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MECHANISMS OF THE ANTINOCICEPTIVE EFFECT OF SUBCUTANOUS BOTOX® : INHIBITION OF PERIPHERAL AND CENTRAL NOCICEPTIVE PROCESSING

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Botulinum toxin A has been used for the treatment of conditions involving excessive muscle contractions as well as painful pathological conditions (low back pain, headache, myofascial pain and migraine). Our recent study demonstrated that subcutaneous (s.c.) BOTOX® inhibited inflammatory pain in the rat formalin model and therefore indicates a direct action of BOTOX® on sensory neurons. To further investigate the mechanism of the antinociceptive effect of s.c. BOTOX®, its effect on formalin-induced local glutamate release, electrophysiological activities of dorsal horn neurons and the spinal expression of C-fos, an indicator of activation of neurons, was assessed in the rat formalin model. Formalin (s.c., 5%, 50 µl) produced prolonged distinct biphasic excitations (spikes) of dorsal horn neurons, which correspond to early (acute nociceptive) and late (tonic nociceptive) phase of the behavioural formalin response. Pretreatment of rats with BOTOX® (1 day, s.c.) significantly inhibited the formalin-induced electrophysiological activities in the late phase but not in the early phase. BOTOX® also dose dependently inhibited formalin-induced glutamate release in the paw and the expression of C-fos in the dorsal horn of the spinal cord. These results demonstrate that the inhibition of neurotransmitter release from primary sensory neurons by s.c. BOTOX® mediates, at least, some of its antinociceptive effect. Local administration of BOTOX® directly inhibits the peripheral sensitisation produced by local neurotransmitter release, which then result in an indirect reduction in the central sensitisation. Inhibition of nociceptive processing at the peripheral site and at the spinal cord level may underline the mechanism of BOTOX® effect in alleviating certain chronic pain conditions.

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