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REPRODUCTIVE ENDOCRINOLOGY

Less estrogen, more neuroinflammation?

Long-term estrogen deprivation in aged mice is associated with increased inflammatory activity in the brain, show Italian researchers. The findings provide a mechanistic link between lack of ovarian function, aging and neuroinflammation.

"We postulated that the decreased estrogen receptor stimulation that occurs after menopause might be one of the causes of the augmented incidence of inflammatory diseases such as atherosclerosis, diabetes mellitus, osteoporosis and neurodegeneration in women," recounts lead researcher Adriana Maggi.

The investigators used a transgenic mouse model in which the luciferase gene is positively regulated by estrogens to assess the transcriptional activity of estrogen receptors. The transcriptional activity of the receptors in the brain decreased with age, being 60% lower in animals aged 18 months than in animals aged 6 months, independently of estrogen receptor expression or ovarian function. Aged mice in which an ovariectomy had been performed 17 months earlier, however, showed an increased expression of inflammatory markers in the brain. Mice aged 12 months that had been ovariectomized 7 months earlier had a greater inflammatory response to stimulation with lipopolysaccharide than mice in which an ovariectomy had been performed 1 month before stimulation or sham-operated animals.

"The study supports the hypothesis that estrogen receptors and estrogen exert a protective action in the brain during aging and that the long-term lack of ovarian function limits such a protective effect," concludes Maggi. The researchers hope that the findings of this and other studies contribute to the design of novel and more efficacious hormone replacement therapies.

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Original article Benedusi, V. *et al.* A lack of ovarian function increases neuroinflammation in aged mice. *Endocrinology* doi:10.1210/en.2011-1925