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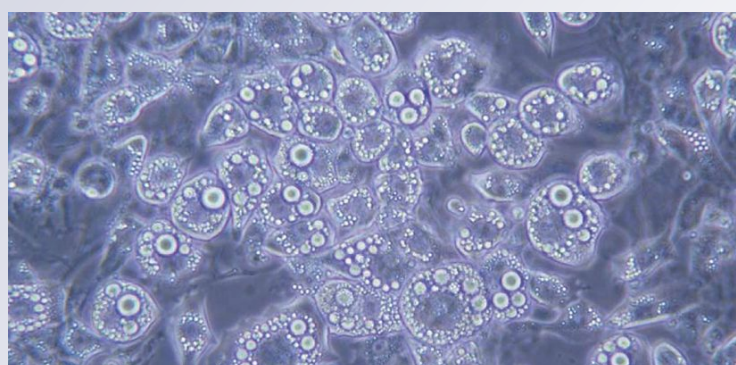
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Estrogens: mechanisms of neuroprotective effects

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Abstract Within the last few years, there has been a growing interest in the neuroprotective effects of estrogen and the possible beneficial effects of estrogen in neurodegenerative diseases such as stroke, Alzheimer's disease, and Parkinson's disease. The concept of neuroprotective effects of estrogen in women remains controversial because these effects may vary with the timing of treatment. Research increasingly suggests that changes in estrogen levels during aging may increase risk for Alzheimer's disease, the most common type of dementia. This update reviews the newest information about estrogen and cognitive aging, including information regarding the role of bio-available estrogen in older women and men.

Keywords Estrogens · Neuroprotection · Aging · Neurodegenerative diseases

Introduction

The brain is an important target organ for estrogen. In addition to direct effects, estrogen influences brain function through effects on the vasculature and the immune system. Two classes of intracellular estrogen receptors, α and β , are expressed within specific regions of the human brain [11].

Many estrogen actions are potentially relevant to cognitive changes occurring after menopause, but for most, the clinical implications are yet unclear. Estrogen enhances synaptic plasticity, neurite growth, hippocampal neurogenesis, and long-term potentiation. The latter is a physiologic process involved in the formation of episodic memories. Estrogen protects against apoptosis and against neural injury in a variety of experimental settings, including toxicity induced by excitatory neurotransmitters, β -amyloid, oxidative stress, and ischemia.

Estrogen influences several neurotransmitter systems, including acetylcholine, serotonin, noradrenalin, and glutamate. Acetylcholine is important in memory processes. Cholinergic neurons in the basal forebrain express estrogen receptors, and estrogen enhances cholinergic function after ovariectomy. These neurons are specifically affected by the pathology of Alzheimer's disease. Other estrogen actions are both pro-inflammatory and anti-inflammatory. Pro-thrombotic properties of some estrogens may contribute to cerebrovascular disease, and vascular pathology increases dementia severity in the presence of Alzheimer's pathology [15].

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