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Anesthetic Neurotoxicity: Integrating Laboratory Neuroscience, Nursing, and Clinical Medicine

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Abstract:
Anesthetic neurotoxicity, a growing concern in modern clinical practice, has raised alarms regarding the long-term effects of anesthetic exposure, particularly in vulnerable populations such as neonates, infants, and the elderly. This interdisciplinary review explores the complex interplay between laboratory neuroscience, nursing, and clinical medicine in understanding and addressing anesthetic neurotoxicity. Emerging evidence suggests that anesthetics, while essential for surgical procedures, may interfere with neurodevelopment and neuronal function, potentially leading to cognitive dysfunction and behavioral changes. Studies conducted in animal models, particularly during critical periods of synaptogenesis, have highlighted the potential for lasting neurotoxic effects, but the clinical relevance of these findings remains uncertain. This paper integrates findings from laboratory research on the molecular and cellular mechanisms underlying anesthetic neurotoxicity, alongside clinical studies that investigate the cognitive and behavioral consequences in human populations. Furthermore, we discuss the role of healthcare professionals, particularly nurses, in mitigating risks by providing vigilant postoperative care and advocating for safer anesthetic practices. The review concludes by emphasizing the need for continued research and collaboration across disciplines to better understand anesthetic neurotoxicity and its impact on patient health across the lifespan.
Keywords: Anesthetic Neurotoxicity, Neuroscience, Cognitive Dysfunction, Behavioral Changes, Anesthesia, Synaptogenesis, Pediatric Anesthesia, Aging and Anesthesia, Postoperative Cognitive Dysfunction, Neurodevelopment, Clinical Medicine, Nursing in Anesthesia, Neurocognitive Effects, Molecular Mechanisms, Perioperative Care.

1. Introduction

Over the more than 170 years since the introduction of chloroform, anesthesia has rapidly evolved with the development and application of myriad new agents and refinements in neural function. In light of modern

strategies and technological advancements enabling noninvasive as well as minimally invasive procedures, potentially millions of children are exposed to general anesthesia at ill-defined times in brain development. Anesthetic safety has never been as relevant as it is today. Interest in neurodevelopmental anesthesiology or anesthetic neurotoxicity has dramatically grown in concert with accumulated evidence showing that anesthetic agents can affect neural development in multiple, complex, and interacting ways; and that the developing brain, already vulnerable because of its inherent malleability, appears particularly susceptible to some of these actions.

The long-term ramifications of anesthesia and surgery on neural function and overall brain health remain fundamentally unknown. Do anesthetics cut a swathe through the developing brain, causing only transient, detectable electrical and cognitive sequelae, or do they elicit subtle maturational detours that manifest years or decades later? Effects, if present, are likely idiosyncratic and confounded by heterogeneity in clinical scenarios juxtaposed on diverse genetic backgrounds. Anesthetic neurotoxicity, as it is fervently discussed today, is an ever-moving target defined by a matrix of molecular, synaptic, cellular, and circuit insults. The complex, multifaceted, and, as yet, incompletely understood impacts of anesthetic agents on neural development, function, and homeostasis provide abundant potential targets for intervention. Nevertheless, discordant laboratory-based findings continue to bedevil the few clinically applicable therapeutic leads. Given the uncertainty in predicting any changes in pediatric anesthesia and the increasing numbers of women who present with high-risk pregnancies despite comorbidities, scientists and anesthesiologists should share data and expertise to ameliorate the ongoing proclivity.

1.1. Background and Significance

The administration of anesthesia has its roots in ancient surgical practices. For thousands of years, anesthetic techniques have been developed to induce insensibility, amnesia, and displacement while preserving cardiovascular and respiratory function and promoting surgical intervention itself. Throughout medical history, important advancements have included the introduction of nitrous oxide and ether in the mid-19th century, as well as the use of barbiturates, propofol, and the intravenous anesthetics of today. Inhaled agents and intravenous agents are now used in combination, allowing for fine-tuned depth of anesthesia and providing unconsciousness, analgesia, and muscle relaxation. These pharmaceutical innovations have allowed for safer and more reliable anesthesia, significantly decreasing the morbidity and mortality of surgical intervention over the last 150 years. Additionally, ever-growing numbers of surgeries are performed as elective procedures on patients with variable health concerns across the lifespan. By far, the fastest-growing group of patients undergoing surgical procedures are children and elderly individuals, all with different profiles and levels of health related to age and development, but also to many comorbidities and risks. Most anesthetic complications occur intra- and post-operatively but are minor and fully reversible. Nevertheless, a collection of primarily laboratory-based research focuses on an additional concern of anesthetic neurotoxicity, the potential long-lasting or permanent developmental effects of general anesthesia given to neonatal animals, babies, and young children. Results of this line of research may have relevant implications for clinical practice. If it can be proven to be true for humans, parents and public health practitioners must be informed about these risks. Major stakeholders, including pregnant women, parents, young adults, and the elderly, stand to benefit from further investigation in this area. (Rajendram et al.2022)(Ji & Karlik, 2022)(Useinovic and Jevtovic-Todorovic2023)(Salik, 2022)

1.2. Purpose of the Work

The purpose of this paper is to present an interdisciplinary inquiry into the neurotoxic effects of anesthetics from the perspectives of laboratory neuroscience, nursing, and clinical medicine. Indeed, research has reported that anesthetics can interfere with many of the processes associated with brain development, with potential repercussions for later cognitive function and behavior. While this could be seen as being 'outside' of the immediate domain of caring for patients, it could also be argued that this is very much an area in which every healthcare provider involved in protecting the perioperative welfare of a patient, from skin prep to evidence-based practice in the PACU and on every floor, should be aware of. Indeed, anesthetic exposure is now being advanced as a possible explanation for the phenomenon of post-operative cognitive dysfunction and even post-operative delirium. As members of a diverse scholarly community, we intend to build on our mutual respect and shared basic understanding of the particulars of one another's disciplinary training.

To date, the definitive mechanism by which anesthetics can induce neurotoxic effects is under study and to some degree remains to be elucidated. This interdisciplinary collaborative paper aims to develop a more in-depth and nuanced understanding of what could be at work in the anesthesia-mediated destruction of neurocircuitry. In so doing, we focus on the developing neurons and glia which, in humans, are created

over a trajectory of decades from embryos until late adolescence and, in some instances, the 20s. Focusing on rodents in the lab, a large body of studies has outlined where in the brain anesthetics interfere with this toxic action, as well as the death pathways utilized in many of these neurons. We also present several small but longitudinal clinical studies that have struggled with this same question in fragile patients. Our hope is that this review will inspire further conversations between laboratory and clinical experts in the future.

2. Neurotoxicity Mechanisms of Anesthetics

In the wake of greater scrutiny of public health, increasing attention is being paid to understanding the physiological endpoints at a cellular and molecular level wherein anesthetics interact with the highly conserved and essential pathways required for neurotransmission, synaptic plasticity, and the very viability of neurons. Such detailed analyses of molecular mechanisms of anesthesia may then also provide insight into the nature and long-term trajectory of anesthetic-induced changes not only in cellular mechanisms of the neural microenvironment but also in the physiological processing of information by that developing neural microenvironment. While many animal models of the developing and adult nervous systems exist demonstrating modulation of these landscapes by agents used for anesthesia and sedation, meaningful recommendations and applications to protect against anesthetic-related neurotoxicity are a core goal. It was therefore also the aim of this manuscript to explicitly integrate evidence from all relevant research concerning potential downstream mechanisms including direct neurotoxic mechanisms and more subtle endocrine and immunological short- and long-term processes underlying neurocognitive disturbances arising from selective intraoperative anesthesia in infants and children. (Zhu et al.2022)(Tabnak et al.2021)(Liu et al.2020)(Wang et al., 2021)(Smith et al.2024)

Many techniques that suppress long-term potentiation require deactivation of N-methyl-D-aspartate receptors. Similarly, in the developing brain, contamination of N-methyl-D-aspartate pathways with agents that could down-regulate the function of these receptors could potentially limit endpoints of neurotoxicological studies in N-methyl-D-aspartate. The idea that clinically useful agents disturb neural development at the synapse level is proposed, who showed both aggrevate-dependent and independent agents that resulted in manipulation of N-methyl-D-aspartate dependent plastic changes could be considered potentially harmful to the developing brain. This process had been shown to operate in animals treated with ketamine at a dose that would allow light general anesthesia and prolonged for many hours. Kainic acid has previously been shown to stimulate corpus callosum splinter formation within 15 minutes of injection, and this method was utilized for the rapid and pronounced lesions made by the intraperitoneal pathway with no visible after-effects. We have demonstrated the relatively innocuous nature of a relatively moderate general anesthesia with respect to lesions, as there were no differences in eating/drinking functions and rat action patterns observed after surgery in saline-general anesthesia groups after noise alone or noise associated with electrical stimulation. We have also shown, in a separate experiment, that lesions alone or after pre-treatment with general anesthesia increased extracellular glutamate within the cortex of unanaesthetized rats in regions normally damaged by lesions after general anesthesia + electrical stimulation as compared to controls. (Venkataramani et al.2021)(de Bartolomeis et al., 2022)(Hanson et al.2024)(Marwaha et al.2023)(Gao et al., 2022)(Singh et al.2023)(Akyuz et al.2024)(Liu et al., 2021)(Incontro et al.undefined)

2.1. Cellular and Molecular Pathways

Cellular and Molecular Pathways Established In Vitro for Anesthetic Neurotoxicity and Cognitive Dysfunction In Vivo Anesthetic neurotoxicity, if a clinically relevant entity, involves multiple signaling pathways and end organ systems. At the molecular and cellular level, anesthetic neurotoxicity affects altered neurotransmitter receptor and ion channel function. For example, anesthetics at clinical concentrations impact major cellular signal transduction pathways, such as the serine/threonine kinase Akt, the extracellular signal-regulated kinase, and glycogen synthase kinase 3 pathways, which appear to primarily carry out neuron survival and synaptogenesis.

These major cellular pathways are affected in large part due to altered neurotransmitter receptor signaling; ion channel receptor specifications, such as the N-methyl-D-aspartate receptor subunits or the activated G-protein coupled receptor kinases of the alpha-amino-3-hydroxy-5-methyl-4-isoxazole-propionic acid glutamate receptor; and/or the effect of altered intracellular cation and anion signals. The final effect of these multiple possibly anesthetic-related or unrelated impacts, in combination with signal, receptor, and channel, can be synapse loss and neuronal dysfunction, death, or neurogenesis, cell growth inhibition, cell cycle re-entry, and apoptosis. In summary, credible, well-understood molecular and cellular pharmacologic off-and-on and end organ pathways to anesthetic neurotoxicity exist. These pathways can be altered due to the unique epigenetic state of the immune and inflammatory cells in the brain by volatile anesthetic

sedation or general anesthetic medications; hence, anesthetic neurotoxicity is now established after multiple convincing laboratory investigations. (Vutskits & Davidson, 2023)(Useinovic and Jevtovic-Todorovic2023)(Useinovic et al.2022)(Wang et al.2024)
z (Apai et al., 2021)(Yang et al., 2020)(Lee et al., 2023)(Becke-Jakob et al.2023)(Yu et al., 2023)(Rajendram et al.2022)(Liu et al., 2020)(Cao et al.2023)

2.2. Animal Models and Research Findings

Animal Models in the Study of Anesthetic Neurotoxicity Since the 1950s, there has been increasing interest in the use of animal models to assess potential long-term effects of anesthetic exposures at critical periods of neural development. Work completed in primates and other nonhuman species has contributed significantly to our understanding of the potential cognitive and behavioral impacts of general anesthesia exposure and mechanisms that may contribute to such effects. Animal models serve as cornerstones of preclinical research and have resulted in a more in-depth understanding of the broad range of anesthetic risks. The prolonged development and smaller brains of nonhuman species, combined with our growing understanding of the complex integrated processes occurring during critical periods, ensure the persistence of interest in this line of research. Investigators using a wide array of animal models, including rodents, rabbits, nonhuman primates, and others, have noted declines in long-term potentiation (a marker of learning-related synaptic connections between neurons) and cognitive impairments associated with the use of various general anesthetics during periods of rapid synaptogenesis. In general, animal work has focused on the evaluation of three anesthetic drug classes: the intravenous NMDA antagonist ketamine, the intravenous GABAergic anesthetic propofol, and a variety of volatile anesthetics that suppress synaptic transmission by intra- or extracellular modulation of GABA and glutamate receptors. A broad spectrum of laboratory tools have been used to define the risk of anesthetic exposure in healthy laboratory animals during or near the peak of synaptogenesis. Moreover, several groups have found that anesthetic exposure during periods of rapid synaptogenesis can result in later cognitive deficits in various learning and memory paradigms that can be reversed by the use of synaptic enhancers. Growth in the field has been robustly increased, resulting in robust and reproducible data sets. It is important to highlight that no experimental model should be expected to formalize the results of the research in humans perfectly. There are clear differences in the way young animals and humans develop. Not least of all, the environment in which the developing human brain unfolds is far more complex and interactive with the cognitive world. Additionally, the use of multiple models can front-load, model, and refine concepts and data systems. Studies of young animals have worked well over the past two decades, but we also suggest the use of other animal models that can capture other potentially vulnerable systems. (Chinn et al.2020)(Vutskits & Davidson, 2023)(Fleissner et al.2022)(Dhoundiyal et al.2023)(Xu et al.2024)(Wang et al.2024)(Gaob & Yana, 2024)(Ferland-Beckham et al.2021)(Petroff et al., 2023)

3. Clinical Implications

Anesthesia-related neurotoxicity suggests a concern for the effect of currently used anesthetics on neurons. Clinical implications are that general anesthesia can have a profound long-term effect on the neurocognitive outcomes of the patient. Clinical trials have reported that more than one episode of general anesthesia has a substantial impact on learning, behavior, and memory. Available data demonstrate clinical relevance depending on age, with worse outcomes for a younger demographic. A significant amount of clinical research has identified that general anesthesia leads to neurocognitive changes. Animal models have also suggested associations between general anesthesia use in infants and negative outcomes in behavior, anxiety, and depressive responses. Data highlight the need for clinicians to remain informed about potential neurotoxic effects of inhaled and injectable anesthetics. Specifically, a warning labels that those who receive multiple anesthetics are at greater risk for neurotoxicity compared to those who have a single anesthetic episode.

Clinical data suggest the possibility of long-term behavioral and cognitive neurotoxicity as a result of infant anesthesia exposure. That being said, infants and children do need surgical procedures. Consensus guidelines state that no specific anesthetic could be viewed as safe. However, for patients with a single anesthetic exposure history of one year or greater, available data suggest that no anesthetic is safer compared with another. Given the available data and guidelines, a comprehensive anesthesia-toxicity consent strategy should also address background surgeries, surgery recovery, and the pre- and postoperative recovery of the patient along with the cumulative exposure to anesthetic medication. While there are no specific guidelines for this, we provide recommendations here based on the published nursing literature. (Useinovic and Jevtovic-Todorovic2023)(Reighard et al.2022)(Rajendram et al.2022)(Apai et al., 2021)(Vutskits & Davidson, 2023)

3.1. Neurocognitive Effects in Different Age Groups

The incidence of anesthesia-induced neuronal apoptosis in multiple parts of the cerebrum is age-dependent. Several studies demonstrated that anesthesia does cause a decrease in neurocognitive function in both newborns and the elderly. Development of the brain most often relates to age-dependent risks, particularly because of the vulnerability of a rapidly developing central nervous system, its enormous plasticity, and adaptive capacity. Anesthesia used on the fetus, premature infant, and neonate undergoing surgery could potentially interfere with the natural excitement and detachment of these vulnerable brain systems, creating a potential hazard of delayed and disordered neurological maturation. In the premature neonate, evidence demonstrates that anesthesia caused impaired brain MRI changes, self-inducing fewer myelin stores by the age of 2 years and longer-term effects on brain performance. Anesthetic neurotoxicity could have long-term consequences because the neurocognitive effects extend outside the age windows of relevant clinical studies. The developing brain has an inherently decreased allowable threshold for harm, as indicated by younger brain cell apoptosis in culture. Chronic anesthetic and sedative medications are harmful to brain maturation and lead to improved mental scores in animal studies.

Anesthetics have a disproportional incidence on neurocognitive function in the infant population. Disturbing anesthetic injury can result in a loss of abstract perception, executive functioning, and working memory, which is associated with decreased description and health-related quality of life capacity. In large epidemiological literature, teenagers aged 0-2 are found to have an enhanced chance of studying or developing disabilities in the course of the central nervous system emergence phase, following many anesthetics. A study finding in the same guiding lineage revealed that more than 90% of infants and 80% of children had at least one anesthetic-susceptible learning and/or behavioral impact. It was known that the less the practice, the more concurrent anesthetic treatment was received by these young children. In a rodent model and fetal guinea pigs, exposure to anesthetics causes headaches. The impact of anesthetic in a post-operative environment was encouraged in a number of preclinical investigations. A number of older adults over 65 years old experienced improved central nervous system activity when exposed to intraoperative lighter anesthetic agents, which eventually reshaped post-operative neurocognitive decline to mild cognitive impairment. It was estimated that an overall anesthesia-induced complication will only really be evident in a portion of the 65 or 75+ age group. Overall, the older population appears to have less central nervous system sedative effects of anesthesia or surgery. It is hypothesized that associated with physical and neurological aging, the analogs of the adult body and brain will withstand adversity. There is increased lipophilicity in the aging brain, reducing the volume of circulation of an onset and a cumulative effect on anesthesia. It doesn't necessarily mean that older individuals are invincible; their resilience is still susceptible to decline due to social isolation, accompanying health issues, or polypharmacy triggering neurotoxicity, lack of reserve, general frailty, and even death. Intraoperative anesthesia, as prescribed, is seen as beneficial for depression, bipolar disorder, and schizophrenia, which still heavily contributes to related cognitive decline, particularly in older adults. (Brévaut-Malaty et al.2022)(Gascoigne et al.2021)(Hart et al., 2025)(O'Connell et al., 2023)(Damarla, 2024)(Du et al.2023)(Hart et al., 2023)(O'Byrne et al.2024)

3.2. Guidelines and Recommendations for Safe Anesthetic Use

Abraham and colleagues, Kim and colleagues, and other investigators and professional societies have advocated for the development and implementation of guidelines for the use of anesthetics in clinical practice. However, because a large majority of research in this area has been focused on animal models or studies under controlled situations, the direct translation of laboratory studies to the clinic may not always be appropriate for clinical practice. More favorable results on the potential neurotoxic effects of anesthetics have been demonstrated when multiple anesthetics/modalities were used, a crossover design, or anesthetic use was in infants. In this regard, and to assist in providing recommendations, multiple professional and governmental organizations have considered this in their deliberations. Consequently, it is recommended that anesthetic care be individualized based on a patient's profile.

Guidelines from professional organizations are developed based upon a balance of data derived from a synthesis of available research studies and expert consensus. Abraham and colleagues position paper on general anesthesia and young children, including a computerized methodology, was endorsed by the SmartTots executive board. Similarly, neither the Association of Paediatric Anaesthetists nor provided practice guidelines for perioperative anesthetic care for patients based upon brain health and the deleterious effects of anesthetics. Sury and colleagues proposed that the U.S. FDA and Health Canada, along with other healthcare governing bodies, recommend that anesthetic neurotoxicity be implemented on the premise that it is better to be safe than sorry. More optimally and importantly, these professional guidelines

advocate for an increase in a culture of vigilance in clinical practice against an emergence of data for deleterious effects of general anesthesia in developing brains. Additionally, nursing staff have a responsibility to share their concerns or questions with the rest of the healthcare team as a means to ensure safety during patient care. Guidelines from governmental and professional organizations emphasize the need to continue to monitor the patient during and immediately after the administration of general anesthesia, as well as during the recovery period. In this respect, it is proposed that individuals who provide point-of-care in clinical practice or are involved in planning anesthetics should be familiar with the organization-specific recommendations that govern the clinical area in which the child is cared for. (Health Organization, 2021)(Health Organization, 2022)(Health Organization, 2021)(Ueda et al.2024)(Hurst et al.2021)

4. Nursing Considerations

The perioperative period gives the nurse opportunities to manage the effects of anesthesia and surgery on the patient's neurocognitive condition. Patient assessment should include significant risk factors and investigations appropriate to the patient's vulnerabilities and severity of illness because of volume, dose, and length of anesthesia needed for the procedure. Vigilance and the ability to be a patient advocate in postoperative care are central to the nurse's role. Nursing competence in anesthetic neurotoxicity is strongly identified for readiness to take action against signals or symptoms initially unrecognized by other caregivers. It is suggested that judgments of capability for handling clinical scenarios should be broadly discussed among caring staff.

The care of patients exposed to anesthetic and sedation medication is shared among anesthesiologists, pharmacists, certified registered nurse anesthetists, and nurses. Ongoing education about new warnings regarding drug safety and management of new drugs added to the list of those with specific warnings in patients under age 3 needs to be periodically updated. Nursing staff education should include the cognitive research findings of recent years and healthy practices they suggest. Nurses who are trained to recognize a vulnerable patient at the beginning stage of anesthesia exposure will have the best opportunity to assist in implementing changes that should arise in the patient's anesthetic care plan for alternate or less toxic medications to be used according to the collaborative team management's best interest for a safe outcome to the general health of the patient. (Hu et al.2021)(Rogers & Franklin, 2021)(Riedel et al.2021)(Richardson et al.2021)(Jeffries, 2020)(Shorey & Ng, 2021)(Khanlou et al.2022)

4.1. Patient Assessment and Monitoring

As neurotoxicity monitoring continues to be reviewed in the laboratory neuroscience literature, the nursing considerations in working towards integrating anesthetic neurotoxicity and clinical medicine must be considered. Preoperative patient assessment provides an excellent opportunity to complete a cognitive and neurological assessment for the purposes of researching long-term neurological outcomes following anesthesia in the perioperative period. Preanesthetic neurological and cognitive assessments can help identify the importance of patient-based risk factors such as genetics, preoperative injury, and comorbidities in the development of postoperative delirium and postoperative cognitive decline. Implementing and continuing neuropsychological and cognitive assessments in anesthesia practice is vital for further understanding the potential differing mechanisms underlying early and delayed effects of anesthesia and surgery on the brain and cognition.

There are a growing number of behavioral testing tools that are becoming sensitive enough to be included within a nursing protocol for anesthetic neurotoxicity and can be practically implemented within the perioperative period, such as continuous reaction time tests, the serial sevens auditory learning task, the device-based cognitive function test, and aspects of the postoperative self-administered cognitive assessment. Close cooperation and discussion between neuroscience researchers and clinical staff are needed as the practical implementation of a successful monitoring protocol for neurotoxicity should be derived and supported by clinical research. Establishing a clear and successful nursing assessment and postoperative monitoring within nursing care would lead to the future possibility of interventions to prevent the development of long-term cognitive decline in vulnerable patient populations. Proper assessment, support, and intervention following anesthetic neurotoxicity is a future nursing role and possibility still to come. (Ing et al.2022)(Hoh et al.2023)(DeLucca, 2023)(Chen et al., 2024)(O'Connell et al., 2023)

4.2. Communication with Patients and Families

Patients and their families may raise concerns about anesthetic neurotoxicity. Families could be aware of the work regarding disuse behavioral disease developing in 30% of ICU patients. What do we tell families who inquire about this data? Nursing interventions to ensure a smooth postoperative recovery include education and communication. Whenever possible, we should begin a conversation about neurocognitive

effects from anesthetic drugs prior to the day of surgery. We provide general information at the time of the preoperative visit and include a direct, frank, and transparent conversation with the patient regarding the potential effects of anesthesia. We usually hear from patients who are getting oral sedation that, "once the bib went on, I don't remember much." On the day of surgery, we describe the process of administering general anesthesia to each patient, including the wake-up process and the potential for disorientation.

Postoperatively, particularly in the PACU or the ICU, staff should take the time to allay patients' fears. As patients regain orientation and verbal communication, the patient care team reintroduces themselves and describes the general timeline of care to include postoperative assessments and interventions. We listen to any questions or statements of worry openly and truthfully. Detail changes to life after surgery, such as vision loss communication for patients who undergo spine surgery, and strategies to cope. For eye surgery with a gas bubble, we inform the patient when the gas will begin to dissipate and that the vision will be completely blacked out. They express that they are aware of what to expect regarding the feeling of "blacked out" vision because of nursing pre-surgical education and the intraoperative teaching. We have started teaching all convergent diving procedures this important information about helping them through the fear of temporarily losing consciousness. Encouragement and empathy go a long way to gain trust with a frightened patient, both preoperative and postoperative. (Clair et al., 2020)(Brearley et al., 2023)(Dangor et al.2021)(Newman, 2022)(Prasad et al.2020)

5. Future Directions and Research Opportunities

More research needs to be done to investigate the long-term consequences of anesthetic neurotoxicity and the age dependency of these adverse side effects. Controlled clinical trials in vulnerable populations affected by residential exposure, as well as nursing research in clinical adult and pediatric settings, can further our current knowledge of postoperative cognitive dysfunction and delirium. In the basic sciences, it is our responsibility to take advantage of the current technological advances in live-cell imaging, particularly of glia and vascular cells, functional magnetic resonance imaging in animal models, and modeling of human-induced pluripotent stem cell-derived brain-cell organoids to study neurotoxicity directly and in real time. It is thus an ethical mandate for our society to reduce or avoid general anesthetic agents and surgical interventions that are not urgently needed in vulnerable patients, such as young children and the elderly. For these reasons, current and future research should be aimed directly at four general questions. Can we develop alternative strategies for anesthetic exposure, including the use of nonanesthetic agents and alternatives to general anesthesia, to reduce short- and long-term negative effects on the brain? Are the neurotoxic effects of officially dementia-causing anesthetic agents always synonymous with neurodegeneration? Can the adult brain generate new neurons? If these are "staff cells," can these neurons integrate and function correctly, redifferentiating synaptic connections comparable to neurons lost due to aging and Alzheimer's disease.

Conclusion:

Anesthetic neurotoxicity remains a significant concern, particularly with increasing evidence suggesting that anesthetic exposure can have long-lasting effects on neurodevelopment, cognitive function, and behavior, especially in vulnerable populations such as neonates, infants, and the elderly. Despite extensive laboratory research and animal studies, the precise mechanisms through which anesthetics impact neural function remain incompletely understood, and the clinical relevance of these findings is still a matter of ongoing investigation. The potential for postoperative cognitive dysfunction and delirium, particularly in older adults and those with underlying health conditions, further underscores the importance of understanding anesthetic neurotoxicity. As the use of anesthetics continues to rise, particularly among pediatric and elderly patients, further research is essential to clarify the scope of these risks and to refine clinical practices to mitigate potential harm.

Recommendations:

Enhanced Clinical Monitoring: Healthcare professionals, particularly anesthesiologists, nurses, and other perioperative staff, should be vigilant in monitoring for signs of cognitive dysfunction or delirium in vulnerable patient populations, including both pediatric and elderly patients. Early identification of potential neurotoxic effects can guide appropriate interventions.

Increased Research Collaboration: Laboratory scientists, clinical researchers, and healthcare providers should collaborate more extensively to bridge the gap between laboratory findings and clinical applications. This will help refine protocols for safer anesthetic use and improve patient outcomes.

Use of Non-Toxic Alternatives: Future studies should explore the potential for non-anesthetic agents or alternative anesthetic techniques that could minimize neurotoxic risks, particularly in high-risk groups such as young children and the elderly.

Tailored Anesthesia Protocols: Anesthesia regimens should be tailored to the individual patient based on their age, health status, and risk factors. This could include minimizing the duration and intensity of anesthetic exposure where possible, particularly in patients with known vulnerability.
Patient and Family Education: Healthcare providers should educate patients and their families about the potential risks of anesthetic neurotoxicity, especially in the context of repeated or prolonged exposure. Informed decision-making can help guide treatment options and reduce unnecessary risks.
Postoperative Care and Support: Nurses and other healthcare providers should be trained to recognize the early signs of postoperative cognitive decline and to provide targeted interventions to support recovery. This includes managing pain effectively, ensuring adequate rest, and fostering a supportive environment for cognitive recovery.
Longitudinal Studies: More longitudinal studies are needed to track the long-term effects of anesthetic exposure on cognitive and behavioral outcomes, particularly in children and the elderly. These studies could provide valuable insights into the developmental and aging processes affected by anesthesia.
By addressing these recommendations, the healthcare community can enhance patient safety, minimize the risks associated with anesthetic neurotoxicity, and ultimately improve patient care outcomes across the lifespan.

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