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Women's posttraumatic stress symptoms and autism spectrum disorder in their children

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Abstract

Maternal posttraumatic stress disorder (PTSD) may be associated with autism spectrum disorder (ASD) in offspring through multiple pathways: maternal stress may affect the fetus; ASD in children may increase risk of PTSD in mothers; and the two disorders may share genetic risk. Understanding whether maternal PTSD is associated with child's ASD is important for clinicians treating children with ASD, as PTSD in parents is associated with poorer family functioning. We examined the association of maternal PTSD with offspring ASD in a large US cohort (N ASD cases = 413, N controls = 42,868). Mother's PTSD symptoms were strongly associated with child's ASD (RR 4-5 PTSD symptoms=1.98, 95% CI=1.39, 2.81; RR 6-7 symptoms=2.89, 95% CI=2.00, 4.18). Clinicians treating persons with ASD should be aware of elevated risk of PTSD in the mother. Genetic studies should investigate PTSD risk alleles in relation to ASD.

Keywords

Autism spectrum disorder; posttraumatic stress disorder; gestational effects

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1. Introduction

Understanding whether maternal posttraumatic stress disorder (PTSD) is associated with offspring autism spectrum disorder (ASD) is important for clinicians treating families with children with ASD. PTSD in parents has been associated with poorer parenting (Jordan et al., 1992; Pears & Capaldi, 2001; Schechter et al., 2005) and poorer family functioning (Davidson & Mellor, 2001; Jordan, et al., 1992), reduced ability to solve problems effectively within and outside the family (Davidson & Mellor, 2001), and lower satisfaction with parenting (Samper, Taft, King, & King, 2004), factors important in themselves and that may also impair treatment of the child with ASD. Additionally, determining whether maternal PTSD is associated with child's ASD may elucidate ASD etiology.

Several lines of evidence suggest PTSD in women may be associated with ASD in their children. Maternal prenatal stress and anxiety have been associated with cognitive (Van den Bergh, Mulder, Mennes, & Glover, 2005), emotional and behavioral problems (O'Connor, Heron, Golding, Beveridge, & Glover, 2002), schizophrenia (Huttunen & Niskanen, 1978), atypical handedness (Glover, O'Connor, Heron, & Golding, 2004), and lower birth weight (Baibazarova et al., 2012) in children. It has been hypothesized that maternal stress affects several biological systems that in turn negatively impact the development of the fetus' brain. Hypothesized mechanisms include effects of maternal cortisol, reduced blood flow (Van den Bergh, et al., 2005) and immune function (Parker & Douglas, 2010) on the development of the fetus' limbic system, prefrontal cortex, hypothalamic-pituitary-adrenal (HPA) axis (Talge, Neal, & Glover, 2007), and immune system (Parker & Douglas, 2010), possibly in part through epigenetic alterations (Gurnot et al., 2013; Monteleone et al., 2014; Oberlander et al., 2008).

Maternal exposure to psychosocial stressors, including physical and sexual abuse in childhood (Roberts, Lyall, Rich-Edwards, Ascherio, & Weisskopf, 2013) and poor family functioning and intimate partner violence during gestation (Kinney, Miller, Crowley, Huang, & Gerber, 2008), has also been associated with greater risk of ASD, although findings have been inconsistent (Li et al., 2009). Maternal exposure to psychosocial stressors may increase ASD risk through dysregulation of the mother and fetus' immune function and HPA axis, possibly leading to higher exposure to cortisol and inflammation in the child's developing brain (Dietert & Dietert, 2008; Patterson, 2009; Talge, et al., 2007). PTSD is a marker of extreme distress occurring in response to a traumatic event and is also indicative of a chronic stress reaction, thus, if such maternal stress leads to ASD, maternal PTSD symptoms may be associated with ASD in offspring through these stress-related pathways.

Alternatively, there could be an association of mother's PTSD with child's ASD because having a child with ASD is associated with low social support and greater parenting-related stress. As risk of PTSD is higher in persons with lower social support (Acierio et al., 2007; Holeva, Tarrier, & Wells, 2001) or who have been exposed to chronic or multiple stressors (Astin, Lawrence, & Foy, 1993; Schumm, Briggs-Phillips, & Hobfoll, 2006), parents of children with versus without ASD may be at increased risk of developing PTSD symptoms following exposure to a traumatic event. A recent meta-analysis found a large effect size on parenting-related stress associated with children with ASD versus both normally developing

children and children with Down Syndrome (Hayes & Watson, 2013). One study using a selected sample of parents of children with ASD found that receiving the diagnosis of ASD induced posttraumatic stress symptoms in some parents (Casey et al., 2012). Parenting stress related to offspring ASD has also been linked with other stressors, such as marital discord (Walsh & O'Leary, 2013), financial stress (Sharpe & Baker, 2011), time pressure (Sawyer et al., 2010), stigma (Gray, 2002; Mak & Kwok, 2010), and decreased social support (Benson & Karlof, 2009; Brooke Ingersoll & Hambrick, 2011). Perhaps as a consequence of exposure to these stressors, parents of children with ASD are at higher risk of stress-related health outcomes, including poorer general mental health (Sawyer, et al., 2010), distress (Estes et al., 2009), depression (Brooke Ingersoll & Hambrick, 2011; B. Ingersoll, Meyer, & Becker, 2011; Sawyer, et al., 2010) and anxiety (Micali, Chakrabarti, & Fombonne, 2004; Rezendes & Scarpa, 2011). In addition to stress-related pathways, maternal PTSD symptoms may be associated with offspring ASD through shared genetics. Accumulating evidence suggests common genetic risk for diverse mental disorders (Cross-Disorder Group of the Psychiatric Genomics Consortium, 2013), although no studies have examined potential genetic overlap between ASD and PTSD.

In the present study, we examine the relationship between PTSD symptoms in women in the Nurses' Health Study II, a US longitudinal cohort, and ASD in their children. To elucidate whether PTSD in the mother may increase risk for ASD in her child and whether the child's ASD may increase risk of PTSD in the mother, we examine the association of women's PTSD and child's ASD both in women whose PTSD onset before the birth of the child and in women whose PTSD onset after the birth of the child.

2. Methods

2.1. Sample

The Nurses' Health Study II (NHSII), an ongoing cohort, enrolled 116,430 female nurses from 14 populous states in 1989 and has followed them with biennial questionnaires. The NHS II cohort was ages 24-44 years at enrollment and was 95.5% white. In 2001, women were asked the year of each of their children's births, the child's sex, birth weight and gestation length, and whether they smoked or drank alcohol during the pregnancy. They were also asked about their experience of childhood abuse. In 2005, women were asked whether they had ever had a child with ASD. In 2008, women were asked about lifetime trauma exposure, PTSD and depressive symptoms. In 2009, women were again asked whether they had ever had a child with ASD. The Harvard School of Public Health Institutional Review Board approved this research. Completion and return of questionnaires sent by U.S. mail constitutes implied consent.

2.2. Case ascertainment and control selection

In 2005, respondents were asked whether they had ever had a child diagnosed with autism, Asperger's syndrome, or other autism spectrum disorder. We mailed a follow-up questionnaire in 2007-2009 to women currently participating in NHS II who responded that they had a child with any of these diagnoses (N=756), 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, or Klinefelter, Down, Angelman, Jacobsen, or Rett syndrome were excluded (n=11). Of the remaining children, 413 had mothers with trauma and PTSD data. In this study we refer to 'cases' as children with autism, Asperger's syndrome, or other autism spectrum disorder who met these inclusion criteria; we use 'ASD' to refer to this case definition.

ASD diagnosis was validated in a subset of 50 randomly selected case mothers willing to be interviewed via telephone administration of the Autism Diagnostic Interview – Revised (ADI-R)(Lord, Rutter, & Le Couteur, 1994) about the child they reported as having ASD. The ADI-R is an extensive diagnostic interview designed to be administered to caregivers of children and adults who may have an ASD. The ADI-R queries behavior in three domains: social, communication, and repetitive and restrictive behavior. Most mothers were willing to be interviewed (81%). Diagnoses reported in the children of women who were willing versus unwilling to participate in the substudy were extremely similar, suggesting that severity of child's ASD did not affect women's willingness to be interviewed (percentage of women willing/unwilling to participate reporting: autism, 25%/25%; Asperger's 51%/49%; pervasive developmental disorder - not otherwise specified, 25%/23%). In this substudy, 43 children (86%) met ADI-R criteria for full 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 either missed full diagnosis by one point in one domain (n=5) or met cutoffs in one or two domains only (n=2). Thus, all children in the validation study demonstrated autistic behaviors and may have been on the autism spectrum even if they did not meet ADI-R criteria for full autistic disorder.

Controls were identified from among women who reported never having a child with an ASD in 2005 and 2009, and who responded to the 2001 questionnaire in which respondents reported calendar year and sex for each of their births. To assure independence of maternal characteristic among controls, we randomly selected one birth per respondent from among live births with data on mother's trauma and posttraumatic stress symptoms and year of birth and sex of the child (N=42,934).

2.3. Measures

2.3.1. Lifetime trauma and PTSD symptoms—Women's lifetime exposure to trauma and PTSD symptoms were queried in 2008. We measured lifetime trauma with a modified version of the Brief Trauma Questionnaire (Morgan et al., 2001; Schnurr, Vielhauer, & Weathers, 1995). The 16-item questionnaire queried exposure to 15 traumas as well as "a seriously traumatic event not already covered." Women were asked the age at which they experienced the first of these events. Women were also asked "which of these events would you consider the worst event?" and were asked the age at which they experienced that event.

We assessed posttraumatic stress symptoms with regard to the worst event using the Short Screening Scale for DSM-IV PTSD (Breslau, Peterson, Kessler, & Schultz, 1999; Roberts et al., 2012; Roberts, Rosario, Corliss, Koenen, & Austin, 2012), which assesses 7 symptoms

of PTSD (e.g., “Since the event, have there ever been times when you: Avoided being reminded of this experience by staying away from certain places, people or activities? Became jumpy or got easily startled by ordinary noises or movements? Felt more isolated or distant from other people?”). Endorsement of 4 or more symptoms identified PTSD cases with 85% sensitivity, 93% specificity, 68% positive predictive value, and 98% negative predictive value, and endorsement of 6 or more symptoms identified PTSD cases with a sensitivity of 38%, specificity of 100%, positive predictive value of 87%, and negative predictive value of 95% in a validation study (Breslau, et al., 1999). We additionally queried women’s age the first time any PTSD symptoms occurred. Trauma exposure and PTSD symptoms were coded jointly as: no trauma exposure; trauma exposure and no PTSD symptoms; 1 to 3 symptoms; 4 or 5 symptoms; and 6 or 7 symptoms.

2.3.2. Childhood abuse—Women’s experience of childhood abuse was 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 (Bernstein et al., 1994). Frequency of unwanted sexual touching or forced or coerced sexual contact before age 18 years by an adult or older child was queried with four questions (Moore, Gallup, & Schussel, 1995). Sexual abuse was coded as: none, mild, moderate, or severe according to the frequency of occurrence.

2.3.3. Depressive symptoms—Women’s current depressive symptoms were assessed in 2008 with the Center for Epidemiologic Studies Short Depression Scale (CES-D10) (Andresen, Malmgren, Carter, & Patrick, 1994). The CESD-10 measures the frequency of 10 past-week depressive symptoms (e.g., “I felt that everything I did was an effort.”), with response options ranging from 0: “rarely or none of the time” to 3: “all of the time.” Responses are summed to create a score that can range from 0 to 30.

2.3.4. Gestational risk factors—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. Maternal smoking and alcohol use, birth weight and gestation length for each pregnancy were assessed in 2001.

2.3.5. Demographic covariates—Calendar year of each birth and child’s sex were queried in 2001. Maternal age at birth was calculated by subtracting the mother’s birth year from the birth year of the child. Calendar year of birth was coded continuously. Women’s childhood socioeconomic status was measured by the maximum of her parents’ education during her infancy, queried in 2005.

2.4. Analyses

To determine whether PTSD symptoms in women were associated with ASD in their children, we examined prevalence of ASD among children by women’s lifetime PTSD symptoms and occurrence of maternal PTSD symptoms by child’s ASD status. To ascertain whether women with children with ASD had higher prevalence of PTSD symptoms and

childhood abuse, we conducted chi-square tests. We then calculated risk ratios of ASD by PTSD symptoms adjusted for demographic covariates. As women's experience of childhood abuse has been associated with risk of ASD in her children (Roberts, Lyall, et al., 2013), to determine whether PTSD was associated with ASD independently of mother's experience of childhood abuse, we examined the association of PTSD and ASD further adjusted for childhood abuse. As current depressive symptoms may have influenced reporting of PTSD and ASD, we further adjusted for depressive symptoms measured in 2008, at the time of PTSD assessment and ASD follow-up.

To determine whether women's PTSD symptoms were associated with offspring ASD in women whose symptoms onset before the birth of the child, we conducted analyses restricted to women who experienced both their worst event and their first PTSD symptoms before the birth of the index child. To investigate whether greater prevalence of gestational risk factors for ASD in women with versus without PTSD symptoms before the child's birth explained possible elevated risk of ASD in children, we added birth weight (Brimacombe, Ming, & Lamendola, 2007), gestation length (Larsson et al., 2005), maternal smoking and alcohol use (Juul-Dam, Townsend, & Courchesne, 2001), preeclampsia (Gardener, Spiegelman, & Buka, 2009) and gestational diabetes (Krakowiak et al., 2012) to the model. We conducted sensitivity analyses excluding women with more than one child with ASD (N=23).

Risk ratios were estimated using generalized estimating equations with a log link and a Poisson distribution (Zou, 2004) using SAS PROC GENMOD.

3. Results

Women's lifetime PTSD symptoms were associated with unwanted sexual contact and physical/emotional abuse in childhood and current depressive symptoms, but not age at child's birth or calendar year of birth (Table 1). Women with children with ASD were more likely to have 4 or more PTSD symptoms than women with children without ASD (34.1% versus 20.6%, $\chi^2=55.79$, $df=4$, $P<0.001$) and to have experienced the highest quartile of physical/emotional abuse (30.8% versus 23.7%, $\chi^2=13.72$, $df=3$, $P<0.001$). Sexual abuse was slightly more common in women with children with ASD, with borderline statistical significance (37.4% versus 33.6%, $\chi^2=2.82$, $df=1$, $P=0.09$; Table 2).

Women who experienced high levels of PTSD symptoms at any time in their lives were substantially more likely to have had a child with ASD than the reference group of women who had not experienced trauma (1.84% of women with 6-7 PTSD symptoms had a child with ASD versus 0.72% of women not exposed to trauma, $RR=2.66$, 95% confidence interval; $CI=1.85$, 3.81 , Figure; Table 3, Model 1a). Adjustment for depressive symptoms in 2008 somewhat attenuated the association between mother's PTSD symptoms and child's ASD, although it remained strong (RR 1-3 symptoms= 1.29 , 95% $CI=0.95$, 1.76 ; RR 4-5 symptoms= 1.77 , 95% $CI=1.25$, 2.50 ; RR 6-7 symptoms= 2.35 , 95% $CI=1.59$, 3.47).

In analyses restricted to women whose worst trauma and symptoms occurred before the child's birth, associations of PTSD symptoms with ASD were similar to those found in all

women (Table 3, Model 2a). Adjustment for women's experience of childhood abuse somewhat attenuated the relationship between PTSD symptoms and ASD, though it remained statistically significant (Table 3, Models 1b and 2b).

Adding gestational risk factors, including birth weight, gestation length, preeclampsia, gestational diabetes, and maternal smoking and alcohol use to the model did not meaningfully change the association between maternal PTSD symptoms before birth and ASD (trauma no symptoms, $RR=0.89$, 95% $CI=0.60, 1.32$; 1-3 symptoms, $RR=1.36$, 95% $CI=0.96, 1.93$; 4-5 symptoms, $RR=1.69$, 95% $CI=1.12, 2.57$; 6-7 symptoms, $RR=2.61$, 95% $CI=1.67, 4.07$). Results were nearly identical in analyses excluding women with more than one child with ASD ($N=23$).

In exploratory analyses, we estimated risk ratios for ASD associated with PTSD symptoms in women whose worst trauma occurred after the child's birth (N controls=23,611, N cases=194). Risk ratios in these women were very similar to those in all women (trauma no symptoms, $RR=0.94$, 95% $CI=0.59, 1.48$; 1-3 symptoms, $RR=1.15$, 95% $CI=0.78, 1.69$; 4-5 symptoms, $RR=2.18$, 95% $CI=1.47, 3.24$; 6-7 symptoms, $RR=2.76$, 95% $CI=1.75, 4.37$, $P_{trend}<0.001$). While some of these women could have had PTSD symptoms from a different trauma prior to the birth of the child, an association between maternal PTSD and child's ASD remained even when further restricting to women with no reported trauma before the birth of the child (1-3 symptoms, $RR=1.08$; 4-5 symptoms, $RR=2.37$; 6-7 symptoms, $RR=1.47$).

4. Discussion

We report for the first time an association between mother's PTSD symptoms and child's ASD. Because stress related to parenting a child with ASD could increase a mother's risk of PTSD, we also restricted analyses to women whose PTSD symptoms onset before the birth of the child. That the results were similar in these analyses to analyses involving all women suggests that stress related to parenting a child with ASD was not the only factor driving the associations we found. Association of maternal PTSD with child's ASD remained after adjustment for mother's experience of childhood abuse, current depressive symptoms, and gestational factors.

Our results are consistent with several possible mechanisms. Maternal PTSD and ASD may be associated due to a common cause of PTSD and ASD, such as shared genetic risk. ASD has been associated with psychiatric disorders in family members, including autism (Bolton, Pickles, Muphy, & Rutter, 1998), schizophrenia (P. F. Sullivan et al., 2012), obsessive-compulsive disorder (Hodge, Hoffman, & Sweeney, 2011), personality disorders (Daniels et al., 2008) and depression (Bölte, Knecht, & Poustka, 2007). These associations have been hypothesized to be primarily a result of shared genetic risk for ASD and other psychiatric disorders, although few shared genetic variants have been identified (Cross-Disorder Group of the Psychiatric Genomics Consortium, 2013; Miller et al., 2009). Evidence from twin studies also suggests that genetic risk for PTSD overlaps with other psychiatric disorders, including depression (Koenen et al., 2008), generalized anxiety disorder and panic disorder (Afifi, Asmundson, Taylor, & Jang, 2010). It is possible that elevated genetic risk for ASD

in case mothers, manifest in them by broad autism phenotype behaviors (Constantino & Todd, 2005), increased risk of trauma exposure and development of PTSD in these women. People who noticeably differ from others, whether due to disability or traits such as gender nonconformity, are at risk of interpersonal violence (Roberts, Rosario, et al., 2012; Roberts, Rosario, Slopen, Calzo, & Austin, 2013; P. M. Sullivan & Knutson, 2000). Additionally, people who do not accurately process social information may be at greater risk of physical and sexual assault (Brownlie, Jabbar, Beitchman, Vida, & Atkinson, 2007; DePrince, 2005; Parks, Hequembourg, & Dearing, 2008). Thus, women who exhibit the broader autism phenotype may be more likely to be victimized. Moreover, lack of social support following trauma exposure has been associated with increased risk of developing PTSD (Acierno, et al., 2007). Persons with ASD and those with the broad autism phenotype who do not meet ASD diagnostic criteria have weaker social networks and less companionable friendships than typically-developing persons (Bauminger et al. 2003; Jobe and Williams White 2007; Locke et al. 2010), which may put them at elevated risk of PTSD following trauma exposure.

In addition to a common cause of PTSD and ASD creating the associations we found, it is also possible that separate mechanisms operating before and after the child's birth could account for these associations. Mother's PTSD symptomatology before the child's birth may affect the developing fetus in ways that increase risk for ASD, and child's ASD may increase risk of mother's PTSD symptoms after the birth due to stressors related to parenting a child with ASD.

Maternal PTSD prior to the child's birth may negatively affect the developing fetus. PTSD has been associated with HPA-axis dysregulation in both women and their children (Yehuda et al., 2005). Dysregulation of the HPA axis has been observed in persons with ASD (Marinovi - urin et al., 2008), and it has been hypothesized that dysregulation of the maternal HPA axis affects the fetal brain (Wadhwa, Dunkel-Schetter, Chicz-DeMet, Porto, & Sandman, 1996). Experiments in primates have shown that manipulation of HPA-axis hormones during gestation induce long-lasting changes to the hippocampus (Sapolsky, Uno, Rebert, & Finch, 1990; Uno et al., 1994). Proinflammatory biomarkers have also been associated with PTSD (von Kanel et al., 2007). Maternal inflammation affects the developing brain and maternal inflammation and immune function have been hypothesized to be causes of ASD, possibly through maternal antibodies directed to the developing brain (Martin et al., 2008; Onore, Careaga, & Ashwood, 2011). Studies of persons with ASD have shown active neuroinflammatory processes in the white matter, cerebral cortex and cerebellum, proinflammatory profiles of cytokine concentration in cerebrospinal fluid (Vargas, Nascimbene, Krishnan, Zimmerman, & Pardo, 2005), and hyperreactivity of the innate immune response (Jyonouchi, Sun, & Le, 2001). Thus, maternal PTSD may increase risk for ASD in offspring through HPA-axis and immune dysregulation. Future research with maternal biomarkers measured during pregnancy should test these hypotheses.

An association of PTSD with ASD among women who reported PTSD after the child's birth could result if having a child with ASD increases risk of mother's PTSD. Parenting children with ASD has been associated with high levels of stress, lower social support, and associated mental health symptoms, including depression, though the association with PTSD

has not been examined, aside from a single study of PTSD related to child's receipt of an ASD diagnosis (Casey, et al., 2012). Studies examining the association of depression with parenting a child with ASD have suggested that greater time pressure, degree of child's impairment (Bebko, Konstantareas, & Springer, 1987; Davis & Carter, 2008; Dumas, Wolf, Fisman, & Culligan, 1991), and the broad autism phenotype in parents, through associations with reduced social support and maladaptive coping, may explain the association (Brooke Ingersoll & Hambrick, 2011; B. Ingersoll, et al., 2011). Thus, studies suggest that a combination of ASD-related parenting stress and genetic risk factors may lead to greater risk of depression in parents of children with ASD.

The association we found between ASD and PTSD symptoms reported after the child's birth must be interpreted with caution, however, because it is hard to rule out in our study setting that PTSD symptoms reported after the birth were not also present prior to the child's birth. Nonetheless, our findings that PTSD reported after the birth was associated with ASD appeared to hold even when analyses were restricted to women who did not report any trauma prior to the birth of the child, although the number of these women was small.

Our study has important limitations. The participants were primarily white professionals, thus, results may not be generalizable to other populations. Trauma, PTSD and childhood abuse were measured retrospectively, potentially biasing our results. ASD was by report of the nurse mothers, which, although validated with the ADI-R, does not constitute a diagnosis. Additionally, we assessed PTSD symptoms with respect to the worst traumatic event. Other traumatic events over their lives may also have triggered PTSD symptoms in women, potentially leading to underestimation of women's lifetime PTSD symptoms. We did not assess family history of mental illness. Had we found that adjustment for family history of mental illness attenuated the association between maternal PTSD and child ASD, these findings would suggest that the association we found was driven in part by genetic overlap between PTSD, ASD and other mental disorders.

Our study also has notable strengths. We assessed the association of maternal PTSD and ASD by directly querying mothers; thus, we have likely captured a much greater proportion of ASD cases and PTSD symptomatology than studies using hospital records (Daniels, et al., 2008). We used a non-clinical sample, thus our results may be more generalizable than studies using clinical samples (Bölte, et al., 2007). Finally, unlike all prior studies examining the association of ASD with family members' mental disorders, we examined mother's childhood abuse as a possible common cause of PTSD and ASD.

We found that mothers of children with ASD had substantially greater prevalence of PTSD symptoms than mothers of children without ASD. Regardless of the mechanisms driving the association of maternal PTSD with child's ASD, clinicians treating children with ASD should screen parents for PTSD, depression and other mental health symptoms that could be treated to improve family functioning (Jovanovic et al., 2011; Parsons, Kehle, & Owen, 1990; Roberts, Galea, et al., 2012; Schechter, et al., 2005). Additionally, parents of children with ASD should be alerted that they may be at risk of PTSD and depressive symptoms, so that they can receive prompt treatment should symptoms arise. Several treatments are effective for PTSD, include eye-movement desensitization and reprocessing, cognitive-

behavioral therapy (Seidler & Wagner, 2006), psychopharmacotherapy, and psychodynamic therapy (Bisson et al., 2007; Foa, Keane, Friedman, & Cohen, 2008). If untreated, PTSD has potentially severe physical and mental health sequelae, including cardiovascular disease, diabetes, and chronic fatigue syndrome (Boscarino, 2004; Kubzansky et al., 2013; Qureshi, Pyne, Magruder, Schulz, & Kunik, 2009). Thus, screening and treatment for PTSD and other disorders is likely to be an effective way to improve the health of this vulnerable population. Additionally, genetic studies of ASD should consider PTSD risk alleles in ASD etiology. Further prospective longitudinal research is needed to elucidate the factors driving associations between maternal PTSD and ASD in children.

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Highlights

- We examined the association between maternal lifetime PTSD symptoms and child's ASD.
- Maternal PTSD symptoms were associated with 2-3 times greater risk of child's ASD.
- Clinicians treating children with ASD should be aware of possible PTSD in mothers.
- Genetic studies should consider PTSD risk alleles in association with ASD.

Figure. Mother's posttraumatic stress symptoms and offspring ASD, Nurses' Health Study II, children born 1960-2003

†Models are adjusted for mother's childhood socioeconomic status, mother's age at the birth of the child, child's sex and child's year of birth.

Table 1
Demographic covariates and risk factors for ASD by mother's PTSD symptoms, Nurses'
Health Study II (N ASD cases = 413, N ASD controls = 42,934), children born 1960-2003

Variable		No trauma	Trauma, no symptoms	1-3 symptoms	4-5 symptoms	6-7 symptoms
Mothers	N	7904	21565	6841	4421	2616
Mother's age at child's birth (years)	Mean	28.4	28.7	28.6	28.5	28.2
Calendar year of birth	Median	1983	1984	1983	1983	1983
Depressive symptoms, CESD 2008	Mean	4.7	4.5	5.9	8.3	10.7
Childhood sexual abuse (any)	%	17.7	32.6	39.6	44.7	53.2
Childhood physical/emotional abuse (highest quartile)	%	11.6	21.1	27.2	35.8	45.3
Maternal childhood socioeconomic status (either parent, 4+ years college)	%	22.6	21.5	22.9	23.0	22.8

Table 2
Maternal trauma/PTSD, demographic covariates and ASD risk factors by child's ASD status, Nurses' Health Study II, children born 1960-2003

Variable		Child without ASD (N=42,934)	Child with ASD (N=413)
Mother's trauma/PTSD			
No trauma	%	18.3	13.8
Trauma no PTSD	%	30.1	20.8
1-3 PTSD symptoms	%	31.0	31.2
4-5 PTSD symptoms	%	13.4	20.1
6-7 PTSD symptoms	%	7.2	14.0
Mother's age at child's birth (years)	Mean	28.8	31.8
Calendar year of birth	Median	1984	1989
Male sex	%	51.7	83.6
Depressive symptoms, CESD, 2008	Mean	5.9	7.1
Unwanted sexual contact in childhood (any)	%	33.6	37.4
Childhood physical/emotional abuse (highest quartile)	%	23.7	30.8
Maternal childhood socioeconomic status (either parent, 4+ years college)	%	20.6	25.5

Table 3
Mother's posttraumatic stress symptoms and risk of offspring ASD, Nurses' Health Study II, children born 1960-2003

	All women			Women with PTSD symptoms before child's birth ^a			
				Model 1a: Base model	Model 1b: Further adjusted for maternal childhood abuse	Model 2a: Base model	Model 2b: Further adjusted for maternal childhood abuse
Trauma and PTSD	N mothers	% children with ASD (N cases)	Risk ratio for ASD (95% confidence interval)			N mothers	Risk ratio for ASD (95% confidence interval)
No trauma	7904	0.72 (57)	1.0 [reference]		1.0 [reference]	7904	1.0 [Reference]
Trauma, no symptoms	13012	0.66 (86)	0.88 (0.63, 1.22)		0.85 (0.61, 1.19)	5747	0.90 (0.61, 1.34)
1-3 symptoms	13419	0.96 (129)	1.32 (0.97, 1.80)		1.24 (0.90, 1.70)	6190	1.39 (0.98, 1.96)
4-5 symptoms	5853	1.42 (83)	1.92 (1.38, 2.68)		1.72 (1.21, 2.44)	2546	1.71 (1.13, 2.60)
6-7 symptoms	3159	1.84 (58)	2.66 (1.85, 3.81)		2.32 (1.59, 3.40)	1425	2.68 (1.72, 4.16)
Test of linear trend			<i>P</i> <.0001		<i>P</i> <.0001		<i>P</i> < 0.001
							<i>P</i> < 0.01

Note: All models adjusted for mother's age at the birth of the child, mother's childhood socioeconomic status, and child's sex and birth year.

^aFor these models, all women with "no trauma" were included. Women in the "trauma, no symptoms" group were women whose worst traumatic event occurred before the birth of the index child and who did not report any PTSD symptoms.