Visual attention in children with prenatal cocaine exposure

AMY HEFFELFINGER,¹ SUZANNE CRAFT,² AND JAYE SHYKEN¹

¹Washington University School of Medicine, St. Louis, MO 63130

²University of Washington, VA Puget Sound Health Care System, Seattle, WA 98108

(RECEIVED February 27, 1995; REVISED April 5, 1996; ACCEPTED May 24, 1996)

Abstract

Previous studies have reported that developmental disruption of dopaminergic systems results in lateralized deficits in visual attention (Posner et al., 1991; Craft et al., 1992). Infants who were prenatally exposed to cocaine were hypothesized to have increased reaction times to targets in the right visual field on measures of visual attention compared with infants who were not exposed to cocaine. Seventeen children without prenatal exposure to cocaine and 14 children who were exposed to cocaine (age range from 8–40 months) completed a visual attention task, the Mental Development Index of the Bayley Scales of Infant Development, Second Edition; and the Preschool Language Scale, Third Edition. Cocaine-exposed children were slower to orient to stimuli in the right visual field after repeated trials, especially after attention was first cued to the left visual field. They were also less likely to orient to the right when given a choice. Results suggest that the left hemisphere visual attention system is disproportionately affected by prenatal exposure to cocaine. (*JINS*, 1997, *3*, 237–245.)

Keywords: Prenatal, Cocaine exposure, Visual attention

INTRODUCTION

The neuropsychological impact of prenatal cocaine exposure in children is a subject of speculation and controversy. The media have presented these children as an increasing problem for schools because of their inattentiveness and hyperactivity (Mayes et al., 1992). Few studies, however, have addressed empirically the question of whether cocaine exposure influences the development of attention systems. In this article we review the literature of neurological and cognitive effects of cocaine exposure. We then describe the results of a study examining the question of impaired visual attention in this population.

Effects of Prenatal Cocaine Exposure

Central nervous system effects

Although there are numerous studies documenting neurological abnormalities in infants prenatally exposed to cocaine, little is known about how cocaine influences the central nervous system of the developing child (Doberczak et al., 1988; Chasnoff et al., 1989; Hite & Shannon, 1992). Chasnoff et al. (1989) reported an increased rate of seizure activity, cerebral infarctions, and abnormal electroencephalogram (EEG) activity in newborns exposed to cocaine. Doberczak et al. (1988) conducted EEGs on cocaine-exposed neonates who had no significant birth complications, and over half of them showed EEG abnormalities for the first few weeks after delivery. In contrast, Link et al. (1991) found no structural differences in the degree of myelination in 8 cocaine-exposed infants as compared to age-matched control children.

One possible mechanism through which prenatal exposure to cocaine may affect the brain is by selectively interfering with the maturation of catecholamine systems. In adults, cocaine acts as a stimulant by specifically blocking the reuptake of catecholamines at postsynaptic terminals (Pitts & Marwak, 1988). Akbari and Azmitia (1992) documented an increased number of dopamine fibers in the anterior cingulate cortex and in noradrenergic fibers in the parietal cortex and the CA1 field of the hippocampus in adult rats that had been prenatally exposed to cocaine. Dow-Edwards et al. (1990) measured the rates of glucose utili-

Reprint requests to: Amy Heffelfinger, Washington University School of Medicine, St. Louis, MO 63130.

zation and the number of dopamine receptors in adult rats with prenatal cocaine exposure. Increased binding of a dopamine agonist occurred in the substantia nigra *pars compacta*. Metabolic activity was decreased in numerous regions, including hypothalamic structures, the nigrostriatal pathway, the nucleus accumbens, amygdaloid structures, and the hippocampus. Minabe et al. (1992) recorded single-cell activity in the midbrain structures of adult rats prenatally exposed to cocaine, finding a decrease in the number of active dopamine cells in the substantia nigra *pars compacta* and in the ventral tegmental area. These studies suggest that cocaine exposure affects dopaminergic pathways.

Cognitive effects

If cocaine selectively influences certain neural systems, then it is possible that children exposed to cocaine may exhibit specific cognitive and behavioral deficits instead of general cognitive impairment. To date, there have been conflicting findings regarding the development of general cognitive functions. On the Neonatal Behavioral Assessment Scale (NBAS; Brazelton, 1973), some studies have found that newborns who were prenatally exposed to cocaine showed significant differences compared to control children on at least one of the clusters (Chasnoff et al., 1989; Eisen et al., 1991; Mayes et al., 1993). However, Neuspiel et al. (1991) and Woods et al. (1993) found no group differences between cocaine-exposed newborns and control children on the NBAS. During infancy, babies exposed to cocaine performed as well as control infants on the Mental Development Index of the Bayley Scales and the Stanford Binet Intelligence Scale (SBIS) (Chasnoff et al., 1992; Griffith et al., 1994). In contrast, Van Barr (1990) found that 24and 30-month-old cocaine-exposed children achieved significantly lower scores on the Mental Development Index than the control group. However, the majority of these children also were exposed to heroin and/or methadone, raising questions about whether the observed deficits were solely attributable to cocaine exposure.

Results of certain studies suggest that cocaine exposure selectively influences the development of language and attention abilities. Bender et al. (1995) reported that cocaineexposed children obtain lower scores on language comprehension tasks. In addition, children exposed to cocaine prenatally have had significantly lower scores than control children on the verbal portions of the SBIS, but not on the nonverbal portions (Griffith et al., 1994).

Prenatal cocaine exposure may also negatively affect a child's ability to direct and sustain attention (Mayes et al., 1993). Cocaine-exposed newborns obtained significantly lower scores than control children on the habituation cluster of the NBAS, which measures the regulation of attention in neonates (Eisen et al., 1991; Mayes et al., 1993). Chasnoff et al. (1989) found that cocaine-exposed children performed more poorly on the orientation and state regulation clusters; a significant number of the children who had been prenatally exposed to cocaine throughout pregnancy

were unable to enter alert states to engage in orientation tasks, whereas all of the control children were alert and responsive to the examiner. Each of these studies demonstrates a deficit in the ability of cocaine-exposed newborns to regulate their level of arousal and attentiveness.

Further research suggests that attentional deficits resulting from cocaine exposure may persist into childhood. Low scores on the Summative Attention Rating Scale, which was created from the 5-point rating scales of the Stanford-Binet Intelligence Scale, were the best predictors of low scores on the Verbal Reasoning portion of the SBIS and of high scores on the aggression and destructiveness scales of the Child Behavior Checklist (Griffith et al., 1994). Cocaine-exposed children had significantly worse scores on each of these measures. These findings indicate that cocaine may affect the ability to be attentive, which in turn may influence the ability to perform cognitive tasks and to interact with other people.

Visual Attention Systems

Visual attention plays an important role in cognitive processing. Although evidence suggests that attentional substrates may be organized differently in young children, understanding the mature system provides a context for examining developmental problems. Posner (1988) and colleagues have developed a theory of visual attention in adults. A posterior attention system mediates reflexive, overt shifts of attention and an anterior attention system is involved in sustained attention and state regulation. Orienting of visual attention involves three cognitive processes: the disengagement, shifting, and engagement of attention, which in adults are mediated by bilateral posterior parietal cortices, the pulvinar and reticular nuclei of the thalamus, and the superior colliculus, respectively.

The anterior attention system is comprised of cortical and subcortical structures that control alertness, vigilance, and voluntary visual actions. In adults, the anterior cingulate gyrus is involved with sustaining attention during voluntary cognitive behaviors, but the level of activity decreases as the subject practices and learns a task (Posner, 1988; Posner & Peterson, 1990). The cingulate gyrus has reciprocal dopaminergic connections with the ventral tegmental nucleus via the caudate nucleus of the basal ganglia (Rothbart et al., 1990; Colby, 1991). The basal ganglia also have reciprocal connections with many cortical areas. The anterior system may serve as a regulating loop for selective and sustained attention for higher cognitive processes.

If the anterior cingulate gyrus receives dopaminergic input and is involved in selecting and maintaining attention and in regulating emotions, then disruption to this dopaminergic system may result in changes in attention and emotional behaviors. This possibility is supported by studies of children with attention-deficit hyperactivity disorder (ADHD), who show anterior attention network dysfunction and who are hypothesized to have disrupted catecholamines (Shaywitz et al., 1977; McCraken, 1991). Similarly, children exposed to cocaine exhibit different patterns of state regulation and attention maintenance than do control children. Therefore, cocaine may have influenced the anterior attention system through prenatal disruption of the dopamine system.

Development of Visual Attention

As an infant develops, certain visual abilities emerge and may represent the maturation of the neural networks mediating visual attention. The development of disengaging processes and anticipatory looking have been studied in healthy infants. According to Johnson et al. (1991), the maturation of the parietal lobe and the pathway from the frontal eye fields to the superior colliculus underlie the infant's ability to disengage visual attention. In this study, 4-month-old children were able to disengage their attention and orient to new stimuli consistently (85% of trials) within 1 s, while 2- and 3-month-olds only looked to the new design 32 and 42% of the time, respectively. These behavioral data coincide with a PET study documenting that parietal lobe metabolism reaches adult levels at 4 months of age (Chugani et al., 1987).

Posner et al. (1984) and Craft et al. (1992) suggest that anterior frontal regions may regulate the parietal lobe's allocation of attention. Craft et al. (1992) found that male children with early-treated phenylketonuria (ETPKU), an inheritable condition that disrupts dopamine metabolism, were slow to respond to right visual field targets after a brief delay when attention had been engaged to a cue in the left visual field. In addition, children with bilateral injury to anterior brain regions had increased reaction times to invalidly cued targets in the right visual field after longer intertrial intervals (Craft et al., 1994). Both populations suffered from developmental damage to bilateral anterior regions, and both had difficulty disengaging towards right visual field targets. These results suggest that, in children, the anterior regions play a role in the disengagement and engagement processes.

Maturation of the frontal eye fields and other prefrontal areas coincides with higher level visual attention phenomena such as anticipatory looking. At age 4 to 5 months, infants are able to anticipate the location of a target because they learn the relationship between cue type and subsequent location (Johnson et al., 1991). Four-month-old infants looked with anticipation 29% of the time after being trained, whereas the 2- and 3-month-old groups only anticipated the target 14% of the time.

In summary, visual attention abilities emerge early in development and are vulnerable to disruption early in infancy. Therefore, if visual attention abilities are mediated by dopaminergic pathways, and these pathways are disrupted by prenatal cocaine exposure, visual attention abilities may be impaired in children who were prenatally exposed to cocaine.

Dopaminergic Influences on Lateralization

Dopamine may influence neural lateralization, which is expressed through behavioral asymmetries. For example, Glick

et al. (1977) found asymmetries in dopamine receptors and metabolism in the nigrostriatal system of rats, and these differences in dopamine distribution were correlated with behavioral indices such as the direction of spontaneous circling. A decrease in the asymmetrical behavior resulted when apomorphine, a dopamine agonist, was administered (Castellano et al., 1989). Also, there was a decrease in the rightside preference if the substantia nigra contralateral to the side of preference was lesioned, but lesioning the ipsilateral substantia nigra did not influence side preference. Furthermore, as Castellano et al. (1989) noted, the distribution of catecholamines may regulate the development of neural asymmetries. Therefore, it is possible that behavioral asymmetries are determined early in development through dopamine's influence on the morphology of neural tissue.

Disruption to the dopamine system early in development can cause behavioral differences throughout development and possibly into adulthood (Santana et al., 1992). As mentioned previously, Craft et al. (1992) found that ETPKU, an inability to synthesize dopamine postnatally, affected performance on a visual attention task. Males with ETPKU had slower reaction times to targets in the right visual field than children without ETPKU. Therefore, if prenatal cocaine exposure disrupts dopamine systems, cocaine-exposed children may demonstrate lateralized differences in behaviors that are influenced by dopamine.

In summary, there is limited information on the effects of prenatal cocaine exposure on the neuropsychological functioning of children. Evidence from animal studies suggests that cocaine interferes selectively with the development of catecholaminergic systems, including the dopaminergic pathways (Dow-Edwards et al., 1990; Akbari & Axmitia, 1992; Minabi et al., 1992). Dopamine is thought to play an important role in the growth and synaptic differentiation of neurons in early development (Santana et al., 1992). In addition, it may influence lateralization, because it is distributed asymmetrically (Glick et al., 1977). In particular, visual attention is likely to be affected. Craft et al. (1992, 1994) found that children with metabolic disorders and children who suffered disruption of dopamineinnervated anterior brain regions at birth displayed abnormal patterns of attending to targets in the right visual field. These results suggest that the left hemisphere attention systems were impaired. We propose that because of cocaine's influence on dopaminergic pathways, children who were exposed to cocaine during gestation will have increased reaction times for targets in the right visual field on measures of visual attention compared to children who were not exposed to cocaine.

METHODS

Research Participants

Thirty-one children between the ages of 8 and 40 months participated. This wide age range was established based on the ages of the available cocaine-exposed infants. The control group consisted of 17 children, and the cocaine-exposed group consisted of 14 children whose mothers had used cocaine during pregnancy. Table 1 provides demographic information about each group. Groups did not differ in age, number of premature subjects, birth weight, or maternal education. There was no difference in representation of sex between cocaine-exposed children and control children. Groups were comparable for ethnicity (cocaine-exposed group: 12 African American and 2 White participants; control group: 14 African American and 3 White participants). The cocaine-exposed group had significantly lower scores on measures of overall cognitive development and receptive language skills; mean scores are presented in Table 1.

The majority of cocaine-exposed participants were recruited from the WISED (Women and Infants Safe From the Exposure to Drugs) program at St. Louis Regional Hospital. This program provides prenatal care for pregnant women who have or are using cocaine and other illegal substances. Abstinence is encouraged, but not required during enrollment. In order to protect confidentiality, each mother was informed about the research study by the WISED coordinators, and their consent was obtained before they were contacted by the investigators. The majority of the mothers who were contacted from the WISED program agreed to participate in the research study. A few participants were older siblings of children in the WISED program or children of mothers who had heard about the study and requested participation. Two of the cocaine-exposed children were in foster care. Inclusion requirements for the study were exposure to cocaine during gestation, as identified by positive urine analysis for cocaine pre- or perinatally and/or parental report. Children with evidence of concomitant opiate or barbiturate exposure were excluded from the study. Two of the mothers had also consumed alcohol during their pregnancy. These children were included in the study because the alcohol use was limited to infrequent occurrences during the initial trimester of pregnancy and because two mothers of control children had similar reports of alcohol use. Nicotine use was not an exclusionary criterion due to the number of mothers who used both cocaine and nicotine. Children were excluded if they suffered any perinatal complications other than prematurity.

The majority of the control subjects were recruited through daycare centers in middle- to low-socioeconomic neighborhoods in St. Louis, Missouri. Letters describing the study's procedures were given to each parent, and the parents were encouraged to call the researcher if interested in participating. Children were excluded from the control group if parental reports indicated drug use during pregnancy and if children had suffered from any perinatal complications except prematurity.

Procedure

The children participated in two testing sessions lasting approximately 75 min at the St. Louis Children's Hospital. Order of tests was counterbalanced so that the Bayley Scales of Infant Development, Second Edition and the Preschool Language Scale–3 were administered on different days. The visual orienting task was administered on the same day as the Bayley; administration order for the visual attention task and the Bayley was also counterbalanced. Tests were administered in a quiet, well lit medical clinic. The parents of participants received \$20.00 per session and written feedback about their children's performance on the standardized tests.

At the beginning of the first session, a brief interview was conducted with each mother to obtain information about the participant's pre- and postnatal development, as well as to obtain demographic information, occupational status of the mother, and drug and alcohol use history. In addition, mothers signed consent forms for participation and release of information forms from the hospital where the child was born.

Cognitive tests

The Mental Development Index of the Bayley Scales of Infant Development, Second Edition (1993) was administered to measure overall cognitive development. In addition, receptive language development of these children was assessed with the Auditory Comprehension component of the Preschool Language Scale–3 (PLS–3; Zimmerman et al., 1992). These measures were administered by a Master's level psychology graduate student and a research assistant who

Table 1. Age, maternal education level, birth weight, and group scores on the Bayley II and the Preschool Language Scale–3

Variable	Control			Cocaine-exposed		
	М	SD	n	М	SD	n
Age (months)	23.7	8.11	17	20.3	9.88	14
Education (years)	13.26	2.57	17	12.07	1.84	14
Birth weight (g)	2893.33	701.15	13	2785.00	756.52	8
Bayley II	99.47	12.18	17	86.64	12.00	14
PLS-3	99.47	12.43	17	87.50	8.89	14

was trained by the Master's level student. Due to the relationship between the researcher and the WISED program, administrators were aware of group status. However, videotapes of the attention measure were scored by two raters who were unaware of group status.

Visual orienting task

The visual attention task was administered on a threemonitor computer system as described in Johnson et al. (1991). Three 30-cm color monitors were arranged side by side about 1 m in front of the child, who was sitting on the parent's lap. Each parent was instructed to remain silent throughout the task. The central display had a visual angle of about 10° and each peripheral display was about 30° from the middle of the central monitor. There were two central designs. One consisted of a green background with colorful spiraling circles, and the other had a blue background with spiraling squares. Each pattern increased in size with time. They were accompanied by a regular low-frequency beat pattern and a tone of increasing frequency, respectively. The peripheral stimuli were two identical geometric figure sets.

Eye movements were monitored by a video camera situated above the monitors. This camera recorded the child and the reflection of the monitors in mirrors located on the wall behind the child. The examiner administered the test by watching the video output to a television monitor. Stimulus presentation was controlled by the examiner with a computer keyboard.

This task consisted of two phases. During the training phase, a series of 18 training trials were administered. For each of these trials, one of two central designs appeared, determining on which peripheral side the test stimulus would appear. The child was required to orient to a central design. The offset of the central display corresponded with the onset of a unilateral peripheral design. The child was allowed 2.5 s to orient; then the stimulus was removed, and the trial ended.

Data were scored by frame-by-frame analysis of video tapes of eye movements by raters who were unaware of group status. Three scores were assigned. First, the percent of trials completed was determined; a 50% completion rate was necessary for the participant's data to be considered valid. Second, the mean reaction time, from the offset of the central design to the beginning of an eye movement, was calculated for right and left visual field trials. Third, the percent of *fast* looks, reaction times under 300 ms, was used to evaluate the consistency of fast reactions for both visual fields.

The testing phase of the task consisted of three types of trials, reinforcement trials, test trials, and disengage trials, and was administered immediately after the training phase. The reinforcement trials were identical to those previously described and were included to reinforce the learned association. During test trials, bilateral peripheral stimuli followed the offset of the central display, regardless of which design was presented. Test trials were included to determine whether the child oriented to the side that had been associated with a given design in the training trials, thus showing that the child had learned the contingent relationship between central design and side of the subsequent target. Disengage trials were identical to reinforcement trials, except that the central stimulus remained present during the peripheral presentation. These trials demonstrated the child's ability to disengage attention from the central stimulus. Six of each trial type, three to each side, were presented in a pseudorandom order in which randomization was constrained by the following limiting factors: no more than two of the same trial type could be presented consecutively and no more than three consecutive targets could appear on the same side.

Reinforcement and test trials were excluded if the child did not orient to the peripheral stimulus within 2.5 s. Four s were allowed before exclusion for disengage trials. Fixation to the central design at the onset of a peripheral stimulus was required during all trial types. At least two, one in each direction, of each of the trial types needed to be complete in order for the test to be scorable. Reinforcement trials yielded scores for each visual field of percent complete, percent fast looks, and mean reaction time. For test trials, the percent complete, percent correct (percent oriented towards peripheral target contingent with the central cue), and mean reaction time were calculated for each visual field. Finally, percent complete, percent correct (whether an eye movement was made within 4 s), and mean reaction time were scored for disengage trials.

RESULTS

Visual Orienting Task

Visual orienting trials

A repeated-measures multivariate analysis of variance (MANOVA) was performed for fast reaction times using group as the between-subjects variable and task phase (training phase vs. reinforcement trials of the test phase) and direction (left vs. right visual field) as the within-group factors. A Group \times Phase \times Direction interaction was present, F(1,1) = 5.01, p < .05. Further ANOVAs were conducted to determine the nature of this interaction. When the reaction times of both phases were combined, cocaine-exposed children had significantly fewer fast looks than did the control children when orienting to targets in the right visual field, F(1,28) = 4.35, p < .05 (Figure 1). Further analysis revealed that cocaine-exposed children had fewer fast looks to the right visual field during the second half of the test than did control subjects, F(1,28) = 6.43, p < .05 (Figure 2). No differences were present between the groups during the training phase of the test or for trials in which the target was in the left visual field. Groups did not differ in the percentage of trials completed or in reaction times.

Two-choice test trials

A main group effect for percent of correct trials for right visual field targets was statistically significant, F(1,27) =



Fig. 1. Percent of fast looks to the right visual field during training and testing phases of the visual orienting task. *Cocaine-exposed children had fewer fast looks to right visual field targets throughout the task than did control children (p < .05).

4.91, p = .05. As shown in Figure 3, cocaine-exposed children had fewer correct trials than controls when the target was in the right visual field. The binomial distribution was used to determine if percent correct was different from chance. Interestingly, only the cocaine-exposed group was significantly different from chance when expected to look to the right, having fewer correct than would be expected. Neither group's percent correct differed from chance when the target was in the left visual field.

Disengage trials

An ANOVA was performed for reaction time with group as the between-group variable and side of target (left or right) as the within-subjects factor. Figure 4 demonstrates that cocaine-exposed children had significantly slower reaction times to right visual field stimuli than did controls, F(1,21) = 6.51, p < .05. There was no difference between groups in reaction times to left visual field stimuli. Further analysis revealed that the controls were faster to disengage to the right than they were to the left, although the difference only approached significance, F(1,11) = 4.13, p <.10. In addition, there was a main effect between group for percent correct on trials in the right visual field (Figure 5), because controls disengaged more often from the central display when the stimuli were in the right visual field than did cocaine-exposed children, F(1,29) = 4.26, p < .05. Once again, the control children showed a tendency to disengage to the right more frequently than they did to the left, F(1,16) = 4.15, p < .10.

DISCUSSION

The results of the present study support the hypothesis that children with prenatal cocaine exposure perform differently on visual attention tasks than control children. In particular, we hypothesized that cocaine-exposed children would have more difficulty with attention to stimuli in the right visual field. Cocaine-exposed subjects were less likely to orient quickly to stimuli in the right visual field, especially after repeated trials, and they took longer to disengage attention to respond to stimuli in the right visual field. After numerous trials, they were less likely to orient towards the right when given a choice.

Lateralized Deficits in Cocaine-Exposed Infants During Simple Orienting

Children who had been prenatally exposed to cocaine were consistently slower to orient toward right peripheral stimuli than were control children on trials requiring them to look to peripheral designs during the test phase of the task. They had significantly fewer fast looks (reaction time < 300 ms) to the right visual field than did the control group. There was no difference in percent of fast looks to the right visual field between the groups during the training phase of the task. However, children who were exposed to cocaine prenatally had significantly fewer fast looks during the reinforcement trials, which were identical to the earlier training trials, than did control children. The fact that this pattern was observed only in the latter portion of the task and not in



Fig. 2. Percent of fast looks during the second phase of training or reinforcement trials in the visual orienting task. *Cocaine-exposed children had fewer fast looks to the right side than did control children (p < .05).



Fig. 3. Percent correct during test trials in the second phase of the visual orienting task. *Cocaine-exposed children had fewer correct trials in the right visual field than did control children (p = .05).

the initial training portion suggests that the deficit is not in simple orienting, a basic function of the superior colliculus. Rather, cocaine-exposed children did not learn to anticipate the location of the target, a skill normal children acquire by 4 months of age (Johnson et al., 1991).

Cocaine-exposed infants may have problems maintaining attention to stimuli in the right visual field after numerous trials. As noted, there were no differences between groups in reaction time or percent of fast looks during the training phase; the difference in time to orient to right visual field targets emerged during the reinforcement trials in the second half of the test. Some studies suggest that neonates prenatally exposed to cocaine have difficulty regulating attention and arousal levels, as demonstrated with lower habituation scores (Eisen et al., 1991; Mayes et al., 1993). However, results of the studies of Neuspiel et al. (1991) and Woods et al. (1993), did not find group differences in ability to regulate attention and arousal levels. The results from the present study indicate that visual attention difficulties are present in early childhood. The slowed response to right visual field stimuli observed in the present study may reflect dysfunction in the left anterior attention system, which plays a role in maintaining directed attention.

Our results suggest that cocaine selectively influences the development of the left anterior attentional system. This system involves frontal regions, the anterior cingulate gyrus, and the substantia nigra, which are part of the nigrostriatal and mesolimbic dopaminergic pathways. Akbari and Azmitia (1992), Dow-Edwards et al. (1990), and Minabe et al. (1992) found that the anterior cingulate gyrus and the sub-

stantia nigra have altered levels of dopamine in rats prenatally exposed to cocaine.

Disengagement of Attention in Prenatal Cocaine Exposure

The results indicate that cocaine also hinders the development of the ability to disengage attention. Cocaine-exposed children exhibited deficits when they were required to disengage their attention from an attractive central stimulus and look towards a target in the right visual field. They were much slower to look to the right than were the controls. Similarly, Craft et al. (1994) found that children with anterior deficits due to metabolic dysfunction or to acute cerebral insult had difficulty disengaging attention to respond to right visual field targets. These results suggest that, for children, the ability to disengage attention involves an anterior neural system. In addition, the anterior left hemisphere may be more vulnerable to disruption than the anterior right hemisphere.

Children with prenatal exposure to cocaine also showed a leftward orienting bias when given the choice to look to the left or right on bilateral test trials in the second part of visual orienting, a pattern that has been observed in children with bilateral anterior cerebral disruption (Craft et al., 1994). This pattern of responding is common in infants throughout the first 18 months of life, but then disappears (Posner & Rothbart, 1989). The appearance of this bias on later trials further suggests that cocaine-exposed children are unable to maintain attention to right visual field stimuli; attentional mechanisms may regress to the previous devel-



Fig. 4. Mean reaction times during disengage trials in the second phase of the visual orienting task. *Cocaine-exposed children were slower than control children to disengage during right visual field trials (p < .05).



Fig. 5. Percent correct during disengage trials in the second phase of the visual orienting task. *Control children disengaged more frequently on right visual field trials than did cocaine exposed children (p < .05).

opmental level of leftward orienting when the left hemisphere attention system is fatigued.

Rightward Bias in Control Children

It has been proposed that the right hemisphere dominates attentional functioning from infancy until about 18 months (Posner & Rothbart, 1989). Results from the present study suggest that the left-hemisphere attentional system may increase in efficiency when a child is 2 years old. On the second half of orienting trials, the control infants looked to the right stimulus consistently faster than they did towards the left. In addition, on bilateral trials, they disengaged from central stimuli to right visual field targets more quickly than to left visual field targets.

These results are consistent with the emergence of language skills, which are also supported by left hemisphere neural structures, at this age. The development of lefthemisphere neural structures may be delayed or disrupted in children who were exposed to cocaine. The present study found that cocaine-exposed subjects obtained significantly lower scores on a measure of receptive language than did control subjects. Griffith et al. (1994) and Bender et al. (1995) reported that cocaine-exposed children have a higher prevalence of language deficits than control children. In addition, our study suggests that the left anterior attention system has been disrupted, resulting in decreased visual attention abilities toward stimuli in the right visual field. Presently, it is unknown whether cocaine-exposed children will experience a subsequent improvement in behaviors mediated by left neural structures, indicating delayed development, or if they will suffer chronic deficits in these abilities.

Implications for Future Research

Although growing evidence suggests that developmental disruption of dopamine affects visual attention, it is possible that attentional impairment in cocaine-exposed children is not solely due to disruption of the dopamine systems (Posner, 1988; Craft et al., 1992). Akbari and Azmitia (1992) found that rats with prenatal cocaine exposure had increased norepinephrine fibers in the parietal lobe. In addition, it has been hypothesized that norepinephrine has a functional role in visual attention (Posner, 1988; Clark et al., 1989). Potentially, cocaine exposure may disrupt the balance within some or all of the catecholamine systems. Further studies may help clarify this issue by relating catecholamine metabolite levels to visual attention performance in cocaine-exposed children.

Information regarding nicotine use was not available for the whole sample. Limited data suggest that an equal number of mothers in each of the groups smoked during pregnancy, making it unlikely that the observed impairments are in fact due to prenatal nicotine exposure. However, future work should examine the effects of nicotine specifically, to determine whether such exposure influences the development of visual attention.

CONCLUSIONS

Exposure to cocaine *in utero* affects dopaminergic systems, which play a role in the mediation of attention. Results from the present study suggest that the left-hemisphere visual attention system is disproportionately affected by prenatal cocaine exposure. In addition, language, which is typically controlled by the left hemisphere, is delayed in these children as well. Further research is necessary to determine the duration of these deficits and the impact they will have on the academic and psychological development of children with prenatal cocaine exposure.

ACKNOWLEDGMENTS

Amy Heffelfinger (now at the Department of Neurology, University of Minnesota); Suzanne Craft, Department of Psychiatry and Behavioral Sciences, University of Washington and the VA Puget Sound Health Care System; Jaye Shyken, Washington University School of Medicine, Department of Obstetrics and Gynecology.

The authors thank Qunyue Siang for subject recruitment and her dedication to the participants of the WISED program, Dale Weininger for his expert computer programming, and Hannah Sierles for her help with data collection. Posters on partial results from this study were presented at the 23rd International Neuropsychological Society Meeting and at the 2nd Cognitive Neuroscience Meeting. Correspondence concerning this article should be addressed to Suzanne Craft, who is now at the Department of Psychiatry and Behavioral Sciences, University of Washington and the VA Puget Sound Health Care System, GRECC-182B Seattle Veterans Affair Medical Center, 1660 South Columbian Way, Seattle, Washington 98108. Electronic mail may be sent to scraft@u.washington.edu.

REFERENCES

- Akbari, H.M. & Azmitia, E.C. (1992). Increased tyrosine hydroxylase immunoreactivity in the rat cortex following prenatal cocaine exposure. *Developmental Brain Research*, 66, 277–281.
- Bender, S.L., Word, C.O., DiClemente, R.J., Crittenden, R.J., Persaud, N.A., & Ponton, L.E. (1995). The developmental implications of prenatal and/or postnatal crack cocaine exposure in preschool children: A preliminary report. *Developmental and Behavioral Pediatrics*, 16, 418–424.
- Brazelton, T.B. (1973). Neonatal Behavioral Assessment Scale. Philadelphia: J.B. Lippincott.
- Castellano, M.A., Diaz-Palarea, M.D., Barroso, J., & Rodriguez, M. (1989). Behavioral lateralization in rats and dopaminergic system: Individual and population laterality. *Behavioral Neuroscience*, 103, 46–53.
- Chasnoff, I.J., Griffith, D.R., Frier, C.J., & Murray, T. (1992). Cocaine/polydrug use in pregnancy: Two-year follow-up. *Pe-diatrics*, 89, 284–289.
- Chasnoff, I.J., Griffith, D.R., MacGregor, S., Dirkes, K., & Burns, K.A. (1989). Temporal patterns of cocaine use in pregnancy: Perinatal outcome. *Journal of the American Medical Association*, 261, 1741–1744.
- Chugani, H.T., Phelps, M.E., & Mazziotta, J.C. (1987). Positron emission tomography study of human brain functional development. *Annals of Neurology*, 22, 487–497.
- Clark, C.C., Geffen, G.M., & Geffen, L.B. (1989). Catecholamines and the covert orienting of attention in humans. *Neuro*psychologia, 28, 131–139.
- Colby, C.L. (1991). The neuroanatomy and neurophysiology of attention. Journal of Child Neurology, 6 (Suppl.), S90–S118.
- Craft, S., Gourovitch, M.L., Dowton, S.B., Swanson, J.M., & Bonforte, S. (1992). Lateralized deficits in visual attention in males with developmental dopamine depletion. *Neuropsychologia*, 30, 341–351.
- Craft, S., White, D.A., Park, T.S., & Figiel. (1994). Visual attention in children with perinatal brain injury: Asymmetric effects of bilateral lesions. *Journal of Cognitive Neuroscience*, 6, 165–173.
- Davis, E., Fennoy, I., Laraque, D., Kanem, N., Brown, G., & Mitchell, J. (1992). Autism and developmental abnormalities in children with perinatal cocaine exposure. *Journal of the National Medical Association*, 84, 315–319.
- Doberczak, T.M., Shanzer, S., Senie, R.T., & Kandall, S.R. (1988). Neo natal neurologic and electroencephalographic effects of intrauterine cocaine exposure. *Journal of Pediatrics*, 113, 354–358.
- Dow-Edwards, D.L., Freed, L.A., & Fico, T.A. (1990). Structural and functional effects of prenatal cocaine exposure in adult rat brain. *Developmental Brain Research*, 57, 263–268.
- Eisen, L.N., Field, T.M., Bandstra, E.S., Roberts, J.P., Morrow, C., Larson, S.K., & Steele, B.M. (1991). Perinatal cocaine effects on neonatal stress behavior and performance on the Brazelton scale. *Pediatrics*, 88, 477–480.
- Glick, S.D., Jerussi, T.P., & Zimmerberg, B. (1977). Behavioral and neuropharmacological correlates of nigrostriatal asymmetry in rats. In S. Haenad, (Ed.), *Lateralization in the nervous* system (pp. 213–249). New York: Academic Press.
- Griffith, D.R., Azuma, S.D., & Chasnoff, I.J. (1994). Three-year outcome of children exposed prenatally to drugs. *Journal of American Academy of Child and Adolescent Psychiatry*, 33, 20–27.
- Hite, C. & Shannon, M. (1992). Clinical profile of apparently healthy neonates with in utero drug exposure. *Journal of Obstetric, Gynecologic, and Neonatal Nursing*, 21, 305–309.

- Johnson, M.H., Posner, M.I., & Rothbart, M.K. (1991). Components of visual orienting in early infancy: Contingency learning, anticipatory looking, and disengaging. *Journal of Cognitive*
- Link, E.A., Weese-Mayer, D.W., & Byrd, S.E. (1991). Magnetic resonance imaging in infants exposed to cocaine prenatally: A preliminary report. *Clinical Pediatrics*, 30, 506–507.

Neuroscience, 3, 335-344.

- Mayes, L.C., Granger, R.H., Bornstein, M.H., & Zuckerman, B.S. (1992). The problem of prenatal cocaine exposure: A rush to judgment. *Journal of the American Medical Association*, 267, 406–408.
- Mayes, L.C., Granger, R.H., Frank, M.A., Scholtenfeld, R., & Bornstein, M.H. (1993). Neurobehavioral profile of neonates exposed to cocaine prenatally. *Pediatrics*, 91, 778–783.
- McCraken, J. (1991). A two part model of stimulant action on attention deficit hyperactivity disorder in children. *Journal of Neuropsychiatry*, 3, 201–209.
- Minabe, Y., Ashby Jr., C.R., Heyser, C., Spear, L.P., & Wang, R.Y. (1992). The effects of prenatal cocaine exposure on spontaneously active midbrain dopamine neurons in adult male offspring: An electrophysiological study. *Brain Research*, 586, 152–156.
- Neuspiel, D.N., Hamel, S.C., Hochberg, E., Greene, J., & Campbell, D. (1991). Maternal cocaine use and infant behavior. *Neuro*toxicology and Teratology, 13, 229–233.
- Pitts, D.K. & Marwak, J. (1988). Cocaine and central monoaminergic neurotransmission: A review of electrophysiological studies and comparison to amphetamines and antidepressants. *Life Sciences*, 42, 949–968.
- Posner, M.I. (1988). Structures and functions of selective attention. In T. Boll & B. Bryant (Eds.), *Master Lectures in Clinical Neuropsychology* (pp. 173–202). Washington, DC: American Psychological Association.
- Posner, M.I. & Petersen, S.E. (1990). The attention system of the human brain. Annual Review of Neuroscience, 13, 25–42.
- Posner, M.I. & Rothbart, M.K. (1989). Attention: Normal and pathological development (Tech. Rep. Vol. 89, No. 11). [Place of Publication]: Institute of Cognitive and Decision Sciences.
- Posner, M.I., Walker, J.A., Friedrich, F.J., & Rafal, R.D. (1984). Effects of parietal injury on covert orienting of attention. *Journal of Neuroscience*, 4, 1863–1874.
- Psychological Corporation, The (1992). *Preschool Language Scale-3*. San Antonio, TX: Author.
- Rothbart, M.K., Posner, M.I., & Boylan, A. (1990). Regulatory mechanisms in infant temperament. In J. Enns (Ed.), *The development of attention: Research and theory* (pp. 47–66). Amsterdam: North Holland.
- Santana, C., Rodriguez, M., Afonso, D., & Arevalo, R. (1992). Dopaminergic neuron development in rats: Biochemical study from prenatal life to adulthood. *Brain Research Bulletin*, 29, 7–13.
- Shaywitz, B.A., Cohen, D.J., & Bower, M.B. (1977). CSF monoamine metabolites in children with minimal brain dysfunction: Evidence for alteration of brain dopamine. A preliminary report. *Journal of Pediatrics*, 90, 671–677.
- Van Barr, A. (1990). Development of infants of drug dependent mothers. Journal of Child Psychiatry, 31, 911–920.
- Woods, N.S., Eyler, F.D., Behnke, M., & Conlon, M. (1993). Cocaine use during pregnancy: Maternal depressive symptoms and infant neurobehavior over the first month. *Infant Behavior and Development*, 16, 83–98.
- Zimmerman, I.L., Steiner, V.G., & Pond, R.E. (1993). *The Bayley Scale of Infant Development* (2nd ed.). San Antonio, TX: The Psychological Corporation.