

# General Anesthesia, Cognition, and Neurological Comorbidities

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DOI: <https://doi.org/10.15354/si.23.re815>

Funding: No funding source declared.

COI: The author declares no competing interest.

**General anesthesia is a frequently employed medical intervention that facilitates the induction of a temporary state of unconsciousness, hence facilitating the execution of surgical procedures in patients. Nevertheless, the cognitive capabilities of patients with neurological comorbidities, such as epilepsy or dementia, may be a subject of worry when contemplating the impact of general anesthesia. Studies have indicated that individuals who have pre-existing neurological diseases may encounter negative consequences on their brain function when exposed to anesthesia. These consequences can manifest as a reduction in cognitive abilities or a worsening of their current coexisting medical conditions. Hence, it is imperative for healthcare practitioners to thoroughly assess the potential advantages and disadvantages of general anesthesia in individuals with neurological comorbidities. This evaluation should encompass exploring alternative methodologies or tailoring anesthetic management strategies to mitigate potential complications and enhance patients' overall results.**

**Keywords:** General anesthesia; Neurological Comorbidities; Central Nervous System; Cognition; Prevention

Science Insights, 2023 October 31; Vol. 43, No. 4, pp.1097-1104.

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**G**ENERAL anesthesia is a commonly used medical procedure that induces a reversible state of unconsciousness and analgesia, allowing surgeons to perform invasive procedures without causing discomfort or awareness to the patient. However, individuals with neurological comorbidities may face unique challenges and risks during anesthesia (1). Neurological comorbidities refer to the coexistence of multiple neurological conditions, such as epilepsy, Alzheimer's disease, or multiple sclerosis, alongside the primary medical condition.

Patients with neurological comorbidities present specific concerns during general anesthesia due to their increased susceptibility to complications (2). For instance, individuals with epilepsy may experience seizures triggered by anesthesia, while those with Alzheimer's disease may exhibit altered cognition, exacerbating postoperative confusion. Multiple sclerosis patients often have reduced mobility and muscle coordination, warranting careful monitoring and positioning during anesthesia. Anesthesiologists need to prioritize patient safety by thoroughly

evaluating preoperative risks and optimizing anesthesia choices based on the specific comorbidities.

The management of general anesthesia in patients with neurological comorbidities necessitates a multidisciplinary approach (3). Collaborative decision-making among anesthesiologists, neurologists, and surgeons is crucial to minimize potential risks and optimize patient outcomes. Comprehensive preoperative assessments should include a detailed patient history, examination of neurological function, and evaluation of comorbidities' severity. Special attention must be paid to the selection of anesthetics and their potential interactions with the patient's medications or disease-specific treatments. Additionally, individualized anesthetic techniques, such as avoiding agents that may trigger seizures or maintaining cerebral perfusion pressure within a specific range, should be considered for patients with specific neurological conditions.

General anesthesia in patients with neurological comorbidities poses unique challenges and requires careful consideration. Anesthesia management should prioritize patient safety and thoroughly evaluate risks associated with the comorbid conditions. Collaboration among different medical specialties is essential to optimize patient outcomes. By considering the individual patients' specific needs and tailoring anesthetic techniques accordingly, healthcare providers can mitigate potential risks and provide safe and effective general anesthesia to patients with neurological comorbidities.

### **General Anesthesia and Physiological Effects**

The central nervous system is the primary target of general anesthesia. It acts by altering the neurotransmission within the brain, resulting in the suppression of consciousness and sensation (4). The exact mechanisms behind this effect are complex and multifactorial, involving anesthetics' interaction with specific receptors in the brain. Additionally, general anesthesia modulates neuronal activity, leading to a reduction in the brain's metabolic rate and cerebral blood flow (5).

Cardiovascular effects represent another crucial aspect of general anesthesia (6). Anesthetics can lead to alterations in heart rate, blood pressure, and cardiac output. Generally, it causes a decrease in sympathetic nervous system activity, reducing the overall stress response and promoting a stable cardiovascular state. However, some anesthetics may depress myocardial contractility, which warrants careful monitoring during surgery to prevent adverse cardiac events (7).

Respiratory system effects are also notable during general anesthesia. Anesthetics reduce the responsiveness of the respiratory centers in the brain, leading to decreased ventilatory drive (8). Consequently, the patient's ability to maintain an adequate level of oxygen and carbon dioxide exchange may be compromised. Therefore, it is essential to manage the airway, provide mechanical ventilation as needed, and carefully monitor blood gases during the administration of anesthesia.

In addition to the central nervous, cardiovascular, and respiratory systems, general anesthesia impacts several other organs and functions (9). Hepatic blood flow and drug metabolism may be altered, requiring adjustments in drug dosing. Renal function may also be affected, as anesthetics can decrease glomerular filtration rate and urine output. Thermoregulation is

impaired, necessitating active measures to maintain a patient's body temperature. Additionally, general anesthesia may suppress immune function, impacting the patient's ability to respond to infections and prolonging post-operative recovery.

Various factors can influence the physiological effects of general anesthesia, such as patient age, medical history, and the choice of anesthetic agents (10). Individual variations in drug metabolism and response can result in differing physiological outcomes. Additionally, the anesthetic technique utilized, whether intravenous or inhaled, can also impact the physiological effects experienced by the patient.

The management of the patient during general anesthesia requires a careful balance between achieving an adequate depth of anesthesia for surgery and minimizing potential adverse effects (11). Monitoring tools, such as electroencephalography, arterial blood pressure monitoring, and capnography, are crucial for assessing the patient's depth of anesthesia and physiological stability. Regular monitoring and adjusting the anesthetics' dose and choice according to the patient's response are essential for patient safety and optimal outcomes.

General anesthesia plays a fundamental role in modern medicine by enabling safe and effective surgical procedures. Its physiological effects are widespread, affecting the central nervous, cardiovascular, respiratory systems, as well as several other organs and functions. Understanding these effects is critical for providing appropriate and tailored anesthetic care, ensuring patient safety and successful surgical outcomes. Ongoing research in the field aims to deepen our knowledge of anesthetic mechanisms and improve patient care during the administration of general anesthesia.

### **General Anesthesia and Cognition Deficiency**

Although general anesthesia is considered safe and effective, concerns have been raised regarding potential cognitive side effects, often referred to as postoperative cognitive dysfunction (POCD).

Several studies have examined the long-term cognitive effects of general anesthesia, with mixed results (12, 13). While some studies report transient cognitive deficits, others show no significant differences compared to the general population. This discrepancy might be attributed to multiple factors, including variations in study design, patient characteristics, and the specific anesthetic agents used. It is essential to consider these factors when interpreting the available data to form a comprehensive understanding of the topic.

One potential mechanism for general anesthesia-induced cognition deficits is the neuroinflammatory response. The brain's immune response to surgery and anesthesia can trigger inflammation, leading to neuronal dysfunction and cognitive impairment (14). Animal studies provide evidence supporting this hypothesis, with anesthetics shown to activate inflammatory pathways and induce cognitive deficits in rodent models (15). However, extrapolating these findings to human populations requires caution, and further research is needed to establish a direct link between anesthesia-induced neuroinflammation and cognitive decline.

Additionally, anesthesia-related changes in neurotransmitter systems, such as gamma-aminobutyric acid (GABA) and

N-methyl-D-aspartate (NMDA) receptors, have been implicated in cognition deficiency. GABA is the main inhibitory neurotransmitter in the brain, and anesthetics that enhance its activity, like propofol, might disrupt normal neural communication (16). NMDA receptors, involved in learning and memory processes, can also be affected by anesthetics, potentially impairing cognitive function (17, 18). Understanding the complex interplay between these neurotransmitter systems and how anesthetics modulate them is crucial for unraveling the mechanisms underlying cognition deficits.

Moreover, factors related to surgery, such as duration, complexity, and hypoperfusion, have been associated with an increased risk of cognitive impairment. Prolonged or invasive surgeries may expose patients to longer periods of anesthesia, increasing the potential for cognitive side effects (19). The presence of underlying medical conditions, such as cardiovascular disease or diabetes, can also confer vulnerability to cognition deficits. These factors highlight the importance of individual patient characteristics in assessing the risks associated with general anesthesia administration.

It is worth noting that the majority of studies investigating cognitive decline after general anesthesia primarily focus on older adults. This is due to the increased susceptibility of older individuals to cognitive impairment, as well as their higher likelihood of undergoing surgical procedures. However, recent research suggests that younger populations might also experience cognitive changes, albeit less severe and transient (20). Further investigations are required to explore the impact of general anesthesia on cognition in diverse age groups and to determine potential age-related differences in vulnerability.

Assessing cognition deficiency after general anesthesia is a complex task that necessitates careful neuropsychological testing. Standardized cognitive tests, such as the Mini-Mental State Examination (MMSE) and Montreal Cognitive Assessment (MoCA), are commonly utilized to evaluate various cognitive domains pre- and postoperatively (21). These tests help identify subtle changes in attention, memory, executive function, and processing speed. Combining such assessments with functional brain imaging techniques, like functional magnetic resonance imaging (fMRI), could offer valuable insight into the neural correlates of anesthesia-induced cognitive changes.

To mitigate potential cognitive impairments associated with general anesthesia, several strategies have been proposed. Preoperative patient optimization, including proper management of comorbidities and optimization of neuroprotective agents, might reduce the risks of cognition deficiency (22). Utilizing alternative anesthetic techniques, such as regional anesthesia or lighter sedation, may also alleviate cognitive side effects (23). Nonetheless, these approaches require careful consideration of both patient and surgical factors to make informed decisions regarding anesthetic management.

In sum, general anesthesia has revolutionized the field of surgery, allowing for intervention without pain or distress to patients. However, the potential cognitive side effects associated with its administration have garnered attention. While evidence regarding the relationship between general anesthesia and cognition deficiency remains inconclusive, ongoing research using comprehensive study designs and cutting-edge neuroimaging

techniques is shedding light on potential mechanisms and risk factors. By advancing our understanding of this complex interplay, we can develop strategies to minimize long-term cognitive impairment and improve patient outcomes following surgery.

## **The Effect of Age on General Anesthesia-Related Cognition**

Cognitive decline is a natural part of the aging process, with numerous studies indicating that older adults exhibit slower processing speed, reduced memory capacity, and decreased executive functioning. General anesthesia poses additional risks to cognitive function, as it is known to disrupt the neural connectivity in the brain. These cognitive changes can include impairments in attention, memory retrieval, and information processing, potentially affecting a patient's ability to comprehend and acquire new knowledge.

One specific factor that plays a substantial role in anesthesia-related cognitive decline is the duration and depth of anesthesia. While the specific mechanisms underlying these changes are not fully understood, it has been suggested that longer exposure to anesthesia may be associated with a higher likelihood of cognitive impairment, particularly in older adults (24). Consequently, patients who undergo extensive anesthesia might experience temporary cognitive deficits that impede their ability to engage in complex academic tasks.

Recent studies have emphasized the need to consider the precise type of anesthesia administered. Inhalational anesthetics, such as isoflurane, are believed to have a more pronounced impact on cognition than intravenous anesthetics like propofol (25). Consequently, the choice of anesthetic agent is a crucial aspect when it comes to understanding the cognitive effects of anesthesia on patients or any individual of advanced age.

While some research suggests that cognitive deficits resulting from general anesthesia may only be transient, several studies have highlighted the potential for long-term cognitive impairments. The mechanisms causing these persistent effects remain unclear, but it is hypothesized that inflammation, oxidative stress, and the induction of amyloid-beta plaques might contribute (26). These underlying molecular events may impact the intelligence and comprehension of patients who have undergone general anesthesia.

Age-related variations in cognitive vulnerability to general anesthesia have been noted. Older individuals tend to exhibit a higher susceptibility to anesthesia-induced cognitive decline compared to their younger counterparts (27, 28). The reasons for this disparity may be multifactorial, including pre-existing cognitive decline, increased vulnerability to neuroinflammation, and reduced resilience of aged brains to insults.

Pre-existing cognitive conditions, such as mild cognitive impairment or Alzheimer's disease, can exacerbate the impact of general anesthesia on cognition. This makes it crucial to thoroughly evaluate the cognitive status of patients before surgery to determine their vulnerability and take necessary precautions to minimize anesthesia-related cognitive decline.

Emerging research on the topic emphasizes the importance of early cognitive assessment and rehabilitation strategies following exposure to general anesthesia. Implementing cognitive interventions targeted at memory and executive func-

tions could potentially mitigate anesthesia-induced cognitive deficits in patients, allowing them to regain their preoperative intelligence and comprehension abilities (29).

Another significant aspect to consider is the impact of anesthesia procedures on brain structure and connectivity. Recent neuroimaging studies have revealed that general anesthesia can lead to alterations in the default mode network, a crucial brain network associated with higher-level cognitive functions (30). These structural changes may contribute significantly to the alteration of intelligence and comprehension abilities in patients who undergo general anesthesia.

To minimize the negative impact of general anesthesia on cognition, individualized anesthesia management strategies may be necessary. Tailoring anesthetic techniques based on the specific needs and health conditions could significantly reduce the risk of cognitive decline associated with anesthesia exposure.

### **Choice of Anesthetic Agents and Neurological Comorbidities**

In the field of anesthesiology, the selection of appropriate anesthetic agents is crucial for ensuring optimal patient outcomes. However, when patients with neurological comorbidities require surgery or procedures under anesthesia, the decision-making process becomes even more intricate. Neurological comorbidities, such as epilepsy, multiple sclerosis, and Parkinson's disease, may interact with anesthetic agents, potentially leading to significant implications for both perioperative and long-term neurological function.

Before proceeding with anesthesia, a comprehensive preoperative evaluation is vital to understanding the patient's neurological comorbidities. This assessment helps identify the specific neurological condition and its severity, as well as the patient's overall neurological status. Examining the patient's medical history, including medication use and previous responses to anesthesia, plays a crucial role in individualizing the anesthetic plan.

Anesthetic agents can affect neurological function in various ways, including altering brain activity, synaptic transmission, cerebral blood flow, and metabolic demands. Different agents have distinct mechanisms of action and therefore impact neurological outcomes differently. Understanding these mechanisms is essential for selecting the ideal anesthetic agent for patients with neurological comorbidities.

Patients with epilepsy present unique challenges due to the potential for seizure activity triggered by anesthesia (31). Intravenous anesthetic agents, such as propofol and etomidate, are commonly preferred for their antiepileptic properties and minimal effect on seizure threshold (32, 33). Inhalational agents, on the other hand, should be used with caution due to their epileptogenic potential.

Anesthetic management of patients with multiple sclerosis demands special attention to avoid exacerbating the disease (34). Agents with immunomodulatory properties, such as intravenous lidocaine or ketamine, may help reduce neuroinflammation. Additionally, maintaining normal body temperature during surgery, as hyperthermia can worsen multiple sclerosis symptoms, is crucial (35). Proper positioning and avoiding prolonged procedures can minimize the risk of exacerbation.

For patients with Parkinson's disease, anesthetic agents must be carefully selected to prevent worsening of motor symptoms and associated complications. Avoiding drugs that hinder dopaminergic transmission, such as metoclopramide, is important. Regional anesthesia techniques can be considered as they reduce the need for systemic medications and may provide better postoperative pain control without exacerbating Parkinson's symptoms (36).

Understanding the pharmacokinetic and pharmacodynamic properties of anesthetic agents in patients with neurological comorbidities is crucial. Altered drug metabolism, clearance, and sensitivity may significantly impact the effect and safety of anesthesia. Elderly patients, commonly affected by neurological comorbidities, might have altered pharmacokinetics, warranting careful dosing adjustments (37, 38).

The choice of anesthetic agents should consider the potential risks and benefits associated with each option. Balancing the necessity for adequate anesthesia and successful intraoperative management with minimizing the risk of perioperative neurological complications is crucial. Shared decision-making with patients, involving a thorough discussion of potential risks and expected benefits, is increasingly important in today's patient-centered care (39).

Advancements in neuroimaging techniques, such as fMRI, can provide valuable insights into the effects of anesthetic agents on the brain. Moreover, investigating the use of neuroprotective agents and personalized pharmacogenomics might lead to improved anesthetic approaches in patients with neurological comorbidities.

Anesthesia management in patients with neurological comorbidities necessitates a thoughtful and evidence-based approach. Understanding the interaction between anesthetic agents and neurological function is crucial for optimizing patient outcomes. While challenges exist, advancements in research and clinical practice are continuously shaping our understanding and refining anesthetic choices for patients with neurological comorbidities, ensuring the best possible perioperative care.

### **Future Studies of Anesthetic Agents and Cognition Dysfunction**

As advancements in anesthesia continue to enhance patient care and surgical outcomes, it becomes crucial to examine their effects on cognitive function. To comprehend the future direction of anesthetic agents and cognition, it is essential to review the existing knowledge in this field. Studies have suggested that anesthetic agents can influence various cognitive domains, such as memory, attention, and executive function. However, more research is needed to understand the underlying mechanisms and long-term effects on cognitive health.

Future studies should aim to identify the optimal anesthetic regimens that yield the least disruptive effects on cognition. Utilizing advanced imaging techniques, such as fMRI and electroencephalography, researchers could evaluate the impact of different anesthetic agents on specific brain regions and networks involved in cognitive processing.

Further investigations should focus on vulnerable populations such as the elderly, children, and individuals with pre-existing cognitive impairments. Anesthesia has been associ-

ated with POCD in older adults. Therefore, future studies could explore ways to minimize these adverse effects, potentially by tailoring anesthetic protocols to individual patient characteristics.

To comprehensively understand the impact of anesthetic agents on cognition, long-term follow-up studies are crucial. Analyzing the cognitive performance of patient months or years after receiving anesthesia would provide a clearer picture of any persistent effects and inform the development of targeted interventions if necessary (40).

The integration of neuroimaging techniques could greatly advance our understanding of the neurobiological basis underlying anesthesia-induced cognitive changes. By combining brain imaging modalities with detailed cognitive assessments, researchers can unravel the precise neural mechanisms involved in the cognitive effects of different anesthetic agents.

Emerging research suggests that certain anesthetic agents, such as xenon and volatile agents with neuroprotective properties, may have the potential to protect the brain from injury during surgery (41). Future studies should aim to investigate the neuroprotective effects of these agents and their impact on cognition, offering new insights into preventative strategies and personalized medicine.

Traditional general anesthesia involves the administration of intravenous or inhaled agents. However, the future study of anesthetic agents and cognition should not only examine the effects of these routes but also delve into alternative modes of drug delivery. Investigating targeted delivery methods, such as inhalation via nasal sprays or transdermal patches, might reduce systemic exposure and minimize cognitive disturbances.

Anesthetic agents are often administered concurrently with other drugs during surgical procedures. Future research should investigate potential interactions between anesthetic agents and common medications, such as analgesics, sedatives, or anticholinergics, to better understand how these combinations affect cognition. Such studies can help optimize drug regimens and reduce any adverse cognitive effects.

Advances in artificial intelligence (AI) and machine learning offer exciting opportunities for future study of anesthetic agents and cognition. AI algorithms could be trained to analyze massive datasets comprising neuroimaging results, cognitive tests, and patient characteristics, allowing for more precise predictions and personalized recommendations in anesthetic administration to optimize cognitive outcomes (42).

As we advance our knowledge in this area, it is imperative to address the ethical considerations surrounding research involving anesthetic agents and cognition. Informed consent should be obtained from patients before participating in studies, ensuring they are aware of potential cognitive risks. Ethical guidelines should be updated, acknowledging the necessity of further research while prioritizing patient safety.

Therefore, future studies of anesthetic agents and cognition holds immense potential for optimizing patient care, refining anesthetic techniques, and deepening our understanding of the intricate relationship between anesthesia and cognitive function. By exploring the impacts of anesthetic agents on vulnerable populations,

## Conclusion

General anesthesia is a critical component of modern medicine, used to induce a reversible state of unconsciousness and immobility in patients undergoing invasive surgical procedures. Despite its benefits, recent research has shed light on the potential association between general anesthesia and neurological comorbidities.

Firstly, it is crucial to comprehend the physiological effects of general anesthesia on the central nervous system. The administration of anesthetic agents aims to inhibit neural transmission, thereby suppressing consciousness and creating a state of unconsciousness. This modulation of neurophysiological processes inevitably affects the CNS, raising concerns about potential long-term neurological consequences.

Secondly, neurological comorbidities such as cognitive decline, dementia, and even stroke have been linked to general anesthesia exposure. Some studies have associated the use of anesthesia with an increased risk of postoperative cognitive dysfunction, a condition characterized by impaired memory, attention span, and executive function. Although the precise mechanisms underlying this relationship are yet to be fully elucidated, researchers hypothesize that anesthesia-induced inflammation, oxidative stress, and synaptic dysfunction may contribute to the development of neurological comorbidities.

Thirdly, it is essential to consider the impact of patient characteristics, such as age, on anesthesia-related neurological outcomes. Older individuals have been shown to be more vulnerable to the neurocognitive effects of anesthesia, potentially due to age-related changes in neuronal reserve, decreased cerebral blood flow, and altered drug metabolism. Additionally, the duration and type of anesthesia seem to influence the risk of neurological comorbidities, with some evidence suggesting that longer exposure to general anesthesia may increase the likelihood of developing cognitive impairment.

Moreover, the choice of anesthetic agents may also play a role in the development of neurological comorbidities. Certain studies have reported that specific drugs, such as inhalational anesthetics and certain intravenous agents, exhibit neurotoxic properties in animal models (43). These findings raise concerns regarding the selection of anesthetic agents, particularly in vulnerable populations, such as pediatric and elderly patients.

Furthermore, the role of preexisting neurological conditions must be considered when exploring the relationship between general anesthesia and comorbidities. Patients with preexisting neurodegenerative diseases, such as Alzheimer's or Parkinson's, may experience exacerbated cognitive decline following anesthesia. Similarly, individuals with a history of stroke or cerebrovascular disease may face an increased risk of postoperative neurological complications.

However, despite the growing body of research examining the potential association between general anesthesia and neurological comorbidities, the current evidence remains inconclusive. Studies present conflicting results, and determining causality in this complex relationship poses significant challenges. Factors such as confounding variables, methodological limitations, and inter-individual variability contribute to the lack of consensus in the research field.

To address these uncertainties, future studies should focus

on enhancing research methodologies, employing rigorous longitudinal designs, and selecting appropriate control groups. Collaborative efforts among researchers and clinicians are also essential to establish standardized protocols for assessing neurocognitive function pre- and post-anesthesia, as well as monitoring and documenting potential neurological sequelae after surgical interventions.

Therefore, the relationship between general anesthesia and

neurological comorbidities represents a multifaceted topic that requires the intelligence and comprehension of a patient to navigate. While evidence suggests a potential link between anesthesia exposure and cognitive decline, dementia, and stroke, many aspects of this relationship remain unclear. Identifying potential risk factors, understanding the underlying mechanisms, and incorporating meticulous research methodologies will be crucial in further unraveling the complexities of this association. ■

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Received: August 10, 2023 | Revised: September 19, 2023 | Accepted: September 25, 2023

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