

The effect of intranasal oxytocin on social interaction and corticosterone levels in rats

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Introduction

- Oxytocin (OXT) is a nine amino acid neuropeptide associated with prosocial and affiliative behaviour in mammals
- OXT has been shown in human studies to increase trust, positive communication, and have a positive impact on social behaviours in autistic individuals
- OXT has also shown to increase social behaviour and decrease social avoidance in rodent students
- OXT has also been shown to reduce the stress response in terms of attenuation of the hypothalamic-pituitary-adrenal (HPA) axis
- Majority of research on behavioural effects of OXT has used central or peripheral administration
- The intranasal (i.n.) route of administration is a novel, clinically relevant route of administration that is non-invasive and allows large peptides to cross the blood-brain barrier (BBB)
- The prosocial effects of oxytocin make this peptide an ideal candidate for investigation using the intranasal route of administration
- There exists a lack of studies in the literature on the effects of intranasal oxytocin on social behaviour and HPA activity in rodents

Objectives

The objective of the present study is to determine the effects of intranasal oxytocin on social interaction and HPA axis activity in rats and compare these effects with those elicited by intraperitoneal administration

Methods

Subjects: Male Sprague-Dawley rats (250-300 g) were maintained on a 12h light/dark cycle and given *ad libitum* access to food and water.

Drugs: OXT was dissolved in 0.9% saline and administered intranasally at doses of 5µg/20µL and 20µg/20µL. The same doses were used for intraperitoneal (i.p.) injections but with a volume of 100µL. Controls received an equivalent volume of saline.

Procedure:

Intranasal administration: i.n. administration was performed as described in Lukas and Neumann (2012). 3 days prior to testing, the rats were habituated to i.n. administration. When administering saline or drug, the animal was restrained and the drug was applied bilaterally to the highly innervated rhinarium, avoiding direct application into the nostrils.

Social interaction paradigm: The paradigm consists of two days of habituation and one day of testing.

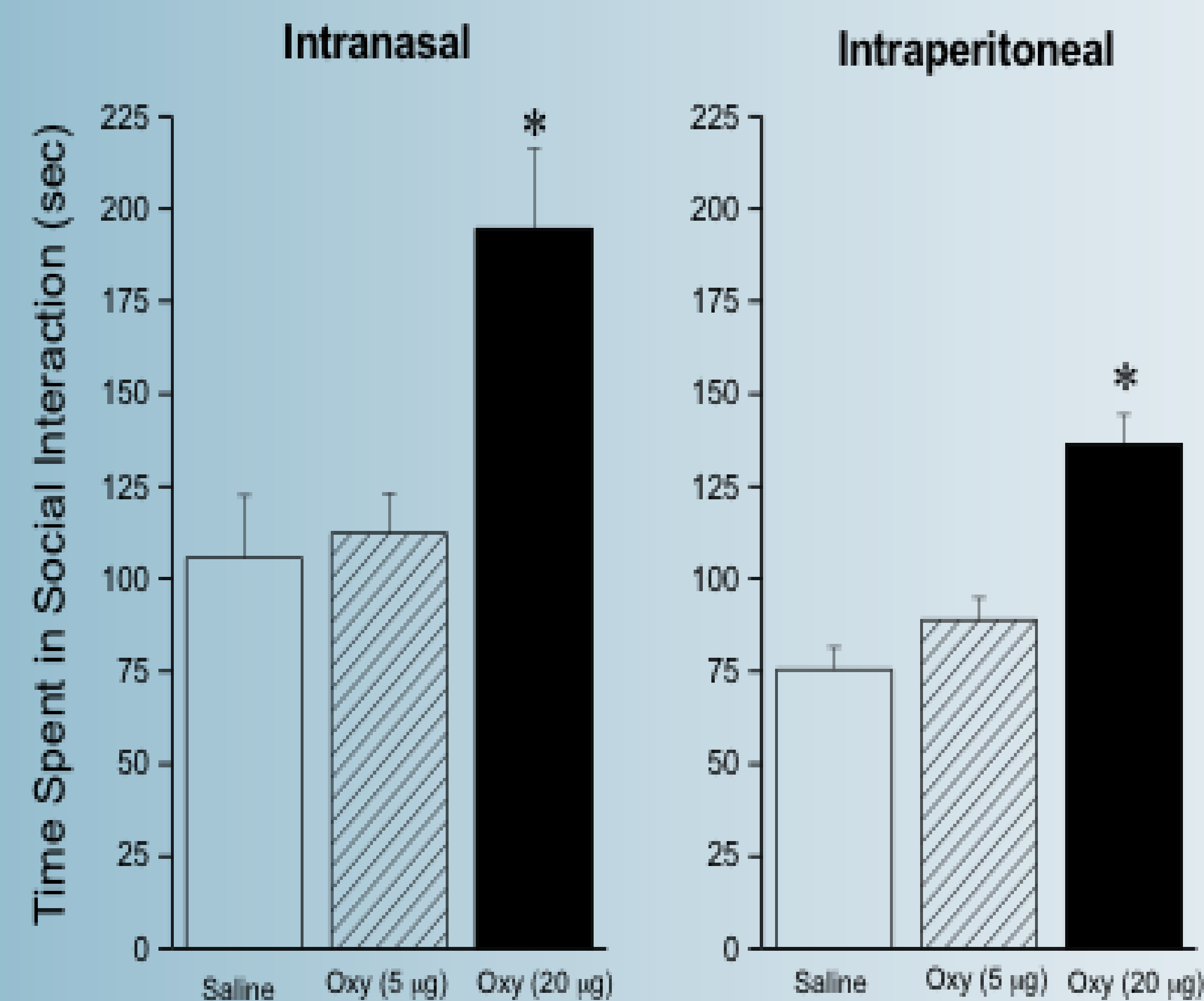
- Day 1: Rat + partner placed in the arena for 4 minutes
- Day 2: Rat individually placed in the arena for 4 minutes
- Day 3: Rats received i.n. or i.p. injection of OXT or saline either 40 minutes (i.n.) or 20 minutes (i.p.) prior to being placed in the arena for 10 minutes

A video camera was located above the arena and total time spent engaging in active social interaction was scored.

Blood collection for corticosterone analysis: Blood samples were obtained using tail venipuncture right before (0 min), 20, 40, 60, and 120 min after either i.p. or i.n. OXT or saline injections. Two blood droplets were collected on Schleicher and Schuell filter paper, dried at room temperature and then stored at -20° C. Corticosterone levels were determined from the eluted blood sample using a commercial RIA kit (MP biomedical) according to the manufacturer's instructions.

Results

Figure 1: Social interaction experiment



As depicted in Figure 1, i.n. administration of oxytocin elicited a significant increase in active social interaction. Post hoc comparison revealed that treatment with 20µg but not 5µg of OXT was effective at increasing time spent engaging in social interaction. Similarly, i.p administration of 20µg of OXT increased levels of active social interaction, but a dose of 5µg did not.



Figure 3: Two rats engaging in active social behaviour in the social interaction apparatus

Figure 2: Corticosterone levels experiment

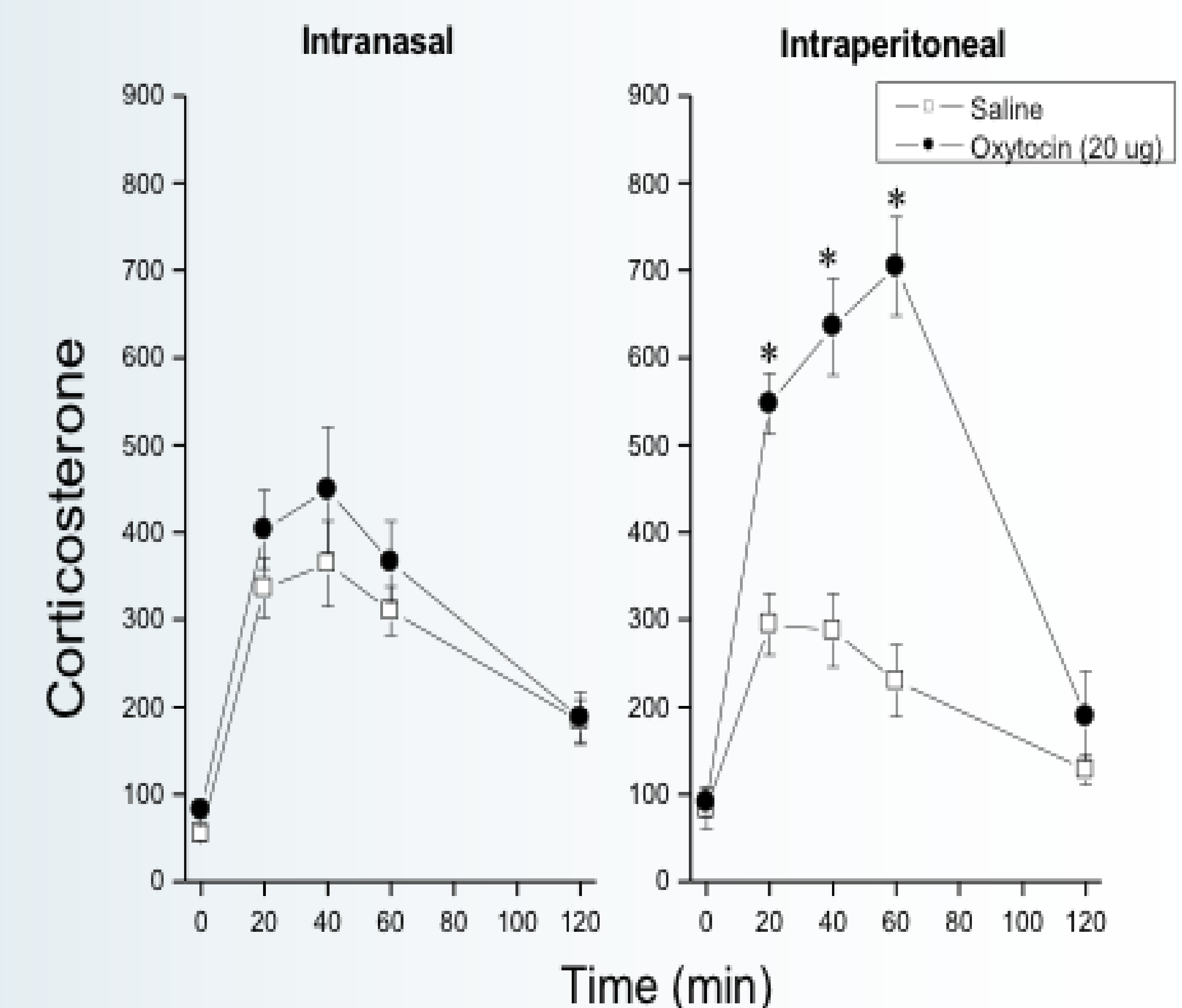


Figure 2 shows blood levels of corticosterone at baseline, 20, 40, 60 and 120 minutes following i.n. administration of OXT. From the figure it can be seen that i.n. OXT administration had no significant effects on blood corticosterone levels. Figure 2 also shows blood levels of corticosterone at baseline, 20, 40, 60, and 120 minutes following i.p. administration of OXT, and it can be seen that i.p. OXT produced a marked increase in blood corticosterone levels.

Discussion

- Promising results for intranasal OXT being a treatment for social anxiety disorders
- Further preclinical and clinical research must be done to explore the neural pathways and mechanisms behind OXT's behavioural effects
- OXT surprisingly increased HPA axis activity, which leads to speculation that 1) the prosocial effects of OXT are not mediated by HPA axis activity and 2) OXT must be administered chronically to attenuate the HPA axis, rather than acutely, as was done in the present study
- The present study showed both i.n. and i.p. OXT increase social interaction in rats, which is in agreement with literature using different administration routes in rodents and human OXT studies
- Intranasal administration is a clinically relevant, highly non-invasive and effective route of administration for neuropeptides

Summary and Conclusion

- The present study looked at the effects of intranasal OXT on social interaction and corticosterone levels in rats
- The intranasal administration of a neuropeptide was compared with intraperitoneal administration of equal dosages
- Social interaction was measured using the social interaction paradigm where active interaction was scored
- Corticosterone levels were measured using tail knicks and a radioimmunoassay
- It was found intranasal OXT significantly increased social interaction but had no effect on corticosterone levels in rats
- Intranasal OXT is promising as a potential treatment for social anxiety disorders and further research must be done into its behavioural effects