter, filled with water up to a height of 30 cm. On the first day, male Wistar rats were forced to swim for 15 min. Rats were re-exposed to the FST for a single 5 min session, after the acute and chronic challenge with vehicle or DHEA. The measurement of locomotor activity was performed in a clear Plexiglas box (40×25×35 cm) for 30 min without any habituation period. In the experiments, the animals received DHEA (2, 10, and 50 mg/kg) or vehicle. Afterwards, the capability of bicuculline (0.5, 1, and 2 mg/kg) to antagonize effects of DHEA was checked. Throughout the study, drugs were given intraperitoneally, 30 min before testing. The data were assessed by one-way ANOVA. If the ANOVA was significant, each treatment condition was compared with control by Dunnett's test ($\alpha = 0.05$). Where appropriate, the influence of the antagonist bicuculline on the effect of DHEA was assessed.

Results: In FST, ANOVA indicated statistically significant effects of DHEA. Dunnett's analysis showed that DHEA significantly decreased the duration of immobility at the dose of 10 mg/kg, exerting acute, but also chronic antidepressant-like effects. These effects were antagonized by bicuculline (2 mg/kg), a specific antagonist of the $GABA_A$ receptor. However, DHEA did not induce significant differences in time of struggling behavior. ANOVA did not show a significant effect of treatment on locomotor activity.

Discussion: These data experimentally support the findings that under certain circumstances, DHEA might have triggered antide-pressant-like effects in rats. Furthermore, these effects were not confounded by change in motor function. Bicuculline abolished the action of DHEA, confirming partially GABA-ergic mediation of the effect. However the molecular and neuronal substrates linking the actions of DHEA to specific $GABA_A$ receptors remain to be further elucidated and linked to human neuropsychiatric disorders.

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