New Research Provides Model for Study of Biological Basis of Social Impairment in Autism: Duke University Study Investigates Brain Circuitry Underlying Social Attention

by Cure Autism Now

Researchers at Duke University Medical Center recently made strides in developing a model of social attention that can lay the groundwork for research into the neurobiological origins of limited social interaction in autism. The research program, led by Michael Platt, Ph.D., has focused on developing an animal model of complex social behavior which can be used as a model to understand human behavior. Animal models are important because they allow researchers to study the underlying neurobiology in a way that is not possible in humans. The models developed by Dr. Platt's laboratory will make it possible to develop biological models of social interaction in autism.

Because children are inherently social, and this social interaction is so important to their development, understanding the brain mechanisms supporting social attention is a fundamental and challenging goal for neuroscience. It is particularly important for understanding autism, in which one of the hallmark characteristics is a lack of, or deficiency in, social skills. In fact, one of the most profound deficits is impaired joint (or social) attention, which is the ability to orient one's attention to where others are directing theirs. Without this skill, it is difficult for children to engage with and learn from other people. The failure to develop appropriate joint attention has now been found to be one of the earliest deficits in autism (seen even by one year of age), and it is believed that many of the other developmental issues may be consequences of this early inability to read and follow simple social cues such as another person's eye gaze. Despite the importance of this skill, the brain mechanisms responsible for moderating social attention and the specific neuronal circuitry and chemicals involved remain relatively mysterious.

Dr. Platt characterizes the importance of an appropriate model system for proper study of the complex and fundamentally human challenge of social attention. "One reason for this knowledge gap is that fundamental brain processes – such as neuronal firing, synaptic changes, and biochemical alterations – cannot be studied directly in people, yet standard animal models like mice and rats do not display the same complex, visually-guided social behavior seen in humans. Finding an animal model system with similar behavioral tendencies as humans is thus vital for understanding the brain mechanisms supporting social motivation and attention and the manner in which these mechanisms break down in autism."

Dr. Platt and his colleagues have now developed methods for scientists to study what motivates individuals to look at social stimuli and how attention is reflexively shifted to follow the view point of another individual. These are the building blocks of shared attention, which seem to be uniquely lacking or deficient in individuals with autism. With support from Cure Autism Now (CAN), Platt and his colleagues have developed a new behavioral model of human social attention in monkeys ideally suited for neurobiological study. They have demonstrated that monkeys, just like typically-developing humans, look at faces and align their attention to where other individuals are looking. These behavioral responses can serve as a superb animal model for probing the brain mechanisms underlying human social attention.

The most recent CAN-funded study by Shepherd, Deaner, and Platt (2006) revealed that while directing their own attention, monkeys not only respond by reflex to other monkeys' faces, they also take into consideration identity and social status in their responses. This finding, that both

reflexive and voluntary brain circuits mediate the way monkeys jointly direct their attention, may provide insight into how the relationship between the two circuits leads to impairments in social attention in autism. The researchers found that the relative strength of these circuits depends upon a monkey's own social status. In nonhuman primates, social status depends strongly on the male hormone testosterone, so one hypothesis is that testosterone in humans is somehow involved in social attention as well. This may be relevant to autism because, as the authors note, autism is much more frequent in males than females.

These findings now pave the way for a range of neurobiological studies that would be difficult, if not impossible, to do in human subjects – particularly children with autism. Dr. Platt's goal is to identify the neural circuitry of social attention and to determine if the circuitry they ultimately identify can be impacted by other domains studied in autism, including many others also funded by Cure Autism Now (among them environmental interactions, hormonal modulations and genetic factors). Dr. Platt and his colleagues have already begun to probe the neural circuits mediating reflexive and voluntary social attention. Moreover, they are beginning to examine monkeys' attention responses following manipulation of hormones. They are especially interested in the role that peptide hormones such as oxytocin, also implicated in autism, may play in these circuits. They also plan to examine the eff ects of various pharmacological agents known to influence reward processing and mood, such as dopamine and serotonin, which are being independently studied for their roles in autism as well.

In the long run, uncovering the biochemistry which is generating the behavioral deficits in autism will make it possible for researchers to develop treatments that target the source of problems, rather than just addressing behavioral outcomes. Cure Autism Now's Science Director Sophia Colamarino, Ph.D. explains, "To understand what biological problems are at the core of autism and to try to fix them immediately, we must understand from where this behavioral break arises. However, sometimes we need to do some backtracking to get to where we understand the basic biochemistry of the behavioral systems that are atypical in autism." Dr. Platt believes that the development of new treatments for autism and related disorders will benefit directly from improved understanding of social attention mechanisms in an animal model. He states, "With the specific neural pathways identified, we will also be that much closer to identifying the underlying etiology of autism – and thus potentially find a way to not only treat, but potentially also to prevent this disorder."

uncovering the biochemistry which is generating the behavioral deficits in autism will make it possible for researchers to develop treatments that target the source of problems

Developing a model to evaluate social motivations and joint attention opens the door to explorations and answers that parents, educators and researchers have wondered about. What types of social cues influence social awareness in autism? What are the pathways that process social attention? What other biological processes in the body impinge upon the fidelity of these pathways? What is the biochemistry of the cells that actually mediate them? What other molecules, such as hormones, modulate social attention? Perhaps, most importantly, what pharmacological or therapeutic interventions can adjust this disrupted circuitry to overcome the deficits in autism? Dr. Platt's work provides a model upon which studies of this type can be based, and what we learn from these monkeys may offer up the clues to how to repair the circuitry that will allow for improved joint attention, imitation and social growth in individuals with autism.

Reference: Shepherd, S., Deaner, R. & Platt, M. (2006). Social status gates social attention in monkeys. Current Biology,16 (4), R119-R120.

This science summary was prepared by the Science Program staff of Cure Autism Now. For more information visit their website www.cureautismnow.org.

As Appeared in the July/August 2006 issue.

www.autismdigest.com