
12 Anxiety Disorders in Parents and Children: a Genetic-Epidemiological Perspective

MYRNA M. WEISSMAN

Introduction

The data presented in this chapter are rooted in clinical psychiatry and derive from the methods of genetic epidemiology. However, the approach and findings have implications for the study of behavioral inhibition. The data derive from a family-genetic study that examined the relations between adult forms of anxiety disorders in parents and childhood forms of anxiety disorders in their offspring. Questions that ultimately may be considered by this strategy include, Is behavioral inhibition or shyness in young children a precursor of adult anxiety disorders? Is behavioral inhibition a latent trait that has variable forms of expression at different ages?

Anxiety as a Clinical Disorder

Anxiety states were first described in the cardiovascular literature in the nineteenth century. However, it was Freud (1977) who offered the first detailed description of anxiety syndromes of relevance to psychiatric practice. He identified several different forms of anxiety states. Many of the subtypes he proposed in his 1917 lecture (simple and social phobias, agoraphobia, panic disorder, and obsessive-compulsive disorder) are remarkably similar to the anxiety disorders now classified in the American Psychiatric Association's

This study was supported in part by Alcohol, Drug Abuse, and Mental Health Administration grant MH 28274 from the Affective and Anxiety Disorders Research Branch, National Institute of Mental Health, Rockville, Md.; and Mental Health Research Network on Risk and Protective Factors in the Major Mental Disorders grant 86-213, "Child and Adult Depressive Disorders: A Test of Continuities Using Family-Genetic Data from the John D. and Catherine T. MacArthur Foundation." A version of this paper was also presented at the Behavioral Inhibition Conference sponsored by the New England Node of the John D. and Catherine T. MacArthur Foundation Network on the Transition from Infancy to Childhood, Harvard University, Cambridge, Mass., 21-22 November 1986.

Diagnostic and Statistical Manual of Mental Disorders, Third Edition (DSM-III).

Despite the description of distinct types of anxiety states as early as 1917, a unitary view of anxiety disorders prevailed in American psychiatry until the 1960s, when it was challenged by new information on the differential efficacy of behavioral and of pharmacological treatments for components of anxiety states.

Anxiety disorders in the DSM-III have been separated into subtypes for adults and children. For adults, these include agoraphobia, social and simple phobia, panic disorder, generalized anxiety disorder (GAD), and obsessive-compulsive disorder. Those anxiety disorders first evident in childhood and adolescence include separation anxiety, avoidant disorder, and overanxious disorder.

The epidemiology of most of the anxiety disorders in adults has been determined through surveys of community samples (Weissman 1985). The familial transmission of some anxiety disorders has also been studied (Crowe et al. 1980; Crowe et al. 1983; Leckman et al. 1983; Weissman, Leckman, et al. 1984). There have been no epidemiological studies of children using current psychiatric diagnostic criteria (Orvaschel and Weissman 1986).

Although the DSM-III includes a separate category of anxiety disorders that originate in childhood, there is no reason not to diagnose the other adult anxiety disorders in children, except for the explicit requirement that generalized anxiety disorder not be diagnosed before age 18. In fact, data from epidemiological, family, and clinical studies suggest that many of the anxiety disorders have their first onset in adolescence or earlier. However, since children have not been studied extensively in epidemiological or in family studies, most of the data on age of onset of anxiety disorders in childhood have been obtained retrospectively from adults. There is some suggestion from clinical studies of children that the first onset of anxiety disorders may occur quite early and that there may be a continuum between the adult and the childhood forms of anxiety disorder.

There has not been one published longitudinal study of individuals first identified as having an anxiety disorder in childhood who have been followed to adulthood to determine the natural history, clinical course, or prognostic significance of the childhood anxiety disorders and their continuity to the adult disorders. One such study has just been undertaken by R. Gittelman-Klein at Columbia University.

Family-Genetic Studies as a Research Strategy

Since the introduction of standardized instruments for assessing psychiatric disorders and of specified diagnostic criteria, there has been considerable in-

terest in testing the validity of diagnostic criteria as well as the relations between adult and childhood forms of the disorder. While there are several approaches to validity in psychiatry (follow-up studies, clinical response to treatment, and association with biological markers), family-genetic studies are another approach to identifying possible etiological homogeneous subgroups.

Evidence for familial aggregation of a disorder does not imply that the origin of a disorder is genetic. Aggregation could result either from shared genes or from common environmental factors such as infection, diet, stress, or social learning. It is both simplistic and erroneous to assume that only genetic or only environmental factors are involved in the etiology of psychiatric disorders, for both undoubtedly contribute. Understanding the degree to which each of the sources contributes and interacts to produce a given phenotype is the aim of genetic-epidemiological studies.

Other study paradigms from which information on familial aggregation can be derived include adoption and twin studies, and these designs have been used to study the major psychiatric disorders (for a detailed discussion, see Weissman et al. 1986).

Although family-genetic studies do not yield evidence for the amount of genetic variance, data from family studies in psychiatry can serve several purposes. One of the most fruitful has been to provide better understanding of diagnostic heterogeneity. It is quite likely that many of the psychiatric disorders are groups of conditions rather than single entities with different etiological and modifying risk factors. The use of family data in the absence of specific neuropathological evidence is one approach to identifying homogeneous diagnostic subgroups. If the diagnostic subgroup under study increases risk of the disorder and "breeds true" within families, potential evidence for the validity of the diagnostic group is suggested. If adult forms of a disorder are related to increased risk of specific disorders in the offspring of affected individuals, this suggests a relation between the adult and childhood disorders.

Because variation in expression of a particular trait within families is assumed to result from the same latent factor, family studies can yield information on the clinical expression of a disorder. This property of family studies can lead to the development of more precise clinical descriptions of the spectrum of disorders, as manifest in the personality, symptoms, or social functioning of relatives. Studies of the young children of adult probands can yield information on the transmission of disorders and/or symptoms across generations, on the early signs and childhood forms of the disorder, and on the risk or protective factors that mediate the development of the disorder.

Of course, these methods are indirect and represent only one strategy that requires replication by similar and alternate strategies. Multiple strategies for validating the diagnosis of anxiety disorders are currently being developed.

Design of a Family-Genetic Study

Case-Control Studies

In a family-genetic study, a proband with the illness under investigation is selected for study and is then matched to a control proband (i.e., an individual who does not have the illness under investigation but who is comparable on other characteristics). Usually, the prevalence of the condition among first-degree relatives is compared to prevalence among relatives of controls. In the absence of control groups, the rates of illness among relatives can be compared to population rates. This design requires accurate information on the population at risk. In either case, these studies usually have a retrospective cohort design in that the lifetime rates of illness in relatives are obtained on the basis of recall of their lifetime incidence of disorder.

Top-Down Studies

In family studies of psychiatric disorders, the probands, or index cases, with the disorder being investigated have nearly always been adults who were selected from treatment settings or from psychiatric or case registries. Family studies that begin with the adult probands and study psychopathology among their offspring as well as other relatives have been called "top down" by Puig-Antich (1984).

Bottom-Up Studies

With the increasing interest in childhood psychiatric disorders during the last decade, children have also begun to be defined as the probands in family studies termed "bottom-up" studies (Strober 1984). In a manner similar to that followed in the adult studies, children who serve as probands generally have been selected from inpatient or outpatient treatment settings. Studies that begin with the child or adolescent as the proband, or index case, tend to find very high rates of illness in the adult relatives, possibly because of sampling bias. Although the proband is the treated child, it is the parent who brings the child for treatment and who grants permission for the child to be included in the study. Ill parents, or parents sensitized to the effects of the illness because of several ill family members, may be more likely than healthy parents to bring their children to treatment and to consent to the child's inclusion in a study.

In order to control for this ascertainment bias, researchers can select a comparison control proband group of children with another treated psychiatric illness. The rates of all types of psychiatric illness will also tend to be high in the adult relatives of the child comparison group. However, the types of illness and the magnitudes of the differences in rates between the relatives of the

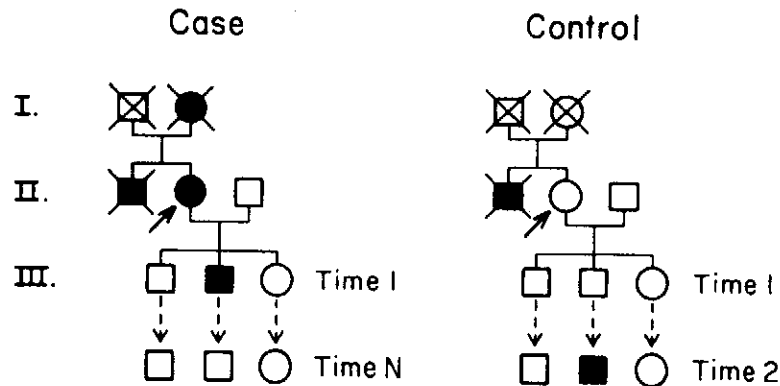


Fig. 1. High-risk study.

cases and the relatives of the comparison control group can provide more important information than the absolute rates of illness in the relatives.

High-Risk Studies

The high-risk paradigm is a variant of the family study (see fig. 1) (Garnezy 1974; Weissman et al. 1986). The focus is usually limited to the young children of ill probands. Usually, there is no assessment of the proband's first-degree or other relatives, although it is quite important to assess the spouse. In high-risk studies, the offspring are usually studied longitudinally in order to identify risk factors that are premorbid to, rather than concomitant with, the disorder or that are manifestations of the disorder. Such factors may serve to identify vulnerable individuals and permit efforts toward prevention and intervention.

Family-Genetic Study

The data reported here derive from a high-risk study imbedded in a family study in which the young offspring are being followed longitudinally (fig. 1) (Weissman, Kidd, and Prusoff 1982; Weissman, Leckman, et al. 1984; Weissman, Prusoff, et al. 1984). Diagnostic information was available on the probands' first-degree relatives and offspring.

The first findings derived from family studies of depressed patients, in which my colleagues and I discovered that many depressed patients had concomitant anxiety disorder. We attempted to understand the relation between anxiety disorders and depression by using familial transmission as an outcome. To do this, we asked whether anxiety disorder in the proband increases risk of depression and/or anxiety in relatives. If an accompanying anxiety disorder increases risk of depression, then this suggests that depression and

anxiety are similar disorders. If anxiety disorder in the proband increases the risk of anxiety in relatives (when compared to relatives of probands with no accompanying anxiety disorder), this suggests that anxiety is a distinct disorder. The more specific questions have to do with the type of anxiety disorder.

Methods

The initial sample included 215 probands (82 normal controls drawn from a community sample and 133 probands with major depression), 1,331 of their adult first-degree relatives, and 194 of their children aged 6–17 years. Children under 6 years of age were not studied because the current interview methods are not suitable for use with these younger age groups. Diagnoses were based on the Research Diagnostic Criteria (RDC) for all probands and adult first-degree relatives and on the DSM-III for the children (Weissman, Leckman, et al. 1984).

In the family study of adults, comprehensive diagnostic estimates of probands, spouses, and all adult first-degree relatives, including children older than 18 years, were obtained through direct interview, family history from multiple informants, and medical records when available. Diagnoses were made by two clinicians uninvolved in the collection of the data on the basis of all available information. The interviewers and the clinicians did not know whether the children came from depressed or normal parents.

Children younger than 18 years were not interviewed directly; instead, information on minor children was obtained by family history from the proband, spouse, and other first-degree relatives. The data presented on the children in the report of this study always refer to the probands' children aged 6–17 years.

A screening instrument, modified from the early work of Herjanic and Reich, was administered to the probands and spouses to determine symptoms of psychopathological condition, behavioral problems, and psychological treatment in any of their children who were aged 6–17 years at the time of the proband interview. First, there was a general probe about problems with the child, and then the informant was read a symptom list, including questions about the child's psychological treatment, school difficulties, and symptoms. Information was obtained separately for each child. When there were positive answers to symptoms, the interviewers were instructed to code them and to record details in a narrative form as well. Medical records were also sought. For 64 percent of children with a diagnosis, information was available from more than one source. Since many of the probands with major depression also had anxiety disorders, we became interested in the effect of a depression plus an anxiety disorder in probands on rates and type of illness in first-degree relatives.

Table 1: Diagnoses in Adult Relatives 18 Years or Older by Proband Diagnosis

Proband Diagnosis	N at Risk	Major Depression	Phobia	Panic	GAD	Any Anxiety
Normal	521	5.6	1.2	.0	4.0	5.2
Major depression						
No anxiety	338	10.7	2.1	2.1	6.2	9.2
With agoraphobia	96	11.5	1.0	2.1	5.2	8.3
With panic disorder	133	19.6	3.8	3.8	10.5	15.8

For these analyses, we looked closely at the specific anxiety disorders in the probands, using a diagnostic hierarchy for probands with depression and anxiety disorders, as follows: agoraphobia > panic disorder > generalized anxiety disorder. Operationally, this meant that depressed probands with both agoraphobia and panic disorder would be classified as depressed with agoraphobia and so on (Leckman et al. 1983). For this chapter, I will concentrate on agoraphobia and panic disorder.

Findings in Adults

Table 1 summarizes the results in adults. In general, the first-degree relatives of probands with major depression and panic disorder had the highest rates of illness. They showed increased rates of major depression, phobia, panic, GAD, and anxiety disorders when compared to the relatives of either the normal controls or the depressed probands without an anxiety disorder.

Findings in Children

Next, we looked at the rates of DSM-III diagnoses in 194 of the probands' children ages 6-17 (table 2) (Weissman, Leckman, et al. 1984). The subgroups of probands were the same as those for the study of adults, with one exception. Probands who had social and simple phobias, as well as agoraphobia, were included in the depression and phobia group since we were examining the outcome of the different phobias in children. As with the adult relatives, the highest rates of illness were in the children of probands with both depression and panic disorder. The rates of major depression (26.3 per 100) and separation anxiety (36.8 per 100) were highest in the children of parents with both depression and panic disorder. These findings support the suggestion of Klein and Gittelman-Klein (1978) that there is an association between childhood separation anxiety and panic disorder.

Several of the children had both depression and anxiety disorders. Table 3 shows the rates of depression and anxiety disorders, singly or together, in children by proband diagnosis. The results show that the children's diagnoses tended to follow those of their proband relatives, with several specific trends

Table 2: DSM-III Diagnosis in Children Ages 6-17 Years by Proband Parent Diagnosis

DSM-III Diagnosis in Children	Proband Parent Diagnosis (Lifetime Rates per 100 in Children)			
	Normal (87)	Depression, No Anxiety Disorder (38)	Depression and Agoraphobia (18)	Depression and Panic (19)
Major depression	.0	10.5	22.2	26.3
Separation anxiety	.0	.0	11.1	36.8
Panic disorder	.0	.0	5.6	5.3
Agoraphobia	.0	.0	5.6	5.3
Social phobia	1.2	.0	11.1	5.3
Simple phobia	.0	.0	.0	5.3
Obsessive-compulsive	1.2	.0	5.6	.0
Any diagnosis	8.1	21.1	27.8	42.1

Note. Numbers in parentheses represent number of children at risk.

visible. For example, (1) there was increased depression in the children of the depressed probands, particularly the children of probands with depression plus agoraphobia and the children of probands with depression plus panic disorder (22.2 and 26.3 percent, respectively); (2) there was increased anxiety disorder in the children of the probands with depression plus panic disorder; (3) the children of probands with depression and no anxiety disorder did not themselves have anxiety disorders; (4) increased rates of phobia were observed in the children of probands with depression plus agoraphobia and among the children of probands with depression plus panic disorder; and (5) there were increased co-occurrences of depression plus any anxiety disorder (26.3 per 100) in the children of probands who also had the co-occurrence of depression and an anxiety disorder, particularly panic disorder (see table 3).

Table 3: DSM-III Anxiety Disorders and Depression in Children by Proband Parent Diagnosis

DSM-III Diagnosis in Children	Children with Diagnosis (N)	Proband Parent Diagnosis (Lifetime Rates per 100 in Children)			
		Normal	Depres- sion, No Anxiety Disorder	Depression and Agoraphobia	Depression and Panic
Any major depression	17	.0	13.2	22.2	26.3
Any anxiety disorder*	13	2.3	.0	11.1	36.8
Any phobia ^b	5	1.2	.0	11.1	10.5
Major depression and any anxiety disorder	8	.0	.0	11.1	26.3

*Includes all phobias, panic, separation anxiety, and obsessive-compulsive.

^b Includes agoraphobia, simple, and social phobia.

Age of Onset and Sex Distribution of Anxiety Disorders

Age-corrected rates of depression and any anxiety disorder by sex were calculated for the children of probands using Lifetime Risk (LTR), which is defined as the risk of onset of a particular disorder between birth and some particular age (age 18 years, in this case). The estimation of LTR is based on the nonparametric product-limit table method for analyzing survivorship developed by Kaplan and Meier (1958), which yields a maximum likelihood estimate of LTR. This method makes a calculation at each point in time there is a change in the number of persons at risk for development of the disorder. The number at risk changes with each onset of the disorder and with each death of an unaffected person. The Biomedical Computer Program P-series (BMDP) program PIL was used to calculate LTR.

The earliest onset age of an anxiety disorder was 3 years. The LTR by age 18 years for developing an anxiety disorder was .08 among boys and .10 among girls. There were no significant differences in rates of anxiety disorders by sex of child for these young groups. The epidemiological data on adults show a strong sex effect in adults, with higher rates in women for all anxiety disorders. Thus, increased risk of anxiety disorder in adult women is not apparent in children. As in depression, the sex difference with increasing risk to women may not become apparent until after puberty.

Using logistic analyses, we also examined the effect of sex of proband on the rates of any anxiety disorder or any depression in children and found no significant effect. Caution must be exhibited in interpreting these findings because of the small sample size of children who were affected and the retrospective nature of the data.

Parent Characteristics as Risk Factors

Several proband characteristics (e.g., sociodemographic variables, early history, and family history of illness) were examined to determine whether these proband characteristics increased the risk of major depression, any anxiety disorder, or any DSM-III diagnosis in the children across the proband groups. The proband characteristics that did not increase the risk were current age, sex, social class, number of children (any age) in family, marital status, childhood history of stuttering or sleepwalking, and separation from parent as a child. The characteristics of probands that did increase risk in the children were number of episodes of depression, childhood history of enuresis, and number of first-degree relatives (i.e., probands' parents, siblings, or adult children or children's grandparents, aunts, uncles, or adult siblings) with major depression or anxiety disorders.

Having found that the proband's number of episodes of depression significantly increased the probability of a major depression in the child, we conducted the following analysis to determine if either the child's age at exposure

or the number of years of exposure to parental illness was critical in increasing risk. We first examined the relation between the child's age at exposure to the parent's first onset of depression and of anxiety; then we controlled for the number of years the child had been exposed to the proband's depression and anxiety. Neither set of analyses yielded any significant differences in rate of disorders in the children; nor were there any interpretable trends.

Summary Findings

The findings of our first family-genetic study of anxiety disorder in the children and parents with depression and anxiety were as follows.

1. Major depression and anxiety disorders are probably heterogeneous diagnostic categories.

2. Probands with both major depression and panic disorder show markedly increased rates of major depression as well as anxiety disorders (phobia, panic disorder, and GAD) compared with the first-degree relatives of normal controls and depressed probands without anxiety disorders.

3. These findings suggest that panic disorder and major depression may partially have a common underlying diathesis. My colleagues and I are testing this hypothesis prospectively in new studies.

4. As compared with the children of normals, the children (ages 6-17) of depressed probands were at increased risk for major depression. Depression plus agoraphobia or panic disorder in the probands conferred an additional risk on the children. If the proband had both depression and panic disorder, the children were at the greatest risk for having a psychiatric disorder, particularly major depression and separation anxiety. More than one-third of the children of probands with depression plus panic disorder had separation anxiety, and more than one-fourth had major depression.

5. As noted elsewhere (Weissman, Leckman, et al. 1984), the risk to children for major depression or any psychiatric disorder increased linearly if two parents were ill. There was a similar, but nonsignificant, trend for anxiety disorders.

6. The proband characteristics that did *not* increase risk of anxiety disorder or any psychiatric disorder in children were current age; sex; social class; marital status; number of other children; age of onset of depression, anxiety disorder, or any psychiatric disorder; childhood history of stuttering or sleepwalking; and separation from parents during childhood. The child's age at exposure or years of exposure to parental illness also did not increase risk (Weissman, Leckman, et al. 1984).

7. The proband characteristics that significantly increased risk of anxiety in children were recurrent depressions, high familial loading of major depression or any anxiety disorder, and childhood history of enuresis.

Are Adult and Childhood Anxiety Disorders on a Continuum?

We have found that major depression in the parent increases the risk of major depression in the children and that depression plus anxiety disorders, particularly panic and agoraphobia, confers an additional risk of depression and anxiety in these children. Panic disorder in the parents, in contrast to other anxiety disorders, confers a greater than threefold increase of separation anxiety in the children.

These data suggest that the children of patients with agoraphobia or panic disorder are beginning to manifest similar disorders themselves, particularly separation anxiety. A number of investigators have made similar observations about the onset of adult anxiety disorder in childhood or early adulthood. One of the earliest observations was made by Klein (1964) in a review of 32 adult patients being treated for panic attacks, with agoraphobia or anticipatory anxiety. At least half the adult patients reported marked separation anxiety and difficulty in adjusting to school as children. The patients who reported childhood separation anxiety had chronically high levels of separation anxiety throughout their lives and suffered significantly more panic attacks under conditions of separation and bereavement.

Roth (1960), in a study of 135 patients with phobic anxiety and depersonalization, noted that onset occurred most often during the early 20s. Sheehan, Sheehan, and Minichiello (1980), in a study of 100 patients treated for agoraphobia and panic attacks, found that 55 percent had an onset of agoraphobia by age 20. Buglass et al. (1977), in a study of 30 agoraphobic housewives, dated the mean age of onset of agoraphobic symptoms at 31 years, with a range of 10–52 years. Agras, Sylvester, and Oliveau (1969), in a community survey of 325 persons, found a high prevalence of fears and phobia in children younger than 14 years. There was also a different pattern of phobias with age. A fear of doctors, injection, darkness, and strangers was short lived and had a sharply declining incidence as the children matured. A fear of animals, heights, storms, enclosed places, and social situations showed slowly declining incidence with age, suggesting that, once acquired, such fears were longer lived.

Others have questioned whether childhood anxiety symptoms are related to adult anxiety disorders or to nonspecific psychiatric problems. Berg and his colleagues (Berg, Butler, and Pritchard 1974; Berg, Marks, et al. 1974) surveyed 786 female members of an agoraphobia correspondence club to learn about incidence of past school phobias. When these women were compared with 58 nonagoraphobic women who were psychiatric outpatients with a neurotic disorder, few differences between the groups were found. A history of school phobias was equally common in both groups. The authors concluded

that childhood school phobias were related generally to adult neurotic illness rather than specifically to adult agoraphobia.

Tyrer and Tyrer (1974) interviewed 60 phobic, 60 anxious, and 120 depressed adult patients, and 120 matched orthopedic and dental patients for comparison, about problems of childhood school attendance that were due to refusal. They found that school refusal occurred more frequently among the patients with psychiatric disorders. There was a nonsignificant tendency for childhood school refusal to be higher in phobic patients. These authors concluded, in agreement with Berg, that there is a link between childhood school refusal and adult neurotic illness. However, the diagnostic criteria for neurotic illness in these studies were unclear. Many of these nonagoraphobic neurotic women might have been suffering from other anxiety or depressive disorders.

Klein's early observations of the possible relation between adult and childhood anxiety disorders, and the successful treatment of these adult anxiety patients with imipramine, led to the first trial of imipramine in school-phobic children by Gittelman-Klein and Klein (1973). Their results suggested that school-phobic children and phobic-anxious adults may share a common psychopathological process, as both adults and children with phobic problems had a similar positive response to imipramine. However, my colleagues and I agree with the investigators' conclusion about the need for long-term studies of phobic children to determine the degree to which these disorders were precursors of adult anxiety or of depressive states. Direct observation of children is important.

Relevance for Studies of Behavioral Inhibition

Very young children and infants have not been included in any of the studies cited. Since anxiety disorders may begin in childhood, it would be quite useful to study children before the onset of a clinical disorder.

There are no family-genetic studies, to our knowledge, that have included the assessment of offspring under the age of 6 years. Direct interviews of children are not very useful for the diagnostic assessment of psychiatric disorders in this age group. Other approaches are required. There is an opportunity here for fruitful collaboration with developmental psychologists who use observational techniques that can be modified for field studies. As an example, the approaches used by Kagan and his colleagues (e.g., Kagan et al. 1984) in their elegant studies of very young shy children may be quite important in assessing children of adult probands with agoraphobia and panic disorder. Is shyness an early form of agoraphobia or panic disorder? Are behavioral inhibitions the latent traits of anxiety disorders? If the design used is a family-case-control or high-risk method, as described here, it would be relatively easy to incorporate young children and infants in the assessment, given

that methods of assessing behavioral inhibition have been developed. These measures could be considered as proxies for anxiety disorders and the results incorporated into the epidemiological and genetic analyses.

If the shy or behaviorally inhibited child is the proband, as in the bottom-up study, then the inclusion of a control group of children is warranted. Perhaps non-behaviorally inhibited children enrolled in the same study would be suitable. Without a control group, if anxiety is found in the parents of behaviorally inhibited children, it will be unclear whether the association might not be due to the tendency of anxious parents to enroll their children in studies.

Finally, it is important that the diagnostic assessment of parents and relatives be made with careful attention to the type of anxiety disorders and their comorbidity with major depression or other disorders. There are several good diagnostic interviews available that cover the variety of anxiety disorders (Weissman et al. 1986). Previous family studies that my colleagues and I conducted began with an interest in major depression, and the findings led us into studies of anxiety because of the high comorbidity with depression and the intriguing results in children. We are currently conducting studies of various anxiety disorders in families. The increased collaboration in such a study of developmental psychologists interested in behavioral traits of infants and young children as well as genetic epidemiologists interested in transmission of psychiatric disorders in families across the generations could be potentially fruitful and exciting.

References

- Agras, S.; Sylvester, D.; and Oliveau, D. 1969. The epidemiology of common fears and phobias. *Comprehensive Psychiatry* 10:151-56.
- Berg, I. 1976. School phobia in the children of agoraphobic women. *British Journal of Psychiatry* 128:86-89.
- Berg, I.; Butler, A.; and Pritchard, J. 1974. Psychiatric illness in the mothers of school-phobic adolescents. *British Journal of Psychiatry* 125:466-67.
- Berg, I.; Marks, I.; McGuire, R.; and Lipsedge, M. 1974. School phobia and agoraphobia. *Psychological Medicine* 4:428-34.
- Buglass, D.; Clarke, J.; Henderson, A. S.; Kreitman, N.; and Presley, A. S. 1977. A study of agoraphobic housewives. *Psychological Medicine* 7:73-86.
- Crowe, R.; Noyes, R.; Pauls, D. L.; and Slymen, D. 1983. A family study of panic disorder. *Archives of General Psychiatry* 40:1065-69.
- Crowe, R.; Pauls, D. L.; Slymen, D. J.; and Noyes, R. 1980. A family study of anxiety neurosis. *Archives of General Psychiatry* 37:77-79.
- Freud, S. 1977. Anxiety Lecture XXV, 1917. In *An introductory lecture on psychoanalysis*, ed. J. Strachey, 392-412. New York: Norton.
- Garnezy, N. 1974. Children at risk: The search for the antecedents of schizophrenia: 2. Ongoing research programs, issues, and intervention. *Schizophrenia Bulletin* 9:55-125.

- Gittelman-Klein, R., and Klein, D. F. 1973. School phobia: Diagnostic considerations in the light of imipramine effects. *Journal of Nervous and Mental Disorders* 156:199-215.
- Kagan, J.; Reznick, S. J.; Clarke, C.; Snidman, N.; and Garcia-Coll, C. 1984. Behavioral inhibitions to the unfamiliar. *Child Development* 55:2212-25.
- Kaplan, E. B., and Meier, P. 1958. Nonparametric estimation from incomplete observations. *Journal of the American Statistical Association* 53:457-81.
- Klein, D. F. 1964. Delineation of two-drug responsive anxiety syndromes. *Psychopharmacologia* 5:397-408.
- Klein, D. F., and Gittelman-Klein, R. 1978. Drug treatment of separation anxiety and depressive illness in children. *Advances in Biological Psychiatry* 2:50-60.
- Leckman, J. F.; Weissman, M. M.; Merikangas, K. R.; Pauls, D. L.; and Prusoff, B. A. 1983. Panic disorder and major depression: Increased risk of depression, alcoholism, panic and phobic disorders in families of depressed probands with panic disorder. *Archives of General Psychiatry* 40:1055-60.
- Orvaschel, H., and Weissman, M. M. 1986. Epidemiology of anxiety disorders in children: A review. In *Anxiety disorders of childhood*, ed. R. Gittelman, 58-72. New York: Guilford.
- Puig-Antich, J. 1984. Affective disorders. In *Comprehensive textbook of psychiatry*, vol. 2, ed. H. J. Kaplan and B. J. Sadock, 1850-61. Baltimore: Williams & Wilkins.
- Roth, M. 1960. The phobic anxiety-depersonalization syndrome and some general aetiological problems in psychiatry. *Journal of Neuropsychiatry* 12:293-306.
- Sheehan, D. V.; Sheehan, K. E.; and Minichiello, W. E. 1981. Age of onset of phobic disorders: A reevaluation. *Comprehensive Psychiatry* 22:544-53.
- Strober, M. 1984. Familial aspects of depressive disorder in early adolescence. In *An update on childhood depression*, ed. E. Weller. Washington, D.C.: American Psychiatric Press.
- Tyrer, P., and Tyrer, S. 1974. School refusal, truancy, and adult neurotic illness. *Psychological Medicine* 4:416-21.
- Weissman, M. M. 1985. The epidemiology of anxiety disorders: Rates, risks, and familial patterns. In *Anxiety and the anxiety disorders*, ed. A. H. Tuma and J. D. Maser, 275-96. Hillsdale, N.J.: Erlbaum.
- Weissman, M. M.; Kidd, K. K.; and Prusoff, B. A. 1982. Variability in rates of affective disorders in relatives of depressed and normal probands. *Archives of General Psychiatry* 39:1397-1403.
- Weissman, M. M.; Leckman, J. F.; Merikangas, K. R.; Gammon, G. D.; and Prusoff, B. A. 1984. Depression and anxiety disorders in parents and children: Results from the Yale Family Study. *Archives of General Psychiatry* 41: 845-52.
- Weissman, M. M.; Merikangas, K. R.; John, K.; Wickramaratne, P.; Prusoff, B. A.; and Kidd, K. K. 1986. Family-genetic studies of psychiatric disorders: Developing technologies. *Archives of General Psychiatry* 43:1104-16.
- Weissman, M. M.; Prusoff, B. A.; Gammon, G. D.; Merikangas, K. R.; Leckman, J. F.; and Kidd, K. K. 1984. Psychopathology in the children (ages 6-18) of depressed and normal parents. *Journal of the American Academy of Child Psychiatry* 23:78-84.