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DOSE-DEPENDENT NEUROPROTECTION BY SODIUM PROPIONATE AGAINST OGD-INDUCED ISCHEMIC INJURY *IN VITRO*

Background/Objective. Sodium propionate (NaProp) is a microbiota-derived short-chain fatty acid (SCFA) with promising neuromodulatory properties mediated via the gut-brain axis. Despite extensive research into SCFA mechanisms, clinical translation is hindered by a biphasic profile, where high concentrations risk toxic intracellular acidification. This study aims to investigate the dose-dependent effects of NaProp under *in vitro* ischemic injury conditions. **Methods.** A long-term hippocampal culture model was subjected to a 40-minute transient oxygen-glucose deprivation (OGD) followed by 4 hours of normoxic reperfusion (RP). Cell viability was assessed via lactate dehydrogenase (LDH) release assay. NaProp (0.2 mM, 1.0 mM, and 5.0 mM) was administered 30 minutes before OGD, maintained during OGD, and continued throughout the reperfusion phase. Data (mean $\pm$ SEM) were compared by one-way ANOVA with Tukey's post hoc test. **Results.** Ischemic stress (OGD + 4 h RP) significantly increased LDH release (0.38 ± 0.026 a.u.) compared to normoxic controls (0.22 ± 0.006 a.u.; $p < 0.05$), indicating a disruption of neuronal plasma membrane integrity. NaProp treatment mitigated OGD-induced injury in a dose-dependent manner. While a low dose (0.2 mM) minimally reduced LDH leakage (0.33 ± 0.022 a.u.), a moderate dose (1.0 mM) further attenuated OGD-induced release (0.26 ± 0.026 a.u.; $p = p < 0.05$ vs OGD). The 5.0 mM dose produced the greatest effect, restoring LDH to baseline (0.20 ± 0.029 a.u.; $p < 0.05$ vs OGD). Although excessive SCFA exposure has been reported to trigger neurotoxicity via intracellular acidification, no signs of injury were detected up to 5.0 mM; higher concentrations were not tested. **Conclusions.** NaProp provides dose-dependent neuroprotection against ischemic injury *in vitro*, with 5.0 mM conferring the greatest protection within the range examined. As concentrations above 5.0 mM were not assessed, the upper limit of the protective window remains to be defined. These findings offer baseline efficacy and safety data for optimizing SCFA-based stroke therapies. **Grants/Funding.** Supported by the National Research Foundation of Ukraine (grant number 2023.05/0023).

Keywords: hippocampal neurons, oxygen-glucose deprivation, lactate dehydrogenase, cell viability, gut-brain axis, short-chain fatty acids, neurotoxicity, cell death, stroke.

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