Anesthesia and the Developing Brain

Essay

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To my father ,

Mother,

Wife

& my son

Anesthetic Developmental Neurodegenerative Effect On Experimental Models

Brain Development

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Abbreviations

- **BDNF** :- brain-derived neurotrophic factor.
- **Caspase** :- cysteine-aspartic proteases.
- **CBCL** :- Child Behavior Checklist.
- **CDER** :- Center for Drug Evaluation and Research.
- **CNS** :- cenral nervous system.
- **CP** :- Cognitive Problems.
- **CSF** :- cerebrospinal fluid.
- **DISC** :- death inducing signaling complex.
- **EA** :- Educational Achievement.
- **EM** :- Electron microscope.
- **FBDP** :- fodrin breakdown product.
- **FDA** :- Food and Drug Administration.
- **GABA** :- gamma-aminobutyric-acid.
- **GSA** :- general somatic afferents.
- **GSE** :- general somatic efferents.
- **GVA** :- general visceral afferents.
- **GVE** :- general visceral efferents.
- **GW** :- gestational week.
- **LD** :- Learning disabilities.
- **MAC** :- Minimal Alveolar Concentration.
- **MAP** :- The mean arterial blood pressure.
- **MRI** :- magnetic resonance imaging.
- **MZ** :- monozygotic.
- **NCTR** :- National Center for Toxicological Research.
- **NMDA** :- N- Methyl- D- Aspartate.
- **NOEL** :- No-observed-adverse-effect level.

- **PC** :- postconception.
- **PET** :- positron emission tomography.
- **PND** :- Postnatal day.
- **Shh**:- sonic hedgehog.
- **SSA** :- special somatic afferents.
- **SVA**:- special visceral afferents.
- **SVE**:- special visceral efferents.
- **SVZ** :- subventricular zone .
- **TEM** :- Transmission electron microscope.
- **VZ** :- ventricular zone .

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Introduction

General anesthesia is a complex pharmacological response produced by a chemically heterogeneous class of drugs involving mechanisms that remain incompletely understood. Current concepts define anesthesia by its core features of amnesia, unconsciousness, and immobility (in the order of decreasing potency), each mediated by pharmacological effects on specific neuronal networks in different regions of the central nervous system. The molecular targets of these region and dose-specific actions on neuronal network function have not been defined for most anesthetics, although likely candidates have been identified and characterized. These include ligand-gated ion channels involved in inhibitory receptors for g-aminobutyric acid (GABA) and glycine or excitatory N-methyl-Daspartate (NMDA) and AMPA subtype receptors for glutamate synaptic transmission, ion channels conducting Na+, Ca2+, and K+ that regulate neuronal excitability and chemical transmission, and pleiotropic intracellular signalling pathways. This diversity of potential targets increases the probability of both positive and

negative non-anesthetic effects***(Hudson AE & Hemmings HC., 2011)***

In 1989, Dr. Olney reported in *Science* that *N*-methyl-D-aspartate antagonists such as MK801 (a well studied neuroprotectant) could produce histopathologic changes suggestive of toxicity in the brains of normal adult rats. Subsequent studies have extended and refined this work to show that many anesthetics can produce what appear to be apoptotic changes, particularly the brains of very young rodents. This has raised the possibility, albeit one that is still very speculative, that even a routine anesthetic using the most routine drugs might pose a risk of neurotoxicity to the fetus, the neonate, or even the young child***(Olney J; et al., 1989)***

Most pediatric anesthetists should be aware of the issue of possible neurotoxic effects of general anesthetics on the developing brain. The subject is regularly discussed in editorials, reviews, and conference meetings. It is also being raised in the lay press. Is it time to go further and develop clinical guidelines based on the available evidence? Some recommendations have indeed already been made. In 2007, the Federal Drug Administration

(FDA) anesthetic and Life Support Drugs Advisory Committee released minutes suggesting that surgery that was truly elective should be postponed until after 6 months of age. This was based on concerns about the neurotoxic effects of anesthetics on neonatal animals. ***(Sanders RD & Davidson A .,2009)*** .

These activities are just the first step. We need to definitively answer the questions of whether anesthetic use in children poses a risk to their development and, if so, under what circumstances. Although withholding anesthesia from children who need surgery is unreasonable, obtaining more information about safe use is imperative. If anesthetic agents are found, in certain cases, to affect the developing brain, strategies for mitigating and managing such risks can be implemented. ***(Rappaport P;et al.,2011)*** **.**

Aim of the Essay

It is an attempt to answer the fundamental question : Is the early exposure to anaesthesia has a harmfull effect on the human developing brain ?