Childhood Onset of "Adult" Psychopathology

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CHAPTER 11

Offspring at Risk: Early-Onset Major Depression and Anxiety Disorders Over a Decade

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The topic of this book—understanding the childhood onset of adult psychiatric disorders, the sequence in which psychiatric disorders develop and the form they take in childhood, and how they evolve over the life span—has important public health and preventive implications. Identification of the timing of onset of any disorder could guide interventions either before symptoms begin, by focusing on risk factors, or

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at the first signs of illness in high-risk individuals. Prevention could be a realistic goal.

Until recently, there were many obstacles to understanding childhood onset of adult depression. Among these were the lack of concepts and of tools for assessment and the lack of an empirical base. Before the 1970s the conventional wisdom was that depression was primarily a disorder of the middle-aged or elderly and that children rarely get depressed. The question of whether childhood depression existed prompted the National Institute of Mental Health in 1975 to hold its first conference on childhood depression. Two groups with opposing views were identified. At one pole were clinicians who described children with symptoms of depression, some of whom were receiving tricyclic antidepressants. At the other end were scientists who argued that childhood depression is not a distinct clinical syndrome, but rather a condition of childhood development "evanescent in nature and dissipating with time" (Lefkowitz and Burton 1978, p. 716). Consistent with the belief that children did not get depressed was the absence of assessment tools. Lefkowitz and Burton (1978) pointed out that the absence of a body of significant research on objective measurement and epidemiological characteristics reflected the lack of interest and skepticism about the existence of the syndrome in children.

In the 1970s the situation began to change dramatically. The late Joaquim Puig-Antich, M.D., modified the leading diagnostic assessment for adults, the Schedule for Affective Disorders and Schizophrenia (SADS; Endicott and Spitzer 1978), for children (the Kiddie-SADS; Puig-Antich and Chambers 1978). He began a systematic study of the symptom patterns, social functioning, treatment, sleep patterns, and neuroendocrine patterns of children and adolescents with depression and anxiety disorders coming for treatment to Babies Hospital at Columbia University (Puig Antich et al. 1989).

In the late 1980s, the Epidemiologic Catchment Area Study, a community survey of psychiatric disorders and the associated ages at onset in more than 18,000 adults, was launched (Robins and Regier 1991). This study was followed by in the 1990s the National Comorbidity Survey, a community survey of psychiatric disorders in about 9,000 persons (Kessler et al. 1994).

During this decade, a number of studies of the families of patients

with depression and anxiety disorders were initiated. The epidemiological studies clearly showed that major depressive disorder (MDD) is associated with an early age at onset. The age-specific rates of first onset of MDD from the 1980 survey of adults and similar data from the subsequent survey in the 1990s are presented in Figures 11–1 and 11–2, respectively. These surveys, as well as the international surveys that followed, made it clear that the peak age at first onset of major depression is in the teens and young adulthood; that prepubertal onset, although uncommon, occurs; and that the rates of MDD are consistently higher in women than in men, even in quite diverse countries (Weissman et al. 1996). Moreover, the results from family-genetic studies showed that early onset of major depression (onset before age 30 years) is the most familial, further suggesting the importance of childhood and adolescent onset of MDD (Weissman et al. 1984).

Longitudinal Study of Offspring at High Risk of Developing Depression

It was against this background that we began a longitudinal study of offspring at high and low risk of developing depression by virtue of their parent's depression. Since it was clear that depression often affected women in their childbearing and childrearing years, we felt that studying the effect on the offspring could have public health implications. Given the increased familial risk of depression in the first-degree relatives of probands with MDD, we expected that the offspring would be at high risk and that if we studied them early enough we would begin to understand the onset, sequence, and course of their disorder.

We have been following up on a cohort of offspring either with one or both parents having MDD (high risk) or with neither parent having MDD (low risk). Follow-up has been carried out over a decade, with the offspring having been assessed three times during this period. The full details of the methods used in this study can be found elsewhere (Weissman et al. 1987, 1997).

At the initial interview, we found that the offspring of depressed parents, ranging in age from 6 to 23 years, compared with those of nondepressed parents, had a significantly increased risk of MDD and anxiety

FIGURE 11–1. *Age-specific incidence rates of depression in the United States, 1950.*
Source. Data from the Epidemiologic Catchment Area Study (N = 15,571) (Robins and Regier 1991).

FIGURE 11–2. *Age-specific incidence rates of major depression in the United States, 1990.*
Source. Data from the National Comorbidity Survey (N = 8,096) (Kessler et al. 1994).

disorders and markedly poorer overall functioning. Two years later, the differences between the groups of offspring were more pronounced, with the offspring of depressed parents continuing to have an increased incidence of depression, high recurrences rates, and slower recovery. There were striking differences in age at onset between each group of offspring. All of the cases of prepubertal-onset depression occurred in the offspring of depressed parents who themselves had early onset of MDD (before age 20 years). No sex differences in the rates of prepubertal-onset MDD were found. After puberty, the female offspring showed a marked increase in onset of MDD that peaked between the ages of 15 and 20 years. For the male offspring, there was a gradual rise in MDD onset after puberty. The results also suggest that the depressed offspring of nondepressed parents had a different course of illness than the depressed offspring of depressed parents and that longer follow-up would be required to capture clinically significant differences between the two groups.

The goal of the original study was to determine whether the lifetime rates of psychopathology, and specifically MDD, in the offspring of depressed probands were greater than those in the offspring of nondepressed parents. Comparisons were made in the overall lifetime rates of disorder (from birth to the time of interview) between the two groups. Because subjects were between the ages of 6 and 23 years, there was a wide variation in their stage of development at the first interview. As a consequence, many of the offspring at the time of first interview had not yet passed through the critical period of risk for the onset of depression, and the estimates of age-specific risks were unstable. With the availability of the 10-year follow-up, more precise estimates could eventually be made of age-specific and cumulative lifetime rates.

During the 10-year follow-up, we found that the offspring of depressed parents, compared with those of nondepressed parents, had higher rates of of MDD and phobias (about threefold higher for both), panic disorder, and alcohol dependence (nearly fivefold higher) (Table 11–1). There was no significant interaction between parental depression status and parental and offspring gender for the risk of MDD, anxiety disorders, or alcohol dependence in offspring (data not shown).

The peak time for the incidence period for MDD for both sexes was between ages 15 and 20 years (Figure 11–3). At all ages, the incidence

TABLE 11–1. *Cumulative rates of DSM-III-R psychiatric disorders (with impairment criteria applied) in offspring, by parental diagnosis*

Diagnosis in offspring	Parental diagnosis		Relative risk[c] (95% confidence interval)
	One or both with MDD,[a] *n* (%)	Neither with MDD,[b] *n* (%)	
Any mood disorder	87 (85.3)	20 (37.9)	2.39 (1.46, 3.89)
MDD	64 (56.4)	13 (25.1)	2.50 (1.38, 4.54)
Bipolar disorder	3 (2.3)	0 (0.0)	—[d]
Dysthymia	7 (6.1)	3 (5.7)	0.922 (0.235, 3.58)
Any anxiety disorder	51 (41.7)	8 (15.1)	2.96 (1.41, 6.24)
Phobias	27 (21.0)	4 (7.6)	2.94 (1.03, 8.41)
Panic disorder	14 (13.4)	0 (0.0)	—[e]
OCD	1 (1.9)	1 (0.75)	—[f]
GAD	0 (0.0)	0 (0.0)	—[g]
ADHD	5 (3.9)	2 (3.5)	0.882 (0.166, 4.67)
Any substance abuse	40 (32.0)	14 (27.8)	1.32 (0.715, 2.42)
Alcohol abuse	15 (14.5)	8 (16.0)	0.934 (0.406, 2.15)
Alcohol dependence	21 (21.6)	2 (7.4)	4.93 (1.16, 21.06)
Drug abuse	7 (5.5)	7 (13.6)	0.414 (0.145, 1.18)
Drug dependence	16 (14.5)	1 (1.9)	6.98 (0.925, 52.74)
Schizophrenia	2 (1.8)	0 (0.0)	—[h]
Childhood disorders			
Separation anxiety	16 (12.4)	6 (11.3)	1.08 (0.424, 2.78)
Conduct disorder	44 (34.1)	11 (20.8)	1.88 (0.969, 3.64)[i]

TABLE 11–1. *Cumulative rates of DSM-III-R psychiatric disorders (with impairment criteria applied) in offspring, by parental diagnosis* (continued)

Diagnosis in offspring	Parental diagnosis: One or both with MDD.[a] *n* (%)	Parental diagnosis: Neither with MDD.[b] *n* (%)	Relative risk[c] (95% confidence interval)
Childhood disorders (*continued*)			
Overanxious disorder	17 (13.6)	1 (1.9)	7.22 (0.959, 54.28)
Any of the above diagnoses	99 (78.4)	25 (47.2)	2.18 (1.40, 3.38)

Note. If the offspring reported, in the Schedule for Affective Disorders and Schizophrenia (SADS) or Kiddie-SADS, during an episode of disorder that they sought help, took medication, were hospitalized, or had impaired functioning at work, school, or home, they were considered impaired. Data on impairment were not collected for conduct disorder. ADHD = attention-deficit/hyperactivity disorder; GAD = generalized anxiety disorder; MDD = major depressive disorder. OCD = obsessive-compulsive disorder.
[a]Data for 129 offspring. [b]Data for 53 offspring. [c]Adjusted for age and sex of offspring. [d]Two-tailed Fisher exact test = 1.25, $df = 1$, $P = 0.56$. [e]Two-tailed Fisher exact test = 6.25, $df = 1$, $P = 0.004$. [f]Two-tailed Fisher exact test = 0.427, $df = 1$, $P = 1.00$. [g]Not estimable because there were no cases. [h]Two-tailed Fisher exact test = 0.551, $df = 1$, $P = 1.00$. [i]Data on impairment were not collected for conduct disorder.
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by sex was higher in the offspring of depressed parents than in those of nondepressed parents. The incidence rates declined after age 20 years except for the rates in male offspring, which appeared to decline slightly after age 25. Prepubertal onset is uncommon in general and in our sample occurred primarily in the high-risk offspring. The incidence rates were higher in female than in male adolescents. After age 20 years, the incidence rates were similar in both sexes.

A different pattern was found for any anxiety disorder, including panic disorder, generalized anxiety disorder, agoraphobia, social phobia, simple phobia, separation anxiety, obsessive-compulsive disorder, and overanxious disorder (Figure 11–4). The peak incidence of anxiety in

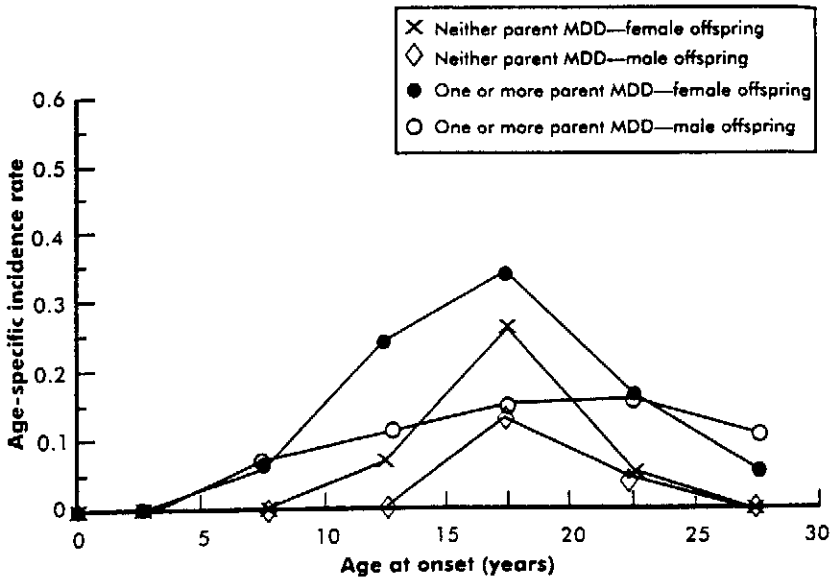

FIGURE 11–3. *Age-specific incidence rates of major depressive disorder (MDD) by parental MDD and sex of offspring (N = 152, lifetime rates).*
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the offspring for both sexes occurred much earlier than that of MDD (age range: 5–10 years), especially in the offspring of depressed parents. Among anxiety disorders, phobias and separation anxiety disorder had, on average, the earliest onset (mean ages at onset: 5.2 and 6.6 years, respectively). Overall, the incidence rates for anxiety disorders appear to decline after age 10 years and converge by sex of offspring and parental diagnosis. The incidence rate for alcohol dependence in both sexes of depressed probands increased at ages 15–20 years (Figure 11–5).

The illness severity at the time of the third interview (i.e., at 10-year follow-up) in the offspring who were depressed at the time of the first or second interviews was greater in the offspring of depressed parents than in those of nondepressed parents (Table 11–2). The depressed offspring of depressed parents were less likely to go for treatment when they felt they needed it and less likely to receive treatment when they were depressed. More than 30% of the depressed offspring of depressed

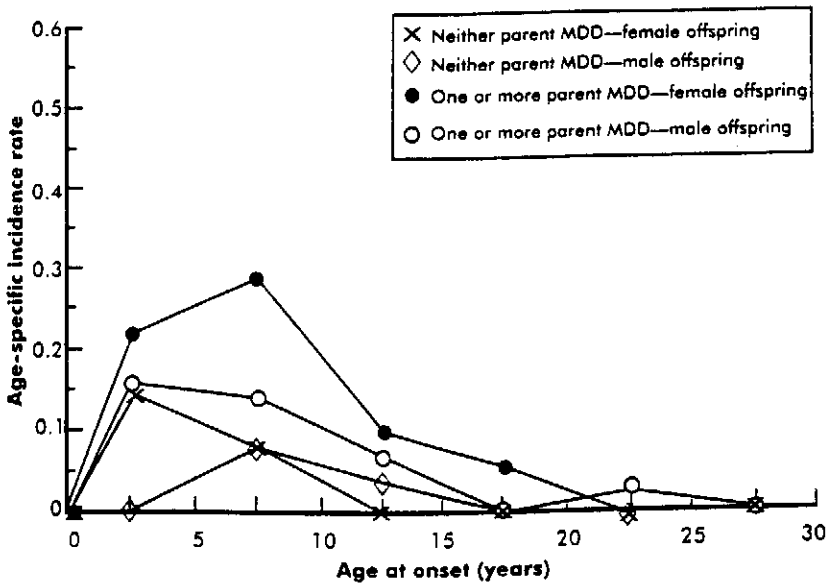

FIGURE 11–4. *Age-specific incidence rates of any anxiety disorder by parental major depressive disorder (MDD) and sex of offspring (N = 182 lifetime).*
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parents never received any treatment; in addition, they had more impairment overall, in work and marriage, than the depressed offspring of nondepressed parents and reported more days on which they felt depressed.

Conclusion

As in previous investigations, we found that 1) parental depression increases the risk of depression in the offspring; 2) the course of depression in children, as in adults, is protracted, 3) the morbidity rate is high, and 4) the overall symptom picture in offspring does not vary by the age at onset of the symptoms and does not differ by proband group. The overall rates and burden of illness are greater in the offspring of depressed parents than in those of nondepressed parents. The former continue to

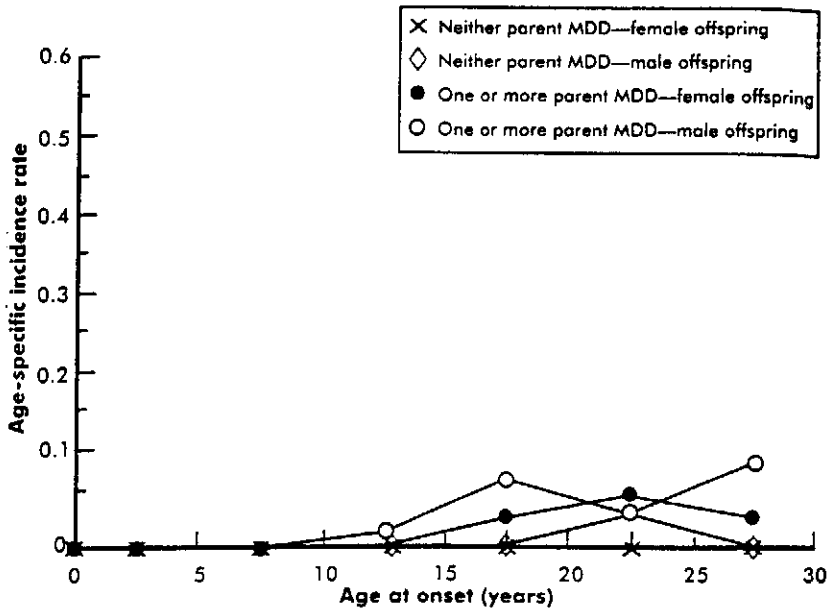

FIGURE 11–5. *Age-specific incidence rates of alcohol dependence by parental major depressive disorder (MDD) and sex of offspring (N = 152 lifetime).*
Source. Reprinted with permission from Weissman MM, Wickramaratne PJ, Moreau D, et al.: "Offspring of Depressed Parents: Ten Years Later." *Archives of General Psychiatry* 54:932–940, 1997. Copyright 1997, American Medical Association.

have markedly higher rates of MDD (threefold higher) and anxiety disorders. As they mature, they also have higher rates of alcohol dependence (fivefold higher) and poorer functioning in work, family, and marriage. The cumulative rate of MDD in the offspring of nondepressed parents (25.1/100) for ages 6–36 years is higher than that in the community sample for ages 15–34 years (17.1/100), and this difference may be explained by our closer surveillance of the sample (i.e., three interviews), as well as by the younger ages of the offspring when interviewing began.

The observed recurrent nature of depression is consistent with findings from longitudinal studies of depressed adults and children. The increased risk of MDD in the offspring of depressed parents is consistent with that found in numerous studies in which the offspring were minors. The familial nature of depression was consistent with that demonstrated in studies in which the probands were depressed children or adults. Although the absolute rates vary with the design and criteria used, the

TABLE 11–2. *Severity of outcome at 10-year follow-up in offspring with any depression at time of first or second interviews, by parental diagnosis*

	Parental diagnosis				
	One or more MDD[a]	Neither MDD[b]			
					Odds ratio[c] (95% CI)
Did not go for treatment when felt such was needed, *n* (%)					
	23 (33.3)	1 (4.2)			12.85 (1.61, 102.54)
GAS ≤71, *n* (%)					
	32 (40.0)	4 (15.4)			4.34 (1.33, 14.14)
			Statistic[d]	*df*	*P*
Social Adjustment Scale, mean (SD)					
Work	1.54 (1.07)	1.30 (0.324)	−3.66	88.5	0.0004
Social and leisure	1.97 (0.567)	1.89 (0.450)	−0.689	49	0.49
Extended family	1.65 (0.509)	1.46 (0.314)	−2.54	64.6	0.01
Marital	1.88 (0.630)	1.47 (0.358)	−3.05	46.1	0.003
Parental	1.44 (0.402)	1.22 (0.405)	−1.44	23.2	0.16
Family	1.78 (0.601)	1.61 (0.502)	−1.37	44.3	0.18
Overall	1.80 (0.455)	1.59 (0.332)	−2.56	55.2	0.01
No. of days depressed during follow-up, mean (SD)					
	118 (401)	11 (49)	−2.33	86	0.02
			Statistic[e]	*df*	*P*
Ever out of work in last 5 years because of psychopathology, *n* (%)					
	11 (13.7)	1 (3.8)	1.92	1	0.29[f]
Number of MDD episodes during follow-up, *n* (%)					
0	53 (66.2)	23 (88.4)			
1	23 (28.7)	2 (7.6)			
2+	4 (5.0)	1 (3.8)	5.10	2	0.08
Suicide gestures or attempts, *n* (%)					
	13 (16.2)	3 (11.5)	0.340	1	0.75[f]

TABLE 11–2. *Severity of outcome at 10-year follow-up in offspring with any depression at time of first or second interviews, by parental diagnosis* (continued)

	Parental diagnosis				
	One or more MDD[a]	Neither MDD[b]	Statistic[c]	*df*	*P*
Treatments over 10 years,[g] *n* (%)					
Outpatient treatment	33 (67.4)	6 (100.0)	2.76	1	0.16[f]
Hospitalization	4 (8.2)	3 (50.0)	5.42	1	0.02[f]
Any treatment	33 (67.4)	6 (100.0)	2.76	1	0.16[f]

Note. Numbers of offspring from which data on parental diagnosis are derived vary, as specified in table notes, because of missing data. CI = confidence interval; GAS = Global Assessment Scale. MDD = major depressive disorder.

[a]Data for 50 offspring, except in category of treatment over 10 years, in which data for 49 offspring are represented.

[b]Data for 26 offspring, except in category of treatment over 10 years, in which data for 6 offspring are represented.

[c]Adjusted for age and sex of offspring. [d]*T* statistic is used for continuous variables.

[e]Chi-square statistic is used for dichotomous variables. [f]Two-tailed Fisher exact test.

[g]Treatment for MDD for offspring with any depression at time of third interview (10-year follow-up).

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magnitude of the effect of familial depression (i.e., a two- to threefold increased risk) is consistent across high-risk and family studies.

More shifts to bipolar disorders occurred among the offspring of depressed parents than in the offspring of nondepressed parents, but the overall rate of bipolar disorder (2.3% in the offspring of depressed parents) was lower than that reported by other investigators. Of note, some of the offspring have not fully passed through the age at risk for the onset of bipolar disorder.

Prepubertal onset of MDD is uncommon, and it did not occur in the offspring of the nondepressed parents. The peak first onset of MDD

in middle and late adolescence is consistent with the findings from epidemiological studies of depressive disorders in adolescents and adults. This peak is consistent in female offspring regardless of proband diagnosis, and this suggests a consistent vulnerability period for focus on detection and intervention. Why the rates should increase so abruptly in young females in middle and late adolescence and early adulthood is still unclear and is an area for further research. Parental affective disorders further increase the risk of first onset in adolescents. However, affective disorders in parents may serve as an identifier of a constellation of risk factors. High rates of comorbid anxiety disorders in depressed parents may be a factor. Alternatively, early expression of anxiety disorders could constitute an underlying vulnerability to psychopathology related to shared genetic or environmental factors.

The current findings support initiatives aimed at early detection and possible treatment intervention in the parents of depressed offspring and the offspring of depressed parents. Physicians who specialize in pediatrics and adolescent medicine, as well as internists, family physicians, and child psychiatrists, are particularly well positioned to inquire about the mental health history of their patients' parents.

Alternatively, psychiatrists who treat adult patients should inquire about the clinical status of the offspring. Successful treatment of parental depression may provide primary prevention by reducing the symptoms of depression that may impair parenting. Secondary prevention may be achieved through the early detection and treatment of high-risk offspring who exhibit early or minor forms of anxiety, depressive, or substance abuse disorders. Finally, the aggressive treatment of established MDD (i.e., tertiary prevention) may reduce the high level of social impairment characteristically found in the depressed offspring of depressed parents.

Only a small proportion of young people with mental disorders receive adequate mental health treatment. In the current study, a large number of the offspring who perceived a need for mental health care accessed no treatment whatsoever. One possible explanation is that the offspring of depressed parents develop negative attitudes toward mental health treatment because they associate it with their parents' chronic course of illness. Alternatively, the depressed parent may deny that his or her offspring have the same disorder. A better understanding of how parental factors influence the seeking of health care for offspring may

help public health planners extend treatment to this vulnerable and underserved population. There are now strong financial incentives to limit treatment costs. Our data suggest that outcomes research should assess the impact of parental depression on the offspring over time.

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