Introduction

Cognitive impairment has increasingly been recognized as a complication after anesthesia (Loepke and Soriano 2008; Wilder et al. 2009). Adult neurogenesis is critical to normal hippocampal function (Zhao et al. 2008). Therefore, it has been suggested to play a role in post-anesthetic cognitive dysfunction. Most studies up to date focus on adult neurogenesis following anesthetics. However, the aim of the present study was to investigate the effects of propofol and isoflurane anesthesia on progenitor cell proliferation, differentiation, migration and maturation in the dentate gyrus. We hypothesize that anesthetic-induced alteration of the nascent cells at one or more of these stages may explain the impairment of cognitive function experienced by some patients.

Methods

3 month-old F344 rats were randomly assigned to four different groups (n=8/group): Propofol, Intralipid, Isoflurane and Control. Rats in the first two groups were continuously infused via tail-vein catheter for 3 hrs with 35 mg/kg/hr of propofol or 10% intralipid, respectively. Rats in isoflurane and control groups were exposed to 3 hrs of 1.5% isoflurane or room air respectively. Three different thymidine analogs (CldU, IdU, and EdU) were intraperitoneally injected at three different time points (21 days, 8 days, and 4 days) prior to the anesthetic or control treatment in order to assessed maturation, migration and differentiation of nascent cells in the dentate gyrus (DG) at the time of anesthesia. Proliferation was assessed by quantification of the endogenous marker Ki67. In addition, phenotype identification at each time point was assessed by co-localization of each thymidine analog with the corresponding histological marker for each stage of neurogenesis.

Results

These results suggest an agent and stage dependent effect. In the young brain, propofol anesthesia appears to be particularly harmful, especially to nascent cells undergoing early and late differentiation in the dentate gyrus.

References


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IN YOUNG RATS, PROPOFOL BUT NOT ISOFLURANE AFFECTS NASCENT CELLS UNDERGOING EARLY AND LATE DIFFERENTIATION IN THE DENTATE GYRUS

Postnatal neurogenesis, a developmental process that includes proliferation and fate specification of adult neural stem cells along with their differentiation, maturation, migration and incorporation into the existing neural circuitry of their progeny in the mature nervous system.

Experimental Time Line