

# STUNNING THE NEURAL NEXUS: MECHANISMS OF GENERAL ANESTHESIA

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*General anesthesia requires managing a complex array of anesthetic agents that act on an intricate web of neural connections or neural nexus. Both inhaled and intravenous anesthetics must intervene at some level of the neural nexus that provides for amnesia, immobility, hypnosis, and suppression of noxious reflexes. These interactions occur at the spinal and supraspinal level and involve spinal pathways and centers of arousal and memory formation centrally.*

*Current research does not support the notion of a unitary mechanism of action for general anesthetics, but rather that anesthetics act by altering neuronal ion channels and neural communication. In general, anesthetics act by either enhancing inhibitory transmission or blocking excitatory conduction in neural impulses. The potent inhaled agents*

*and most intravenous agents enhance the inhibitory  $\gamma$ -aminobutyric acid subtype A (GABA<sub>A</sub>) and glycine channels and depress the excitatory neuronal nicotinic acetylcholine (nACh) receptors. Nitrous oxide and ketamine act primarily by depressing the excitatory N-methyl-D-aspartate (NMDA) receptors and enhancing the opioid  $\mu$  receptors. The extent, distribution, and subunit composition of these receptors determine the effects of various anesthetic agents on an individual patient. This variability, both within the patient and among the mechanisms of action of anesthetics, provides a reasonable degree of flexibility to the clinical practice of anesthesia.*

**Key words:** General anesthesia, ion channels, theories of anesthetic action.

In order to induce general anesthesia, the anesthesiologist draws on an armamentarium that provides for an assortment of neurological effects: amnesia, analgesia, loss of consciousness, muscle relaxation, and suppression of noxious reflexes.<sup>1</sup> However, these components of neural function are widely dispersed within the central nervous system (CNS), and the drugs that provide these elements of anesthesia have variable profiles regarding their effects. For example, blockade at the level of the spinal cord can provide analgesia and immobility in response to noxious reflexes, but only interventions within the brain can bring about amnesia and hypnosis. In fact, minimum alveolar concentration (MAC), as measured by the absence of movement to noxious stimuli, is defined by the spinal, not supraspinal, contribution to the anesthetic state. The traditional 3-neuron models of the spinothalamic tract (pain and temperature) and posterior columns (touch and proprioception) allow modification at both presynaptic and postsynaptic sites within the pathways and via a variety of neurotransmitters.

At the supraspinal level, the reticular formation in the brainstem processes sensory information before it continues to the hypothalamus, thalamus, and cortex; further, midbrain reticular neurons play a key role in the control of arousal and consciousness. Neurons

within the hippocampus, which plays a critical role in new memory formation, are subject to input from an array of other CNS neurons. This implies that general anesthesia may require actions at different neural sites and via different molecular mechanisms.<sup>2,3</sup> Thus, the anesthesiologist is faced with pharmacologically manipulating an elaborate web of neural connections, or neural nexus, in order to achieve general anesthesia.

There is international agreement that the investigation of the mechanism of general anesthetics must include (1) defining the clinical endpoints of these agents, (2) identifying the neuronal networks involved in achieving these endpoints, (3) characterizing each network with regard to its biomolecular function, and (4) exploring the integration of these networks.<sup>4</sup> This article will review the basic neurophysiology underlying communication within the CNS and discuss the neural networks and cellular mechanisms currently believed to support the actions of the intravenous and inhaled anesthetics.

## Defining clinical anesthesia

Specific components of anesthesia are not generally agreed on; amnesia and immobility are typically expected outcomes, while unconsciousness, analgesia, and suppression of reflexes to noxious stimuli are apparently debatable.<sup>5</sup> Among patients who request

# Neural Mechanisms Of Anesthesia

**M Carnoy**



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### **Table of Contents Neural Mechanisms Of Anesthesia**

1. Understanding the eBook Neural Mechanisms Of Anesthesia
  - The Rise of Digital Reading Neural Mechanisms Of Anesthesia
  - Advantages of eBooks Over Traditional Books
2. Identifying Neural Mechanisms Of Anesthesia
  - Exploring Different Genres
  - Considering Fiction vs. Non-Fiction
  - Determining Your Reading Goals
3. Choosing the Right eBook Platform
  - Popular eBook Platforms
  - Features to Look for in an Neural Mechanisms Of Anesthesia
  - User-Friendly Interface
4. Exploring eBook Recommendations from Neural Mechanisms Of Anesthesia
  - Personalized Recommendations
  - Neural Mechanisms Of Anesthesia User Reviews and Ratings

- Neural Mechanisms Of Anesthesia and Bestseller Lists
- 5. Accessing Neural Mechanisms Of Anesthesia Free and Paid eBooks
  - Neural Mechanisms Of Anesthesia Public Domain eBooks
  - Neural Mechanisms Of Anesthesia eBook Subscription Services
  - Neural Mechanisms Of Anesthesia Budget-Friendly Options
- 6. Navigating Neural Mechanisms Of Anesthesia eBook Formats
  - ePub, PDF, MOBI, and More
  - Neural Mechanisms Of Anesthesia Compatibility with Devices
  - Neural Mechanisms Of Anesthesia Enhanced eBook Features
- 7. Enhancing Your Reading Experience
  - Adjustable Fonts and Text Sizes of Neural Mechanisms Of Anesthesia
  - Highlighting and Note-Taking Neural Mechanisms Of Anesthesia
  - Interactive Elements Neural Mechanisms Of Anesthesia
- 8. Staying Engaged with Neural Mechanisms Of Anesthesia
  - Joining Online Reading Communities
  - Participating in Virtual Book Clubs
  - Following Authors and Publishers Neural Mechanisms Of Anesthesia
- 9. Balancing eBooks and Physical Books Neural Mechanisms Of Anesthesia
  - Benefits of a Digital Library
  - Creating a Diverse Reading Collection Neural Mechanisms Of Anesthesia
- 10. Overcoming Reading Challenges
  - Dealing with Digital Eye Strain
  - Minimizing Distractions
  - Managing Screen Time
- 11. Cultivating a Reading Routine Neural Mechanisms Of Anesthesia
  - Setting Reading Goals Neural Mechanisms Of Anesthesia
  - Carving Out Dedicated Reading Time
- 12. Sourcing Reliable Information of Neural Mechanisms Of Anesthesia
  - Fact-Checking eBook Content of Neural Mechanisms Of Anesthesia
  - Distinguishing Credible Sources

13. Promoting Lifelong Learning
  - Utilizing eBooks for Skill Development
  - Exploring Educational eBooks
14. Embracing eBook Trends
  - Integration of Multimedia Elements
  - Interactive and Gamified eBooks

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