



*Foundation for Anesthesia  
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## **How Local Anesthetics Disrupt Intracellular Calcium Stores and the Impact on Synaptic Function and Neurotoxicity**

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Local anesthetics are essential drugs in modern medicine, with particular importance to anesthesiologists in treating pain due to surgery. With an overdose of these medications, local anesthetic systemic toxicity (LAST) may occur, affecting primarily the brain and heart and potentially leading to death. In most patients who suffer LAST, the symptoms of brain toxicity occur before heart problems. Thus, the brain may be particularly sensitive to the toxicity of local anesthetics. Although LAST is the most worrisome adverse effect of local anesthetics, the cause of this disorder is not well understood. Ryanodine receptors are channels that control the flow of calcium ions within cells. They have been shown to contribute to toxic effects of local anesthetics in muscle cells, but it is not known if ryanodine receptors can explain toxicity in the brain. Thus, this research will use neuronal cultures and microscopic techniques to study if local anesthetics target ryanodine receptors to alter calcium levels in neurons of the brain, leading to abnormal communication between neurons. The goal is to better understand the toxicity of local anesthetics so safer drugs can be designed.