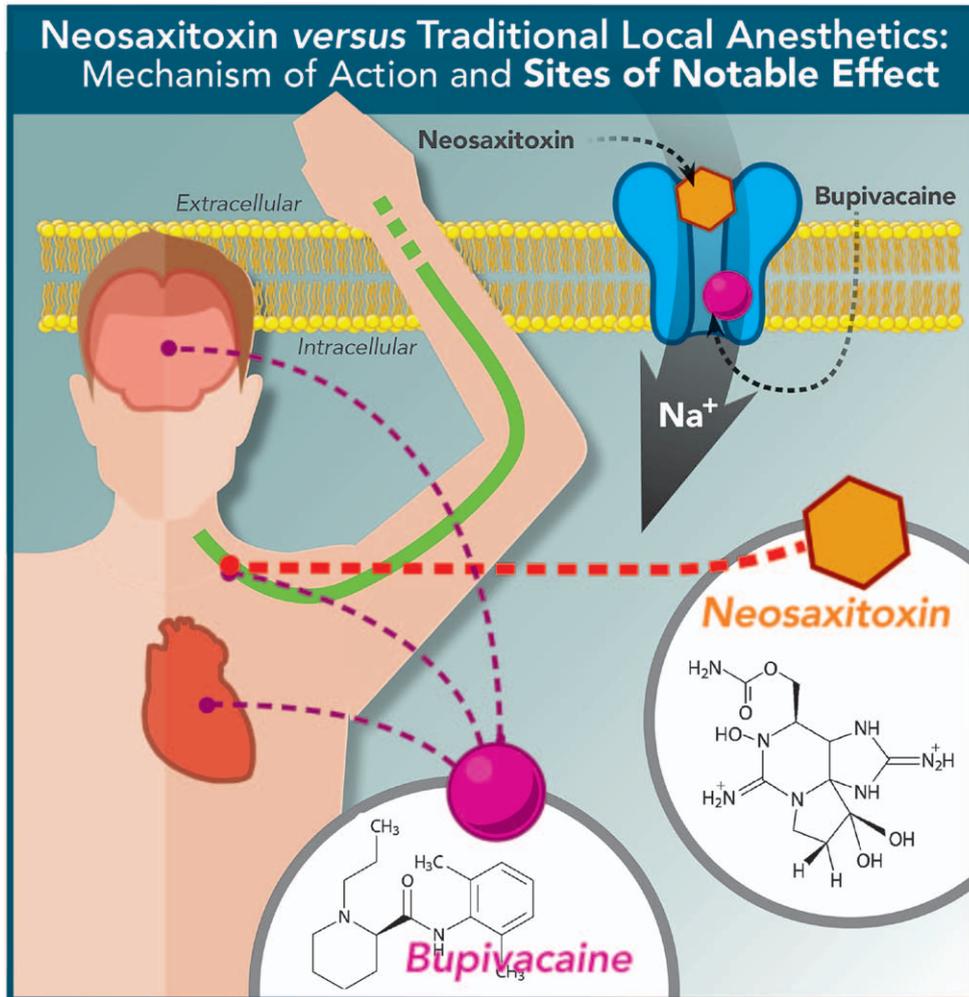


ANESTHESIOLOGY



Traditional local anesthetics act by inhibiting the voltage-gated sodium channels that are responsible for neuronal conduction. Local anesthetics, including lidocaine, bupivacaine, and tetracaine, diffuse across the plasma membrane and bind deep within the pore of the transmembrane sodium channel, thereby completely blocking the entry of sodium into the cell and thus preventing neuronal conduction. In contrast, there are a group of toxins that bind with varying degrees of affinity to the extracellular domain of the sodium channel, preventing neuronal discharge *via* a discrete mechanism of action. Tetrodotoxin, the molecule derived from the puffer fish, a delicacy that when poorly prepared can be fatal, is the best known of these so-called “site 1” sodium channel blockers. Saxitoxin and neosaxitoxin, small molecules synthesized by marine dinoflagellates and freshwater cyanobacteria, are also site 1 sodium channels blockers. Neosaxitoxin has poor affinity for the cardiac isoform of the sodium channel and does not cross the blood-brain barrier, thus this compound is virtually devoid of cardiac and central nervous system toxicity—the limiting toxicities of traditional local anesthetics. Nonetheless, systemic distribution at higher doses of saxitoxins does lead to facial paresthesias and respiratory insufficiency. As demonstrated in this issue of *ANESTHESIOLOGY*,^{1,2} when neosaxitoxin and bupivacaine are administered concomitantly, a prolonged-duration sensory block is created without evidence of added cardiac or central nervous system toxicity, demonstrating the potential for prolonged, but reversible, neural blockade.

Infographic created by James P. Rathmell, MD., Brigham and Women’s Hospital/Harvard Medical School; Gary Strichartz, PhD., Brigham and Women’s Health Care; and Jonathan Wanderer, MD., Vanderbilt University School of Medicine. Illustration by James P. Rathmell, MD., and Annemarie Johnson, Vivo Visuals. Dr. Wanderer is funded by the Foundation for Anesthesia Education and Research, Schaumburg, Illinois, and Anesthesia Quality Institute’s Mentored Research Training Grant—Health Services Research, Schaumburg, Illinois. Address correspondence to Dr. Rathmell: jrathmell@bwh.harvard.edu.

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