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Application of neural stem cells to assess general anesthetic-induced neurotoxicity

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Every year, approximately 6 million children in US and 2% of pregnant women in North America undergo general anesthesia. There is an increasing concern about the potential adverse effects of anesthetics on the developing brain. Neural stem cells (NSCs) are able to recapitulate most critical events of CNS development *in vivo* and, therefore, represent a valuable *in vitro* model for evaluating xenobiotic-induced developmental neurotoxicity. The potential toxic effects of ketamine and propofol and two commonly used pediatric anesthetics were examined using NSCs and NSC-derived neural cells. NSCs were harvested from gestational day (GD) 16 rat brain and confluent cell cultures were exposed to either ketamine or propofol at different doses and durations, followed by systematic evaluation of cytotoxicity. At clinically-relevant doses, propofol resulted in a significant reduction of NSC viability and proliferation rate, whereas ketamine did not show such effects. The different results may be attributed to the different mechanisms through which they cause neurotoxic effects: ketamine-induced neuronal damage was detected after NSCs differentiated. These data suggest that anesthetic-induced neurotoxicity depends upon the concentrations of drugs used, the durations of exposure, the receptor subtype activated and the developmental stages at the time of exposure.

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