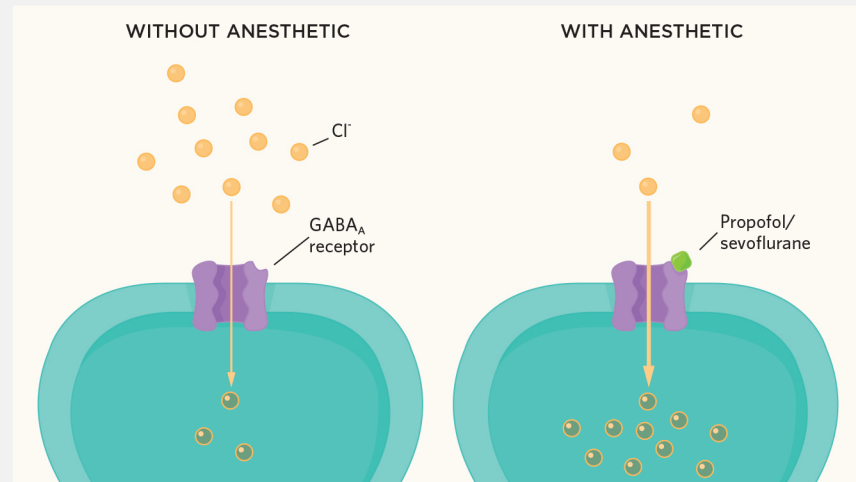


ANESTHETICS AND NEURONAL RECEPTORS

General anesthetics work by altering the activity of specific neurons in the brain. One main class of these drugs, which includes propofol and the ether-derivative sevoflurane, work primarily by increasing the activity of inhibitory GABA_A receptors, while a second class that includes ketamine primarily blocks excitatory NMDA receptors.

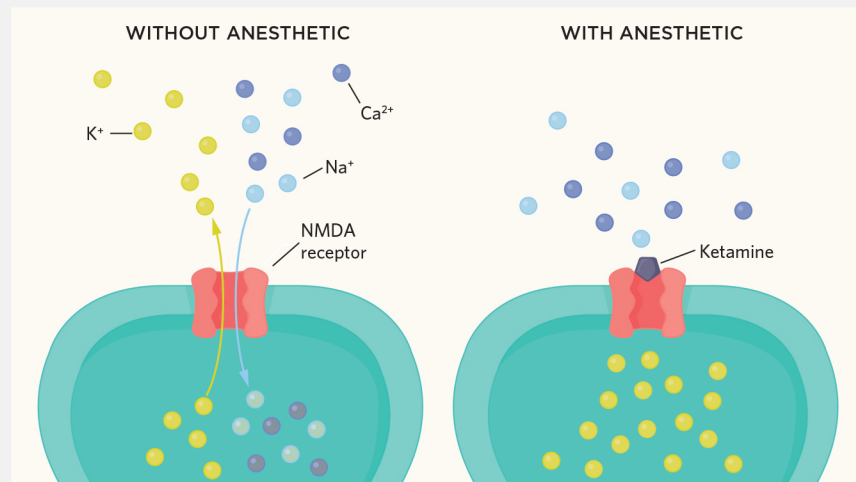
PROPOFOL AND SEVOFLURANE

The GABA_A receptor is a channel that allows chloride ions to flow into the neuron, decreasing the voltage within the cell relative to the extracellular space. Such hyperpolarization decreases the probability that the neuron will fire. Propofol and sevoflurane increase the chloride current going into the cell, making the inhibition more potent.



KETAMINE

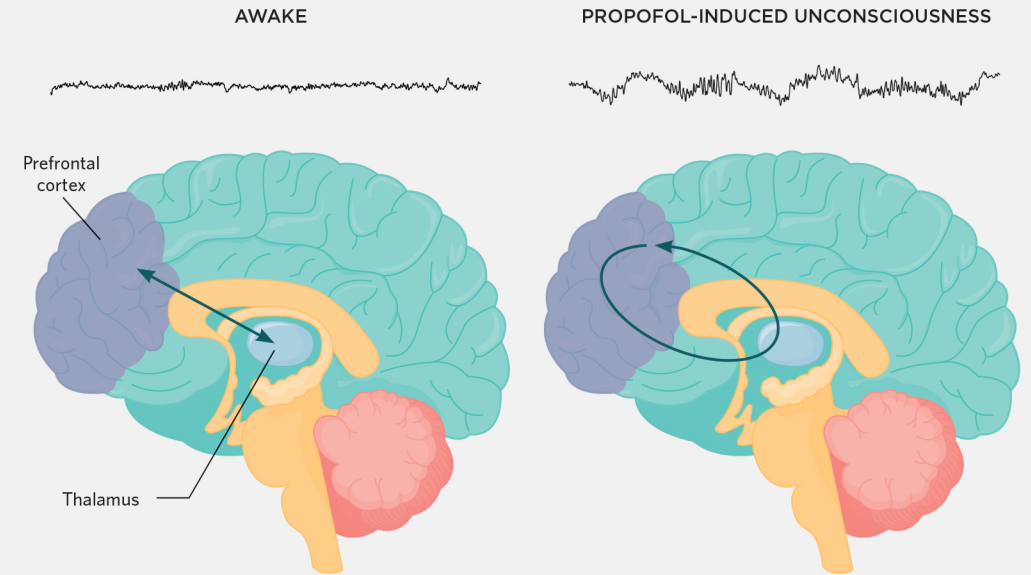
The NMDA receptor allows sodium and calcium ions to flow into the cell, while letting potassium ions out, increasing the voltage within the cell relative to the extracellular space and increasing the probability of neural firing. Ketamine blocks this receptor, decreasing its excitatory actions.



OSCILLATIONS IN THE ANESTHETIZED BRAIN

Anesthetics' interactions with neural receptors alter how neurons work, and as a consequence, how different brain regions communicate. These alterations manifest as highly structured oscillations in brain activity that are associated with the dramatic behavioral changes characteristic of general anesthesia.

The changes in brain activity can be readily observed using electroencephalogram (EEG) electrodes on the scalp. Slow oscillations of less than 1 Hz are seen in the brains of patients treated with any of the anesthetics in clinical practice. In addition, anesthetics elicit oscillations of other frequencies, such as the alpha oscillations observed following propofol administration (illustrated at right; see online for an animation of the activity patterns). These oscillations are directly related to the anesthetized state, and can be used to monitor level of unconsciousness.



DRUG	PRIMARY RECEPTOR	ANESTHETIC-SPECIFIC OSCILLATIONS	EEG READOUTS
Propofol	GABA _A	Alpha (8-12 Hz) oscillations result from synchronization of neural activity in the cortex and thalamus.	
Ketamine	NMDA	Beta/gamma (25-50 Hz) oscillations, perhaps due to an increased spiking rate of excitatory neurons in the cortex following ketamine-induced reduction of activity in nearby inhibitory neurons	

INTERPRETING THE EEG: The colored graphs, known as spectrograms, aid in visualizing the frequency and temporal dynamics of the oscillations by assigning hot colors to frequencies that are particularly prominent in the raw signal (black lines above spectrograms). Clinicians are beginning to use both types of readouts to monitor depth of anesthesia.