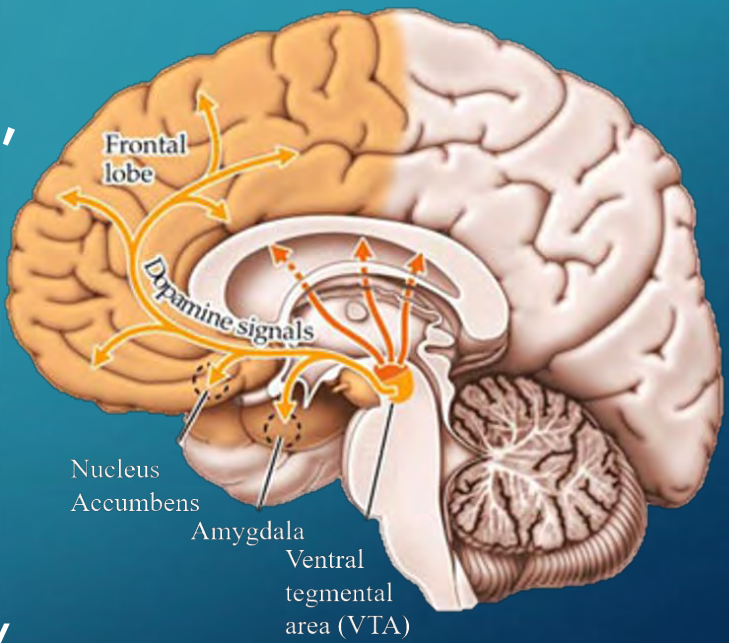
# Effects of intranasal oxytocin on cocaine-conditioned locomotion and anxiety-like behaviors in rats.

Mentor: Carmen S. Maldonado-Vlaar, PhD

Amanda V. Marti Mendoza
NeuroID Research Program

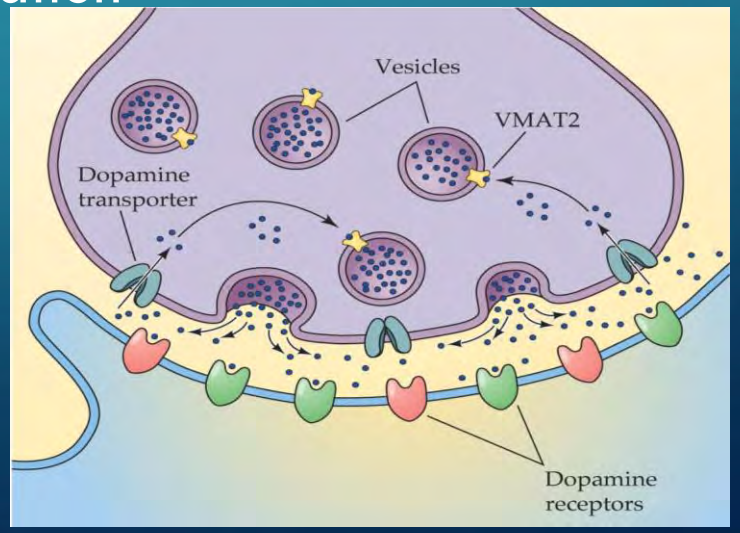
# ADDICTION

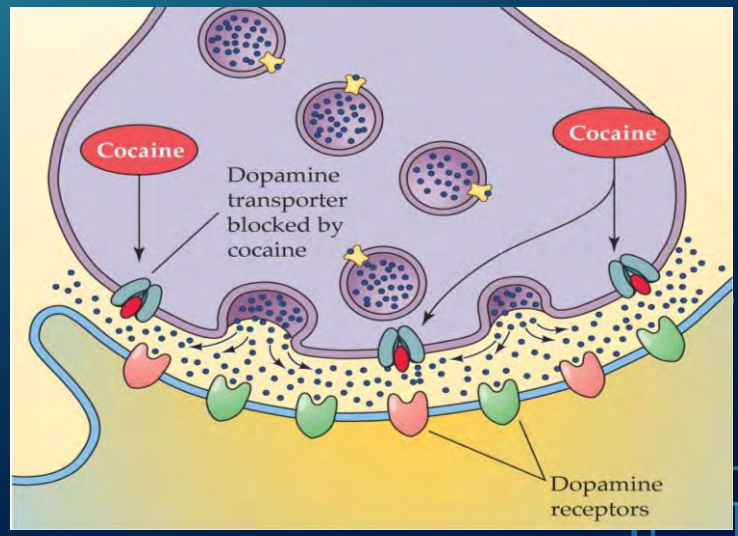
- Addiction is a chronic disease characterized by compulsive, or uncontrollable, drug seeking and use despite harmful consequences and changes in the brain, which can be long lasting.
- Psychostimulants have a sympathomimetic effect as the result of the activation of the Sympathetic Nervous System (“Fight or flight”).
- Mesolimbic Pathway (Dopaminergic) – Reward Pathway
  - Ventral Tegmental Area (VTA)
  - Nucleus Accumbens
  - Prefrontal Cortex




# COCAINE

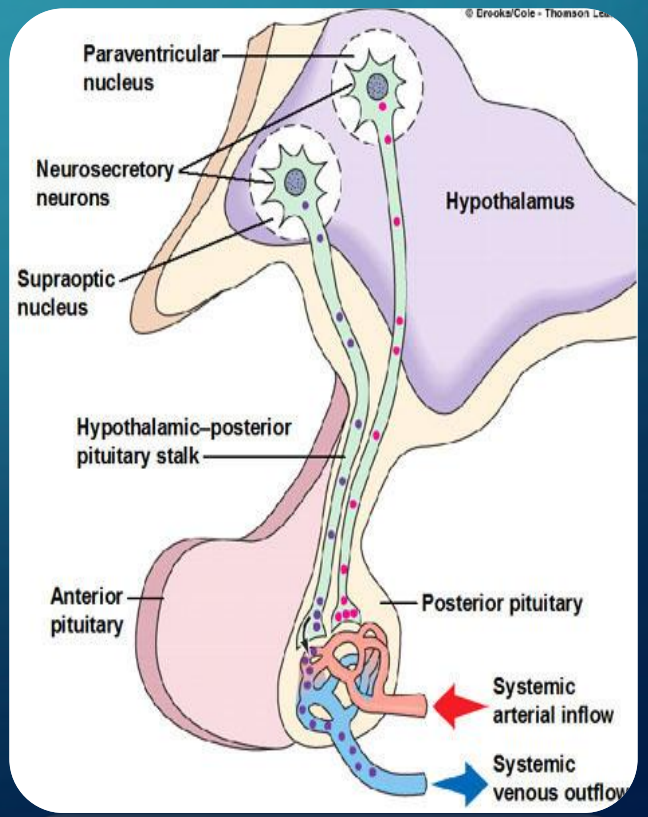
- Is a psychostimulant that produces changes in brain regions implicated in drug reward.
- Has specific cellular actions within the Nucleus Accumbens – Potentiates pleasure
- Acts as inhibitor of the dopamine transporter, therefore inhibiting this neurotransmitter's reuptake.
- Produces behavioral sensitization



# 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.

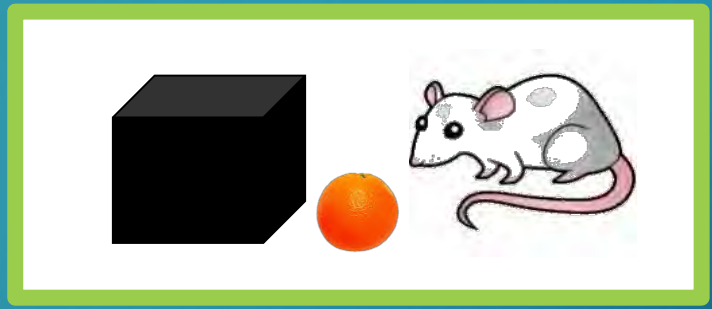
# HYPOTHESIS

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 (1µg/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

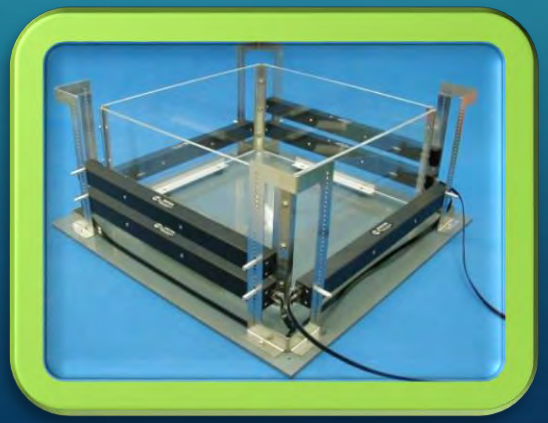
**Intranasal infusion**
Oxytocin (n=10)
Vehicle (n=10)

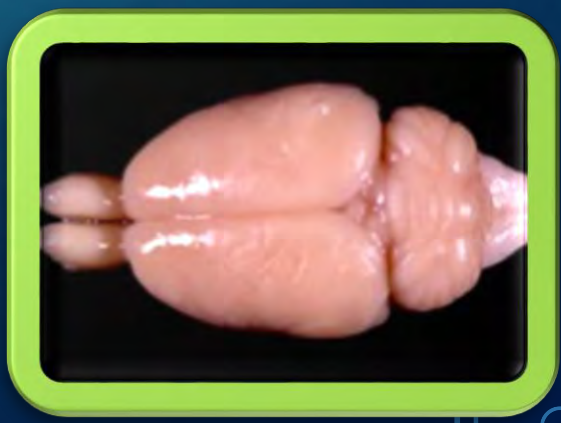
**Conditioning Chamber**

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

**Euthanasia and Brain extraction**

Min -30 ---------- 0 ---------- 60 ---------- 65 ----------





# RESULTS - CONDITIONING

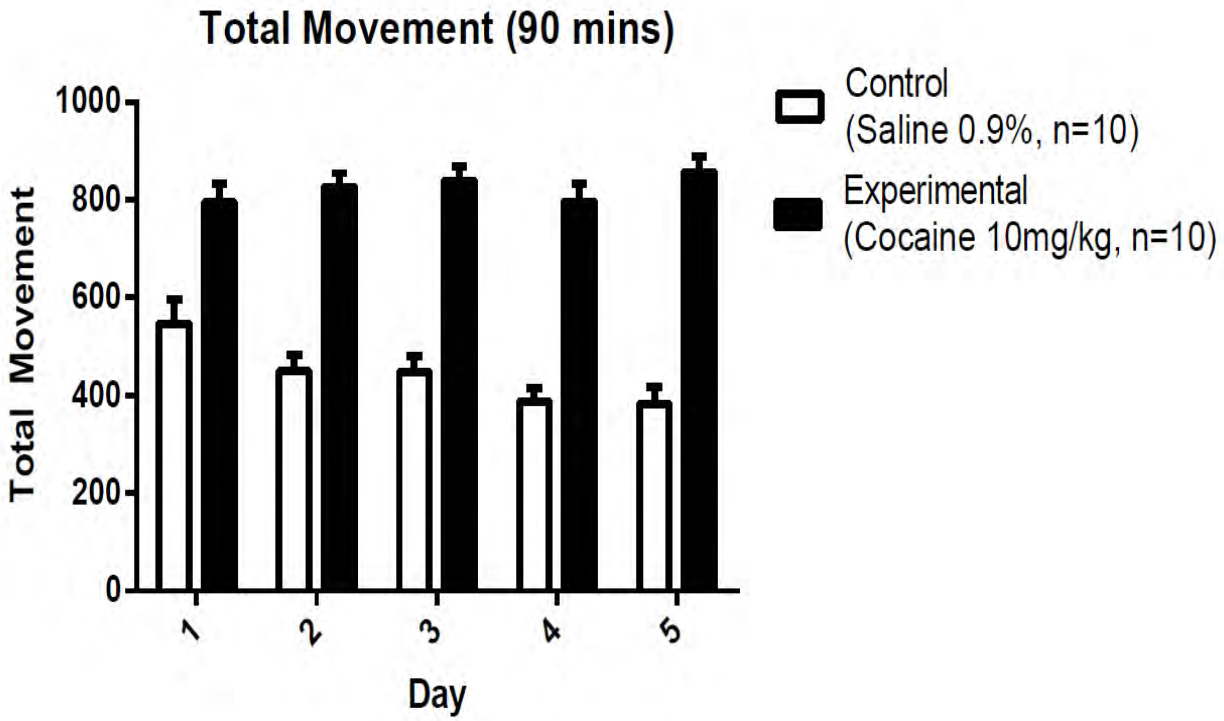



Figure 1: Experimental group moved more than controls in total movement (TM) from Day 1 to Day 5.

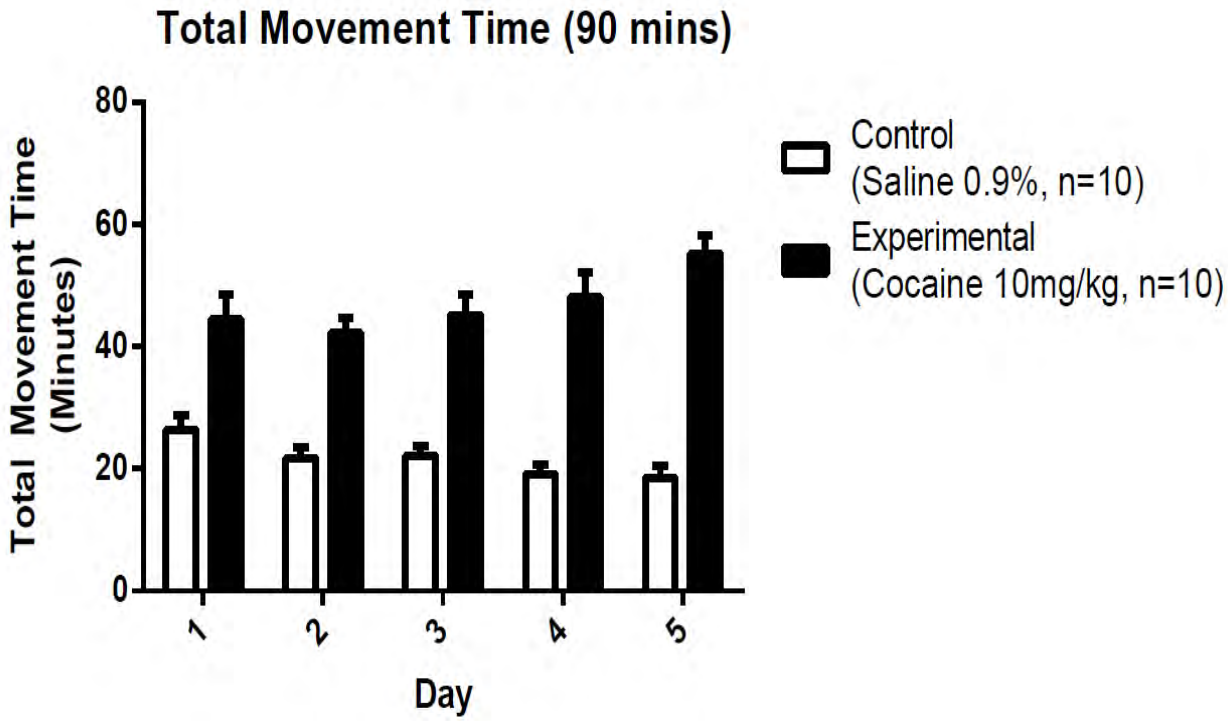



Figure 2: Experimental group spent more time moving than controls in total movement time (TMT) from Day 1 to Day 5

# RESULTS - CONDITIONING

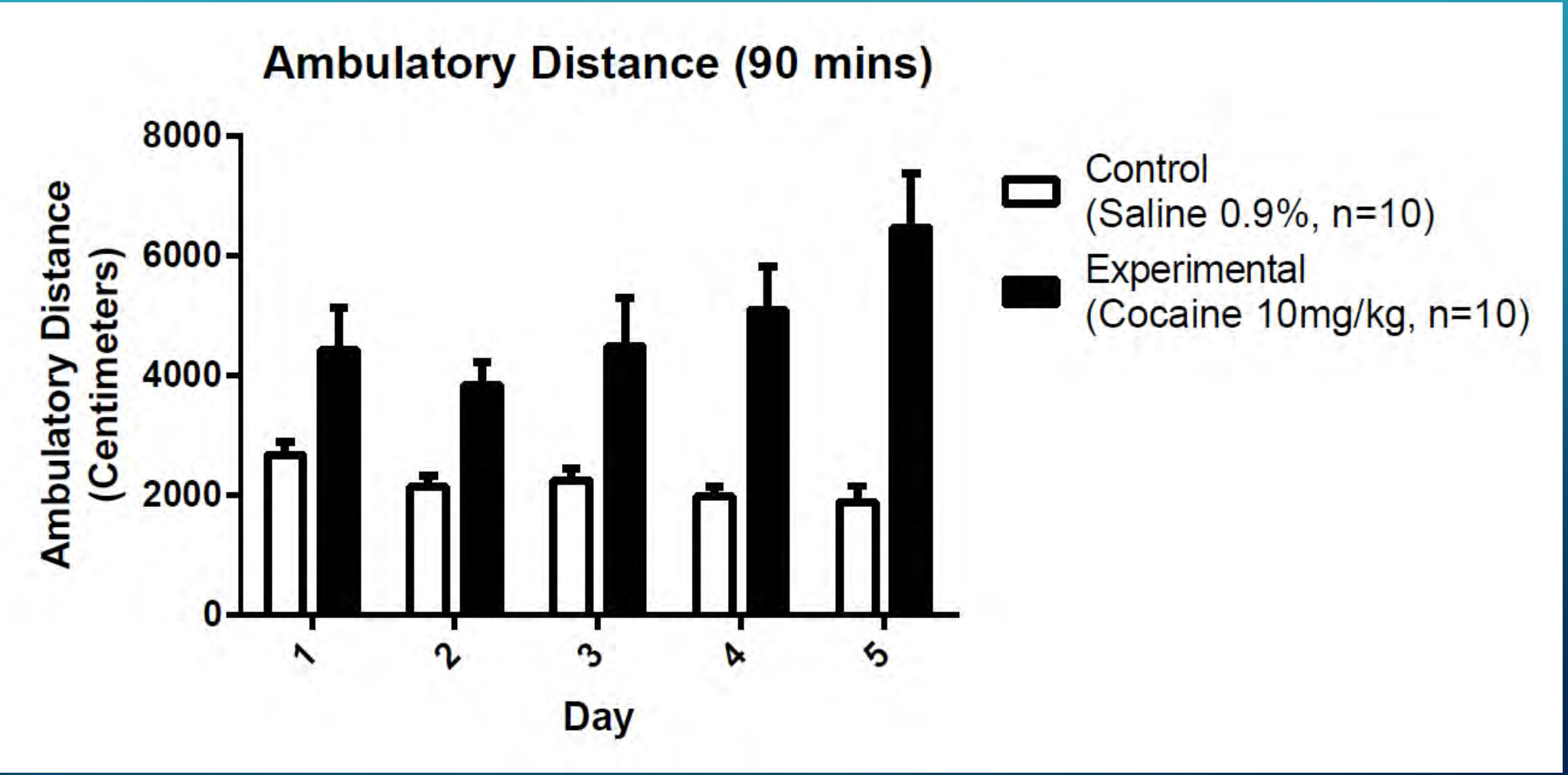



Figure 3: Ambulatory distance (AD) increased from Day 1 to Day 5 in experimental animals when compared to controls.

# RESULTS – TEST DAY (CUES ONLY)

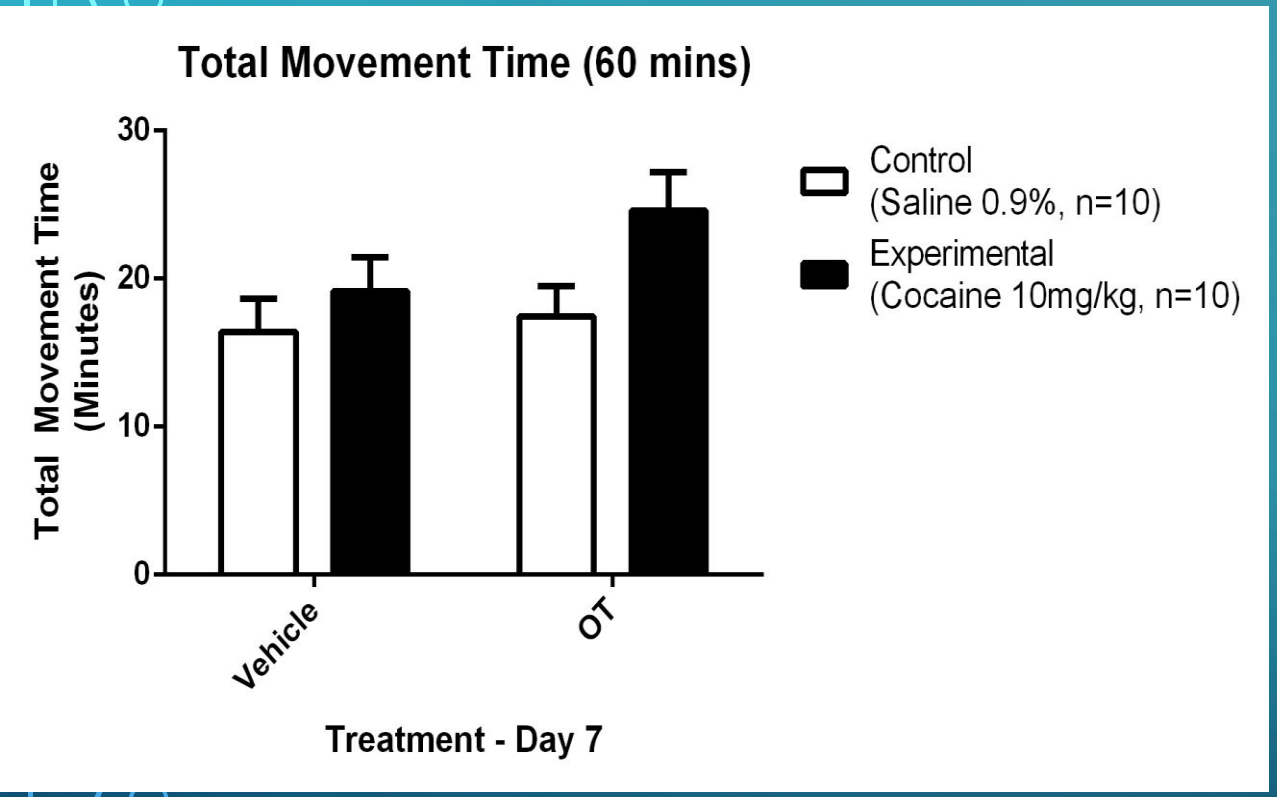



Figure 4: Experimental group treated with OT moved for a longer time (TMT) than those treated with Vehicle

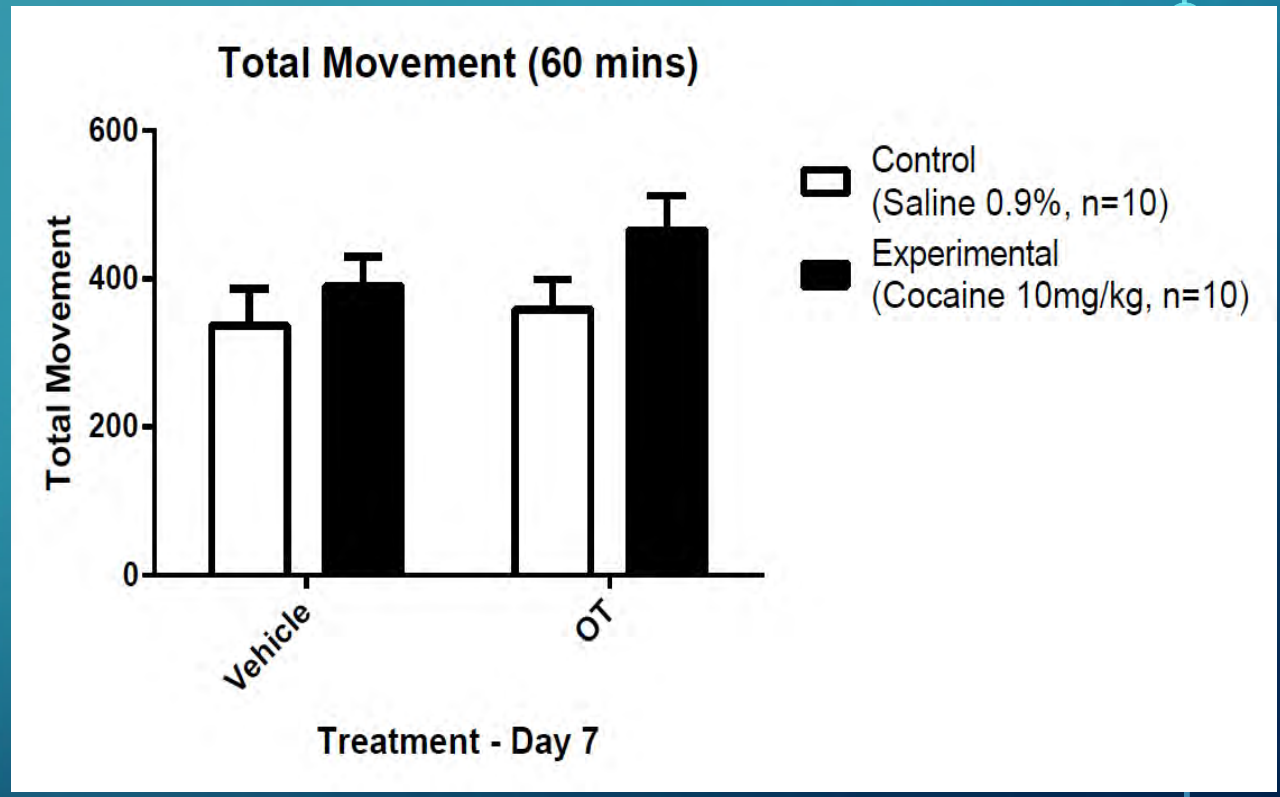



Figure 5: Experimental group treated with OT moved more (TM) than those treated with Vehicle

# RESULTS – TEST DAY (CUES ONLY)

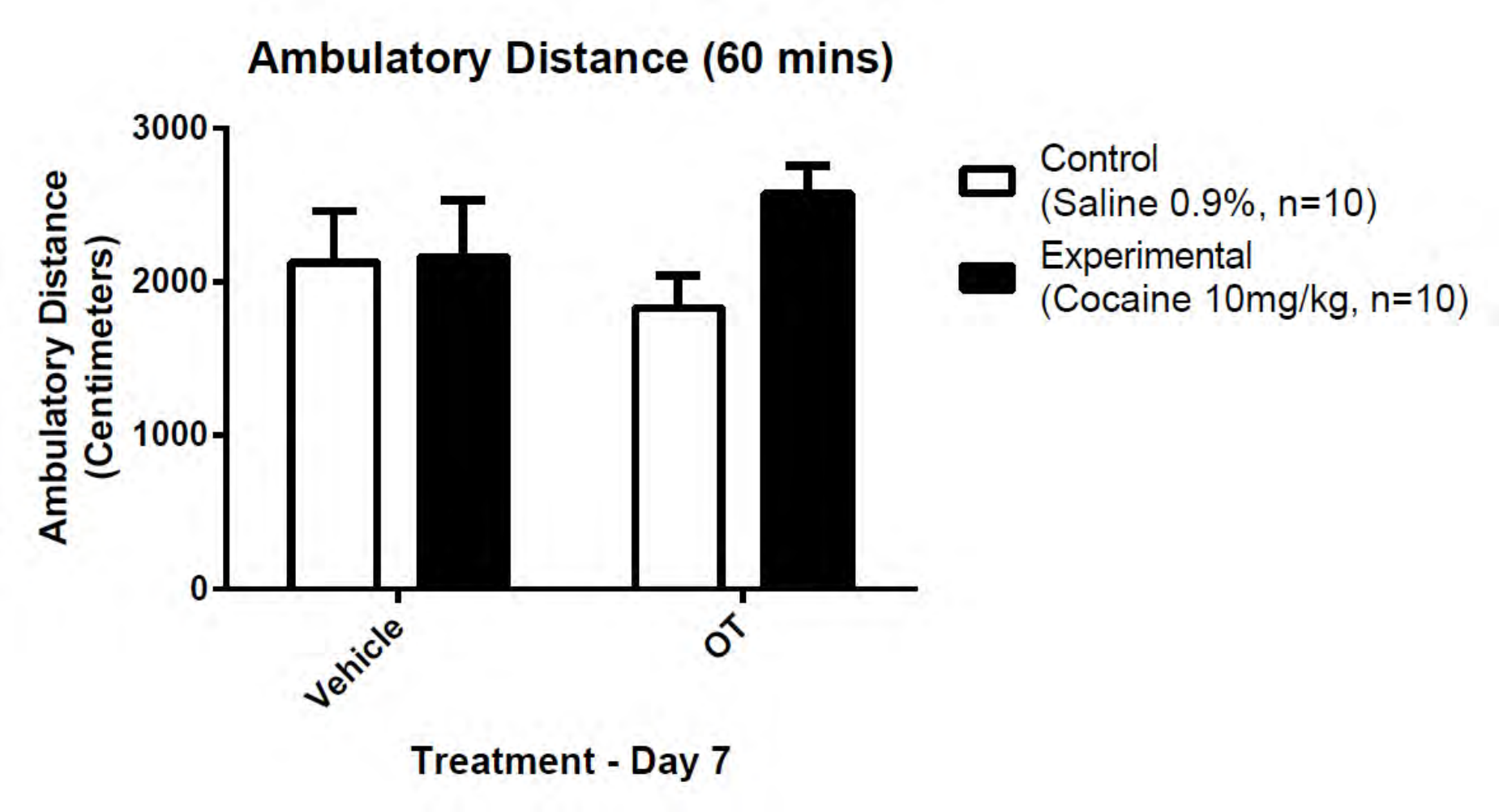



Figure 6: Experimental group treated with OT showed more ambulatory distance (AD) than the one with Vehicle treatment

# RESULTS – TEST DAY

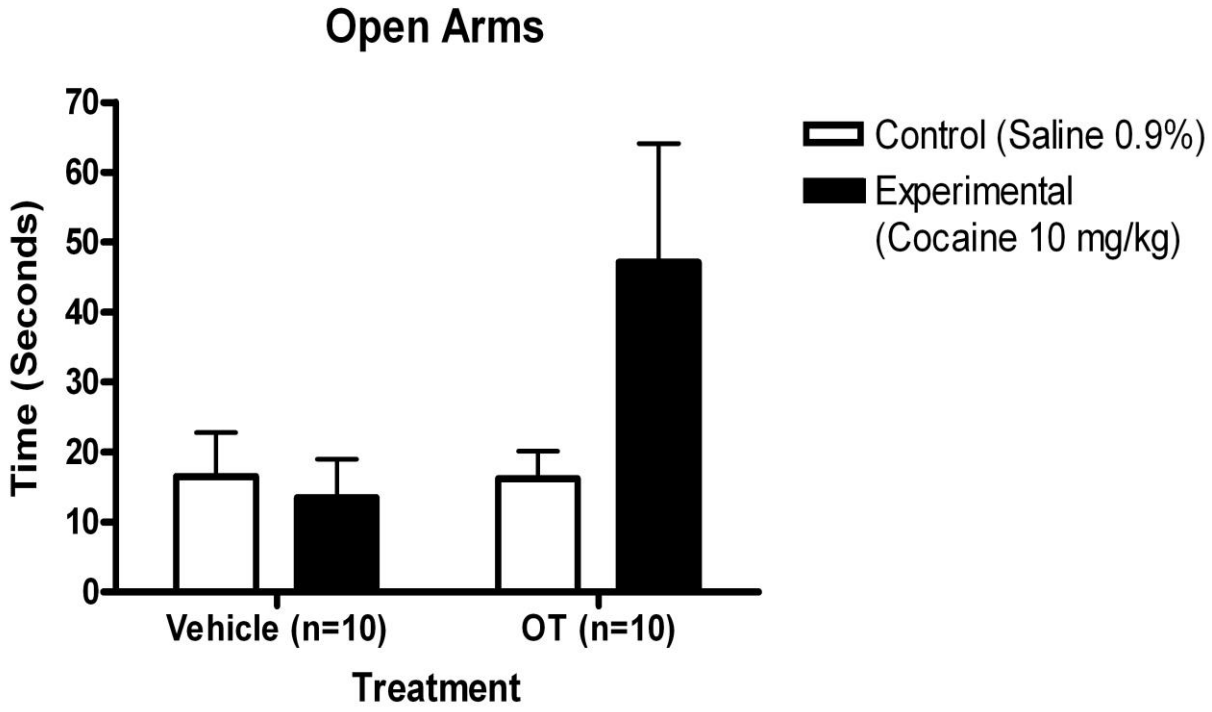



Figure 7: Experimental group treated with OT spent more time in the Open Arms of the EPM than the group with Vehicle treatment

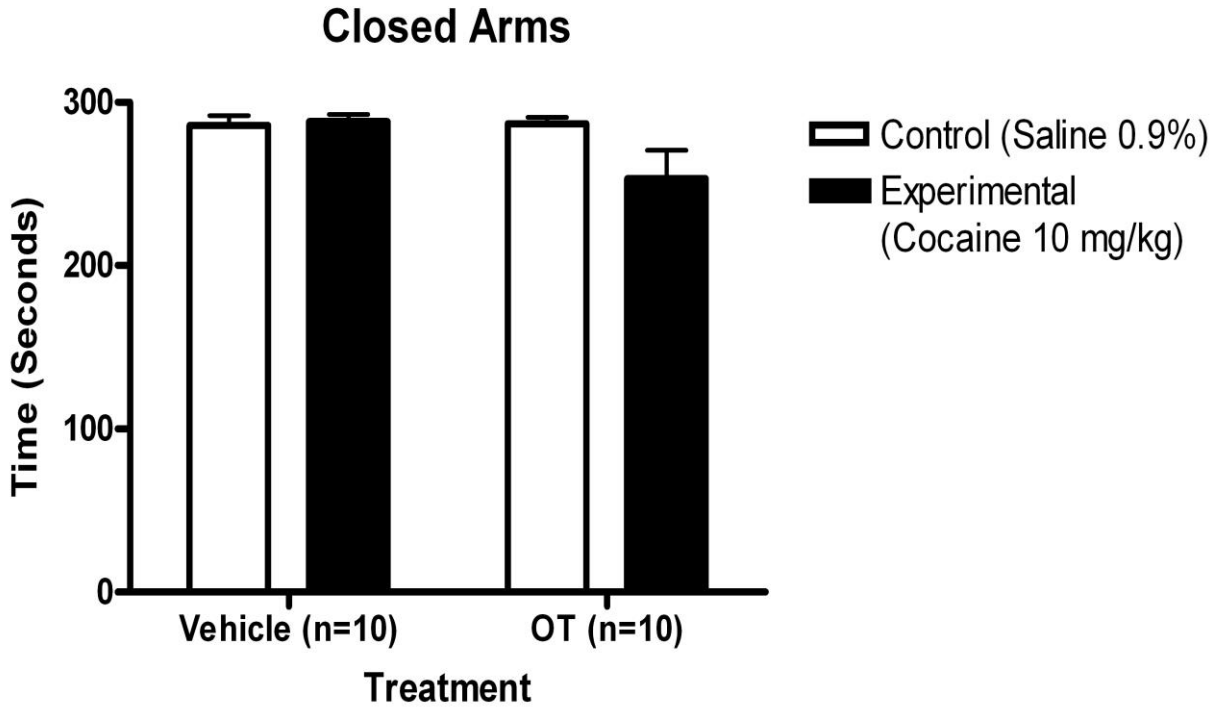



Figure 8: Experimental group treated with OT spent less time in the Closed Arms of the EPM than the group with Vehicle treatment

# 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.

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