The Role of Behavioral Genetics in Child and Adolescent Psychiatry

Robert R. Althoff, MD, PhD & James J. Hudziak, MD

Perhaps more than any other discipline, the field of Behavioral Genetics (BG) has provided a clear path to the understanding of why some children suffer and others do not. While other scientific and pseudoscientific schools of thought got lost in the miasma of their own dogma, it was BG that provided a sensible foundation to understand causality in child psychiatry. To explain, entire schools of thought were devoted to proving that child psychopathology was “due to” a variety of causes such as “refrigerator mothers”, “fixation on specific phases of development” and other psychodynamic (i.e. environment-only) focused theories. On the other hand, the ‘medical-model’ set out to discover a single gene explanation for schizophrenia, autism, and most other psychopathologies using a “biology-only” approach. While both of these categorical approaches are clearly lacking and are now thought to be obviously silly (Hudziak & Faraone, 2010), it is important to point out that the field of Behavioral Genetics did not buy into either approach from the beginning. Instead, the proponents of twin, adoption and family studies soldiered on by providing evidence of genetic contribution balanced with environmental contribution and ultimately explained the ideas of gene-environment correlation, gene-environment interaction, and epigenetic processes as they relate to child psychiatry. The Gene-by-Environment (GxE) argument, the gold standard of our field is the direct result of the work of Behavioral Genetics. We should be thankful for their clear minded approach. Now that we have this plausible explanation for causality of developmental psychopathology, why do we still need BG approaches? The answers are relatively obvious. Just like the science of molecular genetics has evolved since the beginning of the human genome project, so has the field of Behavioral Genetics. Gone are the times when simple reports of genetic and environmental contribution to traits are the product of this field. Instead, BG is using its extraordinary large samples of twins, siblings, and families to do the ultimate molecular genetic studies. Further, they are using these same samples to do the ultimate study of environmental risk and protective factors using monozygotic twins discordant for traits, extended twin-sib designs, twin-imaging designs, family studies and twins-of-twins models. These are all examples of how BG scientists have superpowered approaches for the discovery of the genes and specific environmental factors that influence traits.

Perhaps the biggest obstacle to identifying the genetic and environmental factors is our phenotypic approach. Scientists who study the GxE non-psychiatric medical conditions like leukemia or other cancers can use simple measures and study the genetic contribution in specific cell types (e.g. leukocytes and cancer cells). In child psychiatry we will never be able to study the genetic expression in brain cells. Moreover, our phenotypic approach is far from a simple measurement. Prior to identifying which genes or environmental factors contribute to the risk or protect a child from a disorder we have a long way to go in defining just what a disorder is. Behavioral Genetics can use its samples, approaches, and bioinformatics to help us better refine the phenotypes we aim to study. For example, even in a disorder that child psychiatrists feel confident in making, Attention Deficit/Hyperactivity Disorder (ADHD), BG scientists have identified that rater bias, rater contrast, informant effects, gender and ethnic variance are all problematic to gene finding. Once we have refined a single phenotype to the point that we feel confident that our search for genetic and environmental mediators will be on target, we are faced with the daunting prospect of what to do about so called “co-morbidity”. Are we interested in the genetic and environmental contributions to ADHD alone, or in combination with reading, autism, mood disorders, and low academic performance? BG studies offer continued study into these combinatorial questions -- allowing us to ask questions like: are the same genes involved in attention problems and poor reading performance? Are candidate genes known to be related to ADHD also related to social problems in these children? If we control for the genetic correlations between ADHD and poor academic performance, do children with attention problems still struggle over time? How do sex and age affect the genetic and environmental contributions to developmental psychopathology?

These are the kinds of questions that we sought to bring to the table for this special edition of the Journal of the Canadian Academy of Child and Adolescent Psychiatry. We asked the experts in Behavioral Genetics to weigh in on topics of
continued interest to child and adolescent psychiatry. What you will find is a set of computationally sophisticated papers, but all with a common goal -- to help define the boundaries of genetic and environmental contributions to developmental psychopathology. We've asked each set of authors to try to make their topic relevant to child and adolescent psychiatrists. This has resulted in a series of papers representing what Behavioral Genetics using twin and family studies can offer the field.

Overall, these papers demonstrate again the continued importance of BG studies using twin and family designs. Because nature and nurture are intimately entwined, untangling them is a critical and important endeavor. We hope that these papers will instill in you the desire to read Behavioral Genetic studies more widely, especially as they relate to developmental psychopathology.

Reference