

## Effects of adult-onset streptozotocin-induced diabetes on the rat brain antioxidant status and the activities of acetylcholinesterase, (Na<sup>(+)</sup>,K<sup>(+)</sup>)- and Mg<sup>(2+)</sup>-ATPase: modulation by L-cysteine.

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### Abstract

Uncontrolled diabetes is known to affect the nervous system. The aim of this study was to investigate the effect of the antioxidant L: -cysteine (Cys) on the changes caused by adult-onset streptozotocin (STZ)-induced diabetes on the rat brain total antioxidant status (TAS) and the activities of acetylcholinesterase (AChE), (Na<sup>(+)</sup>,K<sup>(+)</sup>)-ATPase and Mg<sup>(2+)</sup>-ATPase. Thirty-eight male Wistar rats were divided into six groups: C(A) (8-week-control), C(B) (8-week-control + 1-week-saline-treated), C + Cys (8-week-control + 1-week-Cys-treated), D(A) (8-week-diabetic), D(B) (8-week-diabetic + 1-week-saline-treated) and D + Cys (8-week-diabetic + 1-week-Cys-treated). All diabetic rats were once treated with an intraperitoneal (i.p.) STZ injection (50 mg/kg body weight) at the beginning of the experiment, while all Cys-treated groups received i.p. injections of Cys 7 mg/kg body weight (daily, for 1-week, during the 9th-week). Whole rat brain parameters were measured spectrophotometrically. In vitro incubation with 0.83 mM of Cys or 10 mM of STZ for 3 h was performed on brain homogenate samples from groups C(B) and D(B), in order to study the enzymes' activities. Diabetic rats exhibited a statistically significant reduction in brain TAS (-28%, D(A) vs C(A);-30%, D(B) vs C(B)) that was reversed after 1-week-Cys-administration into basal levels. Diabetes caused a significant increase in AChE activity (+27%, D(A) vs C(A); +15%, D(B) vs C(B)), that was further enhanced by Cys-administration (+57%, D + Cys vs C(B)). The C + Cys group exhibited no significant difference compared to the C(B) group in TAS (+2%), but showed a significantly increased AChE activity (+66%, C + Cys vs C(B)). Diabetic rats exhibited a significant reduction in the activity of Na<sup>(+)</sup>,K<sup>(+)</sup>-ATPase (-36%, D(A) vs C(A);-48%, D(B) vs C(B)) that was not reversed after 1-week Cys administration. However, in vitro incubation with Cys partially reversed the diabetes-induced Na<sup>(+)</sup>,K<sup>(+)</sup>-ATPase inhibition. Mg<sup>(2+)</sup>-ATPase activity was not affected by STZ-induced diabetes, while Cys caused a significant inhibition of the enzyme, both in vivo (-14%, C + Cys vs C(B);-17%, D + Cys vs C(B)) and in vitro (-16%, D(B) + in vitro Cys vs C(B)). In vitro incubation with STZ had no effect on the studied enzymes. The present data revealed a protective role for Cys towards the oxidative effect of diabetes on the adult rat brain. Moreover, an increase in whole brain AChE activity due to diabetes was recorded (not repeatedly established in the literature, since contradictory findings exist), that was further increased by Cys. The inhibition of Na<sup>(+)</sup>,K<sup>(+)</sup>-ATPase reflects a possible mechanism through which untreated diabetes could affect neuronal excitability, metabolic energy production and certain systems of neurotransmission. As concerns the use of Cys as a neuroprotective agent against diabetes, our in vitro findings could be indicative of a possible protective role of Cys under different in vivo experimental conditions.