Neonatal exposure to the anesthetics sevoflurane, ketamine and propofol differentially affect GABAergic inhibition, seizure activity and/or social interactions in adulthood

Ira S. Kass PhD, Jinyang Liu MS, Daisy Lin PhD, James E. Cottrell MD,
Anesthesiology Dept, Physiology and Pharmacology Dept SUNY Downstate Health Sciences University, Brooklyn, NY 11203

The early developing brain is especially vulnerable to insults from different anesthetics, which can result in long lasting functional changes. Anesthetics target $GABA_A$ receptors, NMDA receptors and/or intracellular signaling pathways. The long-term functional changes after exposure to anesthetics during the neonatal period are not known. We compared the effects of early-life propofol and sevoflurane, ketamine and propofol on adult behavior, excitatory-inhibitory balance and drug-induced seizure activity.

Postnatal day 7 (P7) mice were exposed to either sevoflurane, ketamine or propofol. Behavior, electrophysiology and seizure experiments were conducted when the mice were adults. The effect of the GABA agonist muscimol (3μM) on hippocampal slice CA1 neurons was used to measure inhibition. Behavior tests included open field, 3 chamber social interaction and novel object recognition. For the drug-induced seizure experiments, mice were given an i.p. injection of 45mg/kg of pentylenetetrazole

The effect of muscimol, demonstrated that adult mice treated with sevoflurane at P7 had significantly less inhibition; there was no significant effect of ketamine or propofol treatment. Sevoflurane treated mice showed significantly increased PTZ induced seizure intensities as adults; P7 ketamine or propofol treatment did not lead to increased induced seizure intensity. Ketamine, but not sevoflurane of propofol reduced time in the center of the open field apparatus.

Neonatal sevoflurane, but not ketamine or propofol, treatment impairs the $GABA_A$ response in adult mice and increases induced seizure intensity in adult mice. Different general anesthetics have unique properties independent of their ability to induce unconsciousness that alter the long-term effects of early-life exposure.