THE HARTWELL FOUNDATION

2016 Individual Biomedical Research Award

Timothy D. Hanks, Ph.D.

Assistant Professor
Neurology

University of California, Davis

Remedying Neural Circuit Dysfunction in a Novel Model of Attention-Deficit/Hyperactivity Disorder

Attention-deficit/hyperactivity disorder (ADHD) is one of the most commonly diagnosed psychiatric conditions of childhood caused by apparent dysfunction at the level of brain neural circuits. While the specific nature of the dysfunction is unknown, a genetic component is thought to involve at least two genes. However, non-genetic causes such as abnormal brain development, brain injury or environmental factors may also play a role. ADHD is characterized by three primary symptoms: inattention, hyperactivity and impulsivity. It is a spectrum disorder with symptoms widely distributed in severity across the general population, with no clear categorical boundary designating individuals affected with ADHD. More than 10% of school-aged children in the United States have received an ADHD diagnosis and over 1000 new children are diagnosed every day. ADHD is associated with multiple adverse outcomes including high risk for school failure, high accident rates, suicide, and drug abuse. The disorder exacts a tremendous burden on society through its direct effects on children, stress to families, and financial costs. Over 6% of all school-age children take ADHD medication; but unfortunately, prescribed drugs often have undesirable side effects, including sleep problems, increased moodiness and decreased appetite, among other issues. Such drugs pose particular challenges for the 30-40% of individuals co-diagnosed with ADHD and autism. Clearly, medications to remedy ADHD require greater specificity and reduced side-effects. Moreover, while existing evidence suggests that brain regions involved in human motor control and impulsivity are a primary source of deficits in ADHD, there are no suitable genetically modified animal models that mimic the observed deficits in which neural activity can be observed or manipulated in response to various target drug therapy. Based upon Tim's remarkable and serendipitous discovery among a population of rats that he could identify individual animals with defects in each of the three primary symptoms of ADHD (inattention, hyperactivity and impulsivity), he proposes a paradigm-shift to deploy this novel animal model for development of targeted interventions to mitigate ADHD. Using rats that exhibit an indication of ADHD, he hypothesizes that it should be possible to change brain circuits by leveraging high-density neural recording methods and newly invented methods of precise neural control (optogenetics) to restore normal neural circuit activity. If Tim is successful, he will identify targeted manipulations of the activity in neural circuits underlying ADHD that will inform the translation of novel drug therapies, with the potential to improve the quality of life for millions of affected children.