The Effects of Estrogen on Intracellular Calcium Release and Amyloid Beta 1-42-induced Cytokine Expression in Human Microglia

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Abstract

Microglia act as the macrophages of the brain. They can secrete proinflammatory molecules that could exacerbate neuronal injury in many models such as ischemia, oxidative stress, and neurodegenerative diseases. Estrogen is known to be neuroprotective in these models. In the present study, amyloid beta peptides (Aβ), the main component of amyloid plaques found in the brains of Alzheimer's patients was used as a stimulator of microglia. There is massive evidence that Aβ cause a number of cytotoxic events that finally lead to neuronal apoptosis and reactive gliosis which seem to be reversed by preadministration of estrogen. The roles of estrogen and Aβ upon glial activation are not as well studied as in neurons. For microglia, estrogen treatment can decrease NO, superoxide, and TNF-α production, thus attenuating the inflammatory responses induced by LPS or Aβ. However, these studies were usually done in murine microglia. The roles of estrogen upon human microglia have never been explored before. We would like to see if estrogen differentially regulate microglia from human compared to murine. By employing human microglia, it should better reflect the response to estrogen in real patients. Cytokine expression was examined to determine the degree of microglial activaiton. Also, the potential molecular mechanism by which estrogen exerts upon microglia was detected using spectrofluorometry to see if estrogen can regulate the intracellular calcium in microglia.

Keywords: Amyloid beta; Estrogen; Human microglia; Intracellular calcium; Proinflammatory cytokines