Effects of Ovariotectomy and ApoE in BNDF Secretion, ERα and ERK and ERKPi Expression in Mouse Brain

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INTRODUCTION: Alzheimer´s disease is the major neurodegenarative disease nowadays. We have shown that lacking of gonadal hormones and ApoE regulates most of the brain molecules associated to cell survival and plaque formation in an opposite fashion. However, when ApoE knock out (APOEKO) mice are ovariotectomized (OVX), this protective effect of reversed in all markers we tested so far, such as brain estrogen receptor alpha (ERα) and brain-derived growth factor (BNDF). One of the main signaling pathways involved in cell survival is AKT/PI3-K/Mtor. **OBJECTIVE:** Evaluate the signaling pathway of AKT/PI3-K/mTOR in both OVX WT and APOEKO mice in two period of time following castration. **MATERIALS AND METHODS:** To do so we have performed Western blottings to most downstream elements of ERα pathway, ERK and ERKPi as well as ELISA to determine the BNDF in mouse brains of WT and APOEKO OVX. **DISCUSSION AND RESULTS:** However, BNDF tissue concentration after OVX decreased time dependently in WT mice (from 7.5 pg/mL in WT SHAM to 5.3 pg/dL to WT OVX 6M to 4.3 WT OX 12 months, r = -0.32), it did not do so in APOEKO OVX mice (from 108 pg/mL in APOEKO SHAM to 9.7 APOEKO OVX 6M to 8.7 PAOEKO OVX 12 months, r = -0.12). Total ERK protein also did not seem to change in any group. Nonetheless, ERKPi, the phosphorylated counterpart of the protein significantly decreased 2-fold in WT OVX after 2 months and 3-fold WT OVX after 6 months surgery when compared to SHAM operared WT mice. **CONCLUSION:** WT and APOEKO mice shown differential pattern of pathways of cell survival involving brain ERK and ERKPi after OVX. The data seem to link this pathway to increase secretion of BNDF in APOEKO mice brain by a mechanism that we are still trying to clarify.

Keywords: Alzheimer's disease, ApoE knock-out mice, molecular biomarkers
Sponsorship: CNPq and FAPES