Promising therapeutic applications of botulinum neurotoxins: nerve regeneration and functional recovery in a spinal cord injury mouse model.

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Treatment of spinal cord injury (SCI) is a dramatic health and social challenge that needs urgent attention by the medical and scientific community. Different experimental approaches are currently being tested, from axon growth promoting or neuroprotection to rehabilitative measures, but none has been able to reverse the consequences of SCI. Considering that the molecular and cellular environment of the spinal cord is constantly changing from the moment of injury until several weeks, or even months later, spinal cord repairing is particularly complex. Our challenge is represented by the identification of pharmacological therapies able to exert neuroprotection reducing the extension of damage and inducing regeneration even through the stimulation of spinal stem cells.

Over the last 20 years, therapeutic utilization of botulinum neurotoxins (BoNTs) has successfully expanded. Established and emerging applications of BoNTs (mainly of serotype A, BoNT/A), from muscular to neurological and pain disorders, are already present in clinical practice. Our previous studies demonstrated that BoNT/A effectively contrasts neuropathic pain inducing analgesic and anti-inflammatory effects and exerting its action on both neurons and glial cells. Currently, we are studying novel and unexpected aspects of BoNT/A that may represent a new and concrete possibility for fighting spinal trauma induced paralysis. We demonstrated the extraordinary capacity of BoNT/A to neutralize the complete paralysis and pain insensitivity induced in a murine model of SCI. We showed that the toxin, spinally administered within one hour from spinal trauma, exerts a long-lasting protective action, up to 60 days after its administration, and induces a complete recovery of muscle and motor function. BoNT/A modulates SCI-induced neuroglia hyperreactivity, facilitating axonal restoration, and preventing secondary cells death and damage. The great power of stimulating axonal regeneration and nerve sprouting of BoNT/A is the new therapeutic potential discovered, which can be of great general interest for the important biological and biomedical implications. Because of the well-documented BoNT/A pharmacology, safety, and toxicity, these findings strongly encourage clinical translation.

References:

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