B-ESTRADIOL PROTECTION AGAINST B-AMYLOID-INDUCED NEUROTOXICITY IN RAT CORTICAL NEURONS VIA JNK SIGNALING AND MODULATION OF BCL-2 FAMILY PROTEINS

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Introduction: Recent studies have shown that female sex hormones, such as β-17-estradiol, are potential neuroprotective agents against damage produced by neurodegenerative diseases, like Alzheimer’s disease.

This evidence is corroborated by several experimental studies documenting the protective role of female sex hormones both in vitro and in vivo.

However, the cellular and molecular mechanisms implicated in their protective actions on the brain are not completely understood.

Aim: The aim of this study is to investigate the neuroprotective role of estradiol against damage induced by β-amyloid peptide (Aβ) and to elucidate the possible mechanism through which this protection is exerted.

Methods: We used primary cultures of cortical neurons from one day old rats treated with 25µM Aβ, 10 µM β-17-estradiol, 100 nM JNK inhibitor, respectively. RT-Real Time PCR, Western Blotting, Immunofluorescence and Cell Viability Assays were also performed.

Results: We observed that estrogen can reverse the effects of Aβ on cell and mitochondrial viability. The ratio Bax/Bclxl is increased upon treatment with the peptide and this trend is reverted by co-treatment with beta-17-estradiol. This result is supported by RT-Real Time PCR, Western Blotting and Immunofluorescence experiments.

β-17-estradiol reduced Aβ-induced JNK activation and Aβ-induced down regulation of Bclxl in a JNK-dependent manner, with subsequent inhibition of mitochondrial release of cytochrome c and activation of Caspase 3.

Conclusions: Our findings indicate that Aβ-induced apoptosis proceeds through the mitochondrial pathway and the JNK signaling cascade plays a role in the regulation of anti-apoptotic effects of β-17-estradiol.