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Fetal Alcohol Spectrum Disorders: A Case Study

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Abstract

This grand rounds manuscript reviews important considerations in developing case conceptualizations for individuals with a history of prenatal alcohol exposure. This case study provides an introduction to fetal alcohol spectrum disorders, diagnostic issues, a detailed description of the individual's history, presenting symptoms, neuropsychological test results, and an integrated summary. We describe a 9-year old girl diagnosed with a fetal alcohol spectrum disorder (FASD): Neurobehavioral Disorder Associated with Prenatal Alcohol Exposure (ND-PAE). This patient is a composite of a prototypical child who participated as part of a research project at the Center for Behavioral Teratology who was subsequently seen at an outpatient child psychiatry facility.

Keywords

Prenatal alcohol exposure; neurobehavioral disorder associated with prenatal alcohol exposure (ND-PAE); fetal alcohol spectrum disorder (FASD); fetal alcohol syndrome (FAS); neuropsychological assessment

Review of Fetal Alcohol Spectrum Disorders

The estimated prevalence of fetal alcohol spectrum disorders (FASD) is conservatively around 1%; however, a recent study in North America found rates as high as 4.8% of the school-age population is affected by prenatal alcohol exposure, indicating a significant public health concern (May et al., 2014; May et al., 2015). While there have been considerable efforts in the public health sector to reduce drinking during pregnancy (Grant et al., 2004), there has not been a meaningful decrease in prenatal alcohol exposure over the past decade (Thomas, Gonneau, Poole, & Cook, 2014). Approximately half of all pregnancies are unplanned and the rates of drinking during childbearing age are substantial; thus, there is ongoing risk of having children born who are affected by prenatal exposure to alcohol (Finer & Zolna, 2011; Green, McKnight-Eily, Tan, Mejia, & Denny, 2016).

Prenatal alcohol exposure results in a heterogeneous clinical presentation, which varies greatly in terms of cognitive and behavioral abilities. Prenatal alcohol exposure remains the

Compliance with ethical standards: This article does not contain any studies with human participants or animals performed by the author. The case study is a composite of cases seen by the first author.

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leading preventable cause of birth defects, developmental disorders, and intellectual disability (American Academy of Pediatrics, 2000). While fetal alcohol syndrome (FAS) has been recognized since the early 1970s (Jones & Smith, 1973), there continues to be difficulty in identifying children affected by prenatal alcohol exposure who do not meet full criteria for FAS. An accepted diagnostic schema to identify children affected by prenatal alcohol exposure has yet to be fully codified in the Diagnostic and Statistical Manual of Mental Disorders - 5th edition (*DSM-5*; American Psychiatric Association, 2013) or other medical diagnostic system, although positive steps have been made. Unfortunately, a majority of children with FASD are undiagnosed or misdiagnosed due to a lack of characteristic physical features and overlapping symptomology with other disorders (Chasnoff, Wells, & King, 2015).

Overview of Clinical Presentation

Prenatal alcohol exposure results in a wide range of central nervous system dysfunction that is apparent neurologically, structurally, and functionally (Bertrand et al., 2005). Underlying changes in the brain have been shown to relate to increased neurological issues including increased rates of seizures, sleep abnormalities, and sensory processing impairments (Bell et al., 2010; Church & Kaltenbach, 1997; Coffman et al., 2012; Jan et al., 2010; Simmons, Madra, Levy, Riley, & Mattson, 2011; Simmons, Thomas, Levy, & Riley, 2010; Steinhausen & Spohr, 1998; Wengel, Hanlon-Dearman, & Fjeldsted, 2011). In addition to neurological signs and symptoms, central nervous system dysfunction can also be evident through the presence of structural brain differences (e.g., microcephaly, structural abnormalities) or functional impairment (e.g., intellectual disability, cognitive deficits).

In some cases, children will meet criteria for a diagnosis of fetal alcohol syndrome (FAS). An FAS diagnosis is characterized by the presence of two or more key facial features (short palpebral fissures, smooth philtrum, thin vermilion border), growth deficits, and evidence of central nervous system abnormalities (e.g., microcephaly, abnormal morphogenesis) (Hoyme et al., 2005). For additional detail, please see Figure 1. It is important to note that the majority of children who are affected by prenatal alcohol exposure do not meet full criteria for an FAS diagnosis and partial phenotypes are important to recognize.

Alcohol is one of the most investigated behavioral teratogens, with decades of research demonstrating the broad behavioral and cognitive effects of prenatal exposure (Glass, Ware, & Mattson, 2014; Mattson, Crocker, & Nguyen, 2011). There are a variety of factors that may affect the neurobehavioral consequences of prenatal exposure including genetics, environment, rate and volume of exposure, and other variables related to the pregnancy and development. The timing and dosage of teratogenic exposure to alcohol to the fetus in utero may directly correlate with impairment in specific areas. For example, exposure to alcohol during the first trimester may lead to cerebellar damage related to movement or habit learning whereas second trimester exposure may relate to behavioral or emotional dysregulation as the amygdala development may be atypical. As of now, there is no safe dosage or timing in which to drink and pregnant women are recommended by the Surgeon General to not drink throughout pregnancy. Further, the exact relations between dosage and timing of exposure and behavioral effects is still largely unknown and likely varies

dramatically based on other characteristics such as speed of metabolism of alcohol, other genetic factors, other potential comorbidities, and environmental effects. Often alcohol is not the only teratogen and there may be concerns related to nutritional status and other factors that affect both the pregnancy and long term behavioral outcomes of the child.

Understanding the relation between neurological insult and behavioral presentation can help inform intervention. However, there have been consistent findings across studies that point to an emerging neurobehavioral profile associated with prenatal alcohol exposure (Mattson & Riley, 2011; Mattson et al., 2013).

Behavioral Deficits/Self-Regulation—Behavioral deficits are often the impetus to seek clinical care for individuals affected by prenatal alcohol exposure. Across studies, there has been repeated confirmation of behavioral concerns related to self-regulation and externalizing problems such as impulsivity and rule-breaking, in addition to inattention, anxiety, depression, and poor social functioning (Glass et al., 2014; Mattson et al., 2011; Streissguth et al., 2004). Children with prenatal alcohol exposure have higher rates of concomitant psychopathology, including increased rates of psychopathology, negative affect, and overall mood lability (Burd, Klug, Martsolf, & Kerbeshian, 2003; Sood et al., 2001; Streissguth et al., 2004). Further, studies consistently support the presence of attention deficits in children who have histories of prenatal exposure to alcohol, with rates of attention-deficit/hyperactivity disorder (ADHD) diagnoses estimated between 40-90% (Bhatara, Loudenberg, & Ellis, 2006; Burd et al., 2003; Fryer, McGee, Matt, Riley & Mattson, 2007).

Adaptive Functioning—Another core feature of the clinical presentation associated with prenatal alcohol exposure is the presence of impaired adaptive behavior. Adaptive behavior deficits have been noted across all domains of adaptive function (i.e., communication, socialization, motor skills, and daily living skills) and appear to worsen with age (Carr, Agnihotri, & Keightley, 2010; Crocker, Vaurio, Riley, & Mattson, 2009; Jirikowic, Carmichael Olson, & Kartin, 2008). In terms of communication, many children with prenatal alcohol exposure demonstrate deficits in aspects of language including phonological processing, speech production, and social communication (Doyle & Mattson, 2015). Social skills are complex and often considered the most severely affected domain of adaptive functioning in children with prenatal alcohol exposure. Alcohol-exposed children have routinely been found to demonstrate poor social interactions and struggle with socially inappropriate behavior (Greenbaum, Stevens, Nash, Koren, & Rovet, 2009; McGee, Fryer, Bjorkquist, Mattson, & Riley, 2008). Children with prenatal alcohol exposure also have difficulty with motor control (Kalberg et al., 2006; Simmons, Thomas, Levy, & Riley, 2006). Daily living skills are often impaired or delayed in children with prenatal alcohol exposure and are apparent both in delayed reaching of developmental milestones (e.g., toileting, following rules, bathing, feeding) and overall difficulty with living independently, although there is minimal research conducted within adult samples (Moore & Riley, 2015). Difficulties in adaptive function often appear to persist into adulthood, although there are anecdotal reports of both improved and worsening behavioral concerns. As prenatal alcohol exposure results in damage to the brain, it is likely that deficits in this area are related to the prenatal neurological striatal insult that can result in poor habit learning requiring

instructions to be repeated more often and not learning effective strategies for functioning in social and practical situations as quickly as typically developing youth. These issues seen in childhood may be exacerbated in adulthood as the gap between what is expected of the individual and what the individual is able to do may grow. Further, as adults individuals often have more freedom and access to situations that may lead to more high risk behavior and negative outcomes. These adaptive behavior problems often lead to secondary disabilities, including high rates of interaction with the justice system, lower rates of independent living, and high rates of substance abuse (Streissguth, Barr, Kogan, & Bookstein, 1996).

Neurocognitive Functioning—In addition to behavioral deficits, cognitive effects of prenatal alcohol exposure are well documented and have been reviewed in depth (see Glass et al., 2014; Mattson et al., 2011 for review). Overall, prenatal alcohol exposure results in cognitive deficits across various domains, including general intellectual function, executive function, learning, memory, and visual spatial reasoning. The literature on impairments in these domains is the basis for the proposed criteria of Neurobehavioral Disorder Associated with Prenatal Alcohol Exposure (ND-PAE), which is in the appendix of the *DSM-5* as a condition for further review (Doyle & Mattson, 2015; Kable et al., 2016).

One of the most robust findings in children with prenatal exposure to alcohol is overall diminished general cognitive function. Average intelligence estimate scores among children exposed to alcohol prenatally fall approximately 1 standard deviation lower than the average non-exposed individual (Glass et al., 2013; Streissguth et al., 2004), although individuals can range from severe impairment to unimpaired (e.g., full scale IQ scores of 40-112; Mattson et al., 2011). Executive dysfunction is often considered a core feature of prenatal alcohol exposure and poor performance on these higher-order domains is seen across parent report and objective standardized assessments (Glass et al., 2014; Mattson et al., 2011; Nguyen et al., 2014). Deficits exist across aspects of executive function including planning, set-shifting, cognitive flexibility, response inhibition, and working memory.

Alcohol-exposed children also struggle with poor performance in learning new material, both in visual and verbal domains, with stronger support for the latter (Mattson et al., 2011; Pei, Rinaldi, Rasmussen, Massey, & Massey, 2008; Willford, Richardson, Leech, & Day, 2004; Willoughby, Sheard, Nash, & Rovet, 2008). Learning deficits are also apparent in the presence of decreased academic performance across domains, with particular weaknesses seen in areas of mathematical functioning (Glass, Graham, Akshoomoff, & Mattson, 2015; Goldschmidt, Richardson, Stoffer, Geva, & Day, 1996; Howell et al., 2006). Memory deficits are also seen across domains (verbal, visual, auditory), and often appear to be associated with initial encoding difficulties with relatively spared retention (Kaemingk, Mulvaney, & Halverson, 2003; Willoughby et al., 2008). Children with prenatal alcohol exposure also have difficulties processing visual information (Mattson et al., 2011; Mattson, Gramling, Delis, Jones, & Riley, 1996; Paolozza et al., 2014), which can relate to poor performance in several areas of functioning (Crocker, Riley, & Mattson, 2015).

Diagnostic Issues

While it appears that training pediatricians on recognizing dysmorphology is effective in increasing awareness and identification of children with FAS (Jones et al., 2006), the vast majority of children affected by prenatal alcohol exposure do not meet criteria for the diagnosis and are at high risk of not receiving necessary services in spite of significant cognitive and behavioral challenges. There are various factors that hinder clinical identification of alcohol-exposed children including high rates of symptoms that overlap with other clinical disorders (e.g., ADHD), no biomarker to date, lack of prenatal exposure information, and often no obvious facial dysmorphology. Objective screening tools, including neonatal testing and the development of potential biomarkers, can assist in the identification of alcohol-exposed children at birth (Koren et al., 2014; Zelner et al., 2010; Zelner et al., 2012); however, these tools have not been introduced as best practice guidelines at this point and remain in a research phase. Ongoing study is needed to determine the accuracy and reduce the risk of disproportionately targeting specific groups, inaccurate screening, and address the concern of stigma and judgment associated with maternal drinking during pregnancy (Drabble, Thomas, O'Connor, & Roberts, 2014; Yan, Bell, & Racine, 2014). A common concern in development of identification tools for alcohol exposure at birth is that even if it is possible to accurately determine prenatal alcohol exposure with adequate sensitivity and specificity, it is not certain that an individual will be negatively affected later in life. As such, tools targeted at identifying affected individuals (vs. exposed individuals) may be most beneficial in assuring proper allocation of interventions and resources.

Further complicating access to services, many children with histories of prenatal alcohol exposure are placed in foster or adoptive care and, unfortunately, documentation of concerns or discussion of the potential effects of prenatal alcohol exposure are often unavailable or unclear. Many reasons exist for the lack of accurate or comprehensive prenatal exposure information such as biological mothers not disclosing for any reason, including stigma related to drinking during pregnancy, and medical professionals not routinely asking about substance use during pregnancy. It is important for clinicians to ask about alcohol exposure (and other teratogenic exposures) both in the preventative context for all women of childbearing age, during pregnancy specifically inquiring about drinking habits pre- and post-pregnancy recognition, as well as in child-visits to ask the parent about prenatal exposure during pregnancy. Conducting a comprehensive interview to understand a woman's baseline alcohol-use pattern can be pertinent in determining rates or risk of alcohol-exposure. Parents may not wish to disclose drinking during pregnancy (affecting both biological and foster care placements) and often it is not until a child develops a significant issue in school that this issue comes to light, at which time records may or may not be reviewed and followed up. Therefore, many affected children may have no information regarding prenatal exposure causing the etiology of behavioral or cognitive dysfunction to never be fully elucidated. Lastly, as there has not been a unanimous agreement for a codified system of diagnostic criteria for alcohol-related diagnoses beyond fetal alcohol syndrome, there is a history of various criteria being used to define or categorize effects of prenatal alcohol exposure. Most recently, the *DSM-5* has proposed the following criteria after consulting with experts in the field. As the *DSM-5* is the most utilized diagnostic manual for

mental health disorders in the U.S., is commonly used in access to services at schools, and informs insurance reimbursement, we have focused on these criteria for the current manuscript. Further, the criteria generally map on to the most recently released updated clinical guidelines related to prenatal alcohol exposure (Hoyme, et al., 2016).

Proposed Diagnostic Scheme

A proposed diagnostic system to identify the effects of prenatal alcohol exposure has been incorporated into the *DSM-5* as a condition requiring further study, referred to as ND-PAE (American Psychiatric Association, 2013). A similar term, Neurodevelopmental Disorder Associated with Prenatal Alcohol Exposure, is listed as a prototypical example under Other Specified Neurodevelopmental Disorder (315.8, F88). The criteria for ND-PAE require indication that the individual was exposed to alcohol at some point during gestation (including prior to pregnancy recognition) and that the exposure was more than “minimal.” The precise dosage is not specific and relies on clinical judgment, although a suggested estimate for minimal exposure is defined as 1–13 drinks per month during pregnancy (and never more than 2 drinks on any one drinking occasion (American Psychiatric Association, 2013). In addition to exceeding a minimal level of prenatal alcohol exposure, the individual must also display impaired neurocognition, self-regulation, and adaptive functioning. As the location of the disorder in the appendix of *DSM-5* (“conditions for further study”) suggests ongoing research is required to determine the feasibility, sensitivity, and specificity of the proposed criteria to accurately identify those affected by prenatal alcohol exposure (Kable et al., 2016).

A common clinical situation occurs when a child presents to an outpatient clinic with myriad other diagnoses – ADHD, adjustment disorder, reactive attachment disorder, mood disorder not otherwise specified, post-traumatic stress disorder (PTSD), and a learning disability – for which a diagnosis of ND-PAE may more parsimoniously encapsulate and holistically conceptualize the case. Pediatricians or mental health professionals may not be adequately trained on how to integrate information regarding prenatal alcohol exposure into their practice or the information regarding prenatal exposure may not readily available (Gahagan et al., 2006; Rojmahamongkol, Cheema-Hasan, & Weitzman, 2015). Further, the diagnosis may be stigmatizing and thus providers may be hesitant to discuss it with the family (Zizzo et al., 2013).

Support for Assessment

Given the heterogeneous neurobehavioral profile associated with prenatal alcohol exposure, a comprehensive neuropsychological examination is recommended. The assessment ideally covers the criteria associated with a diagnosis of ND-PAE (see Figure 2; American Psychiatric Association, 2013). Doyle and Mattson (2015) have reviewed variety of valid, reliable neuropsychological and parent-report measures that assess neurocognitive functioning, behavioral self-regulation, and adaptive functioning. Once a full assessment is conducted, a comprehensive case conceptualization requires a significant records review. Often the diagnosis, as discussed, is difficult as there may be a variety of distinct diagnostic categories that are met for each child. There is a strong emphasis on clinical judgment to

determine the most parsimonious and accurate diagnoses, while also considering access to needed services.

Once a diagnosis is given, advocacy for the child becomes a priority both at school and at home (Boys et al., 2016), ideally with collaboration across various settings and providers. A behavioral analysis to understand what factors are contributing to poor performance is beneficial in order to develop effective treatment recommendations. Clinicians and researchers have advocated for the importance of specific modifications in teaching strategies and classroom environments to aid children with histories of prenatal alcohol exposure (Green, 2007; Kalberg & Buckley, 2006; Kodituwakku & Kodituwakku, 2011; Premji, Benzie, Serrett, & Hayden, 2007). Despite advances in understanding the precise neuropsychological deficits associated with FASD, very few empirically supported interventions are available (Burd et al., 2003; Kodituwakku & Kodituwakku, 2011). Targeted interventions (Adnams et al., 2007; Kable, Taddeo, Strickland, & Coles, 2015; Kable, Coles, & Taddeo, 2007; Peadon, Rhys-Jones, Bower, & Elliott, 2009) and patient advocacy (Boys et al., 2016; Duquette, Stodel, Fullarton, & Hagglund, 2006) can facilitate outcomes, although this is a significant area of need both in terms of development and dissemination. Early identification and effective treatments for alcohol-exposed children could result in better outcomes; however, both are currently limited in terms of access to services and the generation of effective interventions (Bertrand et al., 2005; Kodituwakku & Kodituwakku, 2011; Premji et al., 2007).

School systems and other providers may or may not be familiar with the effects of prenatal alcohol exposure and may benefit from additional psychoeducation. Support for the child in the development of an individualized education plan or special services, as indicated by the effect of prenatal alcohol exposure on learning, may be necessary. Additional considerations could include repurposing interventions targeted within other populations for children with alcohol-exposure, although they may need to be substantially modified to be successful in this population.. Often, alcohol-exposed individuals are complex and require evaluating the situation from a holistic, multifaceted bio-psychosocial perspective, including collaboration between various settings and providers and implementing interventions in a number of systems and environments (e.g., school, home, parent-training, outside support, physical therapy, occupational therapy, speech and language pathology, vocational training). Additional information regarding interventions and treatment recommendations will be discussed at the end of the case study.

CASE STUDY

REASON FOR REFERRAL AND BACKGROUND HISTORY

The case presented here, referred to as Jane, is a composite of cases seen in a research project at the Center for Behavioral Teratology who were then subsequently seen at an outpatient child psychiatry facility. Thus, the data represents a prototypical child seen at the facility. Jane is a 9-year-old, right-handed, monolingual English speaking girl in the 3rd grade. She was referred by her primary care physician for a neuropsychological evaluation to assess her current level of neurocognitive functioning due to parent reported behavioral problems, emotional concerns, and poor school performance. The following background

history was obtained from an interview with Jane and her adoptive mother, Mrs. Smith. Mrs. Smith expressed significant concerns regarding fears of Jane being held back at school and inability to “control Jane” at home and around other children.

Per clinical interview with Mrs. Smith and review of records, Jane has had significant behavioral concerns since she was a toddler. These include explosive tantrums, aggressive behavior, and difficulty with emotional regulation and self-soothing. Jane had been in three different residential/foster care placements and was most recently transitioned to a foster-to-adopt placement in first grade with Mr. and Mrs. Smith. She has adapted well to this placement and was officially adopted by Mr. and Mrs. Smith in the beginning of this year, prior to starting 3rd grade. Jane has been engaged in family therapy, which has focused on attachment issues and evidence based treatment and parent-training for behavioral concerns; however, she still shows significant deficits that require “round the clock care” according to Mrs. Smith. While social skills training has been recommended, they have not been able to fit it into their schedules at this time.

Mrs. Smith noted that Jane has had significant tantrums and difficulties with self-control. She often provokes fights with other children and can have significant tantrums that last for over an hour, which include crying, screaming, destroying property, and hurting others. This in part led to the frequent changes in placement early in her life as other foster parents “could not handle her behavior.” Behavioral concerns also included impulsivity, difficulties with maintaining attention on specific tasks, difficulty following directions, and some aggressive behaviors including hitting and kicking her peers and parents. As she grew older, her behaviors continued and became more sophisticated: she began lying (for example, she broke several toys and then blamed it on another foster child in the home), and stealing items from others in the household. The new placement, engagement in therapy, and utilization of parent-training has successfully reduced the frequency of tantrums to approximately once a week, although they maintain similar severity, which is not developmentally appropriate. These behaviors most often occur at home, although she repeatedly needs to be redirected to on-task behavior at school as well. Her teachers express concern regarding her ability to stay on task and complete work, though have not witnessed the same frequency or severity of behavioral outbursts that are reported at home.

Jane has been seen by several different mental health professionals and continues to be engaged in both behavioral therapy and psychopharmacological intervention. She has a current clinical diagnosis of Attention-Deficit/Hyperactivity Disorder (ADHD), combined presentation, that was originally diagnosed at age 6. Due to difficulties in social interactions, she was assessed for an autism spectrum disorder at the age of 3, which was ruled out at that time. Jane was able to perform adequately in elementary school through second grade, with some difficulties surrounding the transition to a new school in first grade. However, since beginning third grade, she has had difficulty with increasing cognitive, behavioral, and social demands and is currently at risk of not transitioning to fourth grade with her peers. She has been suspended twice from this elementary school due to inappropriate behavior (i.e., inappropriately touching another peer, throwing her chair, not following directions, and breaking a computer).

The potential for Jane to be assessed for and potentially qualify for an individual education plan (IEP) had been brought up by her parents and teachers in 2nd grade, though the school district decided that at that time she has yet to meet criteria for significant services as she was not significantly behind in her academic achievement. She currently has a 504 plan that provides minimal behavioral accommodations. Her parents are currently in process of requesting another IEP evaluation at the school. Jane was assessed by a school psychologist at the age of 7 upon entering first grade and was not found to meet criteria for intellectual disability (IQ = 78, no evidence of specific learning disability), though had significant difficulty with aspects of adaptive functioning. In that evaluation she also received a diagnosis of ADHD and a prescription of a non-stimulant medication (Strattera). Her mother reports that this medication has been minimally effective though expressed concern regarding additional medications or stimulant medication due to potential side effects. For example, there has been concern regarding maintaining weight gain, given that she has a relatively low body mass index. She was assessed for services by the school under the other health impairment (OHI) criterion and a 504 plan was initiated at that time in which she received several accommodations including preferential seating at the front of the task and extra time on assignments.

In many cases regarding prenatal exposure, a comprehensive review of records is imperative as there are often complex biopsychosocial risk factors that may impact functioning. Many children with histories of prenatal alcohol exposure have backgrounds remarkable for social service involvement and potential foster/adoption care. In this case, Jane was born after 32 weeks gestation. Per the hospital records and adoption telling, her biological mother reported drinking before and during pregnancy (several drinks during the day and generally in a binge drinking pattern, 4-5 drinks a day on weekends, “sometimes that much on a weekday”). Per these records, the biological mother and father also reported occasionally using methamphetamine and marijuana. The biological mother reported pregnancy recognition at 5.5 months, at which time she attempted to cut down on her alcohol and substance use. She reported only binge drinking “occasionally” since knowing she was pregnant, though continued to drink greater than four drinks per occasion on several weekends during her third trimester. This pattern of reducing drinking later during pregnancy appears to be common based on our clinical and research interviews, therefore detailed maternal screening for alcohol exposure to the fetus both pre and post pregnancy recognition is imperative. Conducting a detailed interview of baseline substance use and lifestyle factors prior to the pregnancy can also provide important information on drinking patterns that may be underreported during pregnancy. Further, patterns of drinking may change during a pregnancy, as in this case, which is important to note and investigate. In this case, Jane's biological mother reported minimal prenatal care and her nutritional status was unclear throughout the pregnancy.

Child protective services removed Jane from her biological mother's care at the hospital when she had a positive toxicology screen at birth for methamphetamine and Jane's biological mother relinquished her rights at that time. Jane was placed in a foster care home after discharge. At the one year well-child pediatric appointment Jane was referred to a dysmorphologist after the foster parent disclosed Jane's prenatal history based on her records. Jane was evaluated by a dysmorphologist with expertise in FAS (See Table 1,

Figure 1). Jane was in the 7th percentile for height and 4th percentile for weight, consistent with FAS criteria for growth deficiency, though she did not meet full facial dysmorphism criteria for FAS. She met all developmental milestones, generally on the later end. Per the foster care records, she did not crawl until she was 17 months and had received “on and off” occupational and physical therapy between the ages of 1 and 4. Her adoptive mother noted that when Jane was placed with them, there were no developmental delays for speech or language, though noted she is still quite “clumsy”.

Psychosocial History—Jane currently lives with her adoptive mother and father along with two other children, who are also adopted. Of note, Jane frequently steals her sibling's toys and will hide broken toys and lie about how they were broken. When confronted, Jane often has tantrums resulting in tears and acting aggressively towards her mother (e.g., kicking, hitting). In these situations, her mother views her as “acting much younger age than she really is.” Jane reported to the examiner that she has many friends; however, her mother reports that she does not get invited to friend's houses and her teachers report repeated difficulty with peer interactions. Generally, Jane gets along better with peers and neighbors who are two to three years younger than she is. As a younger child, Jane's mother reported that Jane had difficulty interacting in peer situations, often talking over others in conversations or invading other's personal space.

Academic History—Jane's educational history is complicated by her frequent placement changes and she switched schools several times before her current stable placement. She attended preschool between the ages of 3-5 and had a series of behavioral concerns including reports of hiding under her desk, attachment difficulties with foster parents, not following directions, not completing assignments, yelling during class, often getting up from her seat, interrupting peers and the teacher, and not responding or listening to consequences. She has previously been assessed for additional services and has an active 504 plan (she sits near the front of the class, gets extra time on assignments, written reminders and a calendar to help with homework). Jane is currently performing poorly in third grade. She often fails to complete assignments (often crumpled at the bottom of her backpack). Further, she almost two grades behind in math, and one grade behind in reading and spelling. Per her teachers she has particular difficulty with complex math word problems and reading comprehension. She is not pulled out of class for any additional help and receives no tutoring.

Psychiatric History—Currently, Jane is being treated for irritability, mood symptoms and diagnosis of ADHD with a combination of outpatient therapy and medications. Despite the earlier concern regarding weight gain and side effects of medications, since the original evaluation at the age of 7 she has moved to a new psychiatrist and currently takes Prozac (10 mg daily), Clonidine (0.1 mg in the morning and 0.2 mg in the evening), Adderall XR (20 mg daily), and Risperdal (0.25 mg), as prescribed. Of note, there is very little research on medication dosage or efficacy in this population. Further, similar to the various diagnoses that a child with this profile may receive, medications prescribed may also be compounded. Jane's prescribed medications are not uncommon for this population as many children with fetal alcohol spectrum disorders are treated psychopharmacologically using multiple medications. There is preliminary evidence that alcohol-exposed children may respond

differently to medication (Doig et al., 2008). Currently psychiatrists familiar with prenatal alcohol exposure may tend to start at lower doses and increase at a slower rate to help effectively treat behavioral symptoms. To date, there has not been case-control studies to inform published guidelines on psychiatric medication for alcohol-exposed children.

Medical History—As previously discussed, Jane's biological parents have a history of substance abuse problems. Per review of records, Jane's birth was unremarkable with the exception of prenatal exposure to alcohol and drugs and lack of prenatal care. Within her first year, records indicate that she exhibited “failure to thrive.” Growth failure has continued and Jane will occasionally refuse to eat or, at other times, not monitor her eating and overeat to the point of vomiting. Other information regarding her biological parents or family history is unknown. She has no history of seizures or traumatic brain injury, and has never been in any serious accidents. Jane, fortunately, does not have a significant medical history or neurological concerns that would further complicate her cognitive profile. If there were cause for concern regarding a neurological insult or injury, a consult with a neurologist or other medical professionals may be recommended. At this point, neuroimaging studies have primarily been conducted in research settings rather than as part of a clinical protocol. While there is a substantial literature on brain injury and imaging findings in this population, the field is not yet at the point where imaging would necessarily lead to meaningful clinical implications in most cases. Potential consults with other disciplines (i.e., occupational therapy, speech therapy, physical therapy, educational specialist, feeding specialist, pediatrician, neurologist, and psychiatrist) may be indicated as well. Please see Figure 3 for general referral process.

Current Testing—Testing was completed across two days. Jane reportedly took all of her medications as prescribed. Jane had been previously examined by a pediatric dysmorphologist and was recently re-assessed as part of her continuing general care. While Jane's height and weight remained below the 10th percentile for her age and sex, indicating a growth deficiency, she did not meet criteria for microcephaly or display facial dysmorphology required for a medical ICD code, and thus would not qualify for an alcohol related diagnosis of FAS or partial FAS (see Table 1, Figure 1).

Neuropsychological Assessment Results: The purpose of this evaluation was to identify any learning or cognitive difficulties, determine whether any observed deficits are consistent with a specific etiology, and provide this information to her family, teachers, and physicians to help formulate a possible diagnosis and treatment plan. Of note, as mentioned this case is a composite of a prototypical child who participated as part of a research project at the Center for Behavioral Teratology who was subsequently seen at an outpatient child psychiatry facility. Depending on the assessment setting, there may be a variations in the amount of neuropsychological testing that is feasible, for example in a general outpatient assessment center, a child may be able to receive a comprehensive neuropsychological battery conducted over several days or if a child is seen within a pediatrician's office, they may only receive very brief assessment or screening. This case attempts to balance a more comprehensive assessment with feasibility concerns as this battery could be completed during one day (for example, only giving certain subtests of the WIAT-III, not giving

additional parent report measures). For additional information on ND-PAE and appropriate assessment protocols, please refer to Kable et al., 2016 and Doyle and Mattson, 2015.

Current Functioning Based on Self-Report—Jane reported that her current mood is “okay.” She did not endorse any difficulties with sleep or appetite. She reported no pain (0/10), though showed the examiner a Band-Aid from a fall the previous week. She reported no weakness or numbness and her gait/balance was grossly within normal limits.

Behavioral Observations—Jane arrived on time accompanied by her mother. She was cooperative and felt comfortable with testing, noting once that some measures appeared familiar. She had adequate frustration tolerance, though repeatedly asked for breaks and “when it would be over.” She understood all test questions and had adequate vision and hearing. She did not wear corrective lenses or a hearing aid. Her levels of attention and concentration were adequate to complete the testing. She was able to understand the test instructions and only occasionally required repetitions. She required redirection to task when given individual subtests without direct interaction with the examiner (i.e., WIAT-III numerical operations, CPT-3). Her speech was at a normal volume, with a normal rate and rhythm. She often asked the examiner questions about her background and had to be redirected to the task at hand.

Jane appeared to be alert and oriented throughout the testing process. She appeared well groomed, with generally good hygiene, casual dress, and appeared her stated age. Jane maintained euthymic affect throughout most of the interview and testing and spontaneously participated in conversation with the examiner. During assessment, she exhibited appropriate eye contact, although was consistently hyperactive and fidgety throughout the testing. Her thought process was logical and goal-directed, and her thought content was normal and appropriate to the situation. She consistently demonstrated effort to perform well on the various subtests administered and performed at expectation on objective measures of validity; thus, these results appear to be a valid indication of her cognitive and behavioral abilities at the time. Jane took her medications as prescribed on the days of the assessment; therefore, her cognitive and behavioral abilities reflected in the results of this assessment are not representative of her abilities without these medications.

Results of Testing

The neuropsychological assessment included measures of global intellectual performance, executive functioning, learning, memory, and visual-spatial reasoning to evaluate neurocognitive functioning as defined by ND-PAE (see Figure 2). The behavioral questionnaires and parent interviews captured information regarding Jane's self-regulation, behavioral functioning, and adaptive behavior. The table below provides information on the scores and descriptions of performance.

Rating	Percentile	Composite Score
Very Superior	98 th and above	130+

Rating	Percentile	Composite Score
Superior	91 st – 97 th	120-129
High Average	75 th – 90 th	110-119
Average	25 th – 74 th	90-109
Low Average	9 th – 24 th	80-89
Borderline	2 nd – 8 th	70-79
Impaired	Below 2 nd percentile	69 and below

Tests Administered

Child Behavior Checklist (CBCL) (Achenbach & Rescorla, 2001)

California Verbal Learning Test, Children's Version (CVLT-C) (Delis et al., 1994)

Conners Continuous Performance Test, Third Edition (CPT-3) (Conners, 2014)

Delis-Kaplan Executive Function System (D-KEFS) (Delis, Kaplan & Kramer, 2001)

Finger Tapping Test, Grooved Pegboard (Norms: Strauss, Sherman & Spreen, 2006).

NIMH Diagnostic Interview Schedule for Children Version IV, Computerized Version (C-DISC-4.0) (Shaffer et al., 2000)

NEPSY, 2nd edition (Korkman, Kirk & Kemp, 2007)

Wechsler Intelligence Test for Children, Fifth Edition (WISC-V) (Wechsler, 2015)

Wechsler Individual Achievement Test, Third Edition (WIAT-III) (Wechsler, 2009)

Vineland Adaptive Behavior Scale, Second Edition (VABS-II) (Sparrow, Cicchetti & Balla, 2005)

NEUROCOGNITIVE FUNCTIONING

General Intellectual Functioning			
Wechsler Intelligence Scale for Children - Fifth Edition (WISC-V)			
Index Scores / Subtest Scores	Score	%ile	Description
<i>Verbal Comprehension Index (VCI)</i>	92	30 th	Low Average
Similarities	9	37 th	Average
Vocabulary	8	25 th	Low Average
<i>Visual Spatial Index (VSI)</i>	84	14 th	Low Average
Block Design	6	9 th	Borderline
Visual Puzzles	9	37 th	Average
<i>Fluid Reasoning Index (FRI)</i>	74	4 th	Borderline
Matrix Reasoning	5	5 th	Borderline

General Intellectual Functioning			
Wechsler Intelligence Scale for Children - Fifth Edition (WISC-V)			
Index Scores / Subtest Scores	Score	%ile	Description
Figure Weights	6	9 th	Low Average
<i>Working Memory Index (WMI)</i>	74	4 th	Borderline
Digit Span	4	2 nd	Borderline
(Digit Span Forward)	7	16 th	Low Average
(Digit Span Backward)	5	5 th	Borderline
(Digit Span Sequencing)	4	2 nd	Borderline
Picture Span	7	16 th	Low Average
<i>Processing Speed Index</i>	77	6 th	Borderline
Coding	4	2 nd	Borderline
Symbol Search	8	25 th	Average
<i>Nonverbal Index (NVI)</i>	76	5 th	Low Average
<i>General Ability Index (GAI)</i>	80	9 th	Low Average
<i>Cognitive Proficiency Index (CPI)</i>	73	4 th	Borderline
<i>Full Scale Index (FSIQ)</i>	79	8 th	Borderline

Learning – Academic Achievement					
Wechsler Individual Achievement Test – Third Edition (WIAT-III)					
Subtest	Standard Score	Percentile	Description	Age Equiv.	Grade Equiv.
Word Reading	90	25 th	Average	7:8	2.3
Pseudoword Decoding	85	16 th	Low Average	6:8	1.5
Oral Reading Fluency	91	27 th	Average	6:8	1.6
Numerical Operations	73	4 th	Borderline	7:0	1.7
Math Problem Solving	69	<2 nd	Impaired	6:7	1.3
Spelling	88	21 st	Low Average	7:4	2.1
Composites					
Basic Reading	87	19 th	Low Average		
Mathematics	71	3 rd	Borderline		

Executive Functioning		
NEPSY-II		
Subtest	Score	Percentile
Auditory Attention Total	3	1 st
Combined Scaled Score	5	5 th
Total Omission (Errors)	(10)	2-5 th

Executive Functioning		
NEPSY-II		
Subtest	Score	Percentile
Total Commission (Errors)	(0)	51-75 th
Total Inhibitory (Errors)	(0)	51-75 th
Response Set Total	4	2 nd
Combined Scaled Score	7	16 th
Total Omission (Errors)	(14)	11-25 th
Total Commission (Errors)	(4)	26-50 th
Total Inhibitory (Errors)	(0)	>75 th

Delis-Kaplan Executive Function System (D-KEFS)		
	SS	Percentile
<i>Verbal Fluency</i>		
Letter Fluency	10	50 th
Category Fluency	11	63 rd
Switching Fluency	9	37 th
Switching Acc.	9	37 th
<i>Trail Making Test</i>		
Visual Scanning	10	50 th
Number Sequencing	3	<2 nd
Letter Sequencing	6	9 th
Number-Letter Sequencing	2	<1 st
Motor Speed	11	63 rd
<i>Color Word Interference</i>		
Color Naming	9	37 th
Word Reading	8	25 th
Inhibition	6	9 th
Inhibition/Switching	5	5 th

Memory		
California Verbal Learning Test (CVLT-C)		
	Raw	Z-score
List A Trials 1-5 Total	24	T-Score = 20
List A Trial 1	3	-2.0
List A Trial 5	7	-2.5
List B	4	-1.5
Short Delay Free	6	-2.0
Short Delay Cued	6	-2.5

Memory		
California Verbal Learning Test (CVLT-C)		
	Raw	Z-score
Long Delay Free	7	-1.5
Long Delay Cued	7	-2.0
Semantic Clustering	0.9	-1.5
Serial Clustering	6.4	2.0
Slope	1.1	-0.5
Total Intrusions	2	-0.5
Recognition Hits	12	-1.0
False Positive Errors	3	1.0
Total Recognition Discriminability	86.67	-1.5

NEPSY-II		
	Scaled Score	Percentile
Memory for Designs	5	5 th
Memory for Designs Delayed	6	9 th
Memory for Faces	10	50 th
Memory for Faces Delayed	10	50 th
Memory for Names	9	37 th
Memory for Names Delayed	11	63 rd
Narrative Memory Free Recall	5	5 th
Narrative Memory Free and Cued	8	25 th

Visual-spatial Reasoning		
NEPSY-II		
	Scaled Score	Percentile
Design Copy	7	16 th
Geometric Puzzles	8	25 th

SELF-REGULATION

Emotional/Behavioral			
Child Behavior Checklist (CBCL)			
	T Score	Percentile	Range
Anxious/Depressed	78	>97 th	Clinical
Withdrawn/Depressed	68	97 th	Borderline
Somatic Complaints	66	95 th	Borderline
Social Problems	77	>97 th	Clinical

Emotional/Behavioral			
Child Behavior Checklist (CBCL)			
	T Score	Percentile	Range
Thought Problems	68	97 th	Borderline
Attention Problems	77	>97 th	Clinical
Rule-Breaking Behavior	68	97 th	Borderline
Aggressive Behavior	63	90 th	Normal

Conners CPT-3					
	T-Score	Percentile		T-Score	Percentile
Omissions	68	97 th	Detectability (d')	53	63 rd
Commissions	57	75 th	Hit Reaction Time	47	37 th
Perseverations	50	50 th	Hit Reaction Time SD	53	63 rd
Variability	61	86 th	Hit RT Block Change	59	82 nd
			HRT ISI Change	54	66 th
*Greater T scores = worse performance					
C-DISC-4.0 Positive Diagnoses					
ADHD - Combined					
ODD					
CD					
Separation Anxiety					

ADAPTIVE BEHAVIOR

Adaptive Behavior			
Vineland Adaptive Behavior Scale – II (VABS-II)			
	Scaled Score	Percentile	Adaptive Level
Communication	75	5 th	Moderately Low
Socialization	78	7 th	Moderately Low
Daily Living Skills	73	4 th	Moderately Low
Overall Composite	74	4 th	Moderately Low

Motor Skills		
Grooved Pegboard Test		
	Z-score	Percentile
Dominant (R)	−1.26	13 th
Nondominant (L)	−.03	49 th
	Score	Percentile
Beery VMI	93	40 th
Finger Tapping Test		
Dominant (R)	.60	73 rd

Motor Skills		
Grooved Pegboard Test		
	Z-score	Percentile
Nondominant (L)	-.11	46 th

INTEGRATED EVALUATION AND DIAGNOSTIC INTERPRETATION

Jane is a 9-year-old, right-handed girl referred by her primary care physician for a neuropsychological evaluation to assess her current level of neurocognitive functioning due to behavioral concerns and poor school performance. Overall, the current neuropsychological evaluation revealed a variety of weaknesses and several strengths on the domains tested. Jane demonstrated low average cognitive abilities, as her full scale IQ estimate, which is a combination of all index scores, was approximately one and a half deviations below the mean (WISC-V, FSIQ=79, 8th percentile). This is in line with research on children with heavy prenatal alcohol exposure with IQ estimates generally between one and two standard deviations below the mean. In her case, this global estimate of functioning should be interpreted with caution as there was significant variability between the index scores with relative strengths seen in verbal comprehension (WISC-V VCI, SS=92, 30th percentile) and relative weaknesses seen on working memory and fluid reasoning (WISC-V WMI, SS= 74, 4th percentile; FRI SS=74, 4th percentile) There was also significant spread within domains, for example on processing, She was in the average range for a task requiring her to have rapidly scan and match a target to a sample of items but was in the borderline range when asked to associate symbols and numbers in a rapid fashion.

In terms of academic functioning, Jane performed below her current grade level (3rd grade) on all achievement measures (reading, writing, math). She demonstrated relative strengths in reading (WIAT-III Basic Reading, SS=90, 25th percentile) and spelling (WIAT-III Spelling, SS=88, 21st percentile) and relative weaknesses in math, evident on both a written math worksheet (WIAT-III Numerical Operations, SS=73, 4th percentile) and math problem solving (WIAT-III Math Problem Solving, SS=69, 2nd percentile). On spelling measures she made errors that were phonemically consistent. In terms of math, she had difficulty completing even simple problems and she often tried to rush through questions if she did not know how to do them or would become upset. When asked to try, she would make mistakes that demonstrated she had no automaticity in regards to number facts..

Taken together, this pattern is emblematic of a specific learning disability in mathematical functioning. Jane has experienced difficulties learning and using academic skills, in particular within the domain of math, for several years based on her parent reports and standardized assessments. She demonstrated low average to low performance on her ability to master calculation, math word problems and number facts. Her mother and teachers note that Jane gets lost in the middle of math problems, forgets the rule she was supposed to follow, and often becomes upset and does not want to continue further. This was consistent with our assessment and an examination of her homework. Jane also had difficulty with mathematical reasoning and applying mathematical concepts to solve problems. She has been able to compensate to some extent with her other cognitive strengths, though continues

to struggle in this domain. Her math skills were substantially and quantifiably below those expected for her age and cause significant interference for her academic performance, especially when considered in the context of standardized testing.

Jane's performance on measures of executive function was also below expectation. She demonstrated impairment on a measure of selective auditory attention and vigilance (NEPSY-II Auditory Attention, SS=3, 1st percentile), and was borderline range in her ability to cognitive shift and inhibit her responses (NEPSY-II Response Set, 2nd percentile). She had average verbal fluency, visual scanning, and motor speed, although demonstrated difficulties on tasks involving inhibitory control or cognitive flexibility, such as in switching tasks (D-KEFS Color Word Interference Inhibition, SS=6, 9th percentile; Color Word Interference Inhibition/Switching, SS=5, 5th percentile; Trail Making Test Number-Letter Switching, SS=2, <1st percentile). She also demonstrated an isolated difficulty in number sequencing (D-KEFS Trail Making Test-Number Sequencing, SS=3, <2nd percentile), which was not seen on letter sequencing. Overall, Jane demonstrates particular difficulty with higher order executive function tasks and selective attention, while basic fluency, color naming, and reading abilities remain intact.

In terms of memory, Jane demonstrated impairment on both verbal and visual memory at immediate and delayed conditions. She had difficulty in learning a list of words, after hearing the list five times she was able to remember only 7 of the 15 words (CVLT-C total list A, T=20, <1st percentile), however a delay she was able to remember all of the words she learned initially illustrating poor encoding, but intact retention. She demonstrated intact performance on some aspects of memory, including memory for faces and memory for names, though had more difficulty with remembering verbal information even when given context (NEPSY-II Narrative Memory, SS=5, 5th percentile) and more complex visual information both immediately and after a delay (NEPSY-II Memory for Designs, SS=5, 5th percentile). Regarding visual-spatial processing, she demonstrated low average ability on the WISC-V visual spatial tasks (Block Design, Matrix Reasoning) and on a measure where she had to copy designs though had intact performance on a separate visual puzzle task and on a measure of visuomotor integration. Jane also completed a computerized measure of attention difficulties and demonstrated elevated omission scores (CPT-3 Omissions, T=67, 97th percentile) and average commission scores (CPT-3 Commissions, T=57, 75th percentile), which indicates the presence of inattention though not hyperactivity. It is important to note that she was on medication for ADHD at the time of testing.

Regarding her emotional functioning, Jane's mother reported clinically significant elevations on several scales, including: anxious/depressed, social problems, and attention problems. Withdrawn/depressed, somatic complaints, thought problems, and rule-breaking behavior were within the borderline range. According to the clinician-assisted interview, she met positive criteria for ADHD, oppositional defiant disorder (ODD), conduct disorder (CD), and separation anxiety. In terms of adaptive behavior, Jane's parents indicated that her communication (VABS-II Communication, SS=75, 5th percentile), socialization (VABS-II Social Skills, SS=78, 7th percentile), daily living (VABS-II Daily Living Skills, SS=73, 4th percentile) and overall adaptive function (VABS-II, Total, SS=74, 4th percentile) were all moderately low for her age. In terms of motor skills, her gross motor abilities were intact

bilaterally. She demonstrated a relative weakness on fine motor skills on her dominant hand (R), though her non-dominant fine motor skills were intact.

Taken together, Jane's neuropsychological profile is characterized by weaknesses in executive function (working memory, cognitive flexibility, inhibitory control), learning, memory (visual and verbal), and academic achievement, in particular concerns with math. She has mixed performance on visual-spatial reasoning, and intact performance on language measures, gross motor skills, hyperactivity, aspects of memory (faces, names), fluency, and motor speed. Per parent and collateral reports with her therapist and teacher, significant mood regulation and adaptive behavior concerns are evident, particularly in externalizing behaviors.

While her math difficulties are potentially related to prenatal alcohol exposure, it is impossible to determine that they would be fully due to an alcohol-related condition and therefore Jane meets criteria for a diagnosis of a specific learning disorder with impairment is math. Likely her math performance is related to her lower working memory and perceptual reasoning abilities, which affected her calculation and problem solving abilities.

Her parents were given a standardized, semi-structured clinical interview, the Computerized Diagnostic Interview Schedule for Children Version IV (C-DISC-4.0) (Shaffer et al., 2000). In other clinical contexts, there are various other published structured clinical schedules or other comprehensive clinical interviews can be utilized. For Jane, while the C-DISC-4.0 illustrates several diagnoses in which she meets *DSM-IV* criteria, her profile of functioning may be most parsimoniously conceptualized as meeting criteria for the Neurobehavioral Disorder Associated with Prenatal Alcohol Exposure diagnosis, which is listed as a condition for further study in DSM-5. Therefore, her symptomology would be best captured by the Neurodevelopmental Disorder Associated with Prenatal Alcohol Exposure, under the Other Specified Neurodevelopmental Disorder DSM Code (315.8, ICD F88). She also continues to meet criteria for ADHD, combined presentation, per clinician, teacher, and parent-reports, as well as behavioral performance based on objective testing. Both poor math performance and symptoms of ADHD are also criteria in ND-PAE. These diagnoses are given in addition to ND-PAE as she qualifies for all three independently. A similar pattern is seen with children who meet criteria for ADHD and depressive disorders or ADHD and ODD, while there are shared characteristics, one may qualify for both independently.

While Jane also demonstrates a clinical phenotype similar to autism spectrum disorders, previous testing has ruled out this diagnosis and she does not demonstrate the communication deficits or repetitive behaviors necessary to meet criteria. Since Jane does not display the necessary facial dysmorphology for a diagnosis of FAS, documentation of more than minimal prenatal alcohol exposure is required, which is apparent from review of social services records.

Often, documentation of more than minimal prenatal alcohol exposure is not present, hindering the ability to potentially give the ND-PAE diagnosis. A decision tree for identification of children affected by prenatal alcohol exposure was recently described by Goh et al. (2016). This decision tree requires a small number of clinically-obtained variables

to determine whether an individual is likely to be affected by prenatal alcohol exposure. As part of the current testing, this decision tree is presented in Figure 4 with a highlighted path to indicate data from Jane's case. In her case, there was clear documentation of heavy alcohol exposure in utero, and application of the decision tree yielded an outcome consistent with this documentation. In many cases, where exposure information is not available, application of the decision tree may be useful to rule in or rule out the possibility of alcohol effects.

DSM-5 Diagnoses

Neurodevelopmental Disorder Associated with Prenatal Alcohol Exposure, Other Specified Neurodevelopmental Disorder (315.8, F88) Attention-Deficit/Hyperactivity-Disorder, combined presentation (314.01, F90.0) Specific Learning Disorder with Impairment in Mathematics (315.1, F81.2)

Rule Out: Conduct Disorder, Oppositional Defiant Disorder, Separation Anxiety. These diagnoses are better captured by the alcohol related neurodevelopmental diagnosis, though continued monitoring and targeted intervention is recommended.

Discussion of treatment recommendations—Treatment recommendations with an evidence base for children with heavy prenatal alcohol exposure are scarce; however, this population may respond well to interventions developed for other developmental disorders. Previous efforts have been successful in creating evidence-based interventions in other areas of functioning for children with FASD by modifying existing programs, such as social skills (O'Connor et al., 2006) and math (Kable et al., 2015; Kable et al., 2007), which supports the feasibility of adapting interventions to suit the specific needs of affected children. The development of evidence-based interventions for FASD is a critical research need that has been repeatedly documented (Kalberg & Buckley, 2006, 2007; Premji et al., 2007).

Preliminary studies have demonstrated that children with FASD can make significant gains with effective instruction (Kable et al., 2015; Kerns, Macoun, MacSween, Pei, & Hutchison, 2016). For example, children with FASD were able to learn a verbal rehearsal strategy that improved their digit span performance (Loomes, Rasmussen, Pei, Manji, & Andrew, 2008). Further, recent studies have found that self-regulation and executive function trainings result in improved parent-reports, inhibitory control, and storytelling (Nash et al., 2015; Wells, Chasnoff, Schmidt, Telford, & Schwartz, 2012). Computerized and attention focused interventions have also been moderately efficacious (Kerns, Macsween, Vander Wekken, & Gruppuso, 2010; Pei, Flannigan, Walls, & Rasmussen, 2016). Math intervention studies that were developed in concert with the neuropsychological profile associated with prenatal alcohol exposure (Math Interactive Learning Experience, MILE) have demonstrated significant gains in both pilot studies and community-based intervention (Kable et al., 2015; Kable et al., 2007). In Jane's case we would recommend this program, given her circumscribed deficits in this area. The MILE intervention focuses on improving math performance within the context of other issues that influence an alcohol-exposed child's ability to learn including emphasizing learning readiness (preparing the environment for

optimal performance), individualized pace of instruction, physical and visual aids, active feedback, and meta-cognitive control (encouraging greater reflection in problem solving).

Children with heavy prenatal alcohol exposure are likely to have an especially complex set of factors contributing to educational attainment including higher likelihoods of history of abuse, foster care or adoptive care, and a distinct, yet heterogeneous neurobehavioral profile. As the majority of children with FASD are enrolled in general education classrooms (Boys et al., 2016; Howell et al., 2006), it is recommended that these children receive a thorough and comprehensive evaluation to uncover potentially ‘invisible’ special needs that may be missed or misinterpreted to be incorporated into an effective educational plan. A recent study found that approximately 50% of alcohol-exposed children had difficulty in academic functioning (Boys et al., 2016), demonstrating minimal improvement in over 25 years from previous studies (Streissguth et al., 1991; Streissguth et al., 1994; Streissguth, Barr, Kogan, & Bookstein, 1997).

The heterogeneity of academic, behavioral, and cognitive function in children with FASD makes it exceedingly difficult to create a “one size fits all” academic curriculum. For instance, the range of intellectual function among these children is quite broad, and therefore effective interventions must cater to a wide range of abilities. In addition, programs must understand and address the interplay between cognitive, academic, social, emotional, and behavioral challenges. For example, poor performance may be due to behavioral impulsivity or executive dysfunction, both of which are common deficits in FASD. Other predictors are correlated with inattentive/overactive behaviors in internationally adopted children (which are overrepresented in the sample used in this study) that indicate older age at adoption, longer time in the adoptive home, and smaller family size are associated with greater parent-rated difficulties. Further, these difficulties were associated with poorer reading performance, expressive language, and adoptive family functioning (Helder, Brooker, Kapitula, Goalen, & Gunnoe, 2016).

Assessment of school-based services for children with FASD is a burgeoning area of research. In the classroom, a combination of evidence-based interventions may be the most efficacious, as they can target various areas simultaneously. Since 60–95% of alcohol-exposed children are diagnosed with ADHD (Fryer, McGee, Matt, Riley, & Mattson, 2007; Mattson et al., 2011), it may be worthwhile to investigate the feasibility of repurposing existing, empirically supported ADHD interventions or interventions for other populations for use in children with FASD. There are several interventions in which utilizing treatment approaches for other populations (such as ADHD or ASD) have been effectively used for prenatal alcohol exposure, although they generally require considerable modification and individual tailoring based on the unique neurobehavioral profile of alcohol-exposed children. Unfortunately, the availability of interventions has fallen far below the needs of alcohol-exposed children, and many of these programs are still being studied to assess generalizability, feasibility, and efficacy.

Access to Services—Currently, the most common and feasible method of receiving services for an alcohol-related neurodevelopmental disorder is to qualify for services under a different diagnosis, such as intellectual disability or ADHD, or to qualify under a specific

catch-all category based on functioning and symptomology. Legal precedents providing services for individuals with intellectual disability, or those requiring similar services, have facilitated access to services. Section 504 plans can help with classroom accommodations, yet fall short of creating an individualized plan and addressing unique needs of the individual (Senturias, 2014).

Individuals with FASD may require services from numerous providers, including primary care, specialist centers, occupational therapy, psychosocial skills training, and educational specialists (Rogers-Adkinson & Stuart, 2007). In general, the coordination between providers, disciplines, and agencies, requires a case manager or social worker to facilitate care. Often these systems of care are referred to as wraparound services that help increase communication and coordination between all parties involved in care (e.g., parents, teachers, mental health professionals, physical/occupational therapists, behavioral therapists, assessment teams, physicians, speech/language, adoption services, foster care services). Wraparound services are not specific to prenatal alcohol exposure and can be utilized for a variety of complex medical or behavioral presentations. In particular for prenatal alcohol exposure, there are several FASD service centers (McFarlane & Rajani, 2007) that provide models for the continued development of resources. However, there is no easy or practical way to standardize the service needs for children, as each child will have unique patterns of deficits and may require a more individualized approach. One study using semi-structured interviews revealed that there were no standardized special education classes that were appropriate for all alcohol-affected children, as each child required individual supports based on their own pattern of functioning (Autti-Ramo, 2000).

It is important to note that prenatal alcohol exposure results in neurological dysfunction and often behavioral and cognitive effects. As is the case with neurodevelopmental disorders, the course of care is not solely focused on full remediation or is curative in nature, but rather emphasizes supports and intervention to build on the strengths of the child, while considering the weaknesses to improve overall function. As the individual grows there are additional concerns and considerations that must be addressed including potential supports for transition to independence, additional contact with high-risk situations, and a widening gap of performance and age-based expectations. A continued holistic approach to consider all aspects of functioning and environment is important to inform effective intervention and high likelihood of positive outcomes.

Summary of the Case—Given Jane's profile of functioning, she was given diagnoses of Neurodevelopmental Disorders Associated with Prenatal Alcohol Exposure (Other Specified Neurodevelopmental Disorder), a specific learning disorder with impairment in math, and ADHD combined presentation, as discussed above. The clinician who provided the assessment also attended the IEP meeting at her school to provide additional support for Jane's parent's request for an IEP and share specific strategies that may be especially beneficial for Jane's behavioral and cognitive outcomes. The IEP meeting consisted of the principal, representatives from special education, current teacher, adoptive mother, and adoption advocate. As is often the case, the clinician provided psychoeducation to the team regarding the effects of prenatal alcohol exposure, as most members had very little training to work with this population. The clinician was able to educate the team and empower the

parent in sharing pertinent information regarding Jane's case. This discussion led to the development of a specific and targeted IEP that included particular focus on providing additional time and training on new concepts (repeating new lessons until competency was achieved) and a new behavioral reinforcement schedule (tying the positive reinforcement directly and immediately to a behavior, for example getting a sticker immediately after turning in an assignment). Jane also received specific targeting intervention at home and at school focused on improving her math abilities including tutoring, online math programs, the use of the MILE program as discussed above, and modified assignments to improve her math facts skills before introducing more complex information. Further, she was also given recommendations for ADHD including creating a work environment to reduce distractions, using a reward system, encouraging ongoing collaboration between all parties involved (e.g., teachers, parents, psychiatrists, therapists, tutors, and other providers).

Understanding Jane's full neurobehavioral profile from a comprehensive neuropsychological assessment led to a parsimonious diagnosis and actionable treatment recommendations. Further, this assessment assisted in less punishment and more support for areas in which she struggles (e.g., instead of getting a grade reduction for not turning in homework, creating a new system for keeping track of homework and additional scaffolding for supporting homework completion by breaking assignments into steps). This level of involvement is not often feasible; however, understanding the full profile of functioning and providing additional support to parents and schools results in improved outcomes.

Parent-training with a focus on antecedent-based strategies (rather than consequence based strategies) may be a more effective approach as it has been successful in other neurodevelopmental disabilities. Further, this strategy directly focuses on compensating for weaknesses observed in ND-PAE, for example difficulty with learning from prior experience and self-regulation. Both parent training, in-home behavioral consultation, or other aspects of wraparound services can be helpful for both the teaching of new skills and generalization of progress. Psychoeducation for all parties involved in care, from parents to teachers to mental and medical health providers, is imperative in effective cross discipline communication and overall improved outcomes while considering the holistic nature of factors that can affect functioning (e.g., environment, social stress, other system level issues).

An interagency collaboration suggested several areas for improving outcomes, including: FASD awareness and education in schools, understanding FASD as a comorbid disorder ideally in the context of a medical diagnosis similar to acquired brain injury, FASD specific interventions including collaboration between clinicians and school psychologists, advocacy for children with FASD, conducting a full neuropsychological assessment, and continuing interagency collaboration (Boys et al., 2016). This case study corroborates these findings and provides additional support for continuing assessment and advocacy for this population.

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FETAL ALCOHOL SYNDROME

Figure 1.

Facial characteristics associated with fetal alcohol exposure. Figure from Warren KR, Hewitt BG, Thomas JD (2011) Fetal alcohol spectrum disorders: Research challenges and opportunities. *Alcohol Research and Health* 34: 4-14. Figure in the public domain. See Table 1 for more information.

- **More than Minimal Prenatal Alcohol Exposure**
- **Neurocognitive Impairment (one or more):**
 1. Impairment in Global Intellectual Functioning
 2. Impairment in Executive Functioning
 3. Impairment in Learning
 4. Impairment in Memory
 5. Impairment in Visual-Spatial Reasoning
- **Self-Regulation Impairment (one or more):**
 1. Impairment in Mood or Behavioral Regulation
 2. Impaired Attention
 3. Impairment in Impulse Control
- **Adaptive Functioning Impairment (one or more):**
 1. Impairment in Communication
 2. Impairment in Social Interactions and Communication
 3. Impairment in Daily Living Skills
 4. Impairment in Motor Skills
- **Onset of Symptoms in Childhood**

Figure 2.

Core symptoms for Neurobehavioral Disorder Associated with Prenatal Alcohol Exposure (ND-PAE). For complete criteria see American Psychiatric Association, 2013, Diagnostic and statistical manual of mental disorders, DSM-5 (5th ed.), pp. 798-799.

Figure 3.

Framework for FAS Diagnosis and Services. Fetal Alcohol Syndrome: Guidelines for Referral and Diagnosis. National Center on Birth Defects and Developmental Disabilities, Center for Disease Control and Prevention, Department of Health and Human Services in coordination with National Task Force on Fetal Alcohol Syndrome and Fetal Alcohol Effect. 2004. http://www.cdc.gov/ncbddd/fasd/documents/FAS_guidelines_accessible.pdf. In the public domain.

Figure 4.

Decision tree for identification of children affected by prenatal alcohol exposure. Data from the current case are indicated are highlighted in red. Figure adapted from Goh et al. (2016). *Note:* AE = alcohol-exposed, CBCL = Child Behavior Checklist - domains included Somatic Complaints, Social Problems, Thought Problems, Attention Problems, Rule-Breaking Behavior, and Aggressive Behavior. Physical exam for FAS includes measuring whether key facial features are present (palpebral fissure length $\geq 10^{\text{th}}$ percentile; philtrum lipometer Score=4 or 5; vermilion border lipometer score=4 or 5). Criteria for FAS diagnoses requires at least two of three KEY facial features (palpebral fissure length $\geq 10^{\text{th}}$ percentile; philtrum lipometer Score=4 or 5; vermilion border lipometer score=4 or 5), and presence of head circumference $\geq 10^{\text{th}}$ percentile OR height and/or weight $\geq 10^{\text{th}}$ percentile. VABS = Vineland Adaptive Behavior Scale, domains included Communication, Socialization, and Daily Living Skills. Physical Exam (extended features) are specified as ptosis and incomplete extension of one or more digits.

Table 1

Summary and Comparison of the Various Diagnostic Schemas for Prenatal Alcohol Related Disorders. Table adapted and updated from Warren KR, Hewitt BG, Thomas JD (2011) Fetal alcohol spectrum disorders: Research challenges and opportunities. Alcohol Research and Health 34: 4-14. In the public domain.

	4-Digit Code (Astley and Clarren 2000)	IOM Guidelines (Hoyme et al., 2005)	National Task Force (Bertrand et al., 2004)	Updated Clinical Guidelines (Hoyme et al., 2016)	Canadian (Cook et al., 2016)
FAS					FASD with Sentinel Facial Features
Facial Characteristics	Simultaneous presentation of short palpebral fissures (2 SDs), thin vermilion border, smooth philtrum.	Two of: short palpebral fissures (10th %ile), thin vermilion border, smooth philtrum.	Simultaneous presentation of short palpebral fissures (10th percentile), thin vermilion border, smooth philtrum.	Two of: short palpebral fissures (10th %ile), thin vermilion border, smooth philtrum. (4 or 5 on UW Lip-Philtrum Guide)	Simultaneous presentation of short palpebral fissures (2 SDs below the mean, <3rd %ile), thin vermilion border, smooth philtrum. 4 or 5 on UW Lip-Philtrum Guide)
Growth Deficiency	Height or weight 10 th %ile.	Height or weight 10 th %ile.	Height or weight 10th %ile.	Height or weight 10 th %ile.	Not listed
Central nervous System (CNS) Involvement	Head circumference (occipital-frontal circumference [OFC]) 2 SDs below norm or significant abnormalities in brain structure or evidence of hard neurological findings or neurobehavioral impairment	Head circumference (OFC) 10th percentile or structural brain abnormality.	Head circumference (OFC) 10th percentile or structural brain abnormality or neurological problems or other soft neurological signs outside normal limits or neurobehavioral impairment	Deficient brain growth as evidenced by head circumference (OFC) 10th percentile or structural brain anomalies, recurrent nonfebrile seizures (other causes of seizures having been ruled out)	Evidence of impairment in three or more identified neurodevelopmental domains (see below) or in infants and young children, evidence of microcephaly
Neurobehavioral Impairment	CNS involvement can also be met by: significant impairment in three or more domains of brain function (2 SDs below the mean).		CNS involvement can also be met by functional impairment as evidenced by global cognitive or intellectual deficits, 2 SDs below the mean or functional deficits 1 SD below the mean in at least three domains.	Evidence of global impairment (global conceptual ability or IQ index scores 1.5 SD below the mean), or cognitive or behavioral impairment in at least 1 neurobehavioral domain (1.5 SD below the mean), or developmental delay (1.5 SD below the mean).	Severe impairment in three or more of the following neurodevelopmental domains: motor skills; neuroanatomy/neurophysiology; cognition; language; academic achievement; memory; attention; executive function, including impulse control and hyperactivity; affect regulation; and adaptive behavior, social skills or social communication. Impairment is defined at 2 SDs below the mean, with allowances for test error. Psychological diagnoses can also be an indication of severe impairment.

	4-Digit Code (Astley and Clarren 2000)	IOM Guidelines (Hoyne et al., 2005)	National Task Force (Bertrand et al., 2004)	Updated Clinical Guidelines (Hoyne et al., 2016)	Canadian (Cook et al., 2016)
					Additional information is provided in their provided appendix.
Alcohol Exposure	Confirmed/unknown.	Confirmed/unknown.	Confirmed/unknown.	Confirmed/unknown	Confirmed/unknown
Partial FAS					
Facial Characteristics	Short palpebral fissures (2 SDs) and either a smooth philtrum or thin vermilion border, with the other being normal OR palpebral fissure (1 SD) and both a smooth philtrum and thin vermilion.	Two or more of the following: short palpebral fissures (10th %ile), thin vermilion border, smooth philtrum.	Not applicable	Two of: short palpebral fissures (10th %ile), thin vermilion border, smooth philtrum.	Not applicable
Growth Deficiency	Not required	Either height or weight 10 th %ile or CNS	Not applicable	Growth deficiency or deficient brain growth only required if there is not documented prenatal alcohol exposure. Height and/or weight 10 th %ile, or CNS	Not applicable
Central nervous System Involvement	Same as for FAS	Head circumference 10 th %ile or structural brain abnormality or behavioral/ cognitive abnormalities inconsistent with developmental level.	Not applicable	Deficient brain growth as either head circumference 10 th %ile, structural brain anomalies or recurrent nonfebrile seizures.	Not applicable
Neurobehavioral Impairment	Same as for FAS	Same as for FAS	Not applicable	Evidence of global impairment (global conceptual ability or IQ index scores 1.5 SD below the mean), or cognitive or behavioral impairment in at least 1 neurobehavioral domain (1.5 SD below the mean), or developmental delay (1.5 SD below the mean).	Not applicable
Alcohol Exposure	Confirmed	Confirmed/unknown.	Not applicable	If documented, only needs facial dysmorphology and neurobehavioral impairment.	Not applicable
ARND	Not proposed. Several categories assessing functional deficits.			Cannot be made in children <3 years of age	FASD without sentinel facial features
Central Nervous System Involvement	Same as for FAS	Either structural brain anomaly or OFC 10 th %ile	Not applicable		Same as for FAS with sentinel face features

	4-Digit Code (Astley and Clarren 2000)	IOM Guidelines (Hoyne et al., 2005)	National Task Force (Bertrand et al., 2004)	Updated Clinical Guidelines (Hoyne et al., 2016)	Canadian (Cook et al., 2016)
		or neurobehavioral impairment			
Neurobehavioral Impairment	Same as for FAS	A complex pattern of behavioral or cognitive abnormalities inconsistent with developmental not explained by genetics, family, or environment.	Not applicable	Evidence of global impairment (global conceptual ability or IQ index scores ≥ 1.5 SD below the mean), or cognitive or behavioral impairment in at least 1 neurobehavioral domain (≥ 1.5 SD below the mean),	Same as for FAS with sentinel face features
Alcohol Exposure	Confirmed	Confirmed	Not applicable	Documented	Confirmed
Notes	The 4-Digit Code provides an assessment of effects in four areas (growth, face, CNS, and alcohol exposure) that results in 256 different codes and 22 diagnostic categories. A specific pattern or level of alcohol exposure is not required, just that alcohol exposure is confirmed or not.	Alcohol exposure is defined as a pattern of excessive intake or heavy episodic drinking.	Alcohol exposure levels are not defined, but the authors cite evidence of alcohol exposure based upon clinical observation; self-report; reports of heavy alcohol use during pregnancy by a reliable informant; medical records documenting positive blood alcohol levels, or alcohol treatment; or other social, legal, or medical problems related to drinking during pregnancy.	Documented alcohol exposure is met by either ≥ 6 drinks/week for ≥ 2 weeks during pregnancy; ≥ 3 drinks per occasion on ≥ 2 occasions during pregnancy; documentation of alcohol-related social or legal problems before or during pregnancy (e.g., DUI, history of treatment of alcohol related condition); documentation of intoxication during pregnancy by blood, breath, or urine alcohol content testing; positive testing with established alcohol-exposure biomarkers during pregnancy or at birth; increased prenatal risk associated with drinking during pregnancy as assessed by a validated screening tool.	Confirmation of prenatal alcohol exposure, with the estimated dose at a level known to be associated with neurodevelopmental effects.