Journal of Pediatric Nursing 35 (2017) 113–119

Contents lists available at ScienceDirect

Journal of Pediatric Nursing

Predictors of Co-occurring Neurodevelopmental Disabilities in Children With Autism Spectrum Disorders

Lauren Head Zauche, MS, BSN, RN [a,*], Ashley E. Darcy Mahoney, PhD, NNP-BC, FAAN [b], Melinda K. Higgins, PhD [a]

[a] Emory University Nell Hodgson Woodruff School of Nursing, 1520 Clifton Rd NE, Atlanta, GA 30322, United States
[b] George Washington University, Autism and Neurodevelopmental Disorders Institute, 2121 Eye Street NW, Washington, D.C. 20052, United States

ARTICLE INFO

Article history:
Received 7 September 2016
Revised 30 March 2017
Accepted 5 April 2017
Available online xxxx

ABSTRACT

Purpose: Co-occurring neurodevelopmental disabilities (including cognitive and language delays and attention deficit hyperactivity disorder) affect over half of children with ASD and may affect later behavioral, language, and cognitive outcomes beyond the ASD diagnosis. However, no studies have examined predictors of co-occurring neurodevelopmental disabilities in children with ASD. This study investigated whether maternal sociodemographic, perinatal and neonatal factors are associated with co-occurring disabilities.
Design and Methods: This study involved a retrospective analysis of medical records for children diagnosed with ASD between 2009 and 2010 at an Autism Center in the southeast United States. Logistic regression was used to identify predictors of co-occurring neurodevelopmental disabilities.
Results: Of the 385 children in the sample, 61% had a co-occurring neurodevelopmental disability. Children whose mothers had less education (OR: 0.905), had never been married (OR: 1.803), or had bleeding during pregnancy (OR: 2.233) were more likely to have a co-occurring neurodevelopmental disability. Both preterm birth and African American race were associated with bleeding during pregnancy.
Conclusions: Several maternal and perinatal risk factors for ASD were found to put children at risk for further diagnoses of co-occurring neurodevelopmental disabilities. While prematurity, a well-established risk factor for ASD, as well as maternal ethnicity was not found to increase the risk of a co-occurring disability, this study suggests that bleeding during pregnancy may moderate these relationships.
Practice Implications: Understanding maternal, perinatal, and neonatal risk factors may inform healthcare provider screening for ASD and co-occurring neurodevelopmental disabilities by helping providers recognize infants who present with multiple risk factors.

Introduction

Autism spectrum disorder (ASD) is the most common neurodevelopmental disability and affects one out of every 68 children (Centers for Disease Control and Prevention, 2014). ASD is characterized by deficits in social communication and interaction and by restricted, repetitive patterns of behaviors that begin in infancy or early childhood (American Psychiatric Association, 2013). Other co-occurring neurodevelopmental disabilities, including language delays, attention deficit hyperactivity disorder (ADHD), and cognitive delays, are highly prevalent in children with ASD (Levy et al., 2010). Data from the Autism and Developmental Disabilities Monitoring (ADDM) Network, an ongoing, population-based public health surveillance established by the Centers for Disease Control and Prevention at 13 sites across the United States, demonstrate that 63% of children with ASD have language delays, 21% have attention deficit hyperactivity disorder (ADHD), and 18% have cognitive delays (Levy et al., 2010). The prevalence of language delays, ADHD, and cognitive delays in children with ASD are much higher than in the general population with prevalence estimates of 3–7%, 4–11%, and 2–4% respectively (Boyle et al., 2011; Brown et al., 2001). Although language delays, ADHD, and cognitive delays share symptoms with ASD, they are disorders separate from ASD that are accorded a distinct set of criteria in the American Psychiatric Association's Diagnostic and Statistical Manual, 5th Edition (DSM-5) (American Psychiatric Association, 2013; Levy et al., 2010). These disabilities are referred to as "co-occurring" neurodevelopmental disabilities; this term indicates disabilities separate from ASD and does not imply a temporal or causal relationship with ASD.

Criteria for language delays, ADHD, and cognitive delays are set by the American Psychiatric Association's and are outlined in the DSM-5. A language delay is defined as persistent difficulty in the acquisition or use of language because of deficits in comprehension and/or production of language below the expected functional ability for the child's age (American Psychiatric Association, 2000). These deficits result in functional limitations in social and/or communication skills and cannot be

* Corresponding author.
E-mail address: lmhead@emory.edu (L.H. Zauche).

http://dx.doi.org/10.1016/j.pedn.2017.04.002
0882-5963/

attributed to impairments in sensory or motor function or explained by any other neurological or medical condition. Similarly, a cognitive delay is defined as deficits in intellectual functioning, such as reasoning, problem solving, and abstract thinking, by scoring two standard deviations below the population mean that are related to deficits in adaptive functioning as well. To meet criteria for a cognitive delay, these deficits must result in impairments in a person's daily activities across multiple settings. Like a language delay, the cognitive delay cannot be explained by any neurological or medical condition. Criteria for ADHD includes six or more symptoms of inattention or hyperactivity-impulsivity for at least six months that impair social, academic, or occupational functioning in two or more settings (American Psychiatric Association, 2000).

Etiology of ASD

Recent work in the field of autism research has investigated the etiology of ASD, which is thought to involve a strong genetic component as well as the interaction of genes and environmental factors (Buchmayer et al., 2009; Maramara, He, & Ming, 2014). While the neuropathology of ASD remains unknown, studies have identified neuroanatomical and biochemical brain differences in children with ASD that may have originated during the prenatal period (Brimacombe, Ming, & Lamendola, 2007). A growing body of research has demonstrated that perinatal, obstetrical, and neonatal complications are implicated in the risk for ASD (Gardener, Spiegelman, & Buka, 2009; Larsson et al., 2005). Two meta-analyses investigating prenatal, perinatal, and neonatal characteristics or complications demonstrated that advanced parental age at birth, bleeding during pregnancy, gestational diabetes, prematurity, and Caesarean sections were all associated with increased risks for ASD (Gardener, Spiegelman, & Buka, 2011). Other studies have pointed to maternal smoking, hypertension and infection during pregnancy, cohabitation of the mother, and low maternal education as risk factors for ASD, although results have not been consistent (Buchmayer et al., 2009; Frenette et al., 2013; Mahoney, Minter, Burch, & Stapel-Wax, 2013; Mandell, Novak, & Zubritsky, 2005; Schendel & Bhasin, 2008; Walker et al., 2015). While minority race and ethnicity have not been found to be risk factors for ASD per se, they are risk factors for delayed ASD diagnosis, leading to more severe ASD when the diagnosis is eventually obtained (Mandell et al., 2005).

Research on mechanisms that explain the relationship between gestational conditions or obstetrical complications and the neuropathology of ASD is lacking, but theoretical explanations have been postulated. During pregnancy, the fetal brain is vulnerable to environmental insults, such as prematurity or fetal hypoxia. Brain tissue is particularly sensitive to disturbances in cell energy metabolism, which can be caused by hypoxia or impaired gas exchange and may contribute to the activation of an inflammatory immune response (Erdei & Dammann, 2014; Gardener et al., 2011; Gonzalez & Miller, 2006). Both the disturbance in cell energy metabolism and the inflammatory response may lead to alterations in the development or loss of the already developed neuronal connections (Erdei & Dammann, 2014; Gardener et al., 2011; Gonzalez & Miller, 2006). Regions of the brain that are especially vulnerable to these insults include the basal ganglia, hippocampus, lateral ventricles, prefrontal cortex, and the thalamus (Gunn & Bennet, 2009; Piven et al., 1995). Neuroimaging studies have demonstrated larger lateral ventricles and hippocampal morphological abnormalities in children with ASD compared to controls (Eiliam-Stock, Wu, Spagna, Egan, & Fan, 2016; Piven et al., 1995; Ecker, Bookheimer, & Murphy, 2015). Furthermore, studies have found that children with ASD have reduced connectivity between the thalamus and the prefrontal cortex, which may be related to impaired sensory processing in children with ASD (Toulmin et al., 2015). Fetal hypoxia also has been shown to result in an increase in dopaminergic activity, and children with ASD have been shown to have over-activation of dopaminergic circuits (Gardener et al., 2009; Previc, 2007). Additionally, several studies have demonstrated that many regions of the brain that are affected in children with ASD are also affected in children born preterm, including volume reduction in the corpus collosum, decreased brain density, and less connectivity in white matter (Chen, Jiao, & Herskovitis, 2011; Padilla et al., 2015). Thus, it appears mechanisms contributing to the neuropathology of ASD may be related to perinatal complications that disrupt the normal neurodevelopmental trajectory of the infant.

Complications in pregnancy, such as bleeding, hypertension, cord abnormalities, placental insufficiency, gestational diabetes, or smoking, may all directly interfere with adequate nutrient and gas exchange and increase the risk for fetal hypoxia (Gardener et al., 2009; Krakowiak et al., 2012). In addition to these complications, previous studies have reported that caesarean delivery and maternal age above 30 are associated with an increased risk for ASD (Bilder, Pinborough-Zimmerman, Miller, & McMahon, 2009; Brimacombe et al., 2007; Gardener et al., 2009). Maternal age may increase the risk of ASD due to older mothers having a higher risk for uterine muscle dysfunction, diminished blood supply, obstetric complications, and nucleotide repeat instability (Kaytor, Burright, Duvick, Zoghbi, & Orr, 1997; Kolevzon, Gross, & Reichenberg, 2007; Zhang et al., 2002). Although Caesarean sections have been found to be associated with ASD, this relationship may be confounded by the indications for the Caesarean, which may relate to other conditions associated with an increased risk of ASD (Brimacombe et al., 2007; Hultman, Sparen, & Cnattingius, 2002). While these conditions or complications can be associated with fetal hypoxia, it is uncertain as to whether fetal hypoxia is the specific mechanism by which these risk factors influence the development of ASD.

Risk Factors for Language Delays, ADHD, and Cognitive Delays

Although the pathology of ASD varies from other neurodevelopmental disabilities, it is possible that risk factors for ASD could also predispose children to other neurodevelopmental disabilities (Barbaro & Dissanayake, 2010; Chawarska, Macari, & Shic, 2013; Deconinck, Soncarrieu, & Dan, 2013; Zwaigenbaum, Bryson, & Garon, 2013). Like ASD, pre- and perinatal risk factors along with sociodemographics have been implicated in the etiology of other neurodevelopmental disabilities. Maternal obesity, gestational diabetes, preeclampsia, placental insufficiency, low levels of maternal education, low maternal age, minority racial or ethnic group, and prematurity are all associated with an increased risk of language delays, ADHD, and cognitive delays (Krakowiak et al., 2012; Oerlemans et al., 2016; Sucksdorff et al., 2015; Williams et al., 2013). Therefore, there is some overlap in risk factors for both ASD and other neurodevelopmental disabilities, independently of each other. However, risk factors for ASD and other neurodevelopmental disabilities have been studied mostly in isolation and little is known about how these risk factors play a role in the shared etiology of ASD and co-occurring neurodevelopmental disabilities.

Purpose of Study

Neurodevelopmental disabilities that co-occur with ASD have effects on outcomes beyond those effects associated with ASD. Consideration of co-occurring disabilities should influence treatment plans and goals. Identifying factors related to co-occurring neurodevelopmental disabilities may help target interventions and identify children with these disabilities. However, no studies have examined predictors of co-occurring neurodevelopmental disabilities in children with ASD. The purpose of this study was to determine whether maternal factors, perinatal or obstetrical complications, or neonatal birth characteristics affect the diagnosis of a co-occurring neurodevelopmental disability (language delay, ADHD, or cognitive delay) in children with ASD. We hypothesized that factors associated with the diagnosis of ASD, including maternal education, maternal age, bleeding during pregnancy, gestational diabetes, and gestational age, would be predictors of a co-occurring neurodevelopmental disability.