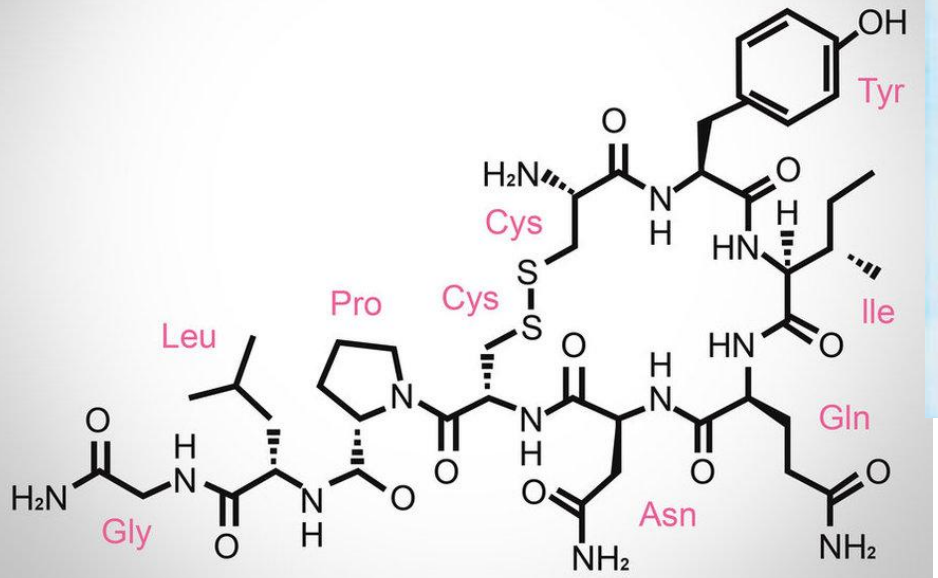
OXYTOCIN–SOCIAL BONDING, AUTISM, AND WOMEN'S HEALTH

Karen L. Bales, Department of Psychology and California National Primate Research Center, University of California, Davis

this is love.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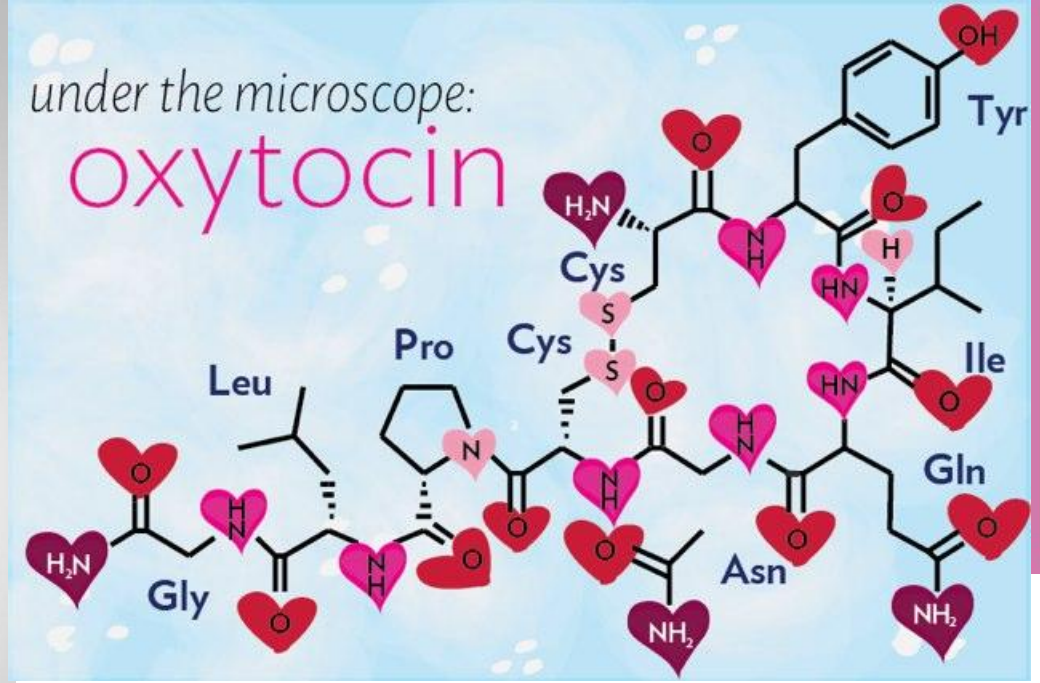
under the microscope:
oxytocin
OH
Tyr
H₂N
Cys
Pro
Cys
Leu
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Gly
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NH₂
NH₂


group
creating
mood
control
attachment
nasally
bonding
hormone
oxytocin
trust
time
loved
effects
feelings
fear
influences
level
amygdala
administered
decision
matter
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OXYTOCIN
bumpybrains.com


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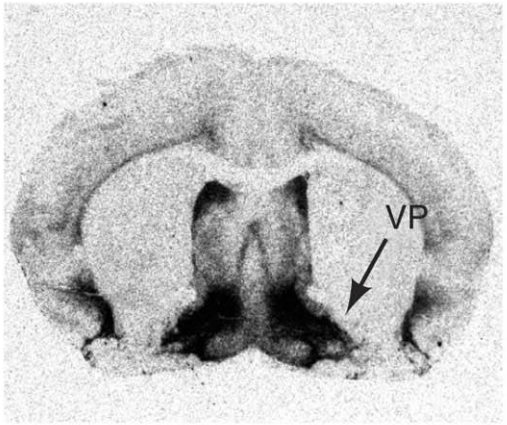
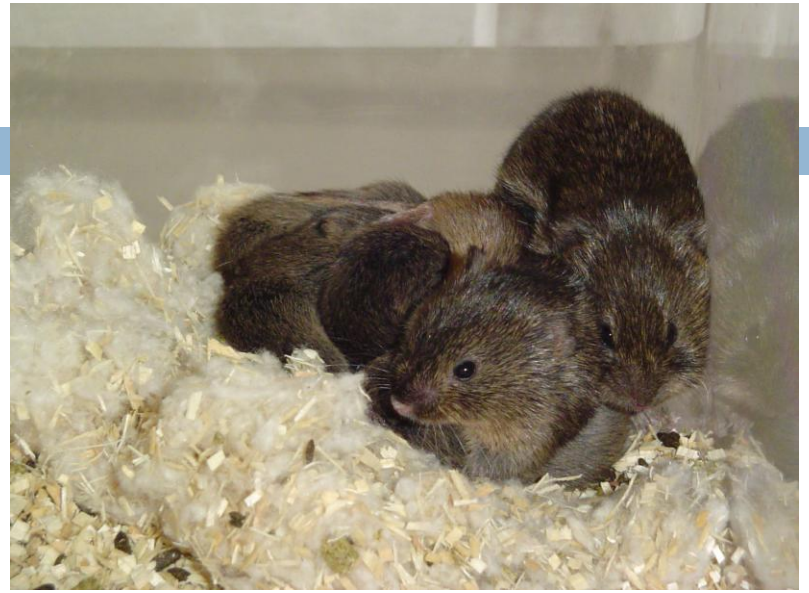
IT'S NOT LOVE.
IT'S OXYTOCIN.

The Prairie Vole Story

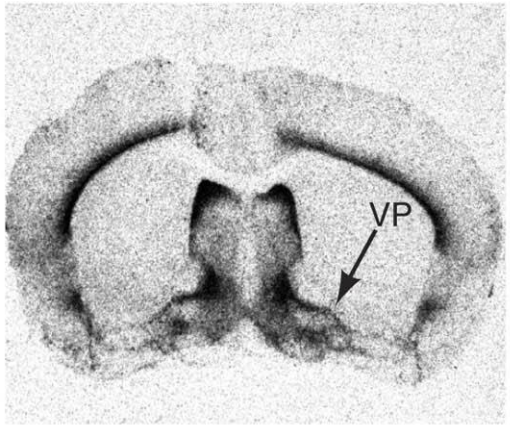
(a)

(b)





(c)



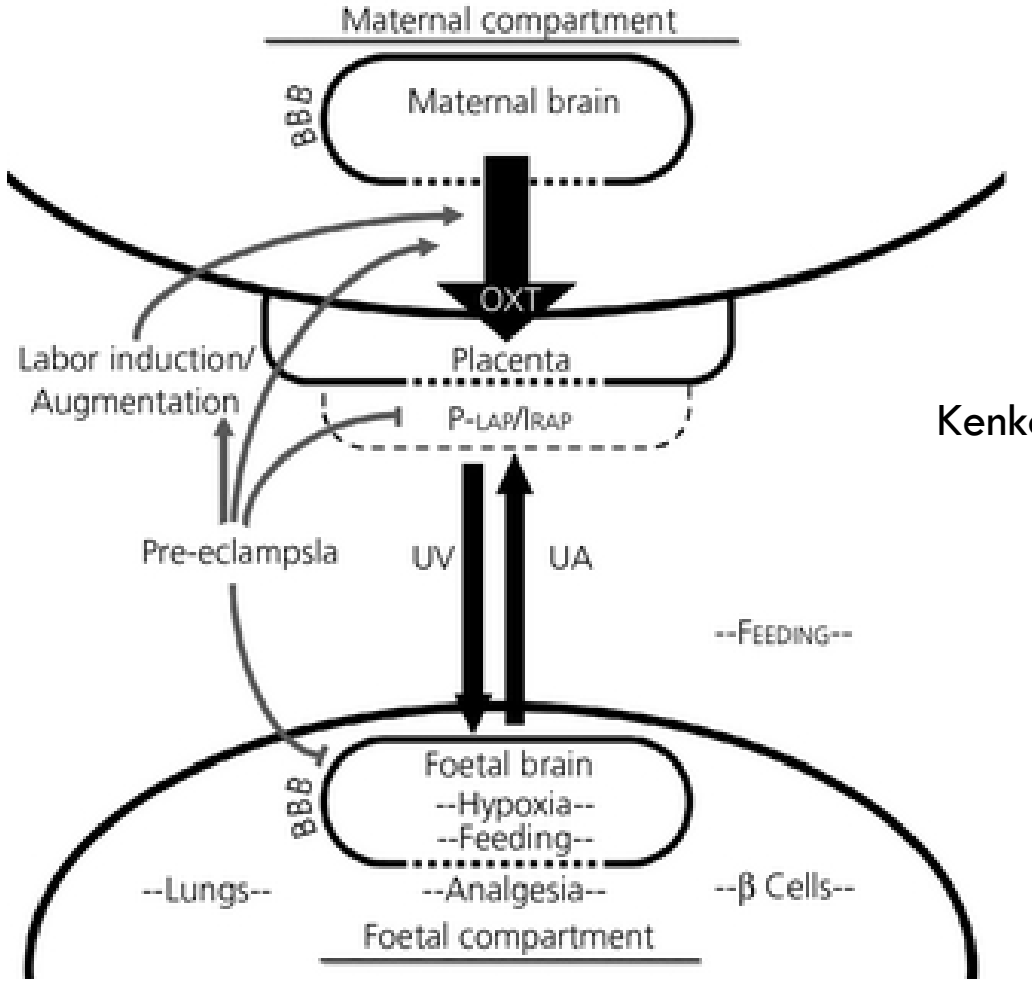
BIOLOGICAL PSYCHOLOGY, Fourth Edition, **Figure 5.20**

Clinical Manipulations of Oxytocin

- "Pitocin" – artificial oxytocin – is used to induce labor in delivery rooms
- Labor induction rate in the U.S. is 30-40%
- Oxytocin antagonists are used to delay preterm labor

Kenkel et al., 2014

Journal of Neuroendocrinology
Volume 26, Issue 10, pages 739-749, 16 SEP 2014 DOI: 10.1111/jne.12186
http://onlinelibrary.wiley.com/doi/10.1111/jne.12186/full#jne12186-fig-0001



Kenkel et al., 2014

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http://onlinelibrary.wiley.com/doi/10.1111/jne.12186/full#jne12186-fig-0002

Pharmacological Manipulation of Oxytocin

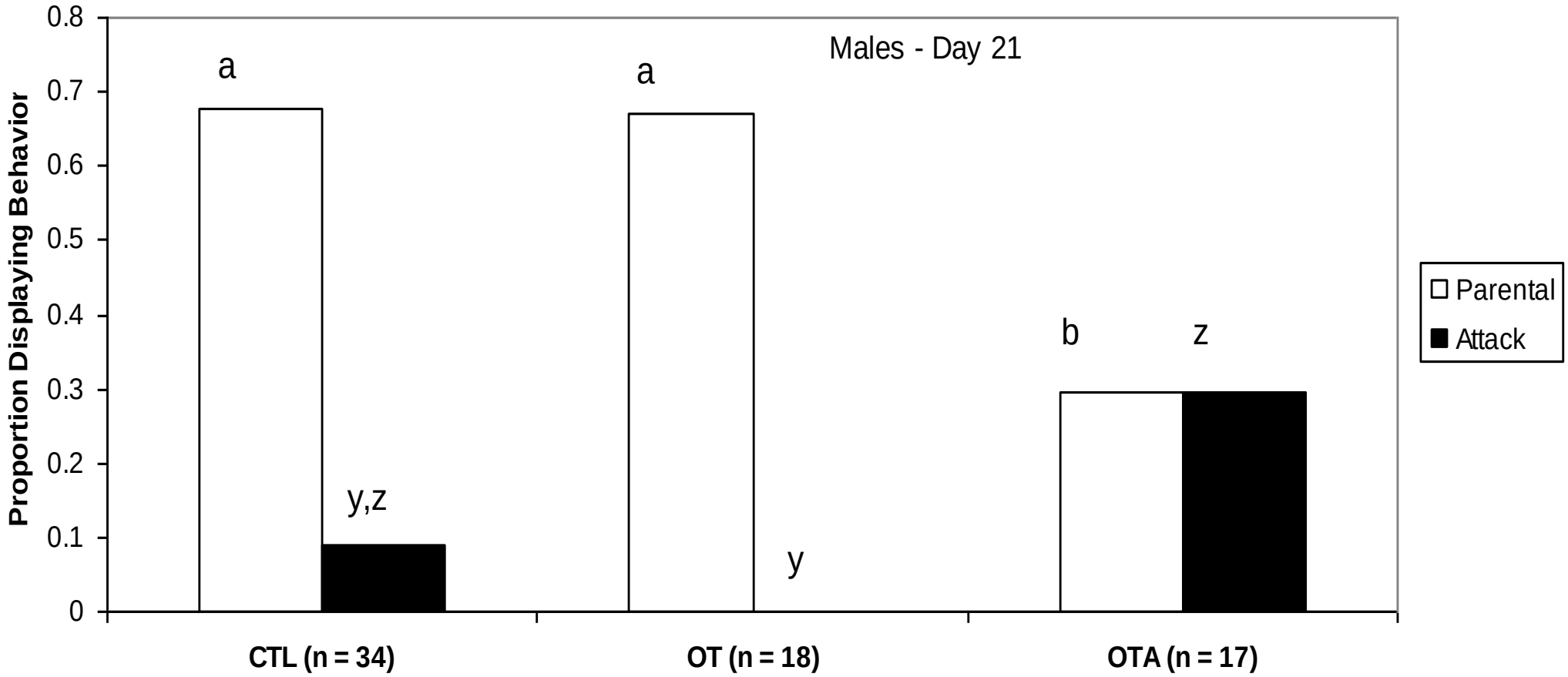
- Gregory et al., 2013 showed that male children who underwent labor induction or augmentation had a 23% higher chance of an autism diagnosis (35% if they received BOTH labor induction and augmentation)
- Female children whose mother's labor was induced or augmented also had a higher risk of autism (but lower than in males)

- These studies modeled PITOCIN or ATOSIBAN administration

Methods

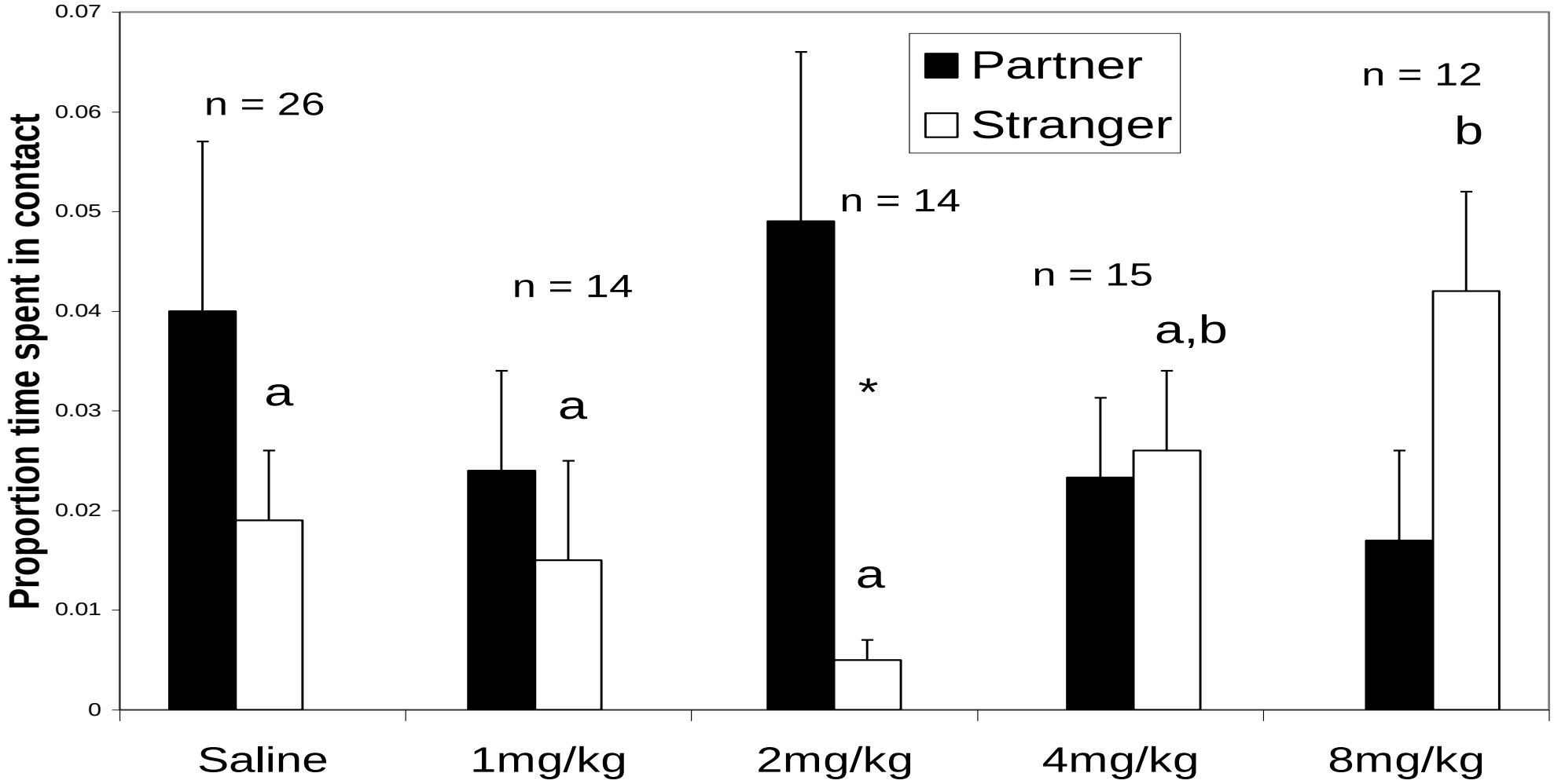
- On day 1 of life, vole pups received an injection of either:
- 1) Oxytocin (OT)
- 2) Oxytocin antagonist (OTA)
- 3) Saline (SAL)
- 4) They are handled only (HAN)
- Tested: alloparental care, partner preference, plus-maze, and intrasexual aggression

Exposure to OTA reduces alloparental care in males



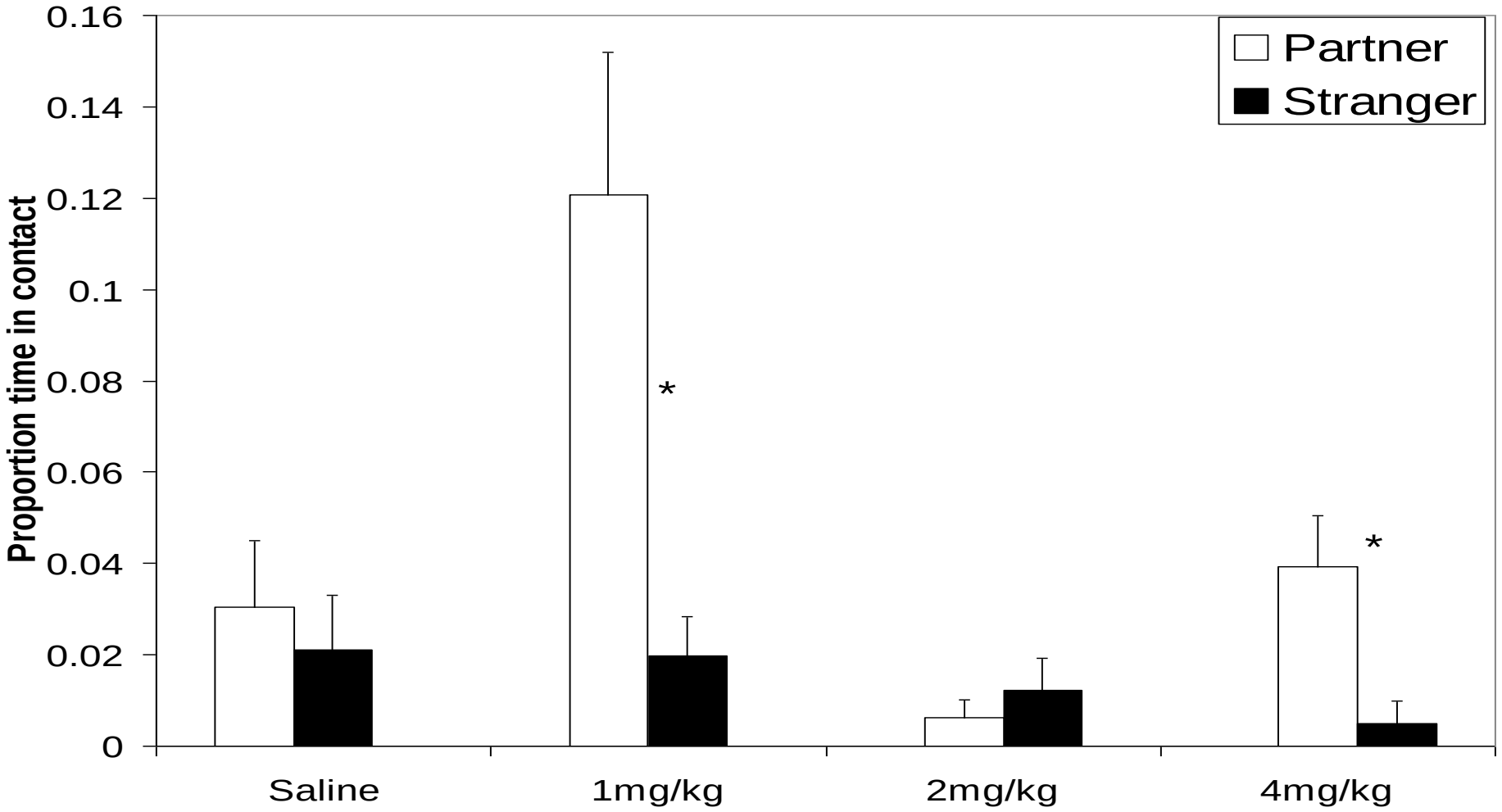
Bales et al., Developmental Psychobiology, 2004

OT shows a dose-response on pair-bonding in females



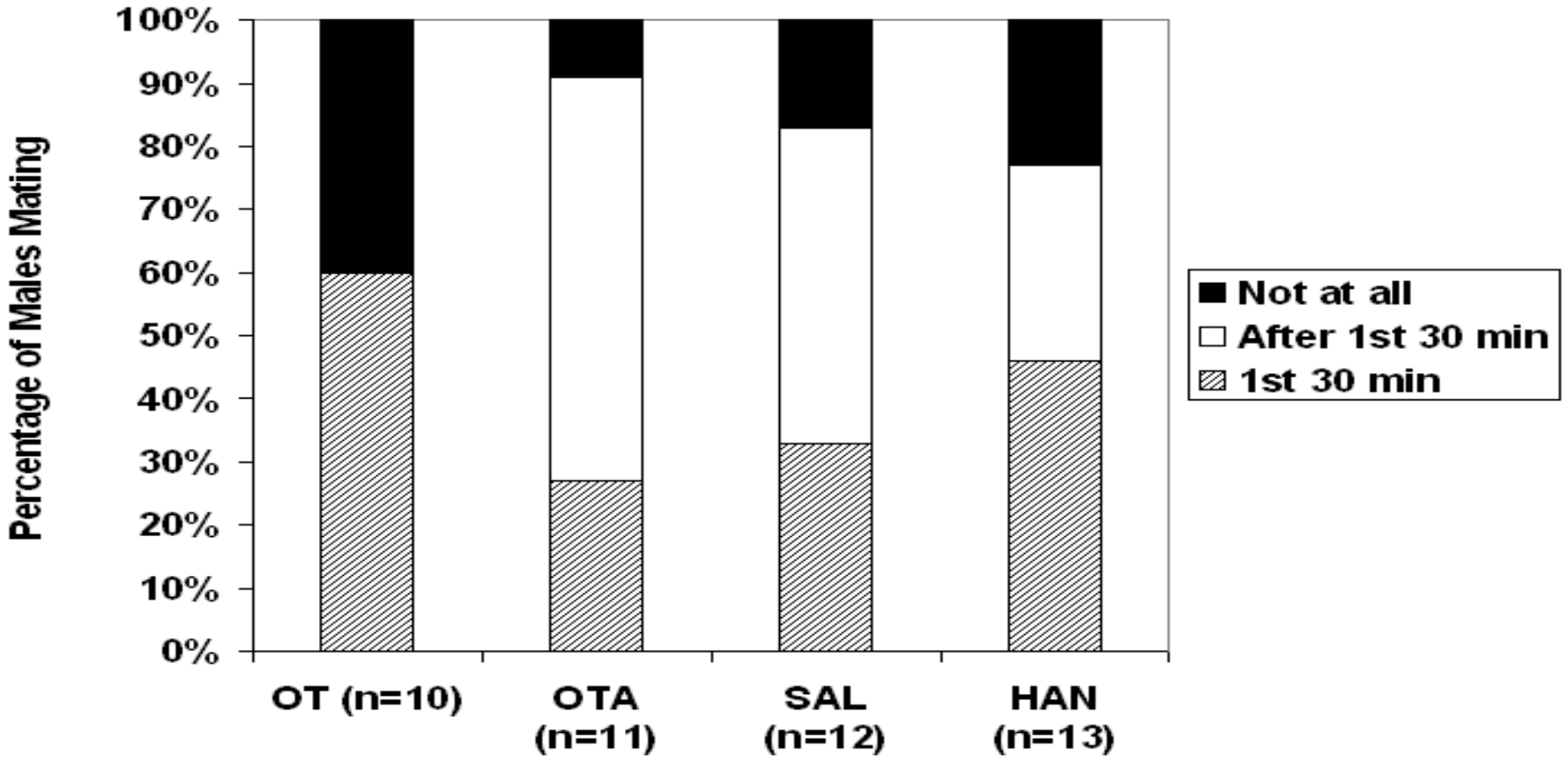
Bales et al., Hormones and Behavior, 2007

Male dose-response

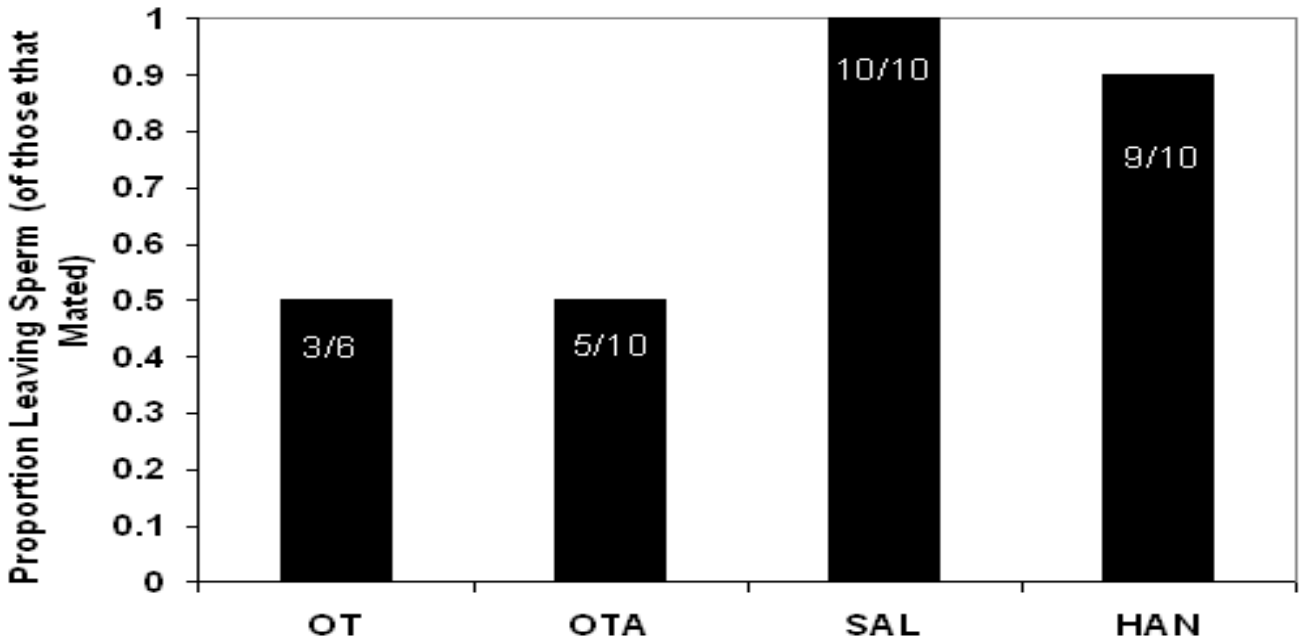


Carter et al., 2008

Early OT/OTA changes reproductive potential in males



Bales et al., Physiology & Behavior, 2004



Bales et al., Physiology & Behavior, 2004

Results of Neuroanatomical Studies

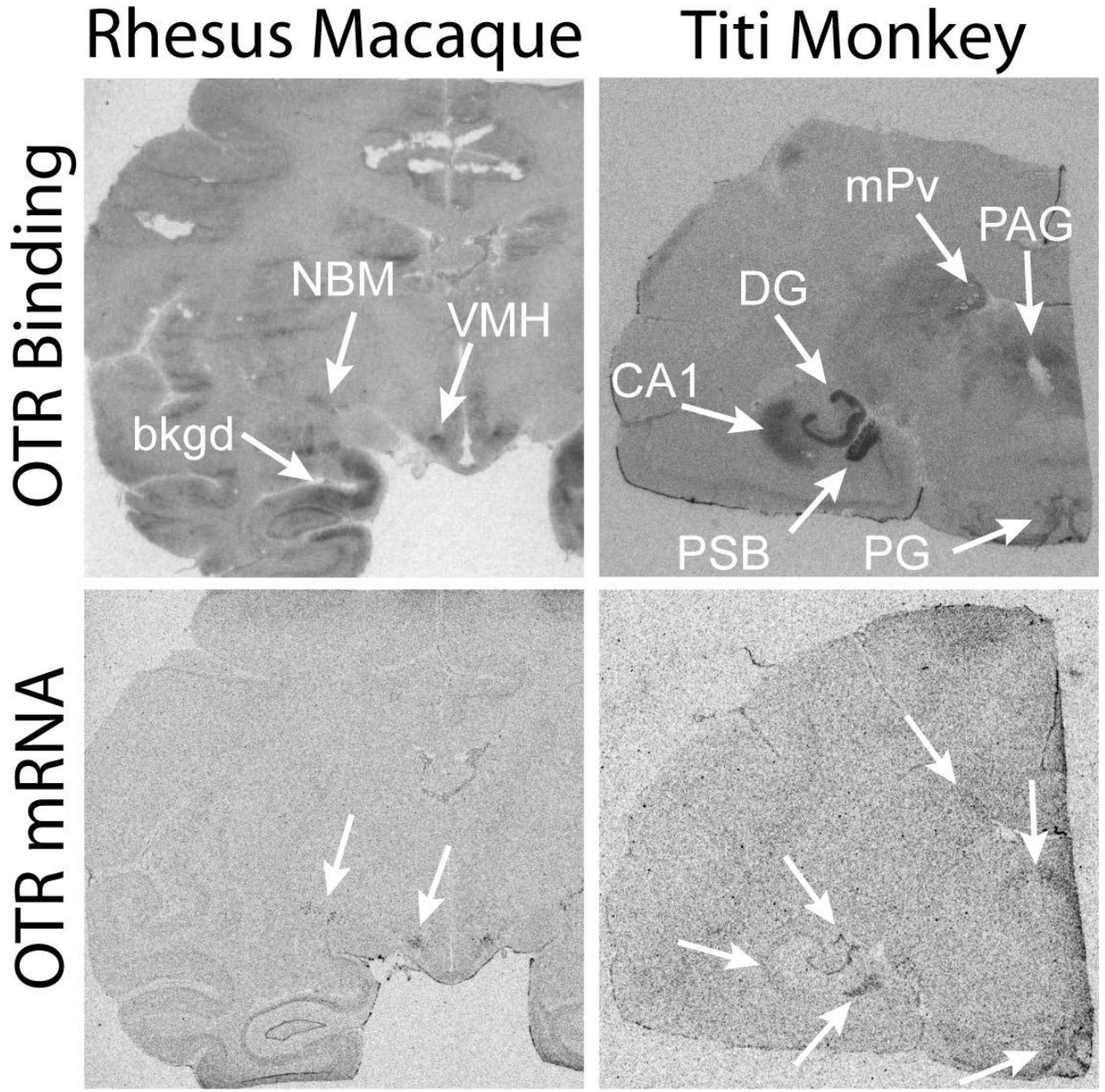
- No changes in OT production at 60 days (Kramer et al., 2007)
- No changes in OT receptors or dopamine D2 receptors at 60 days (Bales et al., 2007)
- Multiple changes in vasopressin V1a receptors in both sexes (Bales et al., 2007)

Titi monkeys (Callicebus cupreus)

Monogamous, New World primates

Small family groups

Adult pair-mates form a bidirectional social bond



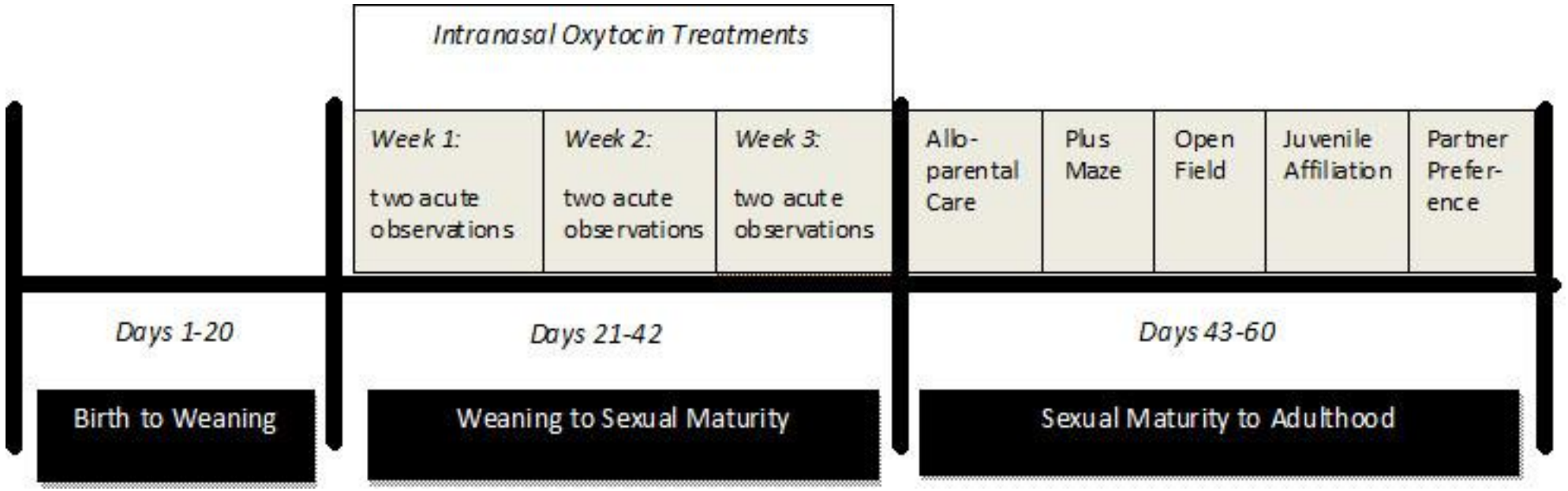
Courtesy of Sara Freeman; Freeman et al., 2014

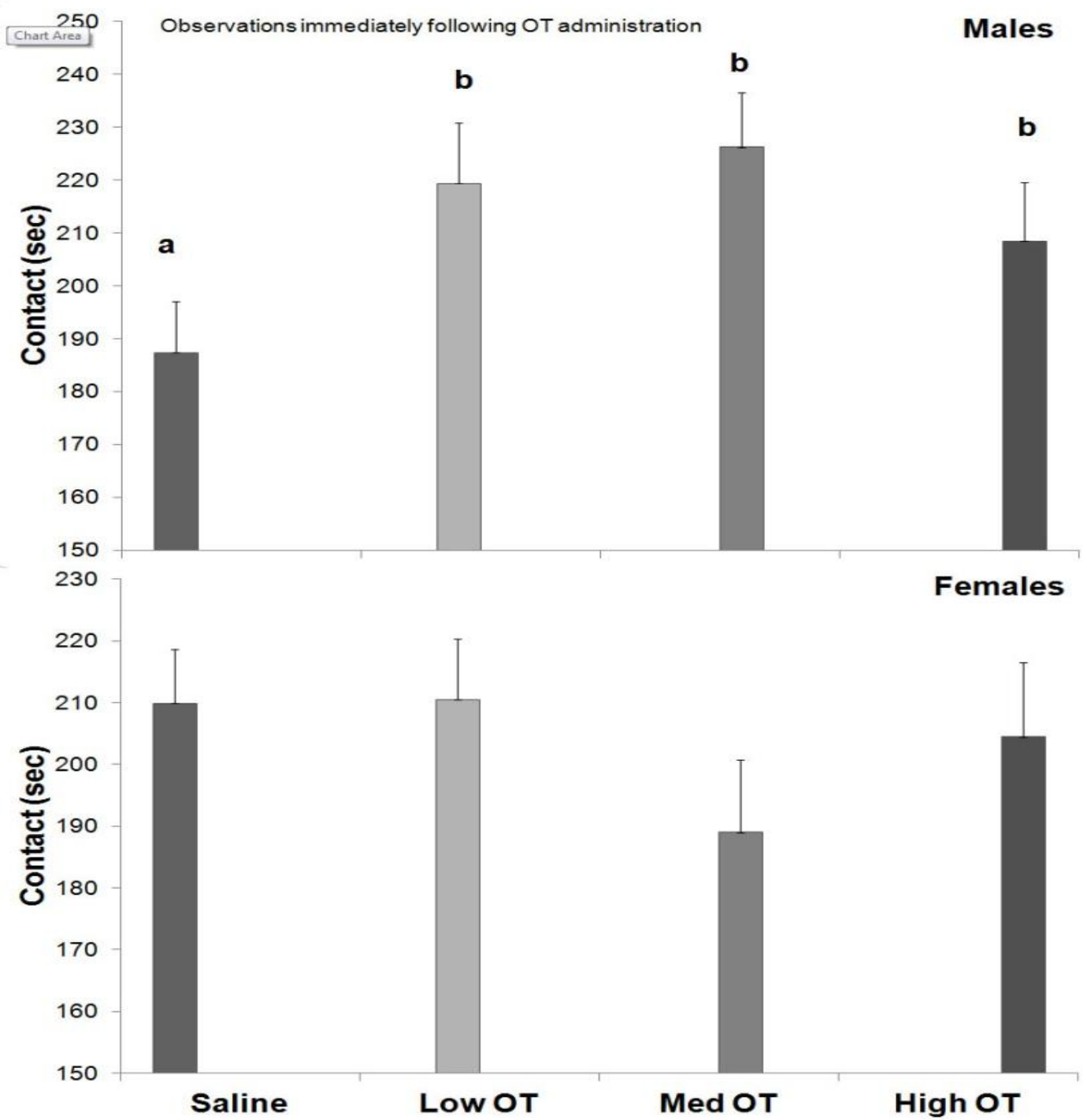
Intranasal Oxytocin

- Chronic intranasal OT is already in clinical trials for use in schizophrenia, autism, social anxiety, etc.
- No previous animal testing for long-term effects
- GOAL OF THIS SERIES OF STUDIES: DETERMINE LONG-TERM EFFECTS OF DEVELOPMENTAL EXPOSURE TO INTRANASAL OXYTOCIN IN:
  - A socially monogamous rodent
  - A rodent model of autism
  - A socially monogamous primate
- Focus on social behavior, repetitive behavior, and neural substrates

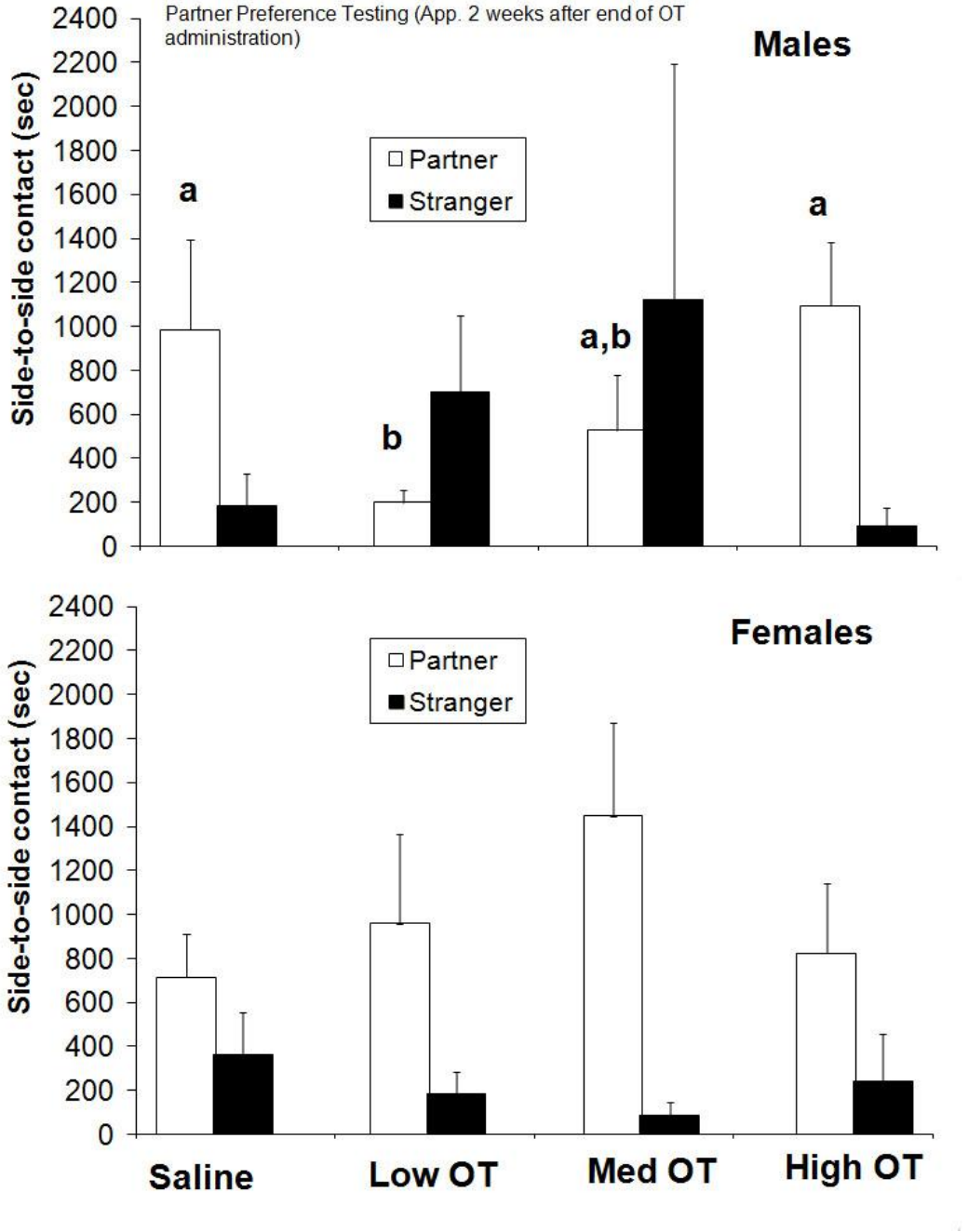
Intranasal oxytocin

Study Timeline - Voles





Bales et al., 2013



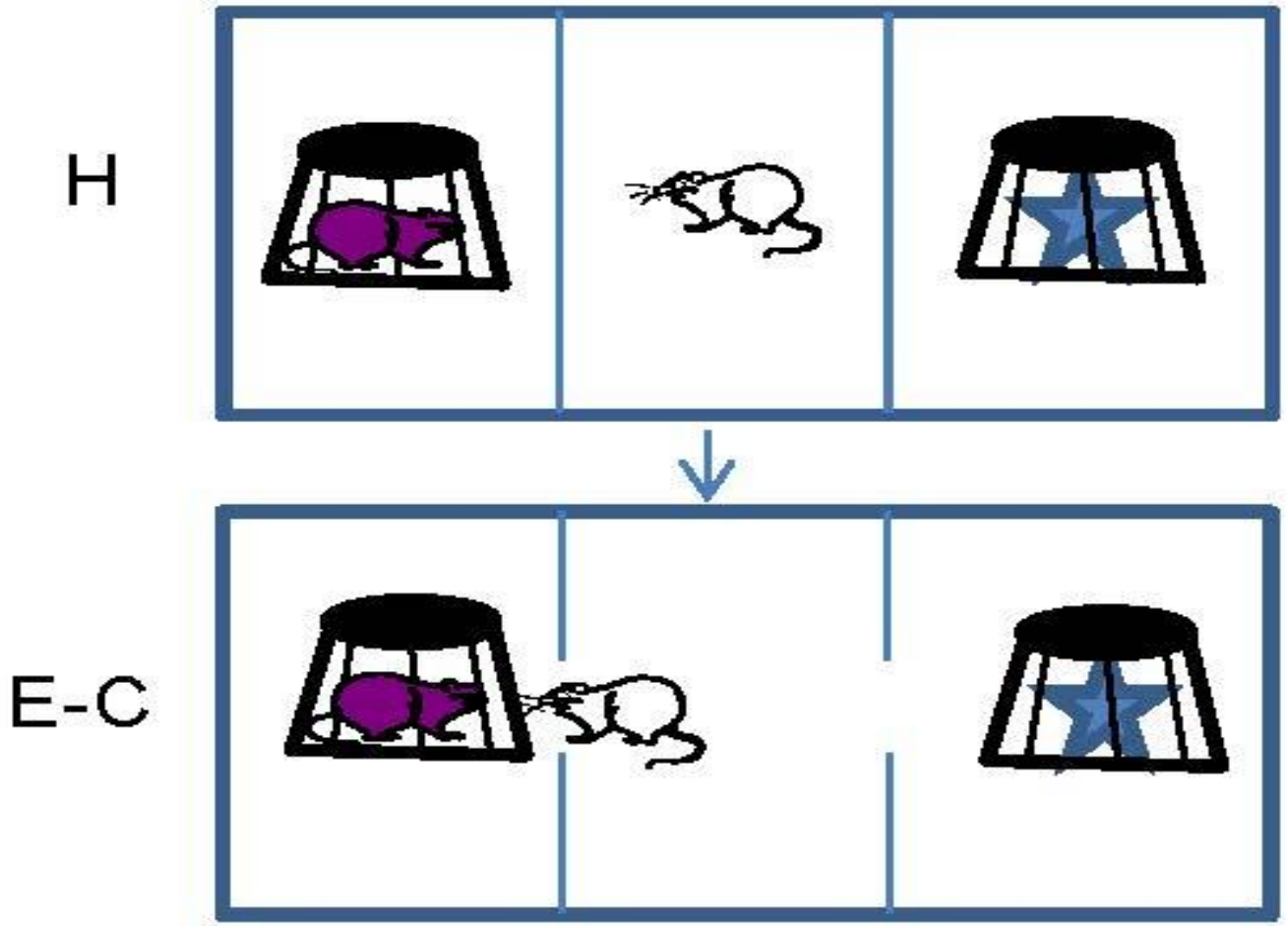
Bales et al., 2013

Intranasal OT administration in mice

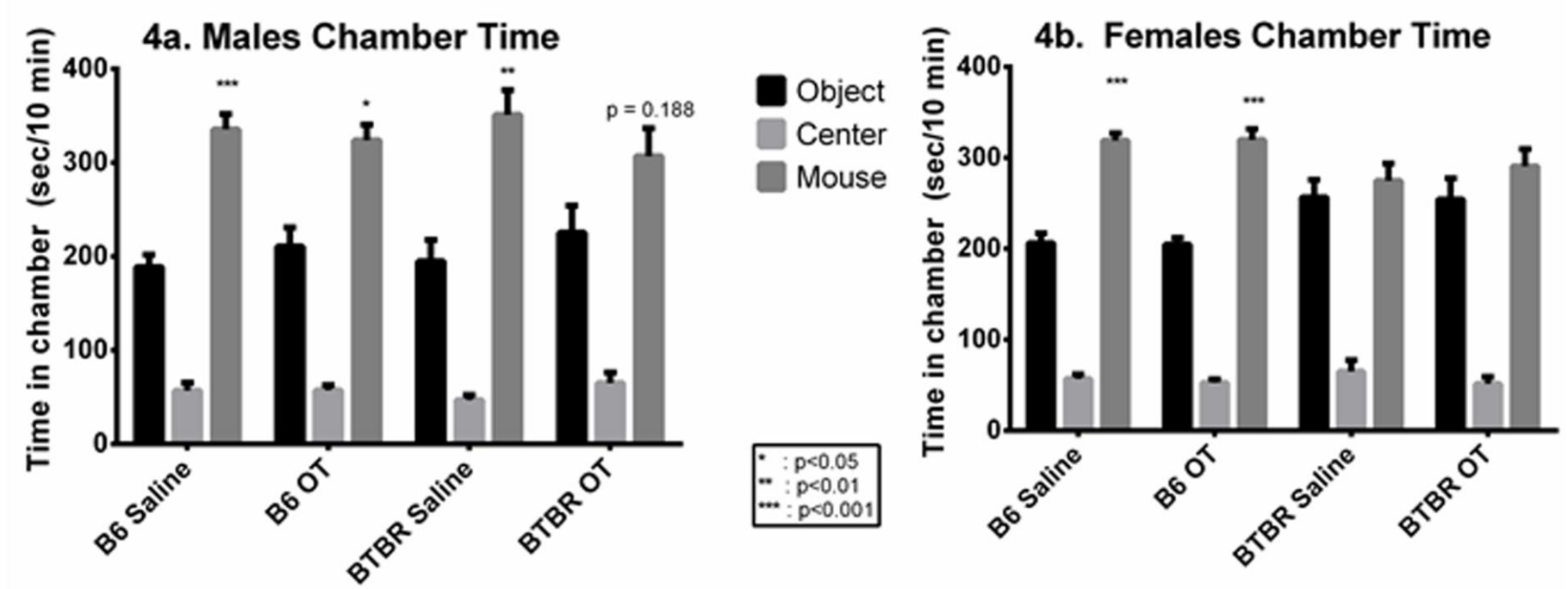
- BTBR T+ Itpr3tf/J (BTBR) mice are a mouse model of low sociability
- C57BL/6J mice are a strain control
- Results: Few to no effects of intranasal OT

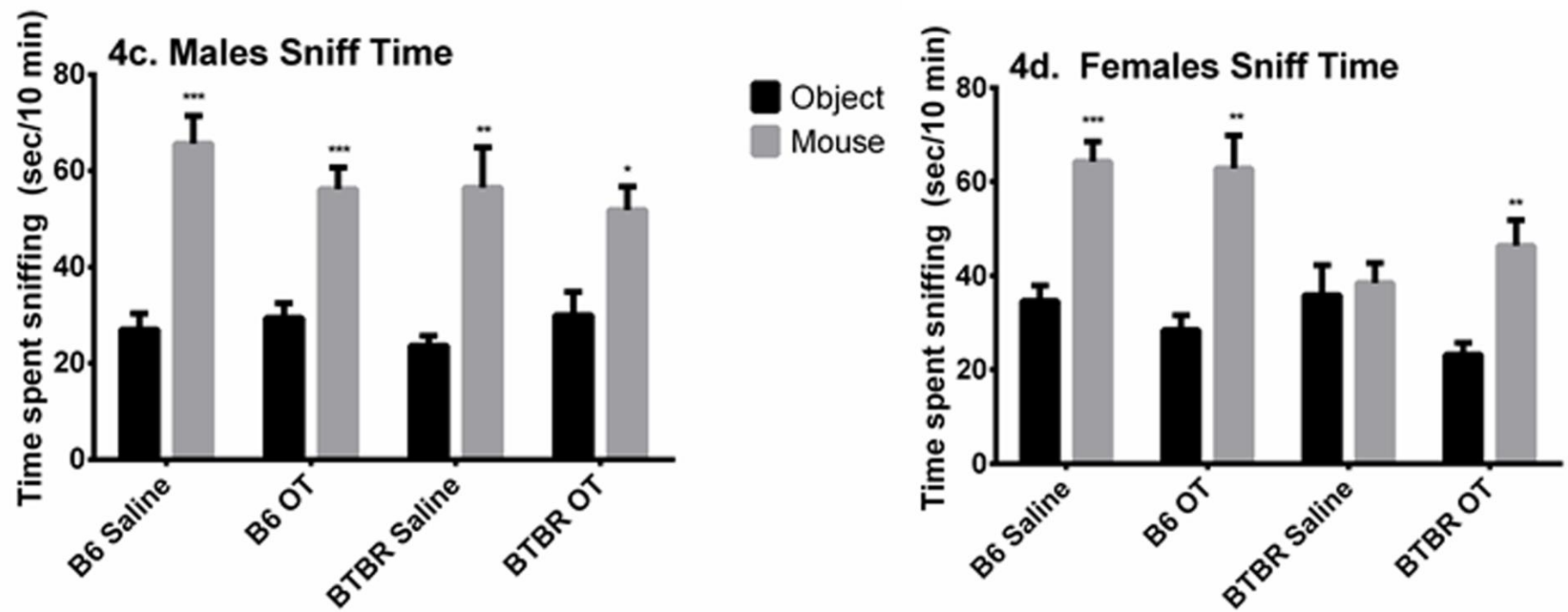
Sociability

Conspecific *vs* control object



"Crawley test"
Diagram from Millan and Bales 2014





Bales et al., Translational Psychiatry, 2014

Intranasal Oxytocin Administration

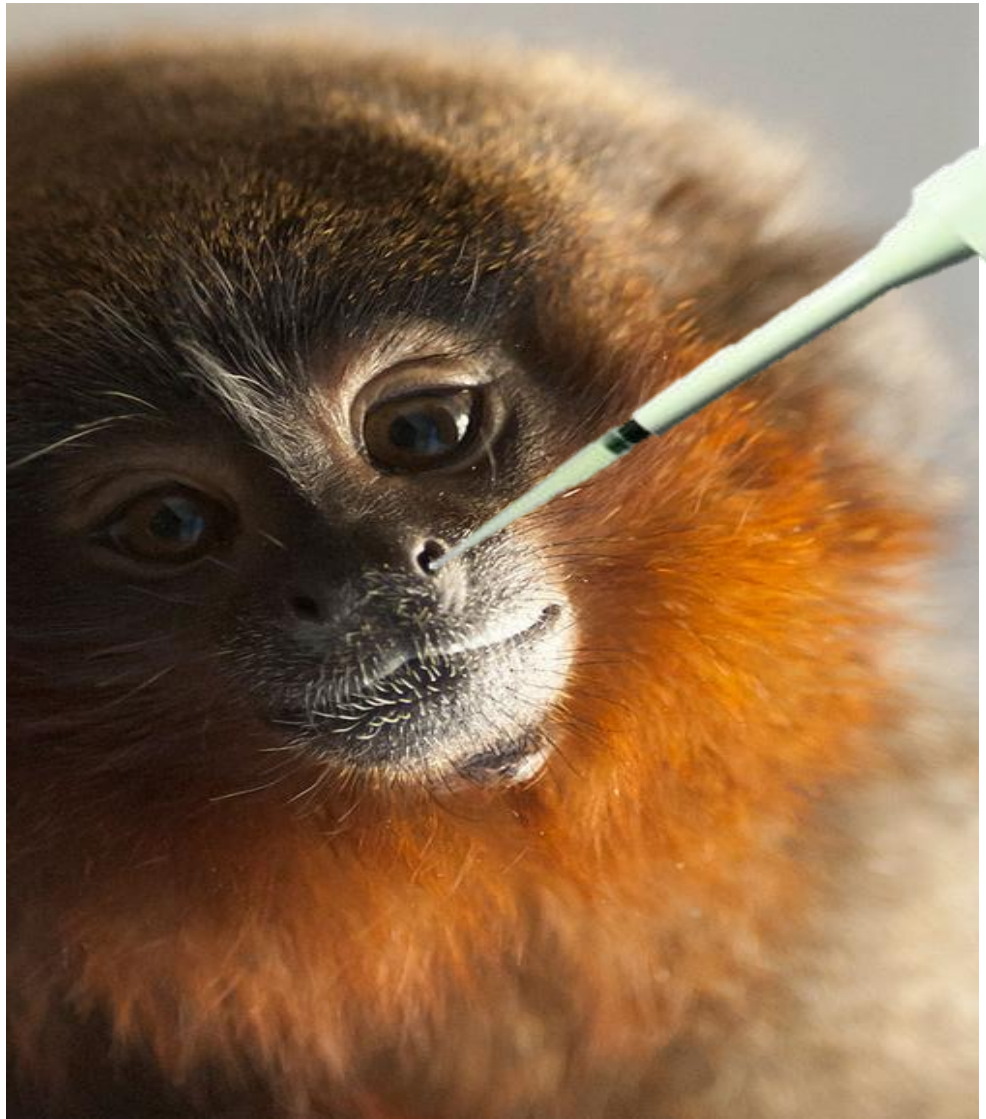
- **Treated monkeys once per day from the age of 12 to 18 months**

- **Chronic intranasal OT at 0.8 IU/kg dissolved in 50ul of saline (n=6) or saline (n=5)**

- **Medium dose**

(based on clinical studies)

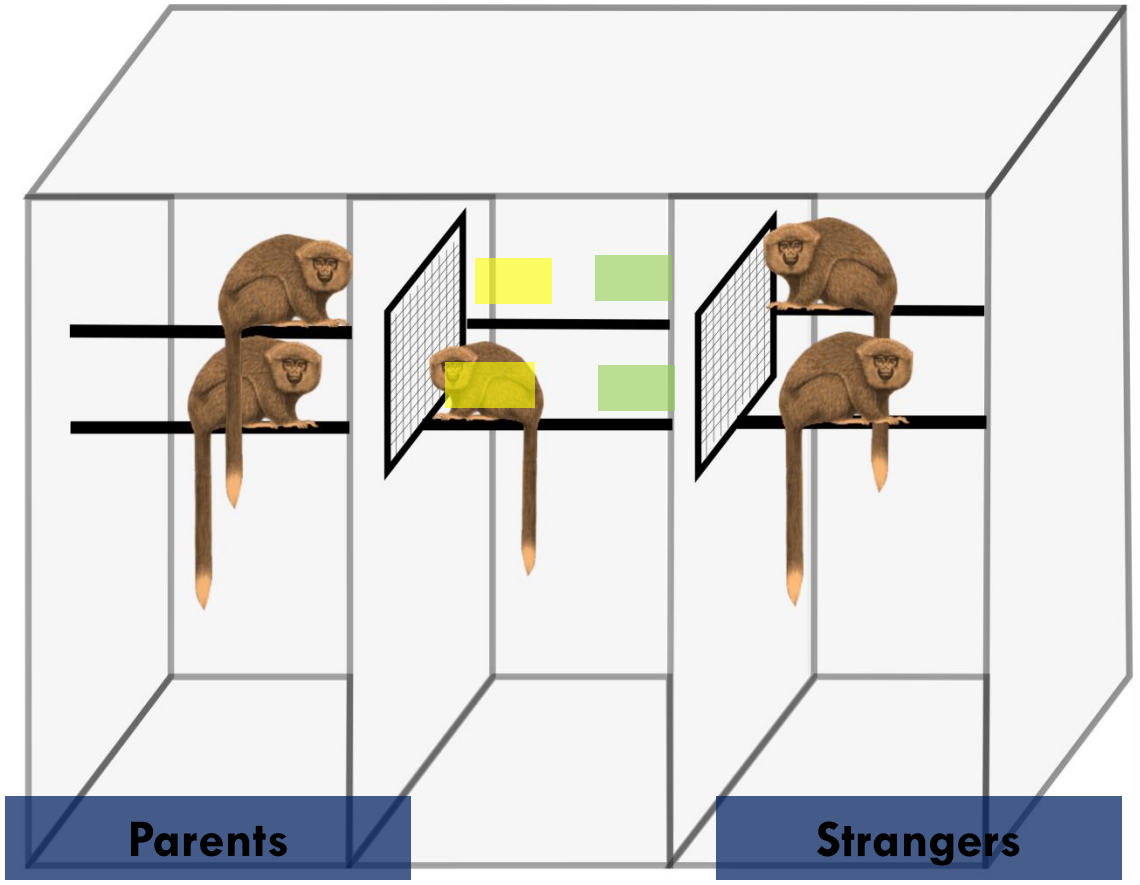
- **Late juvenile and pubertal period**



Titi monkey Parent Preference Test

Prairie vole Partner Preference Test

Williams et al. 1992



Carp, Rothwell, et al., in review

(Unpublished data slides removed)

Conclusions – intranasal studies

- **Effects of intranasal oxytocin may be long-lasting, different by sex, may differ between rodent species and between rodents and primates.**

- **Obstetric and other clinical uses of oxytocin may have long-lasting effects on offspring – and the effects on mothers are mostly unstudied.**

- Collaborators: Drs. Sally Mendoza, Suma Jacob, Marjorie Solomon, Jacki Crawley, Jill Silverman, Al Conley, Trish Berger, Helena Snyder
- Post-docs: Drs. Tamara Weinstein, Sara Freeman and Adele Seelke
- Graduate Students: Dr. Benjamin Ragen, Dr. Allison Perkeybile, Emily Rothwell, Rebecca Larke, Rocio Arias del Razo, Trent Simmons
- Technical Staff: Julie Van Westerhuyzen, Jessica Bond, Sarah Carp, Charlotte Blanz, Griffin Downing, Elizabeth Sahagun, Leana Goetze, Kyle Puhger, Mike Pride
- Many excellent undergraduates
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- Monkey photos by Kathy West

Questions??