Differences in Early Childhood Risk Factors for Juvenile-Onset and Adult-Onset Depression

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Background: Family and twin studies suggest that juvenile-onset major depressive disorder (MDD) may be etiologically distinct from adult-onset MDD. This study is the first to distinguish prospectively between juvenile- and adult-onset cases of MDD in a representative birth cohort followed up from childhood into adulthood.

Method: The study followed a representative birth cohort prospectively from birth to age 26 years. Early childhood risk factors covered the period from birth to age 9 years. Diagnoses of MDD were made according to *DSM* criteria at 3 points prior to adulthood (ages 11, 13, and 15 years) and 3 points during adulthood (ages 18, 21, and 26 years). Four groups were defined as (1) individuals first diagnosed as having MDD in childhood, but not in adulthood (n=21); (2) individuals first diagnosed as having MDD in adulthood (n=314); (3) individuals first diagnosed in childhood whose depression recurred in adulthood by age 26 years (n=34); and (4) never-depressed individuals (n=629).

Results: The 2 juvenile-onset groups had similar high-risk profiles on the childhood measures. Compared with the adult-depressed group, the juvenile-onset groups experienced more perinatal insults and motor skill deficits, caretaker instability, criminality, and psychopathology in their family-of-origin, and behavioral and socioemotional problems. The adult-onset group's risk profile was similar to that of the never-depressed group with the exception of elevated childhood sexual abuse.

Conclusions: Heterogeneity within groups of psychiatric patients poses problems for theory, research, and treatment. The present study illustrates that the distinction between juvenile- vs adult-onset MDD is important for understanding heterogeneity within depression.

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SEVERAL FINDINGS suggest that juvenile- and adult-onset major depressive disorder (MDD) have distinct origins.[1] First, although a significant proportion of depressed children become depressed adults,[2,3] most individuals who experience depression in adulthood were not depressed as children.[4] Second, juvenile-onset MDD is associated with increased risk for MDD among the first-degree relatives of depressed probands in clinical and community samples.[4-8] Third, the children of depressed parents are at high risk for juvenile-onset MDD compared with the children of nondepressed parents, and this association is explained by early parental age at onset of MDD.[9]

These findings implicate genetic risk factors in juvenile-onset MDD. However, depressed children and adolescents may also experience unique psychosocial risks, such as poor parenting or family discord, especially if these risks are genetically mediated.[10,11] Additional support for the hypothesis that juvenile- and adult-onset MDD are distinct subtypes would be demonstrated if early childhood psychosocial risks were differentially associated with juvenile- vs adult-onset MDD.

A range of childhood psychosocial risk factors have been associated with depression, including characteristics of the child (eg, behavioral and socioemotional problems, poor school performance), characteristics of the parents (eg, parent psychopathology, rejecting or intrusive behavior), and family circumstances (eg, the loss of a parent, physical or sexual violence, family

discord).[12-15] However, it has not been shown decisively whether these risks distinguish juvenile- from adult-onset MDD. To our knowledge, the only study to have assessed the impact of a wide range of childhood risk factors on juvenile- vs adult-onset MDD[14] found that family violence, parental psychopathology, and the early death of a parent increased the risk for early onset of depressive symptoms (by age 20 years) but not for later onset. However, these results were limited by the use of a single screening question to assess depression and retrospective recall of age of onset.

Despite increasing evidence for an early- vs late-onset distinction, a small body of research suggests there is also heteroge-

SUBJECTS AND METHODS

SUBJECTS

Participants are part of the Dunedin Multidisciplinary Health and Development Study, a longitudinal investigation of health and behavior in a complete birth cohort.[22] The study members were born between April 1, 1972, and March 31, 1973, in Dunedin, New Zealand. Of these, 1037 children (91% of eligible births; 52% male) participated in the first follow-up at age 3 years, forming the base sample for the longitudinal study. Cohort families are primarily white and represent the full range of socioeconomic status in the general population of New Zealand's South Island.

The Dunedin sample has been assessed with a diverse battery of psychological, medical, and sociological measures with high rates of participation at age 3 (n=1037), 5 (n=991), 7 (n=954), 9 (n=955), 11 (n=925), 13 (n=850), 15 (n=976), 18 (n=993), 21 (n=992), and, most recently, 26 years (n=980; 96% of the living cohort members). The research procedure involves bringing 4 study members per day (including emigrants living overseas) to the research unit within 60 days of their birthday for a full day of individual data collection. Each research topic is presented, in private, as a standardized module by a different trained examiner in counterbalanced order throughout the day. In addition, data are gathered from sources such as parents, partners, and courts.

At ages 11, 13, and 15 years, study members were administered the Diagnostic Interview Schedule for Children.[23] Major depressive disorder was diagnosed according to *DSM-III* criteria. The Diagnostic Interview Schedule for Children has shown good interrater reliability in this cohort ($\kappa > 0.86$). The modifications and descriptive epidemiology of the Diagnostic Interview Schedule for Children in this sample have been described by McGee et al.[24] At ages 18, 21, and 26 years, study members were administered the Diagnostic Interview Schedule.[25] Major depressive disorder was diagnosed according to *DSM-III-R* criteria at ages 18 and 21 years and *DSM-IV* criteria at age 26 years. The Diagnostic Interview Schedule demonstrates good interrater reliability ($\kappa > 0.85$) and validity in this cohort, as demonstrated by the disordered group who sought treatment frequently and had high levels of functional impairment.[26] For both the Diagnostic Interview Schedule for Children and the Diagnostic Interview Schedule, the reporting period was 12 months prior to the interview (eg, at age 11 years [hereafter, age-11] interviews assessed depression while the child was age 10 years). Interviewers were blind to the study members' psychiatric history and had tertiary degrees and experience in social work, medicine, and clinical psychology.

To be included in the analyses, study members must have completed psychiatric interviews in both childhood (at ages 11, 13, or 15 years) and adulthood (at ages 18, 21, or 26 years); 998 study members (96% of the birth cohort) met this criterion. Of the 998, 66% completed all 6 psychiatric interviews, 24% completed 5 interviews, 6.4% completed 4 interviews, 2.4% completed 3 interviews, and 0.8% completed 2 interviews (ie, 1 child and 1 adult interview). Here we report findings based on the full study cohort (N=998). In addition, all analyses were rerun on the subsample that had all 6 interviews.

The juvenile-depressed group comprised study members who were first diagnosed as having MDD at age 10, 12, or 14 years but who had no subsequent episode (n=21; 8 women [38%]). The adult-depressed group comprised those who were first diagnosed as having MDD at age 17, 20, or 25 years (n=314; 201 women [64%]). The juvenile/adult–depressed group comprised those who were first diagnosed as having MDD at age 10, 12, or 14 years and whose depression recurred in adulthood by age 26 years (n=34; 22 women [65%]), and the never-depressed group comprised those who were never diagnosed as having MDD (n=629; 252 women [40%]). A χ^2 analysis revealed that the sex distribution across the 4 groups was not equal because depressed adults were more likely to be women ($\chi^2_3 = 53.92$; $P \leq .001$).

We defined adult-onset MDD as a first diagnosis at 17 years or older because (1) this cutoff was consistent with the definition of adult-onset MDD used by Harrington et al[2] and (2) the incidence of new cases of depression in this sample spiked between the ages of 15 and 18 years and declined thereafter, suggesting that onset of depression at or before age 15 years is unique (**Figure**).[27]

The juvenile-depressed group had a significantly earlier age of MDD onset (mean [SD], 12 [1.84] years) compared with the juvenile/adult–depressed group (13 [1.47] years; $t_{366} = 2.93$; $P \leq .01$). The juvenile-onset and juvenile/adult–onset groups had a significantly earlier age of onset compared with the adult-depressed group (20 [3.12] years; $t_{366} = 24.22$; $P \leq .001$). The mean age at menarche in this sample was 13 years (range, 8.5-15 years), and 46% of the adolescent boys had their growth spurt from ages 13 to 15 years. On this basis, a significant proportion of the juvenile-depressed group was prepubertal and the juvenile/adult–depressed group was pubertal or postpubertal at MDD onset.

EARLY CHILDHOOD RISK FACTORS FOR DEPRESSION

Early childhood risk factors for depression included many of those identified in the literature, such as neurodevelopmental characteristics, parental characteristics, family circumstances, and child behavior and temperament. The risk factors associated with the diagnosis of depression covered the period before age 9 years so as to be temporally nonoverlapping with the period covered by the age-11 diagnosis of depression. Although a review of these risk factors and their links to depression would be beyond the scope of this article, excellent reviews are available.[10-12,28]

Neurodevelopmental characteristics encompassed a count of perinatal insults, which included any of 12 pre-

neity within juvenile-onset groups as a function of whether the child was prepubertal or postpubertal at onset. Prepubertal onset has been associated with lower risk of recurrence[16,17]; higher risk of bipolar disorder, suicide attempts, alcohol dependence, and conduct disorder[17]; and lower heritability.[18,19] Results from family studies have been inconsistent. Some results have shown higher rates of crimi-

nality and family discord and lower rates of depressive disorder among relatives of prepubertal- vs postpubertal-onset MDD probands,[20] and others have shown no significant differences in rates of disorder among relatives in these 2 groups.[21] Although the findings are not entirely consistent, they do suggest heterogeneity within early-onset MDD.

natal or 12 neonatal problems recorded by physicians during the mother's pregnancy.[29] Gross motor skills (eg, standing long jump, balance) were measured with the Bayley Motor Scale[30] at age 3 years, the McCarthy Motor Scales[31] at age 5 years, and the Basic Motor Ability Test[32] at ages 7 and 9 years. Scores on these measures were standardized and summed (α = .71). Intelligence quotient was measured with the Wechsler Intelligence Scale for Children (Revised)[33] at ages 7 and 9 years and was averaged (r = .79).

Parental characteristics included mother's internalizing symptoms, which were assessed with the Rutter Malaise Inventory[34] when the study members were ages 5, 7, and 9 years. This includes 23 items measuring physical and psychological symptoms of depression and anxiety. The total number of symptoms endorsed by mothers was summed, and scores were averaged across the 3 assessments (α = .90). At age 3 years, mother-child interactions were observed and rated across 8 categories during a 1-hour testing session and during the child's physical examination. To construct the rejecting behavior composite, 1 point was awarded for each behavior that was rated by psychometricians and physicians as hostile or rejecting (eg, if the mother's expression of affect was consistently negative or if she was unresponsive to her child's needs; α = .71).[35] Parents' criminal conviction history was assessed via a questionnaire posted to parents who were asked to report if they had ever been convicted of a crime; 3% of the mothers and 12% of the fathers reported that they had been. Parental disagreement about discipline was reported by mothers when the study children were ages 5, 7, and 9 years as part of an interview about how parents dealt with misbehavior. Mothers indicated whether they and their partners disagreed about how to discipline the child and how often they disagreed in front of the child. Scores were standardized and averaged across ages 5 to 9 years (α = .62).

Family circumstances included the number of residence changes and parent-figure changes that each study member experienced from birth to age 9 years. Socioeconomic status was measured with a 6-point scale that places each occupation into 1 of 6 categories based on the educational level and income associated with that occupation in the data from the New Zealand census.[36] Measures of socioeconomic status were averaged from birth to age 9 years (α = .79). Unwanted sexual contact by age 11 years (having one's genitals touched, touching another's genitals, and sexual intercourse)[13] was assessed retrospectively at age 26 years as part of an interview about sexual behavior and reproductive health. Eighteen percent of females and 7% of males reported having experienced unwanted sexual contact, which is consistent with rates reported elsewhere.[37] Finally, it was recorded whether study members lost a parent by age 9 years because of death, divorce, or separation (12.6%).

Child behavior and temperament were measured from ages 3 to 9 years. When the study members were aged 3 years, mothers reported on a 3-point scale whether their child had been difficult to manage as a baby (0, "easy all of the time" to 2, "very difficult to manage"). At age 3 years,

children were observed during a 1-hour psychological examination, and their behavior was rated across 15 categories. Three factors emerged from these ratings and these were cluster analyzed, yielding temperament profiles.[38] Of interest are the inhibited and undercontrolled temperament profiles. Inhibited children were shy, fearful, and passive; engaged in little verbal communication; exhibited flat affect; and were distractible. Undercontrolled children were irritable, distractible, emotionally labile, and rough and uncontrolled in their behavior. From ages 5 to 9 years, teachers completed the Rutter Child Behavior Scale,[39] which assesses children's worried/fearful, hyperactive, and antisocial behavior. Children were scored on a 3-point scale (0, "does not apply" to 2, "certainly applies"). Teachers' reports were chosen instead of parents' reports, which may be biased by their own psychopathology.[40,41] Scores on these 3 scales were averaged over time (all, $\alpha \geq$ .70). In addition, 2 items from the Rutter Scale were chosen to measure peer problems ("Not much liked by other children" and "Tends to do things on his own. Rather solitary."). Scores on these items were summed across ages 7 and 9 years (α = .60). Finally, at age 9 years, study members completed an interviewer-administered depression checklist. A total score was created by summing positive responses to the items. Because the checklist did not show acceptable criterion validity against clinical judgment,[42] it is included as a measure of depressive symptomatology and not clinical depression.

STATISTICAL ANALYSIS

χ^2 Analyses were conducted to show associations between depression-onset status and other juvenile and adulthood diagnoses of mental disorder. A second set of analyses evaluated group differences on the childhood risk factors within a regression framework. To test specific predictions about group differences, orthogonal-planned contrasts were conducted.[43] The first contrast tested the prediction that the juvenile-depressed and juvenile/adult–depressed groups would differ from the adult-depressed group because a growing body of research suggests that juvenile-onset MDD is distinct from adult-onset MDD. The second contrast tested the prediction that the adult-depressed and never-depressed groups would not differ significantly on the early childhood risk factors because the effects of childhood adversity on depression onset decline with age.[14] The third contrast compared the juvenile-depressed and juvenile/adult–depressed groups on the early childhood risk factors. Given the inconsistent findings in the literature regarding heterogeneity within juvenile-onset MDD, no predictions were made regarding the direction of effects. All comparisons were adjusted for sex because of its unequal distribution across groups. Group differences were considered statistically significant at $P \leq$ .05, 2-tailed. The magnitude of the effect size for group differences was also evaluated. An effect size of 0.2 is small; 0.5, moderate; and 0.8, large.[44]

The present study is the first to trace prospectively the course of depression in a representative birth cohort from childhood to adulthood, using *DSM* diagnoses of MDD. The longitudinal design allowed us to determine whether early childhood risk factors were differentially associated with juvenile- vs adult-onset MDD and to assess heterogeneity within the juvenile-onset group.

RESULTS

PATTERNS OF COMORBIDITY

Juvenile-onset MDD was highly comorbid, with 33% to 62% of the juvenile-depressed group and 27% to 47% of

the juvenile/adult–depressed group having a diagnosis of conduct disorder, attention deficit disorder, or anxiety disorder by age 15 years (**Table 1**). The combined juvenile-depressed and juvenile/adult–depressed groups did not differ from the adult-depressed group in rates of comorbid disorder at age 26 years, except in the case of schizophreniform disorder (Table 1, column 7). However, the adult-depressed group had elevated rates of disorder at age 26 years compared with the never-depressed group (Table 1, column 8).

EARLY CHILDHOOD RISK FACTORS FOR DEPRESSION

Comparison of the combined juvenile-depressed and juvenile/adult–depressed vs the adult-depressed groups shows that juvenile-onset MDD is associated with worse risk across a range of variables (**Table 2**). Compared with the adult-depressed group, the combined juvenile-depressed and juvenile/adult–depressed groups experienced more
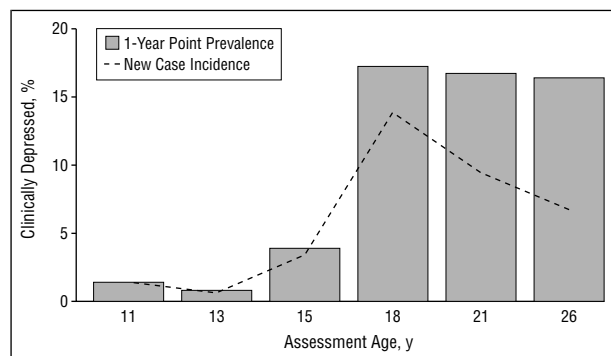
Assessment of age.

perinatal insults and had poorer motor skills. Their mothers reported more symptoms of depression and anxiety and their parents were more likely to have a criminal conviction. The juvenile-depressed and juvenile/adult–depressed groups experienced more parent figure changes and were more likely to have lost a parent because of death, divorce, or separation. They had more peer problems; and were more worried/fearful, hyperactive, and antisocial, as reported by teachers. Finally, the juvenile-depressed and juvenile/adult–depressed groups reported more symptoms of depression at age 9 years and were more temperamentally inhibited compared with the adult-depressed group. Additional analyses were conducted to determine whether these effects remained statistically significant after controlling for juvenile conduct disorder, attention deficit disorder, and anxiety. Compared with the adult-depressed group, the juvenile-depressed and juvenile/adult–depressed groups' risk profile remained significantly worse except in the case of mothers' internalizing symptoms, the likelihood of having lost a parent, teacher ratings of antisocial and hyperactive behavior, and self-reports of depression symptoms at age 9 years.

Comparison of the adult-depressed vs never-depressed groups (Table 2) shows an overall pattern of similarity, although the adult-depressed group experienced more residence changes and unwanted sexual contact. Lastly, comparison of the juvenile-depressed vs juvenile/adult–depressed groups (Table 2) shows an overall pattern of similarity, although the juvenile-depressed group had more perinatal problems. The small sample sizes of these 2 groups may have hindered our ability to detect significant differences, and nonsignificant trends will be discussed herein.

Table 1. Depressed and Never-Depressed Groups With Juvenile (DISC-C Report) and Adult Diagnoses (DIS Report)

	Base Rate†	Never Depressed (N) n = 629	Adult-Depressed (A) (MDD at 18, 21, or 26 y) n = 314	Juvenile-Depressed (J) (MDD at 11, 13, or 15 y) n = 21	Juvenile/ Adult–Depressed (J/A) n = 34
Juvenile diagnoses					
Conduct disorder at age 11, 13, or 15 y	18.4 (181)	15.2 (94)	19.9 (62)	61.9 (13)	35.3 (12)
Any anxiety disorder at age 11, 13, or 15 y‖	16.2 (155)	9.1 (54)	23.9 (73)	57.1 (12)	47.1 (16)
Attention-deficit disorder at age 11, 13, or 15 y	6.3 (60)	5.7 (34)	3.3 (10)	33.3 (7)	26.5 (9)
Adult diagnoses (age 26 y)					
Any anxiety disorder‖	24.3 (237)	14.7 (90)	38.8 (121)	38.9 (7)	55.9 (19)
Manic disorder	2.7 (26)	0.5 (3)	6.1 (19)	5.6 (1)	8.8 (3)
Antisocial personality disorder	4.1 (40)	2.8 (17)	5.8 (18)	11.1 (2)	8.8 (3)
Alcohol dependency	17.2 (168)	13.4 (82)	24.0 (75)	16.7 (3)	23.5 (8)
Marijuana dependency	9.4 (92)	7.5 (46)	12.5 (39)	11.1 (2)	14.7 (5)
Schizophreniform disorder	3.7 (36)	1.3 (8)	5.8 (18)	16.7 (3)	21.2 (7)
Suicide attempt at age 18, 21, or 26 y**	3.9 (39)	1.1 (7)	7.6 (24)	14.3 (3)	14.7 (5)

*The values are percentages (number) unless indicated otherwise. DISC-C indicates Diagnostic Interview Schedule for Children; DIS, Diagnostic Interview Schedule; and MDD, major depressive disorder.

†The base rate for the juvenile diagnoses refers to the percentage of the cohort who were diagnosed as having conduct, attention-deficit, and/or anxiety disorders at age 11, 13, or 15 years (diagnoses available for 954-983 study members). Base rates for adult disorders refer to the prevalence of disorder at age 26 years when diagnoses were available for 970-977 study members.

‡$P \le .001$.

§$P \le .01$.

‖Juvenile anxiety disorders included overanxious disorder, separation anxiety, simple phobia, or social phobia. Adult anxiety disorders included simple phobia, social phobia, agoraphobia, panic disorder, obsessive-compulsive disorder, posttraumatic stress disorder, and generalized anxiety disorder.

¶$P \le .05$.

#All cases of antisocial personality at age 26 years in the juvenile-onset groups were men. The odds ratio for the comparison between the J and J/A groups is less than unity because 18.2% of the J men vs 25% of the J/A men had a diagnosis of antisocial personality.

**Study members reported in the DIS interview whether they had attempted suicide.

Finally, all analyses were rerun on the subsample of study members having data from all 6 psychiatric interviews (66% of the sample). The results regarding group differences on childhood risk factors were unchanged (Table 2). Findings regarding adult comorbidity (Table 1) showed 1 change: group differences on alcohol dependency at age 26 years were no longer statistically significant.

COMMENT

This study is the first to our knowledge to distinguish prospectively between juvenile- and adult-onset MDD in a representative birth cohort that has been followed up from childhood into adulthood. These findings replicate and extend the work of Kessler and Magee[14] by showing that early childhood risks differentiate juvenile- from adult-onset cases. With few exceptions, the adult-depressed group resembled the never-depressed group in having experienced low levels of early childhood risk factors. In contrast, the combined juvenile-depressed and juvenile/adult–depressed groups experienced significant risk factors: neurodevelopmental problems in the form of perinatal and motor skill problems, more psychopathology and instability in their family of origin, and more behavioral and socioemotional problems. Many of these group differences were specific to childhood depression because they remained statistically significant after controlling for comorbidity with other childhood disorders. It is also important to highlight that the early childhood risk factors we measured were specifically associated with MDD onset and not simply recurrence. That is, regardless of whether MDD persisted beyond childhood, the early childhood risk factors distinguished the juvenile-onset groups from the adult-onset group.

Several limitations to these findings must be noted. First, these results are limited to a single, contemporary cohort of New Zealand young adults. Although current prevalence rates of psychiatric disorder in New Zealand match rates from national US surveys,[26,46] further studies are required to determine whether our results will extend to other times and places. Moreover, studies with larger samples of juvenile-onset cases are needed.

Second, because diagnoses of MDD covered the year prior to the scheduled assessment periods and assessments were separated by a year or more, it is possible that we failed to detect episodes of MDD that emerged between interviews. Moreover, at age 26 years, the sample had not passed completely through the age of risk for MDD and study members will experience more episodes of MDD in the future. Thus, individuals in each of the 4 groups might have been misclassified. However, misidentification would have exerted a conservative effect on our analyses by making it more difficult to detect group differences. Misclassification may also have occurred because we included in the analyses study members who did not complete psychiatric interviews at all 6 assessments. However, excluding these study members did not change the results.

Third, the identification of risk factors for juvenile-onset MDD in no way ensures their causal status.[47] Although the early childhood risk factors (except childhood sexual abuse) covered the period prior to the first diagnosis of MDD (and could thus be ruled out as consequences of depression), future research is needed to determine whether changes in any of the childhood risk factors would decrease the likelihood of MDD, thus implying their causal status. Moreover, our list of early childhood risk factors was not exhaustive. For example, although we assessed mothers' symptoms of depression and anxiety, parental history of psychiatric disorder is an important risk factor for depression that was not measured.

With these limitations in mind, the strengths of the study can be noted. Because of its unique prospective, longitudinal design, this study makes several improvements over the existing literature. First, despite the possibility that we failed to detect episodes of MDD, there were opportunities for MDD to be observed at 3 points in childhood and in adulthood. Second, diagnoses of MDD were made prospectively, thus eliminating problems associated with long-term retrospective recall.[48] Third, diagnoses of MDD were made in a birth cohort as opposed to a clinical sample. Thus, the observed associations between juvenile-onset and early childhood risk factors were not caused by high-risk families selectively coming to clinical attention. Lastly, the predicted group differences were observed and were consistent with the extant literature on the distinction between juvenile- vs adult-onset MDD.

The findings differentiating juvenile- and adult-onset MDD are consistent with results from family studies, suggesting that juvenile-onset MDD may be a distinct subtype associated with both genetic and early childhood psychosocial risk factors. Future research is needed to determine whether these early childhood risk factors are genetically mediated[49] and how these risks may be causally implicated in the origins of depression.

of Other Mental Disorders*

χ^2_{df}	Orthogonal Contrasts, Odds Ratios (Confidence Intervals), Adjusted for Sex		
	J + J/A vs A	A vs N	J vs J/A
37.52_3‡	3.21 (1.73-5.94)§	1.77 (1.22-2.57)§	2.43 (0.76-7.74)
84.77_3‡	3.38 (1.87-6.11)‡	2.99 (2.02-4.42)‡	1.58 (0.53-4.77)
54.90_3‡	12.03 (4.97-29.11)‡	0.75 (0.36-1.57)	0.97 (0.28-3.38)
86.76_3‡	1.65 (0.91-2.97)	3.55 (2.56-4.93)‡	0.52 (0.16-1.68)
30.80_3‡	1.17 (0.38-3.64)	16.80 (4.85-58.20)‡	0.47 (0.04-4.98)
9.21_3¶	1.45 (0.48-4.37)	3.83 (1.90-7.73)§	0.69 (0.09-5.12)#
17.40_3‡	0.74 (0.35-1.57)	2.91 (2.00-4.24)‡	0.45 (0.10-2.05)
7.24_3	0.98 (0.40-2.36)	2.39 (1.49-3.83)§	0.52 (0.09-3.10)
50.34_3‡	3.80 (1.63-8.85)§	5.57 (2.35-13.20)‡	0.60 (0.13-2.74)
41.33_3‡	1.98 (0.84-4.68)	8.18 (3.43-19.53)‡	0.86 (0.18-4.11)

Table 2. Group Differences on Continuous and Categorical Early Childhood Risk Factors*

	Never Depressed (N) n = 629	Adult-Depressed (A) (MDD at Age 18, 21, or 26 y) n = 314	Juvenile-Depressed (J) (MDD at Age 11, 13, or 15 y) n = 21	Juvenile/Adult– Depressed (J/A) n = 34
Neurodevelopmental characteristics				
Total perinatal insults	0.73 (0.97)	0.68 (1.03)	1.48 (1.60)	0.76 (0.96)
Gross motor skills, ages 3-9 y, *z* scores	0.06 (1.81)	0.15 (1.81)	–1.94 (2.89)	–0.92 (2.98)
IQ, full-scale WISC, ages 7-9 y	106.0 (13.79)	106.4 (13.44)	100.7 (18.38)	103.8 (19.01)
Parental characteristics				
Mother's internalizing symptoms, child: ages 5-9 y	1.93 (2.15)	2.14 (2.31)	3.81 (3.49)	2.67 (2.63)
Mother's rejecting behavior, child: age 3 y	0.54 (1.27)	0.56 (1.34)	1.05 (1.80)	0.62 (1.04)
Parents' criminal conviction history, % (No.)	12.3 (70)	13.2 (39)	40.0 (6)	28.1 (9)
Parental disagreement about discipline, child: ages 5-9 y (*z* scores)	–10 (3.79)	0.35 (3.86)	0.33 (3.72)	0.49 (3.14)
Family-of-origin characteristics				
No. of residence changes, birth to 9 y	1.68 (1.99)	2.16 (2.56)	3.05 (2.25)	2.59 (2.43)
No. of parent figure changes, birth to 9 y	0.27 (0.75)	0.23 (0.66)	0.56 (1.09)	0.80 (0.89)
Socioeconomic status, birth to 9 y	3.52 (1.18)	3.57 (1.28)	2.92 (0.80)	3.41 (1.17)
Unwanted sexual contact by age 11 y, % (No.)	8.1 (49)	19.7 (61)	16.7 (3)	17.6 (6)
Parental loss by age 11 y, % (No.)	11.4 (72)	13.1 (41)	19.0 (4)	29.4 (10)
Child temperament/behavior				
Difficult baby, age 3 y	0.86 (0.49)	0.85 (0.47)	0.95 (0.59)	1.00 (0.49)
Teacher-rated peer problems, child: ages 7-9 y	1.06 (1.30)	0.98 (1.27)	2.21 (1.75)	1.68 (1.85)
Teacher-rated worried/fearful, child: ages 5-9 y	1.32 (1.20)	1.27 (1.14)	2.07 (1.37)	1.68 (1.70)
Teacher-rated hyperactive, child: ages 5-9 y	1.06 (1.23)	0.79 (1.05)	1.76 (1.44)	1.48 (1.82)
Teacher-rated antisocial, child: ages 5-9 y	0.95 (1.58)	0.71 (1.17)	1.34 (1.27)	1.96 (2.14)
Child's rating of depression, age 9 y	3.95 (3.07)	4.14 (2.91)	5.94 (2.91)	4.80 (2.92)
Undercontrolled temperament, % (No.)	9.2 (57)	11.3 (35)	19.0 (4)	11.8 (4)
Inhibited temperament, % (No.)	7.6 (47)	7.1 (22)	9.5 (2)	23.5 (8)

*All values are mean (SD) unless indicated otherwise. MDD indicates major depressive disorder; WISC, Wechsler Intelligence Scale for Children (Revised).

†All values are degrees of freedom unless indicated otherwise.

‡All values are *t* statistics (effect sizes) unless indicated otherwise. Effect size of 0.2 is small; 0.5, moderate; and 0.8, large.[43] Odds ratios were converted to effect sizes according to the formula provided by Haddock and colleagues.[45] The referent group for the ORs in the J + J/A vs A group is the A group; for the A vs N group, the N group; and for the J vs J/A group, the J/A group.

§$P \le .01$.

‖$P \le .05$.

¶$P \le .001$.

With the exception of having experienced unwanted sexual contact (which was measured retrospectively), adult-onset MDD does not seem to have an early developmental diathesis. This finding calls for renewed vigor in the search for adolescent and early-adult life events that trigger adult-onset MDD. A question for future research is whether risk factors exert their effects for only a limited period (suggesting that the same risk factors we measured in early childhood, such as losing a parent, would predict adult-onset MDD if they occurred in late adolescence) or whether risk factors are developmentally sensitive, and those that predict juvenile-onset MDD are qualitatively different from those that predict adult-onset MDD. A history of depression should be included as a control variable in analyses that assess the relationship between childhood risk factors and adult depression. Otherwise it is unclear whether the risk variables are related to the current episode or whether they exert their effect via past episodes of depression.[14]

A developmental perspective on psychopathology illustrates how the course and correlates of disorder vary as a function of age at onset. Thus, findings from longitudinal studies have important nosological implications.[50] Although our findings differentiated juvenile- and adult-depressed groups, we also draw attention to a pattern of nonsignificant findings that suggest heterogeneity within juvenile-depressed groups. The juvenile-depressed group had a higher proportion of males and exhibited a pattern reminiscent of externalizing behavior, characterized by more perinatal problems and somewhat higher rates of comorbid conduct disorder, attention deficit-disorder, crime by parents, and temperamentally undercontrolled behavior. In contrast, the juvenile/adult–depressed group had a higher proportion of girls and exhibited a pattern reminiscent of internalizing behavior, characterized by somewhat more temperamentally inhibited behavior, adult anxiety, and parental loss (but also more antisocial behavior). However, given the small size of our juvenile-depressed groups, the small effect sizes, and the statistical nonsignificance of the estimates, studies with larger samples of juvenile-onset cases are needed to determine whether there is meaningful heterogeneity within juvenile-onset MDD.

Heterogeneity within groups of psychiatric patients who present with the same symptom profile poses problems for theory, research, and treatment. Distinctions based on age of onset have proven important for understanding heterogeneity within attention-deficit/hyperactivity disorder[51] and antisocial disorder,[52,53] in

F†	Orthogonal Contrasts, t Statistics (Effect Sizes), and Odds Ratios (ORs) (Effect Sizes; Confidence Intervals) Coefficients Adjusted for Sex‡		
	J + J/A vs A	A vs N	J vs J/A
4.10§	2.38 (0.34)‖	0.59 (0.05)	2.55 (0.60)§
8.86¶	4.73 (0.66)¶	0.45 (0.05)	1.70 (1.02)
1.27	1.82 (0.27)	0.65 (0.03)	0.84 (0.17)
5.25¶	2.67 (0.40)‖	1.57 (0.10)	1.67 (0.39)
1.05	1.06 (0.17)	0.67 (0.02)	1.07 (0.32)
$\chi^2 = 15.57$¶	OR = 3.06 (0.62; CI = 1.52-6.16)§	OR = 1.10 (0.05; CI = 0.72-1.70)	OR = 1.67 (0.28; CI = 0.46-6.11)
1.13	0.08 (0.06)	1.95 (0.45)§	0.24 (0.16)
6.42¶	1.90 (0.24)§	2.90 (0.22)	0.78 (0.19)
4.55§	3.59 (0.68)¶	0.94 (0.06)	0.93 (0.25)
2.00	1.93 (0.28)	0.54 (0.04)	1.46 (0.48)
$\chi^2 = 26.84$¶	OR = 0.89 (0.06; CI = 0.38-2.11)	OR = 2.28 (0.45; CI = 1.44-3.62)§	OR = 1.94 (0.37; CI = 0.37-1.09)
$\chi^2 = 10.23$‖	OR = 2.33 (0.47; CI = 1.17-4.65)‖	OR = 1.10 (0.05; CI = 0.72-1.68)	OR = 0.60 (0.28; CI = 0.16-2.24)
1.23	1.81 (0.27)‖	0.03 (0.02)	0.42 (0.09)
7.57¶	4.47 (0.67)¶	0.56 (0.06)	1.34 (0.29)
3.49‖	3.02 (0.46)	0.69 (0.04)	1.11 (0.25)
7.58¶	4.16 (0.70)¶	1.41 (0.23)	0.36 (0.17)
8.11¶	4.45 (0.80)¶	1.22 (0.17)	1.80 (0.34)‖
$\chi^2 = 2.88$‖	2.08 (0.38)‖	1.33 (0.06)	1.02 (0.39)
3.01	OR = 1.26 (0.13; CI = 0.55-2.91)	OR = 1.46 (0.21; CI = 0.92-2.31)	OR = 1.51 (0.23; CI = 0.33-6.92)
$\chi^2 = 11.69$§	OR = 3.09 (0.62; CI = 1.36-6.98)§	OR = 0.82 (0.11; CI = 0.48-1.41)	OR = 0.39 (0.52; CI = 0.07-2.07)

which childhood onset has worse implications for course, recurrence, familial transmission, and treatment resistance.[54] Research on schizophrenia is also benefiting from a focus on childhood neurodevelopmental processes[55] and juvenile-onset symptoms.[56] The present study and others[1] illustrate that the distinction between juvenile- vs adult-onset MDD is important for understanding heterogeneity within depression as well.

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