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Profiles of Drug Endangered Children: Investigation in a Clinical Sample

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Profiles of Drug Endangered Children: Investigation in a Clinical Sample

by

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Each person whose signature appears below certifies that this doctoral project in his/her opinion is adequate, in scope and quality, as a doctoral project for the degree of Doctor of Psychology.

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ABSTRACT

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Dr. Kimberly Freeman, Chairperson

Despite the increase in children born prenatally exposed to methamphetamine, little is known about the cognitive and neuropsychological outcomes of these children. Research specific to prenatal-methamphetamine exposure is extremely limited and has been primarily restricted to rat studies. This research combined with the few studies examining children prenatally exposed to methamphetamine suggests that methamphetamine-exposure is associated with various cognitive and neuropsychological delays and is impacted by both biological and environmental factors. Given the scarcity of research in this area, the current study used archival data from a psychological assessment clinic to (1) describe the frequency of prenatal methamphetamine-exposure cases, (2) describe the profiles of prenatal methamphetamine-exposed children, and (3) compare a matched sample of methamphetamine-exposed and clinical non-drug exposed groups for any differences. The methamphetamine-exposed group was also compared to the non-clinical normative group to examine any differences.

A total of 25 children participated in the study (14 prenatally methamphetamine exposed children and 11 non-drug exposed children). Of the total clinic population, 3.07% were identified as exposed to methamphetamine. Descriptive analysis indicated

that the methamphetamine-exposed group performed in the low average range in the areas of processing speed, verbal comprehension, attention/executive functions, memory and sensorimotor functioning as measured by the Wechsler intelligence scales and the Neuropsychological Evaluation for Children (NESPY). An examination of the subtests indicated that the methamphetamine exposed children scored lower than both the non-drug exposed group and the normative sample. Of particular concern were the comprehension, arithmetic, symbol search and coding subtests that all fell in the below average range. A series of t-tests indicated a significant difference between clinic based non-drug exposed children and methamphetamine-exposed children in the area of processing speed. When compared to the non-clinical normative sample, the methamphetamine-exposed group scored significantly lower in the areas of verbal comprehension and processing speed. In addition to being statistically significant, the findings were also clinically significant indicating potential areas of delay for these children. Although these findings provide some insight regarding the functioning of prenatally methamphetamine exposed children, more research is needed as the impact of environment factors and other confounding variables could not be ruled out.

Introduction

Methamphetamine use is a significant public health issue in the United States. According to the National Survey on Drug Use and Health (NSDUH, 2007) in 2005 an average of 10.4 million Americans over the age of 12, of which approximately half are female, have tried methamphetamine at least once in their lifetime (NSDUH, 2007). This is a significant finding as methamphetamine abuse among women has gained increased attention in recent years; particularly due to the unique consequences related to drug use and pregnancy. Specifically, women who are pregnant and using drugs are of considerable concern due to the potential harmful psychosocial and biological effects drugs have on developing children both from being exposed to drugs in utero and by being exposed to environmental factors associated with drug use (Azuma & Chasnoff, 1993; Chasnoff, Griffith, Freier, & Murray, 1992; Hawley, Halle, Drasin, & Thomas, 1995; National Center on Addiction and Substance Abuse at Columbia University, 2003).

Due to the deleterious child outcomes associated with prenatal drug exposure, systematic investigations to determine drug effects on the developing child are needed. Although research does much to identify issues associated with prenatal drug exposure in general, specific effects of particular drugs such as methamphetamine are unknown. As such, much of the literature involving drug exposure and consequent child development issues focuses on children exposed to cocaine in utero. This focus is primarily in response to the increased use of cocaine in the late 1980s and the 1990s. In addition to cocaine, infants exposed to amphetamines, alcohol, and polysubstances have also been widely studied (Azuma & Chasnoff, 1993; Chasnoff et al., 1992; Chasnoff, Griffith, MacGregor, Dirkes, & Burnes, 1989; Hawley et al., 1995; National Center on Addiction and

Substance Abuse at Columbia University, 2003). The literature examining cocaine and stimulant drugs have important implications in providing hypotheses about methamphetamine-exposed children given that few studies have examined developmental outcomes of methamphetamine-exposure.

Even though methamphetamine and cocaine are often grouped together because they are both stimulant drugs, methamphetamine and cocaine may impact the development of the central nervous system differently (Dixon & Behar, 1989; Lake & Quirk, 1984; Meredith et al., 2005). As such, it would be important to study the specific effects of methamphetamine to understand its impact on child development. Additionally, neurodevelopmental studies of prenatally methamphetamine-exposed brains have discovered neurochemical and structural differences in the prenatally methamphetamine-exposed brains when compared to non drug-exposed brains (Smith, Chang, Yonekura, Gilbride et al., 2001). Given these anatomical differences, it would be important to investigate any cognitive and/or neuropsychological differences that may exist in methamphetamine-exposed children.

Most research in the area of methamphetamine has been limited to animal studies and chronic methamphetamine use in adults. In light of this scarcity of literature, it is important to explore these early animal studies in order to provide a better understanding of prenatal methamphetamine-exposure on offspring outcomes. Additionally, a few studies have been conducted that examine child outcomes on prenatal methamphetamine-exposure (Chang, et al., 2001; Smith, Chang, Yonekura, Grob, Osborn, and Ernst, 2001; Smith, Yonekura, Wallace, Berman, Kuo, & Berkowitz, 2003). These early studies suggest potential problems with visual motor integration, sustained attention and memory; thus indicating that further research is needed in this area. As such, the goals and objectives of the current study are to describe the frequency of methamphetamine-exposed children in the clinic, describe the profiles of methamphetamine-exposed children, and to compare methamphetamine-exposed children with non-methamphetamine exposed children as well as a non-clinical normative sample on a number of cognitive factors.

Literature Review

Currently, the United States is experiencing an epidemic in methamphetamine use (Office of National Drug Control Policy, 2003), especially with the increase of superlabs, which have the capacity to produce methamphetamine in mass. According to the U.S. Department of Justice (2001), the Riverside and San Bernardino County area is referred to as the "methamphetamine capital of the United States." Methamphetamine has gained popularity because of its low price and relatively uncomplicated production process, which makes it more easily available than cocaine and heroin (Marwick, 2000; Meredith, Jaffe, Ang-Lee, & Saxon, 2005). The U.S. Attorney for the Central District suggests that methamphetamine will soon become the most readily available drug in the in the central district, which includes the Los Angeles, Orange, Riverside, San Bernardino, San Luis Obispo, Santa Barbara, and Ventura counties (U.S. Department of Justice , 2001).

According the 2005 NSDUH (2007) 2 million Californians over age of 12 have tried methamphetamine at least once in their lifetime. Estimates further indicate that the proportion of women using methamphetamine is nearly equal to men, which is dissimilar from other drug use ratios that show men typically use more than women (Cohen, Greenberg, Uri, Halpin, & Zweben, 2007). In a study examining type of drug use it was found that of the 17% of female drug abusers who reported being primarily methamphetamine users, 38% had used during pregnancy (Marwick, 2000). Methamphetamine use among pregnant US women has doubled over a six year span from 1998 to 2004 and appears to be steadily increasing (Cox, Posner, Kourtis, & Jamison, 2008; Marwick 2000). It has been suggested that methamphetamine may be popular among women of childbearing age and even pregnant women due to the drug's properties of increasing energy and weight loss (Cohen, Greenberg, Uri, Halpin, & Zweben, 2007; Cox, Posner, Kourtis, & Jamison, 2008; Marwick, 2000).

Much of the literature which involves drug exposure and consequent child development issues focuses on children exposed to cocaine in utero because of the increase in cocaine use in the late 1980s and the 1990s. In addition to cocaine, infants exposed to amphetamines, alcohol, and polysubstances have also been widely studied (Azuma & Chasnoff, 1993; Chasnoff et al., 1992; Chasnoff, Griffith, MacGregor, Dirkes, & Burnes, 1989; Hawley et al., 1995; National Center on Addiction and Substance Abuse at Columbia University, 2003). This literature has important implications in examining development in methamphetamine-exposed children as few studies have been conducted in this area. Specifically the prenatal cocaine-exposure literature is particularly important as methamphetamines and cocaine both belong in the class of psychostimulant drugs.

Prenatal Drug Exposure

The increase of drug use in women of child-bearing age has resulted in an increase of children being born drug exposed. Maternal drug use generates an adverse environment for the fetus with a variety of interacting factors, which becomes a health threat to the developing fetus. Drug exposure effects on the fetus do not simply mean exposure to toxins, rather it is a complex interaction of genetics, nutrition, toxicity, social, and environmental variables all of which contribute to fetal growth and development (Chasnoff, Griffith, Freier, & Murray, 1992; Dixon, 1994).

Prenatal drug use places the fetus at risk directly as well as indirectly (Dixon, 1994). Stimulants can easily cross the placental barrier and can be delivered to the fetus quickly, in higher concentrated doses, and at longer exposure duration than the maternal levels. Further, the drugs are directly delivered to the fetus through the placenta by diffusion and then supplied again to the fetus by mixing with the amniotic fluids (Dixon, 1994; Chasnoff, Burns, & Burns, 1987). In addition, the drug effects on the mother's body also negatively affect the fetus. The vasoconstriction which results from maternal stimulant use causes decreased oxygen and blood flow, and decreases supply of nutrients to the fetus which adversely effects fetal development and places the fetus at high risk for postnatal developmental delays (Woods, Plessinger, & Clark, 1987; Dixon, 1994).

Pregnant women addicted to stimulants further compromise their fetus' well-being through the lifestyle choices they make. Typically women who abuse stimulants tend to have poor appetite and consequently poor nutrition, which in turn affects fetal development. Many women tend to under utilize prenatal care services and abuse multiple substances such as cigarettes, alcohol, and other illegal substances to counter the unpleasant aspects of the stimulants, which further compromises fetal and infant well-being (Brook, Whiteman, Shapiro & Cohen, 1996; Dixon, 1994). Overall, research corroborates that in utero drug-exposure result in poor overall development for the child.

Postnatal physiological effects. According to many studies, drug-exposed children typically demonstrate poor physiological outcomes. Several studies indicate that drug-exposed infants tend to exhibit significantly lower birth weight, are shorter in length, have considerably smaller head circumference at birth, are premature, and have increased prenatal mortality (Azuma & Chasnoff, 1993; Chasnoff et al., 1992; Chasnoff, Griffith, MacGregor, Dirkes, & Burns, 1989; Hawley et al., 1995; National Center on Addiction and Substance Abuse at Columbia University, 2003). Other research findings suggest that immediately after birth, drug exposed children have problems with habituation, muscle tone, and primitive reflexes (Morrison, Cerles, Montaini-Klovdahl, & Skowron, 2000). Several studies examining physiological effects of prenatal drug-exposure will be highlighted in the following section.

Chasnoff et al. (1992) compared three groups of infants in a 2-year outcome study. The first group of infants was prenatally exposed to cocaine and marijuana and/or alcohol, the second group of infants was prenatally exposed to just marijuana and/or alcohol, and a control group had no prenatal exposure to drugs. It was discovered that the cocaine exposed infants had reduced head circumference, length, and birth weight. The group exposed to marijuana and alcohol but not cocaine (group 2) also exhibited reduced head circumference at birth. Both drug exposed groups had significantly smaller head circumference than the control group, but the group with cocaine-exposure exhibited more severe physiological effects. Both drug-exposed groups' head size was significantly smaller than the control group through 2-years of age.

Neuroimages of cocaine-exposed and drug-unexposed children were examined in another study to investigate possible differences in neuronal loss, cell membrane injury, and ischemic changes (Smith, Chang, Yonekura, Gilbride et al., 2001). Volumetric tests of the brain indicated a trend toward lower midbrain volumes in cocaine exposed children. However, no significant differences were found in brain volumes of the cocaine-exposed group and non-exposed group of children.

In addition to looking at structural differences, metabolite concentrations were measured in the frontal white matter and striatum, to investigate biochemical changes in the brains of cocaine-exposed children (Smith, Chang, Yonekura, Gilbride et al., 2001). Although significant structural differences in the two groups were not found, neurochemical alterations in the children exposed to cocaine were noted. Specifically, in the cocaine-exposed group of children, creatine (a bioenergetic metabolite) was increased significantly in the white matter of the frontal lobe. This possible abnormality in energy metabolism in the frontal lobe of the cocaine-exposed children suggested that exposure to cocaine might cause frontal lobe injury by forcing cerebral metabolism to go in overdrive mode, exceeding the available energy supply (Smith, Chang, Yonekura, Gilbride et al., 2001). The authors further indicated that the results of the study implied that because executive functioning is thought to be mediated in part by the frontal-striatal pathway, altered energy metabolism in the striatum may have important clinical implications. Nonetheless, they did not discuss the clinical implications of the findings more specifically.

In another study, Dixon and Bejar (1989) examined nervous system abnormalities among three groups of infants; stimulant drug- methamphetamine and cocaine exposed group, encephalopathic injury group, and no drug exposure or brain injury infant group. The results illustrated that the drug-exposed and encephalopathic injury groups had similar and significantly more abnormal encephalographic results than the infants of the control (no drug exposure or brain injury) group. However, Dixon and Bejar (1989) found that the stimulant drug group had more abnormal white matter cavities and intraventricular hemorrhage than the brain injury group. Moreover, the cocaine-exposed infants had more abnormalities in white matter cavities than the methamphetamine-exposed infants. However, the methamphetamine-exposed infants had increased rates of intraventricular and subarachnoid hemorrhages. The consensus among researchers is that children subjected to prenatal drug-exposure generally exhibit more negative physiological outcomes than non-exposed infants (Azuma & Chasnoff, 1993; Chasnoff et al., 1992; Chasnoff, Griffith, MacGregor, Dirkes, & Burns, 1989; Hawley et al., 1995; National Center of Addiction and Substance Abuse at Columbia University, 2003). Given the structural and metabolic abnormalities that drug exposed children experience, it would be important to examine any associated cognitive deficits.

Cognitive and neuropsychological outcomes. Cognitive functioning of drug exposed children has been a topic of interest due to the deleterious effects prenatal drug exposure has on brain development and functioning. Griffith, Azuma, and Chasnoff (1994) evaluated a sample of participants using a standardized measure of intelligence (Stanford-Binet Intelligence test-4). In this study cocaine-exposed children (three-year olds) showed no difference in overall performance on the Stanford-Binet when compared to a non drug-exposed control group. However an examination of the index scores found that the cocaine-exposed group scored in the below-average range for verbal and abstract/visual reasoning when compared with non drug-exposed children (Griffith, Azuma, & Chasnoff, 1994).

Another study conducted by Singer et al., (2004) also showed no significant differences in full scale IQ, verbal IQ and performance IQ (Wechsler Pre-school and Primary Scales of Intelligence-Revised edition) between cocaine-exposed and non-drug exposed groups of four-year olds. However, there were subscale differences in visual-spatial skills, general knowledge and arithmetic (Singer et al., 2004). Additional differences in drug-exposed and non exposed-children were noted by Morrison et al. (2000). Specifically, cocaine and poly-substance exposed children were studied using the Mullen Scale of Early Learning (MSEL), which assesses development in five domains:

gross motor, visual reception, visual motor integration, language reception, and language expression. The drug-exposed group of children exhibited delays in gross-motor skills, visual motor expression, visual reception, and receptive language skills when compared to a non drug-exposed group. The drug-exposed group scored significantly lower on the expressive language domain than the non drug-exposed group (Morrison et al., 2000).

Singer et al. (2002) further supported that prenatal cocaine-exposure was related to significant cognitive deficits and developmental delays. Using two groups of infants, poly-drug exposed including cocaine and poly-drug exposed without cocaine, the researchers did a comparative study of mental functioning and development delays of the two groups using the Bayley Scales of Infant Development. It was discovered that the poly-drug including cocaine-exposed group exhibited mental retardation (Mental Development Index < 70) at age two at a rate five times higher than what was expected for the general population of infants. Moreover, the poly-drug including cocaine-exposed infants also exhibited delays (defined as Mental Development Index <80) at age two at a rate two times greater than the poly-drug exposed without cocaine infant group. However, the study did not specify if the delays were attributed to cognitive, motor or language deficits. Chasnoff et al. (1992) also reported lower development in cocaine-exposed children. Although it was found that the mean developmental scores of the groups did not vary greatly, there were a greater proportion of cocaine-exposed infants scoring significantly lower in the mental development index and psychomotor index of the Bayley Scales of Infant Development than the control group infants (Chasnoff et al., 1992).

The literature is very limited in discussing the neuropsychological effects of stimulant drug-exposure. A single research study discussing neuropsychological effects of cocaine-exposed children was found. With regards to neuropsychological performance patterns, cocaine-exposed children exhibited more errors on an executive functioning task (assessed by AB task). The cocaine-exposed children made more preservative errors and had more difficulties with inhibition than the non drug-exposed group (Epsy, Kaufmann, & Glisky, 2000). The study findings indicate that the cocaine-exposed group made more AB errors than was expected given their overall cognitive skill, which supports differences in neuropsychological development in drug-exposed children. Research supports that prenatal stimulant-exposure impacts cognitive and neuropsychological development negatively. However, due to differences in study methodology the findings are inconsistent in identifying the specific areas negatively affected.

Although not directly related, negative effects on cognition and memory have been found in individuals who chronically use methamphetamine as adults. Although the method of exposure is different for methamphetamine abusers than for fetuses, and developmentally they are less vulnerable than fetuses to drug-exposure effects, additional meaningful information can be gained in examining adult chronic methamphetamine-users and the long-term effects of methamphetamine.

Adult chronic methamphetamine abusers experience cognitive impairment and exhibit impaired verbal memory, as well as impaired performance on tasks involving perceptual speed and information manipulation (Meredith, 2005). Chronic methamphetamine users also exhibit deficits in abstract reasoning, planning, behavioral flexibility and episodic memory tasks (Kalechstein, Newton, & Green, 2003). There are also associations with poor attention, working memory, processing speed and episodic memory in chronic methamphetamine users (Nordahl, Salo, & Leamon, 2003). Methamphetamine dependent adults exhibit impairments in neurocognitive functioning even after abstinence, and are significantly slower than cocaine abusers to normalize (Meredith, 2005). Research supports that chronic methamphetamine-abuse in adults result in cognitive deficits, especially in memory and attention. In focusing on deficits experienced by chronic methamphetamine-abusers, information may be generalized to shed light on some of the mechanisms in which methamphetamine can affect the cognitive development of infants exposed in utero.

Environmental influences. Researchers have also linked drug exposed children's development to environmental factors such as environmental stimulation, care-giver child environment, poverty, unstable households, and physical and emotional neglect (Eriksson et al., 1989; Hawley et al., 1995). There is a considerable amount of literature that suggests that postnatal environmental factors play a significant role in determining developmental outcomes.

In one such study examining the differences between drug-exposed and non-exposed groups matched for age, ethnicity, gender, and SES no differences were found between a matched sample of cocaine-exposed and non-exposed children (Phelps, Wallace, & Bontrager, 1997). Both of these groups scored approximately one standard deviation below the mean on auditory comprehension and expressive language (Phelps, Wallace, & Bontrager, 1997). These findings were supported by another study that compared cognitive and motor development of three groups; prenatally opiate-exposed group, prenatally non-opiate-exposed group and a non-drug exposed group matched along demographic variables (Chasnoff, Burns, Burns & Schnoll, 1986). No differences were found in the groups on mental development and psychomotor indices, but all the infants in the study exhibited a decreasing trend in cognitive and motor functioning. Chasnoff et al. (1986) suggested that environmental characteristics such as a non-stimulating environment have a direct influence on development, more so than maternal drug use during pregnancy. Both of these studies support that variables other than just drug-exposure may have an effect on cognitive development. However, a more focused review of the literature is needed to understand the specific effects of environmental variables on cognitive development.

Pulsifer, Radonovich, Belcher and Butz (2004) studied two groups of children, exposed to drugs and not exposed to drugs. The results indicated that the exposed group of children scored significantly lower than the non-exposed group in intelligence and school readiness; the caregivers of drug-exposed children also scored significantly lower in intelligence and reading achievement than the caregivers of non-exposed children. Further, the caregivers' reading achievement was significantly correlated with child school readiness. The study concludes by stating that genetics interact with the environment in drug exposed children's school readiness. Although literature supports the idea of a link between prenatal drug exposure and difficulty in school (Dixon & Behar, 1989; Pulsifer et al., 2004), it is difficult to determine if poor school performance is due to prenatal drug exposure, to lack of a stimulating environment, and/or to heritability. The research seems to suggest that it is likely a combination of these variables.

In studying ties between environment and intelligence, socioeconomic status is an important variable to examine. Some studies indicate that approximately 60% of variability in IQ can be attributed to SES in impoverished families while in affluent families a smaller percentage of SES is attributed to the variability in IQ (Turkheimer, Haley, Waldron, D'Onofrio & Gottesman, 2003). Low SES and poverty was found to have a noticeable effect on child functioning and development (Hanson, 1975; Nair, Black, Ackerman, Schuler, & Keane, 2008). Hanson (1975) reported that home environment was directly related to measures of IQ, and further elaborated that home environment was most impactful in the first 10 years of life.

It appears that environmental factors are confounding variables related to drug-abuse and child outcomes. Johnson, Nusbaum, Bejarano, and Rosen (1999) reported that environmental variables affect the development of prenatally drug-exposed children. Specifically, this research stated that exposure to adverse social conditions is more likely to result in poor developmental outcomes than prenatal drug-exposure because women who abuse drugs typically come from impoverished environments where resources, finances, social support, and knowledge are limited. Due to the limitations of resources, more energy has to be exerted to secure basic necessities which leave less available energy to channel into ensuring the most advantageous opportunities for optimal child development. Further complicating matters of optimal development is that the addicted mother tends to have more problems and fewer social and coping resources, which sets up a highly stressed and distracted mother to take care of the infant's needs (Johnson, et al., 1999).

The above research indicates a limited effect of drug-exposure itself and suggests that drug-exposure results are more of an end product that combines the effect of the drug with the effects of an improvised non-stimulating environment. This is evidenced by research supporting there are cognitive and developmental differences in groups prenatally-exposed to drugs compared to groups not exposed to drugs (Azuma & Chasnoff, 1993; Chasnoff et al., 1992; Pulsifer, Radonovich, Belcher and Butz, 2004; Singer at al., 2002; Watson & Westby, 2003) and research supporting that these differences are primarily due to environmental variables. (Eriksson et al., 1989; Johnson, et al., 1999; Nair, Black, Ackerman, Schuler, & Keane, 2008; Turkheimer, Haley, Waldron, D'Onofrio & Gottesman, 2003). Based on the research, it is apparent that a drug addicted parent's circumstances (poverty, poor nutrition, lack of care, high stress, poor health, mental health issues) create an unsuitable environment that is unfavorable to optimal development. It appears that an interaction of environmental variables along with the drug-exposure itself determines developmental outcomes.

Although the above research does much to identify issues associated with prenatal drug-exposure in general, not much is specifically known about the effects of prenatal methamphetamine-exposure. As such, most research in this area has been limited to animal studies will a few human outcome studies. In light of this deficit, it is important to explore these early animal studies in order to provide a better understanding of prenatal methamphetamine-exposure in offspring outcomes. Additionally, the few studies examining child outcomes on prenatal methamphetamine-exposure directly speak to the goals and objectives of the current study.

Effects of Prenatal Methamphetamine Exposure in Rodents

As mentioned previously, there is a paucity of literature that specifically addresses the outcomes of prenatal methamphetamine exposure. Therefore, rodent studies will be reviewed here to gain a basic understanding about methamphetamine-exposure outcomes. Scientists attempt to examine the effects of prenatal methamphetamine exposure by designing controlled experiments to inspect biological and developmental functioning of drug exposed rodent offspring. However, it should be noted that Cho, Melega, Kuczenski and Segal (2001) report major differences in rats' metabolic rate of methamphetamine. The authors caution there are significant differences in the elimination half-life of methamphetamine between rats (70 minutes) and humans (12 hours), which can be accounted for by altering the dosages of methamphetamine given to the rat subjects.

Martin, Martin, Radow, and Sigman (1976) observed the effects of prenatal methamphetamine exposure by injecting three groups of Sprague-Dawley rats. The study used nicotine, methamphetamine, or saline (control group) injected rats, as well as non-injected rats (second control group). There were changes in the length of gestation in the nicotine and methamphetamine injected groups, with a lengthened gestation period for the nicotine injected group and shortened gestation period for the methamphetamine injected group. Both the nicotine and methamphetamine groups' litters were light weight, with the methamphetamine group litter being the lighter. The methamphetamine injected group's offspring were underweight at birth and were not able to achieve the rate of weight gain noted in the control groups and remained significantly below the control group weight. In the methamphetamine group some developmental delays were noted such as eye opening, while no developmental delay were observed in the other groups.

Additionally, the rat pups in the drug-exposed group were also more avoidant (Martin, Martin, Radow, & Sigman, 1976).

Martin et al. (1976) discovered locomotor activity changes in the long-term for methamphetamine-exposed rats. Methamphetamine-exposed rats exhibited consistently high activity levels when compared to nicotine-exposed and non-drug exposed control groups. In another study, rats administered a higher dose of methamphetamine failed to deliver a viable litter (Martin, 1974). Also, the litter size decreased as the dose of drug given to the rats increased (Martin, 1974). Wistar rats were used to investigate learning in methamphetamine injected, non-injected, and saline injected groups (Slamberova, Pometlova, Syllabova, & Mancuskova (2005). The rats exposed to methamphetamine were slower in navigation learning than the control groups. The authors suggested that this may be due to the methamphetamine effects on the developing hippocampus which is central to memory and learning.

In a similar study, using the same three groups Slamberova et al., (2006) found that the methamphetamine-exposed rats exhibited slower reflexes in that they were slower to turn themselves when they were placed on their backs. This study also examined the effects of prenatal methamphetamine-exposure on sensory-motor coordination. The methamphetamine-exposed rats fell from a rotating cylinder task, which was thought to be due to impaired sensory inputs or to delayed development of control of locomotion. However, the results contradicted previous studies by Martin et al. (1976) noting that the methamphetamine-exposed rat pups opened their eyes earlier than the control groups, and were able to catch up to the weight of the control groups. The authors speculate that the disparity in the studies may be due to the different type of rats used in the two experiments.

Vorhees, Ahrens, Acuff-Smith, Schilling, & Fisher (1994) examined the effects of post-natal methamphetamine exposure in rats. The authors investigated the developmental differences when drug-exposure occurs during brain development of rats during a period equivalent to the third-trimester brain development in humans. Sprague-Dawley rats were separated into three groups: distilled water injections, methamphetamine injections early (1-10 days) in the postnatal development and methamphetamine injections later (11-20 days) in the postnatal development. The methamphetamine-exposed groups exhibited increased acoustic startle responsiveness as they were hyper-reactive. The methamphetamine-exposed groups also demonstrated impaired leaning in a multiple-T maze task. It appears that the neonatally exposed rats, especially those exposed on days 11-20, had long-term deficits in associative memory and/or memory processes that depend on stable cues and on determining spatial cues. In the methamphetamine injected 11-20 days group, multiple forebrain effects involving associative processes that also affected learning were noted.

Williams, Moran, & Vorhees (2004) investigated behavioral and growth effects induced by neonatal low dose methamphetamine exposure at a time analogous to third trimester human development. Sprague-Dawley rats were administered low doses of either methamphetamine (equivalent to low-dosage used by humans) or saline through an injection. Commensurate with previous literature, the investigators found the methamphetamine exposed rats displayed impairment in learning on Morris water maze tasks, as well as indications of deficits in spatial learning. The study suggested that even low doses of methamphetamine can have negative effects on learning and memory.

In summary, research supports that methamphetamine-exposed rats exhibited differences from the control groups. Rats injected with methamphetamine had shorter gestation periods and delivered premature and non-viable litters. Methamphetamine-exposed rats were born underweight and had difficulty gaining weight over time. Developmental delays such as eye-opening and slower reflexes in the methamphetamine-exposed group were observed in several studies (Martin et al., 1974; Martin et al., 1976; Slamberova et al., 2006). However, it should be noted that the research is somewhat inconsistent as there was one study contradicting the findings that methamphetamine-exposed rat pups had delayed eye opening and poor weight gain over time (Martin et al., 1976). Methamphetamine-exposed rats also exhibited negative effects in learning, memory, visuo-spatial abilities, and sensory-motor coordination problems, than their non-exposed counterparts (Slamberova, Pometlova, Syllabova, & Mancuskova, 2005; Vorhees, Ahrens, Acuff-Smith, Schilling, & Fisher, 1994; Williams, Moran, & Vorhees, 2004). Based on the animal models, results suggest that differences in learning and memory, visuo-spatial skills and visuo-motor integration might be expected in children exposed to methamphetamine.

Effects of Prenatal Methamphetamine Exposure in Humans

As mentioned previously, few studies have examined the negative effects of prenatal methamphetamine exposure on the development of children, while the knowledge of the effects of prenatal methamphetamine exposure on fetal growth is also inadequate. Furthermore, the available research yields mixed conclusions due to methodological differences and variations in measurement tools used to examine outcomes.

In one study, two groups of full-term infants (methamphetamine exposed and non-exposed) were compared, it was discovered that there were no significant differences in weight, length or head circumference. However, a higher percentage of infants in the methamphetamine exposed group were small for their gestational age (Smith, Yonekura, Wallace, Berman, Kuo, & Berkowitz, 2003). It is theorized that a majority of stimulant users tend to also smoke cigarettes to decrease the unpleasant effects of stimulant use (Dixon, 1994). Dixon found that simultaneous exposure to methamphetamine and nicotine resulted in small infant size. In addition, methamphetamine exposure during all three trimesters of pregnancy resulted in decreased birth weight and head circumference compared to infants exposed to methamphetamine for only a part of the pregnancy.

Smith, Chang, Yonekura, Grob, Osborn and Ernst (2001) examined the neurotoxic effects of prenatal methamphetamine-exposure on the brain. Children were age-matched into groups of methamphetamine exposed and non-exposed groups and were evaluated with MRI and H-MRS. No visible structural abnormalities were found in either group. However, the methamphetamine-exposed group had higher levels of creatine, which indicates altered energy metabolism. N-acetyl-containing compounds were normal, which according to the authors suggested a lack of significant neuronal loss or damage. There were no differences noted in the two groups in behavior problems.

Chang et al. (2001) also examined the neurotoxic effects of prenatal methamphetamine exposure on the brain and cognition. Groups of methamphetamine exposed children and non-exposed children were evaluated using MRI to examine structural differences. These children were also given a battery of neurocognitive assessments which included Visual Motor Integration (VMI), Purdue pegboard, Test of Variable attention (TOVA), The Developmental Neuropsychological Assessment (NEPSY), Wechsler Preschool and Primary Scale of Intelligence-Revised (WPPSI-R), Children's Memory Scale-Dot location subtest, Expressive One Word Picture Vocabulary Test-Revised (EOWPVT-R), Peabody Picture Vocabulary Test (PPVT-III), Controlled Oral Word Association Test, Vocabulary and Block Design-Wechsler Intelligence Scale for Children-Third Edition (WISC-III), and Children's Depression Inventory (CDI) to examine differences in cognition.

In this study, MRI results were analyzed using a MRI segmentation program to segment the brain from the skull, muscle, skin, etc. in order to gather intracerebral brain volume and global CSF volume. Results showed that, relative to the whole brain, the methamphetamine exposed children had smaller volumes of subcortical gray matter, putamen, globus pallidus and smaller hippocampal volumes. Compared to the control group (non drug-exposed), the methamphetamine exposed group had significantly lower volumes of putamen and globus pallidus, which was reported by the authors to be associated with poorer attentional task performance (Chang et al., 2001).

The methamphetamine-exposed children performed worse than the unexposed children on a visual motor integration task (VMI), but there was no difference between the groups in fine motor function as measured by the Purdue Pegboard. Furthermore, the methamphetamine exposed children performed significantly worse than the unexposed children on a measure of sustained attention (TOVA), while there were no differences between the groups in visual attention and psychomotor speed. Verbal memory (long delay and short delay) was also significantly lower in the methamphetamine group when compared to the unexposed group. The long-delay spatial memory scores in the methamphetamine exposed group were lower, even though both groups were within normal limits. Both groups performed within the normal range on the measures of visuo-constructional skills and ability to define words, but the methamphetamine-exposed group scored lower than the non-exposed group in vocabulary (Chang et al., 2001).

Summary of the Literature

In summary, given that the methamphetamine abuse among pregnant women is increasing, it is important to examine the effects of prenatal methamphetamine-exposure on children. Current research on methamphetamine-exposure on cognitive development is sparse. However, research examining prenatal effects of cocaine was used to gain an understanding of the effects of methamphetamine-exposure, because although the two drugs have individual differences they are both of the stimulant class of drugs.

Overall the research examining the effects of drug-exposure has focused on physiological effects such as premature birth, lower birth weight, smaller head circumference, brain volume differences and metabolic differences of neurochemicals (Azuma & Chasnoff, 1993; Chasnoff et al., 1992; Hawley et al., 1995; Smith, Yonekura, Wallace, Berman, Kuo, & Berkowitz, 2003), which has led to exploring cognitive and neuropsychological correlates. With regards to cognitive development, research findings are inconsistent due to methodological differences but most studies found differences between stimulant-exposed and non-exposed groups (Chasnoff et al., 1992; Griffith, Azuma, Chasnoff, 1994; Kalechstein, Newton, & Green, 2003; Meredith, 2005; Morrison et al, 2000; Singer at al., 2002). Specifically, it was determined that drug-exposed children had difficulties in the areas of verbal and visual reasoning, expressive and receptive language skills, memory impairment, processing speed and attention (Chasnoff et al., 1992; Griffith, Azuma, Chang, et al., 2004; Chasnoff, 1994; Kalechstein, Newton, & Green, 2003; Meredith, 2005; Morrison et al, 2000).

Environmental factors were also found to contribute to outcome and must be considered. Consistent variables identified in the literature that contributes to cognitive and neuropsychological developmental outcomes are mother's lifestyle choices (poor nutrition, poor prenatal care) during pregnancy and postnatal environmental variables such as SES, maternal stress, neglectful parenting, and chaotic households (Eriksson et al., 1989; Johnson, et al., 1999; Nair, Black, Ackerman, Schuler, & Keane, 2008; Turkheimer, Haley, Waldron, D'Onofrio & Gottesman, 2003).

Research specific to prenatal methamphetamine-exposure has been very limited and has been primarily restricted to rat studies used to serve as a basic model to gain additional information. These studies generally indicated that methamphetamine-exposed litters were less viable, length of gestation was less and rat pups were lighter in weight than non exposed-rats (Martin et al., 1976). The methamphetamine-exposed rats also exhibited developmental delays and slower reflexes. Additionally, they had negative effects related to learning, memory, visuo-spatial abilities, and sensory-motor coordination. The results of the few studies that examined children prenatally-exposed to methamphetamine suggested there are volumetric, and neurochemical differences in the brain (Smith, Chang, Yonekura, Grob, Osborn and Ernst , 2001; Smith, Yonekura, Wallace, Berman, Kuo, & Berkowitz, 2003), as well as delays in visual motor integration, sustained attention, and memory when compared to non drug-exposed children (Chang, et al., 2001). Given the scarcity of research examining the effects of prenatal methamphetamine-exposure, more research exploring methamphetamine-exposure is necessary.

Methods

Statement of Problem

Methamphetamine is becoming a primary drug of choice as it is relatively inexpensive and, easily available due to an increase in the number of methamphetamine laboratories in Inland Empire. Methamphetamine appears to be a preferred drug among pregnant women due its highly addictive properties along with its other desired effects including increased energy levels and weight loss. As a result of the increase in methamphetamine abuse in women of child bearing age, more babies are born with prenatal exposure to the drug.

Stimulant drug use when pregnant has been shown to have adverse effects on children later in life. Specifically, children have been found to have deficits in the areas of verbal and visual reasoning, expressive and receptive language skills, memory impairment, processing speed and attention (Chasnoff et al., 1992; Griffith, Azuma, Chang, et al., 2004; Chasnoff, 1994; Kalechstein, Newton, & Green, 2003; Meredith, 2005; Morrison et al, 2000). Although this research offers some insight into understanding the effects of prenatal drug-exposure in general, the extent that these finding apply to children prenatally exposed to methamphetamine is unknown.

Existing research on methamphetamine-exposure on long-term cognitive effects is very limited. However, early animal and adult human studies seem to support that methamphetamine-exposure is related to impairments in learning, memory, visuospatial abilities, perceptual speed, attention, and abstract reasoning (Slamberova, Pometlova, Syllabova, & Mancuskova, 2005; Williams, Moran, & Vorhees, 2004). These findings were generally supported by the only study examining cognitive and neuropsychological outcomes in prenatally methamphetamine exposed children, which found that methamphetamine-exposure has a significant effect on sustained attention and verbal memory, and trends in lower visual motor integration, spatial memory and verbal ability (Chang et al., 2001).

Given the above, the current study will examine the cognitive trends and profiles of children prenatally exposed to methamphetamine. It should be noted that children were being seen for behavioral and/or academic problems through the Loma Linda University (LLU) Pediatric NeuroAssessment Clinic. Therefore it is assumed and expected that deficits will be found in these children. Further, due to 'referral to clinic' bias the children in this sample may not represent the larger population of methamphetamine affected children. As such this study will be primarily exploratory in nature, focusing on patterns of deficits.

Study Objectives and Hypotheses

The first objective of this study will utilize neuropsychological archival data to describe the frequency and characteristics of clinically referred children prenatally exposed to methamphetamines. Specific factors to be explored include the following:

1. Prenatal methamphetamine-exposed cases will be specifically identified and described in respect to sample demographics (i.e. age, gender, ethnicity, referral question).
2. Profiles of prenatal methamphetamine-exposed children seen in the LLU PNAP clinic will be described. This will include examining trends in the Wechsler intelligence factor scores (verbal comprehension index, perceptual organization/perceptual reasoning index, freedom from

distractibility/working memory index, and processing speed index). Wechsler intelligence subtest trends and Neuropsychological Evaluation for Children (NEPSY) domain scores of attention/ executive functions, language, sensorimotor functioning, visuospatial processing, and memory and learning will also be explored. Descriptive comparisons to the normative sample will also be discussed.

The second objective of this study will compare a matched sample (by age, gender, ethnicity and referral question of behavior concerns, academic concerns or psychosocial concerns) of prenatal methamphetamine-exposed and a clinic-based non-prenatal drug exposed children to address if there are any significant differences in the perceptual reasoning index, verbal comprehension index, processing speed index, and working memory index as measured by Wechsler Intelligence Scale for Children-III (WISC-III) or Wechsler Intelligence Scale for Children-IV (WISC-IV). The prenatal methamphetamine-exposed group will also be compared to the non-clinical normative sample on the same Wechsler index scores indicted above.

It is expected that effects of sustained attention and memory deficits would affect processing speed and working memory index scores due to the fact that attention and memory are especially necessary to complete the processing speed tasks and the working memory tasks. The lower score trends in verbal ability would probably lead to low scores in the verbal comprehension index, and visual motor integration and visuo-spatial ability would lead to lower scores in the perceptual reasoning index. As such, the following hypotheses will be investigated:

1a. There will be a significant difference between methamphetamine-exposed and the clinic based non-drug exposed groups on the Wechsler intelligence scale, verbal comprehension index factor scores.

1b. There will be a significant difference between methamphetamine-exposed children and the non-clinical normative sample on the Wechsler intelligence scale, verbal comprehension index factor scores.

2a. There will be a significant difference between methamphetamine-exposed and clinic based non-drug exposed groups on the Wechsler intelligence scale, perceptual reasoning index factor scores.

2b. There will be a significant difference between methamphetamine-exposed children and the non-clinical normative sample on the Wechsler intelligence scale, perceptual reasoning index factor scores.

3a. There will be a significant difference between methamphetamine-exposed and clinic based non-drug exposed groups on the Wechsler intelligence scale, working memory index factor scores.

3b. There will be a significant difference between methamphetamine-exposed children and the non-clinical normative sample on the Wechsler intelligence scale, working memory index factor scores.

4a. There will be a significant difference between methamphetamine-exposed and clinic based non-drug exposed groups on the Wechsler intelligence scale, processing speed index factor scores.

4b. There will be a significant difference between methamphetamine-exposed children and the non-clinical normative sample on the Wechsler intelligence scale, processing speed index factor scores.

Participants

Children participating in this study were clients of the LLU Pediatric NeuroAssessment Program (PNAP), which is a comprehensive assessment and diagnostic program that addresses the needs of preschool and school-aged children with behavioral and academic problems. Children were primarily referred to the PNAP program by their primary care physicians, although some were school, friend, or self-referred. A neuropsychological evaluation including cognitive, psychosocial, and neurological assessments was a part of the standard care at PNAP these clients received. This study included archival data from children who had a neuropsychological evaluation including a Wechsler Intelligence scale (WISC-III or WISC-IV) and/or a Neuropsychological Evaluation of Children (NEPSY). All participants identified for this study had informed parental consent for the participant information and data to be used in research.

A total of 15 children with prenatal methamphetamine-exposure were identified from the PNAP participants through chart review. Of the 15 participants, one participant was excluded from the study due an existing diagnosis of Autism, which along with traumatic brain injury was determined as an exclusionary criterion for this study. Of the 14 remaining participants, 11 participants were matched with a non-drug exposed group; the remaining three participants were unable to be matched. However, the 11 participants who were matched all had a Wechsler scale of intelligence (WISC-III or WISC-IV) and three had some NEPSY domains in their battery. The three participants without matches all had some or all of the NEPSY domain scores included in their battery.

Chart review and PNAP database review was used to identify the non-drug exposed sample of participants eligible to be matched. The non-drug exposed participant group was matched to the methamphetamine-exposed participants by age, gender, ethnicity, and referral question (behavioral, academic or psychosocial). Participants were also matched according to the version of the WISC or NEPSY administered. In respect to referral question, none of the methamphetamine-exposed participants were primarily referred for psychosocial challenges, and therefore no participants in the sample were coded for psychosocial referral question. Primarily behavioral referral questions included behavior difficulties, attentional challenges, and aggressive behaviors. The academic referral question was coded for participants who were referred for concerns about school achievement, academic ability and cognitive/academic functioning. Participants were coded as the behavioral/academic (both) referral question when they were referred for a combination of behavior and academic challenges. It should also be noted that the participants were not matched along the variable of family SES or other environmental variables due to the unavailability of this information.

Measures

Wechsler intelligence scales. Currently, the Wechsler intelligence tests (e.g., Wechsler Adult Intelligence Scale-fourth edition, 2008; Wechsler Intelligence Scale for Children-fourth edition, 2003) are the most widely used intelligence measures because of their excellent reliability and validity demonstrated through decades of research (Kaufman, 2000; Rispens et al., 1997; Watkins, Kush, & Glutting, 1997).

The Wechsler Intelligence Scale for Children, third edition (WISC-III) is an assessment instrument that assesses intelligence of children 6 years, 0 months through 16 years 11 months (Wechsler, 1991). It was standardized on a nationally representative sample of children (*N* = 2200) closely following the 1988 U.S. census demographics (Wechsler, 1991). The WISC-III is comprised of four factor-based indexes of intelligence, verbal comprehension index (VCI), perceptual organization index (POI), freedom from distractibility index (FDI) and processing speed index (PSI). The WISC-III has 13 subtests (ten standard and three supplementary subtests) that make-up the test (*M* = 10, *SD* = 3). The WISC-III has strong reliability demonstrated both by measures of average internal consistency coefficients of 0.96 for FSIQ, 0.94 VCI, 0.90 for POI, 0.87 for WMI and 0.85 for PSI, and also by test-retest coefficients which was 0.95 for FSIQ, 0.93 for VCI, 0.87 for POI, 0.86 for WMI, and 0.85 for PSI (Wechsler, 1991).

The most recent revised and updated edition of WISC-III is the Wechsler Intelligence Scale for Children, fourth edition (WISC- IV). The WISC-IV "is an individually administered, comprehensive clinical instrument for assessing the intelligence of children ages 6 years 0 months through 16 years 11 months" (Wechsler, 2003 , p.1). The WISC-IV was standardized on a nationally representative sample of children (*N* = 2200) closely following the 2000 U.S. census demographics (Wechsler, 2003). The WISC-IV provides four index scores of verbal comprehension index (VCI), perceptual reasoning index (PRI), working memory index (WMI) and processing speed index (PSI), in addition to a measure of general intellectual functioning. The WISC-IV is comprised of ten core subtests and five supplementary subtests) (*M* = 10, *SD* = 3). The WISC-IV has strong reliability demonstrated both by measures of average internal consistency coefficients of 0.97 for FSIQ, 0.94 VCI, 0.92 for PRI, 0.92 for WMI and 0.88 for PSI, and also by test-retest coefficients which was 0.93 for FSIQ, 0.93 for VCI, 0.89 for PRI, 0.89 for WMI, and 0.86 for PSI (Wechsler, 2003).

The WISC-III and WISC-IV have notable similarities as well as differences. The WISC-III and WISC-IV are both comprised of four indexes. WISC-III and WISC-IV both have the verbal comprehension index (VCI), a measure of verbal reasoning and comprehension, acquired knowledge and attention to verbal stimuli. The correlation between WISC-III and WISC-IV verbal comprehension index is strong, $r = .88$ (Wechsler, 2003). The perceptual organization index (POI) on the WISC-III and perceptual reasoning index (PRI) on the WISC-IV, which measures non-verbal, fluid reasoning were moderately correlated $r = .72$ (Wechsler, 2003). The freedom from distractibility index (FDI) on WISC-III and the working memory index (WMI) on WISC-IV, which measures short-term memory, sustained attention, concentration, and the ability to hold and manipulate information in the short-term memory were moderately correlated, $r = .72$ (Wechsler, 2003). The processing speed index (PSI), which is a measure of speed, acuity, discrimination of visually presented information is a factor of both WISC-III and WISC-IV. The PSI on WISC-III and WISC-IV was strongly correlated, $r = .81$ (Wechsler, 2003). In addition to the four factors, a full scale intelligence quotient (FSIQ) can also be determined for the WISC-III and WISC-IV. The FSIQ is strongly correlated ($r = .89$) on both tests. Wechsler intelligence scales are reported as standard scores, and are therefore numerically comparable. WISC-III and WISC-IV both have a norm-referenced mean of 100 and a standard deviation of 15.

Although the WISC-III and WISC-IV are well correlated with one another, there are differences in the subtests that make up each index. Three of the four WISC-III verbal comprehension index subtests (similarities, vocabulary, and comprehension) were retained to compose the WISC-IV. Among the changes to the verbal comprehension index from the WISC-III to WISC-IV was that the Information subtest is now an optional subtest (not included to calculate VCI or FSIQ as in WISC-III) on the WISC-IV (Wechsler, 1991; Wechsler, 2003). The perceptual reasoning index on the WISC-IV also has three instead of four subtests, block design, picture concepts, and matrix reasoning. The WISC-III perceptual organization index was comprised of picture completion, picture arrangement, object assembly and block design (Wechsler, 1991; Wechsler, 2003). The WISC-III freedom from distractibility index was made-up of digit span and arithmetic subtests, but WISC-IV working memory index is comprised of the digit span and letter-number sequencing (Wechsler, 1991; Wechsler, 2003). The processing speed on both WISC-III and WISC-IV include the coding and symbol search subtests (Wechsler, 1991; Wechsler, 2003). There are also differences between the tests in the way FSIQ is determined. On the WISC-IV, all four of the working memory index and processing speed index subtest scores are included in determining FSIQ, while only two of the four subtest scores from the freedom from distractibility index and processing speed index are included to determine FSIQ on the WISC-III (Wechsler, 1991; Wechsler, 2003). It should be noted that the norms on the WISC-III and WISC-IV are different, and as such it may be problematic to combine scores from the two versions of the test. However the standard approach to combine the scores currently found in the literature was used in this study.

Verbal comprehension index measures by the Wechsler intelligence scales require verbal conceptualization, language processing, verbal reasoning, memory and the ability to orally describe the nature or meaning of words (Sattler, 2001; Wechsler, 2003). The verbal comprehension index measures knowledge acquired from one's environment (Wechsler, 2003). The perceptual organization index and perceptual reasoning index indexes will be combined and referred to as the perceptual reasoning index throughout this study. This index requires visual perception, visuospatial processing, visual-motor coordination, planning and organization, attention, memory and reasoning with visually presented, nonverbal material to solve novel problems (Sattler, 2001; Wechsler, 2003). The freedom from distractibility and working memory index will be combined and referred to as the working memory index. Working memory requires working memory processes to be applied to the manipulation of orally presented verbal sequences. The ability to temporarily retain information in memory, by performing some operation/manipulation with it, and to generate a result is measured by freedom from distractibility/working memory indexes. It involves attention, concentration, mental control, reasoning, which are all essential components of other cognitive higher order progresses. The processing speed index (PSI) requires visual perception and organization, visual scanning, attention, concentration, and accurate and effective motor responses (Wechsler, 2003).

NEPSY- Neuropsychological Evaluation for Children. The NEPSY is an individually administered test of neuropsychological development which measures skills in the core domains of attention/ executive functions, language, sensorimotor functioning, visuospatial processing, and memory and learning in children between the ages of 3 years and 12 years to determine neuropsychological functioning (NEPSY; Korkman, Kirk, & Kemp, 1998).

The attention/ executive functioning domain functions are subjective to their operational definitions. Korkman, Kirk, and Kemp (1998) outline the specific facets of the attention and executive function measured in the NEPSY as follows: auditory and visual attention, response set stability and change and nonverbal problem solving. For the age band 5-12 years, three subtests make-up the attention/executive core function sections, and two subtests make-up this section for the 3-4 year band. Of all the core domains of the NEPSY, attention/ executive function is thought to be the most conceptually problematic due to the lack of agreement among researchers of the exact constitution of tasks aimed at measuring executive functions (Saadia & Warriner, 2001).

The Language functioning core domain is based on three subtests for the 5-12 year-old band and three subtests for the 3-4 years-old band. The language domain of the NEPSY assess phonological processing, repetition of nonsense words, comprehension of instructions and speeded naming (Korkman, Kirk, & Kemp,1998). The sensorimotor domain of the NEPSY is based on three subtests for the 5-12 year-old band and two subtests for the 3-4 year-old band. This domain includes imitation of hand positions, production of repetitive finger movements and speeded precise pencil usage. The visuospatial processing domain is based on two subtests for the 5-12 year-old band and two subtests for the 3-4 year-old band. The visuospatial processing domain requires the ability to put together parts to form a whole and judge object orientation and location. The fifth domain of the NEPSY, memory and learning is based on three core subtests for the 5-12 year-old band and two subtests for the 3-4 year-old band. The memory and learning domain is assessed by narrative memory and both delayed and immediate memory for names and faces (Korkman, Kirk, & Kemp, 1998). Saadia and Warriner (2001) reported that the NEPSY does not allow for delineation of assessment in different types of memory.

The average internal consistency coefficients for the NEPSY for the 3 to 4 year band are 0.70 for attention/executive functioning, 0.90 for language, 0.88 for sensorimotor functioning, 0.88 visuospatial processing and 0.91 for memory and leaning, which means that the core domains exhibit moderately high reliability scores. The domain of attention/executive function shows somewhat lower reliability for this age band. The internal reliability of the core domains for the 5 to 12 year band are 0.82 for attention/executive functioning, 0.87 for language, 0.79 for sensorimotor functioning, 0.83 for visuospatial processing and 0.87 for memory and learning, which indicates reliability of the core domains are moderately high. In this study, all domains were examined.

Procedure

Parent consent was obtained prior to their child's participation for all components of the program, including for research purposes. Only archival data from participants was utilized. The initial database was gathered as part of a routine clinic evaluation of PNAP program participants. However, it was found that the clinic database did not indicate drug-exposure information. Subsequently, with permission from the clinic director, individual intakes and charts were reviewed to ascertain methamphetamine-exposure. No identifying information was included in the final database created for this study. The data used were from assessments conducted during the period of 2001 to 2008.

Analyses

The analyses of the first objective utilized descriptive statistics including frequency, central tendency, and variability to describe frequency and profiles of the prenatally methamphetamine-exposed children.

The second objective included four, two part hypotheses comparing the methamphetamine-exposed group to the non-drug exposed group and to the normative sample in respect to the Wechsler Intelligence scale indexes of verbal comprehension, perceptual organization/perceptual reasoning, freedom from distractibility/working memory and processing speed. These hypotheses were analyzed using independent and one-sample t-tests.

Supplementary analyses were conducted in order to obtain additional information regarding the variables. Specifically, one-sample t-tests were performed to compare the non-drug exposed sample to the normative sample in respect to differences in Wechsler intelligence factor index (verbal comprehension, perceptual organization/ perceptual reasoning, freedom from distractibility/working memory, processing speed) scores. Additionally, descriptive information was provided comparing the methamphetamine-exposed group to the clinical non-drug exposed group along the Wechsler intelligence subtests scores.

In examining the study objectives, WISC-III and WISC-IV scores were combined due to the small sample size. This is a potential methodological issue due to the WISC-III and WISC-IV differences in test construction and the fact that children consistently score slightly higher on the WISC-III (Wechsler, 2003). However, the standard approach found in the literature, which was to combine the standard scores was utilized. Although this approach is somewhat problematic, there does not appear to be an effective solution in the literature that addresses the differences in WISC-III and WISC-IV scores. In interpreting all significance tests a p-value of < .05 was used. All analyses were performed using SPSS statistical software, version 17.0 (SPSS, 2008).

Results

Objective One

The first objective was to describe the frequency and characteristics of prenatal drug exposure in the neuropsychology clinic demographic. Review of the PNAP clinic database indicated a total of 489 patients. Through review of intakes and patient charts, 15 methamphetamine exposed patients were identified. Of the total clinic population, 3.07% were identified as exposed to methamphetamine. For the purpose of this study, one participant was excluded from the study per previously established exclusionary criteria of a diagnosis of Autism. Although the intake questionnaire used in the clinic asks about drug use, it does not specifically ask about methamphetamine use. As a result, it is possible that information specific to methamphetamine use was not gathered during the intake. It was noted during the review of the intakes, that some questionnaires indicated the presence of prenatal drug-use, but did not specify the type of drug(s) that was used.

The methamphetamine-exposed sample demographics for each participant are listed on Table 1. The methamphetamine-exposed sample was made-up of 9 males (64 %) and 5 females (36 %). With regards to ethnicity, the sample included 8 Caucasian participants, 3 African-American participants, 1 Hispanic participant, 1 Asian participant, and 1 Native-American Participant. In the methamphetamine-exposed sample, 6 participants were referred for Academic concerns, 2 participants were referred for behavioral concerns, and 6 participants were referred for academic and behavioral concerns. The methamphetamine-exposed participants' mean age was 9.36 (SD = 3.5) with a range of ages from 4 to 14.

Table 1

Methamphetamine-exposed sample demographic information

Clt.	Age	Gender	Ethnicity	Referral[a] Question	Measure
1	14	Male	Caucasian	Both	WISC-III
2	14	Male	Caucasian	Both	WISC-IV
3	6	Male	Hispanic	Behavioral	WISC-III
4	11	Male	Caucasian	Academic	WISC-III
5	14	Male	Caucasian	Academic	WISC-IV
6	10	Male	African-American	Both	WISC-IV/NEPSY
7	11	Male	Native-American	Both	WISC-IV
8	11	Female	Caucasian	Both	WISC-III
9	4	Male	African-American	Academic	NEPSY
10	9	Female	Asian	Academic	WISC-III/NEPSY
11	6	Male	Caucasian	Both	NEPSY
12	7	Female	Caucasian	Academic	WISC-IV
13	10	Female	African-American	Academic	WISC-IV/NEPSY
14	4	Female	Caucasian	Behavioral	NEPSY

[a] On Referral Question column, 'Both' refers to primary referral questions of Academic and Behavioral nature.

Of the 14 methamphetamine-exposed participants, 11 participants (with Wechsler intelligence scale included in their battery) were matched with non drug-exposed participants from the clinic. The participants' demographic information from both groups is depicted on Table 2.

In further addressing objective one the cognitive and neuropsychological profiles of prenatal methamphetamine-exposed children were examined. First, the data were screened for missing data, and accuracy of data entry. Given the clinical nature of the sample where standard procedure of selecting the assessment battery is determined based on referral question, not all participants had Wechsler intelligence scales and NEPSYs

Table 2

Participant Demographics

Demographic	Methamphetamine-exposed group	Non-exposed group	Total
Gender			
Female	5	4	9
Male	9	7	16
Ethnicity			
Caucasian	8	6	14
African-American	3	2	5
Hispanic	1	1	2
Asian	1	1	2
Naïve-American	1	1	2
Referral Question			
Behavior	2	1	3
Academic	6	5	11
Behavior/Academic	6	5	11

administered as a part of their assessment battery. Of the fourteen methamphetamine-exposed participants in this study, six participants in the sample had NEPSY scores available, and only four of those participants had all the domains of the NEPSY administered. Specifically, four scores were available for the NEPSY-memory domain and NEPSY-language domain, and five scores were available for NEPSY-attention/executive functions domain. Due to the very small sample size, NEPSY scores of the methamphetamine-exposed participants can only be examined descriptively.

Of the total methamphetamine-exposed group, 11 participants had Wechsler intelligence scores (WISC-III or WISC-IV). There were five methamphetamine-exposed participants whose assessment battery included the WISC-III, while six participants whose assessment battery included the WISC-IV. Participants (n = 11) not exposed to any drugs were matched by age, gender, ethnicity and referral question to the methamphetamine-exposed subsample. Three of the 11 participants with a Wechsler intelligence measure also had various NEPSY domain scores available.

Profiles of the methamphetamine-exposed group. The Wechsler intelligence scale index scores and NEPSY domain score profiles of methamphetamine-exposed children seen in the neuropsychology clinic are illustrated on Table 3.

Table 3.

Standard score mean, median and standard deviation for methamphetamine-exposed children

	n	Mean	Median	SD	Range
Wechsler Intelligence Test[a]					
Verbal Comprehension Index	11	86.18	87.00	15.35	68-108
Perceptual Reasoning Index	11	91.45	88.00	19.79	56-129
Working Memory Index	11	90.27	98.00	16.00	71-113
Processing Speed Index	11	81.64	78.00	14.04	59-111
NEPSY Domains					
Attention/Executive Functions	5	87.40	88.00	18.87	60-113
Language	4	90.00	90.00	8.41	81-99
Sensorimotor Functions	6	88.33	91.50	20.27	50-107
Visuospatial Processing	6	100.00	102.00	16.62	79-118
Memory and Learning	4	87.75	83.00	13.67	78-107

Note: Standard score mean (*M* = 100) and standard deviation (*SD = 15)* for normative population. Average range 80-119 (Sattler, 2001).
[a] WISC-III and WISC-IV were used to calculate Verbal ability,
Performance ability, Working Memory and Processing Speed means and standard deviations.

An examination of the processing speed index (*M* = 81.6) for the methamphetamine-exposed participants indicates that it was the lowest of the Wechsler intelligence scale factors. The other Wechsler intelligence scale variable mean scores in increasing order are verbal comprehension (*M* = 86.2), working memory (*M* = 90.3) and perceptual reasoning (*M* = 91.4). Both the processing speed index mean and the verbal comprehension index mean fell in the low average range classification, while the working memory index and the perceptual reasoning fell in the average range (Sattler, 2001).

In looking at the NEPSY domain scores, the attention/executive functioning domain (*M* = 87.4) was the lowest. The remainder of the NEPSY domains in increasing mean score order are memory (*M* = 87.7), sensorimotor functioning (*M* = 88.3), language (*M* = 90.0) and visuospatial processing (100.0). The domains of attention/executive functioning, memory, and sensorimotor functioning fell in the classification of the low average range (Sattler, 2001).

Variability of index scores was also examined for the methamphetamine-exposed sample as illustrated on Table 4. For the Wechsler intelligence test scores, the greatest variability was found on the perceptual reasoning index (Range = 73) and the least variability was on the verbal comprehension index (Range = 40). For the NEPSY domains, the greatest spread was on the sensorimotor functioning (Range = 57) and the smallest spread was on the Language Domain (Range = 18). The methamphetamine-exposed group appears to have a large spread in perceptual reasoning and sensorimotor functioning, which means that participants' scores fall in a variety of ranges from severely delayed to above average.

Table 4

Variability of the index scores for methamphetamine-exposed children

		Standard Scores		
	n	Minimum	Maximum	Range
Wechsler Intelligence Test				
Verbal Comprehension Index	11	68	108	40
Perceptual Reasoning Index	11	56	129	73
Working Memory Index	11	71	113	42
Processing Speed Index	11	59	111	52
NEPSY Domains				
Attention/Executive Functions	5	60	113	53
Language	4	81	99	18
Sensorimotor Functioning	6	50	107	57
Visuospatial Processing	6	79	118	39
Memory	4	78	107	29

[a] based on 11 participant scores (assessed with WISC-III, WISC-IV); [b] based on 5 participants' scores; [c] based on 4 participants' scores; [d] based on 6 participants' scores.

Descriptive comparison of methamphetamine-group by Wechsler intelligence scale subtests. The methamphetamine-exposed sample was further examined by subtest. Only the subtest scores that comprised the four factors of verbal comprehension, perceptual reasoning, working memory and processing speed indexes were used in this analysis. The optional subtests such as mazes subtest from WISC-III and WISC-IV subtests cancellation, picture completion, and word reasoning were excluded from the analysis because they were optional subtests and did not contribute to the factor scores. Subtest means and standard deviations were compared to the non-clinical normative-sample subtest mean ($M = 10$) and standard deviation ($SD = 3$) to describe the methamphetamine-exposed group profiles. Descriptive analyses of scale scores were performed. The means and standard deviations for each of the subtests are exhibited in Table 5, and standard deviations for each subtest by edition of Wechsler intelligence test (WISC-III or WISC-IV) Table 6.

Table 5

Wechsler intelligence test overall subtest means (scale scores) for methamphetamine-exposed participant group

Subtest	*n*	Overall Mean[a]	*SD*	Range
VCI				
Similarities	11	7.6	2.9	4-12
Vocabulary	11	7.7	3.7	3-13
Comprehension	11	6.8	2.9	2-11
Information	5	8.0	4.2	2-14
PRI/POI				
Block Design	11	7.7	4.0	1-14
Picture Concepts	11	9.5	2.1	6-12
Matrix Reasoning	11	10.0	5.8	3-18
Picture Completion	5	9.0	3.5	3-13
Picture Arrangement	5	7.4	3.9	1-11
Object Assembly	5	7.4	3.1	4-12
WMI/FDI				
Digit Span	11	9.1	2.3	6-14
Letter-Number Seq.	6	8.2	4.7	3-14
Arithmetic	5	6.8	3.2	5-14
PSI				
Coding	11	6.6	3.1	3-11
Symbol Search	11	6.4	2.8	3-13

Note. Means are reported in Scaled Scores ($M = 10$, $SD = 3$). Average range is 8-12 (Sattler, 2003).
[a] Overall mean combines WISC-III and WISC-IV.

Table 6

Wechsler intelligence test subtest means for WISC-III and WISC-IV for methamphetamine-exposed participant group

	WISC-III				WISC-IV			
Subtest	*n*	Mean	*SD*	Range	*n*	Mean	*SD*	Range
VCI								
Similarities	5	7.8	2.8	4-11	6	7.3	3.3	5-12
Vocabulary	5	7.6	4.5	3-13	6	7.8	3.3	4-12
Comprehension	5	6.4	3.6	2-10	6	7.2	2.4	5-9
Information	5	8.0	4.2	2-13				
PRI/POI								
Block Design	5	8.0	4.5	1-13	6	7.5	4.0	3-14
Picture Concepts					6	9.5	2.1	6-12
Matrix Reasoning					6	10.0	5.8	3-18
Picture Completion	5	9.0	3.5	3-12				
Picture Arrangement	5	7.4	3.9	1-11				
Object Assembly	5	7.4	3.1	4-12				
WMI/FDI								
Digit Span	5	9.6	3.0	6-14	6	8.7	1.6	7-11
Letter-Number Seq.					6	8.2	4.7	3-14
Arithmetic	5	6.8	3.2	2-9				
PSI								
Coding	5	6.4	3.0	3-11	6	6.8	3.4	2-11
Symbol Search	5	6.6	3.8	4-13	6	6.3	2.1	3-8

Note. Means are reported in Scaled Scores (M = 10, SD = 3). Average range is 8-12 (Sattler, 2003).
[a] Overall mean combines WISC-III and WISC-IV (n = 11). Mean is separately reported is for WISC-III (n = 5) and WISC-IV (n = 6) scores of the participants.

WISC-III subtest means were looked at in comparison to the WISC-IV subtests to check for significant differences between the two versions of tests with this database for the purpose of quality control. Any differences in subtest means between the two versions were within 1 point of each other and no significant difference were noted in the two versions. It was determined that the overall mean (WISC-III and WISC-IV combined) is appropriate to use in examining subtest patterns in the methamphetamine-exposed group.

In examining the subtest means of the Wechsler intelligence test, it appears that while some subtests scaled scores fell within the average range defined as between scores of 8-12 (Sattler, 2001), most fell in the below average range. The overall means for the subtests Comprehension (*M* = 6.8), Arithmetic (*M* = 6.8), Coding (*M* = 6.6) and Symbol Search (*M* = 6.4) were below the expected level, and appears to indicate the most problematic areas with regards to subtest scores for the methamphetamine-exposed participants. With regards to the indices the subtests belong to, both subtests that make-up the processing speed index were below average range (Sattler, 2001). The overall means for the subtests Picture Arrangement (7.4), Object Assembly (7.4), Similarities (7.6), Vocabulary (7.7), and Block Design (7.7) fell slightly below the low average range for the methamphetamine-exposed group (Sattler, 2001). The highest subtest was matrix reasoning (*M* = 10) which was equal to the normative mean. It should be noted that none of the methamphetamine-exposed group subtest means were higher than the normative mean.

The subtest score ranges had significant variability as illustrated in Tables 5 and 6. There was considerable variability of scaled scores within each subtest. The subtests which had the most variability were matrix reasoning, block design, letter-number sequencing and information, and the subtests with the least variability were picture concepts, digit span and arithmetic. With regards to variability ranges, the subtests that formed the perceptual index had the highest dispersion (range = 10.5), the subtests that formed the verbal comprehension index and the processing speed index had a range of

9.5, and the subtests that formed the Working Memory Index had the smallest range (range = 8.3).

Descriptive comparison of methamphetamine-group by NEPSY scale subtests. The methamphetamine-exposed sample was further examined by NEPSY subtest. In examining the subtest means of the NEPSY, it appears that most subtests scaled scores fell within the average range defined as between scores of 8-12 (Sattler, 2003). The overall means for the subtests statue ($M = 6.5$), speeded naming ($M = 6.5$), and memory for names ($M = 6.3$) were below the expected range, and appeared to be the most problematic areas in respect to subtest scores for the methamphetamine-exposed participants. Furthermore, the means for subtests visual attention and response set ($M = 7.2$), and sentence repetition ($M = 7.5$) fell slightly below the low average range for the methamphetamine-exposed group. In contrast to the WISC subtest scores, some NEPSY subtest means were above the normative mean ($M = 10$). However, the NEPSY subtests should be interpreted with extreme caution due to very small sample size contributing to most subtest (see Table 7).

In looking at the overall profile of scores, the methamphetamine-exposed group demonstrated low average performance in the areas of processing speed, verbal comprehension, attention/executive functions, memory and sensorimotor functioning. The scores also indicate a great deal of variability, especially in the areas of perceptual reasoning, sensorimotor functioning, and attention/executive functioning. In respect to the Wechsler intelligence subtests, comprehension, arithmetic, coding and symbol search, and in respect to the NEPSY subtests speeded naming, memory for names and statue fell in the below average range (scale score < 7) as defined by Sattler (2003) and appears to be the most problematic areas for the methamphetamine-exposed group.

Table 7

NEPSY subtest means (scale scores) for methamphetamine-exposed participant group

Domain / Subtest	*n*	Overall Scores: Mean	*SD*	Range
Attention/Executive Func.				
Tower	3	10.0	1.7	9-12
Auditory Attn.	3	9.0	0	9
Visual Attn.*	5	7.2	2.6	4-11
Statue**	2	6.5	3.5	4-9
Language				
Phonological Processing*	4	8.3	4.3	4-14
Speeded Naming	2	6.5	0.7	6-7
Comprehension of Instru.*	4	8.3	2.1	6-10
Body Part Naming**	2	8.0	2.8	6-10
Sensorimotor				
Fingertip Tapping	3	11.6	1.5	10-13
Imitating Hand Posit.*	5	8.8	2.3	6-12
Visuomotor Precision*	5	8.8	2.9	5-12
Visuospatial				
Design Copy*	5	10.6	2.2	7-12
Arrows	3	12.0	3.5	8-14
Block Construction**	2	9.5	2.1	8-11
Memory and Learning				
Memory for Faces	3	11.3	4.6	6-14
Memory for Names	3	6.3	2.8	3-8
Narrative Memory*	5	9.6	2.4	7-12
Sentence Repetition**	2	7.5	2.1	6-9

Note: includes subtests for age bands 3-4 years and 5-12 years.
** the subtests that make-up domains of both age bands (3-4 and 5-12)*
*** the subtests found only in the 3-4 age band*

Objective Two

The second objective of this study required statistical comparison of a matched sample (by age, gender, ethnicity, and referral question of behavior concerns, academic concerns or both) of prenatal methamphetamine-exposed children to clinic based non-drug exposed children and to established norms to assess any significant differences in the perceptual reasoning index, verbal comprehension index, processing speed index, and working memory index as measured by Wechsler intelligence scales (see Tables 8 and 9).

Table 8

Methamphetamine-exposed group scores compared to the clinical non-drug exposed group.

Wechsler Intelligence factor	Meth-exposed mean	Non-exposed mean	t-value	sig.
Verbal Comprehension Index	86.18	95.55	-1.621	.12
Perceptual Reasoning Index	91.45	95.82	-0.616	.54
Working Memory Index	90.27	96.46	-1.049	.31
Processing Speed Index	81.64	93.73	-2.091	.05

Table 9

Methamphetamine-exposed group scores compared to the non-clinical normative group.

Wechsler Intelligence factor	Meth-exposed mean	Normative mean	t-value	sig.
Verbal Comprehension Index	86.18	100.00	-2.986	.01
Perceptual Reasoning Index	91.45	100.00	-1.432	.18
Working Memory Index	90.27	100.00	-2.016	.07
Processing Speed Index	81.64	100.00	-4.337	.00

In order to address this objective, the data of the two groups was first examined to see if the assumptions for parametric tests were met. To assess for univariate outliers, boxplots for each continuous variable were assessed for the methamphetamine-exposed group and non-exposed group. Outliers were defined as any value greater than 2.5 standard deviations from the mean. Two outliers were identified for the methamphetamine-exposed group on the processing speed variable with each case being on the opposite extreme. A t-test was used to compare the scores of the group with and without outliers, and no significant differences were found, the mean differences of the groups was less than 1 point different (outliers included: $M = 81.64$, $SD = 14.05$; outliers excluded, $M = 80.89$, $SD = 8.61$). While these two cases pose a threat to the representative nature of the sample, due to the small sample size and the importance of looking at the variability in the performance, it was decided to include the outliers in the sample when analyzing the data. It was determined that because the outliers were on the opposite extremes, they did not affect the skew of the data distribution. To examine data for normality, skew and kurtosis were examined (Howell, 2006). Results of the Kolmogorov-Smirnov indicated no significance thus suggesting that the sample was distributed normally. With regards to homogeneity of variance, the variance of the two groups was significantly different on the WISC working memory variable, and the unequal variance t-statistic was used for this index. Given the above, the assumptions of the t-test were met and the analysis was conducted.

Hypothesis One: Part a. The first hypothesis proposed that there would be a significant difference between methamphetamine-exposed and the clinic based non-drug exposed groups on the Wechsler intelligence scale, verbal comprehension index scores.

An independent sample t-test was performed comparing the mean verbal comprehension index score of the methamphetamine-exposed group (*M* = 86.18, *SD* =15.35) to the clinic based non-drug exposed group (*M* = 95.55, *SD =11.47)*. The alpha level was .05. There was no statistical difference, t (20) = -1.62, *p* = .12 in verbal comprehension index scores between the methamphetamine-exposed and clinic based non-exposed groups. These results suggest that there is no difference in verbal comprehension between the children exposed to methamphetamine prenatally and children not exposed to drugs prenatally in the clinic based sample.

Hypothesis One: Part b. The next hypothesis proposed that there would be a significant difference between methamphetamine-exposed children and the non-clinical normative sample on the Wechsler intelligence scale, verbal comprehension index factor scores. A one-sample t-test was performed to compare the mean verbal comprehension index score of the methamphetamine-exposed group (*M* = 86.18, *SD* =15.35) to a non-clinical normative population (*M* = 100, *SD* = 15). The methamphetamine-exposed group was statistically different t (10) = -2.98, *p* = .01 from the non-clinical normative group on the verbal comprehension variable. This suggests that the methamphetamine-exposed group performed significantly lower on verbal comprehension than the non-clinical normative group.

Hypothesis Two: Part a. The second hypothesis proposed that there would be a significant difference between the methamphetamine-exposed and the clinic based non-drug exposed groups on the Wechsler intelligence scale, perceptual reasoning factor index scores. An independent sample t-test was performed comparing the mean perceptual organization index/perceptual reasoning index score of the methamphetamine-exposed group (*M* = 91.45, *SD* =19.79) to the clinic based non-drug exposed-group (*M* = 95.82, *SD* = 12.69). There was no statistical difference, t(20) = -0.616, *p* = .54 in perceptual organization index/perceptual reasoning index scores between the methamphetamine-exposed and the clinic based non-drug exposed groups.

Hypothesis Two: Part b. This hypothesis suggested that there would be a significant difference between the methamphetamine-exposed group and the non-clinical normative sample on the Wechsler intelligence scale, perceptual reasoning index factor scores. A one-sample t-test was performed to compare the mean perceptual reasoning index score of the methamphetamine-exposed group (*M* =91.45, *SD* =19.79) to a non-clinical normative population (*M* = 100, *SD* = 15). The methamphetamine-exposed group was not statistically different t (10) = -1.43, *p* = .18 from the normative group on the perceptual reasoning index variable. This suggests that there is no difference in perceptual reasoning ability of children exposed to methamphetamine prenatally and children in the normative sample.

Hypothesis Three: Part a. The third hypothesis proposed that there would be a significant difference between the methamphetamine-exposed and the clinic based non-drug exposed groups on the Wechsler intelligence scale, freedom from distractibility/working memory factor index scores. An independent sample t-test was performed comparing the mean freedom from distractibility/working memory index score of the methamphetamine-exposed group (*M* = 90.27, *SD* =16.00) to the clinic based non-drug exposed group (*M* = 96.46, *SD* = 11.21). There was no statistical difference, t (20) = -1.049, *p* = .31 in freedom from distractibility/working memory index scores between the methamphetamine-exposed and non exposed groups. These results suggest that there is no difference in working memory ability between the children exposed to methamphetamine prenatally and children not exposed to drugs prenatally in the clinic based sample.

Hypothesis Three: Part b. This hypothesis proposed that there would be a significant difference between the methamphetamine-exposed group and the non-clinical normative sample on the Wechsler intelligence scale, working memory/freedom from distractibility index factor scores. A one-sample t-test was performed to compare the mean perceptual reasoning index score of the methamphetamine-exposed group (M = 90.27, SD =16.00) to a non-clinical normative population (M = 100, SD = 15). The methamphetamine-exposed group was not statistically different t (10) = -2.016, p = .07 from the non-clinical normative group on the working memory/freedom from distractibility index variable. These results suggest that there is no difference in working memory ability between the children exposed to methamphetamine prenatally and a normative sample.

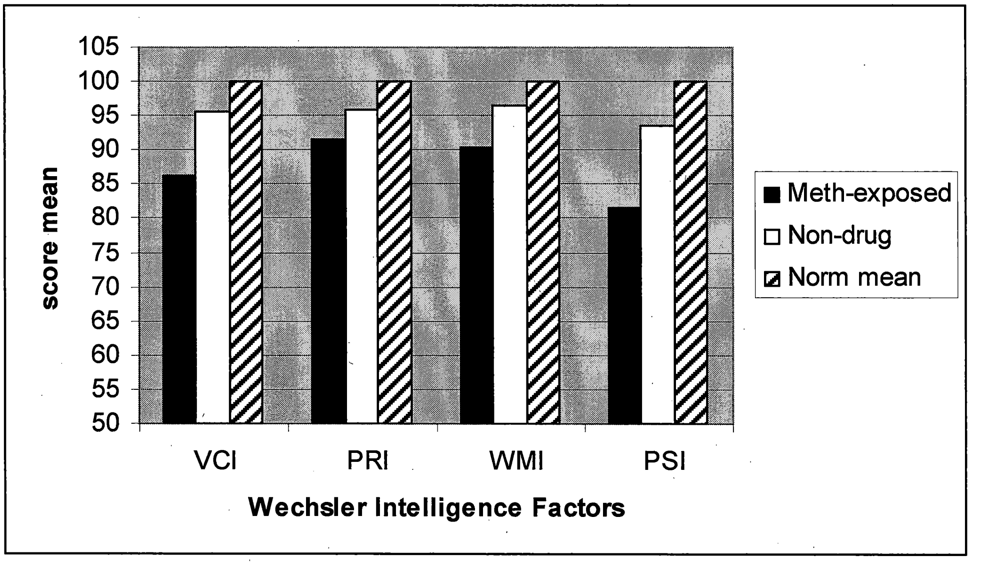
Hypothesis Four: Part a. The fourth hypothesis proposed that there would be a significant difference between the methamphetamine-exposed and the clinic based non-drug exposed groups on the Wechsler intelligence scale, processing speed factor index scores. An independent sample t-test was performed comparing the mean processing speed index score of the methamphetamine-exposed group (M = 81.64, SD =14.04) to the clinic based non-drug exposed group (M = 93.73, SD = 13.06). There was a statistical difference t (20) = -2.091, p = .05 in processing speed factor index scores between the methamphetamine-exposed and the clinic based non-drug exposed groups. These results suggest that there is a significant difference in processing speed between the children exposed to methamphetamine prenatally and children not exposed to drugs within a clinical sample.

Hypothesis Four: Part b. This hypothesis suggested that there would be a significant difference between the methamphetamine-exposed group and the non-clinical normative sample on the Wechsler intelligence scale, processing speed index factor scores. A one-sample t-test was performed to compare the mean processing speed score of the methamphetamine-exposed group (M = 81.64, SD =14.04) to a non-clinical normative sample (M = 100, SD = 15). The methamphetamine-exposed group was statistically different t (10) = -4.337, p = .001 from the non-clinical normative group on the processing speed index variable.

Overall, results indicated that when compared to a similar non-drug exposed clinical sample the methamphetamine-exposed group had statistically lower index scores in the area of processing speed. However, when compared to the non-clinical normative sample the methamphetamine-exposed group scored significantly lower in the areas of verbal comprehension and processing speed. In addition to being statistically significant, these findings are also clinically significant as the index means fall in the low average range representing potential areas of delay for these children (Sattler, 2001). Finally, it should be noted that the difference between the methamphetamine-exposed group and the normative sample approached significance on the working memory index. As such, a larger sample resulting in increased power would have likely resulted in a significant difference between the indicated groups.

Although the methamphetamine-exposed group was not significantly different from the drug-exposed group and the normative sample on all the Wechsler intelligence indexes, the methamphetamine-exposed group generally had lower Wechsler index means on all four indexes than the non-drug exposed group and the normative sample (see Figure 1).

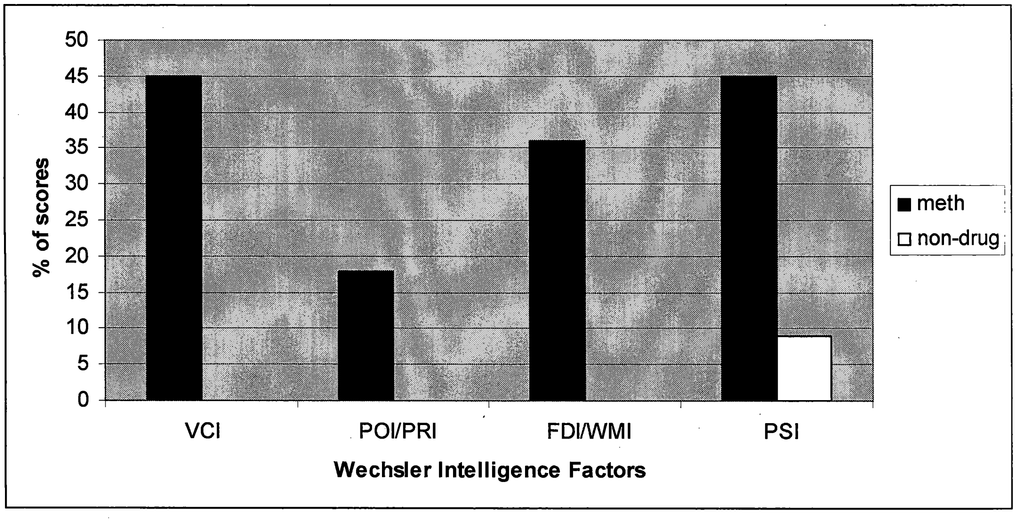
Figure 1. Score means for the methamphetamine-exposed, non-drug exposed and normative sample.



To further highlight the clinical differences between the methamphetamine-exposed group and the clinic based non-drug exposed group the number of occurrences of low scores between the two groups was explored (see Figure 2). Low scores were defined as any score falling 1.5 standard deviations below the normative mean or a score of 77 or less.

The general patterns of the index scores indicate more occurrences of low scores for the methamphetamine-exposed group as compared to the clinic based non-drug exposed group. Based on these trends, areas of notable concern include the processing speed, verbal comprehension and working memory variables.

Figure 2. Percentage of scores (1.5standard deviations) below the normative mean



Supplemental Analysis

To gain additional information about the methamphetamine-exposed group, two supplementary analyses were conducted. Specifically, one-sample t-tests were performed to compare the clinic based non-drug exposed sample to the non-clinical normative sample in respect to differences in Wechsler intelligence index scores Also, the methamphetamine-exposed group was descriptively compared to the non-drug exposed clinical group along the Wechsler intelligence subtests scores.

Clinical non-drug exposed sample compared to normative mean. To supplement the information gleaned with hypotheses testing, one sample t-tests were conducted to look at differences between the clinic based non-drug exposed group and the non-clinical normative sample (see table 10) on index scores.

Table 10

Clinical non-drug exposed group scores compared to the non-clinical normative group.

Wechsler Intelligence factor	Non-drug mean	SD	Norm mean	SD	t-value	sig.
Verbal Comprehension Index	95.55	11.5	100.00	15	-1.288	.23
Perceptual Reasoning Index	95.82	12.7	100.00	15	-1.093	.30
Working Memory Index	96.45	11.2	100.00	15	-1.049	.32
Processing Speed Index	93.73	13.1	100.00	15	-1.59	.14

Note: The means are standard scores.

This suggests that the clinic based non-drug exposed group fell in the average range along all four of the Wechsler intelligence indexes. Additionally, the clinic based non-drug exposed group did not have statistically significant differences from the non-clinical normative group on any of the Wechsler intelligence indexes.

Methamphetamine-exposed group compared the clinical non-drug exposed sample on subtest scores. The Wechsler intelligence scale subtests were compared descriptively for the methamphetamine-exposed and clinical non-exposed groups as illustrated in Table 11.

Table 11

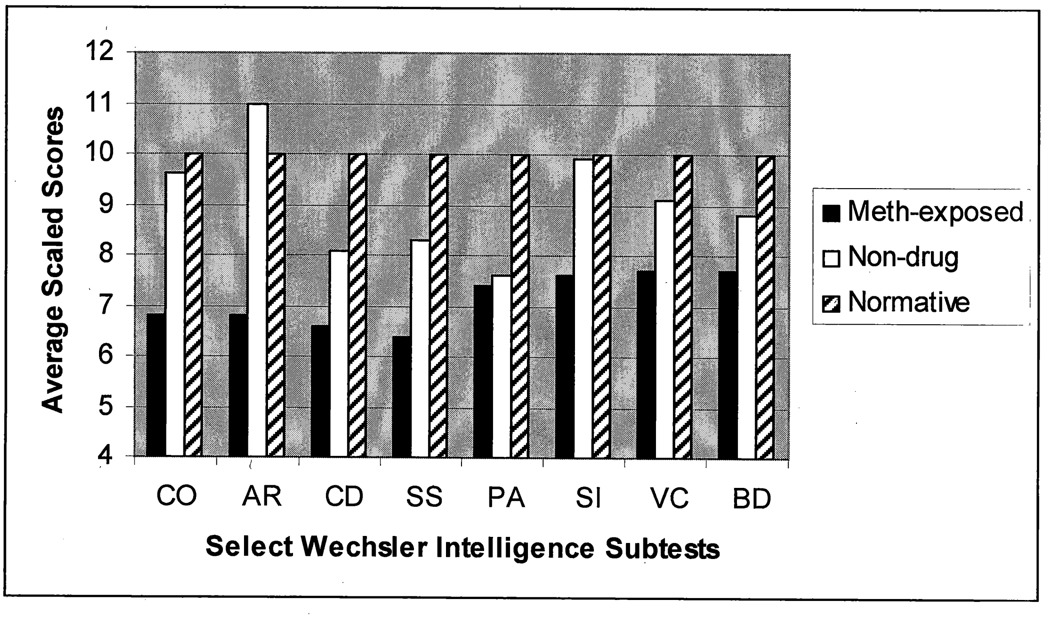
Subtest score means for methamphetamine-exposed group and non-drug exposed group

Subtest	Meth-exposed Mean[a]	Meth-exposed *SD*	Non-exposed Mean	Non-exposed *SD*
VCI				
Similarities	7.6	2.9	9.9	2.7
Vocabulary	7.7	3.7	9.1	3.1
Comprehension	6.8	2.9	9.6	2.7
Information	8.0	4.2	10.0	0.7
PRI/POI				
Block Design	7.7	4.0	8.8	3.2
Picture Concepts	9.5	2.1	9.8	2.4
Matrix Reasoning	10.0	5.8	10.2	2.9
Picture Completion	9.0	3.5	10.5	2.2
Picture Arrangement	7.4	3.9	7.6	3.4
Object Assembly	7.4	3.1	10.4	2.0
WMI/FDI				
Digit Span	9.1	2.3	8.8	1.5
Letter-Number Seq.	8.2	4.7	9.8	1.2
Arithmetic	6.8	3.2	11.0	1.6
PSI				
Coding	6.6	3.1	8.1	2.5
Symbol Search	6.4	2.8	8.3	1.7

Note. Means are reported in Scaled Scores ($M = 10$, $SD = 3$). Average range is 8-12; means reported are average (WISC-III ($n = 5$) and WISC-IV ($n = 6$)) scores of the participants.

Overall, the methamphetamine-exposed group subtest mean scores were generally lower than the clinical non-drug exposed subtest mean on every subtest (selected subtests illustrated in Figure 3). The methamphetamine-exposed group had four mean subtests scores in the below average range, while the non-drug exposed group did not have any subtest means in the below average range of functioning. For the methamphetamine-exposed group, the subtest areas that appeared to have the most difference between groups were arithmetic, object assembly and comprehension. In looking at the trend of scores, all the clinic based non-drug exposed subtest means were higher than the methamphetamine-exposed subtest means. With regards to subtest scores, it appears that methamphetamine-exposed participants generally scored lower than the clinic based non-drug exposed group, as well as the non-clinical normative sample on all of the cognitive subtests.

Figure 3. Selected Wechsler subtest scores for the methamphetamine-exposed, non-drug exposed and normative sample.



Discussion

Methamphetamine use among pregnant women has been steadily increasing in the United States, which has subsequently resulted in an increase in the number of children born prenatally exposed to methamphetamine (Young, 2005). As such, there is considerable concern regarding the well-being of children exposed to methamphetamine due to the potential harmful effects the drug may have on development. Although general drug-exposure effects have been a topic of research interest for some time, research specific to methamphetamine exposure is extremely limited. Therefore, review of similar research is necessary and has demonstrated that prenatal stimulant drug-exposure poses problems in children's cognitive and neuropsychological development. Specifically, Mayes, Bornstein, Chawarska, & Granger (1995) suggest that prenatal drug-exposure may affect arousal and attention, which in turn could affect learning and emotional responsivity, which then may also affect the infants' later cognitive and social development (Mayes, Bornstein, Chawarska, Haynes, & Granger, 1996). With regards to intellectual development prenatal drug-exposure has been found to be associated with difficulties in verbal and visual reasoning (Griffith, Azuma, & Chasnoff, 1994), visuo-spatial skills (Singer et al., 2000), visual-motor functioning (Morrison, Cerles, Montaini-Klovdahl, & Skowron, 2000), verbal memory (Chang et al., 2004), language development (Chang et al., 2004; Griffith, Azuma & Chasnoff, 1994; Morrison, Cerles, Montaini-Klovdahl, & Skowron, 2000), and attention (Chang et al., 2004).

Although the existing research provides an understanding of prenatal stimulant drug-exposure effects, the effects of prenatal methamphetamine-exposure are not well documented. In fact, only one study could be found suggesting that methamphetamine-exposed children performed worse on visual motor integration tasks and significantly worse on verbal memory and sustained attention when compared to non drug-exposed children. Given the lack of research in this area and the growing concern for the development of these children, the current study examined the overall cognitive and neuropsychological profiles of children prenatally exposed to methamphetamine and evaluated how they compared to non-drug exposed children and established norms. Outcomes were measured using the Wechsler scales of intelligence (WISC-III and WISC -IV) and the NEPSY.

Profiles of Methamphetamine-Exposed Children

The first objective of the study was to describe the frequency and characteristics of clinically referred children prenatally exposed to methamphetamines. Within the LLU PNAP clinic population, 15 participants out of 489 were identified as methamphetamine-exposed for a total of 3.07%. Given that the Inland Empire is known to have high rates of methamphetamine abuse, this was a surprising finding (U.S. Department of Justice, 2001). In examining the clinic intake questionnaire it was found that the section assessing substance use did not have a prompt asking about specific types of illicit drug use during pregnancy. As a result, it is possible that many clinicians' overlook asking the caregiver about methamphetamine use during pregnancy. Additionally, in looking through the intake questionnaires, it was observed that in some cases, the clinicians indicated that illicit drug were used during pregnancy but failed to specify the name of the substance used. Another reason drug-use may have been underreported is that during the intake assessment, drug-exposure was determined through parent self-report. It is possible that the self-report of illicit substances was biased due to the stigma attached to drug-use during pregnancy, and for drug use in general. Furthermore, some of the children seen at the clinic were adopted, in foster care or in kinship-care, and the caregivers may have had limited information about the children's prenatal history. For example, it was noted that some intake questionnaires reported prenatal drug-exposure but the caregiver was unaware of the types and amounts of drug use. The frequency of methamphetamine-exposed children may also be low in this particular clinic population due to those receiving services at the clinic typically have medical insurance, and the parents have better employment. This could indicate that the clinic patients' parents maybe less likely to abuse illicit drugs.

With regards to the methamphetamine-exposed participants' demographics, the sample was primarily Caucasian and male. However, the sample was ethnically varied and had at least one representative from the major ethnic groups (U.S. census bureau, 2006). It is possible that a majority of the sample was male (9 of the 15 were male) due to the possibility that boys exhibit more frequent and/ or higher severity of externalizing behaviors when compared with girls (Maughan, Rowe, Messer, Goodman, & Meltzer, 2004) and therefore have a higher likelihood of being identified as needing a referral for testing and/or intervention services. A majority of the sample was school-aged and ranged in age from 4 years to 14 years, which is unsurprising given that many academic and behavioral issues are identified during school years (Dixon, & Bejar, 1989; Johnson, et al., 1999). A majority of the referral questions for the participants were primarily academic, or a combination of behavioral and academic; none of the participants had a primarily psychosocial referral question. This finding is expected given that the majority of the participants were school-aged, and that any problems related to school performance or functioning would typically be identified first (Verhulst, & Akkerhuis, 1989). Environmental variables such as SES and child custody type (biological parent, adopted, kinship care or foster care) were not accounted for in this study due to the lack of information available in the archival data set.

In examining the Wechsler intelligence scales (WISC-III & WISC-IV) of the methamphetamine-exposed participants, it was observed that all four WISC factor index means were lower than the normative means. This shows a general trend in methamphetamine-exposed groups' tendency to score lower than the non-clinical normative sample. This finding is supported by research indicting lower cognitive functioning in stimulant-exposed groups as compared to non-drug exposed groups (Chasnoff, et al., 1992; Singer, et al., 2002).

The methamphetamine-exposed group's Wechsler intelligence scale scores were described at the subtest level to examine the group's subtest profile. Results indicated that the overall subtest means for coding, symbol search, arithmetic and comprehension all fell in the below average range. The methamphetamine-exposed children performed below average on both of the processing speed subtests (coding and symbol search), which indicates a delay in the ability to fluently and automatically perform cognitive tasks and to maintain attention and concentration under time pressure (Wechsler, 2003). This finding is supported by literature that associates processing speed difficulties with methamphetamine-abuse in adults (Nordahl, Salo, & Leamon, 2003). Zasler, Katz and Zafonte (2006) also report that the processing speed index is particularly sensitive to brain dysfunction because coding and symbol search subtests tend to be sensitive, which could also be a reason that processing speed index differences were noted in this study.

The methamphetamine-exposed group also performed below average on the arithmetic and comprehension subtests, which may suggest that the methamphetamine-exposed children have some difficulties in numerical reasoning ability, attention, concentration, and with knowledge of conventional standards. Differences on the arithmetic subtest, although not significant was a finding in literature comparing stimulant-exposed children to non-drug exposed children (Singer, 2004). Low comprehension scores were not supported in the literature. However, there is literature support for differences in receptive language and significant differences in expressive language in stimulant/ploy drug-exposed children (Morrison et al., 2000), which has a notable impact on comprehension scores.

A few caveats must be made about comparing current findings to the literature. For example, direct comparisons with previous research cannot be made due to a lack of literature examining Wechsler subtest differences within this population. Further, it is difficult to pin point a specific ability "purely" measured as each Wechsler subtest requires multiple abilities (attention, memory, hand-eye coordination, tracking skills, motor speed, etc.) to complete the tasks. Therefore, definitive statements about problems with specific skills in the methamphetamine-exposed group cannot be made until more research is completed and consistent findings emerge.

Upon examining the NEPSY scores of the methamphetamine-exposed participants, all domain scores were within average to low average range when compared to the normative sample mean. Specifically, the attention/executive functioning and memory domains represented the lowest scores on the NEPSY and fell in the low average range. These findings are consistent with existing research that reported deficits in memory and attention in stimulant-exposed children (Kalechstein, Newton, & Green, 2003; Meredith, 2005). Even more important, these findings are consistent with one study examining cognitive and neuropsychological factors in prenatally methamphetamine-exposed children (Chang, et al., 2001). Specifically, these researchers found that children exposed to methamphetamine performed significantly worse on sustained attention and verbal memory than non-drug exposed children. Also falling in the low average range was the Sensory Motor domain, which was supported by rat studies. Methamphetamine-exposed rats exhibited difficulties with sensory motor coordination by falling off of a rotating cylinder task more frequently than their non-drug exposed counterparts (Slamberova et al., 2006).

The methamphetamine-exposed group's NEPSY scores were described at the subtest level to examine the group's subtest profile. However, extreme caution should be exercised in interpreting these subtests due to the very small number of participant scores available. Results indicated that the overall subtest means for speeded naming, memory for names, sentence memory, statue, and visual attention were lower than average. Two of these subtests (visual attention and statue) were from the attention and executive functioning domain, two subtests (memory for names and sentence repetition) were from the memory domain, while one subtest (speed naming) was from the language domain. The lower than average scores on the attention and executive functioning subtests may indicate a trend toward lower scores and is supported by the research evidencing significantly lower sustained attention in methamphetamine-exposed children and methamphetamine-dependant adults (Chang et al., 2001; Nordahl, Salo, & Leamon, 2003), as well as increased errors in executive functioning in stimulant-exposed children

(Epsy, Kaufman, & Glisky, 1999). In the NEPSY subtest analysis, two memory subtests (one from each age group) also exhibited low scores, which could indicate a trend in low memory scores if the sample of scores were larger. The literature provides support that memory delays are associated with prenatal stimulant exposure (Meredith, 2005). Additionally, rat studies demonstrated memory deficits in methamphetamine-exposed rats (Vorhees, Ahrens, Acuff-Smith, Schilling, and Fisher, 1994; Williams, Moran & Vorhees, 2004) therefore further supporting the low average memory trend observed in this study. Research evidence also demonstrated difficulties in expressive and receptive language (Morrison et al., 2000) which supports some difficulties in the language domains for methamphetamine-exposed children. Although literature offers support for various low subtest scores, it should be noted that within each domain, the subtests with below average scores were the minority. Given the very small number of subtest scores available for analysis, it is very difficult to discuss even trends in the subtests with any true confidence.

Taken together, the descriptive profile of prenatally methamphetamine-exposed children generally supports previous research (Chang et al., 2001; Morrison et al., 2000 Vorhees, Ahrens, Acuff-Smith, Schilling, and Fisher, 1994; Williams, Moran & Vorhees, 2004). Further, results suggests that these children may have delays in the speed in which they process information, in comprehending verbal information, in maintaining attention, in memory, and in manipulating their body within the environment.

Comparative Differences in Methamphetamine-Exposed Children

The second objective of the study was to compare a matched sample of prenatal methamphetamine-exposed children to both non-drug exposed children and to a normative non-clinical sample to assess any differences on the Wechsler intelligence index scores. This objective was broken down into 4 two part hypotheses.

Verbal comprehension index. The first hypothesis sought to examine the difference between methamphetamine-exposed children, clinic based non-drug exposed children, and a non-clinical normative sample on the Wechsler intelligence scale, verbal comprehension index. Results did not indicate a significant difference in verbal comprehension index between the methamphetamine-exposed and clinic based non-drug exposed groups. However, the methamphetamine-exposed group had a lower verbal comprehension mean score than the non-exposed group, which was in the expected direction. Alternatively, there was a significant difference found in verbal comprehension of the methamphetamine-exposed group as compared to the non-clinical normative sample.

Because the non-drug exposed sample was referred to the clinic for academic and behavioral problems, it was expected that this group would have lower means than the normative sample. This could account for the lack of difference in the non-drug exposed group and the significant differences found in the normative sample when compared to the methamphetamine-exposed group. This finding also has important clinical implications in that the methamphetamine-exposed children had low average skills indicating poorer verbal problem solving skills when compared to the general population of non-drug exposed children. It would be unexpected to find indications of neurological impairment on the verbal comprehension index due to its limited sensitivity to impairment. However, the significant difference (between the normative sample and methamphetamine-exposed sample) in verbal comprehension is somewhat supported in the literature. The literature indicates that stimulant-drug exposed children have delays in receptive language skills and deficits in expressive language skills, both of which are required for verbal comprehension (Morrison et al., 2000). Research also discovered trends in below average verbal reasoning skills (measured by Stanford-Binet) in stimulant exposed children (Griffith, Azuma, & Chasnoff, 1994). In contrast, Verbal IQ (on the WPSSI) was demonstrated to not be significantly different in stimulant-exposed and non-drug exposed children. The mixed results in research are likely due to methodological differences, differences in measurement tools (Stanford-Binet, MSEL, WPPSI-R), differences in the development of children at the time of testing, and possibly the differences in substances children were exposed to.

Perceptual reasoning index. The second hypothesis proposed that there would be a significant difference between methamphetamine-exposed children, clinic based non-drug exposed children and a non-clinical normative sample on the Wechsler intelligence scale, perceptual reasoning index. Results did not indicate a significant difference between the methamphetamine-exposed group and clinic based non-drug exposed group. However, it should be noted that the methamphetamine-exposed sample demonstrated some difficulties in subtests that required perceptual motor skills (block design, picture arrangement, and object assembly). A significant difference was also not found between the methamphetamine-exposed group and the non-clinical normative sample. However, it is important to consider that there may be an age effect in the perceptual reasoning index measure. It is possible that deficits may not be noted in children until they are older due to the method in which perceptual reasoning is measured. Therefore, it may be beneficial to group participants by age in future studies to maximize isolating any differences between groups.

The current study results suggest that perceptual reasoning skills are not significantly different between the methamphetamine-exposed group and the clinic-based non-drug exposed group, as well as the methamphetamine-exposed group and the non-clinical normative sample. These findings are supported by the literature that discovered no differences in Performance IQ (on WPPSI-R) between stimulant-exposed and non-drug exposed children (Singer et al., 2004). However, there is also evidence in the literature that visual abstract reasoning (measured by Stanford-Binet) along with memory and attentions were found to be below average in stimulant-exposed children (Chang et al., 2001; Griffith, Azuma, & Chasnoff, 1994). As visual abstract reasoning, attention and memory contribute to the perceptual reasoning index, it would be expected that perceptual reasoning index would have been significantly different. Again, it is possible that these differences are due to methodological and measurement differences between different studies.

Working memory index. The third hypothesis examined differences between methamphetamine-exposed children as compared to clinical non-drug exposed children and a normative sample on the working memory index. Results indicated average performance with no significant differences between the methamphetamine-exposed and non-drug exposed groups or between the methamphetamine-exposed group and the non-clinical normative sample. However, it should be noted that there were trends toward significance, especially when compared to the normative sample, and that a larger sample size would have likely resulted in a significant difference between the groups.

Given the above, the results are generally consistent with research reporting associated differences in working memory in methamphetamine abusing adults (Nordahl, Salo, & Leamon, 2003). The literature indicates that stimulant/methamphetamine-exposure has negative effects on memory. However, due to different types of measurement tools and different functions of memory measured by these tools, it is difficult to narrow down the type of memory affected by stimulant-exposure. In examining the working memory index subtest scores, it appears that the below average score on the arithmetic subtest is decreasing the overall mean of the working memory subtest. The lower score in the arithmetic subtest may be due to difficulties in numerical reasoning, attention and concentration, as well as complex working memory abilities.

Processing speed index. The fourth hypothesis examined differences between methamphetamine-exposed children as compared to clinic based non-drug exposed children and a normative sample on the Wechsler intelligence scale, processing speed index scores. Findings were significant for both comparisons in that the methamphetamine-exposed group had significantly lower scores on the processing speed index than the clinic based non-drug exposed group and the non-clinical normative sample.

The above results are consistent with the existing literature related to adult methamphetamine addicts indicating that deficits in processing speed are negatively associated with methamphetamine-exposure (Nordahl, Salo, & Leamon, 2003). In addition to being statistically significant, this finding is also clinically significant as the index means fall in the low average range representing a potential area of delay for these children. Results are also consistent with literature suggesting associated deficits in sensory motor coordination deficits based on rat studies (Slamberova et al., 2006) and deficits in sustained attention and memory (Chang et al., 2001) in methamphetamine-exposed children. These abilities indirectly contribute to and negatively effect processing speed. In further examining the literature, there is support for components that contribute to the processing speed index, such as attention, and motor coordination (Wechsler, 2003). However, similar to the other indexes, it is difficult to find literature that examines stimulant-exposure and index scores. Rather, the stimulant-exposure effects have to be inferred based on the skills and abilities that make up the index. The literature report (Zasler, Katz & Zafonte, 2006) that the processing speed index is particularly sensitive to brain dysfunction because coding and symbol search subtests tend to be very sensitive, which can be attributed to the significant difference noted in the processing speed index in this study.

Supplemental Findings

Due the small sample size, it is theorized that differences between the groups may not be observed readily, and therefore the groups were also examined descriptively. To inspect the clinical differences between the methamphetamine-exposed group and the clinic based non-drug exposed group the number of occurrences of low scores between the two groups was explored. Low scores were defined as any score falling 1.5 standard deviations below the normative mean or a score of 77 or less. The methamphetamine-exposed group had consistently higher percentages of low scores, when compared with the clinic based non-drug exposed group. This is an interesting finding due to both samples being from a clinic setting. The clinic based non-drug exposed group had fewer low scores than the methamphetamine-exposed group. It appears that when the means are compared, the differences may not be as apparent because the scores are aggregated. This could be one possible explanation that there were not significant differences along many of the index variables between the groups when the group means were compared. Areas of notable concern include the processing speed, verbal comprehension and working memory variables, which indicates that there may be methamphetamine-exposed children with potential for delays in these areas.

To further understand trends in the data, the Wechsler intelligence scale subtests were compared descriptively for the methamphetamine-exposed and clinical non-exposed groups. The methamphetamine-exposed group subtest mean scores were consistently lower than the clinical non-drug exposed subtest mean on every subtest. The methamphetamine-exposed group had four mean subtests scores in the below average range (symbol search, coding, arithmetic, comprehension), while the clinic based non-drug exposed group did not have any subtest means in the below average range of functioning. For the methamphetamine-exposed group, the subtest areas that appeared to have the most difference between groups were arithmetic, object assembly and comprehension. There is no current research that discusses Wechsler intelligence subtest score profiles or subtest deficits of stimulant-exposed children. However, the areas of concern related to these subtests include memory, attention, visual motor integration, verbal reasoning, and verbal knowledge, and there are some studies consistent with stimulant-exposure associated with deficits in these areas (Chang et al., 2001; Nordahl, Salo, & Leamon, 2003; Griffith, Azuma, & Chasnoff, 1994). Again, indirect associations can only be made between the necessary skills and the subtests.

Implications

Caution should be taken when considering the results of the current study due to small sample size. However, the implications produced by this study provide valuable inquiry for future research. The current study revealed that the methamphetamine-exposed group performance fell in the low average range in the areas of processing speed, verbal comprehension, attention/executive functions, memory and sensorimotor functioning through descriptive analysis.

Statistical results indicated that when compared to a similar clinical non-drug exposed sample the methamphetamine-exposed group had statistically lower index scores in the area of processing speed. Furthermore when compared to the non-clinical normative sample, the methamphetamine-exposed group scored significantly lower in the areas of verbal comprehension and processing speed. These findings are also clinically significant as the index means fell in the low average range representing potential areas of delay for these children. Finally, it should be noted that there was no statistically significant difference in any of the Wechsler intelligence factors between the clinic based non-drug exposed group and the non-clinical normative group.

To further examine the clinical differences between the methamphetamine-exposed group and the clinic based non-drug exposed group the number of occurrences of low scores between the two groups were examined. The general trends exhibited a disproportionate number of low scores for the methamphetamine-exposed group when compared to the non-drug exposed clinical group. Processing speed, working memory, and verbal comprehension were areas that were noted to have more low scores. This has implications for methamphetamine-exposed children in that they may potentially exhibit delays in these areas.

In comparing the methamphetamine-exposed group to the clinic based non-drug exposed group, subtest scores were compared for any differences. The clinic based non-drug exposed group consistently had higher subtest means than the methamphetamine-exposed group on all of the subtests. This emphasized a general trend in overall lower scores for the methamphetamine-exposed group when descriptively compared to both the clinical non-drug exposed group and to a non-clinical normative sample. The methamphetamine-exposed group had the largest difference from the non-drug exposed group on the object assembly, comprehension and arithmetic subtests. Further, subtest falling in the in the below average range when compared to the normative sample included comprehension, arithmetic, coding and symbol search. These differences imply developmental delays in areas of visual motor integration, sustained attention, concentration, numerical operations, working memory, visual acuity and speed, social knowledge, and verbal reasoning skills in methamphetamine-exposed children.

Limitations

One of the most significant limitations in regards to this study is the small sample size, which limits the generalizability of findings to the larger population. Also, the small sample size and low-power created some difficulty with hypothesis-testing, analyzing the data and inferring results.

Additional limitations of the current research were due to the study's archival nature and subsequent unavailability of information. Only information obtained through the intake and assessment process was available for review. Although, sufficient information was collected via an assessment intake interview, considerable variability among clinicians (interviewers and assessors) in the amount of detail gathered and recorded in the intake and assessment report were noted. As the written intake interview questionnaire and assessment reports were only available archivally, it is possible that all information gathered in the interview was not recorded and accessible to the researcher of this study.

In conducting the study it was difficult to identify methamphetamine-exposed children due to insufficient information gathered and recorded on the intake interview. Although the intake questionnaire included a section about drug-exposure, a specific prompt for methamphetamine use was lacking. Additionally, information about frequency and duration were not addressed in most of the intake interviews. This information was also probably not available due to the historians' knowledge and awareness of their child's prenatal history, as a portion of the children serviced by the PNAP clinic were in foster care or were adopted, and their caretakers were not likely to have through information about drug-exposure. Adding to the difficulty of identifying methamphetamine-exposed children is the stigma attached to drug-use in general and especially when pregnant. Due to this stigma, it is possible that parents who used drugs while pregnant did not disclose that information during the intake interview and assessment.

Another limitation to this study was in matching the methamphetamine-exposed group with the non-exposed group. Socioeconomic status (SES) and home/out-of-home placement have been shown to be important variables to consider when examining cognitive functioning (Duyme, Dumaret, & Tomkiewicz, 1999; Nelson et al., 2007). SES and placement type were not available for some participants of the sample. Therefore, it was not possible to match the two groups along these two variables. Other environmental variables identified in the literature such as instability of household, abuse and neglect, maternal care-giving style, stimulating/non-stimulating environment, prenatal care and nutrition during fetal development were also unavailable and could have significantly impacted the current findings. These challenges are also characteristic of those encountered by researchers pursuing drug-exposure research.

The measures used in this study were not ideal in pin pointing specific areas of deficits. Wechsler intelligence measures are widely accepted and used to assess cognitive abilities. However, they are not able to provide a pure measure of abilities. Rather the indexes and subtests tap into a variety of abilities and skills. For example, the processing speed index requires the ability to process information speedily and accurately, but it also necessitates hand-eye coordination, attention, memory, and visual discrimination and tracking. As such, difficulties in any of the above mentioned abilities could lead to poor performance in the processing speed index. Although at this time a pure measure that neatly measures specific aspects of cognition or other abilities does not exist, the current measures complicate the capability to focus on specific areas of deficits. Another challenge encountered in this study was the need to combine WISC-III and WISC-IV scores. Although the two versions of the test were well-correlated, some difficulty was presented in that the two versions had index scores comprised of different subtests. It is problematic to combine WISC-III and WISC-IV due to the different normative samples used for each version. Even though the standard approach of combining the scores from the two versions was utilized, there is a methodological limitation in this approach in the existing literature and in this study.

The amount and duration of drug use was unknown in this sample, and was also a limitation of this study. There is research support that the amounts and trimester (developmental period) the fetus is drug-exposed can affect postnatal development (Vorhees, Ahrens, Acuff-Smith, Schilling, & Fisher, 1994; Williams, Moran, & Vorhees, 2004). Based on the intake information, the amount of drug-exposure and the duration of exposure could not be accounted for, which is also a problem encountered in the drug-exposure literature. It is well known and documented in the literature that many drug users abuse multiple substances, as methamphetamine users tend to do (Brooke, Whiteman, Shapiro, & Cohen, 1996; Dixon, 1994). This is a significant limitation found in the drug related literature and was also a problem in the current study. For example, many of the participants identified as being exposed to methamphetamine also had polysubstance-exposure. However, in some cases the different types of drugs were not known. This complicates research in that the different interactions of the drugs could have their own unique effect that cannot be easily accounted for. Nevertheless, polysubstance exposure is common in the research dealing with drug use and exposure, and is a challenge researchers frequently encounter in the process of this type of research.

An additional limitation was the lack of a "standard" protocol of tests. Although it is the standard of practice to form a testing battery based on the referral question, the variations in measures used makes research difficult. In the present study, each participant was administered an individualized battery appropriate to answer the referral question. However, this produced a complication for research due to the challenge of not being able to compare participants along the same variables due to differences in measures used.

Future Direction

The current study suggests several implications relating to long-term effects of methamphetamine-exposed children in this clinic population. The present study looked at Wechsler intelligence index scores and NEPSY domains to describe a methamphetamine-exposed sample. The study also compared the methamphetamine-exposed sample to a matched sample from the clinic population and a non-clinical normative sample.

The current study demonstrated some trends and differences in the methamphetamine-exposed sample. However, further research of these trends with a larger and a more representative sample is necessary to better understand the profiles of these drug-endangered children. Future studies should also be conducted using a closely matched, control sample including environmental variables such as SES and living situation (adopted, foster care, etc.). Although a considerable amount of research about prenatal drug exposure exist, more research examining the long-term effects of methamphetamine-exposure is necessary, as most of the existing literature is focused on young children who may not have developmentally grown into their potential delays.

Future research might extend this investigation to also look at other variables such as visual-motor integration using the Beery-Buktenica Developmental test of Visual-Motor Integration, sustained attention using the Test of Everyday Attention for Children (TEAch), and verbal and visual memory utilizing the Children's Memory Scale (CMS). It would also be interesting to examine behavioral components by using a Behavioral Assessment System for Children- 2 (BASC-II). This approach would provide valuable information about the particular ways methamphetamine-exposed children are affected and add to the limited body of research that exists in this area. As such, going investigation on the effects of methamphetamine exposure on child development is needed to increase the understanding of drug-effects and to generate relevant interventions for these children.

In future studies, separating the participants by age group may be beneficial as not to loose any subtle differences between age groups. This approach may also assist in isolating differences in groups while accounting for any age effects. In examining the methamphetamine-exposed population, a mixed-design or qualitative approach may be effective in future studies so as to gather a comprehensive representation of the methamphetamine-exposed child. Quantitative studies may have the potential to overlook the subtle differences in the methamphetamine-exposed children. Qualitative studies or mixed-design studies may be more appropriate to collect the information that is not quantifiable. In order to gather the qualitative information as well as the non-quantifiable information, a study should be designed using assessment measures looking at IQ variables, motor skills, memory measures, attention measures, parent reports and teacher reports of behavior, as well as behavioral observations that is qualitatively categorized.

In order to further study the effects of methamphetamine exposure in the PNAP clinic, a specific protocol (standard battery) should be designed and in-place to supplement the assessment battery used to answer the referral question. This will allow the clinic to collect data in a uniform and useful manner for research. There should also be a supplemental questionnaire for children with drug-exposure to gather information about specific drugs, frequency, dosage, and duration of use. This would provide more uniform data and solve problems of missing information, which, in turn, would allow studies to be conducted in a more efficient and effective manner.

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