Time-course of analgesic effects of botulinum neurotoxin type A (BoNTA) on human experimental model of pain induced by injection of glutamate into temporalis muscle

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1 Introduction

- Analgesic effects of BoNTA develop within few hours in animal studies and within days in human studies. [1]
- We have previously shown that BoNTA can block glutamate-induced mechanical sensitization and neurogenic vasodilation in rat temporalis muscle within 3 hours. [2]

2 Aim

The present translational study was designed to explore the time-course of analgesic effects of BoNTA on pain, sensitization and vasomotor responses in a glutamate-evoked human experimental pain model.

3 Methods

- BoNTA (5U) and saline were injected (30min interval) into the left and right temporalis muscles (Fig 1) of 12 healthy males (24.2±2 years).
- Several measurements were made during the experimental session. The design of the study is shown in Fig 1.
- Pressure pain threshold (PPT), skin temperature (thermo camera) and tissue perfusion (laser Doppler) were measured every hour for 3 hours.
- Afterwards, subjects received an intramuscular injection of glutamate (MSG) (1M-0.2mL) into the left and right temporalis muscles.
- Pain intensity (VAS) was recorded for 10min after injection and pain distribution was then mapped.
- PPT was measured at 15 and 30min following the glutamate injections, while skin temperature and tissue perfusion were recorded at 5, 15 and 30min.

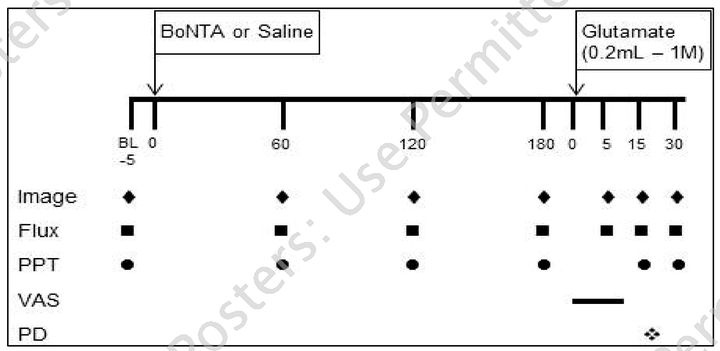

Fig 1: Timeline of the measurements.

4 Results

- BoNTA significantly reduced glutamate-evoked peak pain intensity compared with saline (P=0.045).
- Expansion of pain area was smaller in the muscles pre-treated with BoNTA (Fig 2).

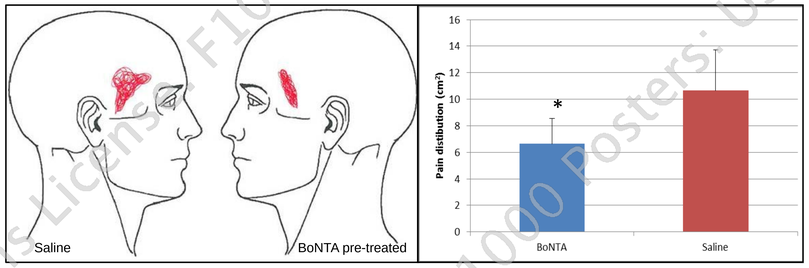

Fig 2: Pain distribution area. Typical drawing after MSG injection (Left panel). Significant difference in the area (Right panel, mean and SEM, *: p<0.05).

- Glutamate-induced vasomotor reactions (tissue perfusion and elevated skin temperature) showed a tendency to decrease in BoNTA pre-treated muscles (Fig 3, 4). Typical blood flux scanning and thermo images after MSG injection are shown in Fig 5 and 6.

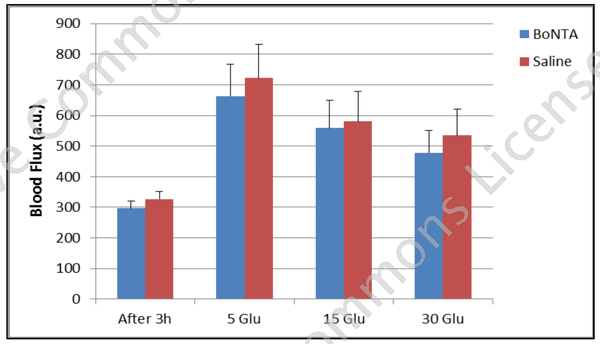

Fig 3 : Temporalis muscle blood flux. (mean and SEM) 3h after pre-treated muscle by BoNTA or saline. 5, 15, and 30 minutes after glutamate injection.

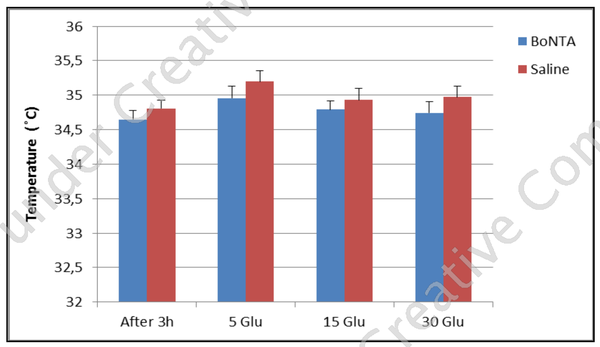

Fig 4: Temporalis muscle temperature. (mean and SEM) 3h after pre-treated muscle by BoNTA or saline. 5, 15, and 30 minutes after ´glutamate injection.

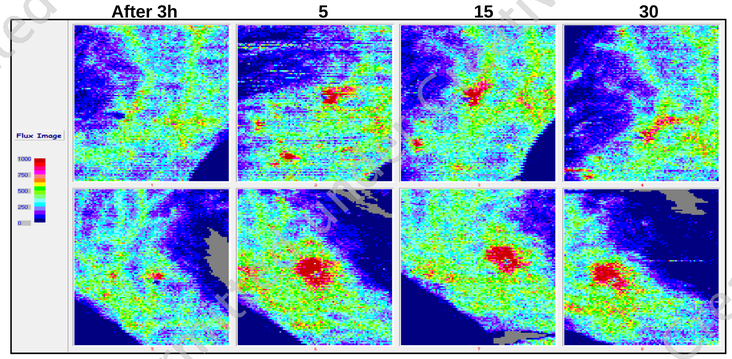

Fig 5: Typical blood flux scanning after injection (Upper panel: BoNTA pre-treated side, lower panel: Saline pre-treated side).

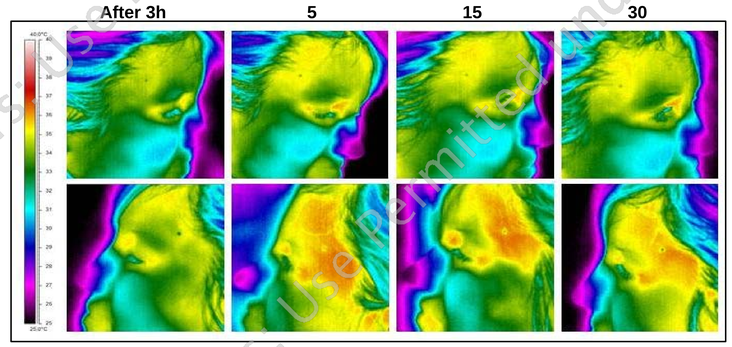

Fig 6: Typical thermo images after glutamate injection (Upper panel: BoNTA pre-treated side, lower panel: Saline pre-treated side).

- Higher PPT values were recorded in BoNTA pre-treated muscles (Table1).

PPT	After 3h	15 Glu	30 Glu
BoNTA	169,61 (14,03)	183,47 (18,16)	172,14 (16,70)
Saline	166,72 (16,15)	173,36 (13,36)	168,52 (16,15)

Table 1: Pressure Pain Threshold in temporalis muscles pre-treated by BoNTA or saline. (mean and SEM)

5 Conclusion

- BoNTA induced a direct analgesic effect within 3 hours of its injection into the temporalis muscle of humans. This phenomenon, at least in part, might be through BoNTA actions on nociceptors.
- BoNTA attenuated glutamate-induced muscle sensitization and vasomotor reactions. This finding may suggest additional effects of BoNTA on the pattern of release of substances which are involved in pain pathways.

References and Acknowledgements

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