Life Sci. 2019 Dec 1:238:116979. doi: 10.1016/j.lfs.2019.116979. Epub 2019 Oct 21.

Effects of progesterone on glucose uptake in neurons of Alzheimer's disease animals and cell models

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PMID: 31647947 DOI: 10.1016/j.lfs.2019.116979

Abstract

Aims: Alzheimer's disease (AD) is closely related to abnormal glucose metabolism in the central nervous system. Progesterone has been shown to have obvious neuroprotective effects in the pathogenesis of AD, but the specific mechanism has not been fully elucidated. Therefore, the purpose of this study was to investigate the effect of progesterone on the glucose metabolism of neurons in amyloid precursor protein (APP)/presenilin 1 (PS1) mice and Aβ-induced AD cell model.

Materials and methods: APP/PS1 mice were treated with 40 mg/kg progesterone for 40 days and primary cultured cortical neurons were treated with 1 μM progesterone for 48 h.Then behavior tests,2-NBDG glucose uptake tests and the protein levels of glucose transporter 3 (GLUT3), GLUT4, cAMP-response element binding protein (CREB) and proliferator-activated receptor γ (PPARγ) were examined.

Key findings: Progesterone increased the expression levels of GLUT3 and GLUT4 in the cortex of APP/PS1 mice, accompanied by an improvement in learning and memory. Progesterone increased the levels of CREB and PPARγ in the cerebral cortex of APP/PS1 mice. In vitro, progesterone increased glucose uptake in primary cultured cortical neurons, this effect was blocked by the progesterone receptor membrane component 1 (PGRMC1)-specific blocker AG205 but not by the progesterone

receptor (PR)-specific blocker RU486. Meanwhile, progesterone increased the expression of GLUT3, GLUT4, CREB and PPARγ, and AG205 blocked this effect.

Significance: These results confirm that progesterone significantly improves the glucose metabolism of neurons.One of the mechanisms of this effect is that progesterone upregulates protein expression of GLUT3 and GLUT4 through pathways PGRMC1/CREB/GLUT3 and PGRMC1/PPARγ/GLUT4.

Keywords: Alzheimer's disease; GLUT3; GLUT4; Glucose uptake; PGRMC1; Progesterone.

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