EARLY CHANGES OF ACETYLCHOLINESTERASE ACTIVITY AND INSULIN SYSTEM IN THE BRAIN OF THE STREPTOZOTOCIN-INTRACEREBROVENTRICULARLY TREATED RAT MODEL OF SPORADIC ALZHEIMER'S DISEASE

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Introduction: Sporadic Alzheimer’s disease (sAD) is associated with central cholinergic deficit and impaired insulin receptor (IR) signaling both in humans and its animal model, rats treated intracerebroventricularly with streptozotocin (STZ-icv) which enable assessment/follow up of alterations starting immediately after the STZ-induced brain damage.

Aims: We aimed to explore the acute changes of central cholinergic transmission and insulin system in the STZ-icv rats, measured 1 day, 1 and 2 weeks after the STZ-icv treatment.

Methods: Adult Wistar rats were administered STZ (0.3-3 mg/kg) or vehicle (controls) icv injections. IR and insulin-degrading enzyme (IDE) protein expression was measured in hippocampus (HPC) by SDS-PAGE electrophoresis and immunoblotting. Acetylcholinesterase (AChE) activity was measured in HPC and parietotemporal cortex (PTC) by Ellman's method. Data were analysed by Mann-Whitney U test (p<0.05).

Results: One day after STZ-icv (1 mg/kg) administration hippocampal IR (45.34%) and IDE (30.83%) protein expression was significantly increased as well as AChE activity (26.3%) which after 1 week was normalized in HPC but significantly increased in PTC (23.37%). No clear dose-dependent effect on AChE activity was found with 0.3-3 mg/kg STZ-icv dose range. IR and IDE protein expression in HPC was normalized 2 weeks after STZ-icv (3 mg/kg) administration.

Conclusion: Cholinergic and insulin brain system are differently affected immediately after STZ-icv induced brain damage; the former showing immediate but mild onset and development of cholinergic deficit and the latter demonstrating acute, stress-induced response in IR signalling which is compensated during the following two weeks.

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