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Brief Report

Prenatal, perinatal, and neonatal factors associated with self-injurious behaviors in children with autism spectrum disorder

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ABSTRACT

Background: Studies that examine the role of factors documented before self-injurious behaviors (SIB) occur are important in establishing a temporal relationship between these factors and SIB. Using data from a population-based surveillance system of 8-year-olds with autism spectrum disorder (ASD), we: (1) explored potential associations between SIB and prenatal, perinatal, and neonatal factors identified from birth certificates, and 2) validated associations between SIB and developmental, behavioral, medical factors accounting for the above prenatal, perinatal, and neonatal factors.

Methods: We included 4343 children from the Autism and Developmental Disabilities Monitoring Network from the 2000, 2006, and 2008 surveillance years. Prenatal, perinatal and neonatal characteristics were obtained from birth certificates. SIB and other potential risk factors were abstracted from children's health or education records. The associations between SIB and various potential risk factors were tested using non-linear mixed models.

Results: Lower maternal educational attainment (adjusted odds-ratio [aOR]: 1.35 [95% confidence interval 1.10–1.67]), prenatal maternal cigarette smoking (1.47 [1.09–1.98]), and electronic fetal monitoring during labor (1.70 [1.02–2.84]) were associated with SIB. In addition, we validated previous associations between SIB and developmental regression, lower IQ, behavioral, sensory and sleep problems, co-occurring developmental and psychiatric diagnoses.

Conclusions: The associations between SIB and maternal smoking, low maternal education attainment may be due to various factors, including low SES and limited access to specialized ASD services. Electronic fetal monitoring may be a marker for unmeasured perinatal complications.

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Findings reported in this study have implications for better understanding of factors associated with SIB to guide prevention and interventions.

1. Introduction

Self-injurious behaviors (SIB) are often reported in ASD with an estimated prevalence varying between 20–53% (Dimian et al., 2017; Soke et al., 2016). SIB are self-directed acts that cause physical damage to the person's own body (Rojahn, Schroeder, & Hoch, 2008) and may include head banging, arm biting, and self-scratching. Some researchers consider SIB as a type of repetitive behavior, a core feature of autism spectrum disorder [ASD] (American Psychiatric Association, 2013). Although, some types of mild, low-frequency SIB (e.g. head hitting) may emerge in typically-developing children around the age of 8 months, these behaviors decline over time and completely disappear by about 36 months (Baghdadli, Grisi, & Aussillloux, 2003; Berkson & Tupa, 2000; Kurtz, Chin, Huete, & Cataldo, 2012). However, in persons with developmental disabilities, including ASD, SIB persist after 36 months and have deleterious consequences extending beyond the physical impact to the individual (Minshawi et al., 2014; Minshawi, Hurwitz, Morriss, & McDougle, 2015).

The etiology of SIB is not completely elucidated and may involve genetic and non-genetic factors (Devine, 2014; Guess & Carr, 1991). In genetic conditions (e.g., Lesch-Nyhan syndrome), hormonal disturbances may contribute to SIB. These hormonal perturbations may affect different neurotransmitter systems, such as dopamine, cholinergic, glutamate, serotonin, GABA, and opioid (Llyod et al., 1981; Minshawi et al., 2015; Weiss, 2002). SIB have been associated with morphologic changes in the brain. For example, a positive correlation between the size of the left caudate nucleus, involved in dopamine metabolism, and SIB was reported in individuals with ASD (Wolff, Hazlett, Lightbody, Reiss, & Piven, 2013). In non-genetic conditions, SIB can be a learned behavior used for social interaction, communication, or self-regulation (Kurtz et al., 2003; Soke et al., 2017). SIB may also be due to impaired control of impulse responses (Oliver & Richards, 2015; Richards, Davies, & Oliver, 2017), and have been associated with other factors, including sleep and sensory problems (Soke et al., 2017).

Identifying factors associated with SIB is crucial to their prevention and effective management. Previous studies in those with ASD were mostly clinic-based and have suggested associations between SIB and developmental regression, low IQ and adaptive skills, sleep, sensory, and behavior problems (Baghdadli et al., 2003; Dimian et al., 2017; Duerden et al., 2012; McClintock, Hall, & Oliver, 2003; Richman et al., 2013; Soke et al., 2017). Most of these previous studies had important limitations, including possible selection bias and limited generalizability of their findings. Further, these studies could not establish a temporal relationship between these factors and SIB since some of these reported risk factors (e.g., sleep problems) could have been consequences rather than antecedents of SIB. Studies that assess associations between factors that are present before SIB occur (e.g., prenatal characteristics) are needed since they can confirm a temporal relationship. Findings from such studies will inform our understanding of predictors of SIB. However, these types of studies are sparse. To our knowledge, there is only one clinic-based study that reported an association between SIB and "an associated perinatal condition" identified from medical records (Baghdadli et al., 2003). However, details on the "perinatal condition" were not provided. Meanwhile, numerous studies have reported associations between prenatal, perinatal and neonatal factors and ASD. For example, advanced parental age (Bilder, Pinborough-Zimmerman, Miller, & McMahon, 2009; Durkin et al., 2008); preterm birth (Schieve, Clayton, Durkin, Wingate, & Drews-Botsch, 2015); maternal cigarette smoking (Larsson, Weiss, Janson, Sundell, & Bornehag, 2009); gestational metabolic conditions (Krakowiak et al., 2012), and obstetric complications (Guinchat, Thorsen, Laurent, Cans, & Bodeau, 2012; Walker et al., 2015; Zhang et al., 2010) were associated with ASD. It seems important to explore whether these same factors are also associated with SIB.

The goal of this analysis was to provide more data on predictors of SIB in ASD. Using a population-based sample, we had two specific objectives: (1) To explore potential associations between SIB and prenatal, perinatal, and neonatal factors from birth certificates, and (2) to validate associations between SIB and developmental (e.g., developmental regression), medical (e.g., sleep problems), and behavioral (e.g., aggression) factors after accounting for prenatal, perinatal, and neonatal factors.

2. Methods

2.1. Participants

We included 8-year-old children from 14 sites of the Autism and Developmental Disabilities Monitoring (ADDM) Network: Alabama, Arkansas, Arizona, Florida, Georgia, Maryland, Missouri, New Jersey, North Carolina, Pennsylvania, South Carolina, Utah, West Virginia, and Wisconsin. We combined data from three surveillance years (2000, 2006, and 2008). Included sites varied depending on the surveillance year. We excluded the 2002 and 2004 study years since data collection procedures were modified during these two surveillance years and this affected accurate documentation of co-occurring conditions including SIB. We only included children who met the surveillance definition for ASD (Centers for Disease Control & Prevention, 2007, 2009, 2012) and whose birth certificates were available.

ADDM is a record-based surveillance system for ASD and other developmental disabilities in selected communities of the United States. All ADDM sites follow a common, validated multi-step process for case determination. ADDM's methodology is detailed in other publications (Centers for Disease Control & Prevention, 2014; Rice et al., 2007; Yeargin-Allsopp et al., 2003). In summary,

during a given surveillance year, health records (available in all sites) and education records (available in most sites) of 8-year-olds living in ADDM catchment areas are reviewed by trained abstractors for: (1) social deficits indicative of ASD, (2) documented ASD diagnosis, and (3) receipt of special education services under autism exceptionalities. These records include standardized testing scores, evaluation reports and provider's notes from birth to the age of 8 years. Records that meet any of the above three criteria are abstracted verbatim and records from various sources for the same child are merged in a summary file. This summary file is reviewed by clinicians at each site who determine whether a child meets the ASD surveillance classification using an algorithm based on the Diagnostic and Statistical Manual of Mental Disorders-Fourth Edition-Text Revision criteria (DSM-IV-TR) (American Psychiatric Association, 2000). The DSM-IV-TR was used since all children included in this analysis were evaluated before DSM5 implementation. Data from each site are combined in to a final ADDM dataset. Birth certificate data, if available, are linked to the final dataset. Linkage to birth certificate is possible only for children born in the same state as their respective ADDM catchment areas, and states may also opt not to send birth certificate data to the ADDM network. In addition to deciding about ASD classification, ADDM clinicians review the child's summary file to document different co-occurring conditions/symptoms, including SIB.

2.2. Variables

SIB were defined to include "any self-directed behavior, such as picking fingers until bleeding, sucking fingers until chapped, slapping self in face, head banging that could causes physical harm or a sign or bodily mark of the act". ADDM reviewers coded SIB (yes/no) based on a review of all available evaluations (ever had SIB) with an inter-reviewer reliability of 0.93. We examined the following birth certificate variables: child's sex, gestational age, birth weight, Apgar score at the 5^{th} minute, maternal and paternal age, mother's education and marital status, maternal cigarette smoking status from the three months prior to pregnancy until the end of pregnancy (referred as" maternal smoking"), maternal weight gain during pregnancy, mode of delivery, type of pregnancy (single vs. multiple births), labor complications (major, minor, others), and obstetric procedures (e.g., amniocentesis, electronic fetal monitoring during labor, ultrasound). A detailed description of birth certificate variables is presented in supplemental Table 1. We also assessed various previously-reported predictors of SIB such as developmental regression, documentation of diagnosis of ASD in the child's records, IQ, behaviors, sleep and sensory problems (Baghdadli et al. 2003; Duerden et al., 2012; Soke et al., 2017). In this analysis, data on these predictors were abstracted from information contained in the child's summary file.

2.3. Analytic strategy

We first compared characteristics of children with and without SIB using chi-square test for categorical variables and a non-parametric test for continuous variables. We analyzed gestational age, Apgar score, birth weight, maternal weight gain during pregnancy and parental age as continuous since their plots versus SIB showed linear relationships. However, we rescaled these variables, defining a unit change to indicate a larger change (e.g., examining 5 years of age as the unit change rather than 1 year of age). To account for missing data on some variables (e.g., IQ, adaptive skills), we imputed 10 datasets using the Fully Conditional Specification (FCS) technique which imputes both continuous and categorical variables (Lee & Carlin, 2010; Van Buuren, 2007). Since we included a high number of variables due to the exploratory nature of this study and to avoid the effect of high correlation between variables, we first estimated the variance inflation factor (VIF) and the tolerance for each variable to assess multicollinearity. Although some variables (IQ and adaptive scores, maternal education and smoking) were highly correlated in bivariate analyses, none of the variables had VIF of > 10 (range: 1.03–3.63) or tolerance < 0.10 (range: 0.28–0.99) in multivariable analyses which indicates that multicollinearity was not problematic (Cheng, Edwards, Maldonado-Molina, Komro, & Muller, 2010). We used non-linear mixed models with site as a random effect to test associations between SIB and the different variables and Rubin's formula (Rubin, 1987) to combine results from the 10 imputed datasets. In a sensitivity analysis, we assessed the same above associations in a complete case analysis.

3. Results

A total of 4343 children were included in this analysis after excluding 2851 children whose birth certificate was not available. The proportion of SIB in children with (27.12%) and without birth certificates (28.55%) were not different. Further, no major differences were observed between the two groups in most of the variables examined in this study. However, children without birth certificates were significantly more likely to live in low income census tracts, and to have adaptive skills scores < 70 and co-occurring sleep problems and developmental diagnoses (data not shown).

The comparisons of birth certificate variables between children with SIB ($n = 1178$) and without SIB ($n = 3165$) are presented in Table 1. We noted differences between the two groups on maternal education, maternal marital status, maternal smoking, and obstetric procedures. The estimates of adjusted associations between SIB and birth certificate variables are presented in Table 2. SIB were significantly associated with maternal education, maternal smoking, and the use of electronic fetal monitoring during labor. The effect estimates of adjusted associations between SIB and predictors reported in previous studies, after accounting for birth certificate variables, are presented in Table 3. As in previous studies, most variables, including developmental regression, IQ, aggression, argumentative behaviors, temper tantrums, sensory and sleep problems, and co-occurring developmental and psychiatric diagnoses were significantly associated with SIB. Overall, the adjusted results from complete case analysis ($n = 1383$), included in supplemental Table 2, mirrored those from multiple imputation on the directionality and significance of the reported associations, but the confidence intervals were larger in complete case analysis versus multiple imputation analysis.

Table 1
Characteristics of participants with birth certificate data in the Autism and Developmental Disabilities Monitoring Network sites* during the 2000, 2006, and 2008 surveillance years.

Variable	Self-injurious behaviors Yes (n = 1178)	Self-injurious behaviors No (n = 3165)	P-value
Child sex (n, %)			
Female	195 (16.6)	564 (17.8)	0.33
Male	983 (83.4)	2601 (82.2)	
Child race/ethnicity (n, %)			
Non-Hispanic African American	228 (19.4)	586 (18.5)	
Hispanic	119 (10.1)	308 (9.7)	0.06
Others	44 (3.7)	186 (5.9)	
Non-Hispanic White	784 (66.5)	2081 (65.7)	
Missing	3 (0.3)	4 (0.2)	
Maternal education (n, %)			
No College degree	812 (68.9)	1852 (58.5)	< **0.0001**
College degree or higher	341 (28.9)	1274 (40.2)	
Missing	25 (2.2)	39 (1.3)	
Maternal marital status (n, %)			
Not married	287 (24.4)	567 (17.9)	
Married	799 (67.8)	2421 (76.5)	< **0.0001**
Missing	92 (7.8)	177 (5.6)	
Maternal smoking status (n, %)			
Smoker	158 (13.4)	243 (7.7)	
Non-smoker	1016 (86.3)	2916 (92.1)	
Missing	4 (0.3)	6 (0.2)	< **0.0001**
Maternal age (years)			
Mean (standard deviation)	28.7 (6.0)	29.6 (5.9)	< **0.0001**
Median (interquartile range)	29.0 (9.0)	30.0 (8.0)	
Paternal age (years)			
Mean (standard deviation)	31.5 (7.2)	32.3 (6.6)	0.002
Median (interquartile range)	31.0 (10.0)	32.0 (8.0)	
Maternal weight gain during pregnancy (pounds)			
Mean (standard deviation)	32.5 (15.9)	32.4 (14.6)	
Median (interquartile range)	30.0 (17.0)	30.0 (16.0)	0.83
Type of pregnancy (n, %)			
Multiple birth	62 (5.3)	137 (4.3)	
Single birth	1116 (94.7)	3028 (95.7)	0.19
Mode of delivery (n, %)			
Not vaginal	447 (37.9)	1209 (38.2)	0.88
Vaginal	731 (62.1)	1956 (61.8)	
Labor complications (n, %)			
Major	100 (8.5)	285 (9.0)	
Minor	161 (13.7)	386 (12.2)	**0.03**
Other	122 (10.4)	331 (10.5)	
None	529 (44.9)	1563 (49.4)	
Missing	266 (22.5)	600 (18.9)	
Obstetric procedures (n, %)			
Electronic fetal monitoring	170 (14.4)	407 (12.9)	< **0.0001**
Ultrasound	768 (65.2)	2111 (66.7)	
Others	153 (13.0)	434 (13.7)	
None	35 (3.0)	157 (5.0)	
Missing	52 (4.4)	56 (1.7)	
Child gestational age (weeks)			
Mean (standard deviation)	38.3 (2.9)	38.4 (2.6)	0.08
Median (interquartile range)	39.0 (2.0)	39.0 (2.0)	
Child birth weight (grams)			
Mean (standard deviation)	3242.1 (745.7)	3293.7 (703.2)	0.04
Median (interquartile range)	3317.0 (793.0)	3348.0 (754.0)	
Child Apgar score at the 5th minute			
Mean (standard deviation)	8.7 (1.1)	8.7 (1.0)	
Median (interquartile range)	9.0 (0)	9.0 (0)	0.72
Census tract median income (quartiles)			
Quartile1 (lowest)	328 (27.84)	689 (21.77)	
Quartile2	336 (28.52)	911 (28.78)	
Quartile3	254 (21.56)	746 (23.57)	< **0.0001**
Quartile4 [highest] (ref)	237 (20.12)	780 (24.64)	
Missing	23 (1.95)	39 (1.23)	
Diagnosis of autism spectrum disorder in the records			
Yes	869 (73.77)	2046 (64.64)	
No (ref)	309 (26.23)	1119 (35.36)	< **0.0001**
Developmental regression			

(*continued on next page*)

Table 1 (*continued*)

Variable	Self-injurious behaviors Yes (n = 1178)	Self-injurious behaviors No (n = 3165)	P-value
Yes	369 (31.32)	724 (22.88)	
No (ref)	809 (68.68)	2441 (77.12)	< **0.0001**
Adaptive behaviors skills			
Delayed (score < 70)	491 (41.68)	1096 (34.63)	
Not delayed (score > =70 (ref)	233 (19.78)	640 (20.22)	< **0.0001**
Missing	454 (38.54)	1429 (45.15)	
Intelligence Quotient			
Delayed (score < 70)	399 (33.87)	875 (27.65)	
Not delayed [score > =70] (ref)	476 (40.41)	1517 (47.93)	< **0.0001**
Missing	303 (25.72)	773 (24.42)	
Aggression			
Yes	823 (69.86)	1334 (42.15)	< **0.0001**
No (ref)	355 (30.14)	1831 (57.85)	
Argumentative behaviors			
Yes	904 (76.74)	1916 (60.54)	
No (ref)	274 (23.26)	1249 (39.46)	< **0.0001**
Temper tantrums			
Yes	864 (73.34)	1481 (46.79)	
No (ref)	314 (26.66)	1684 (53.21)	< **0.0001**
Sensory problems			
Yes	312 (26.49)	575 (18.17)	
No (ref)	866 (73.51)	2590 (81.83)	< **0.0001**
Sleep problems			
Yes	469 (39.81)	736 (23.25)	
No (ref)	564 (47.88)	2065 (65.24)	< **0.0001**
Missing	145 (12.31)	364 (11.50)	
Associated developmental diagnoses**			
Yes	542 (46.01)	1332 (42.09)	
No (ref)	636 (53.99)	1833 (57.91)	**0.02**
Associated psychiatric diagnoses**			
Yes	92 (7.81)	117 (3.70)	
No (ref)	1086 (92.19)	3048 (96.30)	< **0.0001**
Associated neurologic diagnoses**			
Yes	98 (8.32)	247 (7.80)	
No (ref)	1080 (91.68)	2918 (92.20)	0.58
Associated genetic diagnoses**			
Yes	5 (0.42)	15 (0.47)	
No (ref)	1173 (99.58)	3150 (99.53	0.83

All the bolded p-values are significant at < 0.05.
The 14 sites below were included in these analyses: Alabama, Arkansas, Arizona, Florida, Georgia, Maryland, Missouri, New Jersey, North Carolina, Pennsylvania, South Carolina, Utah, West Virginia, and Wisconsin.** **Developmental diagnoses** (Attention-deficit hyperactivity disorder, language disorder, learning disability); **Psychiatric diagnoses** (anxiety, mood disorder, emotional disorder); **Neurologic disorders** (epilepsy, cerebral palsy, encephalopathy, vision impairment, and hearing loss); **Genetic disorders** (Down syndrome, Fragile X syndrome, Tuberous sclerosis).

4. Discussion

We found significant associations between SIB and three prenatal factors (maternal education, maternal smoking, and electronic fetal monitoring during labor). In line with findings from previous studies, various developmental, behavioral, and medical factors, were still significantly associated with SIB even after accounting for birth certificate factors (Baghdadli et al., 2003; Dimian et al., 2017; Duerden et al., 2012; McClintock et al., 2003; Richman et al., 2013; Soke et al., 2017).

To our knowledge, the association between SIB and maternal smoking in ASD has not been reported before and needs confirmation in future studies. This association may not be causative but instead due to residual confounding or chance alone. Nevertheless, other studies have reported associations between maternal smoking during pregnancy and deleterious long-term neurodevelopment outcomes in the offspring, including ASD, hyperactivity/attention problems (Han et al., 2015; Langley, Heron, Smith, & Thapar, 2012; Larsson et al., 2009; Linnet et al., 2003); anxiety and depressive symptoms (Moylan et al., 2015); impairment in executive functions (Daseking, Petermann, Tischler, & Waldmann, 2015); low IQ scores (Mortensen, Michaelsen, Sanders, & Reinisch, 2005). Some of the characteristics, such as low IQ scores, hyperactivity, have been associated with SIB in previous studies (Oliver & Richards, 2015; Richards et al., 2017; Richman et al., 2013; Soke et al., 2017). It is also possible that the association that we found reflects the direct effects of smoking or effects of other factors related to smoking. Chemicals found in cigarettes may alter neurological pathways during brain development. A review by Ross, Graham, Money, and Stanwood (2015) suggested that nicotine, and its metabolite cotinine, can bind to nicotinic acetylcholine receptors and disrupt the cholinergic system. The involvement of the cholinergic system in SIB has been described in Lesch-Nyhan syndrome (Llyod et al., 1981). In addition to nicotine, the fetus is exposed to other substances (Behnke & Smith, 2013), which may act independently or synergistically with nicotine and affect brain development (Ross et al., 2015). Further, maternal smoking may also be a marker for other risk factors, including lower educational

Table 2
Association between self-injurious behaviors and prenatal, perinatal, neonatal characteristics from birth certificates in the Autism and Developmental Disabilities Monitoring Network sites during the 2000, 2006, 2008 surveillance years.

Variable	Unadjusted OR and 95% CI*	Adjusted** OR and 95% CI*
Child sex		
Female	0.91 (0.75, 1.14)	0.88 (0.69, 1.12)
Male (ref)	1.00	1.00
Child race/ethnicity		
Non-Hispanic African American	1.04 (0.85, 1.26)	0.88 (0.67, 1.15)
Hispanic	1.03 (0.79, 1.34)	1.07 (0.78, 1.47)
Others	0.66 (0.40, 1.08)	0.75 (0.49, 1.16)
Non-Hispanic White (ref)	1.00	1.00
Maternal education		
No college degree	**1.61 (1.36, 1.91)**	**1.35 (1.10, 1.67**)
College degree or higher (ref)	1.00	1.00
Maternal marital status		
Not married	**1.53 (1.27, 1.85)**	1.12 (0.88, 1.43)
Married (ref)	1.00	1.00
Maternal smoking status before and during pregnancy		
Smoker	**1.86 (1.20, 2.47)**	**1.47 (1.09, 1.98)**
Non-smoker (ref)	1.00	1.00
Maternal age (for every 5-year decrease)***	**1.14 (1.07, 1.22)**	1.03 (0.92, 1.15)
Paternal age (for every 5-year year decrease)***	**1.08 (1.02, 1.14)**	1.04 (0.95, 1.14)
Maternal weight gain during pregnancy (for every 5 pounds decrease) ***	1.00 (0.97, 1.02)	0.99 (0.96, 1.02)
Type of pregnancy		
Multiple birth	1.23 (0.86, 1.75)	1.29 (0.83, 2.02)
Single birth (ref)	1.00	1.00
Mode of delivery		
Not vaginal	0.99 (0.85, 1.16)	0.98 (0.81, 1.19)
Vaginal (ref)	1.00	1.00
Labor complications		
Major	1.09 (0.83, 1.44)	1.06 (0.79, 1.42)
Minor	1.22 (0.97, 1.53)	1.22 (0.94, 1.58)
Others	1.14 (0.89, 1.46)	1.01 (0.77, 1.33)
None (ref)	1.00	1.00
Obstetric procedures		
Electronic fetal monitoring	**1.92 (1.20, 3.08)**	**1.70 (1.02, 2.84)**
Ultrasound	**1.68 (1.08, 2.80)**	1.28 (0.80, 2.06)
Others	**1.66 (1.07, 2.56)**	1.27 (0.75, 2.13)
None (ref)	1.00	1.00
Gestational age (every decrease in 4 weeks) ***	1.09 (0.97, 1.21)	0.98 (0.80, 1.19)
Child birth weight (every decrease in 1 kilogram)***	1.10 (0.99, 1.23)	1.09 (0.90, 1.31)
Apgar score (for every decrease in 1 unit)**	1.01 (0.94, 1.09)	1.04 (0.94, 1.15)

*CI; Confidence interval; ** adjusted for census tract median income, diagnosis of autism spectrum disorder in the child's records, developmental regression, adaptive behaviors skills, Intelligence Quotient, aggression, argumentative behaviors, temper tantrums, sensory and sleep problems, associated developmental diagnoses, associated psychiatric diagnoses, associated neurologic diagnoses, associated genetic diagnoses *** Assessed the effect of decreasing scores.

attainment, alcohol or illicit drug abuse, poor coping skills, or lower family income, which may limit child's access to specialized ASD interventions that can affect SIB occurrence (Ebrahim & Gfroerer, 2003; Maxson, Edwards, Ingram, & Miranda, 2012; Weaver, Campbell, Mermelstein, & Waksclag, 2008; Yu, Park, & Schwalberg, 2002). Except for maternal education, we could not adjust for other aforementioned factors in this study. Studies that may able to tease out the effects of maternal smoking from those of alcohol or illicit drugs are needed.

The association between electronic fetal monitoring during labor and SIB may be due to chance alone and requires replication by others. It is also possible that electronic fetal monitoring during labor may be a proxy for perinatal complications that affect brain development. While we did adjust for obstetric complications, other complications not measured or not reported on the birth certificate, e.g., congenital malformations that may affect brain development were not included in these analyses. A true association is also possible; the effect of perinatal complications on behavior problems have also been reported in attention-deficit hyperactivity disorder (Ben Amor et al., 2004).

We found SIB in children with ASD to be more likely if the mother lacked a college degree. In families of children with ASD, maternal low education attainment has been associated with limited access to interventions, maternal engagement in unhealthy behaviors including smoking and substance abuse, a lower level of health literacy, and differences in reporting of child behaviors (Mathews, 2001; Moody et al., 2017; Rosenberg et al., 2018). All these factors or other unmeasured characteristics associated with maternal low educational attainment may explain this association with SIB. Similar to other researchers (Smedberg, Lupattelli, Mardby, & Nordeng, 2014; Varner et al., 2014), we confirmed an association between lower education level and high smoking prevalence in our study.

Table 3
Associations between self-injurious behaviors and previously-reported risk factors in Autism and Developmental Disabilities Monitoring sites during the 2000, 2006, and 2008 surveillance years.

Variable	Unadjusted OR and 95% CI*	Adjusted OR** and 95% CI*
Census tract median income (quartiles)		
Quartile1 (lowest)	1.57 (0.74, 1.20)	1.03 (0.76, 1.39)
Quartile2	1.21 (0.97, 1.51)	0.90 (0.69, 1.17)
Quartile3	1.12 (0.88, 1.42)	0.96 (0.74, 1.25)
Quartile4 [highest] (ref)	1.00	1.00
Diagnosis of autism spectrum disorder in the child's records		
Yes	**1.54 (1.29, 1.83)**	**1.35 (1.11, 1.66)**
No (ref)	1.00	1.00
Developmental regression		
Yes	**1.54 (1.29, 1.83)**	**1.37 (1.12, 1.68)**
No (ref)	1.00	1.00
Adaptive behaviors skills		
Delayed (adaptive score < 70)	**1.30 (1.00, 1.67)**	1.17 (0.96, 1.43)
Not delayed (adaptive score > =70 (ref)	1.00	1.00
Intelligence Quotient		
Delayed (score < 70)	**1.44 (1.22, 1.70)**	**1.34 (1.10, 1.63)**
Not delayed [score > =70] (ref)	1.00	1.00
Aggression		
Yes	**3.18 ((2.70, 3.75)**	**2.15 (1.77, 2.61)**
No (ref)	1.00	1.00
Argumentative behaviors		
Yes	**2.15 (1.80, 2.56)**	**1.24 (1.01, 1.54)**
No (ref)	1.00	1.00
Temper tantrums		
Yes	**3.13 (2.64, 3.71)**	**2.19 (1.80, 2.66)**
No (ref)	1.00	1.00
Sensory problems		
Yes	**1.62 (1.35, 1.95)**	**1.35 (1.10, 1.67)**
No (ref)	1.00	1.00
Sleep problems		
Yes	**2.29 (1.93, 2.72)**	**1.61 (1.33, 1.94)**
No (ref)	1.00	1.00
Associated developmental diagnoses***		
Yes	**1.17 (1.00, 1.37)**	**1.21 (1.00, 1.47)**
No (ref)	1.00	1.00
Associated psychiatric diagnoses***		
Yes	**2.21 (1.59, 3.06)**	**1.77 (1.21, 2.59)**
No (ref)	1.00	1.00
Associated neurologic diagnoses***		
Yes	1.07 (0.81, 1.42)	1.12 (0.79, 1.58)
No (ref)	1.00	1.00
Associated genetic diagnoses***		
Yes	1.49 (0.73, 3.02)	1.47 (0.64, 3.40)
No (ref)	1.00	1.00

†CI: confidence interval; * Adjusted for child sex, race/ethnicity, maternal education, maternal marital status, maternal age, paternal age, maternal weight gain during pregnancy, type of pregnancy, mode of delivery, labor complications, obstetric procedures, gestational age, child birth weight, and child Apgar score. *** **Developmental diagnoses** (Attention-deficit hyperactivity disorder, language disorder, learning disability); **Psychiatric diagnoses** (anxiety, mood disorder, emotional disorder); **Neurologic disorders** (epilepsy, cerebral palsy, encephalopathy, vision impairment, and hearing loss); **Genetic disorders** (Down syndrome, Fragile X syndrome, Tuberous sclerosis).

In line with previous studies (e.g., Carroll et al., 2014; Duerden et al., 2012; Goldman et al., 2011; Richards et al., 2017; Richman et al., 2013; Soke et al., 2017), SIB were associated with developmental regression, lower IQ, aggressive behaviors, sensory and sleep problems, and temper tantrums even after adjusting for prenatal, perinatal, and neonatal factors. These results highlight a number of behavioral and developmental characteristics associated with SIB. The consistency of our findings with those previously reported support the validity of these associations. Therefore, these findings have relevance for screening and management of SIB in ASD.

To our knowledge, this is the first study to examine associations between SIB and various prenatal, perinatal, and neonatal factors in birth certificates using a large population-based sample. Since these factors were assessed before SIB occurrence, it was possible to establish a temporal relationship between these factors and SIB. Furthermore, the use of multiple imputation provided more precise estimates. Despite these strengths, this study has some limitations. Although we used a detailed SIB definition, the characterization of SIB (yes/no) does not provide details on the type or severity of SIB. Further, assessing lifetime (ever) occurrence of SIB could have resulted in over reporting of SIB by including transient SIB. Maternal smoking may be subject to under-reporting on birth certificates (England et al., 2007). However, Howland et al. (2015) found good agreements between birth certificate smoking data and maternal worksheets and medical records. Other variables of interest such as family history of ASD or the presence of other psychiatric

diagnoses in the family were not available. Despite the use of multiple imputation, we cannot completely discount the effect of missing data in our analysis. However, our findings were quite similar before and after multiple imputation. Some of our findings may be due to chance alone as we did not adjust for multiple comparisons to avoid the possibility of introducing a type II error in this exploratory study (Greenland, 2008). It should also be noted that ADDM sites are not selected to be a representative sample of children with ASD, thus caution is required when generalizing these findings to locales not included in this study.

This study found significant associations between SIB and lower maternal educational attainment, maternal smoking, and the use of electronic fetal monitoring during labor. In addition, this study confirmed previously documented behavioral, medical and developmental associations after controlling for birth certificate variables. Since SIB have a tendency to persist in to adolescence and adulthood, confirmation of previously reported associations suggests that clinicians may consider assessing children with SIB for related factors, such as sleep and sensory problems, and provide appropriate interventions. Finally, there is a need for additional studies that include details on the type and severity of SIB in children with ASD and assess other factors not examined in this study, including maternal psychiatric comorbidities.

Compliance with ethical standards

All procedures performed in studies involving human participants were in accordance with ethical standards of the institutional and /or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This study is a secondary data analysis of de-identified data previously collected in a surveillance system. Therefore, formal written consent is not required. All authors report no conflicts of interests.

Disclaimer

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

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A version of this work was presented at the 2015 Society for Epidemiology Research meeting in Denver, Colorado and was part of Dr. Soke's doctoral dissertation.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.rasd.2019.01.007.

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