Connecting the Dots Between Biology and Addiction

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With \$2.3 million from the National Institutes of Health Director's Pioneer Award, Emory University psychological scientist Rohan Palmer is mining huge datasets to study how genetic differences leave some people vulnerable to substance addiction.

How did you become interested in behavioral genetics, and in addiction?

I have always been fascinated by individual differences. I initially focused on a career in medicine, but opted to pursue behavioral genetics because it allowed me to be at the intersection of so many areas of science at a time when whole genome data was becoming readily accessible. I quickly learned that studying the effects of genes, environments, and gene *x* environment interaction within developmental contexts are integral to understanding human behavior. Studying addiction has allowed me to understand and give back to an area of science, communities, and individuals struggling with substance misuse. In much of my work, I highlight the fact that although substance involvement may appear normative, there are many underlying diseases and traits, such as depressive symptoms, that undercut individual differences that are masked by a focus on diagnostic outcomes.

What specifically are you investigating with the funding from the NIH Director's Pioneer Award?

My team and I are investigating two central questions in the field of addiction genetics. First, how can we enhance our ability to prioritize genetic variants of interest from genome-wide association studies (GWAS)? Second, what components are necessary for a robust genomic prediction model of substance addiction?

How is the research being conducted? What are the methods you're using?

Part of what we are doing involves the use of raw genomic data to estimate the kinship between tens and hundreds of thousands of individuals who differ in their level of substance involvement. One way we are addressing the first goal is by working with other model-organisms to understand which genes and gene regulatory regions influence sensitivity to the presence of alcohol, cocaine, nicotine, and other substances. Our goal with these data has been to determine how networks of genetic variation play a greater role in substance behaviors than we would expect by chance. For our second goal, we are developing and testing theoretical models of substance use behaviors using genome-wide association evidence for different substances (e.g., our recent GWAS on Opioid Dependence), as well as integrating evidence across relevant traits and diseases using multivariate methods.

What outcomes/societal benefits are you hoping will come from your work?

With each set of studies, we bring additional clarity to the role of various sets of genetic variants in substance addiction. In addition to that, this project brings insight to how we utilize genome-wide data to understand risk for substance addiction by developing a reference resource for inferring addiction risk. The current method for risk prediction is the use of polygenic scores, but sample sizes are still too small to realize the full potential of genome-wide association studies. The platform that we envision for researchers will allow them to apply predictive models in a quasi-experimental manner, which will help to realize the implications of genome-wide risk in society.