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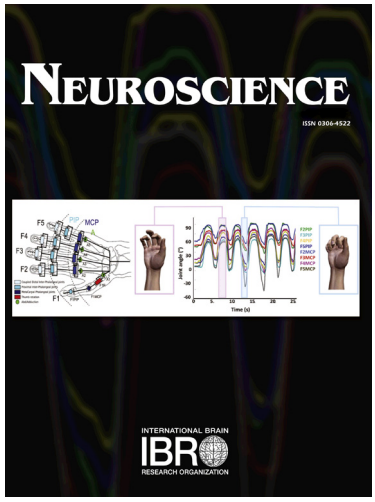

Propofol protects rat hypoglossal motoneurons in an *in vitro* model of excitotoxicity by boosting GABAergic inhibition and reducing oxidative stress

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Propofol protects rat hypoglossal motoneurons in an *in vitro* model of excitotoxicity by boosting GABAergic inhibition and reducing oxidative stress

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ABSTRACT

In brainstem motor networks, hypoglossal motoneurons (HMs) play the physiological role of driving tongue contraction, an activity critical for inspiration, phonation, chewing and swallowing. HMs are an early target of neurodegenerative diseases like amyotrophic lateral sclerosis that, in its bulbar form, is manifested with initial dysphagia and dysarthria. One important pathogenetic component of this disease is the high level of extracellular glutamate due to uptake block that generates excitotoxicity. To understand the earliest phases of this condition we devised a model, the rat brainstem slice, in which block of glutamate uptake is associated with intense bursting of HMs, dysmetabolism and death. Since blocking bursting becomes a goal to prevent cell damage, the present report enquired whether boosting GABAergic inhibition could fulfil this aim and confer beneficial outcome. Propofol (0.5 μM) and midazolam (0.01 μM), two allosteric modulators of $GABA_A$ receptors, were used at concentrations yielding analogous potentiation of GABA-mediated currents. Propofol also partly depressed NMDA receptor currents. Both drugs significantly shortened bursting episodes without changing single burst properties, their synchronicity, or their occurrence. Two h later, propofol prevented the rise in reactive oxygen species (ROS) and, at 4 h, it inhibited intracellular release of apoptosis-inducing factor (AIF) and prevented concomitant cell loss. Midazolam did not contrast ROS and AIF release. The present work provides