Effects of intranasal oxytocin on cocaine-conditioned locomotion and anxiety-like behaviors in rats.

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ADDICTION

• Addiction is a chronic disease characterized by compulsive, or uncontrollable, drug seeking and use despite harmful consequences and changes in the brain, which can be long lasting.

• Psychostimulants have a sympathomimetic effect as the result of the activation of the Sympathetic Nervous System (“Fight or flight”).

• Mesolimbic Pathway (Dopaminergic) – Reward Pathway
  • Ventral Tegmental Area (VTA)
  • Nucleus Accumbens
  • Prefrontal Cortex
COCAINE

• Is a psychostimulant that produces changes in brain regions implicated in drug reward.

• Has specific cellular actions within the Nucleus Accumbens – Potentiates pleasure

• Acts as inhibitor of the dopamine transporter, therefore inhibiting this neurotransmitter’s reuptake.

• Produces behavioral sensitization
**OXYTOCIN (OT)**

- Is a neuropeptide produced within the hypothalamus, specifically within the paraventricular nucleus neurons (PVN).
- Modulates emotions, social interactions, sexual behavior, learning, and memory.
- It is known to produce anxiolytic effects in humans.
- OT within the brain show peak levels at 30-60 minutes after intranasal administration.
- Attenuates locomotion and stereotyped behaviors associated to cocaine.
OBJECTIVE

To examine the effects of intranasal administration of oxytocin on cocaine-conditioned locomotion and anxiety-like response in male rats.
Intranasal infusions of oxytocin will reduce cocaine-conditioned locomotion and anxiety-like behaviors in male rats.
METHODS

- Intraperitoneal Injections: 20 Sprague Dawley male rats were injected intraperitoneally with Saline 0.9% (Control) or Cocaine 10 mg/kg (Experimental).

- Cocaine Conditioning for 5 days: Rats were exposed to activity chambers with olfactory (orange) and visual (black box) cues for 90 minutes.

- Day 7 Test Day: Rats were exposed to activity chambers 30 minutes after intranasal infusions of oxytocin (1 μg/μL) with olfactory (orange) and visual (black box) cues only for 60 minutes. Rats were then exposed to Elevated Plus Maze.
TEST DAY EXPERIMENTAL DESIGN

**Intranasal infusion**
- Oxytocin (n=10)
- Vehicle (n=10)

**Conditioning Chamber**

**Elevated Plus Maze**
- Open Arms = ⬇️ anxious
- Closed Arms = ⬆️ anxious

**Euthanasia and Brain extraction**

Time points:
- Min -30
- 0
- 60
- 65
RESULTS - CONDITIONING

Figure 1: Experimental group moved more than controls in total movement (TM) from Day 1 to Day 5.

Figure 2: Experimental group spent more time moving than controls in total movement time (TMT) from Day 1 to Day 5.
Figure 3: Ambulatory distance (AD) increased from Day 1 to Day 5 in experimental animals when compared to controls.
RESULTS – TEST DAY (CUES ONLY)

Figure 4: Experimental group treated with OT moved for a longer time (TMT) than those treated with Vehicle

Figure 5: Experimental group treated with OT moved more (TM) than those treated with Vehicle
Figure 6: Experimental group treated with OT showed more ambulatory distance (AD) than the one with Vehicle treatment
RESULTS – TEST DAY

Figure 7: Experimental group treated with OT spent more time in the Open Arms of the EPM than the group with Vehicle treatment.

Figure 8: Experimental group treated with OT spent less time in the Closed Arms of the EPM than the group with Vehicle treatment.
DISCUSSION

Experimental animals showed a trend of enhancement of cocaine-conditioning when exposed to only cocaine-paired cues.

Intranasal OT showed an enhancement of cocaine-conditioned locomotion.

Intranasal OT showed an anxiolytic effect in cocaine-conditioned male rats exposed to EPM.
CONCLUSIONS

Intranasal OT attenuates anxiety-like response triggered by cocaine-paired cues in male rats.

Intranasal OT could have anxiolytic effects in drug seeking behaviors in a dose-dependent manner.

Our results suggest a therapeutical potential of OT treatment in cocaine-addiction.
REFERENCES

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