THE HARTWELL FOUNDATION

2022 Individual Biomedical Research Award

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Leveraging Genetics in Anxiety Disorders to Predict Mental Health Outcomes

Anxiety is the most commonly diagnosed psychiatric disorder in children and adolescents. Approximately 7% of U.S. children ages 3-17 are diagnosed each year. Characterized by significant and uncontrollable feelings of distress, anxiety can make children irritable, angry, have trouble sleeping, as well as experience symptoms like fatigue, headaches, or stomachaches. Among the earliest psychiatric conditions to manifest, with a mean age of onset at just 6 years of age, anxiety disorders place children at great risk of subsequent mood disorders during adolescence, including disruptive behaviors, suicidal behavior, and educational underachievement. There is therefore a great need for prediction strategies to ensure that children at high risk for serious outcomes are identified early and connected with appropriate mental health services and treatment. Genetics holds great promise for informing this process: a person's genome only needs to be sampled once in a person's lifetime, can be used to predict risk for many disorders simultaneously, and can be re-analyzed as new discoveries are made. Recent research in psychiatric genetics has made significant progress in identifying genetic risk factors in a multitude of conditions. However, the majority of effort focuses on specific categories of genetic information in single disorders, which limits the clinical utility of prediction models. Cross-disorder studies highlight shared genetic factors, but only recently have rare and common genetic variants been examined to better understand genetic risk. My preliminary data from a pilot DNA sequencing analysis of childhood anxiety disorders demonstrates, for the first time, the important role of rare de novo variants in the development of childhood anxiety, especially how genes harboring such damaging mutations overlapped with genes associated with other neuropsychiatric disorders, indicating that affected individuals may be at risk for other conditions as well. To improve prediction models, I propose to integrate different categories of genetic information in combination with in-depth clinical assessments of multiple anxiety-related conditions during the critical transition from childhood to adolescence. I will assess individual risk for anxiety and other related psychiatric conditions by analyzing whole-exome DNA sequencing and genome-wide microarray data in 200 parent-child trios with childhood anxiety initially assessed in 2016-2019. Follow-up assessments in the same cohort will be used to establish if genetic risk factors predict children's mental health symptoms 5 years later. If I am successful in identifying children at greatest risk for developing significant mental health outcomes, it will ensure timely clinical monitoring and effective treatment for those likely to experience worsening psychiatric symptoms during adolescence.