VT School of Neuroscience
Faculty Recruitment Seminar

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"Mapping oxytocin receptors in primate brains: Implications for human social cognition"

October 12, 2017
11:00am – 12:00pm
Biocomplexity Institute Conference Room

Decades of research have shown that the hormone oxytocin (OT) acts as a potent neuromodulator in a variety of species to influence complex social behaviors, including social bonding, social memory, affiliation, and social reward. Administering intranasal OT to healthy humans can affect a suite of social behaviors, such as trust, eye contact, emotion recognition, socially-reinforced learning, and pair-bonding-related behaviors. Due to its ability to modulate social function in animals and humans, the OT system has been highly implicated in the neurobiology and treatment of autism spectrum disorder (ASD), a condition that is characterized in part by deficits in sociality. Clinical studies designed to test the effectiveness of intranasal OT treatment in adults and children with ASD have shown that intranasal OT can improve some aspects of social functioning in ASD. However, it has remained unclear where OT acts, i.e. where OT receptors (OXTR) are expressed, in the human brain.

Mapping the locations of OXTR in human brain tissue has previously been unreliable, due to the pharmacological cross reactivity and structural homology between OXTR and the closely related vasopressin 1a receptor (AVPR1a). The radioactively tagged ligands that are available to visualize OXTR and AVPR1a in brain tissue bind to both receptor types when they are used in primate brain. To remedy this problem, I developed a pharmacologically optimized modification of receptor autoradiography that finally accurately visualizes OXTR and AVPR1a in primate brain tissue. I mapped these receptors in two nonhuman primate species that differ in their social organization: the non-monogamous rhesus macaque and the monogamous titi monkey. Although there are some interesting species differences that may reflect differences in mating strategy between these two species, there are notable areas of conserved OXTR expression across all monkey species studied to date. Specifically, I found that the OXTR distribution in primates strongly co-localizes with the neural circuitry that underlies visual processing and attention. This result is interesting in comparison to the OXTR distribution across rodent species, where OXTR expression overlaps strongly with the regions responsible for olfactory processing. Thus, it seems that over evolutionary time, OXTRs are found in ecologically relevant brain regions that process stimuli from the sensory modality that is primarily used by that species to navigate its social environment (i.e. vision for primates and olfaction for rodents).

We have now begun to examine OXTR in postmortem human brain tissue and have evidence that OXTR expression is dysregulated in specific subregions of the ASD brain. In our analysis of OXTR density across five specific regions of interest, we found a significant effect of ASD diagnosis only in the nucleus basalis of Meynert (NBM) and the ventral pallidum (VP). In the NBM, which modulates visual attention, ASD specimens had significantly higher OXTR binding compared to controls, which may underlie the aberrant patterns of attention to social stimuli in ASD. In the VP, which is a reward area, ASD specimens had significantly lower OXTR binding compared to controls; low OXTR levels in VP may be related to a reduced experience of social reward in ASD. We also found a significant effect of age only in the VP, where OXTR binding decreases with age across all samples. Further analysis revealed a transient increase in OXTR in early life in control specimens, which was missing in ASD specimens. This result may reflect a critical period for maximal sensitivity to OT in this reward area of the brain in early childhood, between ages 2-5.

We have also reliably mapped OXTR and AVPR1a throughout the neurotypical male and female human brain. These receptors are located in regions that mediate functions like learning, memory, emotion regulation, and reward processing. These receptor maps can now be used to design targeted studies of the human brain in the future.

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