CORRELATION OF COGNITIVE DEFICITS AND CEREBRAL AMYLOID ANGIOPATHY DEVELOPMENT IN THE STREPTOZOTOCIN-RAT MODEL OF SPORADIC ALZHEIMER DISEASE


Department of Pharmacology, University of Zagreb, School of Medicine, Zagreb, Croatia, Department of Child and Adolescent Psychiatry, University Zürich, Zürich, Switzerland, Clinical Neurochemistry, National Parkinson Foundation Centre of Excellence Laboratories, Clinic and Polyclinic for Psychiatry, Psychosomatic and Psychotherapy, Medical School, University of Würzburg, Würzburg, Germany

Introduction: Streptozotocin-itracerebroventricularly (STZ-icv) treated rats represent experimental model of sporadic Alzheimer’s disease (sAD) which demonstrates both cognitive deficits and β-amyloid aggregation in the blood vessel wall, investigated up to three months after STZ-icv treatment so far.

Aims: We aimed to compare the onset and time-course of cognitive deficit and cerebral amyloid angiopathy (CAA) development in the STZ-icv rat model of sAD.

Methods: Adult Wistar rats were administered STZ (3 mg/kg) or vehicle (controls) icv injections and sacrificed at different time points up to 9 months afterwards. Amyloid precursor protein (APP) mRNA was measured in hippocampus by RT-PCR and β-amyloid fibrils in blood vessels visualized by modified alkaline Congo Red staining. Learning and memory functions were tested by Morris Water Maze Swimming (MWM) and Passive Avoidance (PA) Test, respectively, and data analyzed by Mann-Whitney U test (p< 0.05).

Results: One week after STZ-icv (0.3-3 mg/kg) treatment no cognitive deficits were found. Significant cognitive deficits (-23%) were found 2 weeks after the STZ-icv 3 mg/kg treatment, gradually progressing to - 38.44% at nine months measured by MWM and to -94.34% at 6 months measured by PA test, respectively. β-amyloid aggregation with unchanged APP mRNA expression was found at earliest 3 months after STZ-icv (3 mg/kg) treatment in meningeal capillaries and spread to intracerebral blood vessels nine months after STZ-icv treatment.

Conclusion: Cognitive deficits in STZ-icv rat sAD model precede and are not triggered by CAA development which is, probably, not caused by APP overexpression..

Acknowledgement: Supported by UKF, MZOŠ (108-1080003-0020) and DAAD.