General-Anesthesia Long-Term Effects on the Brain in Children and Elders

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Abstract

General anesthetic has many affects when given, most are positive and make the patient feel good during and after surgery. However, more recent studies have suggested there are some negative long-term effects on children and elders brain development. Researchers have found that young children who go under general anesthetic multiple times have a higher chance of developing learning disorders and ADHD. They also found that elders that go under general anesthetic for major surgeries have been linked to them developing postoperative cognitive disorder (POCD) or postoperative delirium (POD). Lastly, general anesthetic causes neurotoxicity in the brain and affects the brains neuron development and synapsis. Given this information, it can be suggested that general anesthesia has short-term effects on the brain, but it can also cause long-term effects at various ages.

Introduction

- Both propofol and Isoflurane have been demonstrated to delay this polarization process and inhibit axonal growth and collapse in response to a repulsive stimulus (Mintz et al., 2012; 2013)
- Exposure to routinely used gaseous and intravenous GAs causes extensive neuro- apoptosis ((Dasgupta and Dumbrell, 2006).

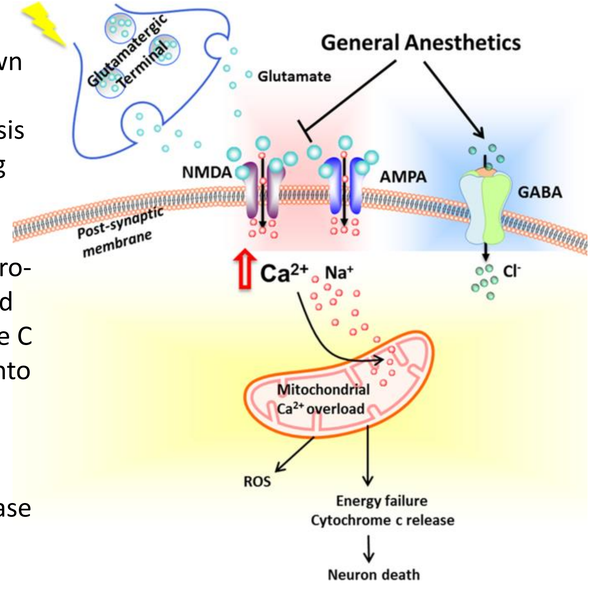


Figure 1. Volatile anesthetics were shown to activate mitochondrial apoptosis pathway, by increasing mitochondrial ROS production, lowering anti-apoptotic Bcl-2/pro-apoptotic Bax ratio and promoting cytochrome C from mitochondrion into cytosol to form apoptosome, which subsequently cleaves pro-caspase 3 to caspase 3 (Wu, et al. 2019)

General Anesthesia on Children Developing Brain

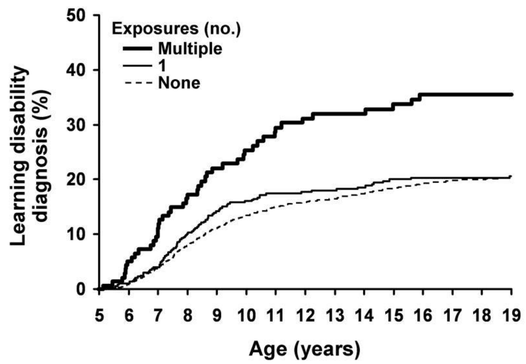
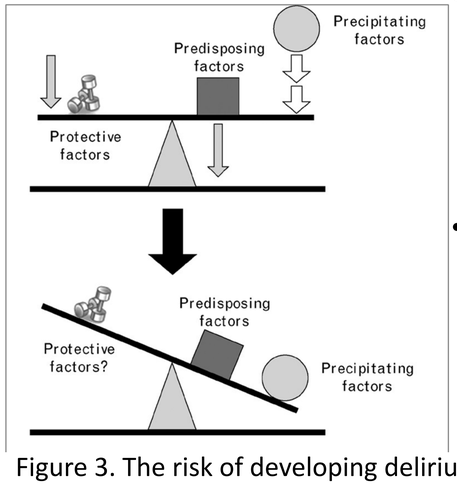


Figure 2.Cumulative percentage of learning disabilities diagnosis by the age of exposure shown separately for those that have 0, 1, or multiple anesthetic exposures under the age of 4 (Wilder, et al. 2009)

- Children who had been exposed to anesthesia before the age of 10 were examined. for their language, cognition, motor skills, and behavior test scores. Language and abstract reasoning problems were more prevalent in these children than in their unexposed counterparts (Ing et al. 2014).

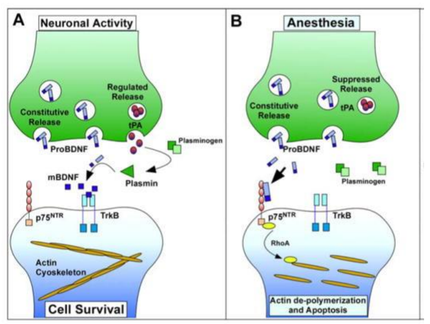
General Anesthesia Affects on Elder's Brain.



- 25% of patients develop POCD one week after surgery with elderly patients being most likely to be affected (Steiner, 2011).
- Memory problems have also been linked to a lack of neurogenesis after early exposure to volatile anaesthetics (Zhu et al., 2010)

Figure 3. The risk of developing delirium can be interpreted as the product of predisposing and precipitating factors. A patient with few or no predisposing factors will only develop delirium when a major precipitating event occurs, whereas a patient with many predisposing factors will develop delirium following a trivial precipitating factor. (Luzius, 2011)

Neurotoxicity in the Brain



- Apoptosis rises with anaesthesia repetition or duration (for both volatile and injectable anesthetics) (Boscolo, et al. 2012)
- Anesthetics toxicity is dose-dependent. Increased anaesthetic doses enhance apoptotic neurons, developmental retardation, cellular differentiation, and synaptogenesis (Sprung, et al. 2012)

Figure 4. Fig.A: mBDNF promotes neuronal survival through TrkB receptors; proBDNF induces apoptosis through p75NTR. Fig.B: Exposure of developing neurons to isoflurane results in reduced tPA release into the synaptic cleft, elevated proBDNF and enhanced activation of p75 neurotrophin receptor leading to apoptosis. (Head, et al. 2009)

Synthesis

- Evidence suggests that a newly discovered family of chemicals may play a substantial role in anesthesia-induced epigenetic modification and neuronal cell apoptosis. They are non-coding RNA molecules called micro-RNAs, and they bind to the messenger RNA (mRNA) in complexes, decreasing translation or promoting mRNA degradation
- Propofol caused increased apoptosis in the neurons with miR-21 knocked down, but the neurons with up-regulated miR-21 were protected (Twaroski et al., 2014). Ketamine-induced neurotoxicity may be caused in part by mi-RNAs (Twaroski et al., 2015). Ongoing studies are looking at the impact of GA on miRNA activity.

References

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