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Differentiating Cognitive Deficits Between ADHD and In Utero Polysubstance Exposure

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Abstract

ADHD is the most prevalent psychiatric disorder in children, affecting their executive and overall well-being as a result (Barkley, 2014; Shaw, Gogtay, & Rapoport, 2010). A rampant increase in new diagnoses of ADHD suggests the potential for misdiagnosis. Stimulants are the first line of treatment and associated with a number of deleterious long-term consequences for those misdiagnosed (Urban & Gao, 2014a). This is of particular concern for children prenatally exposed to substances as in utero use acts on similar neural mechanisms impacted by ADHD – leaving the children vulnerable to misdiagnosis and contraindicated intervention (Derauf, Kekatpure, Neyzi, Lester, & Kosofsky, 2009; Telford, 2012). Additionally, in drug-affected brains, inappropriate treatment with stimulants results in manic episodes, irritability, and other clinical issues (Uban et. al., 2015; Hoffman, 2017). The current study aimed to parse out subtle cognitive differences between ADHD and in utero polysubstance exposure toward clarifying definitive diagnoses and proper treatment planning. Participants were from an archived database from multiple school districts. Cognitive domains from the Woodcock Johnson III and IV were compared between students with ADHD or prenatal polysubstance exposure. Fluid Reasoning most potently predicted a diagnosis of prenatal polysubstance exposure. No cognitive domain predicted a diagnosis of ADHD. Significant differences were also observed for General Intellectual Ability, Long-term Retrieval, and Comprehension Knowledge, with lower scores for those prenatally exposed. These differences suggest an emergent cognitive profile for those prenatally exposed that differs from students with an ADHD diagnosis. This information may aid clinicians in differential diagnosis and proper treatment planning.

Keywords: ADHD, prenatal, polysubstance, exposure, cognitive, deficits

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Chapter 1

Introduction

Relevance

Attention Deficit Hyperactivity Disorder (ADHD) is a highly prevalent neurodevelopmental disorder estimated to impact 3-4% of students in the United States education system (Nyarko et al., 2017; Polanczyk, Salum, Sugaya, Caye, & Rohde, 2015). As such, ADHD is the most common mental health disorder in children (Polanczyk et al., 2015). About 5-10% of minors in the United States between the ages of 6-18 have an ADHD diagnosis which is an increase of approximately 500% over the last 20-30 years (Behnke & Smith, 2013; Hoffman, 2017; Thapar & Cooper, 2016). This striking increase suggests a propensity in over diagnosing the disorder, impugning the validity of traditional diagnostic procedures (e.g., family physicians diagnosing without a mental health specialist). Specific to Oregon, Klein and colleagues (Klein, Panther, Woo, Odom-Maryon, & Daratha, 2016) found that physicians prescribed more than 81% of all ADHD medications to Medicaid patients between the ages of 3-18.

When misused, stimulant medications may have lasting implications on the developing brain's plasticity, resulting in paradoxical symptoms such as hyperactivity, distractibility, and inability to control impulses (Urban & Gao, 2014). Beyond neurotypical brains, those exposed to noxious substances in utero may have even more significant functional consequences including manic and irritable behaviors (Behnke & Smith, 2013; Hoffman, 2017; Uban et al., 2015; Zhu et al., 2017). This is of particular concern as the cognitive ramifications of in utero polysubstance exposure implicate similar neural mechanisms to that of ADHD (e.g., attention and cognitive systems mediated by the pre-frontal cortex; Derauf, Kekatpure, Neyzi, Lester, & Kosofsky, 2009; Mick, Biederman, Faraone, Sayer, & Kleinman, 2002), resulting in a population vulnerable to misdiagnosis and the concomitant, deleterious outcomes of stimulant treatment (Telford, 2012; Uban et al., 2015; Zhu et al., 2017).

Attention Deficit Hyperactivity Disorder

As a neurodevelopmental disorder, Attention Deficit Hyperactivity Disorder (ADHD) is often first recognized in childhood and persists into adulthood (Biederman, Petty, Evans, Small, & Faraone, 2010). Etiologically, there is strong evidence for a genetic component according to twin studies and hereditability estimates ranging between 70-90 %, with an average of 76% (Faraone et al., 2005; Franke, Neale, & Faraone, 2009). Executive dysfunction represents the hallmark symptoms in ADHD including difficulty concentrating, hyperactivity/impulsivity, and motoric activity. More recent research has noted additional deficits in problem solving and reinforcement learning (Ziegler, Pedersen, Mowinckel, & Biele, 2016).

These deficits are attributed to deficiencies in the cognitive and reward systems largely mediated by 5-HT system activity (Serotonin) and sub-cortical dopaminergic projections to the limbic system and pre-frontal cortex (Bralten et al., 2013; Oades, 2008; Volkow et al., 2009). A review of ADHD etiology by (Sharma & Couture, 2014) implicated the prefrontal cortex, caudate, and cerebellum as the primary implicated regions in ADHD. Additionally, an overall reduction in cortical thickness was found in the temporal lobe, striatum, and overall cerebral cortex (Fernández-Jaén et al., 2014).

Behavioral correlates of ADHD. These dysfunctional neural connections manifest behaviorally including difficulties with organization, sustained attention, ignoring impositions, goal directed behavior, hyperactivity, and the inhibition of one's behaviors, feelings, cognitions, and verbalizations that deviate from the social norm and/or one's general well-being (Barkley, 2014). Poor response inhibition or subpar task performance may be associated with anomalous under-activation in the dorsal striatum, inferior frontal gyrus, as well as an inability to recruit the frontal faculties required by the task (Fernández-Jaén et al., 2014; Nymberg et al., 2013). Additionally, differences in reward-cognitive control, mediated by the ventral striatum, have also been documented (Plichta & Scheres, 2014). School settings often highlight these functional difficulties, catalyzing Individual Education Plan (IEP) referrals in many cases. IEPs generally include a broadband behavioral measure, cognitive battery, and achievement tests aimed at addressing a Specific Learning disability, Emotional Disturbance, or Other Health Impairment (e.g., ADHD). Diagnostic threshold for ADHD is generally reached via parent, teacher, and self-reports of behavioral consequences and cognitive deficits believed to underlie ADHD; research supports a comprehensive method integrating multiple domains and perspectives (e.g., behavioral and cognitive) for accurate diagnosis (Barkley, 2014).

Relationship between behaviors, executive functions, and self-regulation. While the behavioral consequences of ADHD are rather pronounced, the cognitive functions influencing these observable difficulties are not as well delineated. It has been well documented that ADHD is a disorder of executive functioning (Barkley, 2014). Executive functions refer to the myriad of neuropsychological processes needed to orient behavior and problem solve toward one's goal (Barkley, 2014). In extrapolating these processes, executive functioning includes inhibition, self-awareness, working memory, emotional regulation, motivation, and overall self-awareness to name a few. An inability to efficiently recruit these faculties is a helpful means of conceptualizing the behavioral manifestations of ADHD. These higher-order cognitive functions are essential for cognitive and emotional self-regulation, or the extent to which one is able to manage themselves in order to attain a specific goal. Barkley (2014) defines self-regulation as any action directed at oneself as a means of altering his or her behavior in order to change the likelihood of a future consequence or achieve a particular objective; further, he postulated that each executive function can be considered a type of self-regulation, or that an executive ability is simply an action in which the purpose is self-regulation. In this manner, behavior presentations are the manifestation of difficulties in self-regulation, which is predominantly localized to the frontal cortices. Understanding ADHD as a disorder of self-regulation emboldens the use of comprehensive behavioral assessment toward accurate diagnosis and prevention of inappropriate treatment. This integrated understanding of ADHD as a disorder of self-regulation engenders more comprehensive behavioral profiles toward accurate diagnosis and prevention of inappropriate treatment.

Neuropsychological Profiles associated with ADHD. The neuropsychological profiles of those with ADHD can provide vital information about this established link between executive deficits and self-regulatory behaviors (Barkley, 2014). Specifically, tests of executive functioning that underlie self-regulatory processes may be particularly sensitive to ADHD. A compendium of research reveals that those with ADHD struggle with tasks requiring working memory, processing speed, mental flexibility, inhibition, verbal fluency, motor control, and sustained attention (Barkley, 2014; Marchetta, Hurks, Krabbendam, & Jolles, 2008; Shanahan et al., 2006).

Two of these constructs of executive dysfunction are typically included in cognitive assessments conducted within the context of IEP testing within school settings: 1) Short-term Working Memory, and 2) Cognitive Processing Speed. Short-term Working Memory (i.e., the ability to hold and manipulate stimuli temporarily in mind; (McGrew, LaForte, & Schrank, 2014) and Cognitive Processing Speed (i.e., rapid and efficient response to a stimuli while maintaining reasonable accuracy; (McGrew et al., 2014) are thought to be aspects of executive functioning mediated by prefrontal and premotor cortices as well their respective frontal posterior connections (McInnes, Humphries, Hogg-Johnson, & Tannock, 2003; Mostofsky & Simmonds, 2008). Profiles featuring relatively low scores in either of these domains should be considered a reliable source of information in diagnosing ADHD. That said, there is debate over whether deficits in Short-term Working Memory and Cognitive Processing Speed scores are significant enough to conform to a reliable cognitive profile in diagnosing ADHD (Barkley, 2014).

In Utero Polysubstance Exposure

A cross-national comparison between younger and older cohorts revealed a steady increase in the prevalence of substances and their abuse over the past 30 years (Degenhardt et al., 2010). Increased use is also reflected in findings that approximately 5.9% of pregnant women in the United States used an illicit substance (Forray, 2016). Findings by Degenhardt and colleagues (2010) delineated a strong association between illicit drug use and use of multiple legal and illegal substances (e.g., a combination of tobacco, alcohol, and cannabis); the relationship was particularly strong between the use of stimulants and multiple substance use. This suggests that users rarely adhere solely to one substance, convoluting the ability to map deficits onto specific drugs. For this reason, prenatal drug use will be referred to as prenatal (or in utero), polysubstance exposure. In this context, poly refers to women who were addicted to substances that likely have a preferred drug of choice but would use any substance available.

Implications of Prenatal Exposure. To render an aggregate effect of a rather heterogeneous construct (e.g., exposure to multiple substances prenatally), it is necessary to explore the behavioral and cognitive implications of specific drugs for children prenatally exposed. Literature associates in utero exposure to methamphetamines with a number of poor behavioral outcomes including increased adversity, externalizing and internalizing, rule-breaking behavior, and aggressive behavior (Eze et al., 2016; L. M. Smith et al., 2015). Additionally, exposed children experienced emotional and neurological deficits such as high emotional reactivity as well as poor inhibitory control; IQ, memory, and spatial performance have also been found to be lower in comparison to nonexposed peers (Eze et al., 2016; L. M. Smith et al., 2015). The use of methamphetamine has been highly associated with alcohol, tobacco, and cannabis use (Degenhardt et al., 2010). Prenatal alcohol exposure had been linked to deficits in executive functioning (e.g., inhibition) and has been found to impact brain regions including the hippocampus, cerebellum, and caudate nucleus (Migliorini et al., 2015; Senturias, 2014). An overview by Senturias (2014) corroborated executive dysfunction and revealed additional deficits in processing speed, sensory integration, memory, non-verbal reasoning, motor control, language, and abstract reasoning for those exposed to alcohol in utero. Prenatal exposure to tobacco use was noted for delinquent, aggressive behaviors and cognitive deficits in learning, memory, executive control (i.e., behavioral inhibition), and hearing in young children (Clark, Espy, & Wakschlag, 2016; Scott-Goodwin, Puerto, & Moreno, 2016). Exposure to cannabis in-utero yields similar, deleterious outcomes such as increased hyperactivity, inattention, and impulsivity, suggesting overall executive dysfunction as a neurological consequence (Marroun et al., 2011; A. Smith et al., 2016); Amassed, in utero substance use has lasting negative effects on the cognitive and attention systems of the developing fetus which are mediated by regions such as the prefrontal cortex and other areas that receive rich, dopaminergic projections from the midbrain (Hoffman, 2017; Telford, 2012).

Dopaminergic pathways are responsible for motivation/goal-driven behavior, attention, and mood regulation (Bergamini et al., 2016). With such pathways implicated, prenatal substance use is closely associated with a number of poor outcomes for the child, including impulsivity, increased stress, and decreased levels of arousal, school achievement, and sustained attention (Behnke & Smith, 2013; Zhu et al., 2017). Cognitively, these poor outcomes are likely associated with deficits in working memory and speed of processing, as these drugs act on the mechanisms implicated in those with ADHD, resulting in executive dysfunction (Senturias, 2014; Telford, 2012). These cognitive abilities are vital for directing and sustaining attention, task monitoring, and other self-regulating behaviors (e.g., goal setting, emotional control, planning, organizing, etc.). As such, cognitive profiles for ADHD and in utero polysubstance are difficult to differentiate as executive dysfunction underpins both disorders.

Purpose of This Study

As ADHD and in utero polysubstance exposure implicate similar neural mechanisms, their resultant cognitive, emotional, and behavioral manifestations are likely similar – resulting in potential misdiagnosis. Additionally, an increase in the co-occurrence of ADHD and documented prenatal substance exposure has led some researchers to postulate in utero substance use as a potential cause of ADHD as opposed to an overlap in symptoms that are the consequences of prenatal exposure (Goh et al., 2016; Telford, 2012). The need to disambiguate this relationship is imperative as the first line of treatment for ADHD are stimulant medications (Fredriksen, Halmøy, Faraone, & Haavik, 2013), which have been shown to have grave consequences on drug affected brains (Hoffman, 2017; Migliorini et al., 2015; Uban et al., 2015). While the cognitive deficits associated with ADHD and prenatal polysubstance exposure have been studied independently, there exists little research differentiating their effects on cognition. Glass and colleagues (2013) found that children with prenatal alcohol exposure demonstrated significantly poorer verbal comprehension and perceptual reasoning than those with ADHD (though scores for both groups were impaired relative to controls). There were no differences between groups on neuropsychological measures, suggesting cognitive scores may best predict diagnosis. The current study aimed to explore what cognitive factors most accurately differentiate an ADHD diagnosis from a child with documented polysubstance exposure: Are there patterns of cognitive differences between a child with an ADHD diagnosis and prenatally exposed child that would aid diagnostic clarity? To that end, two subgroups demarcated the dependent variable: "Group" (ADHD collapsed and Polysubstance) and the independent variables included the following predictors: Cognitive processing speed, Short-term Working Memory, General Intellectual Ability (GIA), Fluid Reasoning (Gf), Comprehension Knowledge (Gc), Gf-Gc composite, Auditory Processing, Long-term retrieval, and Visualization. As previously noted, differences in the prefrontal cortex, striatum, cerebellum, and vermis are largely thought to underly the difficulties characterized by ADHD (Sharma & Couture, 2014). Fluid Reasoning and Long-term Retrieval involve parietal and temporal regions (O'Hare et al., 2009; Wendelken, Ferrer, Whitaker, & Bunge, 2016), which may be spared in ADHD and instead differentially impact Polysubstance. The hypotheses for this study were as follows:

H1: Fluid Reasoning would yield the greatest relationship with Polysubstance and most potently predict group membership. Because Fluid Reasoning loads onto GIA, GIA would also predict a Polysubstance diagnosis.

H2: Long-term Retrieval would have a negative relationship with Polysubstance.

H3: Fluid Reasoning and Long-term Retrieval would lack an association with ADHD.

H4: Cognitive Processing Speed and Short-term Working Memory would be lower for ADHD compared to Polysubstance.

H5: Auditory Processing, Visualization, and Comprehension Knowledge would not yield a relationship with either diagnostic group.

Chapter 2

Methods

Participants

Data from 54 participants were collected for the study. Participants were from an archived database within a psychological service group for rural schools. Participant ages ranged from 7-18 years of age. Other demographic variables included ethnicity, gender, and age. Informed consent was initially collected for the purposes of comprehensive psycho-educational assessment, informing eligibility for an IEP.

Table 1

Demographics of the Sample

Item	Category	Frequency	Percentage
Ethnicity	European American	36	66.6
	Latino/Latina	8	14.8
	Multiple Ethnicities	3	5.6
	Black/African American	3	5.6
	American Indian/Alaska Native	2	3.7
	Asian American	2	3.7
Gender	Male	33	61
	Female	21	39
Age	7-9	10	18.5
	10-12	16	29.6
	13-15	16	29.6
	16-18	12	22.2

Materials

Demographics. Demographic data were collected from the psychological reports in each student's file. List areas included on the demographic survey (See Table 1).

Woodcock Johnson Tests of Cognitive Abilities. Scores from the Woodcock Johnson Tests of Cognitive Abilities (WJ-IV-Cognitive; McGrew et al., 2014) were used as a means of comparison. The WJ-IV-Cognitive is a standardized, norm-referenced measure of cognitive strengths and weaknesses. This test contains eight domains of cognitive abilities comprised of 14 subtests. The domains measure various cognitive abilities including Cognitive Processing Speed (i.e., rapid performance of simple and complex tasks), Short-term Working Memory (i.e., the holding and manipulating of transient information) Fluid Reasoning (i.e., ability to form concepts and flexibly solve novel problems on the spot), Comprehension Knowledge (i.e., one's crystallized intelligence or acquired knowledge), Auditory Processing (i.e., the encoding, manipulation, and discernment of auditory stimuli), Long-term Retrieval (i.e., the storage and subsequent retrieval of learned information), and Visualization (i.e., thinking and reasoning with visual stimuli; McGrew et al., 2014).

Scores are derived from comparing an individual's scores to those of age-matched peers. Performance is presented in Standard Scores (SS) with scores between 90 and 110 falling in the *Average* range. A score greater than or equal to 90 represents a cognitive strength while a score lower than or equal to 85 is representative of a cognitive weakness according to district guidelines. The assessment reports a median reliability and concurrent validity of .80 or higher for all tests. This suggests that the test is a consistent and accurate representation of one's general intellectual abilities. Depending on when data were collected, the Woodcock Johnson III test of Cognitive Abilities (Woodcock, McGrew, & Mather, 2001) will also be examined. Concurrent validity yielded correlations in the .70 range and reliability ranged from .80 - .90. Thus, this test contains 10 standard domains that are psychometrically related to the domains measured in the WJ-IV-Cognitive, albeit under a slightly different name. For clarity, variables used the domain names provided by the WJ-IV-Cognitive (see Table 2).

Table 2

Descriptive Statistics

Measure or Diagnosis	Frequency	Percentage
WJ-IV Cognitive	34	63
WJ-III Cognitive	20	37
ADHD	31	57.4
Polysubstance	23	42.6

Note. WJ-IV and III are the Woodcock Johnson Test of Cognitive abilities, 4th and 3rd edition respectively

Procedure

Following IRB approval, participant files were screened and retrospectively assigned to distinct groups based on the documented diagnosis. Diagnosis was informed by a battery that typically included: a developmental questionnaire, Woodcock Johnson Test of Cognitive abilities (III & IV), the Behavior and Emotional Screening System (II & III; Self, Teacher, and Caregiver reports), the Behavior Rating Inventory of Executive Function (I & II). All diagnoses/diagnostic impressions were confirmed and signed off by the supervising licensed psychologist and found at the conclusion of the student's psychological report. The version of the test analyzed (e.g., Woodcock Johnson III or IV) was contingent on the year the data were collected. The groups included ADHD (collapsed) and those exposed to substances in utero. Those that met diagnostic threshold for ADHD (e.g., based on cognitive and behavioral profiles as well as approved by supervisor) were assigned to the ADHD group, and those with a parent report of in utero polysubstance exposure (garnered from a developmental questionnaire) were placed in the polysubstance group. WJ-IV-Cognitive domain scores were compared and included: General Intellectual Ability (GIA), Cognitive Processing Speed, Short-term Working Memory, Fluid Reasoning (Gf), Comprehension Knowledge (Gc), Gf-Gc Composite, Auditory Processing, Long-term Retrieval, and Visualization.

Chapter 3

Results

Two logistic regressions were employed to seek out the combination of independent (predictor) variables that statistically predict the dependent variables (outcome). Predictor variables included: 1) General Intellectual Ability (GIA), 2) Cognitive Processing Speed, 3) Short-term Working Memory, 4) Fluid Reasoning (Gf), 5) Comprehension Knowledge (Gc), 6) Gf-Gc Composite, 7) Auditory Processing, 8) Long-term Retrieval, and 9) Visualization. The outcome variables were 2 diagnostic groups: 1) ADHD (collapsed) and 2) Polysubstance exposed.

A Pearson-Product Moment correlation examined relationships between the cognitive domains (predictor variables). The appropriate assumptions were met. Cognitive Processing Speed, Auditory Processing, Visualization, Gf-Gc Composite, and Long-term Retrieval did not yield significant correlations with every variable and thus were excluded from further analyses. Notably, Cognitive Processing Speed did not significantly correlate with any other cognitive domain (see Table 3). As such, Short-term Working Memory, Gf, GIA, and Gc served as the predictor variables.

Table 3

Cognitive Domain Correlations

	Domain	*CPS*	*STWM*	*Gf*	*GIA*	*AP*	*LTR*	*VP*	*Gc*
1	CPS	--	.096	.061	.173	.082	.083	.122	-.074
2	STWM	.096	--	.443**	.676**	.273	.218	.455**	.470**
3	FR	.061	.443**	--	.838**	.538**	.345*	.369**	.615**
4	GIA	.173	.676**	.838**	--	.718**	.454**	.467**	.782**
5	AP	.082	.273	.538**	.718**	--	.113	.135	.448**
6	LTR	.083	.218	.345*	.454**	.113	--	.328*	.587**
7	VP	.122	.455*	.369**	.467**	.135	.328*	--	.389**
8	Gc	-.074	.470**	.615**	.782**	.448**	.587**	.389**	--

Note. CPS is Cognitive Processing speed, STWM is Short-term working memory, Gf is Fluid reasoning, GIA is General Intellectual Ability, AP is Auditory processing, LTR is Long-term retrieval, VP is Visual processing, and Gc is Comprehension Knowledge.
* $p < .05$; ** $p < .01$

Logistic regression analysis was used to determine which variables (cognitive domains) predict group membership (diagnosis). Two logistic regressions were conducted independently for each diagnostic group, using the same predictor variables. The associated assumptions were met, including a dichotomous outcome variable, continuous dependent variables, independent observations, linearity between logit outcome and dependent variables, minimal multicollinearity, and appropriate sample size. For the Polysubstance group, regression results indicate that Fluid Reasoning (see Table 4) significantly predicted a Polysubstance exposure diagnosis. Regarding the ADHD group (see Table 5), no cognitive domain significantly predicted group membership.

Table 4

Logistic Regression Analysis: Polysubstance Exposure

	B	SE	Exp(β)	Wald	Sig. (*p*)
(Constant)	10.449	3.422	34513.947	9.324	.002
Gf	-.115	.046	.892	6.220	.013
Gc	-.078	.045	.925	2.984	.084
GIA	.050	.060	1.051	.690	.406
STWM	.025	.031	1.025	.636	.425

Note. Gf is Fluid Reasoning, Gc is Comprehension knowledge, GIA is General Intellectual Ability, and STWM is Short-term Working Memory

Table 5

Logistic Regression Analysis: ADHD (collapsed)

	B	SE	Exp(β)	Wald	Sig. (*p*)
(Constant)	-2.460	2.224	.972	1.223	.269
Gf	.007	.031	1.007	.051	.822
Gc	.005	.032	1.057	3.021	.082
GIA	-.008	.041	.992	.035	.852
STWM	-.028	.025	.972	1.296	.255

Note. Gf is Fluid Reasoning, Gc is Comprehension Knowledge, GIA is General Intellectual Ability, and STWM is Short-term Working Memory

Given that some cognitive domains were excluded from the logistic regressions, a repeated measures MANOVA was also utilized to investigate the effect each cognitive domain on the diagnosis (ADHD vs. Polysubstance). There was a main effect for diagnosis on Fluid Reasoning, GIA, Long-term Retrieval, and Comprehension Knowledge, with Polysubstance

Exposed featuring lower scores for each cognitive domain. Having a diagnosis of Polysubstance exposure had moderate to large effects for General Intellectual Ability ($F(1,40)= 5.614$, $p=.023$, $\eta_p^2= .123$, Fluid Reasoning ($F(1,40)= 10.425$, $p<.002$, $\eta_p^2= .207$, Long-term Retrieval ($F(1,40)= 6.232$, $p= .017$, $\eta_p^2= .135$), and Comprehension Knowledge ($F(1,40)= 9.122$, $p<.004$, $\eta_p^2= .186$. Many, but not all, cognitive scores differed significantly for the Polysubstance group. However, it is worth noting that mean scores were lower in every cognitive domain for the Polysubstance group relative to ADHD (see Tables 6 and 7).

Table 6

Cognitive Domain Means and Standard Deviations for ADHD

Cognitive Domain	M	SD
Fluid Reasoning	93.55	14.54
Comprehension Knowledge	92.32	12.07
General Intellectual Ability	83.04	13.13
Short-term Working Memory	84.58	12.11
Auditory Processing	99.37	17.18
Long-term Retrieval	87.19	13.91
Gf-Gc Composite	86.00	5.35
Visualization	101.07	13.01
Cognitive Processing Speed	83.39	15.09

Note. Standard scores are presented with a mean of 100 and a standard deviation of 10.

Table 7

Cognitive Domain Means and Standard Deviations for Polysubstance

Cognitive Domain	M	SD
Fluid Reasoning	82.65	13.23
Comprehension Knowledge	80.96	14.27
General Intellectual Ability	83.04	13.13
Short-term Working Memory	84.58	12.11
Auditory Processing	93.09	17.70
Long-term Retrieval	77.48	16.16
Gf-Gc Composite	82.13	14.79
Visualization	95.17	12.46
Cognitive Processing Speed	87.09	15.54

Note. Standard scores are presented with a mean of 100 and a standard deviation of 10

Chapter 4

Discussion

To date, no study has examined the cognitive differences between children with an ADHD diagnosis and those prenatally exposed to polysubstance. Across the cognitive domains analyzed, only Fluid Reasoning significantly predicted a Polysubstance diagnosis. Consistent with research impugning the utility of diagnosing ADHD with a cognitive profile (Barkley, 2014), no cognitive domain significantly predicted a diagnosis of ADHD. This finding contrasts with literature suggesting that an ADHD diagnosis has a modest effect on tasks requiring working memory and processing speed (Barkley, 2014; Marchetta et al., 2008; Shanahan et al., 2006). Conversely, a diagnosis of Polysubstance Exposure significantly affected the following cognitive domains: 1) General Intellectual Ability, 2) Fluid Reasoning, 3) Long-term Retrieval, and 4) Comprehension knowledge. Across cognitive domains, mean scores for those with Polysubstance Exposure were lower compared to an ADHD analog. These findings are consistent with literature suggesting implicated intellectual functioning in drug exposed brains (Derauf et al., 2009; Eze et al., 2016; Mick et al., 2002; L. M. Smith et al., 2015). These results add that prenatal polysubstance exposure may also affect aspects of novel problem solving, mental flexibility, and concept formation.

Interestingly, Cognitive Processing Speed did not correlate with any other cognitive domain on the WJ-IV-Cognitive. This suggests that Cognitive Processing Speed may be unrelated to other thinking skills comprised by the General Intellectual Ability. This is problematic because Cognitive Processing Speed loads into the General Intellectual Ability score, which assumes a certain degree of collinearity that was not found for this sample. As such, it is unclear what is assessed by the WJ-IV Cognitive Processing Speed domain, which is further problematic given that this domain is often used for diagnosing ADHD.

Discussion of the Hypotheses

Hypothesis one. Fluid Reasoning will yield the greatest relationship with Polysubstance Exposed and most potently predict group membership. Results confirmed this hypothesis: Exposed participant results displayed the largest effect on Fluid Reasoning, and Fluid Reasoning was the only cognitive factor that predicted group membership. Students prenatally exposed may particularly struggle with aspects of novel problem solving, mental flexibility, and concept formation. Considering this, Polysubstance Exposure may differentially affect frontoparietal circuitry. Given that schooling requires learning new concepts and problem solving, students prenatally exposed will likely struggle academically and need additional supports. Specifically, providing example problems and frequently checking for understanding will likely benefit such students.

Hypothesis two. Long-term Retrieval will have a negative relationship with Polysubstance exposure. Results partially confirmed this hypothesis. Long-term Retrieval did not predict a diagnosis of Polysubstance exposure. This finding contrasts previous literature asserting memory difficulties for those prenatally exposed (Eze et al., 2016; L. M. Smith et al., 2015). The WJ-IV domain of Long-term Retrieval does not contain a delay component and instead requires the participant to immediately recall information previously read as well as use associative memory. This difference may help explain why Long-term Retrieval does not capture the memory deficits consistently observed across studies (Senturias, 2014). That said, this domain significantly differed for those with Polysubstance exposure compared to those with ADHD - with lower scores for those prenatally exposed.

Hypothesis three. Fluid reasoning and Long-term retrieval will lack an association with ADHD. This hypothesis was confirmed. Neither variable predicted an ADHD diagnosis. Similarly, neither variable was significantly lower relative to Polysubstance exposure. Long-term Retrieval and Fluid Reasoning (involving the hippocampus and parietal networks, respectively; (O'Hare et al., 2009; Wendelken et al., 2016) may be spared in ADHD. Across the studies reviewed, parietal and hippocampal differences were not documented. Instead, ADHD etiology is thought to primarily involve problems with frontostriatal-connectivity (e.g., Sharma & Couture, 2014). Taken together, tests involving memory and novel problem solving may not be useful for diagnosing ADHD.

Hypothesis four. Cognitive Processing Speed and Short-term Working Memory will be lower for ADHD compared to Polysubstance. This hypothesis was not confirmed, which contrasted previous literature showing that an ADHD diagnosis had a modest effect on tasks requiring working memory and processing speed (Barkley, 2014; Marchetta et al., 2008; Shanahan et al., 2006). Every cognitive domain, including Cognitive Processing Speed (CPS) and Short-term Working Memory (STWM), were lower for the Polysubstance group relative to ADHD. Given that STWM and CPS scores did not predict a diagnosis of Polysubstance exposure, or differ significantly from an ADHD analog, STWM and CPS are unlikely a core feature of Polysubstance in this study. Instead, lower IQ for those prenatally exposed is a more likely explanation (Eze et al., 2016; L. M. Smith et al., 2015).

Hypothesis five. Auditory Processing, Visualization, and Comprehension Knowledge will not yield a relationship with either diagnostic group. Only visualization did not yield a relationship. Visual skills may be spared for both diagnostic groups. While lacking an ability to predict either diagnosis, Comprehension Knowledge and Auditory Processing were significantly lower for the Polysubstance exposure group. Comprehension Knowledge and Auditory Processing are predicated on temporal lobe integrity (Han et al., 2016). Recent research has even suggested contributions from the parietal lobe in auditory processing and language (Boscariol et al., 2015; Farahani, Wouters, & van Wieringen, 2019). Taken together, prenatal polysubstance exposure may differentially affect both parietal-temporal circuitry and temporal brain regions.

Limitations and Future Directions

In this sample using archival data, students were referred by school officials for psychological evaluations due to academic, emotional, and behavioral concerns. As such, this study was not able to include healthy controls as an additional comparison group because of the lack of availability. If the implicated processing ability found in this study also differentiated Polysubstance from healthy controls, results would suggest Fluid Reasoning deficits as a core feature of Polysubstance. Additionally, comparing ADHD to healthy controls would be helpful toward engendering a WJ-IV cognitive profile for ADHD. Further, both diagnostic groups included students with comorbid mood and learning problems. While this accurately reflects the high prevalence of comorbid conditions among children and adolescents with ADHD (Shroff & Sanchez-Lacay, 2018) and with prenatal exposure to teratogens (e.g., alcohol; Dirks et al., 2019), it is then difficult to definitively attribute differences to a single diagnosis. As such, mood and learning problems were not co-varied due to the sample featuring only four participants with a pure ADHD or Polysubstance exposure diagnosis. Relatedly, Polysubstance Exposure makes it difficult to determine the differential impact of an isolated teratogen. Thus, it is challenging to generalize these findings to students who were prenatally exposed to only one noxious substance.

Finally, all students were from rural communities, limiting the generalizability to children in suburbs or urban settings. This is because communities vary with respect to psychosocial and environmental factors, potentially affecting cognitive and emotional presentations. Future studies with larger, more diverse samples are needed to confirm cognitive differences between ADHD and prenatal polysubstance exposure. Additionally, the addition of a healthy control group as well as mood/learning disorder comparison groups, would better control for the role of cognition on diagnosis. Further, future studies may wish to examine the implicated cognitive domains (e.g., Fluid Reasoning) with other validated assessment tools. This would promote generalizability of the current results. This is because Fluid Reasoning is a broad construct, assessed by a number of different tasks with other tools; consistently lower Fluid Reasoning would suggest the results are not unique to the WJ-IV. Replication is needed to investigate the lack of relationship between Cognitive Processing Speed (CPS) and other domains. Such replication may hinder the utility of CPS to investigate IQ as measured by the WJ-IV.

Implications

These findings suggest that Fluid Reasoning, as measured by the WJ-IV Cognitive, differentiates Polysubstance Exposure from an ADHD diagnosis. Additionally, the cognitive domains on the WJ-IV-Cog may not be sensitive enough to detect the cognitive difficulties in children and adolescents with ADHD. Absent the evidence of a cognitive profile, behavioral/informant measures and detailed clinical interview may prove more useful in diagnosing ADHD in school-based settings (Barkley, 2014). Conversely, WJ-IV cognitive domains are sensitive to Polysubstance exposure sequelae. However, only the cognitive domain of Fluid Reasoning predicted a diagnosis of Polysubstance. Diagnostically, Fluid Reasoning may serve as a reliable indicator means of differentiating Polysubstance exposure from ADHD. Interestingly, Cognitive Processing Speed did not correlate with any other cognitive domain. As processing speed and working memory differences are often thought to cognitively indicate

ADHD, clinicians should be wary of this domain's diagnostic utility. Finally, intervention recommendations may differ with this understanding. With Fluid Reasoning as the significant deficit, behavioral/classroom recommendations will want to ensure novelty is reduced (e.g., providing practice problems and checking for understanding). These findings help to provide more accurate treatment recommendations. Strategies should not be limited to targeting traditional ADHD symptomology.

Conclusions

ADHD deficits overlap significantly with prenatal exposure sequelae, both behaviorally and cognitively. This is problematic for a number of reasons. First, stimulant medication (first line treatment) for children with ADHD is contraindicated in those prenatally exposed to teratogens, highlighting the importance of proper diagnosis. Second, In utero exposure to polysubstance is often only suspected for many children. This is because children's biological parents, who may be able to confirm exposure, often no longer have custody. According to the National Organization on Fetal Alcohol Syndrome, approximately 85% of children with FAS do not live with their biological parents (n.d.). Consistent with literature, many students in the present study only had a suspected diagnosis and were not able to be included. Only students with noted history of exposure, or those screened and subsequently diagnosed with FAS, were retrospectively analyzed. Taken together, objective cognitive differences are crucial toward diagnostic clarity and proper treatment planning. When prenatal exposure is suspected, and/or when students have responded poorly to stimulants, deficits in Fluid Reasoning, as measured by the WJ-IV Cog, should cue the clinician to consider diagnoses other than ADHD.

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