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ACCEPTED MANUSCRIPT

Insulin deprivation decreases Insulin Degrading Enzyme levels in primary cultured cortical neurons and in the cerebral cortex of rats with streptozotocin-induced diabetes

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ABSTRACT

Background: Many studies have indicated a relationship between diabetes and Alzheimer's disease (AD). However, the molecular mechanism underlying this association has not been clarified. Among several factors, insulin degrading enzyme (IDE), which plays roles in the degradation of both insulin and amyloid β (Aβ), has gained interest as a potential target in efforts to solve this puzzle. This study sought to examine the effects of varying insulin and/or glucose concentrations on IDE expression.

Methods: Experiments were performed on primary cultured rat neurons and cortices of rats with streptozotocin (STZ) - induced diabetes. IDE protein and mRNA expression levels were measured by western blot and RT-PCR, respectively.

Results: In primary cultured cortical neurons, removal of insulin for 5 days reduced the expression of IDE. A five-day treatment with a high concentration of glucose in insulin-free media reduced IDE levels, while a high concentration of glucose in the presence of

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