Estradiol activates PI3K/Akt/GSK3 pathway under chronic neurodegenerative conditions triggered by perinatal asphyxia

Saraceno G.E.

Bellini M.J.

Garcia-Segura L.M.

Capani F.

Perinatal asphyxia (PA) remains as one of the most important causes of short-term mortality, psychiatric and neurological disorders in children, without an effective treatment. In previous studies we have observed that the expression of different neurodegenerative markers increases in CA1 hippocampal area of 4-months-old male rats born by cesarean section and exposed for 19 min to PA. We have also shown that a late treatment with 17? estradiol (daily dose of 250 ?g/kg for 3 days) was able to revert the brain alterations observed in those animals. Based on these previous results, the main aim of the present study was to explore the mechanism by which the estrogenic treatment is involved in the reversion of the chronic neurodegenerative conditions induced by PA. We demonstrated that estradiol treatment of adult PA exposed animals induced an increase in estrogen receptor (ER) a and insulin-like growth factor receptor (IGF-1R) protein levels, an activation of the phosphatidylinositol 3-kinase/Akt/glycogen synthase kinase 3 beta/?-catenin signaling pathway and an increase in Bcl-2/Bax ratio in the hippocampus in comparison to PA exposed animals treated with vehicle. Taking together, our data suggest that the interaction between ERa and IGF-IR, with the subsequent downstream activation, underlies the beneficial effects of estradiol observed in late treatment of PA.

Hippocampus

Neuronal survival

Neuroprotection

Signaling pathway

Western blot

beta catenin

estradiol

estrogen receptor alpha

glycogen synthase kinase 3

phosphatidylinositol 3 kinase

protein Bax

protein bcl 2

protein kinase B

somatomedin C receptor

adult

animal experiment

animal model

animal tissue

Article

controlled study

degenerative disease

down regulation

drug effect

drug mechanism

enzyme activation

female

hippocampal CA1 region

male

nerve cell plasticity

neuromodulation

neuroprotection

nonhuman

perinatal asphyxia

protein protein interaction

rat

signal transduction