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# Prenatal and perinatal influences on risk for psychopathology in childhood and adolescence

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**Abstract**
The relationship between a range of prenatal and perinatal events and risk for psychopathology in offspring was examined. Prenatal and perinatal events investigated included maternal experiences, health, and substance use during pregnancy, obstetric complications, feeding practices, and infant health during the first year of life. Offspring diagnosis was based on structured interviews conducted with 579 adolescents on two occasions. Risk for later psychopathology was associated with a number of prenatal and perinatal factors. Major depression was associated with not being breast fed and maternal emotional problems during the pregnancy. Anxiety was chiefly associated with fever and illness during the first year of life and maternal history of miscarriage and stillbirth. Disruptive behavior disorder was associated with poor maternal emotional health during the pregnancy and birth complications. Risk for substance use disorder was associated with maternal use of substances during the pregnancy. Mediating effects of maternal depression, maternal–child conflict, and physical symptoms in the child, and moderating effects of gender of child and parental education were also evaluated. The limitations of this study are discussed and future research directions are suggested.

Indicators of risk for the development of psychopathology are sometimes present from the earliest phases of life. For example, the children of parents with major forms of psychopathology are known to be at heightened risk for psychopathology themselves (e.g., Downey & Coyne, 1990; Goodman, 1987; Hammen, 1991; Weintraub, 1987; Weissman et al., 1987). In some instances these children have been shown to exhibit differences from other children in the earliest stages of infancy. For example, the infants of depressed mothers have been shown to exhibit less positive affect and more flat affect during interactions with their mothers as early as 2 and 3 months (Cohn, Campbell, Matias, & Hopkins, 1990; Field, 1984; Pickens & Field, 1993), and have also been shown to manifest differences in psychophysiological systems related to emotion at 3 and 6 months of age (Field et al., 1995a, 1995b). The purpose of this paper is to contribute to this body of knowledge about the early determinants of risk for later psychopathology by examining the association between a range of prenatal and perinatal factors and the incidence of depression, anxiety, substance use, and disruptive behavior disorder during childhood and adolescence.

## Types of Prenatal and Perinatal Factors

Risk factors during the earliest phases of development may include (a) the prenatal environment, for example maternal physical health during the pregnancy, maternal experiences during pregnancy (such as stressful life events, dysphoric mood, and episodes of mental disorder; O'Hara, 1995), and maternal use of prescribed and nonprescribed drugs during

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pregnancy (Behnke & Eyler, 1993); (b) intrapartum events, such as birth difficulties and associated physical trauma to the child (Guth, Jones, & Murray, 1993; McNeil, 1988); (c) the effects of immediate postpartum environment and health problems (e.g., prematurity, anoxia, hematological problems such as rhesus incompatibility); and (d) aspects of the later neonatal environment, such as general infant health during the first year of life, and the infant's psychosocial environment.

The relationship of obstetric complications (OCs) to later psychopathology has received considerable attention. McNeil (1988) has pointed out that OCs can be divided temporally into pregnancy complications (PCs, covering the period from conception until the onset of labor), birth complications (BCs, occurring during labor and delivery), and neonatal complications (NCs, noted in offspring from the moment of birth until the first 1–4 weeks postpartum). PCs, BCs, and NCs, as described by McNeil, map respectively on to the classes of events described in points (a), (b), and (c) above. Pasamanick's pioneering work in this area was guided by the hypothesis that OCs produce a "continuum of reproductive casualty extending from death through varying degrees of neuropsychiatric disability" (Pasamanick & Knobloch, 1961, p. 91). Unfortunately many studies examine the relationship between global counts of OCs and risk for later psychopathology without reference to the temporal differentiation described above, or differentiation of the systems affected or damaged.

### *Obstetric complications and risk for psychopathology*

Most work has focused on the association of OCs with risk for schizophrenia. In reviewing the evidence, McNeil (1988) concluded that increased rates of OCs have been found in a variety of schizophrenic samples, with oxygen deprivation the strongest risk factor for schizophrenia. Studies have demonstrated associations between OCs and risk for nonschizophrenic disorders, but they have typically not differentiated between the effects of different types of OCs. For instance, Guth, Jones, and Murray (1993) found an association between early onset unipolar affective disorder and the presence of any OC. Similarly, Cohen, Velez, Brook, and Smith (1989) found OCs (in which they included unwanted baby, emotional problems during the pregnancy, low birth weight, physical trauma during the pregnancy, and problems during the delivery) were related to a range of forms of childhood psychopathology, including attention deficit, conduct problems, and oppositional, anxiety and depressive disorders. Vocisano, Klein, Keefe, Dienst, and Kincaid (1996) found that inpatients with "deteriorated affective disorder" (an excessively prolonged and functionally impairing form of major depressive disorder) were more likely to have experienced OCs (low birth weight, birth complications, length of term) than were a comparison group of less impaired outpatients with major depressive disorder. Although some studies have also found an association between OCs and bipolar disorder (Kinney et al., 1993), others have not (Verdoux & Bourgeois, 1995). In contrast to these generally positive findings, Buka, Tsuang, and Lisitt (1993), in a prospective study that assessed the influence of OCs on lifetime diagnosis of a range of mental disorders at age 18 to 27 years, only found nonsignificant trends for one specific OC, chronic fetal hypoxia, to be associated with higher rates of cognitive impairment and psychotic disorders. A possible explanation for the lack of congruence between this latter study and others is Buka et al.'s use of the Diagnostic Interview Schedule (Robins, Helzer, Croughan, & Ratcliff, 1981) to evaluate lifetime prevalence of psychopathology. The Diagnostic Interview Schedule has been criticized for underestimating lifetime prevalence of psychopathology in the Epidemiologic Catchment Area program (Parker, 1987). Thus, although there is considerable evidence suggesting a link between OCs and nonschizophrenic psychopathology, most studies have not attempted to pinpoint the specific OCs which are associated with specific types of subsequent psychopathology.

### *Prenatal stress and risk for psychopathology*

With regard to maternal exposure to stress during pregnancy, animal research has demonstrated that the offspring of stressed mothers show an increase in what are presumed to be behavioral manifestations of depression, and alterations in dopamine transmission (Alonso, Arevalo, Afonso, & Rodreiguez–Diaz, 1991; Alonso, Navarro, & Rodreiguez–Diaz, 1994). In humans, maternal dysphoria during the pregnancy has been linked to high fetal motor activity (Van Den Bergh, 1990), interuterine growth retardation (Goldenberg, Cliver, Cutter, & Hoffman, 1991), and unconsolability and excessive crying in the infant (Zuckerman, Als, Bauchner, Parker, & Cabral, 1990). One of the considerations with these human studies is that they usually do not control for the fact that high levels of distress during pregnancy may be indicative of a more generalized vulnerability to negative affect in the mother. In other words, the distress noted during pregnancy may be a trait rather than a state feature of the mother. Consequently it is impossible to assert that it is the experiences during the pregnancy per se that are exerting an influence on infant behavioral tendencies, especially given the demonstrated continuity between antenatal and postnatal psychological problems (Kelly & Deakin, 1992).

### *Prenatal substance use and risk for psychopathology*

There is voluminous literature on the effects of prenatal exposure to various substances on child development (Behnke & Eyler, 1993). Caffeine is the most frequently used substance by pregnant women (Barr & Streissguth, 1991) making examination of its effects important. Barr and Streissguth prospectively examined the association between prenatal exposure to caffeine and measures of physical and cognitive achievement at 4 and 7 years of age. The results did not show an association of caffeine use with many measures of child outcome. However, an association of caffeine use with breech birth was found. Other less frequently used substances, such as tobacco, alcohol, cannabis, opiates, and cocaine have been shown to elevate risk of congenital abnormalities (such as Fetal Alcohol Syndrome), pregnancy outcome (such as increase in spontaneous abortions, prematurity), fetal growth, and postnatal problems (such as slow infant growth or Sudden Infant Death Syndrome) (Behnke & Eyler, 1993). With regard to the *behavioral* development of children prenatally exposed to substances, most research has focused on the neonatal period, where the acute effect of exposure to the drug can still be observed (Coles & Platzman, 1993). Effects on behavioral and emotional development in later years, however, have received relatively little attention, although there have been studies which have reported deficits in cognitive, language, attentional, and academic performance associated with prenatal exposure to alcohol, cigarettes, cocaine, cannabis, and opiates (see Coles & Platzman, 1993, for a review). The abovementioned studies indicated deficits which could lay the foundation for a wide range of future problems of adjustment. To our knowledge, no study has yet systematically explored the influence of prenatal exposure to substances on the development of psychopathology during childhood and adolescence.

### *Early neonatal factors and risk for psychopathology*

In addition to the early neonatal effects that are often included in studies of OCs (e.g., prematurity, respiratory or hematologic problems evident immediately after birth) there are a number of other aspects of the infant's early environment that seem relevant. Feeding methods (i.e., breast vs. bottle) may be an influential aspect of the early postnatal environment, as a large proportion of an infant's waking hours are spent in feeding interactions. Although most recent accounts of the potential benefits of breast feeding have emphasized nutritional factors (American Academy of Pediatrics, 1982), classical psychoanalytic, classical learning, and object-relations approaches to child development have long as-

serted that breast feeding is important for the development of healthy infant–mother attachment (e.g., Abraham, 1954; Bowlby, 1969; Davis & Wallbridge, 1981). Although the evidence that breast feeding per se is important for healthy attachment is not strong, maternal characteristics that are evident during feeding, such as sensitivity and responsivity to the infant, are strongly related to the quality of infant–mother attachment (Rosenblith & Sims–Knight, 1985). Given the evidence that maternal depression precipitates early cessation of breast feeding (Cooper, Murray, & Stein, 1993) and that maternal enjoyment of feeding is strongly related to quality of attachment (Ainsworth, Blehar, Waters, & Wall, 1978), it seems reasonable to hypothesize an effect of breast feeding on risk for psychopathology. To our knowledge, there has been no previous study that has investigated the impact of feeding method in early life on long term outcomes in psychopathology.

Health problems such as serious illness, infection, fever, or poor nutrition during the first 12 months of life can also be hypothesized to contribute to vulnerability to psychopathology. For example, two recent studies have shown an increased risk for schizophrenia associated with rhesus incompatibility (Hollister, Laing, & Mednick, 1996) and prenatal famine (Susser et al., 1996). Furthermore, Vocisano et al. (1996) found that deteriorated affective disorder patients were more likely to have experienced physical disorders in infancy than were nondeteriorated affective disorder controls. We therefore chose to examine the role of illness in general during the first year of life on risk for psychopathology.

### *Models of the relationship between prenatal and perinatal factors and psychopathology*

It is important to note that to the extent that an association between a particular prenatal or perinatal factor and later psychopathology is demonstrated, a number of possible models to explain such an association can be advanced. Firstly, the association could be due to the fact that the particular event is more likely to occur throughout the child's life, not just during the pregnancy or postpartum, and as such the effects of this factor may not be due to its influence on prenatal or neonatal development specifically. In other words, the event might reflect a trait rather than state feature of the mother during the pregnancy and puerperium. Secondly, the association may be due to the fact that the prenatal/perinatal factor caused some kind of neural or other physical damage to the developing child and that this damage directly caused the child to have heightened risk for psychopathology. This is the hypothesis advanced by Pasamanick and Knobloch (1961). A variant of this model is that the neural or other physical damage does not cause the risk for later psychopathology directly but causes it indirectly through some kind of psychosocial disruption that follows the physical damage, such as when a child with a birth related physical disability is unable to interact normally with other children (e.g., during sporting games), and subsequently suffers a loss of confidence, self-esteem, and social support, which then in turn confers risk for the development of psychopathology. A third possibility is that the prenatal or perinatal factor themselves will lead to psychosocial disruption in the absence of any physical damage, such as where the relationship between a mother and child is negatively affected by prenatal or perinatal complications. The final possibility we will enumerate is that both the event and the later childhood psychopathology might be independently caused by a third factor, such as a genetic or environmental factor that affects both the mother and child. These possibilities are graphically described in Figure 1. This complexity has been recognized by a number of authors in this area (Cohen et al., 1989; Coles & Platzman, 1993), who stress the importance of examining the covariation between prenatal and perinatal events, childhood psychopathology, and other possible intervening mechanisms.

In this study we included a number of factors that may serve as mediating variables in the association between prenatal/perinatal factors and psychopathology in offspring (Baron & Kenny, 1986). These included maternal symptomatology and attitudes during the child's lifetime, which might reflect life-long maternal behaviors or traits as described in

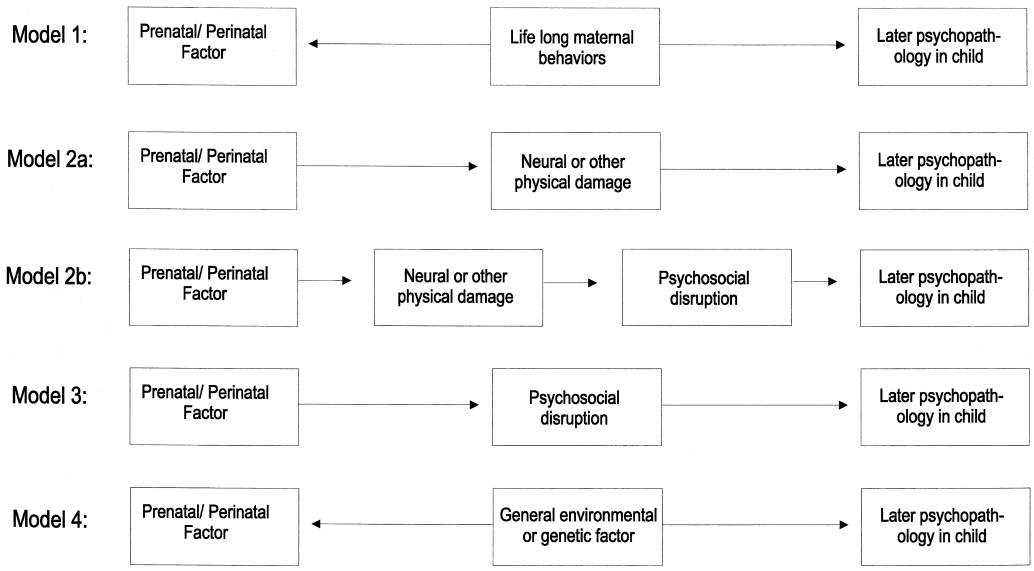


**Figure 1.** Models explaining the association between prenatal and perinatal factors and later psychopathology.

Model 1 in Figure 1. Furthermore, Cohen et al. (1989) proposed two other mechanisms which may mediate the relationship between prenatal and perinatal events and child psychopathology. One is that significant vulnerability to physical illness in early childhood might follow particular prenatal events, and this vulnerability to illness may in turn lead to risk for psychopathology in the child (cf. Model 2b, Figure 1). The second is that particular prenatal and perinatal events may lead to disruptions in the relationship between the mother and child, or in family cohesiveness more generally, and these disturbed relationships may increase risk for child psychopathology (cf. Model 3, Figure 1). As well as these hypothesized *mediating* function of these variables (i.e., variables that account for, or act as a vital link in, the relationship between prenatal factors and later psychopathology), we also considered two other variables that may function as *moderators* (i.e., variables that affect the direction and/or strength of the relation between prenatal factors and later psychopathology), namely gender and parental SES (as estimated by parental education) (Baron & Kenny, 1986). To evaluate the role of these variables in mediating associations between prenatal factors and childhood psychopathology we included indicators of the mother's depressive symptomatology at the time of reporting the pre/perinatal influences, maternal social desirability, the family's cohesiveness, distress in the mother–child relationship, and the child's lifetime rate of physical symptomatology in the analyses as covariates. To assess the role of child gender and parental education in moderating associations between prenatal factors and child psychopathology, interaction terms between these moderating variables and each of the prenatal factors were added to the models predicting later psychopathology.

This report is one in a series in which we describe findings from the Oregon Adolescent Depression Project (OADP), a community based study of a large sample of adolescents which has been conducted in order to describe the prevalence, incidence, risk factors, and consequences of a range of psychopathological disorders during childhood, adolescence, and young adulthood (e.g., Lewinsohn, Gotlib, & Seeley, 1995; Lewinsohn, Hops, Roberts, Seeley, & Andrews, 1993; Lewinsohn, Roberts, Seeley, Rohde, Gotlib, & Hops, 1994; Lewinsohn, Rohde, & Seeley, 1995a). As such, the OADP includes comprehensive information on lifetime history of psychopath-

ology based on structured interview data. In a subset of the sample ($n = 579$) information was obtained from the biological mothers of probands concerning a range of medical complications, symptoms, and substance use behaviors during the pregnancy, birth, and postpartum periods of the proband child. Although this information is based on maternal recall when the child was between 14 and 18 years of age, and is thus subject to biases in such recall, previous studies that have evaluated the validity of maternal recall of obstetric complications (O'Callaghan, Larkin, & Waddington, 1990) and substance use during pregnancy (Jacobson et al., 1991) have found adequate congruency between maternal recall and more objective measures.

The specific aims of this study were threefold. First, to describe univariate associations between a range of prenatal and perinatal factors and risk for non-schizophrenic psychopathology in offspring up to age 18 years. The prenatal and perinatal factors examined cover a range of effects during the pregnancy, intrapartum (birth), and neonatal periods. The second aim was to evaluate the role of putative mediating and moderating variables (as described above) in observed associations between prenatal and perinatal factors and psychopathology in offspring. Finally, due to the high degree of comorbidity between mental disorders in this age group (Lewinsohn, Rohde, & Seeley, 1995a; Lewinsohn, Rohde, Seeley, & Hops, 1991), the specificity of the associations between prenatal and perinatal factors and each particular disorder were evaluated by controlling for the influence of all other diagnoses.

## Method

### *Subjects and procedure*

The initial pool of participants was randomly selected in three cohorts from nine senior high schools (approximately 10,200 students) representative of urban and rural districts in western Oregon. Sampling fractions of 10, 18.5, and 20% were used for each cohort; sampling within each school was proportional to size of the school, size of the grade within the school, and the proportion of males and females within the grade. A total of 1,709 adolescents completed the initial ($T_1$) assessment (interview and questionnaires) between 1987 and 1989, with an overall participation rate of 61%. At the second assessment ($T_2$), 1,507 participants (88.2%) returned for a readministration of the interview and questionnaire ($M$ $T_1$–$T_2$ interval = 13.8 months, $SD = 2.3$).

The representativeness of the sample was evaluated using several procedures. Demographic characteristics of the sample were compared with 1980 census data provided by the school districts. No differences were found on gender, ethnicity, or parental education level, although participants had a slightly higher proportion of two-parent families. Second, participants were compared to those who declined. The two groups were similar on gender of head of household, family size, number of parents in the household, and ethnicity. Students who declined had a slightly lower socioeconomic level (although both groups represented the middle class), 12th grade students (67%) were more likely to participate than 9th grade students (59%), and female students (68%) were more likely to participate than male students (60%). Overall, participants in the sample at $T_1$ were representative of high school students in western Oregon.

Small but statistically significant differences emerged due to attrition in the $T_1$–$T_2$ panel sample, with attrition being associated with lower parental education, smaller household number, male gender, ever used cigarettes, current cigarette use, past diagnoses of disruptive behavior disorders, and past substance use disorders (males only). Additional details regarding the sample are provided in Lewinsohn et al. (1993).

Information on prenatal and perinatal events was only collected from a subset of the $T_1$–$T_2$ sample. Following the completion of the $T_1$ assessment, 1,165 adolescents and their parents were contacted and asked to participate in a study that required participation of both the adolescent and their parents (Hops & Seeley, 1992). Of the 1,165 families contacted, 697 (59.8%) participated in the extended investigation. No significant differences were found between participant and

nonparticipant families with regard to gender of adolescent, gender of head of household, socioeconomic status, adolescent BDI, or adolescent psychiatric disorder assessed at $T_1$. As part of this investigation, parents were asked to complete the prenatal and perinatal events questionnaire. For the purposes of this study, the sample to be analyzed was restricted to the 579 subjects who completed the $T_2$ assessment and where the prenatal and perinatal events questionnaire was complete by the adolescent's biological mother. The demographic characteristics were as follows: 58% female, 92% White, $T_1$ mean age = 16.4 ($SD$ = 1.2), 56% were living with both biological parents, parental education (highest value for mother or father) consisted of 1% having not completed high school, 12% completed high school, 39% had some college, and 48% had an academic or professional degree. Compared with the $T_2$ subjects for whom prenatal and perinatal data were not available ($n$ = 928), the subsample of the 579 adolescents was comprised of slightly more female subjects, 58% versus 51%, $\chi^2$ (1, $n$ = 1507) = 5.36, $p < .05$, and were slightly younger, mean $T_1$ age of 16.4 ($SD$ = 1.2) versus 16.6 ($SD$ = 1.2), $t$ (1505) = 3.94, $p < .001$; no significant differences were found for race, parental education, number of biological parents within household, or lifetime history of psychopathology at $T_2$.

### *Diagnostic interview*

Adolescents were interviewed at $T_1$ with a version of the Schedule for Affective Disorders and Schizophrenia for School-Age Children (K-SADS) that combined features of the Epidemiologic version (Orvaschel et al., 1982) and the Present Episode version (Chambers et al., 1985), and included additional items to derive diagnoses of most disorders as per the Diagnostic and Statistical Manual of Mental Disorders, Third Edition-Revised (DSM-III-R) criteria (American Psychiatric Association, 1987).

At $T_2$, subjects were diagnostically interviewed using the Longitudinal Interval Follow-up Evaluation (Keller et al., 1987), which provides detailed information about the course of psychiatric symptoms and disorders since the initial K-SADS interview, with rigorous criteria for recovery from a disorder (i.e., symptom free for 8 or more weeks). Interviewers also elicited information and rated the presence and severity of depression symptoms and other psychiatric disorders since $T_1$ using the K-SADS format. Therefore, lifetime diagnostic information was available regarding the occurrence and duration of all disorders prior to and at $T_2$.

Diagnostic interviewers were carefully trained and supervised. For reliability purposes, all interviews were either audio- or videotaped and a second interviewer reviewed the recordings of 12% of the interviews. Interrater reliability was evaluated by the kappa statistic (Cohen, 1960). With four exceptions (diagnoses for current and lifetime anxiety disorders, lifetime dysthymia, and lifetime eating disorders, $\kappa$s = .60, .53, .58, and .66, respectively), all kappas at $T_1$ were equal to or greater than .80. Because of the low frequency of disorders at $T_2$, kappas were computed across all disorders. Kappas for the presence of any disorder versus no disorder at $T_2$ and for the occurrence of any disorder between $T_1$ and $T_2$ were .87 and .72, respectively.

### *Psychiatric disorders*

The psychiatric disorders studied included current and past diagnoses of major depressive disorder (MDD; $n$ = 141); anxiety disorders ($n$ = 54) which included diagnoses of panic disorder, agoraphobia, simple phobia, social phobia, obsessive–compulsive disorder, separation anxiety, and overanxious disorder; alcohol and other drug abuse/dependence ($n$ = 68); and disruptive behavior disorders ($n$ = 38) which included attention-deficit hyperactivity disorder, conduct disorder, and oppositional defiant disorder.

### *Measures*

*Lifetime physical symptoms.* Adolescents reported on the lifetime occurrence of 88 physical symptoms (e.g., broken bones, ulcers, double vision; $\alpha$ = .90, $T_1$–$T_2$ $r$ = .48) using a

yes/no response format as part of the $T_1$ assessment (Lewinsohn et al., 1994).

*Parental education.* Adolescents reported on the highest education level achieved by their mother and father using a 7-point Likert type scale; the maximum value for mother or father was used ($T_1$–$T_2$ $r = .90$).

*Prenatal and perinatal events.* Mothers were asked to complete a questionnaire that obtained information on a wide range of prenatal and perinatal factors. These included child's birth date, parent's age at time of birth, child's weight at birth, obstetric history prior to this pregnancy (e.g., prior miscarriages, prior still births), complications during the pregnancy (e.g., bleeding from vagina, swelling of face, hands, ankles, high blood pressure, diabetes mellitus), emotional problems during pregnancy (e.g., anxiety, depression), symptoms requiring prescribed medication during the pregnancy (e.g., morning sickness, pain), substance use during pregnancy (cigarettes, alcohol, coffee/tea, marijuana), delivery complications (e.g., caesarean, breech, blue baby), and aspects of the early postnatal environment such as method and duration of feeding (i.e., breast vs. bottle fed) and incidence of high fever or serious illness or infection in the first 12 months of life. The mother checked which of these had occurred to her during the pregnancy with this child using a yes/no response format. For some items, such as use of substances or feeding method, further information was obtained regarding the amount of use or length of time.

Based on a review of previous literature on perinatal risk screening scales (Molfese, 1989) we assigned each variable to one of 12 scales representing rationally derived dimensions of prenatal events. These scales were classified as either Prenatal Factors, Intrapartum Factors, Early Neonatal Factors, and Late Neonatal Factors. These four broad time frames and the scales within each of them are described in Table 1, along with the prevalence of each variable in our sample. Latent trait analysis was used to test the fit of the prenatal events to the 12 rationally derived dimensions. The NOHARM program (Fraser,

**Table 1.** *Assignment of prenatal and perinatal items into 12 scales and four time frames with the prevalence of each variable*

| Time Frame/Scale/Items | Percent |
|---|---|
| Prenatal | |
| Maternal physical health | 29 |
| Bleeding from vagina | 12 |
| Premature contractions | 14 |
| Swelling of face and hands | 40 |
| High blood pressure | 8 |
| Seizures and convulsions | 2 |
| Rubella | 1 |
| Any other infectious diseases | 1 |
| Diabetes mellitus | 1 |
| Anemia | 17 |
| Serious injury | 2 |
| X rays | 13 |
| Maternal emotional health | 18 |
| Depression during pregnancy | 15 |
| Anxiety during pregnancy | 10 |
| Use of prescribed drugs | 29 |
| Morning sickness | 23 |
| Pain | 4 |
| High blood pressure | 1 |
| Hormones | 1 |
| Valium | 3 |
| Thyroid medication | 4 |
| Maternal substance use | 30 |
| Cigarettes | 21 |
| Alcohol | 21 |
| Coffee/tea | 57 |
| Marijuana | 6 |
| Maternal obstetric history | 21 |
| Previous miscarriage | 18 |
| Previous stillbirth | 3 |
| Medications to prevent miscarriage | 3 |
| Intrapartum | |
| Surgical delivery | 18 |
| Caesarean delivery | 9 |
| General anesthesia | 14 |
| Difficult delivery | 17 |
| Local anesthesia | 54 |
| Breech birth | 6 |
| Forceps used | 18 |
| Early neonatal | |
| Prematurity | 18 |
| Low birth weight | 2 |
| Premature delivery | 13 |
| Baby required incubator | 9 |
| Acute anoxia/hypoxia | 13 |
| Cord around neck | 5 |
| Blue baby | 4 |
| Slow heart beat | 2 |
| Baby did not breathe | 4 |
| Baby had convulsions | 0 |
| Baby required oxygen | 4 |
| Hematological problems | 24 |
| Rhesus incompatibility | 12 |
| Baby had jaundice | 15 |
| Baby required blood transfusion | 1 |
| Late neonatal | |
| Illness in first year | 33 |
| Fever | 22 |
| Infection | 26 |
| Breast feeding | 64 |

1988), which fits multidimensional normal ogive models of latent trait theory (McDonald, 1985), was used to confirm the 12 factor model. The model was specified such that the prenatal events were constrained to load only on their respective factors. A good fit was obtained for the 12 factor model, root mean square residual = .0044, Tanaka index of goodness of fit (Tanaka, 1993) = .998.

To compare the relative effect sizes of the odds ratios that are reported in the results section, each of the 12 dimensions was reduced to a binary variable, where the cutoff score for each variable was designated such that the factor was considered present for those subjects in the upper quartile of the distribution of that variable. Test–retest reliability was calculated on a subset of 120 mothers who completed the questionnaire again at the $T_2$ assessment. Test–retest kappa statistics were calculated for the dicotomized variables. All of the variables exhibited excellent test–retest reliability (all $\kappa > .70$) except for the following: maternal emotional health during pregnancy ($\kappa = .58$), maternal substance use during pregnancy ($\kappa = .62$), surgical delivery ($\kappa = .57$), and difficult delivery ($\kappa = .61$). In addition, we examined the relation between the mother's social desirability (Crowne & Marlowe, 1960) and her reports of the prenatal and perinatal events. Social desirability was significantly albeit weakly related to only 1 of the 12 derived scales, Maternal Physical Health During the Pregnancy ($r = -.08$, $p < .05$). The weakness of this correlation, along with the nonsignificant association with the other 11 scales, suggests that the socially desirable response set did not have much impact on their reporting of prenatal and perinatal events.

*Maternal depressive symptoms.* Maternal depressive symptoms at the time of completing the questionnaire were assessed using the Beck Depression Inventory ($\alpha = .82$, $T_1$–$T_2$ $r = .67$) (BDI; Beck & Steer, 1987).

*Familial relations.* Aspects of the familial relations from the point of view of the mother were assessed. Family cohesiveness was assessed using the Cohesion subscale of the Family Environment Scale (5 items; $\alpha = .80$, $T_1$–$T_2$ $r = .54$) (Moos, 1974), and the degree of conflict between the mother and the child was assessed with the Mother's Appraisal of Dyad subscale of the Conflict Behavior Questionnaire (7 items; $\alpha = .62$, $T_1$–$T_2$ $r = .37$) (Prinz, Foster, Kent, & O'Leary, 1979). These scales have been abbreviated on the basis of several extensive pilot studies (Andrews, Lewinsohn, Hops, & Roberts, 1993).

## Results

### *Associations among predictor variables and mediating/moderating variables*

To begin with, it was of interest to examine the interrelations between the dichotomized prenatal and perinatal event scales using bivariate correlations. Only one correlation exceeded .20, which was between Acute Anoxia/Hypoxia and Prematurity, $r = .25$, $p < .001$. Likewise, the associations between the prenatal and perinatal event scales and the mediating/moderating variables were calculated. Only one correlation exceeded .20, which was between Maternal Emotional Problems During the Pregnancy and Maternal Depression in Later Life, $r = .27$, $p < .001$.

### *Associations between prenatal and perinatal events and later psychopathology*

Next, bivariate associations were calculated between the prenatal/perinatal scales and the four diagnostic outcome measures, in order to choose the variables to be included in the logistic regression equations for the prediction of each diagnostic entity. Table 2 shows the unadjusted odds ratios with 95% confidence intervals for each of the variables that showed significant, $p < .05$, associations with the diagnostic variables. As can been seen, major depression was associated with poor maternal emotional health during the pregnancy and with not being breast fed. Anxiety disorder was associated with poor maternal emotional health during the pregnancy, poor maternal obstetric history, and illness in the infant during the first year of life. Disruptive behavior disorder was associated with poor maternal

**Table 2.** *Summary of the logistic regression analyses predicting adolescent psychopathology*

| Disorder/Prenatal Variable | Unadjusted OR (95% CI) | Adjusted[a] OR (95% CI) | Adjusted[a,b] OR (95% CI) | Adjusted[a–c] OR (95% CI) |
|---|---|---|---|---|
| Major depression | | | | |
| Maternal emotional health | 2.08 (1.32–3.28)* | 2.10 (1.33–3.31)* | 1.63 (0.99–2.68) | 1.50 (0.89–2.54) |
| Not breast fed | 1.66 (1.13–2.45)* | 1.68 (1.13–2.47)* | 1.71 (1.14–2.56)* | 1.64 (1.07–2.51)* |
| Anxiety | | | | |
| Maternal emotional health | 2.09 (1.12–3.92)* | 1.78 (0.94–3.40) | 1.49 (0.76–2.95) | 1.28 (0.62–2.62) |
| Maternal obstetric history | 2.20 (1.21–4.00)* | 2.11 (1.14–3.88)* | 2.13 (1.14–3.98)* | 2.34 (1.23–4.47)* |
| Illness during first year | 2.62 (1.49–4.62)* | 2.49 (1.40–4.43)* | 2.47 (1.38–4.44)* | 2.82 (1.53–5.20)* |
| Disruptive behavior | | | | |
| Maternal physical health | 2.17 (1.09–4.33)* | 1.73 (0.84–3.55) | 1.64 (0.77–3.46) | 1.75 (0.81–3.46) |
| Maternal emotional health | 2.94 (1.43–6.05)* | 2.83 (1.34–5.98)* | 2.49 (1.14–5.43)* | 2.39 (1.06–5.37)* |
| Anoxia/hypoxia | 3.00 (1.38–6.53)* | 3.02 (1.35–6.73)* | 3.00 (1.31–6.87)* | 3.20 (1.36–7.55)* |
| Substance use | | | | |
| Maternal drug abuse | 2.43 (1.45–4.05)* | NA | 2.29 (1.36–3.86)* | 2.49 (1.44–4.30)* |

*Note:* OR, odds ratio; CI, confidence interval; NA, not applicable.
[a]Adjusted for the prenatal variables that were significantly associated with adolescent psychiatric disorder.
[b]Adjusted for the set of covariates (maternal depression, family cohesion, family conflict, adolescent physical symptoms).
[c]Adjusted for the other adolescent psychiatric disorders.
*$p < .05$.

physical health during the pregnancy, poor maternal emotional health during the pregnancy, and acute anoxia/hypoxia. Substance use disorder was only associated with maternal substance use during the pregnancy. All other variables showed nonsignificant associations with the diagnostic variables.

### *Multivariate analyses*

To assess whether maternal depression, family cohesion, family conflict, or adolescent physical symptoms functioned as mediating variables, each significant univariate association was submitted to a hierarchical logistic regression. Odds ratios (ORs), and their attendant 95% confidence intervals (CIs), are presented in Table 2 for each step in the hierarchical regression. The second column presents ORs and CIs for the predictors when controlling for the other significant prenatal/perinatal predictors, whereas the third column presents the ORs when controlling for these predictors and the putative mediating variables. In those cases where inclusion of the mediating variable block rendered the association between the prenatal/perinatal factor and offspring psychopathology nonsignificant, we examined the effect of each of the mediating variables separately in order to establish which might be responsible for the effect. The final column of Table 2 assesses the specificity of the observed associations by showing ORs obtained when controlling for the other prenatal/perinatal predictors, the putative mediators, and the other diagnoses.

With respect to the predictors of major depression, the major effect of controlling for these variables was that maternal emotional health was no longer significant after the inclusion of the mediating variable block. Post hoc breakdowns of the effects of the individual variables revealed that the key variable in reducing the association between maternal emotional health during the pregnancy and later major depression was maternal ratings of depressive symptoms later in life, suggesting that this may act as a mediating variable in the association between maternal prenatal emotional health and offspring major depression. Amongst the predictors of later anxiety, maternal emotional health became nonsignificant after the inclusion of the other prenatal/perinatal predictors. Likewise with the predictors of disruptive behavior disorders, maternal physical health during the pregnancy became nonsignificant after the inclusion of the other predictors. All other predictor variables remained significant after the inclusion of all the other variables in the equation.

To assess the role of child gender and parental education as moderating variables, an additional block was added to the hierarchical multiple logistic regression models described above. In this block, the main effects of child gender and parental education, and the interaction terms between these moderators and the prenatal/perinatal predictors, were entered into each model. Only one of these interaction terms made a significant contribution to the prediction of the outcome variable: the interaction between child gender and maternal physical health in the prediction of disruptive behavior disorder, Wald = 4.01, $p < .05$. Further examination of this effect revealed that it was due to the fact that maternal physical health was significantly associated with disruptive behavior disorder in females offspring, $\chi^2(1, N = 333) = 9.01$, $p < .005$, but not in male offspring, $\chi^2(1, N = 246) = .0998$, *ns*. This suggests that gender does moderate the relationship between maternal physical health during the pregnancy and later disruptive behavior disorder in offspring.

## Discussion

### *Strengths and limitations of the study*

One strength of this study is that it examined the relationship between a wide range of prenatal and perinatal factors and risk for non-schizophrenic psychopathology. Also the measurement of the dependent variables, (i.e., lifetime occurrence of psychopathology during childhood and adolescence) was carefully conducted using well-developed interview techniques. This not only enabled us to examine the presence of such disorders with confidence, but also to examine the specificity of the associations between particular risk factors and particular syndromes. Finally, the fact that this study was based on a representative community sample enabled the testing of associations without the influence of selection biases that apply to the clinical samples that have been used in previous studies (e.g., Guth et al., 1993).

There are also a number of limitations that must be borne in mind when interpreting the results of this study. The greatest potential weakness of this study is probably the manner in which the data on prenatal and perinatal factors was collected. Although the information was obtained from biological mothers only, it did require these mothers to recall incidents that occurred 14 to 18 years previously. This obviously raises the questions as to what effect the vicissitudes of memory and self-presentation might have had on the reporting of this information, and therefore its reliability. As pointed out in the introduction, previous studies which have compared maternal recall to more objective indices have found adequate concordance between these two sources of information. Jacobson et al. (1991) asked 361 African American inner city mothers to report on their use of alcohol, cocaine, and marijuana during pregnancy antenatally and at 13 months postpartum. They found the two reports to be moderately well related for all three substances. Most relevant to this study, however, are the results reported by O'Callaghan et al. (1990), who interviewed biological mothers of schizophrenic and other patients about obstetric complications with their offspring. The offspring were aged between 22 and 43 years old at the time of the interview. These maternal reports were compared with hospital records, which revealed important inconsistencies in only 9.5% of the cases. O'Callaghan et al. (1990) concluded that maternal recall can be a "surprisingly accurate" source of obstetric information. Furthermore, the test–retest reliabilities over a 1 year period for the information provided by mothers in the present study indicated relative consistency. Thus, although maternal recall of prenatal and perinatal events is probably an inferior form of measurement of these factors than more objective indices, such as hospital records, results suggest that information obtained here is an acceptable alternative. Indeed, some studies have presented data questioning the assumption that medical record data are necessarily more accurate and acceptable (Hewson & Bennett, 1987).

Another interesting aspect of the prenatal and perinatal factors studied was the low degree of correlation between them, and the fact that only 1 of the 12 derived scales was even

weakly correlated with social desirability. This adds to the impression that subjects' responses were not determined by a generalized response bias associated with either a jaded or idealized recall of the pregnancy and birth experiences.

Another potential limitation is that the psychiatric syndromes (e.g., anxiety disorders, substance use disorders, disruptive behavior disorders), which have been treated as relatively homogenous entities for the purposes of this study, may indeed consist of diagnostically and etiologically heterogeneous conditions. Given the relatively small number of subjects in each of the specific diagnostic groups (e.g., obsessive–compulsive disorder), we chose to aggregate psychopathological outcomes in order to retain adequate statistical power. Thus, for example, the risk factors identified for anxiety may be relevant to all or only some anxiety disorders. Given all the above-mentioned limitations, our results may be best seen as providing hypotheses for closer investigation in future work, rather than providing the basis for firm conclusions.

### *Predictors of risk for major depression*

With regard to the substantive findings, a number of associations were observed between the prenatal and perinatal factors and various psychopathological outcomes in childhood and adolescence. Major depression was predicted by maternal emotional problems during the pregnancy and not being breast fed. The fact that maternal emotional health was no longer a significant predictor after adjusting for the putative mediating variables, especially the variable reflecting maternal depression later in life, suggests two possibilities. The first is that the risk for future depression in the child is conferred by the effects of maternal depressive behaviors throughout the child's lifetime, rather than specifically during the prenatal period (i.e., maternal depression during the child's lifetime acts as a necessary mediating variable in that it is responsible for the mechanism by which prenatal emotional problems and offspring depression are associated). This is the kind of relationship represented by Model 1 in Figure 1. Indeed, there is a considerable literature which catalogues the deleterious effects of maternal depressive behavior on children in both infancy (Field, 1992) and later childhood (Downey & Coyne, 1990). The other possibility is that this association between maternal depression and child depression is due to a common environmental or genetic factor that influences both individuals, as outlined in Model 4 in Figure 1. Unfortunately, the data presented in this study cannot distinguish between these alternatives, but they do seem more consistent with these models than with a model which posits a specific effect of maternal prenatal depression on the developing fetus and its subsequent risk for depression.

Not being breast fed was strongly and specifically associated with greater risk for major depression. As far as we are aware, this is the first study to demonstrate an association between feeding method in infancy and long term psychopathological outcomes. Whether this association is due to something intrinsically important about breast feeding, or to an association of breast feeding with other aspects of the mother–infant relationship, such as the general amount of closeness of mother–infant contact, cannot be determined on the basis of the available data. In this regard it is important to note that adjusting for the putative mediating variables, which included current maternal depression and overall ratings of the maternal child relationship, did *not* appreciably reduce the association between feeding method and depression. The role of breast feeding for the development of future depression deserves more careful scrutiny in future research, including the effects of duration of breast feeding and the timing of weaning.

### *Predictors of risk for anxiety disorders*

With regard to the future occurrence of anxiety disorders, the strongest, and perhaps most intriguing predictors were serious illness or infection in the first 12 months of life and poor maternal obstetric history. These associations are robust in that they were not appreciably reduced by adjusting for the putative me-

diating variables, and appear to be quite specific to the anxiety disorders. Again, the question can be raised as to whether these associations reflect a causal link between early illness and later anxiety disorder, or whether both of these are jointly determined by a third factor. Relevant to the link between early illness and later anxiety are the results of studies suggesting a link between social anxiety in childhood and allergies, especially hay fever. Kagan, Snidman, and Julia–Sellers (1991) found a greater prevalence of hay fever among first degree relatives of socially anxious, as compared with nonsocially anxious children. Kagan et al. suggest a genetically mediated link between social anxiety and selected atopic allergies. Relatedly, Arcus (1994) has conjectured that the heightened sympathetic nervous system activity typical of anxious children may be immunosuppressive, leading to the observed vulnerability to hay fever and eczema. Thus it is possible that the association between anxiety and early illness reflects the effects of some common genetic or constitutional factor.

The association of anxiety with previous maternal obstetric history is also challenging. In this study, poor previous maternal obstetric history was largely defined by previous miscarriages and stillbirths. Interestingly, there has been a link demonstrated between maternal anxiety and the experience of stillbirth. For instance, Radestad, Steineck, Nordin, and Sjogren (1996) found that women who had a stillborn child scored higher on an anxiety inventory 3 years after the stillbirth than a comparison group of women who had given birth to a nondeformed live child. Phipps (1985–1986) found that a previous experience of stillbirth was associated with markedly increased anxiety during subsequent pregnancies. Finally, Stray–Pedersen and Stray–Pedersen (1984) presented evidence suggesting that stress and anxiety may occasionally play a role in the etiology of stillbirth, by showing that in a group of women with a history of spontaneous abortion, receiving counseling and psychological support significantly increased the pregnancy success rate in subsequent pregnancies. All these results point to a link between stillbirth and anxiety in affected mothers, although whether the maternal anxiety is caused by the stillbirth, or whether it is somehow involved in risk for stillbirth remain unclear. In light of these findings, however, it is intriguing to note the strong and specific association between previous miscarriage/stillbirth and anxiety disorders in the offspring. Once again, this finding requires further specific research scrutiny, with special emphasis on the mechanisms that might be implicated in such an association.

### *Predictors of risk for disruptive behavior disorders*

This was the only class of disorders that showed a significant association with physical problems during pregnancy and delivery, especially acute anoxia/hypoxia. Other research has suggested that neuropsychological deficits, especially in language and executive function, are associated with conduct disorders (Moffitt, 1993). Moffitt has proposed that causes of neuropsychological deficit associated with risk for conduct disorder might include "maternal drug use, poor prenatal nutrition, or pre- or postnatal exposure to toxic agents" and brain insult due to complications during birth (p. 138). Furthermore, brain injuries associated with birth complications have been related to antisocial behavior in previous research (Kandel & Mednick, 1991; Szatmari, Reitsma–Street, & Offord, 1986). The results presented here further support the association between birth complications and risk for disruptive behavior disorders. The role of child gender in moderating the association of maternal prenatal physical health and disruptive behavior disorder (the association being present for females but not for males) suggests that females may be more susceptible to such effects, although given the number of interaction terms that were tested, replication of this finding will be important to exclude the possibility that it was the result of Type I error.

Maternal emotional health during the pregnancy also predicted risk for disruptive behavior disorders. Although previous surveys have indicated that the children of depressed parents have higher rates of conduct disorder and

attention deficit disorder than comparison groups (Downey & Coyne, 1990), risk for these disorders is not as great as for affective disorders. Nevertheless, the fact that children whose mothers reported experiencing emotional difficulties during their pregnancy were 2.4 times more likely to have met criteria for a disruptive behavior disorder, even after controlling for the covariates such as maternal depressive symptoms later in life and family conflict/cohesion, suggests there may be a specific association between maternal emotional problems during pregnancy and risk for disruptive behavior disorders.

### *Predictors of risk for substance use disorders*

The fact that substance use disorders in the child were predicted by maternal use of alcohol, cigarettes, caffeine, and marijuana during the pregnancy is not unexpected. The link between maternal substance use and later child substance abuse could be mediated by shared genetic predisposition, parental modeling, or in utero effects of the substances. Previous research has provided support for both the genetic and modeling mechanisms (Hawkins, Catalano, & Miller, 1992). As we do not have information regarding maternal substance use throughout the child's lifetime, it is not possible to differentiate between these effects, but the specificity of the association between maternal and child substance use disorders is notable.

### *Results in relation to models in Figure 1*

Although the data in this study did allow for the testing of some of the models described in Figure 1, clearly not all the relevant variables have been measured to allow exhaustive tests of them. Nevertheless, we were able to control for a number variables that are known to exert a strong and pervasive influence on adjustment during childhood and adolescence (e.g., quality of parental and familial relationships, maternal depressive symptoms) and in most cases these variables did not reduce the associations between reported prenatal/perinatal factors and later psychopathology. These results do suggest a number of hypotheses for future research. In particular, risk for depression appears to associated with lifelong maternal depressive tendencies rather than specific affects of emotional distress during the pregnancy. This may reflect either common environmental or genetic influences on mother and child (Model 4) or the effects of maternal behaviors throughout the child's lifetime (Model 1). Breast feeding appears to have a more direct effect on risk for depression, although the mechanism is unclear at this stage. Risk for anxiety does seem to be associated with poor infant health, and this may reflect either a common genetic predisposition towards both (Model 4) or the physical and psychosocial sequela of early illness (Models 2 and 3). Likewise, previous maternal miscarriage and stillbirth is associated with risk for anxiety, possibly reflecting the effects of maternal anxiety during the pregnancy or later in the child's lifetime (Models 1 and 2), or a shared genetic propensity towards both anxiety and pregnancy loss in both mother and child (Model 4).

Risk for disruptive behavior disorder appears to be linked to specific delivery complications, suggesting an effect of minimal brain damage on risk for these disorders (Model 2). There also appears to be an association between maternal emotional difficulties during the pregnancy and disruptive behavior disorders, suggesting a role for the in utero effects of maternal stress (Model 2). Finally, substance abuse/dependence is specifically related to maternal substance use during the pregnancy, but we are unable to distinguish here between the effects of modeling (Model 1), shared genetic predisposition (Model 4), or in utero effects of substances (Model 2).

In future studies, we hope to be able to refine and extend the findings reported in this paper. The participants in this research are currently being assessed again at the age of 24 years, which will allow examination of the association between prenatal and perinatal events and risk for psychopathology between 18 and 24 years (i.e., during young adulthood). Also, data is currently being collected on the

family history of psychopathology of each of these probands. These data may help to clarify the relationships reported here, especially when genetic mechanisms are implicated.

In summary, these results suggest that there are a number of associations between prenatal and perinatal events and later risk for psychopathology in offspring that deserve further investigation. Although the analyses presented here cannot fully elucidate the mechanisms by which these associations occur, it is our hope that these results will stimulate further research into such mechanisms so that the influence of this formative stage of human development on later outcomes can be more fully understood.

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