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# THE EFFECT OF N-STEAROYLETHANOLAMINE ON THE STRESS HORMONES LEVELS IN OLD RATS WITH INDUCED CHRONIC INFLAMMATION

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The ontogenesis is directly related to the organism's ability to adapt, which is provided by the neurohumoral regulation system formed by the hypothalamo-pituitary-adrenal axis. It has been established that the neurohumoral system is closely associated with the endocannabinoid system (ES). It is known that glucocorticoids influence the synthesis of endocannabinoids in the CNS, shaping stressor perception and modulating anxious behavior [1, 2]. At the same time, it has been shown that endocannabinoids play a role as a regulatory factor in activating signaling events of the hypothalamo-pituitary axis [3]. Often, ontogenesis is accompanied by the development of pathological conditions, most of which are characterized by metabolic disorders and the course of diseases initiated by pathogenic bacteria. These changes lead to the depletion of adaptive action systems and, consequently, to a decrease in the organism's ability to adapt to new conditions of existence.

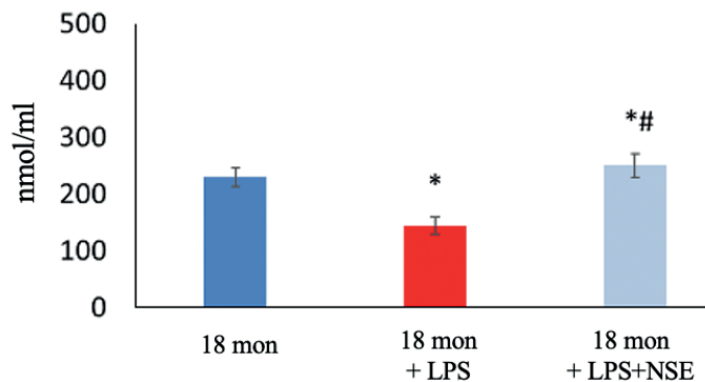
**Aim.** In view of this, the purpose of this study was to investigate the effect of N-stearoyl-ethanolamine (NSE) on the state of the hypothalamo-pituitary-adrenal and sympathoadrenal systems in the presence of complicated chronic inflammatory aging processes.

**Methods.** In the study, 18-month-old male rats were used. Animal experiments were conducted in accordance with the International Convention on the Work of Animals under the law of Ukraine "On the Protection of Animals from Cruel Treatment". The animals were divided into three groups, with one serving as a control "18 mon." ( $n = 6$ ). In rats of the second group ("18 mon. + LPS"  $n = 7$ ) and third groups, chronic low-grade inflammation was induced by intraperitoneal administration of lipopolysaccharide from *E. coli* at a dose of 250 µg/kg once a week for 6 weeks (total of 7 injections). In the rats of the third group, after 5 injections of LPS, a water suspension of NSE was administered orally at a dose of 50 mg/kg daily for 10 days ("18 mon. + LPS + NSE";  $n = 7$ ). The development of inflammation was monitored by the levels of pro-inflammatory cytokines (IL-1β and TNFα) in the animals serum. The levels of corticosterone, adrenaline, and adrenocorticotrophic hormone (ACTH) in rat's blood plasma were determined using the enzyme-linked immunosorbent assay method.

**Results.** The course of chronic inflammatory process is accompanied by a decrease in the corticosterone content (Fig. 1), indicating the influence of the pathological condition on the mechanisms of adaptive response development. Administration of NSE to rats with chronic inflammation contributed to the restoration of circulating corticosterone levels to values corresponding to the control group.

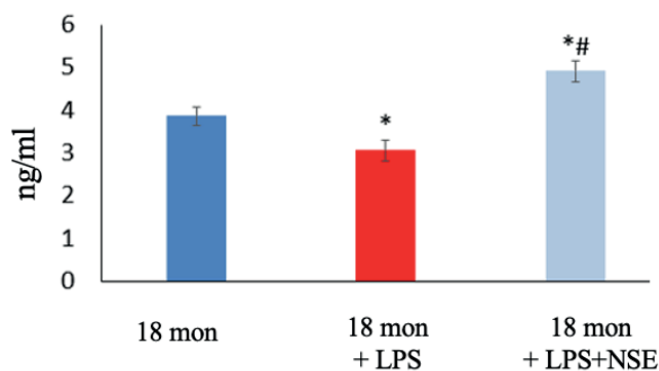
Also, a decrease in adrenaline levels was observed compared to its age norm (Fig. 2). Administration of NSE to old rats with chronic inflammatory processes prevented the decrease in circulating adrenaline levels and promoted its increase in plasma compared to the control group.

An increase in the level of ACTH in the blood of rats was detected in response to a decrease in corticosterone levels induced by chronic inflammatory processes (Fig. 3). Administration of NSE prevented the rise in circulating ACTH due to normalization of corticosterone levels in the blood plasma of animals with chronic inflammation.



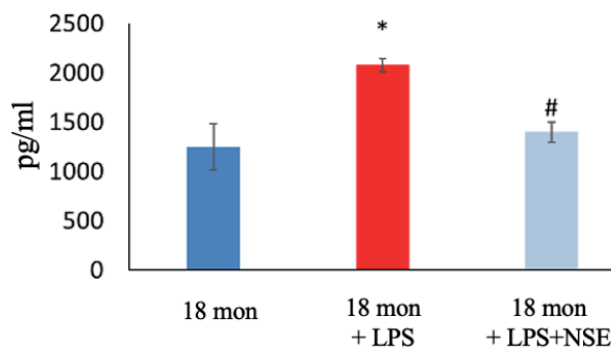
**Fig. 1. The corticosterone content in the blood plasma of rats**

\* —  $P < 0.05$  compared to control (18 mon.); # —  $P < 0.05$  compared to group 18 mon. (18 mon. + LPS)



**Fig. 2. The adrenaline content in the blood plasma of rats**

\* —  $P < 0.05$  compared to control (18 mon.); # —  $P < 0.05$  compared to group 18 mon. (18 mon. + LPS)



**Fig. 3. The ACTH content in the blood plasma of rats**

\* —  $P < 0.05$  compared to control (18 mon.); # —  $P < 0.05$  compared to group 18 mon. (18 mon.+LPS)

**Discussion.** Our results indicate the stimulating effect of NSE on the level of circulating corticosterone in old rat with chronic inflammation. This effect of NSE is explained by its anti-inflammatory action, which was investigated in our previous experiments [4, 5].

Based on the fundamental principles regarding age-related changes in the activity of the sympathoadrenal system, we conducted a study to investigate the impact of NSE on the level of circulating adrenaline in old rats with induced chronic inflammation. It is known that catecholamines, by their biological nature, are pro-inflammatory agents and are sensitive mediators for many immunocompetent cells [6]. Chronic inflammatory processes inhibit the functions of the sympathetic nervous system and, consequently, affect the immune status of the organism. The results obtained in our work indicate a probable decrease in circulating adrenaline in the blood of old rats with chronic inflammatory processes. The application of NSE prevented the development of inflammatory reactions and hindered changes in the activity of the sympathoadrenal system in rats with chronic inflammation.

**Conclusions.** Today, it has been proven that the endocannabinoid system is involved in the regulatory cascades of the hypothalamo-pituitary-adrenal axis, both under physiological conditions and under the influence of stress factors. Age-related inhibition of the activity of the endocannabinoid system is accompanied by functional disturbances in negative feedback, which directly affects the nature and capacity of the organism's adaptive ability. Analysis of the obtained results suggests that saturated N-acyl ethanolamines (NAEs), including NSE, may act as direct modulators of endocannabinoid system activity or indirect regulators by regulating steroidogenesis, integrating into the system of humoral regulation.

**Key words:** stress hormones, endocannabinoids, aging, inflammation, hypothalamic-pituitary-adrenal axis.

**Author's contribution.** K.V. Ibrahimov worked on the corticosterone and adrenaline determination, H.V. Kosiakova carried out the general management of the work and determined the levels of pro-inflammatory cytokine, and T.M. Horid'ko reproduced a model of chronic inflammation in rats and analyzed ACTH levels.

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