Caffeine Consumption Prevents Memory Impairment, Neuronal Damage, and Adenosine A2AR Receptors Upregulation in the Hippocampus of a Rat Model of Sporadic Dementia

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Introduction: The consumption of caffeine correlates inversely with the incidence or evolution of memory impairment upon aging or sporadic Alzheimer’s Disease (AD). The icv administration of STZ leads to brain insulin insensitivity and induces pathological and behavioral alterations similar to those observed in AD and is thus considered an experimental model of sporadic AD. Since caffeine (an adenosine receptor antagonist) and selective antagonists of adenosine A\(_{2A}\) receptors modify the course of memory impairment in different amyloid-β-based experimental models of AD, we now tested the impact of caffeine on STZ-induced dementia and associated neurodegeneration in the hippocampus as well as on the expression and density of adenosine receptors. Materials and Methods: Adult male rats were allowed to consume ad libitum either drinking water or caffeinated drinking water at 1 g/L during two weeks prior to vehicle or STZ (3 mg/kg) infusion. After surgery, caffeine consumption was maintained for 4 additional weeks. Four weeks after STZ or vehicle infusion, rats were submitted to the object recognition test. 24h later the hippocampal adenosine receptors were analyzed by Western blot and quantitative PCR and the neurodegeneration was evaluated by NeuN immunofluorescence. Results and Discussion: STZ infusion triggered memory deficits after 4 weeks, as gauged by impaired object recognition memory. This was accompanied by a reduced NeuN immunoreactivity in the hippocampal CA1 region and an increased expression and density of A\(_{2A}\), but not A\(_1\) receptors, in the hippocampus. Caffeine consumption prevented the STZ-induced memory impairment and neurodegeneration as well as the upregulation of A\(_{2A}\) receptors. Conclusions: These findings provide the first demonstration that caffeine prevents sporadic dementia and implicate the control of central A2AR as its likely mechanism of action.

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