Title: Association of Gestational Age at Birth with Symptoms of Attention-Deficit/Hyperactivity Disorder in Children and Adolescents with Down Syndrome

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Introduction: Attention-Deficit/Hyperactivity Disorder (ADHD) symptoms are frequently reported in individuals with Down syndrome (DS) (Oxelgren et al., 2017), with up to a 40% meeting diagnostic criteria (Ekstein, Glick, Weill, Kay, & Berger, 2011). Considering the variation in ADHD symptoms in this population, a key challenge is to identify mechanisms underlying this variability. The association between prematurity and ADHD is well established in the euploid population. Indeed, it has been shown that even late preterm children score higher on ADHD symptoms compared to children born at gestational week 40 or later (Ask et al., 2018; Sucksdorff et al., 2015). However, the impact that a low gestational age has on later ADHD is unknown for those with DS, and potentially has implications for targeted early intervention. The current study was designed to investigate the association between gestational age (GA) at birth and symptoms of ADHD in 106 children and adolescents with DS while adjusting for confounder factors such as chronological age CA, sex, and IQ.

Method: 106 individuals with DS (50 males and 56 females) between the ages of 6 and 18 years at evaluation (mean CA=10.7 years, SD= 3.4) were included in the current study. Participants were drawn from the Down Syndrome Cognition Project. This study had an exclusion criterion of gestational age less than 35 weeks, as well as other exclusion criteria associated with birth trauma. Symptoms of ADHD were assessed using the Conners Parent Rating Scale, Third Edition (Conners-3) (Conners, 2008), which reflects criteria for ADHD in the DSM-IV (Achenbach, Dumenci, & Rescorla, 2003). For the analyses, we used T-scores for the Inattentive and the Hyperactive-Impulsive subscales, as well as the Global Index T-score. IQ was assessed using the Kaufman Brief Intelligence Test, 2nd Edition (KBIT-2; Kaufman & Kaufman, 2004). Data regarding pregnancy history was obtained through medical records and a phone interview. Prior to examining the independent variable of interest (GA), we examined the association of the following covariates with each of our dependent variables (i.e., ADHD outcomes on the Conners-3): age at testing (continuous), sex of the participant (female, male) and IQ (≤40, > 40). We then used multiple regression models to examine the effect of GA on ADHD symptoms, while adjusting for those covariates that were significantly associated with any of our dependent variables.

Results: CA at testing was inversely related to the Inattentive and Hyperactive-Impulsive subscales, as well as to the Global Index T-score from the Conners-3 (p<0.03). However, IQ and sex were not related to any of the ADHD outcomes. Multiple regression models showed that lower gestational age at birth was associated with higher T-scores for the Inattentive subscale (p=0.04, β=-0.19), the Hyperactive-Impulsive subscale (p=0.03, β=-0.21), and the Global Index (p=0.01, β=-0.24).

Discussion: Our results are similar to those previously reported in the euploid population, suggesting that lower gestational age may increase ADHD symptoms in children and adolescents with DS. Although much remains to be explored, our findings indicate that variation in gestational age should be addressed when considering ADHD outcomes in children and adolescents with DS. Doing so may guide early behavioral interventions to optimize neurodevelopmental outcomes in this population. Implications of our results will be further discussed.

References:


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