

Objective

- Maternal-offspring interaction highlights key moments in which social bonding and somatosensory experience are combined to allow for proper maturation from infancy into juvenile life stages.
- The purpose of this project is to evaluate circuit-specific mechanisms of maternal touch in infant brains.
- OXT may act as a modulatory agent in the periphery through maternal-offspring interactions and may modulate touch activity within the thalamus during social touch.
- In this study, we will evaluate if there are sex and/or treatment effects of OXT stimulation on c-Fos activity in specific thalamic nuclei through a model of social touch in early postnatal mice.

OXTR ligand binding is present in neonatal mouse

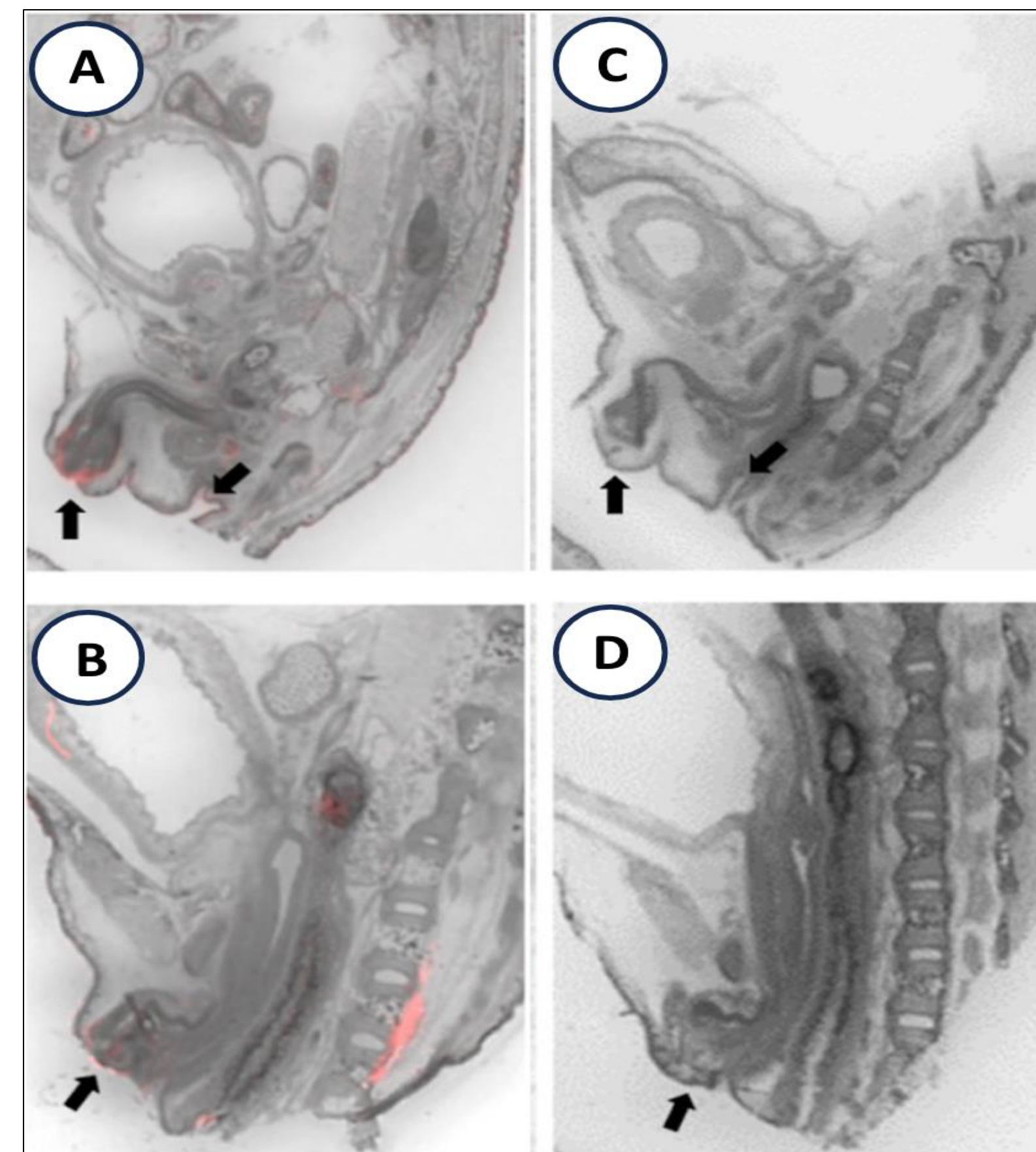


Fig 1. OXTRs are present in the external anogenital area of neonatal OXTR WT mice, A and C display a male P0 C57BL/6J mouse, and B and D display a female P0 C57BL/6J mouse. OXTR was identified by receptor autoradiography and pseudo-colored red. A and B convey OXTR's in the anogenital region (black arrow); C and D represent OXTR KO mice (P0 C57BL/6J mice), with no site for OXTR ligand binding. Image copied from Greenwood and Hammock, 2017(3).

- Exogenous OXT interacts with peripheral OXT receptors (OXTRs). Peripheral OXTRs were found in the oronasal cavity, eye, whisker pads, adrenal gland, and anogenital region in the neonatal OXTR WT mouse(1).
- Peripheral manipulation of OXT or OXT antagonists within neonatal mice affected the development of social behaviors(2).

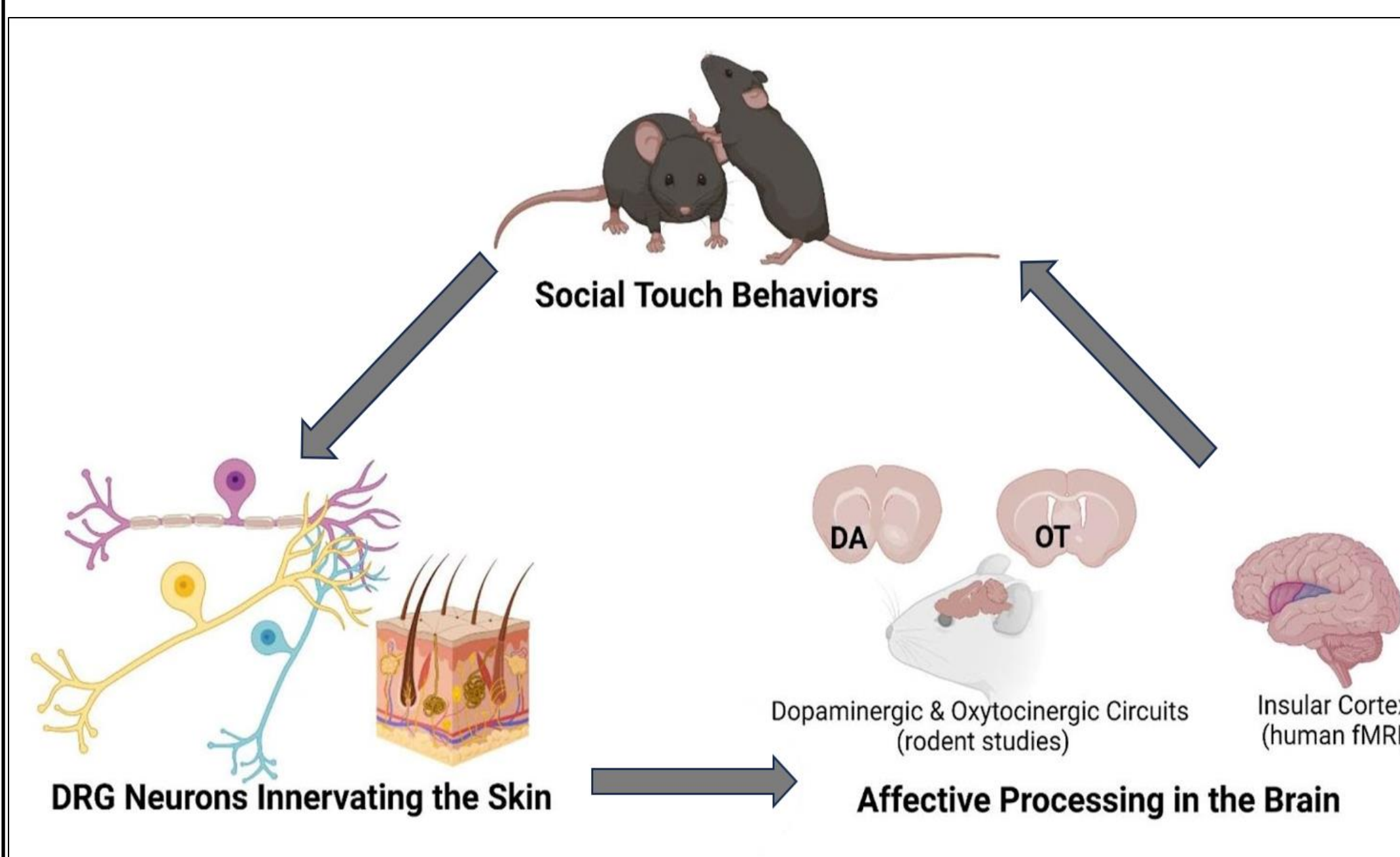
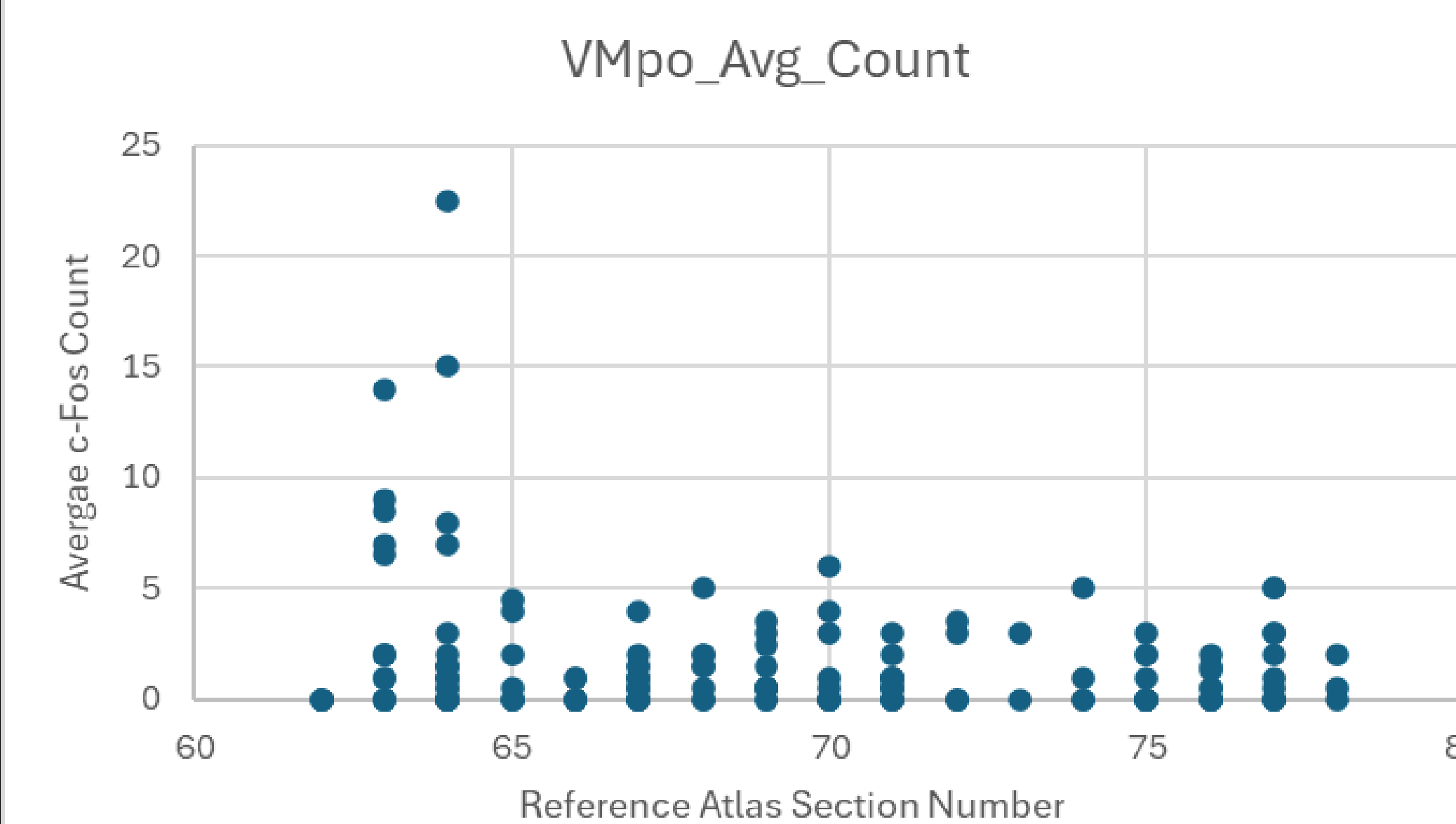
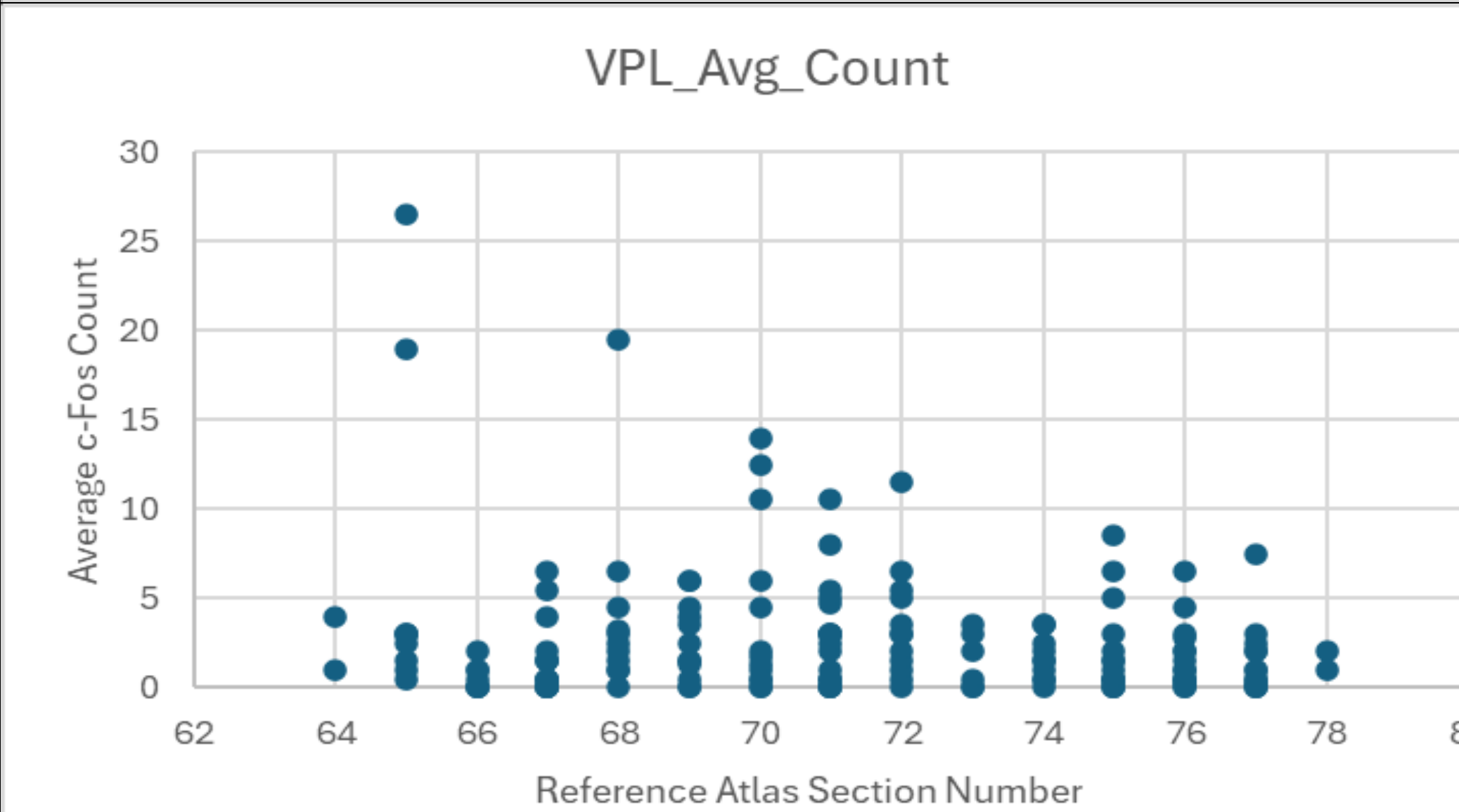
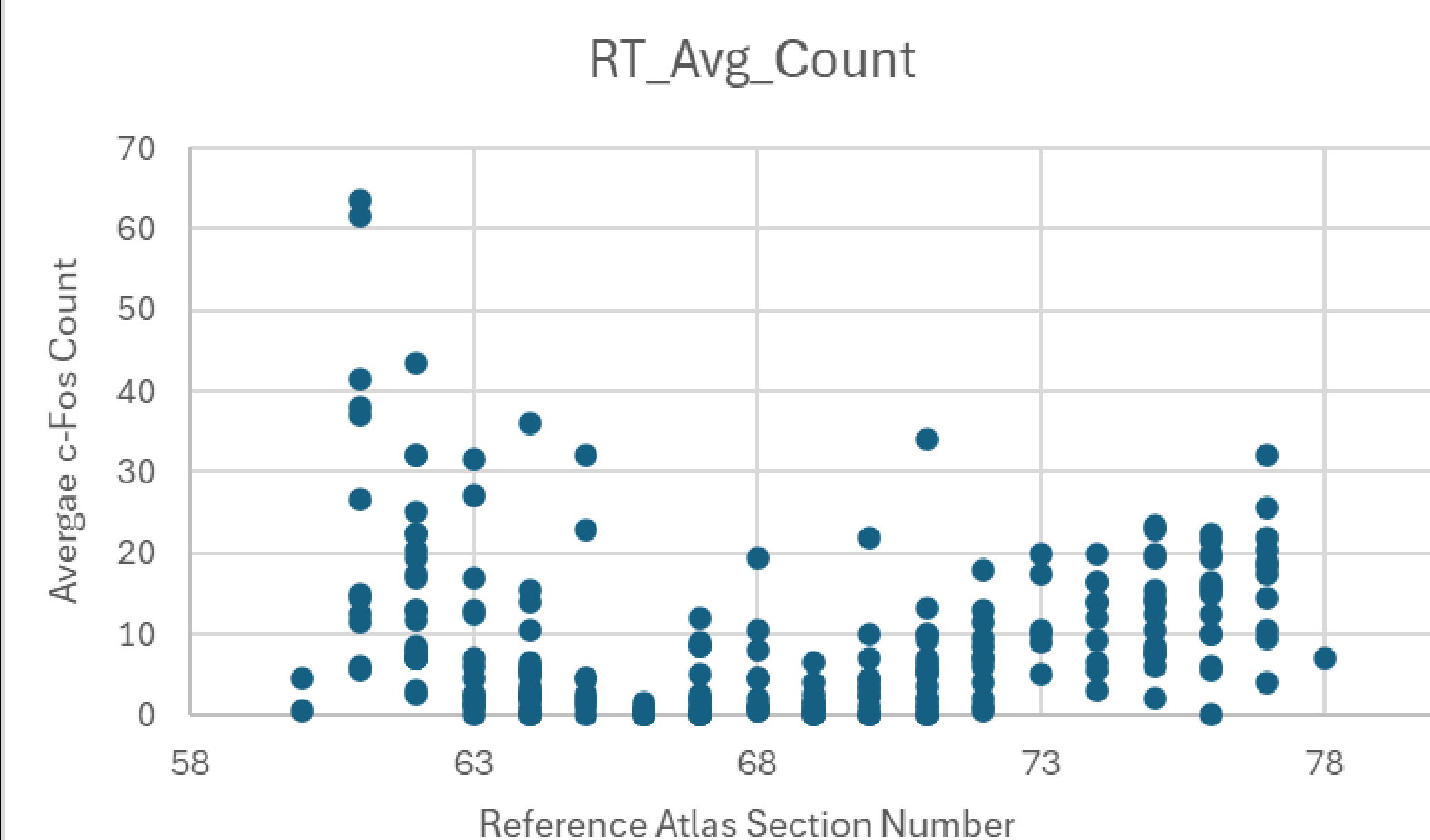


Fig. 2 peripheral activation of somatosensory neurons leads to activation of neural circuitry related to social touch behavior. Image copied from Elias and Abdus-Saboer, 2022(4).

- “Social touch” model mimics the maternal-offspring interaction by emulating the **anogenital stimulation** that occurs during maternal licking of infant rodents, which is required in neonates to induce micturition.
- Infant mice possess OXTR in the anogenital region, in which salivary levels of OXT may act upon these receptors during the grooming process.

Rostral to caudal anatomic changes in thalamic nuclei

- Differences in total representative atlas section images per nuclei
- Anatomical coordinate system to investigate effects of changing nuclei shape and size on treatment effects
- Changes in average c-Fos count for different Reference Atlas sections
- Lead to differences in c-Fos density and total percent area within the nuclei



Summary

1. OXTR ligand binding is observed in neonatal C57BL/6J mice.
2. Initial ANOVA analysis indicated no treatment effects or interactions with sex.
3. C-Fos activity is not uniform across the rostro-caudal axis of thalamic nuclei.
4. Use variability in c-Fos activation across Reference Atlas sections of nuclei to subset analysis for treatment effects and/or interaction with sex.

Implications

Investigation into activity-dependent changes in thalamic nucleus c-Fos activation as a result of social touch is important in understanding the influence of maternal care in postnatal development, specifically social bonding interactions. This project will allow for us to breakdown the mechanisms by which peripheral OXT reception and OXTR activation can modulate CNS activation. This has implications for when there are deficits in OXT signaling, which may be connected to atypical sensory-social responses associated with ASD.

This will be tested in future experiments by investigating differences in c-Fos activation based on treatment effects for specific subsets of Reference Atlas sections within each thalamic nucleus. Additional investigation into treatment effects on a specific subpopulation of cells involved in sensory gating and their c-Fos activation will be conducted within the RT based on anatomical changes.

Acknowledgements

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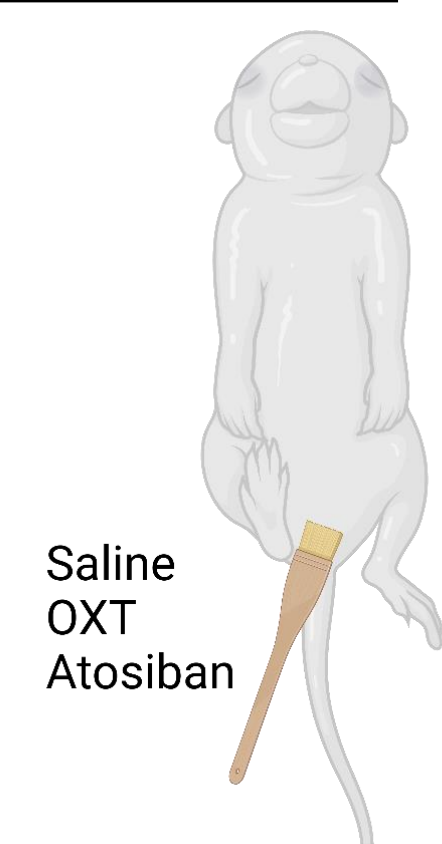
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References

1. Tabbaa, & Hammock, E. A. D. (2020). Orally administered oxytocin alters brain activation and behaviors of pre-weaning mice. *Hormones and Behavior*, 118, 104613.
2. Mogi, Kazutaka, Ooyama, R., Nagasawa, M., & Kikusui, T. (2014). Effects of neonatal oxytocin manipulation on development of social behaviors in mice. *Physiology & Behavior*, 133, 68–75.
3. Greenwood, & Hammock, E. A. D. (2017). Oxytocin receptor binding sites in the periphery of the neonatal mouse. *PLoS One*, 12(2), 1–15.
4. Elias, & Abdus-Saboer, I. (2022). Bridging skin, brain, and behavior to understand pleasurable social touch. *Current Opinion in Neurobiology*, 73, 102527.

Materials and Methods

Treatment

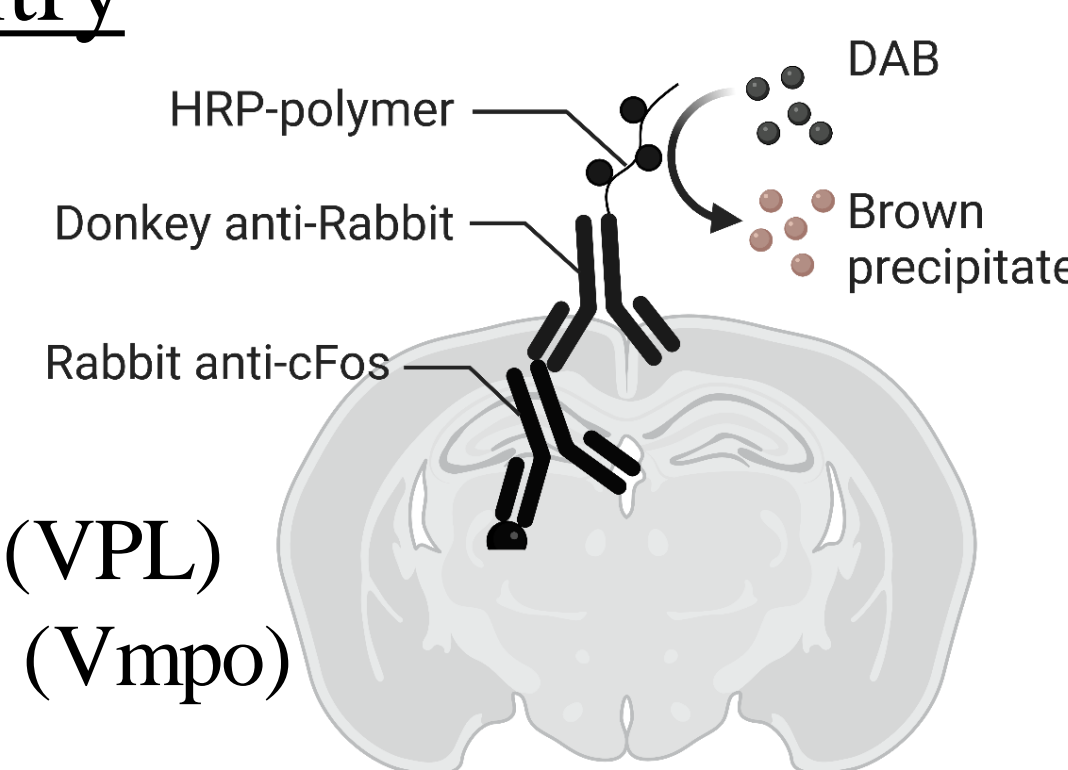


Male and female postnatal day 8 mice (P8) were randomly placed in one of four treatment groups.

- Handled
- Saline
- OXT (1µm)
- Atosiban (1µm)

Immunohistochemistry

c-Fos activity was labeled for quantification in three thalamic nuclei involved in somatosensation.



- Ventral posterior lateral (VPL)
- Ventral medial posterior (VMpo)
- Reticular (RT)

Analysis

2X Images corresponding to specific Allen Brain Reference Atlas image (Sections 60-77) for proper ROI analysis.

c-Fos density was obtained with Image J. An analysis for main effects of sex or treatment or their interaction will be conducted through a 2-way ANOVA.