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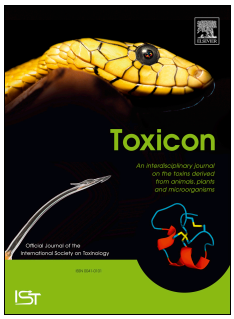

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THE BINDING OF BOTULINUM NEUROTOXINS TO DIFFERENT PERIPHERAL NEURONS

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Abstract

Botulinum neurotoxins are the most potent toxins known. The double receptor binding modality represents one of the most significant properties of botulinum neurotoxins and largely accounts for their incredible potency and lethality. Despite the high affinity and the very specific binding, botulinum neurotoxins are versatile and multi-tasking toxins. Indeed they are able to act both at the somatic and at the autonomic nervous system.
In spite of the preference for cholinergic nerve terminals botulinum neurotoxins have been shown to inhibit to some extent also the noradrenergic postganglionic sympathetic nerve terminals and the afferent nerve terminals of the sensory neurons inhibiting the release of neuropeptides and glutamate, which are responsible of nociception. Therefore, there is increasing evidence that the therapeutic effect in both motor and autonomic disorders is based on a complex mode of botulinum neurotoxin action modulating the activity of efferent as well as afferent nerve fibres.

Introduction

Botulinum Neurotoxins (BoNTs) are a large group of bacterial protein exotoxins produced by phylogenetically distinct strains of the genus *Clostridium*, and they are the causative agents of botulism characterized by a flaccid neuromuscular paralysis (Rossetto et al., 2014; Williamson et al., 2016; Pirazzini et al., 2017). A recent and ongoing major revolution in the BoNT field is the identification of dozens and dozens of novel BoNT isoforms (Peck et al., 2017; Montecucco and Rasotto, 2015). Many toxin variants named