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BRAIN RESEARCH

Research Report

Coexistences of insulin signaling-related proteins and choline acetyltransferase in neurons

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ABSTRACT

Type 2 diabetes recently has been identified as a risk factor for developing Alzheimer's disease (AD). The main reason for this appears to be insulin signaling failure in the brain. Furthermore, cholinergic neurons are particularly affected in the brains of AD patients. The aim of the present study is to investigate if insulin signaling-related proteins are co-located with cholinergic neuron in the CA1 region of hippocampus of mice, which could explain the early loss of cholinergic neurons in AD. Using immunohistochemistry, the insulin signaling-related proteins, such as insulin receptor (InsR), insulin receptor substrate-1 (IRS-1), protein kinase B (PKB, also named Akt), glycogen synthatase kinase-3bteta (GSK-3bteta) and insulin-degrading enzyme (IDE) were analysed. Choline acetyltransferase (ChAT) was selected as a marker of cholinergic neurons. In the CA1 region of hippocampus of mice, several of the insulin signaling-related proteins we had chosen are co-located with ChAT, and most double immunoreactive positive cells were pyramidal cells. The coexistences indicated that the insulin signaling may play an important part in the activities of cholinergic neurons, and the impairment of the pathway may be important in the mechanisms that underlie neurodegeneration in AD.

1. Introduction

Alzheimer's disease (AD) is an age-related cerebral degenerative disorder with cognitive and memory decline. The impairment of cholinergic neurons is one of the central pathologic changes and occurs early. The mechanism of AD is unknown at present, but the relationship between insulin signaling and AD is increasingly becoming a subject of interest in the study of AD (Craft, 2007; Li and Hölscher, 2007).

Insulin signaling pathways are important in the function of sustaining the survival and the function of neurons, and PI-3K/Akt/GSK-3beta signaling pathway of which might play a key role (Duarte et al., 2008). The hypothesis that impaired insulin signaling in the brain which is causally linked to neurodegeneration is a novel theory that could be helpful to understand the possible mechanisms of AD (Li and Hölscher, 2007). More and more evidence provided by epidemiologic studies, *in vivo* or *in vitro* experiments and clinical tests supported this hypothesis (Biessels and Kappelle, 2005; Craft, 2007). We therefore set out in this anatomical study to investigate if there is any connection between insulin signaling that would be of importance for neuronal development,

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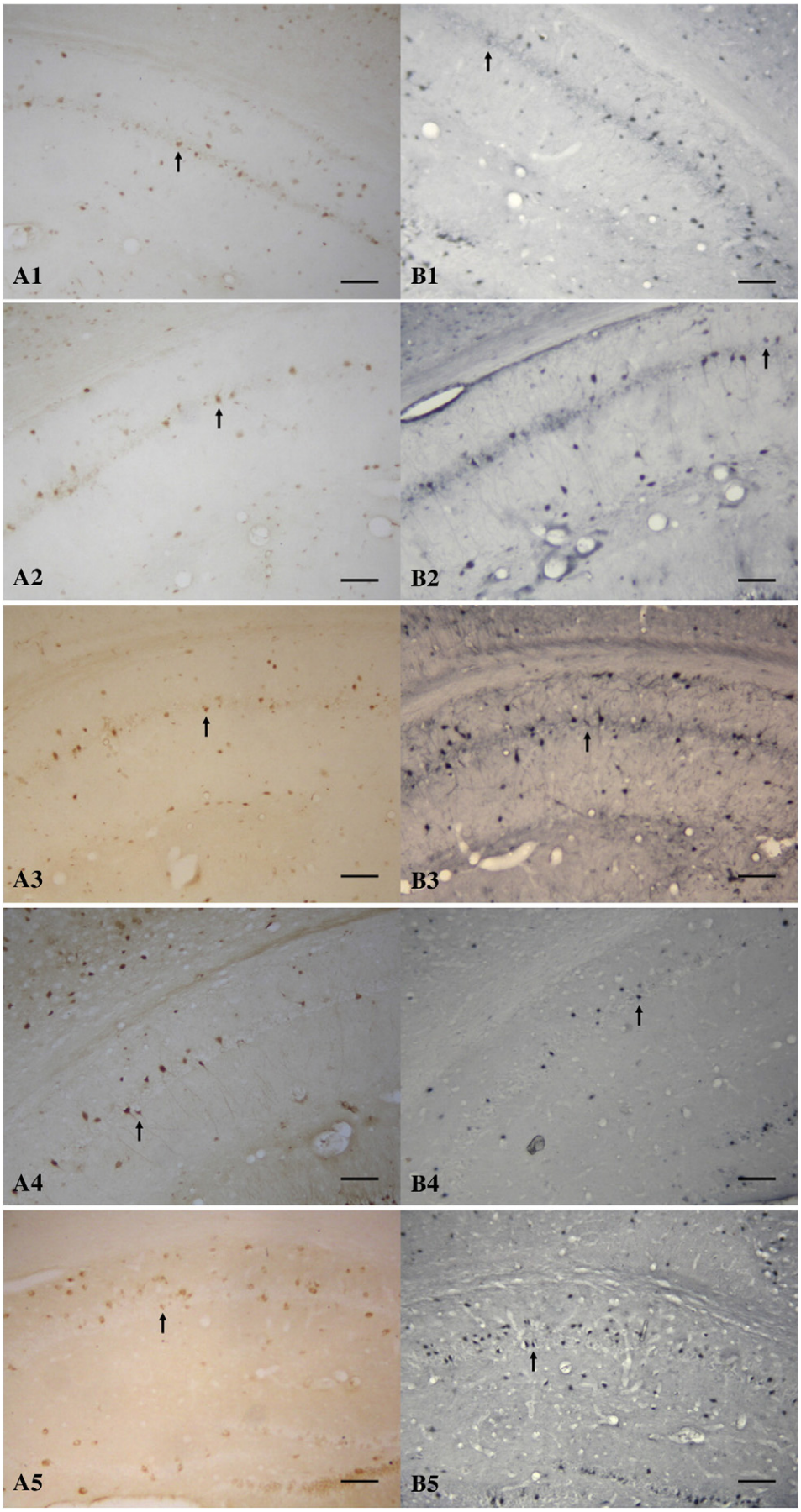
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