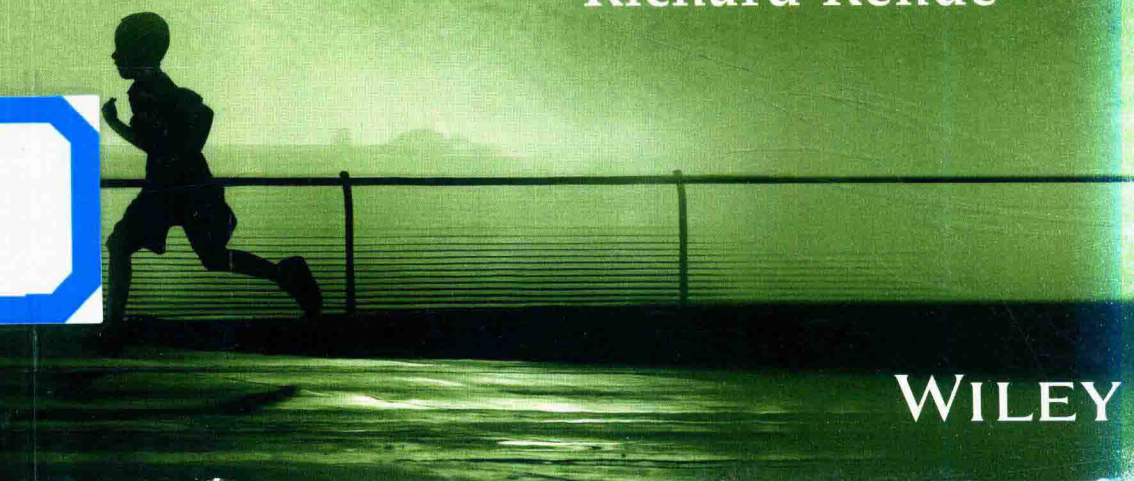
Psychosocial Interventions *for* Genetically Influenced Problems *in* Childhood *and* Adolescence

Richard Rende



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Preface

We assume genes play a role in all behavioral and emotional disorders of childhood and adolescence. The magnitude of the genetic impact, the processes underlying how genes contribute to both risk and protection, and the ways in which genes and environments intersect have all been investigated intensively over the past two decades. What are the implications of this ongoing work for preventing and treating children and adolescents now and in the future?

When the Human Genome Project (HGP) was completed – over a decade ago – there were claims (and perhaps promises) that identification of genes would revolutionize treatment. We envisioned that gene discovery would lead to the development of biological techniques that target those genes (or the effects of those genes) in a fundamental way. Gene discovery would also rewrite how we diagnose disorders – including the behavioral and emotional disorders of childhood and adolescence – leading to more valid identification of risk processes that could be eradicated biologically. A similar idea – but perhaps one with more tempered expectations – is that gene identification would at least lead to a clearer identification of individuals at risk for disorder and provide a platform for treatments tailored to their DNA profile.

While these various perspectives were in a sense the promised deliverables of HGP, we have not yet seen the realization

of that promise. We are finding that the etiology is more elusive than anticipated by HGP, and more in line with prior conceptual models of complex disorders. *Many* genes are typically involved, none of which is so independently and directly responsible to warrant our thinking that it can be "manipulated" biologically to fully or substantially reduce risk. These multiple genes all operate in the context of robust environmental influences. There is emerging evidence of how genes and environment intersect. It may be argued that one important deliverable of the HGP, relative to behavioral and emotional disorders, is to confirm what we had thought previously – that the etiology of every disorder is multifactorial with influences arising at both the genetic and environmental level.

Since we know that both genes and environment are at play, what are the implications for prevention and intervention? To begin, we need to eliminate the word "promise" from our discussions of genetics as applied to prevention and intervention. Genetically tailored biological interventions are simply a possibility, perhaps an unlikely one given the number of etiological influences that underlie behavioral and emotional disorders. Another possibility – one that is argued here to be more realistic – is that psychosocial interventions hold the most promise for making substantial traction in prevention and intervention efforts.

That is not to say that genetic research will not be influential. Our accumulating understanding of genetics will in fact help us devise and implement more effective psychosocial interventions. The last decade has witnessed unprecedented growth in empirical efforts to understand the joint effects of genes and environment. While this work has also proven to yield somewhat murky results at times, overall the overwhelming conclusion is that we need

more, not less, approaches that cast gene effects in relevant psychosocial contexts. Even more compelling is the idea that, when we step back and have a good look at the evidence to date and the emerging conceptual models that both support this line of research and continue to evolve from it, gene–environment studies indicate that the best way to alter the developmental trajectories of youth at high genetic risk for behavioral and emotional disorders is to change their environment. And a critically important way to support that goal is to continue to study genetics – but only if the deliverables of the DNA laboratories are not divorced from the need to deliver and improve psychosocial interventions that hold promise for immediate and long-term improvement in the functioning of children and adolescents.

Here we take a highly selective look at research on genes and environments to ascertain different models of how genetic research may inform psychosocial interventions – and why psychosocial interventions are taking on greater importance post HGP. We consider autism spectrum disorder (ASD), attention-deficit/hyperactivity disorder (ADHD) and reading disorder (RD), conduct problems (CP) and substance use (SU), depression (MDD), pediatric bipolar disorders (PBD), and anxiety disorders (AD). In each chapter, one major theme from ongoing research is highlighted to illuminate a principle about how the environment matters, why we should learn more about it, and why it might provide the most likely route for prevention and intervention. For example, research on ASD will highlight the complexities of gene identification for this disorder – and the compelling new evidence that gene–brain-behavior pathways may be altered by carefully crafted and intensive psychosocial interventions. While we think of ADHD and RD as highly heritable disorders, current thinking suggests that this doesn't

mean that their expression is not substantially influenced by environmental context – and that the psychosocial environment offers much room for modifying the effects of these disorders on development. Both conduct problems and substance use have been shown to reflect environmental factors that lead to similar behaviors in family members (shared environment) – and current promising psychosocial interventions are shown to target hypothesized shared environmental processes. Depression runs in families – and treatments that reduce levels of depression in parents offer similar direct benefits on their children via changes in parenting. Pediatric bipolar disorder is a complex disorder that typically arises in a very complex context of environmental risk – yet we haven't seen enough support for developing psychosocial interventions especially given that there are few biological treatments that are optimally effective. And a consideration of the anxiety disorders reveals intriguing evidence that environmental traumas not only act on genetic vulnerabilities but may in fact alter gene expression through the lifespan – leading to a consideration that early interventions may help undermine this maladaptive biological process.

The real promise for the future will lie in accelerated efforts to apply, refine, and develop psychosocial interventions using our interdisciplinary knowledge base on genes, environments, and their interplay across developmental time. It's time to abandon another round of promises about the deliverables of genetic research that aren't expected to pay off for decades. In contrast, psychosocial interventions have been shown to be effective in the here and now – and by more fully investing in their potential we can learn even more about genetics while evolving more effective interventions that hold promise for improving children's lives today.

Acknowledgments

Writing a book that offers speculations about the future of genetics and intervention is a dicey proposition. Both fields provide moving targets as new (and potentially unexpected) findings can dramatically alter our perspective. Thus, I am particularly grateful to Patricia Rossi for her extraordinary guidance – and patience – as an editor who navigated the interesting process of deciding when it felt right to say that we were done.

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Prelude: Great Expectations

Over a decade ago, when the race to decode the human genome was in full stride, the expectations were great – and then some. The rhetoric focused not on the possibility, but on the promise, that the Human Genome Project (HGP) would revolutionize clinical practice, including the diagnosis and treatment of developmental, behavioral, and emotional disorders in infancy, childhood, and adolescence. This was no basic science endeavor focused on an intellectual holy grail. The HGP came with a very large promissory note – to uncover the genetic origins of disease and disorder and point directly and quickly to biological interventions that would have unprecedented success.

Once the completion of the HGP was formally announced in 2003, the expectations were that we would now be positioned to find the answers to questions that genetic research had promised (and failed) to answer in the past. The primary questions that lingered centered on the speed and scope of the impact. Would the knowledge derived from the HGP lead to "magic bullet" therapies that could inhibit pathological

processes caused by rogue genes? Or would it lead to a better understanding of the role that genes play in disease and rapidly inform us about strategies that could be taken to compensate for genetic risk? In either case, we would have the knowledge to either circumvent or inhibit deleterious genetic influences by biological means, or at a minimum develop tailored interventions that would scan your DNA and tell you how to prevent, or eradicate, a pathological condition. The question that was harder to envision back then – now a decade ago – was whether it would simply illustrate how difficult it would be to move from identifying pathogenic genes to actually doing something about them or, for that matter, even actually identifying those genes.

These questions were prominent in the minds of those who study developmental, behavioral, and emotional disorders in children and adolescents. During the 1990s, there had been an explosion of research that used genetic methods and concepts in developmental psychopathology. Behavioral genetic approaches (such as twin and adoption studies) generated an impressive amount of informative data that were consistent with the idea that DNA is implicated in virtually every form of child and adolescent psychopathology. So just like researchers and practitioners who studied cancer or heart disease, developmental psychopathologists eagerly awaited to see how the HGP would transform what we do, and most importantly, how it would impact our ability to improve children's lives. And this wasn't just speculation. Go back a decade, and you will see that nearly every major longitudinal study of childhood psychopathology made some level of investment in the collection of DNA, in anticipation of some type of major advancement.

So, where do we stand right now? A quick Internet search today will reveal that the HGP revolution – with respect to intervention – has not happened. Numerous articles in the popular press over the past few years have documented the very gradual slope involved in identifying disease genes that could inform new therapeutic techniques. Some have drawn an analogy to business bubbles, in that the great expectations that surrounded the HGP has given way to the sober reality that a decade later few (if any) radical advances have been made with respect to therapeutics. *National Geographic* ran a piece that focused on the five breakthroughs from the HGP and five predictions. Developing gene therapies to cure disease was listed as a *prediction* – not a breakthrough – as it was proposed that this could *start happening* sometime in the *next* decade (or two decades after the completion of the HGP).

One could speculate that the popular press may be inclined to skew perceptions. However, the collective voice extends to the world of science. In July 2011, the prestigious journal *Human Genetics* devoted a special section to the yield to date of the HGP with respect to intervention. It included articles such as "*Translating Human Genomics into Population Screening: Hype or Hope?*" Other papers focused on the substantial challenges that scientists anticipate in moving from the extraordinary knowledge base derived from the HGP to the ultimate deliverable: genetically informed and tailored treatment strategies that work for a range of diseases. Even Francis Collins, who led the HGP initiative at the National Institutes of Health, has acknowledged in multiple interviews that the HGP has not had the massive immediate practical impact on treatment and prevention that was anticipated by many during