

Inhibitory effect of oxytocin receptor antagonist intracerebroventricularly delivered on 7-hydroxy-(dipropylamino)tetralin-induced ejaculation

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OBJECTIVE

- Several lines of experiments indicate a facilitator effect of the nonapeptide oxytocin (OT) on ejaculatory process although the mechanism of action is still not clearly established.
- The present study was undertaken in order to clarify this issue by testing the effect of cerebral injection of a selective OT receptor antagonist (OTantag) on ejaculation induced by intracerebroventricular (i.c.v.) delivery of the selective D₃ receptor agonist 7-hydroxy-(dipropylamino)tetralin (7-OH-DPAT) in urethane-anaesthetised rats.

MATERIALS & METHODS

Surgical preparation

Under urethane anaesthesia, male Wistar rats were stereotaxically implanted with a guide cannula aimed at the lateral cerebral ventricle. A catheter was inserted into one seminal vesicle for measurement of seminal vesicle pressure (SVP). Recording electrode was passed throughout the bulbospongiosus muscle (BS) for measurement of BS electromyogram (BS-EMG).

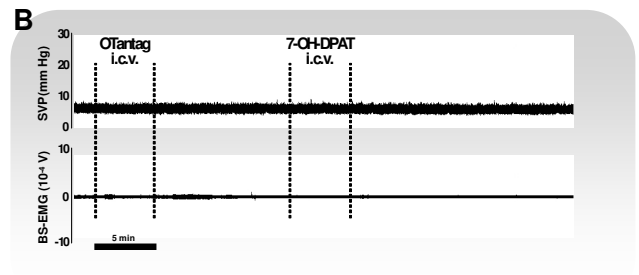
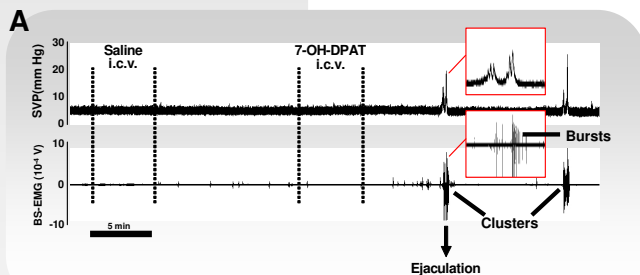
Drugs and injection procedures

The dopamine D₃ preferential agonist R(+)-7-hydroxy-(dipropylamino)tetralin (7-OH-DPAT) and the peptidergic selective oxytocin antagonist d((CH₂)₅¹, Tyr(Me)², Orn³)-oxytocin (OTantag) were dissolved in NaCl 0.9% (saline). After a 5-min baseline period, saline or OTantag (0.1 µg / 5 µl) was i.c.v. delivered and, 15 min later, 7-OH-DPAT (1 µg / 5 µl) was i.c.v. injected. SVP and BS-EMG recordings were continued over 30 min following 7-OH-DPAT injection.

Data analysis

Ejaculation, clusters of BS contractions, and SVP rises were numerated during the 30-min recording period following 7-OH-DPAT i.c.v. delivery. Duration of clusters and frequency of bursts within a cluster of BS contractions as well as duration and amplitude of SVP increases were determined.

RESULTS

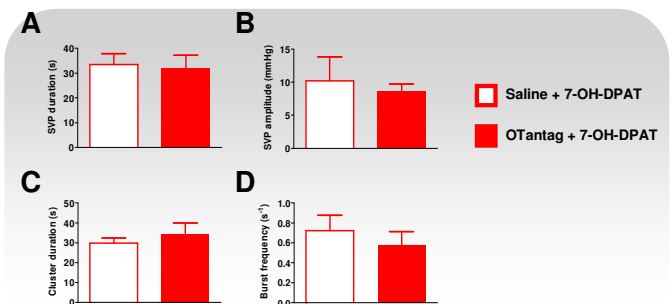


- Typical recordings of seminal vesicle pressure (SVP; upper traces) and bulbospongiosus electromyogram (BS-EMG; lower traces) obtained in anaesthetised rats i.c.v. injected with saline + 1 µg 7-OH-DPAT (A) or 0.1 µg OTantag + 1 µg 7-OH-DPAT (B). A magnification of the recording is displayed in inset (A) and shows the constituent elements (i.e. bursts) of the BS cluster of contractions.

Effects of the oxytocin antagonist d((CH₂)₅¹, Tyr(Me)², Orn³)-oxytocin i.c.v. delivered on ejaculation, contractions of bulbospongiosus muscles (BS), and seminal vesicle pressure (SVP) increases induced by i.c.v. 7-OH-DPAT in anaesthetised rats.

i.c.v. treatment	Ejaculating rats	Mean number of ejaculation	Rats displaying BS contractions	Mean number of BS clusters of contraction	Rats displaying SVP increases	Mean number of SVP increases
7-OH-DPAT + saline	3/6	0.5 ± 0.2	6/6	4.0 ± 0.6	6/6	3.0 ± 0.5
7-OH-DPAT + OTantag	0/6	0	2/6	0.8 ± 0.5 **	1/6	0.5 ± 0.5 **

Data were determined during the 30-min recording period following i.c.v. delivery of 7-OH-DPAT, which was preceded, 15 min earlier, by i.c.v. delivery of d((CH₂)₅¹, Tyr(Me)², Orn³)-oxytocin (OTantag). Mean number ± sem of BS muscle clusters of contraction and SVP increases were determined in 6 rats for each treatment group. Statistics: unpaired Student's t-test; asterisks (**p<0.01) indicate a significant difference between treatment groups.



Effects of selective oxytocin antagonist i.c.v. delivered on duration (A) and amplitude (B) of seminal vesicle pressure (SVP) increases, duration of cluster of bulbospongiosus muscle (BS) contractions (C), and frequency of bursts of BS contractions (D) induced by i.c.v. 7-OH-DPAT. Statistical analysis (unpaired t-test) did not yield significant differences between treatment groups.

CONCLUSIONS

- Ejaculation induced by i.c.v. delivery of 7-OH-DPAT was abolished in rats i.c.v. pretreated with a selective oxytocin antagonist.
- Seminal vesicle and bulbospongiosus muscle (BS) contractions induced by i.c.v. administration of 7-OH-DPAT were reduced in rats i.c.v. pretreated with a selective oxytocin antagonist indicating that both emission and expulsion phases of ejaculation were inhibited.
- The absence of effects of the selective oxytocin antagonist on quantitative parameters characterising seminal vesicle and BS responses elicited by i.c.v. 7-OH-DPAT suggests that the triggering of a programmed ejaculatory response was inhibited.

This study shows that intracerebral delivery of peptidergic selective oxytocin antagonist was capable of reversing ejaculation elicited by dopamine D₃ brain receptor stimulation thus providing new insights on the mechanism of action by which brain oxytocin modulates the ejaculatory process.