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Objective assessment of ADHD core symptoms in children with heavy prenatal alcohol exposure

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HIGHLIGHTS

- Inattention is a core deficit in children prenatally exposed to alcohol.
- Findings are consistent with parent reports of hyperactivity in children with FASD.
- Concurrent measurement of ADHD symptoms may offer a more complete assessment of FASD.

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ABSTRACT

Attention deficits are often observed in children with prenatal alcohol exposure and attention-deficit/hyperactivity disorder (ADHD) is commonly diagnosed in this population. This study used an objective assessment tool to examine differences between alcohol-exposed and non-exposed children on core symptoms of ADHD: inattention, impulsivity, and hyperactivity. Two groups of individuals, aged 7–14 years, participated in the study: alcohol-exposed children (AE, $n = 43$), and non-exposed children (CON, $n = 54$). Subjects were evaluated with the Quotient ADHD System, which provides objective data on ADHD core symptoms by combining an infrared motion tracking system and a computerized continuous performance task. Twelve separate ANCOVAs controlling for the effects of age and sex, were conducted on attention and motion variables. Results revealed that in comparison to the CON group, the AE group was significantly (p's $< .05$) less accurate, made an increased number of omission errors, had longer response latencies, and increased variability in response time. Moreover, the AE group spent less time staying still, and made an increased number of head movements, which traveled a larger distance, covered a greater area, and demonstrated a less complex movement pattern. No significant group differences were observed on the number of commission errors and temporal scaling. Our findings provide further support for the notion that inattention is a core deficit in children prenatally exposed to alcohol. Results from this study are also consistent with parent reports of increased hyperactivity. The Quotient ADHD System may be a useful objective measure of ADHD symptomatology in children with FASD.

1. Introduction

The most widely known outcome of heavy prenatal alcohol exposure is the fetal alcohol syndrome (FAS), which is characterized by a unique pattern of facial dysmorphia, pre- and/or post-natal growth deficiency, and central nervous system (CNS) dysfunction [1,2]. Since FAS was first identified over 40 years ago, it has become increasingly apparent that individuals with histories of prenatal alcohol exposure, with or without a diagnosis of FAS, demonstrate qualitatively similar cognitive and behavioral impairments. This suggests that CNS dysfunction may be a better indicator of alcohol exposure than facial dysmorphia and growth deficiency [3]. Fetal alcohol spectrum disorders (FASD) encompass the full range of physical, cognitive, and behavioral outcomes associated with prenatal alcohol exposure [4].

Although neuropsychological studies have demonstrated deficits associated with prenatal alcohol exposure across a wide range of cognitive and behavioral domains (for review, see [5]), attention deficits are thought to be a hallmark characteristic in children with histories of prenatal alcohol exposure [6,7]. Alcohol-exposed children are also more likely to be described as hyperactive (e.g., [8–10]). Therefore it is not surprising that many children with histories of heavy prenatal alcohol

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exposure have a co-occurring diagnosis of attention-deficit/hyperactivity disorder (ADHD) [11,12].

Several studies have reported that children with FASD have attention deficits when assessed with objective measures such as continuous performance tests (CPTs) [6,8,13–15]. However, objective measurements of hyperactivity in children prenatally exposed to alcohol are limited. To the best of our knowledge only one study has objectively measured hyperactivity in FASD [8]. This study examined the correspondence of parent report and laboratory measures of inattention (CPT) and hyperactivity (non-dominant wrist actigraphy) in children prenatally exposed to alcohol, non-exposed children with ADHD, and non-exposed controls. Non-exposed children with ADHD were found to be hyperactive based on both parent reports and laboratory-measured actigraphy. However, parent ratings and objective measures were discordant for the FASD group. While parents indicated that children with FASD were hyperactive, the laboratory test found similar activity levels in the FASD and control groups. Attention deficits and hyperactivity have also been observed in animal models of FASD (e.g., [16–18]); however, findings are dependent upon numerous factors, including the pattern and timing of alcohol exposure, the age of the animal at the time of testing, and other methodological factors [19]. Given the animal findings and the parental reports of hyperactivity, further objective measurement of activity level is warranted in children with FASD.

The Quotient® ADHD System (Pearson) [20] is a tool developed to provide objective information on ADHD core symptoms of inattention, impulsivity, and hyperactivity by combining an infrared motion tracking system and a computerized CPT [21]. In one study using the Quotient ADHD System, unmedicated boys with ADHD had more attention shifts and spent less time on task than controls; these group differences were more robust than differences on a standard CPT [22]. Quotient motion variables also differ between typically developing children and those with ADHD [21]. Children with ADHD make more whole body movements in less complicated patterns, whereas movements in the control group were limited to the extremities. Using this tool, we tested children with histories of heavy prenatal alcohol exposure and age-matched non-exposed controls. Given the high rates of ADHD in children with histories of heavy prenatal alcohol exposure, we hypothesized that all three ADHD core symptoms of inattention, impulsivity, and hyperactivity will be elevated in these children in comparison to non-exposed controls.

2. Materials and methods

2.1. Subjects

Subjects were children, between the ages of 7 and 14 ($M = 11.50$, $SD = 2.20$), with confirmed histories of heavy prenatal alcohol exposure (AE, $n = 43$) and non-exposed control children (CON, $n = 54$). The data from an additional 20 subjects could not be included in the analyses due to ADHD medication during the 12-hour washout period ($n = 4$), and equipment malfunction or experimenter error ($n = 16$). Subjects were drawn from larger ongoing studies taking place at the Center for Behavioral Teratology (CBT) at San Diego State University and were recruited via several mechanisms including professional or self-referral and community outreach.

History of prenatal alcohol exposure was determined through multi-source collateral report, including review of available medical, social service, and adoption agency records or maternal report when available. Alcohol-exposed children with or without a diagnosis of FAS were included in this study. Direct maternal report was not common for children in the AE group, as many of these children no longer resided with their biological families. However, in these cases, mothers were reported by family members, adoption agencies, social workers or medical health records to be “alcoholic” or alcohol abusing or dependent during pregnancy. When maternal report was available, heavy alcohol exposure was defined as consumption of an average of at least 4 drinks per occasion or 14 drinks per week at least several times during pregnancy. Direct maternal report was available for two children (0.05%) in the AE group. A diagnosis of FAS was accepted as a de facto indication of heavy alcohol exposure. Twelve children (27.91%) in the AE group met criteria for FAS based on a dysmorphology exam (for details, see [23]). All but two of the non-exposed children resided with their biological mothers and alcohol exposure histories for these children were determined through direct maternal report. Mothers of these children reported little (less than 1 alcoholic drink per week on average and never more than 2 drinks per occasion during pregnancy), if any, alcohol use during pregnancy.

The mental health status for each child was assessed using the National Institute of Mental Health Computerized Diagnostic Interview Schedule for Children (C-DISC-IV) [24], a structured diagnostic interview administered to the child's parent or primary caregiver, and/or report of a parent or primary caregiver of a psychiatric diagnosis. Children in the CON group were excluded if they had an ADHD diagnosis by parent report or if they demonstrated clinical (6 or more) or subclinical (3–5) symptoms of ADHD on the C-DISC-IV. Thirty-five children (81%) in the AE group met criteria for ADHD, which is consistent with previous reports [11,12]. Sixteen of these children were prescribed medications often used to treat ADHD that included stimulants such as amphetamines and methylphenidates, and non-stimulant medication such as atomoxetine and guanfacine. In addition, many of these children were also being treated with other types of psychiatric medication. Exclusion criteria for all groups were: primary language other than English, head injury with loss of consciousness greater than 30 min, any known physical or psychiatric disability that would prohibit participation, or any cause of mental deficiency that would prevent successful completion of the task.

2.2. Procedure

Informed consent was obtained from the parent or legal guardian and assent from the child. Children were evaluated using the Quotient ADHD System, described below. As part of larger ongoing studies at the CBT, Full Scale IQ (FSIQ) scores were available from the Wechsler Intelligence Scale for Children, Third Edition [25] or the Wechsler Intelligence Scale for Children, Fourth Edition [26]. Parents or primary caregivers of children who met criteria for ADHD diagnosis were asked to refrain from giving prescribed medication for the treatment of ADHD to their children on the day of their testing appointment. If this washout was not possible the child was allowed to participate, but the data were excluded from the data analyses ($n = 4$). The Institutional Review Board at San Diego State University approved all procedures.

2.2.1. The Quotient ADHD System

As described above, the Quotient ADHD System captures and quantifies motor movements or activity levels in subjects while they are engaged in a computerized CPT. Duration of the test is 15 min for children under age 13 ($n = 73$), and 20 min for adolescents over age 13 ($n = 24$). For ages 14 and under, the test uses a Go/No-Go paradigm in which one of two different types of stars (8-pointed or 5-pointed) are displayed on the computer screen at random screen positions for 200 ms, with a 2-second interstimulus interval. Children are asked to respond by pressing a button on the keyboard when the target (8-pointed star) appears on the screen, while withholding responses to the non-target (5-pointed star). While subjects are engaged in the task, an infrared motion tracking system captures and records movement using the two-dimensional location of a reflective marker placed on a headband worn by the child. The system collects and records motion data at a rate of 50 times per second and with sub-millimeter accuracy. A movement (i.e., microevent) is created every time the reflector moves at least 1 mm from its current location. The trajectory as defined by the microevents is plotted and displayed in 5-minute segments. CPT attention measures and measures