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3 Family Studies of Affective Disorders

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INTRODUCTION

Until recently, the conventional wisdom was that children were not capable of becoming depressed. With the increasing use of systematic diagnostic assessments and direct interviews of children, it has become clear that depression occurs in prepubertal children and is common in adolescents (Weissman, 1988: 143). It is also quite clear from systematic studies that depression runs in families. The offspring of depressed parents and the first-degree relatives of depressed children are at increased risk for depression and other psychiatric disorders. Research efforts are underway to better understand the clinical characteristics, familial aggregation, treatment, and course of depression in children.

The purpose of this chapter is to review recent data concerning the familial nature of major depression and bipolar disorder and to discuss the implications of these findings for pediatricians. This information is of particular importance to pediatricians because they are in a unique position to identify early signs of these disorders in children. They are often the first and, sometimes, the only medical professionals that parents consult concerning their children's psychiatric problems. Parents may consult a pediatrician before anyone else because this relationship is already established and also because it may be too threatening to directly contact a mental health professional.

In addition, some parents may not recognize the signs and symptoms of psychiatric illness in their child. Pediatricians themselves may miss the diagnosis of depression or other psychiatric disorders in children (Chang *et al*, 1988:736–739). As we will demonstrate, depression or bipolar disorder in a parent increases the risk for psychiatric illness in the children and, therefore, it is important for pediatricians to be knowledgeable about the familial aspects of affective disorders.

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BACKGROUND

Before we discuss the research findings, we will first describe two basic types of studies which provide information on the familial nature of affective disorders. For a more detailed discussion of family study designs, see Weissman *et al* (1986: 1104–1116). "Top down" studies begin with a depressed or bipolar parent as the patient (called the proband or index case) and study the patient's offspring and spouse. Sometimes the patient's other first-degree relatives (siblings and parents) are also studied. These are also referred to as "high risk" studies since the children are at high risk for psychiatric problems by virtue of the parent's illness.

"Bottom up" studies start with the depressed or bipolar child as the patient (proband or index case) and then study the child's first-degree relatives (parents and siblings). In this chapter we will review some of the more recent "top down" and "bottom up" studies of major depression and bipolar disorder.

To put the recent findings in perspective, it will be helpful to review the changes that have occurred in the methodology of family studies which involve children. Earlier studies were described by Orvaschel (1983: 53–66) in a review of research on the effects of parental depression on psychopathology in children. Many of the studies she described had methodological problems, including small numbers of children, absent control groups, or non-blind interviews.

Methodological differences made it difficult to compare findings between studies. For example, there were differing types of parental affective disorders, differing types of control groups, varying diagnostic criteria and diagnostic methods, differing informants, and varying methods of calculating rates of disorders. Even given these problems, Orvaschel concluded from the available data that the children of depressed parents are at increased risk for depression and behavior problems. In an independent review, Beardslee *et al* (1983: 825–832) reached similar conclusions.

CHARACTERISTICS OF RECENT FAMILY STUDIES

With the increasing availability and use of systematic assessment methods for diagnosing psychiatric disorders in children, there are now a number of well-designed "top down" and "bottom up" studies of major depression and bipolar disorder. In addition, there is a continuing study involving the direct observation and follow-up of the young offspring of parents with bipolar disorder (Zahn-Waxler *et al*, 1988: 506–509).

We will review a subset of these studies which we feel are the best-designed, have reasonable numbers of patients, and use modern diagnostic criteria. Those to be described have used probands, either parents or children, with lifetime histories of either major depression or bipolar disorder. Tables 3.1 and 3.2 present the characteristics of nine selected studies. These studies have looked at children and adolescents (age six and older) and some have included young adults (up to age 23).

In the "top down" studies described in Table 3.1, one parent in each family was chosen as a proband on the basis of having a current episode or lifetime history of either major depression or bipolar disorder. Occasionally the co-parent had the same disorder. At least one parent proband in each family, and many of the co-parents, were directly evaluated. The parent proband samples were obtained from outpatient and inpatient settings and also from community derived samples. Therefore, the probands reflect a range of severity of affective illness.

Table 3.1 Characteristics of recent "top down" studies of parent probands with affective disorder

Investigator	*Diagnoses of Parent Probands*	*Diagnostic Assessment*		*Ages of Children (Years)*
		Parent	*Child*	
Breslau *et al.* (1987)	MDD[a] Anxiety Not ill[b]	DIS	DISC	8–23
Gershon *et al.* (1985)	BP[c] Not ill	SADS-L	K-SADS-E	6–17
Klein *et al.* (1985)	BP Other psychiatric disorders	SADS	SADS-L	15–21
Klein *et al.* (1988)	MDD Medical illness Not ill	SADS	SADS-L	14–22
Orvaschel *et al.* (1988, 1990)	MDD Not ill	SADS-L	K-SADS-E	6–17
Weissman (1988)	MDD Not ill	SADS-L	K-SADS-E	6–23

[a] MDD = major depressive disorder. In this study, only mothers were included and only one child in each family was studied.
[b] No lifetime history of psychiatric illness.
[c] BP = bipolar disorder.

Table 3.2 Characteristics of recent "bottom up" studies of child probands with affective disorder

Investigator	*Diagnoses of Child Probands*	*Diagnostic Assessment*		*Ages of Children (Years)*
		Child	*Adult Relatives*	
Mitchell *et al.* (1989)	MDD Other psychiatric disorders	K-SADS	SADS-L	7–17
Puig-Antich *et al.* (1989)	MDD Anxiety Not ill	K-SADS	SADS-L	6–12
Strober *et al.* (1988)	BP Schizophrenia	SADS	SADS-L	13–17

The "bottom up" studies, described in Table 3.2, selected as probands children with current or recent episodes of either major depression or bipolar disorder. The child probands came from both outpatient and inpatient samples.

The parents in these "top down" and "bottom up" studies were directly interviewed using systematic diagnostic interviews, either the Schedule for Affective Disorders and Schizophrenia (SADS) (Endicott and Spitzer, 1978: 773–782) or the Diagnostic

nterview Schedule (DIS) (Robins *et al*, 1981: 381–389). The children were evaluated sing the Diagnostic Interview Schedule, Children's Version (DISC) (Edelbrock and Costello, 1984: 286–287), the Schedule for Affective Disorders and Schizophrenia or School-Aged Children, Epidemiologic Version (K-SADS-E) (Puig-Antich *et al*, 1980), or the SADS, lifetime version (SADS-L), used here with adolescents. These interviews yielded diagnoses based upon DSM-III (American Psychiatric Association, 1980: 1–494) or Research Diagnostic Criteria (RDC) (Spitzer *et al*, 978: 773–779; Endicott and Spitzer, 1979: 52–59).

All of the studies used control proband groups. Studies which do not use control roups cannot demonstrate that the increase in risk of a disorder in relatives is due o the presence of the affective disorder in the probands. The control groups in he "top down" studies consisted of parents with no history of psychiatric illness, vith nonaffective psychiatric disorders (e.g., anxiety), or with chronic medical lnesses. In the "bottom up" studies, the control groups consisted of children with o history of psychiatric illness or with nonaffective (e.g., anxiety) psychiatric disrders. Strober *et al* (1988: 255–268) used children with schizophrenia as a control roup.

The studies assessed psychiatric illness in the first- and, sometimes, second-degree elatives of the children, either by direct interview or by using the family history ıethod (Andreasen *et al*, 1977: 1229–1235). Diagnoses for most of the relatives of robands were made blindly, without knowledge of the proband's group status ıffected or nonaffected). Most of the diagnoses of relatives were made on the asis of the consensus of several clinicians, using all available data from multiple ıformants. Some of the studies had a follow-up component.

The Breslau *et al* (1987: 285–297) study was not designed for the purpose of udying the familial aggregation of psychiatric disorders, but it does provide some ata about the risks to children of having depressed parents. It reports annual, not fetime, prevalence rates and so the rates cannot be directly compared with those om the other studies, which have used lifetime rates. A "lifetime prevalence rate" r a disorder refers to the number of people/100 who had the disorder at any time ı their lives. An "annual prevalence rate" refers to the number of people/100 who ad the disorder at any time in a specified one-year time period.

The Hammen *et al* (1987: 736–741) study of children of depressed and bipolar ıothers is very well-designed, but it is not included here because the published ndings have grouped bipolar and non-bipolar probands. For this review, we are resenting findings separately for the two disorders.

INDINGS OF RECENT FAMILY STUDIES

ables 3.3 and 3.4 summarize the findings, from the studies described in Tables 3.1 nd 3.2, on the rates of a number of psychiatric disorders in the relatives of probands vith affective disorders as compared to the relatives of control probands.

Table 3.3 Comparison of rates of disorders in relatives of depressed probands with rates in relatives of control probands

Investigator	*Any Psychiatric Disorder*	*Major Depression*	*Bipolar Disorder*	*Any Anxiety Disorder*	*Substance Abuse*
Rates of Disorders in Children of Depressed Parent Probands[a]					
Breslau *et al.* (1987)[b]					
8–17 yrs.		N.S.		Increased[c]	
18–23 yrs.		Increased		N.S.	
Klein *et al.* (1988)	Increased	Increased[d]	N.S.		
Orvaschel *et al.* (1988)	Increased	N.S.[e]	N.S.[e]	N.S.	
Weissman (1988)	Increased	Increased		Increased	Increased
Rates of Disorders in First-Degree Relatives of Depressed Child Probands[f]					
Mitchell *et al.* (1989)					
Mothers		N.S.	N.S.	Increased[g]	Increased
Puig-Antich *et al.* (1989)	Increased	Increased	N.S.		Increased[h]

See bottom of Table 3.4 for an explanation of notations.

Table 3.4 Comparison of rates of disorders in relatives of bipolar probands with rates in relatives of control probands

Investigator	*Any Psychiatric Disorder*	*Major Depression*	*Bipolar Disorder*	*Any Anxiety Disorder*	*Substance Abuse*
Rates of Disorders in Children of Bipolar Parent Probands[a]					
Gershon *et al.* (1985)	Increased	N.S.	N.S.	N.S.	N.S.
Klein *et al.* (1985)	Increased	N.S.	N.S., but increased for cyclothymia	N.S.	N.S.
Rates of Disorders in First-Degree Relatives of Bipolar Child Probands[f]					
Strober *et al.* (1988)		Increased	Increased	N.S.	N.S.

[a] A notation of "increased" means that the lifetime prevalence rate of the disorder was significantly higher in children of affected parent probands than in children of control parent probands. "N.S." means that there was no significant difference in rates between children of affected parent probands and children of control probands.
[b] One-year prevalence rates.
[c] Overanxious disorder.
[d] There was a significant difference for RDC major depression, but not for DSM-III major depression.
[e] Rates for affective disorder were increased in children of affected parent probands.
[f] A notation of "increased" means that the rate of the disorder was significantly higher in the first-degree relatives of affected child probands than in the relatives of control probands. "N.S." means that there was no significant difference in rates between the two groups of first-degree relatives.
[g] Panic disorder and/or agoraphobia.
[h] Alcoholism.

Any psychiatric disorder

As can be seen in Table 3.3, the lifetime rates of "any psychiatric disorder" were significantly increased in the children of depressed parents in three studies and in the relatives of depressed children in one study. The rates of "any psychiatric disorder" were increased in both studies of children of bipolar parents.

For the children of parents with major depression or bipolar disorder, the lifetime rates of "any psychiatric disorder" were high (not shown in the tables), ranging from 41/100 (Orvaschel *et al*, 1988: 21) to 76/100 (Weissman, 1988: 150) for the children of depressed parents and from 43/100 (Klein *et al*, 1985: 119) to 72/100 (Gershon *et al*, 1985: 287) for the children of bipolar parents. In the Puig-Antich *et al* (1989: 409) "bottom up" study of depressed children, the rate of "any psychiataric disorder" in first-degree relatives was 64/100. These rates are lifetime prevalence rates and are not age corrected.

While noting the high rates of disorder in the relatives of affected probands, it is important to point out the high rates of disorder, in some of the studies, in the relatives of control probands. The highest rate of "any psychiatric disorder" in relatives of control probands was found in the Weissman (1988: 150) study (57/100). However, when impairment criteria were applied to diagnoses, this rate dropped considerably (Weissman *et al*).

Affective disorders

Table 3.3 presents findings from four studies of children of depressed parents. In three studies, there were increased rates of major depression in the children of depressed parents as compared to the children of control parents. There was a wide variation among the studies in the rates of major depression in the children, ranging from 9/100 (Klein *et al*, 1988: 269) to 28/100 (Weissman, 1988: 150). It is interesting to note that the Breslau *et al* (1987: 290) study found an increased rate of major depression in the older children (age 18–23) of mothers with major depression, but not in the younger children (age 8–17).

As shown in Table 3.3, in one "bottom up" study (Puig-Antich *et al*, 1989: 409), the first-degree relatives of prepubertal depressed children were at increased risk for major depression. However, neither of the two studies demonstrated an increased risk for bipolar disorder in these relatives.

Table 3.4 shows some findings from two studies of children of bipolar parents. The only significant difference in the rates of disorders was in the Klein *et al* (1985: 119) study which found an increased rate of cyclothymia in the children. Cyclothymia is considered to be a mild form of bipolar disorder. As shown in Table 3.4, one "bottom up" bipolar study (Strober *et al*, 1988: 260) found increased rates of major depression and bipolar disorder in the first-degree relatives of the bipolar children.

Anxiety disorders

The findings for anxiety disorders are less clear. The rates of anxiety disorders were increased in the children of depressed parents in two studies, but not in the other two (Table 3.3). Weissman (1988: 150) found a rate of 40/100 for "any anxiety disorder". Breslau *et al* (1987: 290) found an increased rate of overanxious disorder in the younger, but not older, children of depressed mothers. One "bottom up" depression study (Mitchell *et al*, 1989: 354) found an increased rate of panic disorder and/or agoraphobia in the mothers of depressed children. None of the studies of parent or child bipolar probands showed any differences between groups (proband vs. control) in the rates of anxiety disorders in relatives.

Substance abuse

Elevated rates of substance abuse in relatives were reported in one "top down" depression study (Weissman, 1988: 150) and in both "bottom up" depression studies (Table 3.3). There were no significant findings for substance abuse in any of the bipolar studies.

Impairment

In one study (Klein *et al*, 1988: 270) (not shown in Table 3.3), the children of depressed parents had more overall social impairment than did the children of control parents. In another study (Weissman, 1988: 149), they had poorer functioning in school, including more special classes for math and attention problems. This poorer school functioning was not explained by lower IQ scores, since there was no significant difference in IQ scores between the two groups of children.

Suicidal behavior

Of the studies discussed, one "top down" study (Weissman, 1988: 150) reported an increased rate of suicidal gestures or attempts in the children of depressed parents (9/100) (not shown in Table 3.3). Both "bottom up" depression studies had significant findings, although in different directions. Mitchell *et al* (1989: 354) found an increased rate of suicide attempts among mothers of depressed children. On the other hand, Puig-Antich *et al* (1989: 409) found a significantly decreased rate of suicide attempts among first-degree relatives of prepubertal depressed children when compared with relatives of psychiatrically ill controls, and no significant difference when compared with relatives of normal controls. None of the bipolar studies reported data on suicidal behavior.

Psychiatric treatment

There were increased rates of psychiatric treatment in the children of depressed parents in three out of four studies (Klein *et al*, 1988: 270; Orvaschel *et al*, 1988: 22; Weissman, 1988: 150). The lifetime rates of treatment were high, up to 39/100 (Weissman, 1988: 150). Increased rates of treatment among relatives were not found in the "bottom up" depression studies. One possible explanation for this difference is that a parent who is treated for depression may be likely to bring a child in for

treatment for psychiatric problems. However, one would not expect that depression in a child would lead to an adult relative being treated.

Developmental and medical problems

The Weissman (1988: 148–49) study found increased rates of a number of developmental and medical problems among the children of depressed parents. These children were born to younger mothers. There was an increased rate of medical problems during pregnancy and an increased rate of adverse perinatal events. The children of the depressed parents were reported by their mothers to be less active and strong, during the first month of life, than the children of the nondepressed parents. They reached several developmental landmarks later, i.e., sitting without assistance and completing urinary and bowel training. In addition, they were at increased risk for seizures and they had an increased rate of surgical procedures requiring hospitalization.

Summary

These findings clearly show that major depression in a parent increases the risk for psychiatric disorders in children, especially for major depression and anxiety disorders and possibly for substance abuse and suicidal behavior. In addition, the children of depressed parents are at increased risk for psychiatric treatment, psychosocial impairment, poor school functioning, and developmental and health problems.

If a parent has bipolar disorder, the children are at increased risk for psychiatric disorder. They are possibly at increased risk for a mild form of bipolar disorder, but elevated risk for other specific psychiatric disorders has not been demonstrated. However, few family studies of bipolar disorder have included children, so the data are limited.

Looking at risk from the point of view of the child's adult relatives, the relatives of depressed children are at increased risk for psychiatric disorder, especially for major depression, anxiety disorders, and substance abuse, but not for bipolar disorder. The findings are mixed concerning suicidal behavior in the adult relatives of depressed children.

If an adolescent has bipolar disorder, there may be an increased risk for major depression and bipolar disorder in relatives. No additional conclusions can be made based upon the studies reviewed because of the small number of bipolar adolescents studied. No conclusions at all can be made concerning the relatives of bipolar prepubertal children because of the absence of data. Moreover, it is unclear if bipolar disorder occurs prepubertally and, if so, what form it takes.

When looking at these findings, one should keep in mind that the absence of significant differences between groups in rates of specific psychiatric disorders does not prove that there were no differences between groups, only that no differences were demonstrated. It is possible that with larger sample sizes, some of the differences in rates between groups might have been significant.

Moreover, even if there is an increased rate of illness in the relatives of depressed or bipolar probands when compared to the relatives of controls, this is not necessarily due to the presence of the affective disorder in the probands. This increased rate may be due to the presence of illness in general (psychiatric or physical) in probands. To determine if the increased rate in relatives is due to the presence of the affective disorder in probands, it is necessary to use control probands who have nonaffective psychiatric illnesses or medical illnesses.

It is not possible from these studies to determine if the affective disorder in the parents caused the children's psychiatric problems or if the children's psychiatric problems caused the parents to become depressed. There may be an interaction of these two processes.

Lastly, while a family study may demonstrate an increased risk for psychiatric problems in the relatives of depressed or bipolar probands, it cannot determine how important genetic factors are, as compared to environmental factors, in producing this increased risk. Most likely, both sets of factors are important. In order to measure the relative contribution of genetic factors, twin, adoption, or genetic linkage studies are necessary.

CLINICAL IMPLICATIONS

Even with the limitations described and recognizing that pediatricians have time constraints and must pay attention to medical problems, these research findings have implications for pediatric practice. Early detection of psychiatric problems in children and referral for appropriate treatment may improve the health of children. More specifically, the findings suggest that if a parent has depression or bipolar disorder, a pediatrician should be watchful for psychiatric problems in all the children in the family. If a child is depressed or bipolar, the pediatrician should suspect psychiatric problems in other family members, especially the parents.

The methods that family studies use to detect psychiatric disorders in the family can also be useful in clinical practice. While the more extended assessments, such as those listed in Tables 3.1 and 3.2, may not be practical in pediatric practice, some self-report questionnaires (completed by the parent, adolescent, or child) may be quite useful as screening tools and can be completed in the waiting room (see Costello and Angold, 1988: 726– 737, for a review of methods).

As pediatricians screen for psychiatric problems, they should keep in mind that psychiatric problems in children will not necessarily be obvious, just as medical illnesses may be hidden. Because of this, a pediatrician should inquire about psychiatric problems in the family, asking the parent about the child, the parent about himself/herself, and the child about himself. In the past, people felt that children were not able to talk with a professional about their psychiatric problems. As a result, professionals did not ask the children about their problems, assuming instead that they could play with the children and learn indirectly about their problems. Now it is clear that children can talk with professionals about their sadness and worries as long as the professionals pay attention to the child's developmental

stage, using language and concepts that the child can understand. Many of the newer diagnostic methods take these factors into account and can be used successfully with children to elicit relevant information for diagnostic purposes.

Not only can the child speak about his own problems, but studies which have asked children directly about their problems, and then independently asked the parent, clearly show that the parent may not be aware of the child's psychiatric problems. Moreau *et al* (1989) demonstrated that parents frequently may not be aware of their children's suicide attempts. In addition, parents and children don't always agree about the child's psychopathology. In a study by Weissman *et al* (1987: 747–753) of children of depressed and normal parents, agreement was poor between parents and children concerning the children's psychiatric illnesses. Children were more likely to report psychiatric illness in themselves than parents were likely to report in the children. A child psychiatrist who evaluated both sets of data was more likely to agree with the child's report.

If children or parents are found to have major depression or bipolar disorder, and especially if these problems are severe and cause impairment in functioning, a pediatrician can refer them for further evaluation and treatment. Both parent and child can be referred if both have psychiatric problems. Treatment of a depressed parent may benefit the children and the family. Likewise, treatment of a depressed child may be beneficial for the family as well as for the child.

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