Chapter 13

GENETIC AND ENVIRONMENTAL INFLUENCES ON WELLNESS, RESILIENCE, AND PSYCHOPATHOLOGY

A Family-Based Approach for Promotion, Prevention, and Intervention

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It is a difficult job for a child to grow up. This job comes with few choices. Your genetic makeup has been determined; you do not get to choose your parents or how many brothers and sisters you will have. You do not get to choose your environment—for example, the town in which you will live, the school to which you will go, and, in most instances, the peer group to which you are exposed. Similarly, you typically do not get to choose whether you will be raised in a religious environment, whether you will be encouraged to play sports, what languages you will be taught, or whether you will be offered

the chance to play a musical instrument. Lastly, you have little control over what life events (good or bad) to which you will be exposed. Taken together, kids do not have a lot of choices about the early trajectory of their lives.

The job of growing up becomes more difficult if you suffer from an emotional-behavioral illness while trying to negotiate the business of growing up. Perhaps most germane to this chapter, growing up is even more difficult if the environment you grow up in is chaotic, particularly if you and your parents both struggle with emotional-behavioral problems. A similar argument can be made from a parental point of view (although there are more choices available to the adult). It is tough to be a parent; it is even tougher to be a parent if your child has an emotional-behavioral illness. Perhaps most important to this discussion, it is terribly difficult to be a good parent if both you and your children suffer from emotional-behavioral illness. It is well known that children's temperaments and psychopathology directly affect their environments and their relations with their parents (Rettew et al. 2006). Similarly, parents' temperament and psychopathological profile will affect their relationships and the environment of the home. Simply put, a child who suffers from severe psychopathology can quickly overwhelm a parent who has otherwise adequate parenting skills.

The interaction between the parents and offspring, as originally discussed by Thomas and Chess (1977) and elaborated by others (Rettew et al. 2006), can either be protective from illness or represent a marked risk for illness. The perspective that all of the conditions that we study (e.g., attention problems, aggressive behavior, anxiety disorders, obsessive-compulsive disorder [OCD], juvenile bipolar disorder) are influenced by multiple genetic and environmental factors is now generally accepted (Althoff et al. 2006; Boomsma et al. 2005; van Grootheest et al. 2007; Rietveld et al. 2003; van Beijsterveldt et al. 2003). The fact that most of these illnesses run in families is also fully accepted.

In this chapter it will be argued that by taking a family-based gene–environment approach (FBA) in the developmental psychopathology (FBA/DP) perspective, researchers and clinicians alike will be able to better understand etiopathology and ultimately treatment. We offer that the FBA/DP perspective is the ideal approach for general medicine to embrace. It should be the goal of all involved in the care and well-being of children and families that we embrace the following strategy. We should aim to devise strategies to keep well children well, prevent at-risk children from developing psychopathology, and intervene on behalf of those who are ill. This movement toward health promotion and prevention is fully supported by the FBA/DP perspective. We argue that in light of recent discoveries it is prudent to once again embrace a full family approach to the assessment and treatment of emotional-behavioral disorders. Further, we will argue that strategies that can be

learned from the FBA/DP perspective can already be useful in the promotion, prevention, and intervention approach simply by embracing the clinical mandate of "do no harm."

GENOMIC MEDICINE AND THE FBA/DP PERSPECTIVE

In the era of genomic medicine we are treated daily to new discoveries relating specific emotional-behavioral problems to specific genetic and environmental influences. Such discoveries are becoming commonplace yet are often misunderstood in the context of their complexity. Typically both the genetic and environmental influences identified in these studies are of small to modest effect and thus only explain a very small part of the story. However, the results are often so intoxicating that the public overvalues the findings in the search for a single diagnostic test or gene treatment. These discoveries doubtless portend a period of rapid discovery that could well lead to new diagnostic, treatment, and prevention strategies for children who suffer from common psychopathologies.

However, in order to ensure proper progression in our field, we must protect these findings from overgeneralization and misuse. Simply put, the experts in our field need to prepare to teach practitioners, families, and patients the lessons that common psychopathologies are best described in the context of complex illnesses, for which complex solutions and approaches will be necessary to ensure that children and their families are receiving the best of care. On the other hand, despite the fact that we are not likely ever to be able to use genetic tests that are diagnostic (e.g., "If you carry this gene you will have a disorder") or even predictive (e.g., "If you carry this gene it is likely that you will have a disorder"), our testing may yield information on relative risk (e.g., "You carry one—or more—of the genes that confer risk for a disorder"). As we move toward discussion of relative risk with our families, this may help change the history of psychiatric treatment by diminishing resistance to treatment because of the stigma and shame often associated with psychiatric illness. In other words, clinical use of relative risk genetic testing may yield advances with patients by "biologizing" and "validating" psychiatric illness, which practitioners have long known to be both biological and valid.

Nonetheless, perhaps the most important lessons of the past 10 years that have emerged have demonstrated that genotypes associated with psychiatric illness are correlated with some environmental stressors but not others. Thus therapeutic avenues of the "environmental type" can be revisited. In this book you will have read a number of examples that provide evidence

of the importance of the FBA/DP perspective. As a result, we focus this chapter on an alternative strategy—the study and implementation of FBA/DP wellness and resilience strategies for both research and clinical medicine.

THE CONCEPTS OF WELLNESS AND RESILIENCE

Societies, cultures, and families have often struggled to promote wellness in children. It is easy to forget that educational programs for children are a relatively recent development in the course of human existence. As with providing an education to all children (see, e.g., *Guns, Germs, and Steel*, by Jared Diamond [1997]), cultures also have spent a great deal of energy trying to make participation in sports a right to all children. Similarly it has long been believed that there are benefits of a musical education (see *The Mozart Effect*, by Don Campbell [1997]), a healthy diet, and religious upbringing. What has been so baffling is the question of why these factors are protective in only some children. Why do some families value these elements of living and others ignore them? We argue that one of the values of using genomically informative designs in family-based research paradigms is the possibility of understanding which children are likely to benefit from one program versus another. To do this properly, we think an emphasis on the study of the environmental and genetic influences on wellness and resilience may be even more important than previously argued. In the study of developmental psychopathology, little attention is paid to the well and the very well child and family. Psychiatry and clinical psychology have focused largely on psychopathology rather than on positive behavior or wellness. This focus has led to a definition of wellness as the absence of emotional and/or behavioral problems. However, we are convinced that variance at the "positive" side of the normal distribution (see Figure 13–1) is as common as variance in psychopathology.

We believe that by studying children, adolescents, and families who are well, happy, and satisfied with their lives in addition to resilient children who once showed psychopathology but have recovered, we can develop new strategies for intervention and prevention.

FBA/DP AND WELLNESS AND RESILIENCE

Unfortunately, bad things happen to all children, but fortunately only some go on to develop psychiatric illness. Pathways into and out of psychopathology need to be better studied using the DP approach. We argue that using the FBA approach will be even more illustrative, because children's problems and family's problems often coexist. One such example is the well-

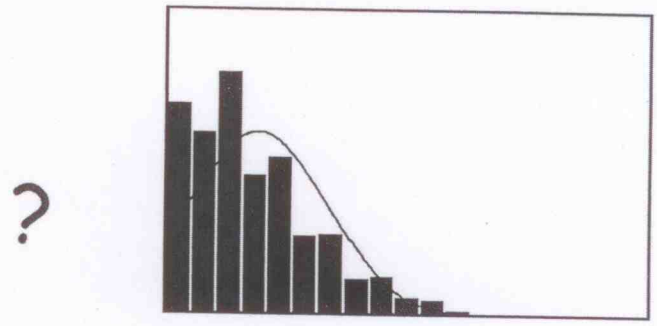

FIGURE 13–1. Gaussian distribution from wellness to problem behavior.

known data on the effects of maternal well-being on the child. Failure to consider the effects of maternal absence or maternal illness when conceptualizing DP pathways will likely lead to spurious findings. Weissman et al. (2006) have nicely demonstrated that in some cases measures of child psychopathology can change with improvement in maternal depression. Similarly, failure to consider genetic factors as playing a role in negative outcomes can also lead to spurious findings. Elegant primate research, detailed elsewhere in this book (see Chapter 7, "Genetic and Environmental Modifiers of Risk and Resiliency in Maltreated Children"), has demonstrated the key role of maternal interaction and offspring genotypes in outcomes in behavior and stress response (Barr et al. 2004; Suomi 2005). Thus, to discover why some children are always well, some children apparently suffer from emotional-behavioral problems from conception through adulthood, and others are sometimes affected and other times well, it may be essential to also understand the family's health and genetic makeup together. Epidemiologic studies show that the majority of the children are free of emotional-behavioral problems at any given time. Emerging evidence from longitudinal studies suggests that within this group of "well" children, many have always been well, whereas others may have been ill at one point but are relatively well at others.

To date, it is not clear what factors influence the shift from illness to wellness or why some children recover from illness and remain well ever afterwards. Suspected factors include life events and risk factors as well as genetic and epigenetic factors.

We believe that in order to study wellness and resilience (i.e., the ability to recover from a prior illness or the capacity to remain well in the face of extraordinary genetic and/or environmental risk factors) in the domain of developmental psychopathology, it is necessary to study children longitudinally using genetically informative strategies. Thus, twin, family, adoption, and molecular genetic studies that measure environmental mediators and modifiers in a longitudinal fashion are needed in order to estimate genetic and environmental factors that put children at risk for or protect them from psychopathology.

To study the factors that promote resilience, we must understand the factors contributing to change and stability in developmental psychopathology. However, when we are examining the etiology of developmental stability and underlying factors for resilience, one caveat is that the mechanisms responsible could differ for genetic and environmental influences (Bartels et al. 2004; Bishop et al. 2003; Haberstick et al. 2005). Bartels et al. (2004), for example, found that stability in internalizing (INT) and externalizing (EXT) behaviors, based on maternal ratings, was accounted for by genetic and shared environmental influences. The genetic contribution to stability (INT: 43%; EXT: 60%) resulted from the fact that a subset of genes expressed at an earlier age was still active at the next time point. Further, a common set of shared environmental factors operated at all ages (INT: 47%; EXT: 34%). The more general conclusion that genetic factors contribute primarily to stability whereas nonshared environments contribute largely to change has also been supported with findings for other phenotypes such as attention problems (Rietveld et al. 2003) and aggression (van Beijsterveldt et al. 2003). The finding of distinct developmental patterns for genetic and environmental influences is important for scientific as well as clinical purposes. The shared environmental influences, for instance, exert a continuous influence from their time of onset. So the children who continue to experience adverse shared environments are at risk for later maladjustment. For additive genetic influences, parts of previous effects are transmitted to later ages. However, the genetic influence is less static owing to new genetic influences that come into play at each age. Nonshared environmental influences seem to be important for age-specific behavior problems and have almost no developmental significance.

Combining these findings from longitudinal studies with knowledge of measured environmental risk and protective factors supports the study of wellness and resilience, which may well yield insight into a wide variety of complex questions. Why for instance do some children benefit from exposure to sports participation, music, nutritious diet, and other widely implemented social programs? Why is it that these social programs, which common sense would indicate should benefit all children, often help only a small percent-

age of children? Why do prevention programs work for only some children and families? Why do pharmacotherapies and psychotherapies not work in all children with the same "diagnosis"? Although the answers are doubtless so complex that many approaches will be needed to dissect the relative contribution of a wide variety of factors, it is suggested that the study of the genetic and environmental influences on wellness and resilience in families may lead to a clearer understanding of which children will respond to which interventions, as well as to design more effective prevention programs.

Such research may lead to strategies that will change the way we assess children with emotional-behavioral illness. To review all of the potential protective strategies is beyond the scope of this chapter, however in order to present some relative simple yet provocative exemplars, we summarize here findings for protective and risk factors known to be mostly environmentally mediated (sports participation, religiosity, and life events).

EXERCISE BEHAVIOR AND SPORTS PARTICIPATION

In our research clinic at the Vermont Center for Children, Youth, and Families (VCYFF), it is not uncommon for parents to leave with a prescription for "team sports" for a child. We have taken this rather atypical approach because it is our contention that participating on sports teams is protective for children, particularly children at risk. There is research that indicates that children who carry genes of risk for attention-deficit/hyperactivity disorder (ADHD) and cigarette smoking are likely to be protected against smoking initiation if they are able to participate on a team (Audrain-McGovern et al. 2006). Just what is the protective value of sports?

Our group has reported results from a large adolescent twin study that found that individual differences in sport participation between ages 13 and 16 years are mainly accounted for by shared environmental factors (78%–84%). In other words, it is the family who is responsible for getting their children to participate in sports (or not). At the ages of 17–18 years, genetic influences begin to appear (36%), and the role of shared environment decreases (Stubbe et al. 2005). This study provides evidence that at one stage of development a mediator may be primarily environmental, but at other stages genetic effects appear.

The relation between exercise behavior and mental health has been described by many researchers (Byrne and Byrne 1993; Folkins and Sime 1981; Gauvin and Spence 1996; North et al. 1990; Salmon 2000; Scully et al. 1998). However, population studies on the association between exercise and mental health are harder to find. Recently, our group (De Moor et al. 2006) studied the association of exercise with anxiety, depression, and personality in a

large population-based adult sample. The primary findings from this investigation are that exercisers are on average less anxious and depressed (effect sizes −0.18 to −0.29 SD), less neurotic (effect size −0.14 SD), more extraverted (effect size +0.32 SD), higher in thrill and adventure seeking (effect size +0.47), and higher in disinhibition (effect size +0.25 SD) than nonexercisers. The differences between exercisers and nonexercisers, although small (Cohen 1969), are very consistent across gender and age and with the previous reports on depression and anxiety.

Further, lack of exercise was found to be cross-sectionally associated with depression in population samples with a broad age range (Farmer et al. 1988; Weyerer 1992) and in samples consisting of young (Steptoe and Butler 1996; Steptoe et al. 1997) or older adults (Kritz-Silverstein et al. 2001; Strawbridge et al. 2002). In a sample of adolescents, however, Allison et al. (2005) found that regular exercise was associated with better social functioning. The latter shows that sports participation might be a moderator of clinical and scientific interest, because besides the significant effects of its absence on depression and anxiety, positive or protective effects are also found. In line with these findings our group found that exercise participation is associated with higher levels of life satisfaction and happiness (Stubbe et al. 2007). It was further found that exercise participation correlates moderately (r=0.20) with self-rated health (De Moor et al. 2007). The genetic characteristics of the latter study provide evidence for overlapping genes influencing both phenotypes (r_g=0.36).

Cross-sectional analyses, as presented here, *cannot* inform us on the causal structure between exercise, personality, anxiety, and depression. An approach to study causality, therefore, is the use of prospective analyses in large longitudinal population-based samples. A prospective association between lack of exercise at baseline and depression or anxiety at follow-up was found in some population studies (Camacho et al. 1991; Farmer et al. 1988; Strawbridge et al. 2002) but was absent in other studies (Allison et al. 2005; Cooper-Patrick et al. 1997; Kritz-Silverstein et al. 2001; Weyerer 1992). These studies did not, unfortunately, examine the reverse causality, where depression or anxiety at baseline may predict reduced exercise participation at follow-up. Further, most of the previously mentioned studies are based on adult samples. Future studies involving children and adolescents are essential to gain insight into the association between sports participation and wellness and psychopathology.

Moreover, since it has been found that variance in exercise behavior in adolescents is accounted for by shared environment, sports participation in itself is a likely target for intervention. Expansion of the previous results that show significant genetic overlap between exercise behavior and self-rated health and satisfaction with life and happiness should be replicated in

children and adolescents. To this end we have completed preliminary analyses in our sample of more than 1,000 adolescent twin pairs and their non-twin siblings. Our data, in which 70% of 13-year-old boys and girls are on sports teams, reveal that in both genders, adolescents who participate in sport on a regular basis generally feel healthier ($P=0.000$) and happier ($P=0.020$) and report a higher quality of life ($P=0.006$).

Given the low risk and potential high return of aiming to include sports participation in a child's life, particularly when at earlier ages the influences are primarily of the shared environmental type, we aim to have more families get their at-risk children to participate in sports (and as a result of these and other studies, other activities such as music training, clubs, and other social programs).

RELIGIOSITY

The concept that being raised in a religious household is protective has long been a staple belief of religious disciplines. Our group has analyzed large sets of twin data revealing that differences between individuals in religious upbringing, affiliation, and participation in church activities are environmentally mediated. The familial resemblance for different aspects of religion is high but can be explained entirely by environmental influences common to family members (Boomsma et al. 1999). In a study of Finnish twins, low heritabilities (11%–22%) and large shared environmental influences (45%–60%) were found (Winter et al. 1999). High levels of religious involvement predict a reduced risk of substance misuse (Gorsuch 1995; Koenig et al. 1994; Larson et al. 1980; Payne et al. 1991). A protective effect of religious involvement and values against adolescent alcohol use was found by Heath et al. (1999).

Furthermore, associations between religiosity and the lower levels of psychopathology and substance use behavior have been suggested. Using data from the National Longitudinal Study of Adolescent Health, Nonnemaker et al. (2003) found religiosity to be protective against cigarette, alcohol, and marijuana use. It has also been found that for boys, low religiosity predicted progression to regular smoking and failure to quit regular smoking (van den Bree et al. 2004).

Spirituality has also been conceptualized by some as a component of personality (Luby et al. 1999). In a population-based adult twin sample, it was found that general religiosity was inversely and significantly linked to nicotine dependence, alcohol dependence, drug misuse and dependence, and adult antisocial behavior. However, general religiosity was significantly related to panic disorder (Kendler et al. 2003a).

Maes et al. (1999) found that genetic factors account for the association between church attendance and alcohol use in males, but in females the association is primarily due to shared environmental factors and genotype–environment covariance. In the Netherlands Twin Register adult twin sample, Koopmans et al. (1999) reported that in females who scored high on religiosity, genetic factors explained 0% of the variance of initiation of drinking. Conversely, in females who scored low on religiosity, genetic factors accounted for 40% of the variance. Subjects with a religious upbringing and who participate in church activities score lower on Sensation Seeking Questionnaire scales, with religiosity being associated with reduced genetic influence on disinhibition, especially in males (Boomsma et al. 1999).

Further, there is a wealth of psychiatric research studying the relationship between OCD, culture, and religious identity and practice (Abramowitz et al. 2002; Chia 1996; Greenberg and Shefler 2002; Greenberg and Witztum 1994; Raphael et al. 1996; Rassin and Koster 2003; Shooka et al. 1998; Sica et al. 2002; Tek and Ulug 2001; Tezcan and Millet 1997). A tentative summary of these studies is that in the normal population there are relations between religiosity and obsessive-compulsive ideation and behavior. However, the literature on OCD and religiosity across a variety of religions, cultures, and ethnic groups shows no proof that religion causes OCD or any other psychopathology.

These data inform the FBA/DP approach. For example, they lead us to ask the question: Are there clinical implications and lessons for family-based activities that extend beyond religion and may relate to other measures of family cohesion (and adversely, family conflict)? Although it is too provocative to imagine recommending participation in religion or religious groups as a "therapeutic intervention," our group and others have been struck by what appears to be the protective qualities of family-based activities and wonder whether the data are already strong enough to support a greater role for family-based approaches aimed at increasing family cohesion as a role for health promotion and prevention strategies.

LIFE EVENTS

A recent study on genetic effects on life events in adolescent and young adult twins and their nontwin siblings reveals no differences in prevalence of life events between monozygotic twins, dizygotic twins, and their siblings. The results indicate familial aggregation of life events, except for traffic accidents in women. Familial resemblance of illness and death of a significant other was mainly due to common environment. For the other life events, it was not possible to distinguish between genetic and common en-

vironmental effects (Middeldorp et al. 2005). Kendler et al. (1993) also reported moderate influences of genes (20%) and shared environment (20%), and relatively large effects of nonshared environment (60%) on life events.

Life event research has shown that both major life events and accumulated daily hassles may serve as stressors with negative implications for mental health. For example, it has been found that stressful life events influence the onset and course of depression (Kendler et al. 1999; Kessler 1997; Pine et al. 2002). However, there is no linear and direct relation (Goodyer 1990), and we are not aware of any study that directly tests the direction of causation. It has also been reported that adolescents initiate smoking to cope with stressful life events (Koval and Pederson 1999; Koval et al. 2000). For example, job loss for a household member is a risk factor for adolescents' involvement in problem behaviors (Unger et al. 2004). Groundbreaking work by Caspi et al. (2003) showed that individual differences in the development of depression caused by stressful life events depend on genetic makeup.

Again, although direction of causation research is under way in many groups around the world using genetically informative designs, it is not clear if genetic predisposition to negative life events is at the root cause of the above relations. However, it can be argued that it is clear that family chaos, conflict, and negative life events, in the genetically informative studies done to date, are associated with higher rates of psychopathology in adults and children. Clearly a strategy aimed modifying the environments of the genetically at risk seems a thoughtful approach that may bring clarity to the questions of why some events lead to impairment in only some of the people. Similarly, why do supportive strategies only help some who have endured negative life events (Kaufman et al. 2004)? Again, studies using the FBA/DP approach are likely to yield important diagnostic and therapeutic advances.

FAMILY CONFLICT

Using data from the large longitudinal database of the Netherlands Twin Register (Boomsma et al. 2006), we are currently investigating the role of familial factors on adolescent wellness and problem behavior. Large studies in our samples of twin children showed moderate to large genetic influences on aggressive behavior during childhood. This classical twin study however, does not reveal information on the possible interacting effects of genes and environment on aggressive behavior. In our new project, "A Twin-Sibling Study of Adolescent Wellness," we have tested the effects of familial conflict, measured with the 11-item Conflict scale from the Family Environ-

ment Scale (Moos and Moos 1974), on the etiology of aggressive behavior from the Youth Self-Report (YSR). The Dutch Health and Behavior Questionnaire has been collected in adolescent twins (n=1,000 pairs) and their nontwin siblings (n=500 individuals).

A main effect of familial conflict on adolescent aggressive behavior (AGG) has been found, with significantly higher levels of AGG in families with high levels of familial conflict (P= 0.00). Preliminary analyses based on twin correlations indicate gene–environment interaction effects, because a higher heritability estimate for AGG is found for the adolescents with low familial conflict in comparison to heritability estimates for the group with moderate familial conflict and the group who reports high familial conflict. Sophisticated model fitting, which will include tests for gender effects and possible effects of gene–environment correlations, will be conducted to gain more insight into the role of familial conflict in AGG. In this way we can begin to estimate the measured genetic and environmental influences on resilience by determining factors that move children into wellness or illness or identifying factors that seem to be protective against inferred genetic and environmental risk factors. Again, these data seem to cry out for family-based intervention approaches (that have long been advocated by a variety of experts) that will reduce family conflict. With a genetically informative approach, these interventions may be tailored more accurately to families who are more likely to respond to them. We argue that while we wait for that evidence it is prudent to move ahead with these strategies now.

OTHER EXAMPLES OF THE FAMILY-BASED GENE–ENVIRONMENT APPROACH

Recent studies reveal the complex interplay between genes and environment when studying family dysfunction in the context of childhood psychopathology. Kendler et al. (2003b), for example, investigated whether dysfunction in the family of origin moderates the impact of genetic factors on liability for psychiatric disorders. They found no evidence for this effect. Furthermore, McGue and Lykken (1992) found that divorce risk was largely caused by genetic influences. An association between genes and environment is also found when neighborhood characteristics (based on zip code) are studied as predictors of adolescent psychopathology. For example, genetic factors account for more individual differences in drinking patterns among adolescents residing in urban areas, whereas shared environmental influences were larger in rural settings (Rose et al. 2001). Similar effects of neighborhood were found for aggressive behavior. Adolescents in high socioeconomic status (SES) neighborhoods were significantly less likely than

their counterparts in low-SES neighborhoods to engage in serious and violent delinquency. Results indicated that risk factors for later repeated violence among adolescents in high-SES neighborhoods, such as physical aggression, may be caused by genetic influences, whereas risk factors for later violence among adolescents in low-SES neighborhoods, such as poor parent–adolescent communication and early intercourse, appeared to be context-dependent (Beyers et al. 2001).

THE GENE–ENVIRONMENT FAMILY-BASED APPROACH AT WORK

Our clinical approach at the VCCYF is inspired by the FBA/DP perspective. We argue that it is no longer sufficient to assess and treat a child's emotional-behavioral problems as if they occur in a vacuum. Put in simple terms, does it really make sense to only treat a 6-year-old boy's anxious depression (with medication and or psychotherapy) when the boy's mother is suffering from panic disorder and his father from alcohol abuse? In this pedigree, for example, all three individuals suffer from disorders that have been identified to be influenced by genetic and environmental factors. We argue that each then contributes to the environmental influences that further can exacerbate the psychopathology. Rather than simply treat the child, we think it prudent to assess the entire family's emotional well-being, health, risk, and protective behavior, and to consider approaches that intervene at the family level and that are developmentally appropriate. While we wait for genetic testing and other promises of our genomic era of medicine, we feel the research to date has already provided us with enough evidence to know that the family-based approach should be implemented in child clinics now.

To operationalize the VCCYF approach, we obtain 1) Child Behavior Checklist (CBCL) data from mothers and fathers and 2) Teacher's Report Forms (TRF) and YSR forms on all children. (We also use DSM interviews, but rely heavily on the CBCL family of instruments because they provide a developmental and gender sensitive perspective absent in the DSM.) These data provide us with a multi-informant, quantitative, developmentally sensitive description of the child's emotional-behavioral health. The CBCL family of instruments generate data on eight syndromes (Attention Problems, Aggressive Behavior, Rule Breaking Behavior, Withdrawn Behavior, Social Problems, Thought Problems, Anxious Depression, and Somatic Complaints) as well as two broadband scales (Internalizing Problems and Externalizing Problems) (Achenbach and Rescorla 2001) and phenotypic markers for obsessive-compulsive behavior and the broad phenotype of juvenile bipolar disorder. Our group has published findings on the genetic

and environmental influences on each of these syndromes. Simply put, in every single instance there is evidence for both genetic and environmental influences on each of these syndromes. We use these data to fuel our family-based explanation of the child's psychopathology. We know each of these child psychopathologic conditions is highly heritable yet influenced by environmental factors. Because children inherit their genes from their parents, and because it is widely known that children with psychopathology often have parents with psychopathology, we considered it prudent to develop an assessment protocol that considered the possibility that parents of children with psychopathology may be struggling against the yoke of their own genetics and the environment that exists in the family. As a result, we also collect emotional-behavioral data on all parents in our clinic.

We obtain the Adult Self-Report on both parents, in which parents describe their own emotions and behaviors on the same syndromes studied in childhood but modified and normed in a developmentally sensitive approach for adults (ages 18–54) and for older adults (ages 55–68 years, Older Adult Self-Report). In addition, we collect the Adult Behavior Checklist, in which partners report on each other's emotions and behaviors, again using the developmental perspective. In addition we collect the Vermont Health Behavior Questionnaire (VHBQ) from parents and children. These data provide us with a detailed description of the child and family's environment with an emphasis on known risk and protective factors, such as happiness (Lyubomirsky and Lepper 1999), life satisfaction (Horley 1984), self-esteem (Kajita et al. 2002), sports participation/physical activity (Babyak et al. 2000), diet/eating habits (Stokes and Frederick-Recascino 2003), academic performance and leisure time (Wilens et al. 2002), and religiosity. We collect data on zip code/SES, medication history, peer smoking/drinking, family relation and family conflict, family structure, cohesion, conflict, life events, parenting styles, and activities such as membership in musical groups, time spent on computers, TV, and electronic games.

The resulting data set forms the foundation for our clinical approach. We have dimensional, developmentally sensitive data on related psychopathological syndromes in the children and their parents (and, in cases in which grandparents are involved, data on the grandparents as well). We can relate a child's anxious depression and inattention syndromes to parental anxiety and inattention. In this way, the child escapes being the identified patient, and the family becomes the focus of treatment. We offer to treat every member of the family who has treatable psychopathology. In addition, we use the data from the VHBQ to identify factors such as family chaos and conflict (see above), which generates a family-based intervention aimed at reducing chaos and conflict in families. With the VHBQ we also learn that many children and families do not participate in sports programs, music

programs, or have healthy diet and exercise programs. Many children leave our clinic with prescriptions to join sports teams, to begin Suzuki violin, to see a dietician, to begin a fitness regimen, or to turn off their TVs, iPods, and computer games. Each of these therapeutic interventions is aimed at modifying the environment and, it is hoped, mediating the genetic expression of these illnesses. Using the CBCL approach as an outcome measure, Weissman et al. (2006) demonstrated that by successfully treating maternal depression, childhood Internalizing and Externalizing scores improved by a full standard deviation, *without* treating the children. Although this remarkable study needs to be replicated, it provides another bit of evidence for the family-based approach. In the near future—indeed, we have a proposal to do this project in review at this time—we would like to provide family genotyping as part of our approach so that we may begin to build a database on which families will benefit from which types of intervention, whether they be of the health promotion, prevention, or intervention (treatment) types. The end game of this approach is to bridge the gap between research findings in the genetic and environmental influences on developmental psychopathology by developing a real-world application. Each of these interventions at worst does no harm and at best may prove to be the types of approaches that will move child psychiatry into the overall family of medical disciplines that embrace health promotion and disease prevention as well as intervention.

CONCLUSIONS

By assessing a child's (and indeed a family's) relative risk for psychopathology using family and molecular genetic approaches, in concert with an assessment of the risk and protective environmental factors, we may be able better to design the complex interventions that are doubtless needed for the complex problems of developmental psychopathology. Although it is clear that molecular genetic testing is a long way from being implemented in clinical settings, it is not too early to learn from the research presented in this book. A more thorough assessment of the child's developmental trajectory, family, and unique environmental risk and protective factors, and, possibly the estimation of the contribution of relative risk genes, may help in the design of more effective treatment and prevention strategies for at-risk children. Indeed, the work of Kaufman et al. (2004) , in which children with one relative risk genotype (S/S allele of the serotonin transporter gene [*SERT*]) were more likely to benefit from social support in the face of extreme environmental disadvantage, offers us the promise of potentially understanding which children will respond to supportive therapies (see Chapter 7, "Genetic and Environmental Modifiers of Risk and Resiliency in Maltreated

Children," this book). Such an advance could well benefit patients, their families, and the clinical teams who serve them. One of the great disappointments of the practice of clinical child psychiatry is the inability to help children achieve wellness despite using all of the methods available in our clinical formulary. It is our contention that the study of resilience, as long as it includes both well and suffering children, while assessing both genetic and environmental factors, is likely to lead to more effective treatments for children and their families and thus improve the efficiency of our clinical efforts.

Routine use of genotyping in clinical practice is probably still decades away. It may well be that through the use of genetic testing, and debunking of damaging misconceptions about etiopathology of child psychiatric illness, families and children will be more likely to seek and accept psychiatric health care. In so doing, we may be able to encourage families to embrace wellness strategies aimed at the family, rather than the child alone. We envision a future that includes assessment of genetic and environmental strengths and weaknesses of the entire family, married to a family-based treatment approach partnered with wellness and therapeutic strategies. It is in this context that we hope to see a reduction in those environmental factors that can be changed in the lives of children and families that contribute to negative outcomes for common psychiatric illnesses. The overall aim is to contribute to healthier, happier families and communities using the research generated by the FBA/DP perspective.

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