1. Using Genome-Wide Data to Find Genes for Externalizing Psychopathology, including Attention Deficit Hyperactivity Disorder, Conduct Disorder, Aggression, Psychopathic Traits, and Antisocial Behavior

Over the past decade, technological and statistical advances have made it possible to economically and efficiently genotype large samples and to test millions of genetic markers for association with traits and disorders. We are using genome-wide data from our own sample and other samples in a series of collaborative studies to conduct genome-wide association scans (GWAS) of various forms of Externalizing Psychopathology, including Attention Deficit Hyperactivity Disorder (ADHD), Conduct Disorder (CD), Aggression, Psychopathic Traits, and Antisocial Behavior. Across these GWAS projects we are particularly interested in the use of gene-based tests and multivariate analyses to increase power and the likelihood of finding replicable associations, as well as exploring similarities and differences in genetic risk factors across different ethnic groups.

- With regard to ADHD, I am part of the Psychiatric Genetics Consortium (PGC) ADHD workgroup and we currently have 12 genome-wide significant loci and a forthcoming paper on this that is currently in preparation.
- For Conduct Disorder, I am co-leading a GWAS of ODD+CD diagnoses in the PGC ADHD plus Danish iPysch samples. I am also leading a GWAS of Conduct Disorder symptoms - and symptoms of the Aggressive and Rule-Breaking CD factors - in the Yale-Penn and SAGE multi-site samples recruited for substance use and abuse. Across the two samples we have ~5000 European-American and ~5000 African-American participants and are in the process of expanding the number of samples.
- For psychopathic traits, we've conducted a GWAS in the TEDS sample in the UK and will be trying to replicate the top associations in my sample here in Georgia, as well as trying to find other youth samples with both GWAS genotypes and similar measures of psychopathic traits.
- And finally, I am part of the BROAD collaboration on GWAS of antisocial behavior broadly construed co-led by Danielle Posthuma and Sarah Medland.

Relevant Publications: In progress.

2. Tests of Specific Genes as Risk Factors for Externalizing Psychopathology

In addition to genome-wide studies, we have conducted and are conducting studies that focus on the association of specific genes with various forms of Externalizing Psychopathology, including Attention Deficit Hyperactivity Disorder, Oppositional Defiant Disorder, Conduct Disorder, Aggression, Psychopathic Traits, and Antisocial Behavior. These genes are chosen based on neurobiological findings in humans and animal models for the biological plausibility of their etiological role in these traits and disorders. These projects include:

a. Association of the Oxytocin Receptor gene with Autism, Aggression, and Social Behavior

Relevant Publications:


*b. Finding Dopamine & Noradrenergic Genetic Risk Factors for ADHD

Relevant Publications:


Kirley*, A., Hawi, Z., Daly, G., McCarron, M., Mullins, C., Millar, N., Waldman, I., Fitzgerald, M., & Gill, M.
3. Meta-Analyses of Genetic and Environmental Influences on ADHD and Antisocial Behavior

Meta-Analysis is a quantitative approach to reviewing the findings in a research literature that bear on a particular question or a set of hypotheses. Using meta-analytic methods allows one to characterize the overall effect size (i.e., the magnitude of an association) and its statistical significance, characterize the precision of that effect size and its heterogeneity across studies, and assess the role of substantive and methodological variables as moderators that may help explain some of the cross-study heterogeneity. We have used meta-analyses to summarize the evidence for genetic and environmental influences on ADHD and Antisocial Behavior.

**Relevant Publications:**


4. Analyses of the Classification and Underlying Structure of Youth Psychiatric Disorders

Despite decades of research, uncertainty remains regarding the valid classification and underlying structure of psychiatric disorders in children and adolescents. Using data from several large population-based twin samples we are conducting sophisticated latent variable modeling and multivariate behavior genetic analyses in an effort to elucidate the underlying structure of both internalizing and externalizing disorders. In our recent efforts in this area we use twin study designs and sophisticated statistical methods to test alternative models for the hierarchical dimensional structure of psychopathology.

**Relevant Publications:**


5. Etiological Relation of Temperament and Personality with Youth Psychiatric Disorders

Contemporary approaches to characterizing psychopathology have emphasized the continuities between normal range function and the abnormal extreme of various quantitative dimensions in contrast to qualitative distinctions among categorical diagnoses. Along these lines we have used multivariate behavior genetic analyses to examine the etiological role of various temperament and personality dimensions in general, internalizing, and externalizing dimensions of psychopathology.

Relevant Publications:

6. Neurocognitive and Social Cognitive Endophenotypes for ADHD and Aggression

Within the context of behavioral and molecular genetic designs, we have examined social cognitive and neurocognitive executive function measures that are putative endophenotypes for ADHD and aggression. These constructs represent specific psychological mechanisms that are posited to underlie the etiology of these disorders and traits and may be influenced by the specific genes that are risk factors for these conditions. Specifically, we are interested in the role of children’s inattention, impulsivity, hostile perceptual biases, and deficits and biases in the processing of facial emotions and others’ intentions in the development of aggression and psychopathic traits, and have examined these and related constructs as endophenotypes for childhood disruptive disorders.

Relevant Publications:

7. Rigorous Tests of Direct Causal Environmental Influences on Child Psychopathology

Traditional approaches to examining putative environmental influences on child psychopathology have relied on simple associations between disorders and variables thought to reflect environmental risk factors. Unfortunately, such associations may reflect background genetic or shared environmental influences rather than the direct causal influences of the “environmental” variables themselves. Over the past decade, in collaboration with a set of colleagues, we have rigorously examined specific
environmental influences for conduct problems and ADHD. Specifically, in a large genetically-informative national representative sample of mothers and their children (i.e., the Children of the National Longitudinal Study of Youth, or CNLSY) as well as in 2 large twin samples, we have conducted both between-family and within-family tests of the effects of several putative environmental risk factors, including mother’s smoking and drinking during pregnancy, mother’s age at the birth of each child, neighborhood effects, effects of family income, and birth weight and gestational age.

Relevant Publications:

8. Exploration of Issues Related to Replicability of Findings of Psychological Research

In addition to testing for replication of behavioral and molecular genetic findings using meta-analysis, I’ve recently co-authored or edited several pieces focusing explicitly on replication issues in our field.

Relevant Publications:

[END]