Effects of Ovariotectomy and ApoE in Increase 1-32βAP Brain Accumulation and HSC70 Expression in Mouse Brain

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INTRODUCTION: Alzheimer´s disease (AD) 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 autolysis and plaque similar in an opposite fashion. However, when ApoE knock out (APOEKO) mice are ovariotectomized (OVX), this protective effect is reversed in all markers we tested so far, such as brain TAU and phosphor(199S) TAU, and 1-32β amyloid peptide (1-32βAP). One of the main signaling pathways involved in cell autolysis such as HSC70 and Beclin. **OBJECTIVE:** Evaluate the association of phosphorylation of TAU protein and 1-32βAP formation in brains of OVX WT and APOEKO mice to two protein associated to autophagossome formation: HSC70 and Beclin. **MATERIALS AND METHODS:** Western blottings has been performed for HSC70 and Beclin in brain extracts of WT and APOEKO OVX mice and their SHAM operated controls compared then to measurements of TAU and phosphor(199S) TAU, and 1-32βAP by ELISA. We found that WT OVX mice exhibited higher (2-fold) TAU, TAU-Pi, HSC70 and Beclin when compared to SHAM operate controls. APOEKO SHAM operated mice showed no changes in HSC70 and Beclin ($p>0.05$, $n=3$) whereas TAU and TAU-Pi were significantly decreased by 50%. OVX also led to increased in HSC70 and Beclin in APOEKO, suggesting that lacking of gonadal hormones and ApoE might work through different pathway in triggering neuronal autolysis. **DISCUSSION AND RESULTS:** Autolysis has been shown to be the last event in neuronal death in AD. We have seen that enhance TAU and TAU 199-S protein, commonly associated to neurofibrillary tangles area, also associated to increased levels of HSC70 and Beclin. Also, these events are associated to increase in 1-32βAP (a neurotoxic peptide) in their brain. **CONCLUSION:** Our data suggest that lacking of gonadal hormones and ApoE experiments are ongoing to better understand this mechanism.

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