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Maternal exposure to intimate partner abuse before birth is associated with autism spectrum disorder in offspring

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Abstract

We sought to determine whether maternal i) physical harm from intimate partner abuse during pregnancy or ii) sexual, emotional, or physical abuse before birth increased risk of autism spectrum disorder. We calculated risk ratios (RR) for autism spectrum disorder associated with abuse in a population-based cohort of women and their children (54,512 controls, 451 cases). Physical harm from abuse during pregnancy was not associated with autism spectrum disorder. However, autism spectrum disorder risk was increased in children of women who reported fear of partner or sexual, emotional, or physical abuse in the two years before the birth year (abuse in the year before the birth year, RR=1.58, 95% confidence interval (CI)= 1.04, 2.40; abuse in both of the two years before the birth year, RR=2.16, 95% CI=1.33, 3.50). Within-family results were similar, though did not reach statistical significance. Association of intimate partner abuse before the child's birth year with ASD in the child was not accounted for by gestation length, birth weight, maternal smoking or alcohol consumption during pregnancy, gestational diabetes, preeclampsia, or history of induced abortion.

The etiology of autism spectrum disorder (ASD) is largely unknown, although strong evidence exists for a genetic contribution to ASD (Hallmayer et al., 2011, Sebat et al., 2007, Constantino et al., 2012, Miles, 2011, Carter and Scherer, 2013, Berg and Geschwind, 2012, Murdoch and State, 2013). There is a less extensive literature on environmental risk factors for ASD, although evidence is beginning to grow in this area, including evidence for an association with several pregnancy-related factors, including maternal gestational diabetes (Roberts et al., 2013b), hypertension, proteinuria, preeclampsia (Gardener et al., 2009), nutritional status (Lyall et al., 2014), and exposure to pollution (Roberts et al., 2013a, Windham et al., 2006, Volk et al., 2011, Volk et al., 2013, Roberts et al., 2007). These data as well as functional genomic studies (Willsey et al., 2013, Parikshak et al., 2013) and post-mortem brain tissue analyses of children ages 2 to 15 years with and without ASD (Stoner et

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al., 2014) suggest that the prenatal period may be a period of vulnerability to environmental factors in the development of ASD.

Maternal exposure to psychosocial stressors during pregnancy has been hypothesized to affect the risk of ASD in offspring through several pathways. Stressors may dysregulate the locus coeruleus-noradrenergic system through the effects of maternal cortisol on epigenetic modification of genes controlling the development of this system (Mehler and Purpura, 2009). Additionally, stressors may disrupt brain development by impairing placental circulation (Kinney et al., 2008) or by dysregulating the hypothalamic-pituitary-adrenal axis in the fetus (Talge et al., 2007, Radtke et al., 2011). Stressors have also been hypothesized to trigger developmental immunotoxicity, through autoimmunity or inflammation of myelomonocytic cells in the brain, potentially increasing risk for ASD (Dietert and Dietert, 2008). Exposure to psychosocial stressors during pregnancy has been linked to cognitive and language deficits (King and Laplante, 2005, Laplante et al., 2008, Bergman et al., 2007), attention deficit/hyperactivity disorder and anxiety in the gestationally exposed child (Talge et al., 2007, Bergman et al., 2007). Exposure to stressors during pregnancy is also associated with having a low birth weight baby, which has been associated with ASD risk (Brown et al., 2011, Schendel and Bhasin, 2008, Kolevzon et al., 2007).

The evidence for an association between maternal perinatal stressors and ASD risk, however, is limited and remains inconclusive. A few studies have suggested an association (Beversdorf et al., 2005, Ward, 1990, Ronald et al., 2011), but these have relied on smaller samples, administrative data, or a case-control study design. Only two studies have used large, population-based samples to examine the association of maternal psychosocial stressors and ASD risk, with opposite findings (Kinney et al., 2008, Li et al., 2009). In both these studies, case ascertainment was based on government treatment records, which likely resulted in large under-ascertainment.

If an association of ASD with maternal prenatal stressors does exist, it might be expected to be stronger the more severe the stressor. Intimate partner abuse is a severe psychosocial stressor (Roberts et al., 2012, Dansky et al., 1999, Roberts et al., 2011a) that has not been examined with respect to ASD. Both physical and psychological abuse victimization have notable effects on the health of the victim, including increased risk for depression, posttraumatic stress disorder (PTSD), anxiety (Dillon et al., 2013, Lawrence et al., 2012), autoimmune disorders, chronic pain, and infection (Coker et al., 2000, Campbell, 2002, Dillon et al., 2013). Victimization by an intimate partner has been linked to hormonal dysregulation (Kim et al., 2015, Inslicht et al., 2006, Pico-Alfonso et al., 2004), poor medication adherence (Lopez et al., 2010), inadequate prenatal care (Cha and Masho, 2013), and maternal behaviors harmful to the fetus, including smoking, substance abuse, suboptimal weight gain, and poor diet (Bailey, 2010, World Health Organization, 2011). As maternal infection (Atladóttir et al., 2010), PTSD (Roberts et al., 2014), hormonal dysregulation (Andersen et al., 2014, Ingudomnukul et al., 2007, Palomba et al., 2012), smoking (Kalkbrenner et al., 2012) and poor diet (Lyall et al., 2014, Schmidt et al., 2011) have been linked to risk of ASD, intimate partner abuse may increase risk of ASD through these pathways. Furthermore, abuse during and before pregnancy has been associated with negative sequelae for the mother and fetus, including premature labor (Silverman et al.,

2006, Shah and Shah, 2010), low birth weight (Silverman et al., 2006, Shah and Shah, 2010, Sarkar, 2008, Alhusen et al., 2014), small for gestational age (Valladares et al., 2009, Alhusen et al., 2014), and neonatal death (Lipsky et al., 2003, World Health Organization, 2011). As premature labor, low birth weight, and small for gestational age are associated with ASD (Kolevzon et al., 2007, Larsson et al., 2005), intimate partner abuse may also increase risk of ASD through these pathways. Thus, if prenatal psychosocial stressors are capable of increasing risk of ASD, this effect may be seen in children of women exposed to intimate partner abuse before the child's birth.

In this paper we examine exposure to intimate partner abuse and risk of ASD in offspring in the Nurses' Health Study II, a cohort of 116,678 female nurses originally from 14 populous U.S. states, established in 1989 and followed up biennially. We examine data from women who reported whether they had ever had a child with ASD and who answered a supplemental questionnaire about abuse (n=54,963 women).

METHODS

Case ascertainment

In the 2005 regular biennial questionnaire, we asked respondents if they had a child diagnosed with autism, Asperger's syndrome, or other autism spectrum disorder. In 2007–2008 we sent a 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 (response rate=84%, n=636).

Cases were excluded for the following overlapping reasons: women reported on the follow-up questionnaire that: they did not have a child with ASD (n=32); the affected child was adopted (n=9); they did not want to participate (n=20); or they did not report the child's birth year (n=71). Women who reported the affected child had trisomy 18, Fragile X, an XXY genotype, or Down, Angelman, Jacobsen's, or Rett's syndrome were excluded (n=11). In this paper we refer to 'cases' as children meeting these inclusion criteria. Of the remaining 549 cases, 98 women did not participate in the supplemental abuse questionnaire assessing intimate partner abuse, leaving 451 cases. An additional 17 women did not respond to questions about physical harm from intimate partner abuse during pregnancy. At NHSII baseline in 1989, case mothers who either did not respond to the entire supplemental abuse questionnaire or to the specific questions about abuse were born slightly more recently (1957 versus 1956), were less likely to be married (79% versus 86%) and were slightly less likely to have smoked ever (64% versus 67%) compared with case mothers who responded to these questions.

We validated the ASD diagnosis in a subsample of 50 randomly selected cases by telephone administration to the mother of the Autism Diagnostic Interview-Revised (ADI-R)(Lord et al., 1994) by a trained professional with extensive experience in administering the ADI-R. In this sample, 43 children (86%) met full ADI-R criteria for a diagnosis of autistic disorder, 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 either missed full diagnosis by one point in one of the other domains (n=5) or met cutoffs in one or

two domains only (n=2). Thus, all children in this subsample exhibited autistic behaviors and may be on the autism spectrum. The Partners Healthcare Institutional Review Board approved this research.

Exposure

Physical harm from abuse during pregnancy was assessed four years before the assessment of ASD, in the supplemental 2001 questionnaire. For each pregnancy, participants were asked “were you physically hurt by your spouse/significant other during this pregnancy?” Response options were: never, once, a few times, more than a few times.

Lifetime exposure to four other types of intimate partner abuse was also assessed in the 2001 supplemental questionnaire with a modified version of the Abuse Assessment Screen (McFarlane et al., 1992). Fear of partner and emotional, physical, and sexual abuse were each assessed with one question: “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, with each year from 1962 through 2001 listed.

We created two dichotomous variables indicating presence or absence of any fear of partner, emotional, physical or sexual abuse in: 1) the calendar year before the birth year and 2) the birth year. Because chronic maternal stress from abuse over multiple years may also affect risk of ASD, we created a count of the number of years exposed to abuse in the 2 years before the birth year (possible range, 0 to 2) and in the 4 years before the birth year (possible range, 0 to 4). As specific months in which abuse occurred were not queried, for abuse in the year before the birth year, we were not able to determine whether abuse occurred before or during pregnancy, or both. For abuse in the year of the birth we could not determine whether abuse occurred before, during, or after pregnancy, or during multiple time periods. Because abuse in the year of the birth may have occurred after the birth of the child, we did not include this year in cumulative measures.

Analyses

For our main analyses, controls were women who reported never having a child with ASD and who responded to a 2001 questionnaire reporting year and sex of each birth. To assure independence of maternal characteristics among controls, we randomly selected one birth per respondent from among live births (n=54,642). Among controls, 54,512 had complete data for analyses of physical harm from abuse during pregnancy and 54,310 had complete data for analyses of intimate partner abuse.

We calculated prevalence of index child’s sex and means for maternal age at birth, birth year, and maternal childhood socioeconomic status by abuse status, separately for physical harm from abuse during pregnancy and any lifetime emotional, physical or sexual abuse (i.e., occurring before or after the index child’s birth). To estimate risk ratios of ASD associated with physical harm from abuse during pregnancy, we used generalized estimating

equations with a Poisson distribution and a log link (Zou, 2004). We ran separate models with any physical harm from abuse and with physical harm from abuse measured in three levels (none, once, or repeated) as independent variables.

To establish whether timing of fear of partner or emotional, physical or sexual abuse with respect to the birth was related to ASD risk, we used generalized estimating equations with a Poisson distribution and a log link to estimate risk ratios for ASD associated with exposure in the year before the birth year and the birth year. We additionally estimated risk of ASD associated with 2 and 4 years of abuse exposure before the birth year in separate models, with number of years of abuse exposure as categorical variables. These models also included terms for abuse in the birth year. All models were adjusted for maternal age at birth, birth year, child's sex, mother's childhood socioeconomic status (SES) measured by the maximum of her parents' education at her birth (Ronald et al., 2011), and mother's experience of physical, emotional and sexual abuse in childhood (Bernstein et al., 1994, Moore et al., 1995). Studies suggest that under-ascertainment of ASD in lower SES families lead to lower prevalence of ASD in lower SES families (Kalkbrenner et al., 2012). As lower SES is associated with greater intimate partner abuse (Khalifeh et al., 2012, Roberts et al., 2011b), maternal SES may be a confounder of the association between abuse and ASD. Similarly, maternal exposure to childhood abuse has been associated with ASD in this cohort (Roberts et al., 2013b), and has been associated with IPV victimization in prior studies (Simons et al., 1993, Stith et al., 2000). Therefore, we adjust for maternal childhood abuse as a potential confounder of the relationship between abuse and ASD.

Pregnancy-related risk factors for ASD may be more prevalent in women exposed to abuse, therefore, we estimated risk of ASD associated with abuse in models further adjusted for smoking and alcohol consumption during pregnancy, gestation less than 37 weeks, birth weight less than 5 pounds, gestational diabetes, preeclampsia, and history of induced abortion prior to index pregnancy. Birth weight, gestational length, smoking and alcohol use were by maternal report in 2001. Smoking during pregnancy was dichotomized as any/none. Alcohol use during pregnancy was coded as: none, 1, or 2 or more drinks/week. Having had an induced abortion prior to the birth of the index child was coded dichotomously based on reported ages at induced abortions, 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 occurrences of preeclampsia during pregnancy, defined for the respondent as "raised blood pressure and proteinuria" was assessed in 1989 and updated biennially.

As women who are exposed to intimate partner violence may differ from unexposed women in ways that affect risk for ASD in their children, we conducted a second set of analyses comparing siblings of the same mother. We restricted analyses to women who had at least one child with ASD and one child without ASD (families comprised only of children with or without ASD would not contribute information to within-family analyses). Of the 451 mothers of a child with ASD, 406 mothers also had at least one child without ASD (their total number of children, N=1097). We conducted conditional logistic regression models conditioned on the mother, with ASD as the dependent variable, to estimate odds ratios. We

conducted a model with physical harm from intimate partner abuse as the independent variable and a second model with fear of partner or emotional, sexual or physical abuse in the year before the birth year and the birth year as the independent variables. In these models we adjusted for the mother's age at the child's birth, the child's birth year, and the child's sex or stratified by the child's sex, using SAS PROC PHREG (SAS Institute, 2002).

RESULTS

Analyses comparing mothers with children with ASD to mothers without children with ASD

In this sample, 2.4% of women were exposed to physical harm from abuse during pregnancy (n=1343) and nearly half of women (48.3%) were exposed to any lifetime intimate partner abuse, i.e., before or after the index birth (Table 1). Of women who experienced physical harm from abuse during pregnancy, nearly half experienced repeated abuse (47.0%, n=652). Mothers who experienced physical harm from abuse during pregnancy or any lifetime intimate partner abuse were younger, had lower childhood socioeconomic status, and had less recent births than mothers who did not have these experiences (Table 1). In adjusted models, neither any physical harm from abuse during pregnancy (RR=0.62, 95% CI=0.24, 1.67) nor repeated abuse (RR=1.16, 95% CI=0.38, 3.57) was associated with ASD.

Prevalence of fear of partner or emotional, physical, or sexual abuse was consistently higher among case versus control mothers until the birth year, at which point prevalence in the two groups was similar. Table 2 shows the prevalence of ASD in children by mother's experienced of abuse in the year before the birth year. As ASD increased in prevalence and intimate partner abuse decreased in prevalence across the years of our study, we show results stratified by child's year of birth. For children born after 1990, for example, prevalence of ASD was 1.6% in children of women who were not abused in the year before the birth year and 2.6% in children of women abused (Table 2). In the model examining fear of partner or emotional, physical, or sexual abuse, we found significantly elevated risk of at least one of these experiences for case versus control mothers in the calendar year before the child's birth year, but not for women exposed in the birth year (Table 3).

Women exposed in both of the two calendar years before the birth year were somewhat more likely to have children with ASD than women exposed in only one of these years, however, confidence intervals for these terms overlapped considerably (Table 4). We did not find a dose-response relationship between number of years exposed over the four calendar years before birth and risk of ASD (1 of 4 years exposed, RR = 0.9, 95% CI=0.6, 1.5; 2 of 4 years exposed, RR = 2.6, 95% CI= 1.7, 3.9; 3 of 4 years exposed, RR = 2.2, 95% CI=1.3, 3.9; 4 of 4 years exposed, RR = 1.5, 95% CI=0.9, 2.5).

Results were nearly identical in models adjusted for smoking and alcohol consumption during pregnancy, gestation less than 37 weeks, birth weight less than 5 pounds, gestational diabetes, preeclampsia, and history of induced abortion prior to index pregnancy.

We conducted several additional analyses to further explore our findings. In order to specifically examine abuse prior to rather than during the pregnancy, we examined whether

abuse two calendar years before the birth year was associated with ASD independently of abuse in the year before the birth year. Abuse two calendar years before the birth year would not include abuse during the pregnancy, whereas abuse in both the calendar year before the birth and in the year of the birth might include abuse during the pregnancy. We entered abuse two calendar years before the birth year in a model adjusted for abuse in the calendar year before the birth. In this model, the association of abuse two calendar years before the birth year was elevated but not statistically significant (RR= 1.40, 95% CI= 0.88, 2.23, p=0.16).

To examine the association of abuse with ASD in additional years before and after the pregnancy, we extended our analyses to the ten calendar years before and four calendar years following the birth year. For these analyses, we also used data from a 2008 follow up to the 2001 supplemental questionnaire, which asked identical questions about fear of partner and emotional, physical and sexual abuse occurring from 2002 to 2008. Because abuse from year to year was highly correlated, we created four terms for any abuse in the: 2^{nd}– 4^{th} year; the 5^{th}– 7^{th} year; and the 8^{th}– 10^{th} year before birth; and the 2^{nd}– 4^{th} year following the birth year and added all these terms to our original model (Table 5). In this model, only abuse in the year before the birth year was statistically significantly associated with ASD. Abuse in the 2 to 10 years before the birth year, the birth year, and all the years following the birth year were not associated with ASD.

Because “emotional abuse” was not defined for respondents, relatively minor instances may have been reported. Therefore we ran analyses excluding women reporting only emotional abuse (n=5494). In these models, the estimated association of abuse in the year before the birth year was somewhat elevated compared with the whole sample (RR=2.23, 95% CI=1.41, 3.51). As abuse following birth of an autistic sibling before the index child may have caused elevated risk of abuse before the birth of the index child, we ran models excluding mothers who reported more than one child with ASD (n=21); results were nearly identical.

Analyses comparing siblings with and without ASD

Of the 406 mothers who had children both with and without ASD, only 19 had been exposed to any physical harm from intimate partner abuse during a pregnancy. As physical harm from intimate partner abuse during pregnancy was rare, models estimating the association of physical harm during pregnancy with ASD within families did not converge.

Risk of ASD associated with fear of partner or emotional, physical or sexual intimate-partner abuse in the year before the birth year was very similar to that found in the main analyses, which compared unrelated children. However, the smaller numbers of children in these analyses resulted in wide confidence intervals (abuse in the year before the birth year, OR =2.06, 95% CI=0.81, 5.22, p=0.13). Further adjustment for birth order did not meaningfully alter estimates.

DISCUSSION

We found increased risk of ASD in children of mothers exposed to abuse in the two calendar years before the child's birth year, but not in women exposed in other years before or after the birth year. Abuse in both the calendar year before the birth year, which may have occurred during pregnancy, and abuse two calendar years before the birth year, which could not have occurred during pregnancy, were marginally associated with risk of ASD. In analyses comparing siblings, the association of prenatal abuse with ASD was remarkably similar to the association found comparing unrelated children, though effect estimates did not reach statistical significance. In contrast, we did not find increased risk of ASD in offspring of mothers who experienced physical harm from abuse during pregnancy. It may be that the small number of women in our sample who experienced physical harm from abuse during pregnancy led to a spurious null association. It is also possible that increased risk of miscarriage, induced abortion and stillbirth in women who experienced physical harm from abuse during pregnancy biased these results toward the null (Howards et al., 2012, Silverman et al., 2007). Given that analyses examining abuse before and during pregnancy yielded different findings, our results should be interpreted with caution.

Findings from studies examining psychosocial stressors during pregnancy and risk of ASD have been contradictory. The largest found that neither maternal bereavement before nor during pregnancy was associated with risk of ASD (Li et al., 2009). Smaller studies examining exposure to life stressors (Ronald et al., 2011, Beversdorf et al., 2005), family discord (Ward, 1990), and hurricanes (Kinney et al., 2008) during pregnancy found significantly increased risk of ASD. These disparate findings may result from stressors of different magnitude and type having different effects on the mother and fetus, although differences in ascertainment of ASD and stress across the studies could easily have contributed as well.

Abuse before pregnancy and abuse during pregnancy may both increase risk of ASD through stress, behavioral, or other pathways. Stressful events before pregnancy may influence maternal health and thereby affect risk of ASD independently of stressors occurring during pregnancy (Croen et al., 2011). A large population-based study found that women abused before pregnancy were at elevated risk of kidney or urinary-tract infection, high blood pressure, placental problems, and gestational diabetes (Silverman et al., 2006). Gestational diabetes has been associated with ASD in several studies (Gardener et al., 2009). However, the association between risk of ASD and abuse in our data was not attenuated after further adjustment for gestational diabetes, preeclampsia, substance use during pregnancy, birth weight and preterm birth, suggesting that abuse is associated with risk of ASD through other mechanisms. It is also possible that intimate partner abuse initiates inflammatory and autoimmune processes in the mother which in turn increase the child's risk for ASD. Inflammatory markers (Slopen et al., 2010, Danese et al., 2009, Danese et al., 2007, Slopen et al., 2012, Miller and Chen, 2010) and autoimmune conditions (Dube et al., 2009, Spitzer et al., 2012) are more prevalent in persons who have experienced violence and other intense stressors. Maternal anti-brain antibodies and autoantibodies have been associated with ASD and ASD severity (Braunschweig et al., 2013, Brimberg et al., 2013, Warren et al., 1990), and persons with ASD have higher prevalence of inflammation,

including neuroinflammation (Dietert and Dietert, 2008, Herbert, 2010, Vargas et al., 2005, Jyonouchi et al., 2005, Jyonouchi et al., 2001, Zimmerman et al., 2005).

We found increasing risk of ASD in children of women abused in none, one, or both of the two years before the birth year, but we did not find a dose-response relationship between number of years exposed to abuse over the four calendar years before birth and risk of ASD. Thus, conclusions about the role of chronic maternal abuse in ASD will require additional research.

Our findings should be interpreted cautiously, in light of several limitations. First, we assessed exposure to abuse retrospectively, thus child's ASD status may have affected reporting of abuse. However, we assessed ASD and abuse in separate questionnaires four years apart, making differential recall of exposure by ASD status less likely than had ASD and abuse been ascertained together. In validation studies in this cohort, self-reports of health-related factors have been highly accurate (Colditz et al., 1997, Colditz et al., 1986, Hankinson et al., 1997, Martinez et al., 1997, Tomeo et al., 1999, Troy et al., 1995). Furthermore, recall bias caused by the child's ASD would likely be strongest in the birth year, yet we found no association between abuse in this year and ASD. Second, we validated maternal report of ASD with telephone administration of the ADI-R, an instrument with good reliability and validity (De Bildt et al., 2004); although this approach is consistent with a large body of epidemiological literature, it does not constitute a clinical diagnosis. Third, we do not know the specific gestational periods during which either physical harm from abuse or fear of partner or emotional, physical, or sexual abuse occurred, nor the severity of these kinds of abuse. The fetus may be more vulnerable to maternal psychosocial stressors during specific gestational stages (Kinney et al., 2008), although evidence is mixed (Li et al., 2009). However, intimate partner abuse is an ongoing circumstance that for most women occurs over a period of consecutive years. In our sample, 85% of women abused two years before the birth year were also abused in the year before birth or in the year of birth, or both. Thus, it is likely that few women would be abused only during a single trimester. Fourth, abuse is associated with adverse circumstances that may explain the association between abuse and ASD we found. However, the association of abuse with ASD was similar in models further adjusted for seven pregnancy-related risk factors, indicating that these adverse circumstances would not include those measured in our study. Our sample was comprised of primarily White medical professionals, therefore a higher prevalence of ASD cases may have been ascertained than in studies including a higher proportion of minorities, lower-socioeconomic-status families, and mothers who do not work in medical fields (Pedersen et al., 2012, Rai et al., 2012, Windham et al., 2011).

Our study also has two notable strengths. We used a large, population-based sample rather than a clinical sample, and we used individual-level data on abuse before, during and following the birth year and child's ASD status rather than the community-level data on stress exposures and ASD prevalence used in some prior research. Although our study has important limitations, it represents the first examination to date of possible associations of prenatal intimate partner violence and risk of ASD and suggests an important area for further research.

Our results suggest maternal exposure to intimate partner abuse before the child's birth may be associated with risk of ASD, possibly due to effects of abuse on the mother or due to paternal genetics. Additional research in humans is needed to complement existing animal models regarding specific brain regions and functions impacted by maternal exposure to psychosocial stressor during gestation (Charil et al., 2010). Studies examining pregnancy-related risk factors for ASD should consider potential confounding by abuse. Additionally, our findings add to prior research suggesting that intimate partner abuse of a pregnant woman may have enduring negative effects on her child.

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Table 1

Maternal exposure to injurious partner violence during pregnancy and any lifetime intimate partner abuse and demographic factors, Nurses' Health Study II, 1963–2002, United States.

		Injurious physical abuse during pregnancy		**Lifetime intimate partner abuse (before or after index birth)**	
		Any (n=1,343)	**None (n=53,725)**	**Any (n=26,501)**	**None (n=28,402)**
Male sex	%	48.9	49.1	49.4	48.8
Birth year	Mean (SD)	1979 (7.3)***	1984 (7.4)	1983 (7.6)***	1984 (7.2)
Maternal age at birth, years	Mean (SD)	25.2 (5.3)***	28.7 (5.0)	28.3 (5.4)***	29.0 (4.7)
Maternal childhood socioeconomic status (range: 1 to 6, 6 is highest status)	Mean (SD)	3.0 (1.0)***	3.2 (0.9)	3.1 (1.0)***	3.2 (1.0)

χ^2 or 2-sided t-test significant at

*$P<0.05$,

**$P<0.01$,

***$P<0.001$

SD: Standard deviation

Table 2

Prevalence of ASD in the child by mother's experience of intimate partner abuse in the year before the birth year, Nurses' Health Study II, 1963–2002

	Intimate partner abuse in the year before the birth year			
	No		Yes	
Birth Year	Child without ASD	Child with ASD	Child without ASD	Child with ASD
	% (N)		% (N)	
1963–1979	99.79 (14791)	0.21 (31)	99.82 (2179)	0.18 (4)
1980–1989	99.29 (20243)	0.71 (145)	98.90 (2244)	1.10 (25)
1990–2002	98.36 (11422)	1.64 (190)	97.39 (894)	2.61 (24)
Total	99.20 (48785)	0.80 (394)	98.98 (5534)	1.02 (57)

Table 3

Risk ratios of child with ASD by year of intimate partner abuse with respect to birth year, Nurses' Health Study II, 1963–2002, United States (N=54319 controls, N=451 cases)

	% (N)	Risk ratio (95% confidence interval)
IPV in the year before the birth year	89.8 (49179)	1.0 [Reference]
No	10.2 (5591)	1.92 (1.28, 2.88)**
Yes		
IPV in the birth year	88.1 (48275)	1.0 [Reference]
No	11.9 (6495)	0.68 (0.44, 1.03)
Yes		
Child's sex	48.3 (26426)	1.0 [Reference]
Female	51.8 (28344)	4.60 (3.60, 0.59)***
Male		1.09 (1.07, 1.12)***
Child's birth year		
Mother's age at child's birth	24.0 (13139)	1.0 [Reference]
Less than 25 years	37.6 (20597)	1.56 (1.04, 2.34)*
25–29 years	26.7 (14622)	1.72 (1.10, 2.88)*
30–34 years	10.1 (5542)	1.72 (1.03, 2.88)*
35–39 years	1.6 (870)	1.94 (1.01, 3.71)*
40 years or older		
Maximum of parent's education in mother's childhood		
Less than 9 years	6.1 (3345)	1.0 [Reference]
1–3 years high school	10.1 (5548)	0.81 (0.47, 1.39)
4 years high school	44.1 (24124)	1.26 (0.82, 1.95)
1–3 years college	20.1 (11023)	1.26 (0.80, 1.98)
4 or more years college	8.3 (4523)	1.05 (0.63, 1.75)
Don't know/missing	11.3 (6207)	0.10 (0.04, 0.25)***
Mother's experience of childhood abuse		
0: None	26.3 (14426)	1.0 [Reference]
1	21.8 (11916)	1.10 (0.83, 1.46)
2	18.9 (10370)	1.18 (0.88, 1.57)
3	19.1 (10466)	1.46 (1.11, 1.92)**
4	8.5 (4634)	1.47 (1.03, 2.10)*
5	3.3 (1797)	1.61 (0.95, 2.72)
6: Severe	2.1 (1161)	3.34 (2.08, 5.37)***

χ^2 test significant at

*$P<0.05$,

**$P<0.01$,

***$P<0.001$

Table 4

Risk ratios of child with ASD by mother's cumulative intimate partner abuse in the two years before the birth year, Nurses' Health Study II, 1963–2002, United States (N=54310 controls, N=451 cases)[†]

	% (N)	Risk Ratio (95% CI)
IPV in the two years before the birth year		
0 of 2 years before the birth year	88.3 (48328)	[Reference]
1 of 2 years before birth year	4.4 (2413)	1.58 (1.04, 2.40)*
2 of 2 years before birth year	7.3 (4020)	2.16 (1.33, 3.50)**
IPV in the birth year		
No	88.1 (48266)	1.0 [Reference]
Yes	11.9 (6495)	0.64 (0.41, 1.00)

[†]Model adjusted for child's sex, child's birth year, mother's age at child's birth, maximum of parents' education in mother's childhood and mother's experience of childhood abuse.

χ^2 test significant at

*$P<0.05$,

**$P<0.01$

Table 5

Risk ratios of child with ASD by year of intimate partner abuse with respect to birth year, including all years from 10 years before to 4 years after the birth year in a single model, Nurses' Health Study II, 1963–2002, United States (N=54235 controls, N=451 cases)[†]

	% (N)	Risk ratio (95% confidence interval)
IPV in any of the 8, 9, 10 years before the birth year		
No	93.4 (49915)	1.0 [Reference]
Yes	6.6 (3516)	0.99 (0.70, 1.38)
IPV in any of the 5, 6, 7 years before the birth year		
No	91.0 (48615)	1.0 [Reference]
Yes	9.0 (4816)	1.14 (0.82, 1.58)
IPV in any of the 2, 3, 4 years before the birth year		
No	87.9 (46951)	1.0 [Reference]
Yes	12.1 (6480)	1.26 (0.91, 1.74)
IPV in the year before the birth year		
No	89.8 (47996)	1.0 [Reference]
Yes	10.2 (5435)	1.68 (1.08, 2.61)*
IPV in the birth year		
No	88.3 (47198)	1.0 [Reference]
Yes	11.7 (6233)	0.69 (0.39, 1.21)
IPV in the year after the birth year		
No	88.2 (47097)	1.0 [Reference]
Yes	11.9 (6334)	0.83 (0.48, 1.43)
IPV in any of the 2,3,4 years after the birth year		
No	84.1 (44947)	1.0 [Reference]
Yes	15.9 (8484)	1.06 (0.73, 1.52)

[†]Model adjusted for child's sex, child's birth year, maternal age at child's birth, maternal childhood socioeconomic status, and maternal exposure to childhood abuse.