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Attention deficit hyperactivity disorder and autism spectrum disorder symptoms in school-age children born very preterm

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ABSTRACT

Background: Very preterm (VP) children face a broad range of neurodevelopmental sequelae, including behavioral problems.
Aim: To investigate prevalence, pervasiveness and co-occurrence of symptoms of attention deficit hyperactivity disorder (ADHD) and autism spectrum disorder (ASD) in school-age children born very preterm.
Methods: Using questionnaire and diagnostic interview data, parent and teacher reported symptoms of ADHD and ASD of 57 VP-children (mean age = 9.2 years) were compared with 57 gender and age matched full-term children using *t*-tests. Intra-class correlation coefficients quantified parent-teacher agreement. Correlation analysis investigated co-occurrence of ADHD/ASD symptoms. ADHD/ASD measures were aggregated using principal component analysis. Regression analyses investigated the contribution of perinatal risk factors, sex and SES to ADHD/ASD symptoms.
Results: VP-children showed higher levels of parent and teacher reported attention problems, social impairment and compromised communication skills. Fair to strong agreement was found between parent and teacher reported ADHD and ASD symptoms, indicating pervasiveness of observed difficulties. Co-occurrence of ADHD and ASD symptoms in VP-children was found. Lower gestational age was associated with higher ADHD and ASD symptom levels, male sex with higher ADHD symptom levels and lower SES with higher ASD symptom levels.
Conclusion: School-age VP-children show higher levels of ADHD and ASD symptoms, and attention, socialization and communication difficulties in particular. Routinely screening for these problems is recommended in follow-up care.

What this paper adds?

Present findings underline the necessity to map out symptoms of both ADHD and ASD in very preterm children, and attention, socialization and communication difficulties in particular. Results also show that ADHD and ASD symptoms frequently co-occur and

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manifest both in the home and school environment, which should be taken into account in the follow-up care of very preterm children.

1. Introduction

Advances in perinatal and neonatal intensive care have markedly increased survival rates of very preterm infants (< 32 weeks of gestation). Unfortunately, a growing number of the surviving very preterm children struggles with neurodevelopmental problems and behavioral impairments (Aarnoudse-Moens, Weisglas-Kuperus, Van Goudoever, & Oosterlaan, 2009; Arpi & Ferrari, 2013; Johnson & Marlow, 2011). In particular, symptoms of attention deficit hyperactivity disorder (ADHD) and autism spectrum disorders (ASD), are often observed in very preterm children (Breeman, Jaekel, Baumann, Bartmann, & Wolke, 2015; Jaekel, Wolke, & Bartmann, 2013; Treyvaud et al., 2013).

Very preterm children have a two to three-fold risk of developing ADHD at school-age and show higher rates of symptoms of ADHD than full-term children (Aylward, 2014; Bhutta, Cleves, Casey, Cradock, & Anand, 2002; Johnson & Marlow, 2011). The inattentive type of ADHD is the most common subtype in very preterm children (Breeman et al., 2015; Jaekel et al., 2013; Johnson & Marlow, 2011). School-age very and extremely (< 28 weeks of gestation) preterm children also show higher levels of ASD symptoms than full-term children (Fevang, Hysing, Markestad, & Sommerfelt, 2016; Hack et al., 2009; Treyvaud et al., 2013), as well as higher rates of ASD diagnoses (5–9%) (Johnson et al., 2010a; Kuban et al., 2016) in comparison to the general population (0.6%) (Fombonne, 2009). A growing body of evidence suggests that ADHD and ASD may have different clinical expressions in very preterm children than in full-term children, described as the “preterm behavioral phenotype” (Jaekel et al., 2013; Johnson & Marlow, 2011; Verhaeghe et al., 2016). In very preterm children, ADHD symptoms could be core attention problems with a neuropathological etiology related to the effects of preterm birth, whereas ASD symptoms may reflect primarily socialization difficulties (Jaekel et al., 2013; Johnson & Marlow, 2011). Multiple studies acknowledge this neuropathological etiology by showing that ADHD and ASD symptoms in preterms are not only inversely related to gestational age (GA) and to birth weight, but are also associated with early brain damage in both white and grey matter (Bora, Pritchard, Chen, Inder, & Woodward, 2014; Limperopoulos et al., 2008; Schendel & Bhasin, 2008; Sucksdorff et al., 2015) due to inflammation and hypoxia-ischemia (Volpe, 2009). However, evidence on the impact of GA on the development of ADHD and ASD is still inconsistent (Gardener, Spiegelman, & Buka, 2011; Wang, Geng, Liu, & Zhang, 2017). Also, precursors of brain abnormalities, including periventricular leukomalacia (PVL) and neonatal infections in very preterm children are inconsistently associated with ADHD and ASD symptoms (Anderson et al., 2011; Hack et al., 2009; Hagberg, Gressens, & Mallard, 2012; Rand, Austin, Inder, Bora, & Woodward, 2016; van der Ree et al., 2011) and in need of further exploration.

ADHD and ASD symptoms frequently co-occur both in the general population and in patients with ADHD and patients with ASD (Leitner, Berger, Di Martino, & York, 2014; Visser, Rommelse, Greven, & Buitelaar, 2016). Visser et al. (2016) suggest that attention problems form the linking factor between ADHD and ASD and the developmental pathway to both disorders. Therefore, it is important to study symptoms of ADHD and ASD in concert. However, studies that included both ADHD and ASD measures in preterms are scarce, and those studies that did, focused on ADHD or ASD diagnoses, not on symptoms, which would provide a more fine grained measure of the problems related to the two disorders (Fevang et al., 2016; Hack et al., 2009; Indredavik et al., 2004; Johnson et al., 2010b; Treyvaud et al., 2013).

Children with the “preterm behavioral phenotype” may not show more problems on all symptom dimensions and therefore may fail to meet criteria for a full diagnosis of ADHD or ASD, yet the impact on daily functioning may be distinct (Brogan et al., 2014; Johnson & Marlow, 2011). Even if children qualify for an ADHD or ASD diagnosis, this may not fully capture the whole clinical presentation (Yaari et al., 2016). Additionally, the degree of pervasiveness of ADHD and ASD symptoms across settings is of clinical importance and can be established with parent and teacher report (Möricke, Buitelaar, & Rommelse, 2016; Wolraich et al., 2004). Yet, many studies rely exclusively on parent reported symptoms (Breeman et al., 2015; Elgen, Sommerfelt, Leversen, & Markestad, 2015; Pinto-Martin et al., 2011; Verhaeghe et al., 2016; Wong, Huertas-Ceballos, Cowan, & Modi, 2014), with only a handful of studies including additional teacher reports (Brogan et al., 2014; Fevang et al., 2016; Johnson et al., 2010b; Treyvaud et al., 2013). Moreover, a great variety of assessment methods has been used to study ADHD and ASD in very and extremely preterm children. Most studies have used questionnaires allowing informants to provide dimensional symptom ratings of ADHD and ASD (Brogan et al., 2014; Dudova et al., 2014; Elgen et al., 2015; Fevang et al., 2016; Wong et al., 2014). Only a few studies have employed a combination of questionnaires and diagnostic classification methods, with the use of standardized psychiatric interviews to assess ADHD (Breeman et al., 2015; Jaekel et al., 2013; Johnson et al., 2010b) or comprehensive observational measures to diagnose ASD (Pinto-Martin et al., 2011; Pritchard et al., 2016; Verhaeghe et al., 2016). Including both diagnostic classification methods and dimensional measures is needed to assess both the presence or absence of the disorder of ADHD and ASD as well as the symptom severity of both disorders.

This current study adds to the body of knowledge by 1) comparing ADHD and ASD symptom levels in very preterm and full-term school-age children using both parent and teacher reported questionnaires and a diagnostic interview; 2) assessing co-occurrence of ADHD and ASD symptoms; 3) investigating pervasiveness of ADHD and ASD symptoms by assessing parent-teacher agreement. In addition, associations between ADHD and ASD symptoms and GA, neonatal infections, PVL, socio-economic status (SES) and sex in very preterm children are investigated.