

## Involvement of both sodium influx and potassium efflux in ciguatoxin-induced nodal swelling of frog myelinated axons

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Résumé en anglais Ciguatoxins, mainly produced by benthic dinoflagellate *Gambierdiscus* species, are responsible for a complex human poisoning known as ciguatera. Previous pharmacological studies revealed that these toxins activate voltage-gated Na<sup>+</sup> channels. In frog nodes of Ranvier, ciguatoxins induce spontaneous and repetitive action potentials (APs) and increase axonal volume that may explain alterations of nerve functioning in intoxicated humans. The present study aimed determining the ionic mechanisms involved in Pacific ciguatoxin-1B (P-CTX-1B)-induced membrane hyperexcitability and subsequent volume increase in frog nodes of Ranvier, using electrophysiology and confocal microscopy. The results reveal that P-CTX-1B action is not dependent on external Cl<sup>-</sup> ions since it was not affected by substituting Cl<sup>-</sup> by methylsulfate ions. In contrast, substitution of external Na<sup>+</sup> by Li<sup>+</sup> ions suppressed spontaneous APs and prevented nodal swelling. This suggests that P-CTX-1B-modified Na<sup>+</sup> channels are not selective to Li<sup>+</sup> ions and/or are blocked by these ions, and that Na<sup>+</sup> influx through Na<sup>+</sup> channels opened during spontaneous APs is required for axonal swelling. The fact that the K<sup>+</sup> channel blocker tetraethylammonium modified, but did not suppress, spontaneous APs and greatly reduced nodal swelling induced by P-CTX-1B indicates that K<sup>+</sup> efflux might also be involved. This is supported by the fact that P-CTX-1B, when tested in the presence of both tetraethylammonium and the K<sup>+</sup> ionophore valinomycin, produced the characteristic nodal swelling. It is concluded that, during the action of P-CTX-1B, water movements responsible for axonal swelling depend on both Na<sup>+</sup> influx and K<sup>+</sup> efflux. These results pave the way for further studies regarding ciguatera treatment.

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