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FULL-TEXT ARTICLE**Female sex steroids: effects upon microglial cell activation.**[Drew PD](#), [Chavis JA](#).

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Multiple sclerosis occurs more commonly in females than males. However, the mechanisms resulting in gender differences in multiple sclerosis are unknown. Activated microglia are believed to contribute to multiple sclerosis pathology, perhaps in part due to production of nitric oxide (NO) and TNF-alpha, molecules which can be toxic to cells including oligodendrocytes. The current study demonstrates that the female sex steroids estriol, beta-estradiol and progesterone inhibit lipopolysaccharide (LPS) induction of nitric oxide (NO) production by primary rat microglia and by the mouse N9 microglial cell line. These hormones act by inhibiting the production of inducible nitric oxide synthase (iNOS) which catalyses the synthesis of NO. Estriol likely inhibits iNOS gene expression since the hormone blocks LPS induction of iNOS RNA levels. The pro-inflammatory cytokines IFN-gamma and TNF-alpha are believed to be important modulators of multiple sclerosis. Here, we demonstrate that estrogens and progesterone also inhibit NO production by microglial cells activated in response to these cytokines. Activated microglia elicit TNF-alpha in addition to NO and we further demonstrate that estrogens and progesterone repress TNF-alpha production by these cells. Finally, estriol and progesterone, at concentrations consistent with late pregnancy, inhibit NO and TNF-alpha production by activated microglia, suggesting that hormone inhibition of microglial cell activation may contribute to the decreased severity of multiple sclerosis symptoms commonly associated with pregnancy.

PMID: 11063824 [PubMed - indexed for MEDLINE]

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Inhibition of microglial cell activation by cortisol. [Brain Res Bull. 2000]

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Retinoic acid inhibits expression of TNF-alpha and iNOS in activated rat [Glia. 2005]

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