

EFFECT OF PROPOFOL ON OXIDATIVE STRESS-ATTENUATED GLUTAMATE TRANSPORTER EAAT4 ACTIVITY

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Background: Propofol (2, 6-diisopropylphenol) has been known to have neuroprotective effects. Excitatory amino acid transporter 4 (EAAT4) is a glutamate transporter predominantly expressed in the cerebellar Purkinje cells, which is vulnerable to ischemic injury. Thus, we hypothesized that propofol reverses reduced EAAT4 activity which was induced by oxidative stress and investigated the effects of propofol on EAAT4 under oxidative stress induced by tert-butyl hydroperoxide (t-BHP).

Methods: EAAT4 was expressed in *Xenopus* oocytes by injection of its mRNA. By using two-electrode voltage clamping, membrane currents were recorded before, during, and after application of L-aspartate (3 μ M) in the presence or absence of t-BHP and propofol.

Results: L-aspartate induced an inward current in EAAT4 expressing oocytes. Exposure of these oocytes to t-BHP (1–20 mM) for 10 min dose-dependently decreased EAAT4 activity. ($1 \pm 0.01 \mu$ C for control; $0.88 \pm 0.05 \mu$ C for 1 mM; $0.83 \pm 0.03 \mu$ C for 2mM; $0.65 \pm 0.04 \mu$ C for 3 mM; $0.51 \pm 0.07 \mu$ C for 5 mM; $0.45 \pm 0.03 \mu$ C for 10 mM and $0.24 \pm 0.06 \mu$ C for 20 mM). IC₅₀ for t-BTH was 6.05 mM and further study was performed with 10 mM t-BTH. Propofol (3–10 μ M) dose-dependently reversed this t-BHP-attenuated EAAT4 activity.

Conclusion: Oxidative stress by t-BHP decreased EAAT4 activity and 3-10 μ M propofol restored oxidative stress-reduced EAAT4 activity

Key Words: excitatory amino acid transporter 4, glutamate transporter, propofol, tert-butyl hydroperoxide, *Xenopus* oocytes.