

Abstract

Frequent exposure of the immature brain to general anesthesia is common. The safety of this practice has recently been challenged in view of the evidence that general anesthetics could be damaging to the developing mammalian neurons. The initial reports were done in immature rats which raised the criticism regarding possibly unique vulnerability of those species, the correlation between the duration of brain development and the duration of anesthesia necessary to activate apoptosis and the importance of maintaining adequate nutritional/cardio-pulmonary homeostasis during anesthesia. Therefore we studied guinea pig whose brain growth is five-times longer than in rats and is completely prenatal phenomenon allowing anesthesia-induced neurotoxicity studies of fetal brain to be performed via anesthetizing pregnant mothers which, due to their size, we made invasive monitoring of maternal (and indirectly fetal) well-being technically feasible. Despite adequate maintenance of maternal homeostasis a single short maternal exposure (4hrs) to general anesthetic isoflurane, alone or with nitrous oxide and/or midazolam at peak of fetal synaptogenesis, induced severe neuroapoptosis in the fetal guinea pig brain which resulted in permanent loss of many neurons in vulnerable brain regions as detected in early post-natal life suggesting that anesthesia-induced neuroapoptosis can cause permanent brain damage.

We started to study also piglets whose brain growth is ten-times longer than in rats and is a prenatal and postnatal phenomenon. We anesthetized piglets 5-10 days-old, due to their large size we made invasive monitoring of their nutritional/cardio-pulmonary parameters. Despite adequate maintenance of piglet homeostasis, the preliminary data show that a single short exposure (4 hrs) to general anesthesia at the peak of synaptogenesis induced severe neuroapoptosis in newborn piglet. The anesthesia-induced developmental neuroapoptosis observed

in the immature piglet brain mimics anesthesia-induced developmental neuroapoptosis observed in the immature rats and guinea pig brain.