

Decreased nitric oxide levels in the hippocampus may play a role in learning and memory deficits in ovariectomized rats treated by a high dose of estradiol

Níveis diminuídos de óxido nítrico no hipocampo podem ser importantes nos déficits de aprendizado e de memória em ratas ooforectomizadas tratadas com alta dose de estradiol

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ABSTRACT

The effects of a high estradiol dose on memory and on nitric oxide metabolites in hippocampal tissues were investigated. Sham-Est and OVX-Est Groups were treated with 4 mg/kg of estradiol valerate for 12 weeks. Time latency and path length were significantly higher in the Sham-Est and OVX-Est Groups than in the Sham and OVX Groups, respectively ($p < 0.001$). The animals in the Sham-Est and OVX-Est Groups spent lower time in the target quadrant (Q1) than those of the Sham and OVX Groups during the probe trial test ($p < 0.05$ and < 0.001 , respectively). Significantly lower nitric oxide metabolite levels in the hippocampi of the Sham-Est and OVX-Est Groups were observed than in the Sham and OVX ones ($p < 0.001$). These results suggest that decreased nitric oxide levels in the hippocampus may play a role in the learning and memory deficits observed after treatment with a high dose of estradiol, although the precise underlying mechanisms remain to be elucidated.

Key words: estradiol, rat, hippocampus, nitric oxide.

RESUMO

Os efeitos de uma alta dose de estradiol na memória e nos metabólitos do óxido nítrico de tecidos hipocámpais foram estudados. Os Grupos Sham-Est e OVX-Est foram tratados com 4 mg/kg de valerato de estradiol por 12 semanas. O tempo de latência e o comprimento do caminho foram significativamente maiores nos Grupos Sham-Est e OVX-Est em relação aos Grupos Sham e OVX, respectivamente ($p < 0,001$). Os animais dos Grupos Sham-Est e OVX-Est passaram menos tempo na meta do quadrante (Q1) do que aqueles dos Grupos Sham e OVX durante o teste inicial ($p < 0,05$ e $< 0,001$, respectivamente). Níveis significativamente menores de metabólitos do óxido nítrico foram observados nos hipocámpos dos Grupos Sham-Est e OVX-Est em relação aos Grupos Sham e OVX ($p < 0,001$). Esses resultados sugerem que os níveis diminuídos de óxido nítrico no hipocampo podem ter um papel nos déficits de aprendizado e de memória, que são observados após tratamento com alta dose de estradiol, embora os mecanismos específicos envolvidos nestes achados ainda precisam ser elucidados.

Palavras-Chave: estradiol, rato, hipocampo, óxido nítrico.

Cognitive impairments occur in both men and women as the age increases. However, the decline in cognitive ability, for example Alzheimer's disease, is more severe in women during menopause^{1,2}. Therefore, it seems that changing the levels of steroid hormones after menopause, and particularly the loss of estradiol, has a role in senile cognitive worsening³.

The main source of sex hormones is the gonads, which reach the brain via the blood circulation. However, estrogens and androgens are synthesized in mammalian brain areas such as the hippocampus⁴. Neuromodulatory actions of gonadal sex hormones in the hippocampus, as an important center involved in learning and memory, are also attractive⁵.

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