LONG-TERM EFFECTS OF MILDRONATE ON THE PROTEIN EXPRESSION IN A RAT MODEL OF PARKINSON’S DISEASE

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Introduction: Recently we have found that mildronate [3-(2,2,2-trimethylhydrazinium) propionate dihydrate] significantly protected alterations in the expression of neural and glial cell biomarkers in 6-OHDA-lesioned striatum (STR) and substantia nigra (SN) of Parkinson’s disease (PD) rat model, as well as in mitochondria-compromising models (Klusa et al., in press; Pupure et al., 2008; 2010).

Aim: These data allow us to suggest that mildronate may influence expression also of other proteins involved in brain functioning, such as heat shock proteins (HSP), nerve growth factors (NGF) and adhesion molecules.

Method: PD was modeled by 6-OHDA intrastriatal injection in rats. Mildronate was administered at doses 10, 20 and 50 mg/kg for two weeks intraperitoneally prior to 6-OHDA injection. Brains were dissected on day 42 after discontinuation of mildronate injections. Expression of HSP70, GDNF (glial-derived NGF) and NCAM (neural cell adhesion molecule) was assessed immunohistochemically.

Results: In 6-OHDA-lesioned STR (also in SN), the HSP70 expression was 3-fold less vs. control (saline), wherease mildronate (20 and 50 mg/kg, but not 10 mg/kg) significantly increased (vs. 6-OHDA values) the number of HSP70 positive cells. 6-OHDA caused a decrease in GDNF expression in STR, while mildronate reversed that to normal level; similar effects were obtained in the case of NCAM.

Conclusion: These data indicate a long-term regulatory effects of mildronate on the expression of endogenous molecular chaperone HSP70, as well as on substances which promote cell survival and neurite outgrowth (GDNF and NCAM). Our data indicate mildronate’s usefulness for the protection/delay of the progression of PD.

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