The Mechanistic Effect of Isoflurane on Crayfish Synaptic Transmission

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Isoflurane is an FDA-approved volatile anesthetic used to induce and maintain general anesthesia. Isoflurane hyperpolarizes membrane potential by selectively enhancing K+ channels and inhibiting GABA, glycine, and NMDA receptors. However, despite clinical relevance, the mechanistic actions of isoflurane are not well-characterized. This study aimed to analyze the effects of isoflurane on synaptic transmission in the model crayfish synaptic preparation, where quantal transmission can be assessed. Proprioceptive sensory activity and muscle tension in the muscle receptor organ (MRO), membrane potential and excitatory junction potentials (EJPs) at the neuromuscular junction (NMJ), and electrical conduction in the leg nerve, were measured. In the MRO, isoflurane induced mixed results at 0.1% and 0.2%, though the activity with isoflurane after five minutes was significantly greater than activity in saline ($p=0.028$; $t=-3.056$). At the NMJ, isoflurane induced muscle contraction. Higher frequency stimulations with isoflurane present resulted in depressed EJP amplitudes. Isoflurane was mostly able to reverse the depolarizing effects of glutamate. Serotonin, an excitatory modulator of the NMJ, was not able to block isoflurane-induced synaptic depression. Isoflurane significantly decreased the area under the curve of compound action potentials. Muscle tension increased without evoked nerve stimulation, likely due to direct actions on the muscle from Ca2+ release by the sarcoplasmic reticulum via ryanodine receptors. These results suggest that the mechanisms of isoflurane are a mix of both pre- and postsynaptic transmission. This study is significant for understanding basic mechanisms of isoflurane, which holds implications for understanding states like malignant hyperthermia.

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