Hippocampal DHCR24 down regulation in a rat model of streptozotocin-induced cognitive decline

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HIGHLIGHTS

• Hippocampal DHCR24 down regulation 14 and 21 days after ICV–STZ administration.
• Hippocampal DHCR24 down-regulation precedes the onset of cognitive impairment.
• Suggestion of potential relation between DHCR24 and cognitive impairment.

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ABSTRACT

The DHCR24 (24-dehydrocholesterol reductase) gene codes a multifunctional protein which consists of enzymatic, antioxidant, and anti-apoptotic activities. It exists in almost all neurons and protects the neural cells against amyloid beta toxicity. Several studies have shown the down regulation of DHCR24 in Alzheimer’s disease. We examined the time profile of DHCR24–mRNA alteration in an animal model of streptozotocin (STZ)-induced cognitive impairment. The DHCR24 mRNA levels of hippocampus and cognitive impairment were evaluated at 7, 14, and 21 days after intracerebroventricular–streptozotocin (ICV–STZ)/Saline administration. The decrease in expression of DHCR24 preceded the onset of the cognitive impairment. These results suggest the potential relation between DHCR24 expression and cognitive impairment.

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1. Introduction

One of the hallmarks of Alzheimer’s disease (AD) is the accumulation of amyloid β (Aβ) proteins [2, 28]. The DHCR24 (24-dehydrocholesterol reductase), a multifunctional protein encoded by DHCR24 gene, encompass the enzymatic, antioxidant, and anti-apoptotic activities [20, 33]. Its gene expression has been shown in almost all neurons and protects the neural cells against Aβ toxicity [9]. Several previous studies suggested the down regulation of DHCR24, in temporal cortex [9, 11], hippocampus, and cingulate cortex [19] of AD patients. Moreover, DHCR24 down regulation in animal [11, 31] model of AD has also been reported in the cortex, and cerebellum. However, little information is available about earlier stages of the disease where cognitive impairment has not yet occurred. It is not clear whether the decrease in DHCR24 transcription precedes a decline in cognitive impairment, or it is a consequence of cognitive destruction. To study this, we monitored the onset of DHCR24 mRNA alteration on different time points, 7, 14, and 21 days after intracerebroventricular–streptozotocin (ICV–STZ)/Saline administration.

ICV–STZ administration induces oxidative stress, as well as cognitive impairment [7, 15, 24, 29]. It has been suggested as an...