ORIGINAL ARTICLE

Association of Maternal Exposure to Childhood Abuse With Elevated Risk for Autism in Offspring

Andrea L. Roberts, PhD; Kristen Lyall, ScD; Janet W. Rich-Edwards, ScD; Alberto Ascherio, DrPH; Marc G. Weisskopf, PhD, ScD

Importance: Adverse perinatal circumstances have been associated with increased risk for autism in offspring. Women exposed to childhood abuse experience more adverse perinatal circumstances than women unexposed, but whether maternal abuse is associated with autism in offspring is unknown.

Objectives: To determine whether maternal exposure to childhood abuse is associated with risk for autism in offspring and whether possible increased risk is accounted for by a higher prevalence of adverse perinatal circumstances among abused women, including toxemia, low birth weight, gestational diabetes, previous induced abortion, intimate partner abuse, pregnancy length shorter than 37 weeks, selective serotonin reuptake inhibitor use, and alcohol use and smoking during pregnancy.

Design and Setting: Nurses' Health Study II, a population-based longitudinal cohort of 116 430 women.

Participants: Nurses with data on maternal childhood abuse and child's autism status (97.0% were of white race/ethnicity). Controls were randomly selected from among children of women who did not report autism in offspring (participants included 451 mothers of children with autism and 52 498 mothers of children without autism).

Main Outcome Measures: Autism spectrum disorder in offspring, assessed by maternal report and validated with the Autism Diagnostic Interview–Revised in a subsample.

Results: Exposure to abuse was associated with increased risk for autism in children in a monotonically increasing fashion. The highest level of abuse was associated with the greatest prevalence of autism (1.8% vs 0.7% among women not abused, $P = .005$) and with the greatest risk for autism adjusted for demographic factors (risk ratio, 3.7; 95% CI, 2.3-5.8). All adverse perinatal circumstances except low birth weight were more prevalent among women abused in childhood. Adjusted for perinatal factors, the association of maternal childhood abuse with autism in offspring was slightly attenuated (risk ratio for highest level of abuse, 3.0; 95% CI, 1.9-4.8).

Conclusions and Relevance: We identify an intergenerational association between maternal exposure to childhood abuse and risk for autism in the subsequent generation. Adverse perinatal circumstances accounted for only a small portion of this increased risk.

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Author Affiliations are listed at the end of this article.

Although the origin of autism is mostly unknown, many hypotheses focus on the perinatal period as potentially critical for the development of autism in offspring. Prematurity,[1] low birth weight,[1,2] gestational diabetes and hypertension,[3] prolonged[1] or very short[4] labor, maternal uterine bleeding,[5] small size for gestational age,[6] and pregnancy length shorter than 35 weeks[7] have been associated with elevated risk for autism in offspring. In addition, maternal smoking,[6] use of selective serotonin reuptake inhibitors (SSRIs),[8] and exposure to intimate partner violence in the prenatal period have been associated with higher risk for having a child with autism. Before and during pregnancy, women exposed to childhood abuse are more likely than those unexposed to experience circumstances and engage in behaviors that may be detrimental to the fetus, including smoking,[9,10] drug use,[10-13] overweight,[14,15] stress,[10,16] and intimate partner violence victimization.[17-19] Maternal exposure to childhood abuse is also associated with unintended pregnancy,[20] preterm labor,[21] and low birth weight.[10] Therefore, maternal exposure to childhood abuse may be a risk factor for autism in offspring. Yet, to our knowledge,

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the association between maternal exposure to childhood abuse and risk for autism in children has not been examined.

In this article, we assess the association between maternal exposure to childhood abuse and risk for autism among offspring in a large population-based cohort. We further examine several perinatal exposures as possible mediators of the potentially elevated risk for autism in children of women exposed to childhood abuse.

METHODS

SAMPLE

We use data from the Nurses' Health Study II, a cohort of 116 430 female nurses originally recruited in 1989 from 14 populous US states and followed up with biennial questionnaires. We examine data from 54 963 women who reported whether they had ever had a child with an autism spectrum disorder and who answered a supplemental 2001 questionnaire about maternal childhood abuse. The Partners Healthcare Institutional Review Board approved this research. Completion and return of questionnaires sent by US mail constitute implied consent.

MEASURES

Selection of Cases and Controls

In the 2005 biennial questionnaire, we asked respondents if they had a child diagnosed as having autism, Asperger syndrome, or other autism spectrum disorder. In 2007-2008, we sent a follow-up questionnaire to 756 women currently participating in the Nurses' Health Study II who responded that they had a child with any of these diagnoses, querying the affected child's sex, birth date, and diagnoses (636 replied, for an 84.1% response rate).

Some women initially reporting a child with autism were excluded based on responses to the follow-up questionnaire. If women reported any of the following overlapping circumstances, they were excluded from the study: the affected child was adopted (n=9), they did not want to participate (n=20), they did not have a child with autism (n=32), or they did not report the child's birth year (n=71). Eleven women who reported that the affected child had Rett syndrome, Down syndrome, 11q deletion disorder, fragile X syndrome, Angelman syndrome, trisomy 18 syndrome, or Klinefelter syndrome were also excluded. Herein, we refer to cases as children meeting these inclusion criteria; we use the term *autism* to refer to autism spectrum disorder. Of the remaining 549 cases, 98 women did not participate in the questionnaire assessing maternal childhood abuse, leaving 451 cases. Women who reported in the 2005 questionnaire that they had a child with autism but were not included in the analyses (n=389) were similar to women who reported that they had a child with autism and were included in analyses (n=451) on year of birth (median, 1957 for both groups), marital status (83.0% of excluded women were married vs 85.8% of included women), and smoking status at Nurses' Health Study II enrollment in 1989 (10.3% of excluded women were smokers vs 11.0% of included women).

Autism diagnosis was validated in a subsample of cases by telephone interview of 50 randomly selected mothers who indicated willingness to complete the interview (81.4% of mothers were willing to be interviewed) using the Autism Diagnostic Interview–Revised (ADI-R).[22,23] Women who agreed to participate in the validation substudy were similar in the autism spectrum disorder diagnoses reported in their child to women who were not willing to participate (among women willing to participate, 24.9% reported autism, 50.9% reported Asperger syndrome, and 25.3% reported pervasive developmental disorders not otherwise specified; among women not willing to participate, 25.5% reported autism, 49.0% reported Asperger syndrome, and 22.6% reported pervasive developmental disorders not otherwise specified). Women not willing to participate in the validation study also did not differ from women willing to participate on the child's sex, prematurity status, child's year of birth, or low-birth-weight prevalence.

In this substudy, 43 children (86.0%; 95% CI, 74.0%-93.0%) met ADI-R criteria for an autism diagnosis, defined by meeting cutoff scores in all 3 domains and having onset by age 3 years. The remaining individuals met the onset criterion and communication domain cutoff and missed full diagnosis by 1 point in 1 domain (n=5) or met cutoffs in 1 or 2 domains only (n=2). The ADI-R provides an algorithm for full autistic disorder but not autism spectrum disorder. All children in the validation study demonstrated autistic behaviors. Children who did not meet full ADI-R criteria narrowly missed and may be on the autism spectrum.

Controls were parous women who reported never having a child with autism and who responded to the 2001 questionnaire reporting year and sex of each birth and maternal childhood abuse. To assure independence of maternal characteristics among controls, we randomly selected 1 birth per woman with data on maternal childhood abuse from among her live births (n=52 498). At baseline in 1989, women included in our analyses were less likely to smoke (29.0% vs 35.6%), more likely to have ever been pregnant (90.9% vs 68.4%), and more likely to be of white race/ethnicity (97.0% vs 94.3%) compared with women not included.

Maternal Exposure to Childhood Abuse

Abuse experiences were assessed in 2001. Combined childhood physical and emotional abuse before age 12 years was assessed with 5 questions from the physical and emotional abuse subscale of the Childhood Trauma Questionnaire[24] querying the frequency of people in the family with the following behavior: (1) hitting so hard it left bruises, (2) punishing in a way that seemed cruel, (3) insulting, (4) screaming and yelling, and (5) punishing with a belt or other hard object. For each item, response options included "never," "rarely," "sometimes," "often," or "very often true." Responses were assigned values ranging from 0 ("never") to 4 ("very often true") and were summed according to questionnaire scoring recommendations. In a validation study, the scale had good internal consistency (Cronbach α=.94) and test-retest reliability (intraclass correlation, 0.82) during a 2-month to 6-month interval.[24] The resulting scale was divided approximately into quartiles to calculate risk ratios and to investigate a possible dose-response relationship between severity of child abuse and risk for autism in offspring.

Sexual abuse occurring in 2 periods was assessed, namely, before age 12 years and age 12 to 17 years. For each period, 2 questions queried unwanted sexual touching by an adult or older child and forced or coerced sexual contact by an adult or older child.[25] Response options included "never," "once," or "more than once." To create a single measure, we assigned 1 point for each "once" answer and 2 points for each "more than once" answer. We then grouped these points for analysis as follows: 0 points was considered no abuse; 1 or 2 points, mild abuse; 3 or 4 points, moderate abuse; and 5 or more points, severe sexual abuse.

Exposure to high levels of both sexual abuse and physical and emotional abuse could be associated with greater risk for

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autism in offspring than exposure to either type alone. Therefore, we also created a measure of combined physical, emotional, and sexual abuse by summing the physical and emotional abuse and sexual abuse measures.

Potential Mediators

In 2001, birth weight, smoking and alcohol use during pregnancy, and lifetime exposure to intimate partner emotional, physical, and sexual abuse was assessed. Birth weight was assessed by maternal report in the following 5 categories: below 5.0, 5.0 to 5.4, 5.5 to 6.9, 7.0 to 8.4, 8.5 to 9.0, and 10.0 lb or higher (to convert pounds to kilograms, multiply by 0.45). Smoking during pregnancy was assessed with a single question: "How many cigarettes did you smoke per day during this pregnancy?" Responses were dichotomized as any or none. Alcohol use during pregnancy was assessed with a question: "On average, how much alcohol did you drink per week during this pregnancy?" Because few women had more than 1 drink per week, response options were coded as none, 1, or 2 drinks or more per week.[26] Lifetime history of intimate partner abuse was assessed in 2001 with a modified version of the Assessing Abuse Scale.[27] Fear of partner and emotional, physical, and sexual abuse were each assessed with one question each: "Have you ever been made to feel afraid of your spouse/significant other?" (fear of partner). "Have you ever been emotionally abused by your spouse/significant other?" (emotional abuse). "Have you ever been hit, slapped, kicked, or otherwise physically hurt by your spouse/significant other?" (physical abuse). "Has your spouse/significant other ever forced you into sexual activities?" (sexual abuse). Following these questions, respondents indicated the calendar years in which any of the types of abuse occurred. We included abuse in the year before the birth year as a potential mediator because abuse in the calendar year before the birth year has been associated with risk for autism in offspring. Having had an induced abortion before the birth of the index child was coded dichotomously based on lifetime history of induced abortions, including ages at occurrences, assessed in 1993 and updated in 1997, 1999, and 2001. Gestational diabetes was coded dichotomously from questions regarding history of gestational diabetes and year of diagnosis, assessed retrospectively in 1989 and updated biennially. Lifetime history and age at occurrence of toxemia or preeclampsia during pregnancy, defined for the respondent as "raised blood pressure and proteinuria," were assessed in 1989 and updated biennially.

Selective serotonin reuptake inhibitor use from 1996 to 2007 was assessed biennially.[8,28] Women were asked whether in the past 2 years they had regularly used Paxil (paroxetine hydrochloride), Prozac (fluoxetine hydrochloride), or Zoloft (sertraline hydrochloride). Women using any of these were coded as having used an SSRI in the perinatal period for births occurring in the 2 years queried by the questionnaire. Because the first SSRI (fluoxetine) was available in 1988 in the United States,[29] all women who gave birth before 1988 were coded as not having used an SSRI during pregnancy. In addition, women were asked in 1993 whether they had ever used fluoxetine hydrochloride or sertraline hydrochloride. Women who reported never having used these substances were coded as not having used SSRIs during pregnancy in 1993 or earlier. Women who reported that they had ever used an SSRI and whose child was born between 1989 to 1993 were excluded from analyses using this variable. Although these women had used an SSRI sometime during the 4-year period queried, it is unknown whether they used an SSRI during the pregnancy that occurred during these years. Maternal age at child's birth was coded as follows: younger than 25, 25 to 29, 30 to 34, 35 to 39, or 40 years or older. Year of child's birth was continuous, and maternal childhood socioeconomic status was measured by the maximum of her parents' education in her infancy.

STATISTICAL ANALYSIS

Using χ^2 tests, we first ascertained whether maternal sexual abuse, physical and emotional abuse, and combined physical, emotional, and sexual abuse were associated with risk for autism in children. We next examined the prevalence of perinatal risk factors by maternal childhood abuse status. To determine whether maternal childhood abuse was associated with risk for autism in children after adjusting for potential confounders, we modeled autism risk with maternal sexual abuse, physical and emotional abuse, or combined physical, emotional, and sexual abuse adjusted for birth year, child's sex, maternal age at birth, and maternal childhood socioeconomic status.

To examine potential mediation by perinatal risk factors, we modeled autism risk as a function of perinatal risk factors, potential confounders, and combined maternal physical, emotional, and sexual abuse. We assessed mediation proportion using SAS Mediate.[30,31] Finally, we conducted models stratified by child's sex to investigate possible sex-specific relationships between maternal childhood abuse and autism risk.

We used generalized estimating equations with a log link and Poisson distribution to estimate risk ratios.[32] To calculate statistical significance for the prevalence of gestational risk factors by combined childhood physical, emotional, and sexual abuse, we modeled each risk factor as a dichotomous dependent variable, with maternal childhood abuse as the independent variable, using generalized estimating equations with a log link and binomial distribution. To calculate statistical significance for the prevalence of alcohol use during pregnancy, which was measured in 3 levels, we used ordered logistic regression with a cumulative logit link and a multinomial distribution.

RESULTS

Approximately 3% of women (1788 [3.4%]) were exposed to serious sexual abuse. Prevalence of autism was elevated but not statistically significantly among children of women exposed to serious sexual abuse compared with children of women unexposed to sexual abuse (1.3% of children of women exposed had autism vs 0.8% of children of women unexposed, $P=.11$). Women exposed to physical and emotional abuse were more likely to have a child with autism (1.1% had a child with autism among mothers with the highest quartile of abuse; 0.7% had autism among mothers with no abuse, $P=.003$). The highest level of mother's combined physical, emotional, and sexual abuse was associated with the greatest prevalence of autism among children (1.8% vs 0.7% of children among women not abused, $P=.005$).

Mother's combined childhood physical, emotional, and sexual abuse was associated with increased prevalence of almost all adverse circumstances in the perinatal period in a dose-response fashion (**Figure**). Compared with women not exposed to abuse, women exposed to the highest level of abuse were more likely to have gestational diabetes (5.3% vs 2.7%), smoke during pregnancy (17.4% vs 8.8%), use SSRIs in the perinatal period (0.4% vs 0.2%), manifest toxemia or preeclampsia (7.7% vs 3.6%), have a previous induced abortion (15.9% vs 10.0%), have a pregnancy length shorter than 37 weeks (9.4% vs 7.1%), use alcohol during pregnancy (5.1% vs 2.8% had >1 drink per

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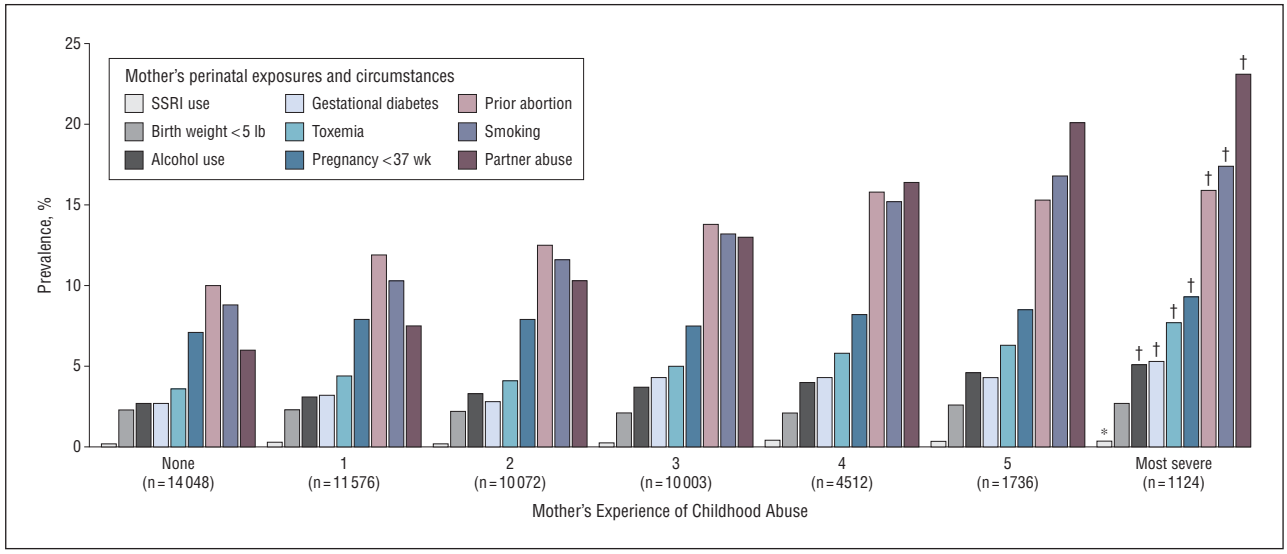

Figure. Perinatal adverse circumstances by mother's exposure to childhood physical, emotional, and sexual abuse from the Nurses' Health Study II (n=53 071). *$P<.05$ and †$P<.001$, Wald χ^2 test. SSRI indicates selective serotonin reuptake inhibitor. To convert pounds to kilograms, multiply by 0.45.

week), and experience intimate partner abuse in the year before the birth year (23.3% vs 6.1%). Women exposed to childhood abuse were not statistically significantly more likely to give birth to a child who weighed less than 5.0 lb; however, they were more likely to have a child who did not weigh 7.0 to 8.4 lb, the birth weight range that has been associated with lowest infant mortality.[33]

In models adjusted for demographic variables (but not perinatal risk factors), women exposed to sexual abuse or physical and emotional abuse were more likely to have a child with autism in a monotonically increasing fashion (**Table 1**, models 1 and 2). Combined physical, emotional, and sexual abuse was also associated with risk for autism among offspring in a monotonically increasing fashion (**Table 2**, model 1). The 1124 women exposed to the highest level of combined physical, emotional, and sexual abuse in childhood were at greatest risk for having a child with autism compared with women unexposed to childhood abuse (risk ratio, 3.7; 95% CI, 2.3-5.8; $P<.001$).

In the model that included perinatal risk factors, maternal childhood abuse remained significantly associated with increased risk for autism in offspring, although risk ratio estimates were slightly attenuated (Table 2, model 2). The perinatal factors we examined statistically accounted for 7.2% of the association between child abuse and autism risk in offspring, although this estimate did not statistically differ from zero. Models stratified by sex showed similarly elevated risk for autism in female and male children of women exposed to childhood abuse, and an abuse × sex interaction term was not statistically significant. Because only 125 women were exposed to SSRIs in the perinatal period, models that included SSRI use would not converge. Therefore, we excluded SSRI use as a potential mediator.

We conducted further analyses to identify which of the perinatal factors were most important in mediating the association between maternal childhood abuse and risk for autism in offspring. We calculated mediation for each perinatal factor separately, adjusted for maternal childhood socioeconomic status and age at birth, as well as the birth year and sex of the child. In these analyses, we found gestational diabetes (mediation, 3.5%) and abortion before giving birth (mediation, 3.0%) to be the strongest mediators of the relationship between child abuse and autism in offspring. Smoking during pregnancy mediated 2.3% of the association, and the remaining variables mediated 1.2% or less.

Because maternal childhood abuse was strongly associated with most of the perinatal factors examined, we conducted additional analyses to investigate whether child abuse might explain the statistical relationship between the perinatal factors and autism in offspring (ie, whether

Table 1. Mother's Exposure to Childhood Sexual Abuse or Childhood Physical and Emotional Abuse and Risk for Autism in Her Child From the Nurses' Health Study II Among 451 Autism Cases and 52 498 Controls[a]
or Childhood Physical and Emotional Abuse and Risk for Autism in Her Child From the Nurses' Health Study II Among 451 Autism Cases and 52 498 Controls

Variable	No.	Risk Ratio (95% CI) Model 1	Risk Ratio (95% CI) Model 2
Childhood sexual abuse			
None	35 175	1 [Reference]	. . .
Mild	12 595	1.2 (1.0-1.5)	. . .
Moderate	3391	1.2 (0.8-1.7)	. . .
Severe	1788	2.0 (1.3-3.1)[b]	. . .
Childhood physical and emotional abuse, quartile			
None	18 342	. . .	1 [Reference]
2	11 516	. . .	1.0 (0.8-1.4)
3	10 545	. . .	1.2 (0.9-1.5)
Top	12 546	. . .	1.6 (1.3-2.1)[c]

Abbreviation: Ellipsis, not applicable.
[a] Models are adjusted for sex of child, mother's age at birth, year of birth of the child, and mother's socioeconomic status in childhood.
[b] $P<.01$, Wald χ^2 test.
[c] $P<.001$Wald χ^2 test.

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Table 2. Mother's Exposure to Combined Childhood Physical, Emotional, and Sexual Abuse and Risk for Autism in Her Child (Unadjusted and Adjusted for Perinatal Risk Factors) From the Nurses' Health Study II Among 447 Autism Cases and 52 478 Controls[a]

Variable	No.	Risk Ratio (95% CI) Unadjusted Model 1	Risk Ratio (95% CI) Adjusted Model 2
Childhood physical, emotional, and sexual abuse			
None	14 008	1 [Reference]	1 [Reference]
1	11 551	1.1 (0.9-1.5)	1.1 (0.8-1.4)
2	10 045	1.2 (0.9-1.6)	1.1 (0.9-1.5)
3	9969	1.5 (1.2-2.0)	1.4 (1.0-1.8)
4	4497	1.6 (1.1-2.3)	1.3 (0.9-1.9)
5	1731	1.7 (1.0-2.9)	1.4 (0.9-2.4)
6, Most severe	1124	3.7 (2.3-5.8)[b]	3.0 (1.9-4.8)[b]
Birth weight, lb			
<5.0	...	...	2.2 (1.2-3.7)
5.0-5.4	...	...	1.3 (0.6-2.9)
5.5-6.9	...	...	1.2 (1.0-1.6)
7.0-8.4	...	...	1 [Reference]
8.5-9.9	...	...	1.1 (0.9-1.4)
≥10.0	...	...	1.3 (0.8-2.2)
Gestational diabetes	...	...	1.8 (1.3-2.5)[b]
Smoking	...	...	1.3 (1.0-1.8)
Prior abortion	...	...	1.3 (1.0-1.6)
Alcohol use, drinks per wk			
None	...	...	1 [Reference]
1	...	...	0.8 (0.6-1.2)
≥2	...	...	0.9 (0.5-1.6)
Toxemia	...	...	0.9 (0.6-1.4)
Partner abuse	...	...	1.4 (1.0-1.8)[c]
Pregnancy, wk	...	...	
<37	...	...	1.1 (0.8-1.6)
37-42	...	...	1 [Reference]
≥43	...	...	0.9 (0.6-1.3)

Abbreviation: Ellipsis, not applicable.
SI conversion factor: To convert pounds to kilograms, multiply by 0.45.
[a] Models are adjusted for sex of child, mother's age at birth, year of birth of the child, and mother's socioeconomic status in childhood.
[b] $P < .001$, Wald χ^2 test.
[c] $P < .05$, Wald χ^2 test.

childhood abuse might confound the association between these factors and autism). We examined the association of autism in offspring with each perinatal factor in separate models and adjusted for demographic factors, with and without maternal childhood abuse as an additional independent variable.

In these analyses, the associations between autism in offspring and prior induced abortion, smoking during pregnancy, and intimate partner abuse were somewhat attenuated after adjustment for maternal childhood abuse (attenuation range, 12.1%-19.2%). The association of gestational diabetes and autism in offspring was slightly attenuated. The associations of pregnancy length less than 37 weeks and low birth weight with autism in offspring were not attenuated after adjusting for maternal childhood abuse. Toxemia and preeclampsia and alcohol use during pregnancy were not associated with autism in children.

COMMENT

We found that maternal exposure to abuse in childhood was associated with elevated risk for autism among offspring in a monotonically increasing fashion. Notably, women exposed to the highest level of physical and emotional abuse, comprising one-quarter of the women in our study, were at 61.1% elevated risk for having a child with autism compared with women not exposed to abuse. In addition, we found that an array of perinatal factors were associated with maternal child abuse history and autism risk in offspring. However, these factors accounted for only a small part of the association between maternal abuse history and autism in children. To our knowledge, no prior studies have examined early-life maternal exposures to stressors as possible risk factors for autism in offspring; however, several maternal stressors in the prenatal period have been associated with risk for autism in children, such as stressful life events,[34,35] although findings are mixed.[36]

Our results are consistent with at least 4 possibilities. First, additional unmeasured perinatal adverse circumstances associated with childhood abuse, such as infection,[37-39] poor diet,[40] insufficient prenatal care,[2] medication use,[8] illegal drug use,[10] and stressful life events,[16,41,42] may account for all of the associations we found.

Second, the experience of maternal childhood abuse and its behavioral, psychological, and physical sequelae may cause alterations to the mother's biological systems, including the hypothalamic-pituitary-adrenal (HPA) axis, the hypothalamic-pituitary-gonadal axis, and the immune system, which may in turn directly increase risk for autism in children. Childhood abuse has been associated with dysregulated HPA axes in women[43-45] and in their infants.[46] Dysregulation of the HPA axis has been observed in persons with autism,[47] and it has been hypothesized that dysregulation of the maternal HPA axis affects the fetal brain.[48,49] In addition, exposure to acute psychosocial stressors may increase secretion of androgen,[50,51] and some evidence suggests that exposure to high prenatal concentrations of androgen is associated with autistic traits.[52,53] However, whether childhood abuse leads to persistently elevated maternal androgens is unknown. Immune dysfunction has also been associated with exposure to childhood abuse.[54-59] Immune dysfunction and inflammation, including neuroinflammation, are more prevalent among persons with autism.[60-65] Maternal inflammation affects the developing brain, and maternal inflammation and immune function[66-68] have been hypothesized to be causes of autism.[69-73]

Third, mother's exposure to childhood abuse may, through epigenetic[74,75] or other mechanisms, increase her biological reactivity to physical and psychological stressors through sensitization of the central nervous system,[44] dysregulation of the HPA axis,[76] and effects on the prefrontal cortex that influence the threat appraisal response system.[77] Hyperreactivity to stressors may in turn negatively influence the developing fetus through effects on the mother and the fetal HPA and hypothalamic-pituitary-gonadal axes and immune system function.[78]

Fourth, maternal exposure to abuse in childhood may be an indicator of genetic risk for autism in offspring; men-

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tal illness in parents is associated with child abuse perpetration,[79-81] and the results of studies[7,82-85] have suggested that genetic risk for autism may overlap with genetic risk for other mental disorders. Therefore, perpetration of child abuse by the grandparents and experience of abuse in childhood by the mother may be indicators of genetic risk for autism in the child.

Our study identifies an intergenerational association between a woman's childhood exposure to violence and risk for a severe developmental disorder in her children. Given the numerous sequelae of the adverse perinatal circumstances we examined,[86-91] it is likely that children of women who were exposed to childhood abuse experience a higher prevalence of a constellation of additional health problems compared with children of women who were not abused. Prior studies[92,93] of the association between childhood abuse and perinatal risk factors have generally been conducted in small samples, with a limited range of outcomes examined. Therefore, the present study is the most comprehensive examination to date of the relationship between maternal childhood abuse and perinatal risk factors in a large population-based sample.

Our results should be considered in light of 2 important limitations. First, child's autism, maternal childhood abuse, and maternal gestational exposures were by participant self-report. Report of autism was validated by the ADI-R, an instrument with good reliability and validity.[23,94] While this approach is consistent with a large body of epidemiological research, it does not constitute a diagnosis. Self-report of health-related circumstances in this cohort of professional nurses has been highly accurate in multiple validation studies.[95-97] Nevertheless, misreporting of autism, childhood abuse exposure, or gestational exposures may have biased our results. Second, women reported their exposure to childhood abuse after knowing that they had a child with autism. If knowledge of their child's autism status affected their report of experience of childhood abuse, this may have biased our results. However, women's experience of childhood abuse was not queried in the context of her children's autism status. Maternal childhood abuse and autism in offspring were assessed in separate questionnaires 4 years apart, reducing the likelihood of bias.

If the association we identify herein between maternal childhood abuse and autism in offspring is in part due to direct or indirect effects of abuse (as opposed to shared genetic risk for abuse exposure and autism), this has several implications for clinical practice. First, we provide another compelling reason to increase efforts to prevent childhood abuse. Second, we identify a population at elevated risk for having a child with autism, namely, women with a history of moderate or serious childhood abuse. Third, given the suggestion of mediation of autism risk in offspring through adverse perinatal circumstances, we suggest a possible means of reducing autism risk in children of these women through prevention of adverse perinatal circumstances.

In terms of research, studies examining perinatal risk factors for autism in offspring should consider potential confounding by maternal childhood abuse. Maternal abuse was strongly associated with almost every perinatal risk factor we examined, and adjustment for abuse attenuated the associations of several perinatal risk factors with autism in children. If maternal abuse increases the risk for autism in offspring through mechanisms not mediated by perinatal risk factors or if maternal abuse is an indicator of genetic risk for autism in children, studies examining perinatal risk factors may find statistical associations with autism even if the factors have no causal role in the origin of autism. If maternal childhood abuse is associated with autism in offspring primarily through shared genetics, mental disorders that specifically increase the risk for child abuse perpetration may overlap genetically with those that increase risk for autism in children. Future work should further investigate causal mechanisms by which maternal child abuse may be associated with autism in offspring.

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Author Affiliations: Department of Social and Behavioral Sciences (Dr Roberts), Nutrition (Drs Lyall and Ascherio), Epidemiology (Drs Roberts, Ascherio, and Weisskopf), and Environmental Health (Drs Ascherio and Weisskopf), Harvard School of Public Health, and Connors Center for Women's Health and Gender Biology, Brigham and Women's Hospital (Dr Rich-Edwards), Boston, Massachusetts; and Medical Investigation of Neurodevelopmental Disorders (MIND) Institute, University of California–Davis, Sacramento (Dr Lyall).
Correspondence: Andrea L. Roberts, PhD, Department of Epidemiology, Harvard School of Public Health, Kresge Bldg, 677 Huntington Ave, Boston, MA 02115 (aroberts@hsph.harvard.edu).
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