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Cross-talk between gonadal steroid hormones signaling and cytokine signaling after experimental traumatic brain injury

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Introduction: It is reported that gonadal steroid hormones may affect the cytokine signaling pathway. To determine the mechanism by which steroids regulates this signaling pathway, here we investigated the effects of administration of exogenous estrogen /progesterone on brain STAT3/SOCS3 in female rats after traumatic brain injury (TBI).
Methods: In this study, ovariectomized female rats were randomly divided into 7 groups: Sham; TBI; Vehicle; Low dose estrogen (E1); High dose estrogen (E2); low dose progesterone (P1); High dose progesterone (P2). The TBI model was established using a Marmarou's weight-dropping method. Brain samples were extracted 24 h following TBI. The expression levels of STAT3and SOCS3 were examined using immunohistochemistry, and brain edema was determined using brain water content (BWC).
Results: This model consistently resulted in increased BWC .Both steroid hormones ameleorated post-injury brain edema. In TBI group, the SOCS-3 positive cells were decreased. While in all groups treated with estrogen or progesterone, the SOCS-3 positive cells were increased; this increase in E1, E2, and P2 groups was statistically significant compared to vehicle group. However, comparisons between treatment groups showed that E2 effect was significant compared to E1 and P2 groups. The p-STAT3 positive cells were significantly increased after TBI; however, only E2 decreased p-STAT3 activation**.**
Conclusion: These results suggest that exogenous estrogen/progesterone increases brain SOCS3 activation and decrease p-STAT3 level after TBI. This represents the initial demonstration of female steroid hormones crosstalk with cytokines signaling in post-injury brain.

Keywords: Estrogen; Progesterone; TBI; SOCS-3; p-STAT3

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