Effects of Sex and Autism on Oxytocin Receptors in the Substantia Nigra of the Human Brain

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I. Introduction

- Oxytocin (OT) has been shown to be vital to social function in animals. Previous work from our group discovered oxytocin receptors (OXTR) in the human substantia nigra (SN), which may play a role in social deficits in individuals with Autism Spectrum Disorder (ASD).
- The SN is composed of two subdivisions: the dopaminergic pars compacta and the GABAergic pars reticulata.
- The aim of the current study is to determine in which subdivision of the SN OXTR are, in order to more accurately evaluate the effects of sex and ASD on OXTR density.
- Future directions of this research are aimed at defining the role of the oxytocin system in individuals with ASD.

II. Methods

- Unfixed, frozen blocks of de-identified human brain tissue were provided by the University of Maryland Brain and Tissue Bank, which is a Brain and Tissue Repository of the NIH NeuroBioBank.
- Sample size of 30 (8 typically developing males, 7 typically developing females, 8 males with ASD, 7 females with ASD)
- Brain blocks stored at -80°C, brought to -20°C and sectioned at 20µm on a cryostat
- Oxytocin receptor autoradiography performed as described previously (Freeman et al. 2018)
- Immunohistochemistry for tyrosine hydroxylase (TH), used to identify the locations of dopaminergic regions
- Images taken with a light microscope at 2.5X

Figure 1 – Examples of autoradiograms showing oxytocin receptor binding density

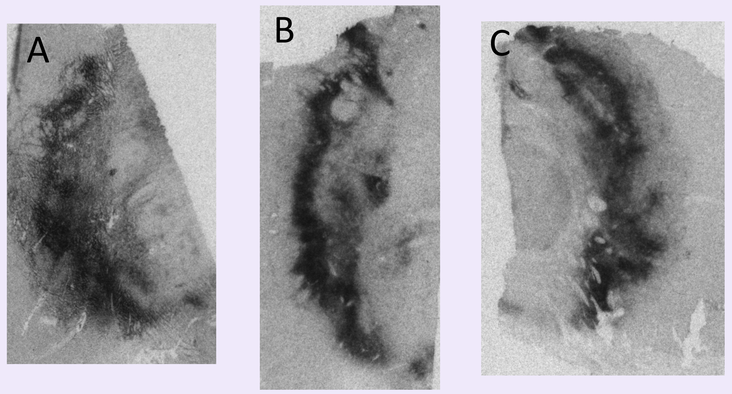
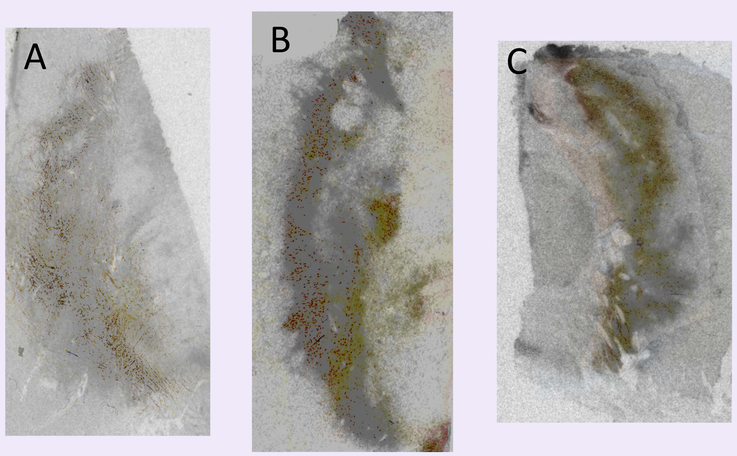


Figure 2 – Examples of dopaminergic neurons (red and orange) superimposed on the films from figure 1



III. Results

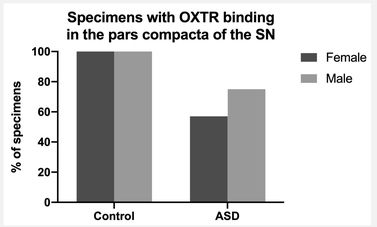


Figure 3 – percentage of specimens showing OXTR binding in the pars compacta. All the control specimens showed overlap with the pars compacta while the ASD specimens expressed greater variance in OXTR density and location.

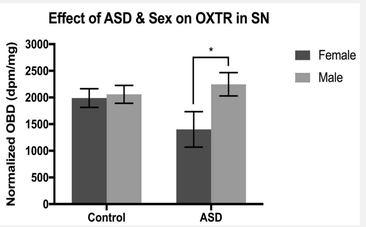


Figure 4 - previous data from our lab quantifying OXTR binding in the entire SN. However, this data was not anatomically informed and did not account for potential differences between subregions of the SN.

IV. Conclusions

- Once a boundary can be drawn between the pars compact and the pars reticulata, further analysis will take place using a digital densitometry system.
- Preliminary results suggest that oxytocin is active in the dopaminergic pars compacta and may play an important role in social reward pathways.
- Although the majority of the slides show overlap between the pars compacta and the dopaminergic neurons, some abnormalities were present in the tissue from individuals with ASD that will be quantified in further analyses.

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