CORRECTION OF STRESS-INDUCED HORMONAL CHANGES BY THE RIL-2 MEDICATION IN EXPERIMENTAL TRAUMATIC BRAIN INJURY

E.E. Fomicheva1, S.N. Shanin1, T.A. Filatenkova1, N.B. Serebryanaya1, 2, 3

1 Institute of Experimental Medicine, Saint Petersburg, Russia;
2 Saint Petersburg State University, Saint Petersburg, Russia;
3 North-Western State Medical University named after I.I. Mechnikov, Saint Petersburg, Russia

Introduction. Traumatic brain injury (TBI) leads to a sustained stress reaction, individual changes in the production of stress hormones and reactions to them can lead to different post-traumatic outcomes due to disruption of the mechanisms of neuro-endocrine-immune interaction [1]. The most important stress-regulating system is the hypothalamic-pituitary-adrenocortical system (HPA axis), its timely activation ensures adequate secretion of corticosterone and counteracts the development of excessive secondary inflammation. Stress also changes the activity of the hypothalamic-pituitary-gonadal system (HPGS), since sex hormones perform their specific roles in the process of adaptation during stress [2]. Testosterone and its metabolites play the role of neurosteroids In the central nervous system, their participation in the formation of training, memory and social behavior has been proven. [3]. The aim of the study was to detect changes in corticosterone and testosterone concentration in blood serum of experimental animals during recovery period after TBI. And also to find possibility of disturbance correction by cytokine preparation rIL-2 (roncoleukin). The injections of a recombinant human interleukin-2 (rIL-2, Roncoleukin (BIOTECH, Saint Petersburg, Russia)) in dose of 30 mg/kg of weight were made to a group of animals, including the control group (without TBI), daily for three days. Measurement

Keywords: stress-hormones; TBI; rIL-2.
of corticosterone (Cs) and testosterone (Ts) concentration in blood serum was made by ELISA kit (DRGDiagnostic). Statistical processing of materials was carried out using the Mann – Whitney test.

Results and discussion. Experiments were done on animals with moderate injury on the 7th day after TBI. Concentration of hormones was measured, and it was shown that the level of corticosterone was decreased in blood serum up to 30% in compare with the control animals (table 1). Injection of rIL-2 to control animals (without TBI) increased the level of Cs in 2-3 times. This fact probably is the result of corticotropic action of IL-2. After the injection of rIL-2 animals in 72 hours after TBI, an additional increase in the Cs level was detected.

Conclusion. Ts slightly changed in animals on day 7 after TBI compared with this indicator in intact animals and control, that only got rIL-2 injections. But it’s level increased when after TBI the injections of rIL-2 were done. The obtained results can be considered as evidence of the stress reaction normalization in animals after TBI. It is well known that levels of IL-2 and high-affinity receptor for IL-2 also change under the stress. Under mild stress they increase, and when acute stress, they are decreased [4]. Under stress, the activated HPA axis has a direct effect on the HPGS, entering into reciprocal relations with it. The lack of corticosterone secretion is the cause of increased secretion of ACTH, which shifts steroidogenesis in the direction of excessive formation of deoxycorticosterone and inhibition of androgen production. It is well known that stress in animals causes suppression of testosterone synthesis, and the duration of action of a stressor is a determining factor for reducing its level [5]. So, the change in the functional activity of HPA axis and HPGS as stress systems for TBI under the influence of rIL-2 is important for the turning on of regulatory mechanisms aimed at overcoming the effects of acute inflammation (including TBI) in the post-traumatic period.

References

<table>
<thead>
<tr>
<th>Animal groups</th>
<th>n = 5</th>
<th>Corticosterone ng/ml</th>
<th>Testosterone ng/ml</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td></td>
<td>70.0 ± 10.0</td>
<td>3.8 ± 0.3</td>
</tr>
<tr>
<td>TBI</td>
<td></td>
<td>50.0 ± 8.0</td>
<td>5.3 ± 0.5</td>
</tr>
<tr>
<td>Control + rIL-2</td>
<td></td>
<td>160.0 ± 25.0*</td>
<td>5.8 ± 0.8</td>
</tr>
<tr>
<td>TBI + rIL-2</td>
<td></td>
<td>220.0 ± 40.0*</td>
<td>8.0 ± 0.8*</td>
</tr>
</tbody>
</table>

Note. * p < 0.05 in compared with hormone levels of intact animals; # p < 0.05 in compared with hormone levels of animals after TBI.