

Faculty Spotlight:

Karen J. Parker, PhD



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Associate Professor, Psychiatry and Behavioral Sciences

“We are transforming health outcomes by developing novel tools to detect and treat social impairments in brain-based disorders.”

Humans are an intensely social species. We experience social interactions as rewarding from infancy, and the social cognitive skills that we develop in the context of our earliest interpersonal attachments are critical for our survival and personal wellbeing. Disruptions to personal relationships, such as social isolation or loss of a loved one, are highly significant risk factors for stress-related depressive and anxiety

disorders, as well as substance abuse initiation or relapse. In some disorders, like autism, social deficits are the defining, core feature. Yet, despite the importance of social functioning in humans, our understanding of the neural mechanisms that control social behavior is limited.

The Parker Lab. As director of the Social Neurosciences Research Program, Dr. Karen Parker’s principal goal is to better understand the biology of social functioning using an integrative approach. Her lab’s behavioral research spans studies of primate social development to studies of behavioral impairments in various clinical populations (e.g., in patients with mood and anxiety disorders; in children with autism; in survivors of hypothalamic-pituitary tumors). A unifying theme of this overall research is Dr. Parker’s abiding interest in two neuropeptides, oxytocin and

vasopressin, which she has shown enhance social functioning and diminish stress and anxiety. She has also found that these neuropeptides are decreased in patients with depressive and anxiety disorders, as well as in those with autism; she is working to formulate these molecules into new medications to treat people with these disorders as described below.

Developing Valid Animal Models for Psychiatric Disorders. It costs at least \$1B to bring a new drug to market. One of the reasons for this exorbitant expense is that most “preclinical” research uses rodent species to test the efficacy of new medications. For brain disorders, over 90% of the compounds that appear to be effective in rodent studies fail in human clinical trials. These challenges underscore the tremendous value in developing new animal models with more reliable biological and behavioral correlates to human disease. Dr. Parker and her team are pioneering the development of several such models. In one monkey model of stress-related depressive and anxiety disorders, this work has yielded important insights into how early life experiences interact with underlying genetic factors to shape brain circuits that regulate emotion, stress reactivity, and cognition, thereby contributing to whether monkeys exhibit stress vulnerability or resilience later in life. Research related to autism includes studies of monkeys that exhibit naturally occurring social impairments and those that are genetically engineered to do so. Dr. Parker’s team has created sophisticated tests which measure monkey behaviors that have direct relevance to core psychiatric symptoms. These tests are enabling her to identify which biological measurements most robustly predict monkey test performance to identify the most promising targets for therapeutic intervention. She and her team are optimistic that these monkey models will facilitate discovery of novel “drugable” targets, provide biological predictors of treatment response, and support creation of a robust therapeutic testing pipeline. Given the genetic relatedness between monkeys and humans, Dr. Parker’s monkey findings stand to enhance the success of subsequent human clinical trials, thereby accelerating development of new medications, enhancing quality of life for people with psychiatric illness, and reducing the emotional and financial burden of brain disease on patients, their family members, and society.

Mood and Anxiety Disorders: Early Experiences, Stress Hormones, and Neuropeptides. It is estimated that for US adults, 20% will experience a mood disorder and 30% will experience an anxiety disorder in their lifetimes. For nearly two decades, Dr. Parker has studied the neurobiology of stress resilience and vulnerability, with a particular focus on how early environmental factors contribute to the development of later stress-related mood and anxiety disorders in both animal models and in human patients. Dr. Parker’s work has shown that patients with depressive and anxiety disorders have increased stress hormone activation and low oxytocin levels. She has also shown that oxytocin administration diminishes stress hormone activation. These findings are important because elevated stress hormones are thought to play a key role in the onset of stress-related psychiatric disorders. She is currently testing whether oxytocin treatment improves behavioral symptoms in anxiety disorder patients.

Autism: A Core Research Direction. Autism is a brain disorder of early childhood onset characterized by pronounced social impairments which can include diminished eye gaze, abnormal facial and emotional processing, lack of perspective taking, and impaired social judgment. These social deficits jeopardize the development of social skills and the formation of close personal relationships. Despite the growing prevalence of autism (1 in 59 US children) and its societal impact (an estimated \$1T to be expended in the US annually by 2025), there are no laboratory diagnostic tests to detect, or medications to treat, autism's core social challenges. To address these barriers to scientific progress, Dr. Parker and her multidisciplinary team are identifying novel biological "signatures" of autism in human tissues, testing promising new medications that improve social abilities, and identifying biological predictors of treatment response to determine which children will benefit most from a given medication. Dr. Parker's current autism research projects include:

Developing Novel Diagnostic Tools. Autism, as well as other psychiatric disorders, is currently diagnosed using behavioral criteria because no robust biomarkers have been identified. Biomarkers are molecules in the body that indicate a disease state, and they improve our ability to more objectively diagnose a disease. Progress in developing accurate laboratory-based diagnostic tests for autism has been hindered by studying biomarkers in blood, which have thus far met with poor results. Because autism is a brain disorder, it stands to reason that studying brain-related tissue samples [e.g., cerebrospinal fluid (CSF) - a fluid that bathes the brain and spine] would enhance the probability of a scientific breakthrough. Indeed, similar approaches to investigating biomarkers in CSF are already being employed with great success in brain diseases such as Alzheimer's and multiple sclerosis. Although opportunities to collect CSF samples are rare, Dr. Parker is leading a multi-site research team that is capitalizing on clinician ordered collection of CSF samples from children with and without autism during medical evaluations. Her team is studying the neuropeptides vasopressin and oxytocin, which are critical for normal social functioning in animals and people, and which are thought to be deficient in some psychiatric populations. Her team is also employing "hypothesis-independent" assessments of CSF biomarkers using liquid chromatography with tandem mass spectrometry (LC-MS/MS), the most comprehensive method available to quantitatively characterize hundreds of potential proteins simultaneously. Dr. Parker hopes to identify a biological "signature" of autism, which would lead to implementation of earlier and more accurate laboratory diagnostic tests and provide new targets for therapeutic development. Lessons learned from autism will provide an important research roadmap for other psychiatric illnesses that Dr. Parker also studies.

Testing Novel Medications to Improve Social Abilities. There are currently only two medications approved by the Federal Drug Administration to treat autism. However, these medications, both antipsychotics, target only associated symptoms such as irritability, have unfavorable side-effects, and do not treat autism's core social deficits. New medications that

improve social abilities in people with autism are therefore urgently needed. For many years, Dr. Parker's laboratory has studied how the neuropeptides vasopressin and oxytocin support normal social behavior. Experimentally reducing the levels of either neuropeptide or their receptors likewise produces social deficits in animal models. In parallel to these animal studies, Dr. Parker's research team has shown that lower oxytocin and vasopressin levels are associated with social impairments in children with autism. Dr. Parker and her team have extended this research to human clinical trials which have tested whether intranasal administration of oxytocin or vasopressin improves social abilities and diminishes anxiety in children with autism and related disorders, such as Fragile-X. Dr. Parker and her team are also studying whether they can identify biomarkers that predict which patients will have a higher likelihood of responding to a certain drug, and therefore identify who will best benefit from treatment. As with her work in the diagnostic space, "best practices" identified in her autism-related therapeutic research will be applied to the other psychiatric illnesses she also studies.

Brain Tumors: New Research Direction to Identify Drug Targets and Novel Therapeutics.

Survivors of hypothalamic-pituitary brain tumors often exhibit pronounced social impairments that adversely impact quality of life. No research, however, has systematically characterized social impairments in these patients or investigated their biological underpinnings. Dr. Parker's team of basic scientists and clinicians is performing comprehensive behavioral testing on these patients and assessing whether disease-induced disruption to hypothalamic-pituitary brain pathways implicated in social functioning (i.e., the neuropeptides oxytocin and vasopressin) underlie these impairments. The ultimate goal of this project is to identify "drugable" targets and develop novel therapeutics to enhance social abilities in this patient population.

Biography

Karen J. Parker, PhD is an associate professor in the Department of Psychiatry and Behavioral Sciences and is the director of the Social Neurosciences Research Program. Dr. Parker received her undergraduate and graduate degrees in Biological Psychology from the University of Michigan and completed her postdoctoral training in Psychiatry Neuroscience at Stanford University. Dr. Parker is also an affiliate scientist at the California National Primate Research Center. She is a recipient of the American Psychological Association's George A. Miller Award, the NARSAD Young Investigator Award, and the University of Michigan's Distinguished Dissertation Award. She is also a U.S. National Academy of Sciences Kavli Fellow and a member of the American College of Neuropsychopharmacology.



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