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Poster Presentation

The Facilitatory Action of Snake Venom Phospholipase A2 Neurotoxins by Which Increase the Release of Acetylcholine, May Improve Alzheimer's Disease Symptoms

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Abstract

Introduction: In a serious brain disorder like Alzheimer's disease, the levels of acetylcholine (ACh) drop significantly. The gradual death of cholinergic brain cells leads to a profound loss of memory and learning ability. Acetylcholine is the chemical messenger that sends messages from one neuron to another in the area of the brain used for memory. Many of the current medications act to enhance the low levels of ACh in the patient's brain. For example; those that inhibit cholinesterase and prevent the normal breakdown of ACh. The presynaptic phospholipase A2 (PLA2) neurotoxins from snake venom including: Bungarotoxin, taipoxin, crotoxin, and ammodytoxin are primarily characterized by their ability to affect ACh release from motor nerve terminals on the indirectly stimulated twitch in vitro and respiratory failure in vivo. **Materials and Methods:** Lyophilized PLA2 neurotoxins, twitch tension recording and whole cell patch clamp recording. **Results:** All these PLA2 neurotoxins exhibit a triphasic modulation of ACh release at the neuromuscular junction on isolated mammalian nerve-muscle preparations. The first phase is a transient initial reduction in the amount of ACh release in response to an action potential, is followed by the second phase or facilitatory phase which is a period of time when ACh release is facilitated and quantal content is increased. Finally, the third phase is a progressive decline, leading to complete block of transmitter release. Although the mechanism of this facilitatory effect is unknown, but several hypotheses such as blockade of some types of K⁺ channels etc, have been suggested. With patch clamp experiments we found evidence that facilitation is not due to direct block of nerve terminal K⁺ channels. **Conclusion:** Despite elusive mechanism, understanding the mechanism by which PLA2 neurotoxins increase the release of ACh in phase II, may facilitate the development of novel therapeutic agents to improve Alzheimer's disease symptoms.

Keywords: Alzheimer's disease, Acetylcholine (ACh), Phospholipase A2 (PLA2) neurotoxins, Facilitatory phase

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