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Modulation of hippocampal gabaergic subpopulations induced by estrogen administration in the Trimethyltin model of hippocampal neurodegeneration

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Estrogens exert neuroprotection through multiple mechanisms, including increased neuronal plasticity [1]. Due to their involvement in the modulation of hippocampal functions, the present study investigates the effects of exogenous 17-beta estradiol (E2) in the rat model of Trimethyltin (TMT)-induced hippocampal neurodegeneration (8mg/kg), characterized by pyramidal cell death selectively localized in CA1,CA3/hilus hippocampal subfields accompanied by glial activation, seizures and cognitive impairment [2,3,4]. After TMT or saline treatment, ovariectomized animals received two E2 (0.2 mg/kg i.p.) or vehicle (oil) doses and were sacrificed 48h or 7 days after TMT- treatment. Our data indicate that E2, although not influencing the extent of neuronal loss in TMT-treated animals, induces the early upregulation of the antiapoptotic gene Bcl2l and of BDNF and TrkB, , essentially involved in neuroprotection and cell survival.

In addition, in the TMT+E2-treated group a significant upregulation of glutamic acid decarboxylase (Gad) 67, neuropeptide Y (npy)- and parvalbumin (pva) genes, as well as the peroxisome proliferator-activated receptor coactivator-1α pathway, involved in both parvalbumin (PV) synthesis and neuroprotection, was detected. Unbiased stereology performed on rats sacrificed 7 days after TMT-treatment pointed out that E2 significantly affects the size of specific hippocampal GABAergic subpopulations in selected hippocampal subfields of TMT-treated animals. In particular, a significant increase of GAD67-expressing interneurons in CA1 stratum oriens, CA3 pyramidal layer, hilus and dentate gyrus, accompanied by a parallel increase of NPY-expressing cells and of PV-positive basket cells in CA1pyramidal layer was detectable. Due the relevance of interneuron role in restoring the inhibitory drive in circuit reorganization, our results add Information on the role of in vivo E2 administration on mechanisms involved in cellular plasticity in the adult brain.

References

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Keywords

Neuroprotection; neurodegeneration; hippocampus; plasticity; interneurons.