The Contribution of Gap Junction and Claustral Dysfunction to General Anesthesia

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The most longstanding research question in anesthesiology is the mechanism of action of the volatile anesthetics. How do these agents, from ether through to modern fluorinated agents, induce an unconsciousness and unresponsiveness that is promptly reversible? Why do these agents work in essentially all multicellular creatures, even those without a brain? The anesthesiology literature has historically focused on anesthetic mechanisms involving chemical synapses such as GABA and NMDA, and on the disruption of either the cortex or thalamocortical loops. The recent elucidation of the BIS algorithm and its reliance on oscillations in the gamma range suggest that other neurologic structures may be involved. The presence of gamma oscillations has been associated with sensory perception in animal and human studies. There is no single mechanism of gamma oscillation production, as they can be created by multiple molecular mechanisms throughout various areas of the cortex. The binding problem is a longstanding problem in consciousness studies that refers to the question of how separate areas of the brain bind together to create a singular, unified sensory experience. The claustrum has previously been proposed to serve this function and may be the anatomic basis of volatile anesthetic action. Volatile anesthetic administration is associated with a loss of positively correlated neuronal activity in animal models. Gap junctions, a form of electrical synapse between cells, maintain neurologic synchrony and may serve as the molecular target of volatile anesthetics. Gap junctions are widely distributed throughout the brain and are evolutionarily conserved. This poster will review the contribution of gap junction and claustral dysfunction to the production of the state of general anesthesia induced by volatile anesthetics.

Several experiments can be performed to determine whether gap junctions, the claustrum or gamma oscillations are involved in the production of general anesthesia in humans. Genetic mutation and optogenetics would help to clarify the role of gap junctions in the induction of general anesthesia. One approach would be to make precise lesions in the claustrum while simultaneously monitoring gamma oscillations throughout the cortex and subcortical regions. The behavioral response to anesthetic exposure in a claustral lesioned animal could then be quantified. Maintenance of the awake state in spite of gap junction and claustral dysfunction would falsify this theory of general anesthesia.