Differential effect of Incobotulinumtoxin A on pain, neurogenic flare and hyperalgesia in human surrogate models of neurogenic pain

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BACKGROUND
The effectiveness of Botulinum-neurotoxin A (BoNT/A) to treat pain in human pain models is very divergent. This study was conducted to clarify if the pain models or the route of BoNT/A application might be responsible for these divergent findings.

METHODS
Sixteen healthy subjects (8 males, mean age 27 ± 5 years) were included in a first set of experiments consisting of three visits: (1) Visit: Quantitative sensory testing (QST) was performed before and after intradermal capsaicin injection (CAPS, 15 μg) on one thigh and electrical current stimulation (ES, 1 Hz) on the contralateral thigh. During stimulation pain and the neurogenic flare response (laser-Doppler imaging) were assessed. (2) Four weeks later, BoNT/A (Xeomin(®), 25 MU) was injected intracutaneously on both sides. (3) Seven days later, the area of BoNT/A application was determined by the iodine-starch staining and the procedure of the (1) visit was exactly repeated. In consequence of these results, 8 healthy subjects (4 males, mean age 26 ± 3 years) were included into a second set of experiments. The experimental setting was exactly the same with the exception that stimulation frequency of ES was increased to 4 Hz and BoNT/A was injected subcutaneously into the thigh, which was stimulated by capsaicin.

RESULTS
BoNT/A reduced the 1 Hz ES flare size (p < 0.001) and pain ratings (p < 0.01), but had no effect on 4 Hz ES and capsaicin-induced pain, hyperalgesia, or flare size, regardless of the depth of BoNT/A injection (i.c./s.c). Moreover, i.c. BoNT/A injection significantly increased warm detection and heat pain thresholds in naive skin (WDT, Δ 2.2 °C, p < 0.001; HPT Δ 1.8 °C, p < 0.005).

CONCLUSION
BoNT/A has a moderate inhibitory effect on peptidergic and thermal C-fibers in healthy human skin.
SIGNIFICANCE
The study demonstrates that BoNT/A (Incobotulinumtoxin A) has differential effects in human pain models: It reduces the neurogenic flare and had a moderate analgesic effects in low frequency but not high frequency current stimulation of cutaneous afferent fibers at C-fiber strength; BoNT/A had no effect in capsaicin-induced (CAPS) neurogenic flare or pain, or on hyperalgesia to mechanical or heat stimuli in both pain models. Intracutaneous BoNT/A increases warm and heat pain thresholds on naïve skin.

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