Available online at www.sciencedirect.com

SCIENCE DIRECT®

Neurotoxicology and Teratology 27 (2005) 797 – 813

NEUROTOXICOLOGY AND TERATOLOGY

www.elsevier.com/locate/neutera

Event-related potentials in cocaine-exposed children during a Stroop task

Linda C. Mayes [a,*], Dennis L. Molfese [b], Alexandra P.F. Key [c], Nicole C. Hunter [a]

[a] *Yale Child Study Center, 230 S. Frontage Road, New Haven, CT 06520, United States*
[b] *Department of Psychological and Brain Sciences, University of Louisville, KY, United States*
[c] *Department of Hearing and Speech Sciences, Vanderbilt University, Nashville, TN, United States*

Received 25 August 2004; received in revised form 22 May 2005; accepted 23 May 2005
Available online 19 August 2005

Abstract

Objective: Prenatal cocaine-exposure may interfere with the ontogeny of prefrontal cortical executive functions due to cocaine's effect on the developing monoaminergic system. This study presents findings regarding cortical functioning in 29 prenatally cocaine-exposed (CE) and non-drug-exposed (NDE) 7- to 9-year-old children participating in event related potential (ERP) studies.
Methods: ERPs were recorded using 128-electrode high-density arrays while children responded to a standard Stroop paradigm.
Results: In the Stroop paradigm, CE children generated prolonged responses to the words while the NDE children produced briefer responses. Effects were noted in the region of the initial positive peak (P1), the second negative peak (N2) and the later positive peak (P3).
Conclusions: Early cocaine exposure may inhibit the specialization and streamlining of brain region involvement during cognitive processing such that task processing is slower to begin, requires more diverse cortical involvement, and requires more time to complete. ERP methodology has considerable potential for studying frontal maturation and may provide additional information to clarify generally the specific effects of prenatal CE on cortical functioning and the developmental course of cognitive functions.

Keywords: Prenatal cocaine exposure; Cortical maturation; Event-related potential

Whether or not prenatal cocaine exposure has an enduring impact on the neurocognitive development of preschool and school aged children is an area of active, and controversial, research. Collected findings from published studies to date suggest at least two models of effect on neurocognitive functioning that may both be expressed functionally as impairment in prefrontal cortical functioning. One relates to arousal modulated attention and related cognitive functioning [96,97]. In this model, neurocognitive impairments in a range of prefrontal cortical functions are expected especially as children are more emotionally aroused. The second model is based on a direct effect of cocaine on cortical morphology and specialization [60,81,84,85]. In this model, neurocognitive deficits might be expected in even non-stressed conditions in a range of functions including impaired inhibition and slowed reaction times [83].

Findings from several groups are consistent with both of these models. A number of investigators have reported difficulties among prenatally cocaine-exposed children in arousal regulatory capacities ranging from increased excitability with poor state regulation, rapid changes in arousal with stimulation (measured by changes in heart rate), to increased arousal from sleep, and greater physiological lability, [5,19,36,52,74,94,95,124,125] with some findings persisting at least through one year of follow-up [132]. A few studies have examined the relation between arousal-modulated attention and impaired information processing in CE neonates and very young infants, [6,29] as well as other aspects of the stress response system, including baseline and peak cortisol response to stressors in which CE infants show a depressed cortisol response to challenge [90] or lower baseline levels [69]. A number of labs also report findings relating to arousal-modulated attention and information processing in infants and toddlers including diminished responsiveness to novel stimuli and recognition memory,

* Corresponding author. Tel.: +1 203 785 7211; fax: +1 203 785 7926.
E-mail address: Linda.Mayes@yale.edu (L.C. Mayes).

0892-0362/$ - see front matter © 2005 Elsevier Inc. All rights reserved.
doi:10.1016/j.ntt.2005.05.011

poor impulse control and task persistence, diminished sustained attention, and greater emotional lability and/or behavioral disorganization [4,5,8,58,59,69,70,97,100,153].

Thus, evidence suggests that cocaine-exposed children may be more easily aroused and hence vulnerable to difficulties in information processing and learning in novel conditions consistent with one model of the developmental impact of prenatal cocaine exposure. At the same time, a number of labs are also reporting neurocognitive deficits under even optimal testing conditions using narrow band assessments to test specific functions such as task switching and inhibition. Collected findings include slower reaction times to visual stimulus presentation [61], slowed reaction times in continuous performance tasks [41], greater perseveration, diminished response inhibition [13,116,117], increased errors of commission or omission on A-not-B or continuous performance tasks [41,44,97,116,117,127], diminished capacity for sustained attention [9,131], and deficits in spatial learning [134]. Several studies have also documented dose–response effects on attention control and a range of executive control functions [5,31,69,70,154] as well as an interactive effect with the level of environmental risk [13].

The range of executive control function effects that seem related to prenatal cocaine exposure may be consistent with preclinical work suggesting a cocaine-related effect on the development of the anterior cingulated cortex [149] and on dopaminergic D1/D2 mediated circuitry critical to regulation of prefrontal cortex [135] and to upregulation of noradrenergic (and serotonergic) systems at a time in early development that could permanently distort the excitatory/inhibitory balance between regulatory systems necessary for optimal cortical function. Preweaning cocaine exposure is associated with a functional decoupling of the D1 receptor from G protein in the striatal DA (D1) system and specifically in the cingulate cortex [54,161], an effect that dampens D1 mediated responses within striatal neurons. Behavioral responses to agonists selective for the D1 receptor are reduced following both prenatal and postnatal exposure [51]. Similarly, differential reduction in cingulate activity in cocaine-exposed animals is associated with an impaired ability to discriminate among salient and/or relevant stimuli [46,129], a finding consistent with emerging data cited above in human studies. Prenatal cocaine exposure is also reported to affect the earliest phases of brain cell proliferation and neuronal migration with attendant disruptions in cortical lamination [60,81,83–85]. Disruptions in cortical architecture might interfere with regional specialization and performance on certain cortically related tasks might be slowed [83].

Behaviorally, findings in preclinical models appear consistent with these neurochemical and structural alterations. Prenatally and/or preweaning exposed animals inhibit approaching novel conditions and open-field exploration [71]. Deficits in learning are suggested by impairments in classical conditioning [21,22,64,148], deficiencies in active and passive avoidance tasks [64], poor short-term memory [113], increased response perseveration [142], diminished proximal cue learning [160], impaired learning on serial reversal tasks [48], impaired habituation [66], impaired reversal learning [26], increased susceptibility to distractors in a visual attention task [50], and less efficient error detection [112]. Prenatally exposed animals appear unable to attend preferentially to less salient but relevant stimuli in the context of more salient but distracting and non-relevant background stimuli [47,129] and have difficulty changing previously learned conditions [65,77].

Taken together, the emerging data suggests that children prenatally exposed to cocaine may experience a range of neurocognitive dysfunctions through a direct effect on neural structure–function relationships. On the other hand, given a range of methodological concerns about the cocaine-exposure literature as a whole [17,18,27,45,80,89,96,115,119,139], questions have been raised about attributing any one disruption in developmental capacities to the prenatal effects of cocaine on emerging neural systems. Prenatal exposure to cocaine is often paired with a simultaneous exposure to other drugs and to severe postnatal environmental deprivation [45,63,79,88,156,159]. Only a few studies have addressed apparent cocaine-related effects on children's development and behavior that are moderated or mediated [10] via pathways of maternal health or quality of caregiving [16,139] or have taken into consideration parental attentional or learning difficulties that may serve as markers of possible genetic contributions to infant functioning [93]. Nonetheless, bearing these cautions in mind, based on these findings in human studies coupled with possible converging data from preclinical models—specifically those findings suggesting slowed reaction times and difficulty inhibiting salient responses even under baseline conditions, the overall goal of the present study is to investigate potential differences in brain organization as a function of early exposure to cocaine via event-related potential (ERP) techniques in a group of 8-year-old children.

Event-related potentials (ERPs) are used as the measure of brain activity during an executive function task, the Stroop Task. The Stroop Color Naming Test [55,152,166] has been useful in examining the relationship between cognitive and brain measures. There is substantial literature on the use of this task to investigate frontal lobe functions in adults and children using both ERP and fMRI [1,7,39,86,91,99,163,168]. Testing generally involves participants attending to a sequence of 3 conditions: (1) a color naming condition where they name a series of color patches, (2) a reading condition where they read a series of color names printed in black ink, and (3) a condition in which they name the color of ink used to spell out different color names. Strong interference from the printed word leads participants to make errors by reading the name instead of identifying the color of the ink. To perform this task flawlessly,

participants must inhibit their inclination to read the color names. An extensive body of literature indicates that this task engages frontal lobe functions [1,7,35,86,91,99,163,168] and pathways relevant to inhibitory control mechanisms [40]. In contrast to the P300 task that requires individuals to attend to infrequent stimuli, the Stroop task places increased demands on participants, requiring them to inhibit attention to intrusive responses, behaviors that engage fronto-striatal circuitry [23,40].

Thus, the hypotheses addressed in the present study included an expectation (1) that the cocaine-exposed (CE) children would exhibit slower ERP responses to stimulus and task demands than that found for non-drug-exposed (NDE) children; and (2) that inhibition-related differences between CE and NDE children would be detected at electrodes over frontal scalp regions.

1. Method

1.1. Participants

Twenty-nine children consisting of 10 females and 19 males were tested. All children were English speaking with no evidence of serious psychiatric disorders (e.g., psychosis). The mean age of the 15 Cocaine-Exposed children was 8.06 years (s.d. = 1.14 years) and the mean age of the 14 Control children was 8.62 years (s.d. = 0.92). There were no differences in age or gender distribution between the two exposure groups. Prenatal cocaine-exposure was determined by a combination of maternal report, urine toxicology in the prenatal or postpartum period, and meconium toxicology. Controls were matched to the CE group based on age, race, SES. Handedness measures were obtained from the children using the Edinburgh Handedness Inventory [118]. Mean handedness laterality quotient for the CE group was 0.42 (s.d. = 0.53), and for Control children it was 0.50 (s.d. = 0.63). There was no significant difference in handedness scores between the two groups $t(24) = -.362$, $p < .721$. (The independent samples t-test for hand preferences was conducted on 26 of 29 due to problems in scheduling the handedness test for three children.) Also, all children had had a standard IQ assessment at age 6 years using the Kaufman Assessment Battery for Children (KABC [75]). There were no significant differences in the mental processing composite between the CE and NDE groups (mean 93.5 (12.3 s.d.) vs. 100.1 (10.2 s.d. respectively) ($F(1,28)$ 2.0; n.s.).

1.2. Sample

The 29 children participating in this study were drawn from a larger sample of 369 children who have been participating in an 11-year longitudinal study of the effects of fetal cocaine exposure on physical, cognitive, social and emotional development of children. Children (and their mothers) who were exposed to drugs other than cocaine (primarily alcohol and marijuana) were also enrolled in the study, as were non-drug using control subjects. The sample was recruited at birth over a 5-year period and children and their parents are seen biannually. Families were originally recruited when they presented for prenatal care at the Women's Center of Yale-New Haven Hospital or, in the case of no prenatal care, when they were admitted to the postpartum ward. The larger sample from which the 29 children for this study were recruited consisted of 81% African American, 6.5% Hispanic and 12.5% Caucasian children, all of who come from the greater New Haven area. The 29 children for this study were recruited from this larger study by asking families of 8-year-olds scheduled for their regular visits over two 1-month periods if they and their child would participate in an additional study. These 29 children include 70% African American, 4% Hispanic, and 26% Caucasian.

Prenatal drug-exposure status was ascertained at the time of recruitment into the longitudinal follow-up study (either prenatally or at the time of delivery). After obtaining verbal consent for an interview, all women were questioned about substance use in a detailed interview that covered lifetime use of cocaine, tobacco, alcohol, marijuana, and other drugs (e.g., sedatives, opiates), and frequency and amount of use of these agents during the preceding 30 days. For all women regardless of drug use history, a urine sample was obtained for toxicology. Standard urine screening for drug level or metabolites of cocaine (e.g., benzoylecognine), opioids, benzodiazepines, and tetrahydrocannabinol (THC) was performed using the Abbott TDx system and the recommended cutoff levels [122]. Urine was rated as positive if the quantity of drug or metabolite was >300 g/ml. The TDx system is highly sensitive and specific for the detection of illicit drug use, and benzoylecognine is detectable for 3 days after use. Prenatal cocaine-exposure status was determined by a combination of maternal report and urine toxicology from the prenatal or immediate postpartum period as well as infant urine and meconium toxicology. Infants were considered cocaine-exposed prenatally if maternal self-reports were positive, even if toxicological results were negative. Conversely, if mothers reported that they did not use cocaine, but clinic or hospital urine toxicological results were positive, infants were also considered exposed. Every mother with a positive history and/or positive urine toxicology for cocaine-use was invited to join the study. Non-cocaine-exposed status was ascertained by negative urine or meconium toxicology and a negative maternal history of cocaine during pregnancy and at the time of delivery.

The fifteen mothers for the present study sample who were identified as cocaine-users had used cocaine since the beginning of their pregnancy and did not stop their use before delivery. None had used cocaine before but not during their pregnancy. No mother in the sample had used opiates. Thus, the terms cocaine-using and non-drug-using refer to the presence of cocaine/crack, and not the use of

alcohol, marijuana, or tobacco up to the time of delivery. The fifteen cocaine-using women had a mean lifetime years of cocaine use of 6.5 years (2.8 s.d.) with a range of 2 to 10 years. On average, they reported using cocaine 6 days out of the thirty prior to the prenatal interview (s.d.=4.4; range 1 to 12). All of the cocaine using women also used tobacco with an average amount of use of 1.1 packs per day (.62 s.d.) in the 30 days prior to the prenatal interview. Similarly, all of the cocaine using women also reported alcohol use on at least 1.7 days (1.3 s.d.) in the 30 days prior to the interview. Eighty percent of the cocaine-using group also reported occasional marijuana use. In contrast, among the fourteen non-drug-using mothers, none reported tobacco use, 46% reported occasional alcohol use, and only one reported any marijuana use. Thus, the comparison group is relatively drug-free except for some alcohol use and any conclusions specific to cocaine-exposure based on this comparison are necessarily limited by the polydrug use of the cocaine-using mothers.

1.3. Stimuli

Based on a standard Stroop paradigm [152] and subsequent modifications [166], three different sets of stimuli were presented. Set 1 consisted of three words representing color names (red, green, blue) printed in lower-case letters in black font. Set 2 included three color-filled rectangles (red, green, blue) matched in height and length to the size of the word stimuli in Sets 1 and 3, and Set 3 included the same three color names printed in lower-case letters in incongruent color (e.g., the word 'red' printed in blue). All stimuli were presented on a white background.

1.4. Procedure

After permission was obtained from the parents, the children were seated 1 m in front of a 17 in. Sony computer monitor where their head was measured to determine the appropriate net size and the reference points (Cz) to guide the correct alignment of the electrode net placement. Next, a high-density array of 128 Ag/AgCl electrodes arranged into a net (Geodesic Sensor Net, EGI Inc.) was placed on the child's head using standard procedures. Prior to placement, the net was soaked in warm potassium chloride solution (KCl) that served as the electrolyte. The KCl solution enabled the detection of brain waves across the scalp even through hair and without the need for abrading the participant's scalp. The filters were set at .1–30 Hz. Brain wave data recording was controlled by the Net Station v.1.0 and 2.0 software package (EGI, Inc.). During recording, all electrodes were referenced to Cz and then later re-referenced for data analysis. All impedances remained at or under 40 kΩ as indicated by impedance measures made immediately before and after the test session. EGIS v.2.2 (EGI, Inc) and E-prime v.1.0 (PST, Inc) software packages controlled stimulus presentation. Each trial began with a fixation point presented for 500 ms, followed by the stimulus (word, color bar, or color word) that remained on the screen for 2000 ms before being replaced by a question mark indicating the time to respond. The question mark was visible until the response (maximum wait time=3000 ms). Although this design resulted in an artificially delayed response and made any analyses of the reaction time or accuracy meaningless, it was necessary to prevent contamination of the ERPs by movement artifacts due to speaking.

During the entire test session, the child's electroencephalogram (EEG) and behavior were continuously monitored so that the stimulus presentation occurred only when the child was sitting still and looking at the monitor. Within a stimulus set, visual ERPs were collected to 42 presentations separated by an intertrial interval that varied randomly between 1400 and 2400 ms to prevent creation of expectation for stimulus onset.

1.5. ERP data analysis

Each ERP epoch included a 100-ms pre-stimulus baseline and 500-ms poststimulus interval. Following artifact rejection, the single trial data were then re-referenced from the vertex (Cz) to the average of all electrodes because the latter was a better representation of a true zero [73] and then averaged separately for each of the 128 electrode sites and each of the three stimulus conditions. In this manner, 384 averages were obtained for each child resulting in a total of 11,136 averaged ERPs from the 29 children. Then, data from the 128 electrodes were clustered into ten regions by averaging the data for electrodes within five anatomical regions in each hemisphere—frontal, central, parietal, occipital, and temporal (see Fig. 1). This approach reflected anatomically based boundaries and represented a modification of the clusters initially proposed by Curran [34] that did not reflect the anatomical boundaries. The purpose of the clustering procedure was to reduce the number of variables to increase statistical power instead of recruiting an unreasonably large number of participants (e.g., $N \approx 1500$).

The clustered ERP data were next submitted to a two-step analysis procedure which first involved the use of a temporal principal components analysis (PCA) followed by an overall MANOVA and then a set of univariate analyses of variance (ANOVAs) conducted separately on the component scores calculated for each principal component. All analyses were performed using the SPSS v.10 software package.

Although there are a variety of different analysis procedures which could be used to analyze ERP data (see for example, Coles and colleagues, pp. 196–198 [32]), a decision was made to utilize a multivariate approach that has produced consistent results in programmatic research across a number of laboratories [20,24,38,49,102,104,

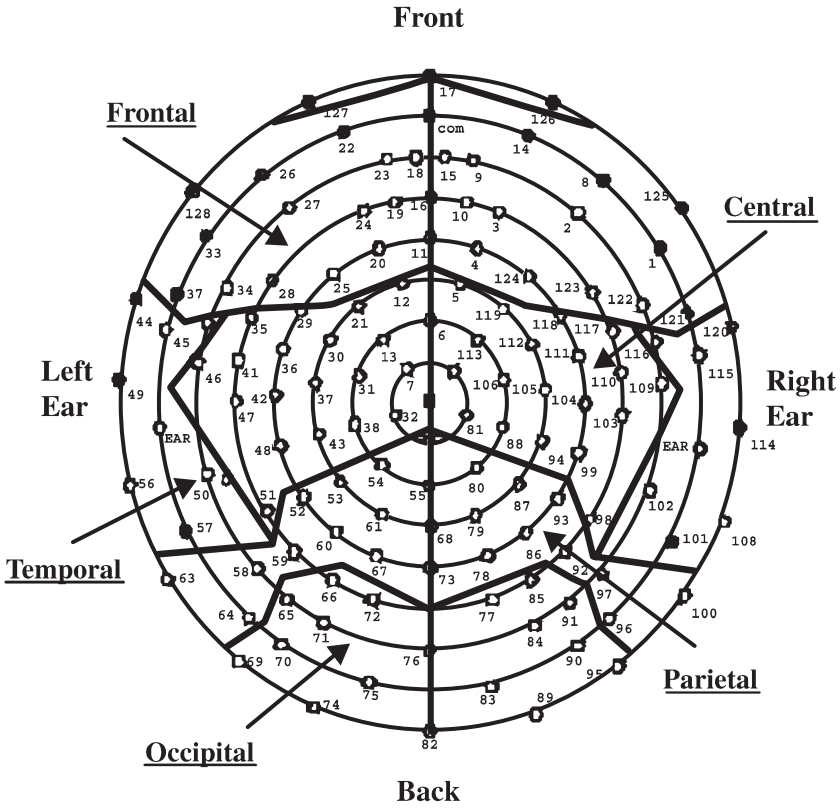


Fig. 1. For analyses, the 128 electrode channels were clustered into 5 regions for each hemisphere, corresponding to neuroanatomical boundaries related to frontal, temporal, central, parietal, and occipital brain regions.

107–109,130,136]. For example, Molfese, in a series of articles investigating speech perception cues such as voice onset time and place of articulation, noted consistent systematic effects across studies for each cue [102–105,110]. Moreover these effects have been independently replicated using comparable analysis procedures [49,136].

The rationale for the use of the temporal PCA procedure is that it has proven successful in identifying regions of the ERP where most of the variability occurred across subjects and conditions. In this way it offers a more parsimonious description of the data, by reducing the original set of measures (ERP time points) to a limited set of more "meaningful" and informative principal components. The PCA procedure itself is blind to experimental conditions and generates the same solutions regardless of the order in which the ERPs are entered. The option of a correlation matrix was selected for the PCA routine. With this method centroid amplitude values for each time-point were first subtracted from the corresponding values of each average ERP. These deviation scores were then normalized by being divided by their respective standard deviation. Thus, variability due to differences among the time-points with respect to the grand-mean, as well as standard deviation, were first extracted before the application of the PCA [37]. While questions have been raised in the literature regarding misallocation of variance in a PCA analysis across immediately adjacent peaks [165], even Wood and McCarthy noted that traditional amplitude and latency approaches are "no less subject to the problem of component overlap" (p. 258 [165]; see also Beauducel and Debner [12] and Chapman and colleagues [25]). Furthermore, when sufficient power is available the likelihood of misallocation is marginalized. "... the results of Wood and McCarthy [165] were due to an excessive and unrealistic statistical power. Moreover, baseline-to-peak measures are not superior to PCA with respect to variance misallocation and thus, this comparison supports the use of the PCA-Varimax strategy for ERP component analysis" (p. 112 [12]). Given our power estimates, we consider the PCA approach reasonable for the present investigation.

Once the PCA identified were within the ERP most of the variability occurred, the MANOVA was used to identify the overall sources of this variability. The MANOVA accomplished this task by determining whether the variability reflected in the component scores assigned for across factors for each component differed as a function of changes in manipulated variables. Subsequently, separate ANOVAs determined whether the variability reflected in the component scores assigned for each component to each averaged ERP differed as a function of changes in the stimulus condition. This procedure directly addressed the question of whether the ERP wave shapes in the region characterized by the most variability for any one component changed systematically in response to the three stimulus conditions

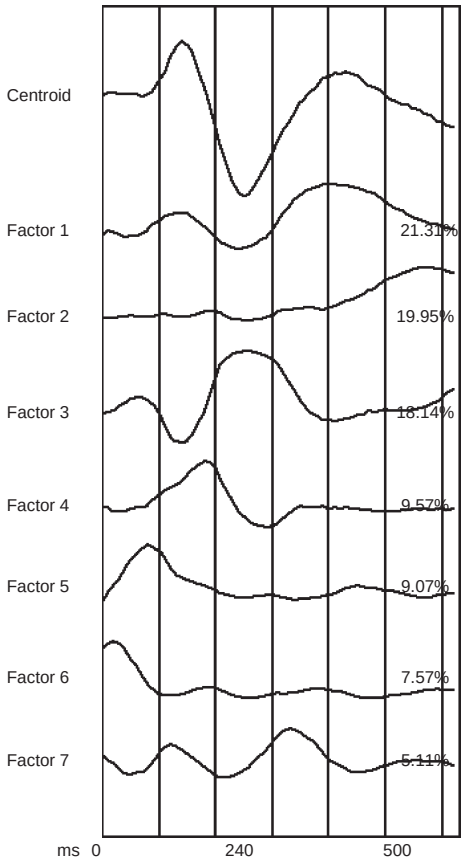


Fig. 2. The group grand averaged ERP waveform from the 29 children that comprised the CE and Control groups. The ERPs were recorded from 128 scalp electrodes positioned over the left and right hemispheres during the Stroop tasks. The seven factors identified by the PCA are displayed below the centroid. ERP duration is 500 ms. Stimulus onset began at 0 ms. Positivity is up. The calibration marker is 10 μV. The percentage of total variance accounted for by each factor is displayed to the right of that factor.

across the different electrode sites over each hemisphere from the two groups of children. The final analysis design included Stimulus Conditions (3: black word, color bar, word in color) × Electrode Regions (5: frontal, central, parietal, occipital, and temporal) × Hemispheres (2: left, right) × Drug group (2: CE, NDE) variables.

2. Results

The PCA resulted in 7 factors accounting for 90.72% of the total variance. The centroid or grand-average waveform of the 11,136 ERPs collected in the present study was characterized by an initial positive-going peak that reached maximum amplitude at 115 ms following stimulus onset. This was followed by a negative deflection peaking at 200 ms and a large positive peak at 350 ms. The last portion of the ERP resolved into a region of broad negativity that reached maximum amplitude at the end of the sampling period. The centroid and the 7 factors derived by the PCA are presented in Fig. 2.

Behaviorally, children in the CE and NDE groups performed similarly on the Black Word and Color Bar conditions. However, there were significant differences in the performance of the two groups on the Color Word condition. CE children had an average of 87.5% correct responses while NDE children had 96.5% ($t(26) = -2.68$, $p = .013$. There were no significant differences in the number of incorrect responses, that is, reading the word rather than naming the color. CE and NDE children produced 3% and 2% errors respectively. However, the CE children had 9% 'no response' trials, suggesting that the CE group required longer to respond in the Color Word condition and in a significantly greater number of trials, were unable to respond before the beginning of the next trial. Based on these behavioral differences, we examined the ERP data for functional differences between the two groups. Analyses focused on whether ERPs to Black Word, Color Bar, and Color Word conditions resulted in differences in ERP component amplitude, latency, and scalp topography and whether these differences changed as a

Table 1
Post hoc comparisons of the Group Condition × Electrode × Hemisphere interaction for frontal, parietal, and occipital electrode regions for the CE and NDE groups for the three tasks

	Effects by Electrode Region			
	CE group		NDE group	
	Left	Right	Left	Right
Frontal	W<Co $t(14) = -2.568$, $p = .022$		W>Co $t(13) = 2.805$, $p = .015$; Co<CW $t(13) = -2.716$, $p = .018$	
Parietal	Co<CW $t(14) = -2.925$, $p = .011$	W>Co $t(14) = 2.832$, $p = .013$; Co<CW $t(14) = -2.978$, $p = .010$		
Occipital		W>Co $t(14) = 3.596$, $p = .003$; Co<CW $t(14) = -2.693$, $p = .018$		W>CW $t(13) = 2.368$, $p = .034$

Condition × Electrode × Hemisphere × Group.
W—Black Word, Co—Color Bar, CW—Color Word.

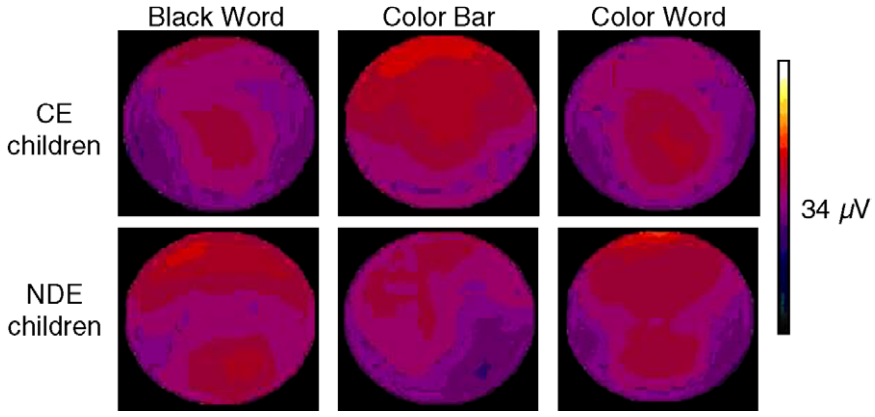
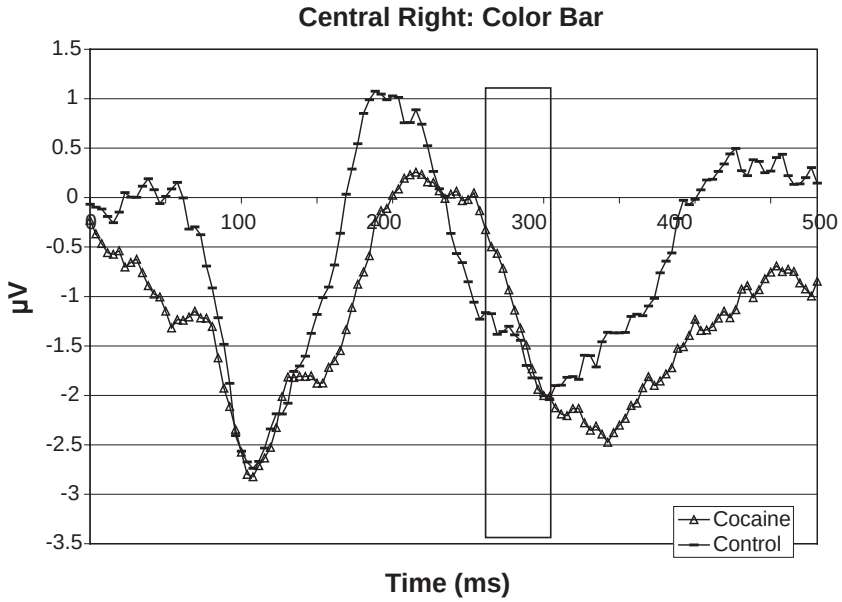


Fig. 3. Scalp topographies reflecting the Group × Condition × Electrode interaction captured by Factor 7 that characterized the ERP region between 256 and 304 ms (maximum—272 ms) following stimulus onset.



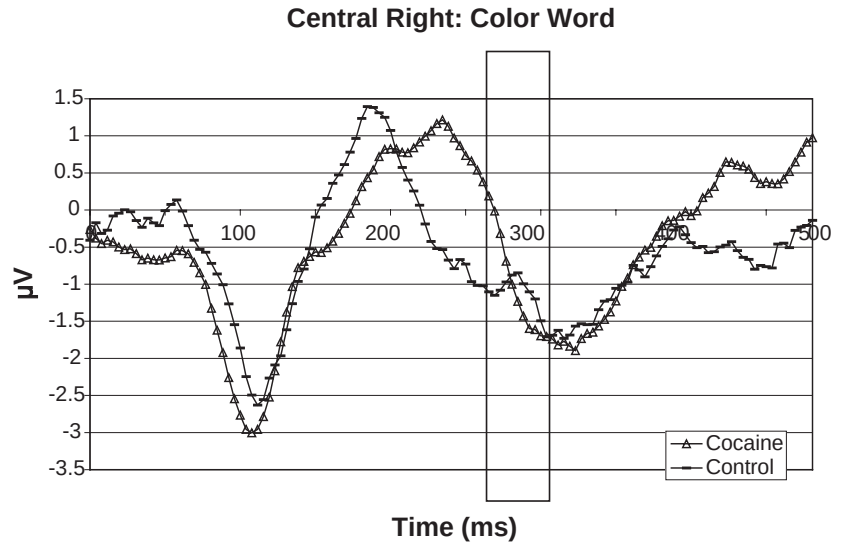


Fig. 4. Averaged ERPs recorded from central scalp regions that were elicited in response to the Color Word and the Color Bar conditions as part of the Group × Condition × Electrode × Hemisphere interaction that characterized the variance described by Factor 1 between 264 and 432 ms (maximum peak = 328).

function of the experimental group to which the child belonged. Based on the hypotheses, it was expected that CE children would produce different ERP responses during the Color Word condition than the Control children. We specifically focus on the Color Word condition inasmuch as this condition taps into inhibitory capacities.

Several group effects were present. An Electrode × Group interaction ($F(4,104)=5.23$; $p<.001$) was noted for the early portion of the ERP between 40 and 104 ms (maximum point of variability=72 ms; Factor 5) where CE group was characterized by larger P1 amplitudes over occipital areas ($F(1,27)=8.028$, $p=.009$) and smaller amplitudes over frontal and central regions ($F(1,27)=4.308$, $p=.048$; $F(1,27)=8.509$, $p=.007$, respectively). Further, a more variable ERP topography was noted for the CE group but not for the NDE group. More specifically, smaller ERPs were recorded from the CE group over the central scalp region than over parietal areas ($t(14)=-2.705$, $p<.017$), while ERPs over occipital regions were larger than those over parietal sites ($t(14)=-3.035$, $p<.009$), and smaller than ERPs over temporal sites ($t(14)=2.177$, $p<.047$).

A Condition × Electrode × Hemisphere × Group($F(8208)=2.44$; $p<.015$) interaction characterized a region of the ERP between 256 and 304 ms (maximum variability reached at 272 ms; Factor 7), corresponding to the N2 component. In line with the hypotheses, post hoc analyses indicated that CE children engaged different brain areas as compared to the NDE children. The NDE group demonstrated the expected pattern of brain activity with the color words eliciting larger brainwaves relative to the color bars over left frontal areas ($t(13)=-2.716$, $p=.018$) and smaller amplitudes relative to the word condition over right occipital regions ($t(13)=2.368$, $p=.034$). Word stimuli elicited larger brainwaves compared to the color bars over left frontal areas ($t(13)=2.805$, $p=.015$).

In contrast, the CE group exhibited a very different pattern of responding. Post hoc data are presented in Table 1.

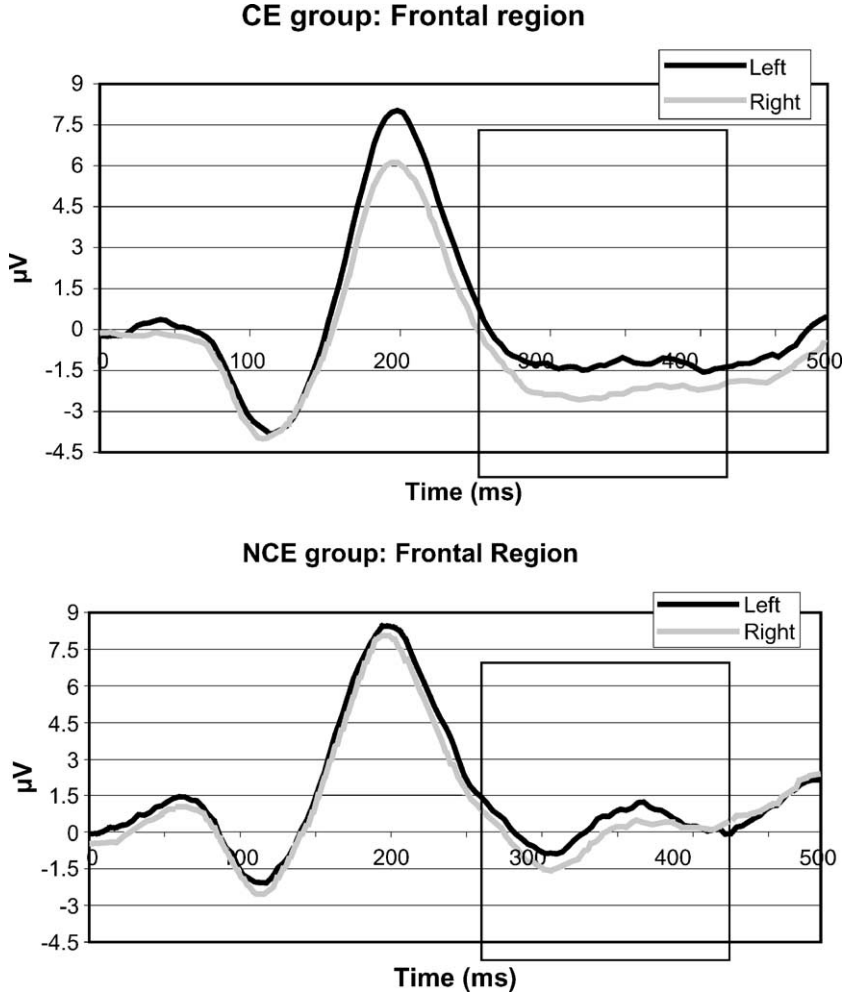


Fig. 5. Averaged ERPs recorded from over left and right hemisphere frontal electrode sites for the CE- and NDE-exposed children as part of the Group × Electrode × Hemisphere interaction. This effect is maximal between 264 and 432 ms (maximum peak=328).

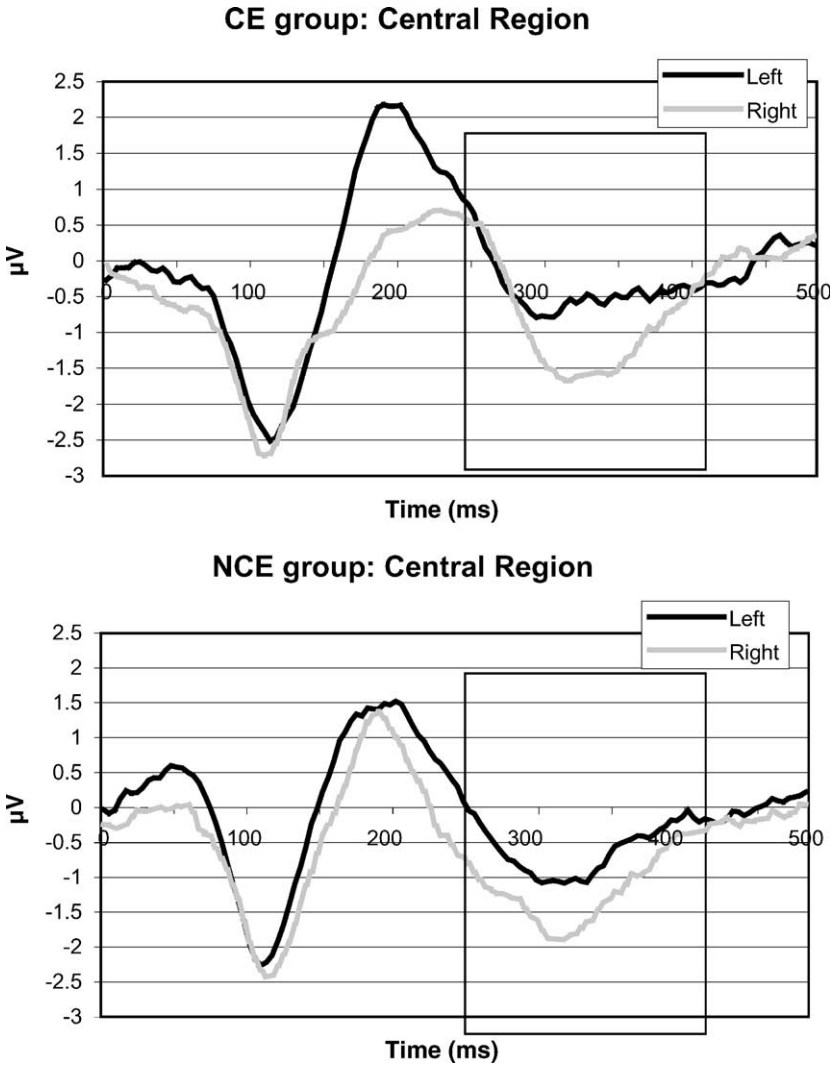


Fig. 6. Averaged ERPs recorded from over left and right hemisphere central electrode sites for the CE- and NDE-exposed children as part of the Group × Electrode × Hemisphere interaction. This effect is maximal between 264 and 432 ms (maximum peak = 328).

Compared to the NDE group, ERPs of the CE children demonstrated greater positivity over right central areas for color words ($F(1,27)=5.571$, $p=.026$) and color bars ($F(1,27)=4.938$, $p=.035$). Further, ERPs from the CE group were larger for color words vs. color bars over left and right parietal ($t(13)=-2.925$, $p=.011$ and $t(13)=-2.978$, $p=.01$, respectively) and right occipital ($t(13)=-2.693$, $p=.018$) locations. The color word condition was associated with smaller brainwaves relative to color bars over left frontal ($t(13)=-2.568$, $p=.022$) and larger over right parietal ($t(13)=2.832$, $p=.013$) areas. These differences in the ERPs between groups can be seen in Fig. 3.

An Electrode × Hemisphere × Group ($F(4,104)=3.07$; $p<.019$) characterized the variability between 264 and 432 ms (maximum variability at 328 ms; Factor 1). The data revealed greater variations between ERP regions in the CE children as compared to the NDE children (Fig. 4) suggesting that the CE children engaged a greater number of brain areas during task performance including more marked hemisphere differences as illustrated in Figs. 5 and 6 for frontal and central electrode sites (see also Table 2). In addition to more positive amplitudes over left vs. right

Table 2
Post hoc comparisons of the Group × Electrode × Hemisphere interaction for each of the electrode regions for the CE and NDE groups

	CE group	NDE group
Effects by Electrode Region		
Frontal	L>R $t(14)=2.382$, $p=.032$	L>R $t(13)=2.290$, $p=.039$
Central	L>R $t(14)=2.634$, $p=.020$	
Effects by Hemisphere		
Left	C<P $t(14)=-2.208$, $p=.044$	C<P $t(13)=-2.925$, $p=.039$
	O>T $t(14)=3.000$, $p=.001$	O>T $t(13)=2.437$, $p=.030$
Right	C<P $t(14)=-4.618$, $p=.001$	C<P $t(13)=-2.277$, $p=.040$
	O>T $t(14)=4.155$, $p=.001$	

Electrode × Hemisphere × Group.
L—left hemisphere, R—right hemisphere.
F—frontal, C—central, P—parietal, O—occipital, T—temporal.

frontal areas observed in both groups ($t(14)=2.382$, $p=.032$ and $t(13)=2.29$, $p=.039$, respectively; Fig. 5), CE children demonstrated similar differences over central areas ($t(14)=2.634$, $p=.02$,Fig. 6). Finally, only the CE group demonstrated electrode differences over right posterior sites (larger amplitudes over occipital relative to temporal sites, $t(14)=4.155$, $p=.001$).

3. Discussion

Overall, brain activity of NDE and CE children during the Stroop task was characterized by different levels and patterns of activation as well as speed of processing. As anticipated, the ERPs detected differences between the two groups that mapped onto differences in executive function processing as characterized by the Color Word condition of the Stroop task. For example, variations in the ERP waveforms between 256 and 304 ms indicated that the brain responses of the NDE group could distinguish between the inhibition condition and the control conditions while those recorded from the CE children did not.

In support of hypothesis 1, differences occurred in the ERP waveforms between the CE and NDE children at a number of latencies. The smaller ERP amplitudes noted over the early portion of the ERP as indexed by Factor 5 (40–104 ms) for only the CE group suggests that the initial encoding of visual stimuli may be altered by prenatal cocaine and other drug exposure. The P1 component typically occurs approximately 60 to 110 ms after the onset of a visual stimulus and is maximal over occipital areas [67]. Variations in P1 amplitude were previously linked to differences in attention across a number of tasks such Posner's attention cueing paradigm [67] and in spatial selective attention experiments [28]. Luck [87] proposed that P1 reflects suppression of noise because the amplitude decreased for unattended locations and did not increase for attended stimuli. The P1 amplitude also increased when speed of response was emphasized, suggesting that P1 may also reflect the level of arousal [158]. The larger occipital P1 response in the CE but not the NDE children could indicate that early exposure to cocaine negatively impacts initial attention mechanisms, an interpretation consistent with findings reported by other laboratories using behavioral and neuropsychological assessments [9,14,62,112,126,127,131].

The fact that only the NDE group ERPs distinguish between the inhibition condition and the control conditions at left frontal electrode sites supports hypothesis 2. While there was a trend toward greater positivity over frontal areas for the NDE group ($p=.06$), the observed group differences over central areas are consistent with increased inhibition of the prepotent reading response. Compared to NDE children, the CE children showed more positivity over central regions (1-tail t $p=.03$). There were no group differences for word or Color Bar conditions suggesting that the inhibitory demands of the Color Word condition were associated with differences in ERP response between the two groups. Similar pattern of findings was observed by Overtoom et al. [120] who studied a group of 7–12-year-old children diagnosed with ADHD and age-matched controls performing a manual stop task that required occasional inhibition of a motor response. In that study, ERPs to inhibited trials were characterized by greater positivity over frontal electrodes in controls while the ADHD group had more positive amplitudes over central regions. Further support comes from the findings that the NDE group discriminated between words, color bars, and color words at frontal electrode sites while the CE group also showed discrimination by condition over posterior scalp regions, that is, the CE group used more diffuse brain regions for the different conditions. These differences in frontal activation between the NDE and CE group may also be consistent with the greater right frontal EEG asymmetry reported in 3- to 6-year-old cocaine-exposed children in response to an emotionally stimulating task [72].

Also, although there were no ERP differences within each group for the Black Word vs. Color Word conditions, if the processes underlying these two conditions were the same (i.e., just reading words) and given the overall within-subject stability of the ERPs, we might predict identical patterns of activity across various electrode sites in both the word and Color Word conditions. This was indeed true for the CE group: Words and color words had similar profiles across electrodes, a finding suggesting the same underlying reading process. In the NDE group the pattern across electrodes was different between the word and Color Word condition: While over the frontal regions the two conditions did elicit a similar response perhaps relating to overall attention to task, over posterior sites means for word and Color Word conditions were quite different: temporal (1-tail t $p=.06$), occipital (1-tail t $p=.04$) with color words looking more like color bars.

In general, slower responses (longer ERP latencies) and reduced amplitudes over anterior regions occurred in the CE children in the Color Word condition, consistent with hypothesis 1. However, larger amplitude ERPs did occur at some latencies for the CE children that were not expected. CE children generated slower but larger initial ERP responses (N1 component) and prolonged responses to the words (as indexed by the P1–P2 inter-peak latencies) while the NDE children produced briefer responses (shorter N1 latency, shorter P1–P2 inter-peak latency). As noted earlier, these effects also occurred across the initial positive peak (P1), the second negative peak (N2) and the later positive peak (P3). Overall initial sensory detection and activation appears more marked in CE children (as indexed by P1 and N2) although later occurring ERP components that are usually associated more with cognitive processing occurred faster with more pronounced amplitudes in NDE children. It is possible that the larger amplitude ERPs at some latencies for the NDE children could indicate that they were more

engaged in focused processing than CE children who spread processing across more cortical areas as reflected by increased ERP differences between electrode regions. Such findings suggest that CE children were both slower to process the task information and exhibited more diffuse and less intense cortical involvement than NDE children.

The level of activation and speed of processing appears more marked in NDE than in CE children. For the CE children, ERPs discriminated task-related effects that occurred over more posterior scalp regions than in the NDE children. Additionally, CE children were both slower to process this information and generated lower voltage levels during task processing than NDE children. Importantly, these differences are apparent without differences in standard measures of IQ or information processing between the CE and NDE groups.

Because of the polydrug exposure in the CE group and the minimal drug exposure in our NDE group (only to occasional alcohol), it is not possible to attribute fully any of the group differences to prenatal cocaine-exposure alone. These findings are best considered preliminary and need to be followed up with a larger sample in which comparison groups may have also used other drugs but not cocaine and with sufficient sample size to permit analyses for other drug effects. This is especially critical since reaction time and other executive control function deficits have been well-documented in studies of prenatal alcohol and nicotine exposure, [30,43,68,76,128,138,140,141,150,151,157,164] and these drugs impact similar neural systems [33,53,133,145,155]. Additionally, while a number of studies of prenatal cocaine exposure have reported slowed response time in infants, preschool, and school-aged children consistent with our longer ERP latencies [42,62,134], at least one group attending carefully to amount of exposure have reported faster responsiveness in more heavily exposed infants in a visual expectancy paradigm along with poorer recognition memory [70]. It may be that combinations of alcohol, nicotine, and cocaine exposure produce different profiles of effect at differing levels of exposure for each drug and the findings we and others report regarding slower response time may reflect the effects of alcohol or nicotine instead of cocaine while the specific effects of cocaine are evident only at higher levels of exposure. Larger sample sizes are required to be able, adequately, to investigate dose–response relationships for the ERP effects found in this initial sample.

Nonetheless, despite this critical caveat regarding the polydrug nature of the CE sample and especially similar behavioral profiles with alcohol and nicotine exposure, these findings are sufficiently provocative to warrant both further follow-up and speculation as to their implication. These findings together may indicate that CE children engage more brain regions and take more time to process the same information that is more quickly and efficiently handled by fewer brain regions in the NDE children. That the CE group seems to use more diffuse brain regions in response to the inhibitory condition may also be consistent with the behavioral data. The CE group was able to inhibit in the Color Word condition as suggested by no difference in errors, but this inhibition of the prepotent response appeared to require more effort and time than the NDE group as suggested by the greater number of trials in which the CE children were unable to respond in time. More effortful inhibition may be consistent with the observation that the CE children exhibited more diffuse and less intense cortical involvement than NDE children. Such findings may suggest that early exposure to cocaine does have marked long-term consequences for brain development and processing. More specifically, it may be that early exposure to cocaine may inhibit the specialization and streamlining of brain region involvement during cognitive processing such that task processing is slower to begin, engages more diverse cortical regions to accomplish and requires more time to complete.

Data are available to support the suggestion that prenatal cocaine-exposure is associated with neuromorphological and functional changes in cortex including cocaine-related effects on the earliest phases of brain cell proliferation and neuronal migration—and thus, on cortical morphology. In rats, prenatal CE interferes with radial gliogenesis and thus, disrupts neocortical architecture [3,56,57,167]. In rhesus monkeys, intermittent prenatal CE resulted in cerebral cortices with highly abnormal structural characteristics including disrupted cortical laminar architecture with an increased number of cells in the underlying white matter suggesting markedly impaired neuronal migration [81,84]. Findings such as these may reflect disrupted monoaminergic system regulated processes that control the genesis of radial glial cells necessary for proper neuronal migration to cortical layers [82,137]. Disruption of such processes may not be compensated for later in gestation inasmuch as neurogenesis appears complete by day 120 to 125 [123] and cortical neuronal migration by the end of the second trimester. Fewer studies are available specifically examining the effects of cocaine on later gestation events such as continuing gliogenesis, synaptogenesis and neuronal connectivity. At least one group has reported decreased striatal neurotrophic activity with cocaine that in turn limits the growth of DA neurons postnatally [162]. Prenatal CE also appears to affect 5-HT and NE connecting fiber density (both to increase and decrease) in different brain regions [2,143].

Disruptions in cortical architecture might interfere with regional specialization such that performance on certain cortically related tasks might be slowed. This suggestion is supported by findings from prenatallly cocaine-exposed monkeys followed through 6 years of age who were tested on their ability to learn a new set of responses following a change in the rules of reinforcement for a simple visual discrimination task [26,121]. The task required inhibition of a previously learned and rewarding response. The prenatally cocaine-exposed animals performed much more

poorly, that is, they took more sessions to attain or never attained pre-reversal type responding when compared to the drug-naive control animals. These findings may parallel the suggestion that the CE group took longer in the Color Word condition and overall used more regions of the cortex in responding.

Two other studies [11,92] with humans also suggest a link between cocaine exposure, brain maturation, and developmental outcomes. In follow-up testing of a longitudinal study conducted by Martin and colleagues [92], infants exposed to non-opiate drugs prenatally were later tested on a series of language, cognitive and executive function tasks as well as a visually presented odd-ball ERP task. There were significant correlations between novelty preferences at 8 months of age and cognitive performance at 5 to 7 years. The drug-exposed children differed in their performance on the McCarthy Scales of Children's Abilities as well as the Tower of Hanoi task, the latter task designed to measure executive functions thought to be mediated primarily frontal cortical regions. Attention as measured by the P300 task also showed marked differences between the two groups with longer P3 latencies and smaller amplitudes for the exposed children. A control visual ERP task (reversing checkerboards) failed to show such group differences, thereby suggesting that the group differences found for P3 were specific to the engagement of attention factors. Such findings both indicate an impact of early non-opiate drug exposure on later cognitive performance and suggest a predictive link between the two that can be measured using ERPs.

A second study [11] reinforces this link between maturational differences in brain development linked to drug exposure and the potential impact on attention and, additionally, behavior disorders. In a study with 94 adolescent males, marked differences were noted in auditory P300 responses obtained during an odd-ball task between boys who had a history of rules violations compared to boys without this history. Boys who historically violated rules did not display the normal maturational increase in P300 amplitude found in the control group. The investigators interpreted the additional topographic analyses of current source densities as indicating that the source of the maturational deficit in the target group involved P300 generators within the frontal region of the brain and speculated that this reflected a decrement in frontal brain maturation among males at risk for substance dependence or antisocial personality disorders.

In light of these findings from the present sample, it is important to conduct further ERP studies in cocaine-exposed children with a specific focus on cortically mediated function. Research over the past 70 years has demonstrated that ERPs can be used effectively to study both general and specific aspects of an individual's response to events in the external as well as internal environment [102,104]. ERP can also be used to study an individual's perceptions and decisions during tasks or following a learning situation [101,114,130]. The ERP technique has a number of advantages over other procedures: (1) Given that ERP techniques do not require a planned and overt response from individuals, it is particularly well-suited for the neuropsychological study of infant, toddler, and child attention and executive control functions [78,106]; (2) It can be used across the life span with virtually identical procedures; (3) It provides very fine temporal information (as short as 1 ms or less) regarding the brain's response to a stimulus, such as a speech sound; (4) The ERP has some gross level spatial resolution capabilities that permit a basis for speculations concerning the distribution of brain mechanisms that subserve functions such as inhibitory control or language.

The addition of ERP and EEG recording procedures to study protocols with prenatally cocaine-exposed children may provide data on the integrity of sensory pathways and brain structures [78], as well as serve as indicators of attentional changes and other aspects of information processing behavior [144]. Continued study of prenatally cocaine-exposed children over time with these more sophisticated techniques permits characterization of developmental trajectories and problems experienced by children with prenatally conveyed neuropsychological vulnerabilities who are also subjected to varying degrees of social–environmental discord. As has been observed in preclinical models, it may also be that some neurocognitive effects first appear (while others may attenuate) as children near or reach puberty [15,98,111,142,146,147].

4. Summary

Twenty-nine prenatally cocaine-exposed and non-cocaine-exposed 7- to 9-year-old children responded to a standard Stroop paradigm. Cocaine-exposed children generated slower and prolonged ERP responses while engaging more brain regions (suggesting more diffuse brain processing) to color names printed in different color ink while the non-exposed children produced briefer responses from a more discrete set of electrode sites. Effects occurred across the first 500 ms of the ERP waveform and included the region of the initial positive peak (P1), the second negative peak (N2) and the later positive peak (P3).

Acknowledgements

This work was supported by several agencies that included NIDA grants RO1-DA-06025 (LCM), RO1 DADA017863 (LCM) and KO2-DA00222 (LCM) and grants from NICHD P01-HD03008 and NICHD R01HD17860, as well as DOE R215K000023 and HHS 90XA0011. Additionally, the work was supported in part by the Yale Children's Clinical Research Center grant MO1-RR06022, General Clinical Research Centers Program, National Center for Research Resources, NIH. The authors gratefully acknowledge the

database management support of Ireneusz Sielski and our close collaboration with Dr. Richard Schottenfeld and his substance abuse treatment programs for pregnant cocaine-using women. Many of the women in our studies were active participants in his studies and much of our information regarding their perinatal drug use was obtained through our collaboration with Dr. Schottenfeld. The authors also gratefully acknowledge the assistance of Natalie Cunningham, Eva Ratajczak, and Jamie Wilson who assisted in the ERP data collection sessions, whose efforts were instrumental in helping the children feel comfortable in the sessions.

References

[1] N.E. Adleman, V. Menon, C.M. Blasey, C.D. White, I.S. Warsofsky, G.H. Glover, A.L. Reiss, A developmental fMRI study of the Stroop color–word task, Neuroimage 16 (1) (2002) 61–75.
[2] H.M. Akbari, H.K. Kramer, P.M. Whitaker-Azmitia, L.P. Spear, E.C. Azmitia, Prenatal cocaine exposure disrupts the development of the serotonergic system, Brain Research 572 (1–2) (1992) 57–63.
[3] H.M. Akbari, P.M. Whitaker-Azmitia, E.C. Azmitia, Prenatal cocaine decreases the trophic factor S-100 beta and induced microcephaly: reversal by postnatal 5-HT1A receptor agonist [published erratum appears in Neuroscience Letters 1994 Jul 4;175(1–2):176], Neuroscience Letters 170 (1) (1994) 141–144.
[4] S. Alessandri, M. Sullivan, S. Imaizumi, M. Lewis, Learning and emotional responsivity in cocaine-exposed infants, Developmental Psychology 29 (6) (1993) 989–997.
[5] S.M. Alessandri, M. Bendersky, M. Lewis, Cognitive functioning in 8- to 18-month old drug-exposed infants, Developmental Psychology 34 (1998) 565–573.
[6] R. Arendt, J. Angelopoulos, A. Salvator, L. Singer, Motor development of cocaine-exposed children at age two years, Pediatrics 103 (1999) 86–92.
[7] C.M. Atkinson, K.A. Drysdale, W.R. Fulham, Event-related potentials to Stroop and reverse Stroop stimuli, International Journal of Psychophysiology 47 (2003) 1–21.
[8] S.D. Azuma, I.J. Chasnoff, Outcome of children prenatally exposed to cocaine and other drugs: a path analysis of three-year data, Pediatrics 92 (3) (1993) 396–402.
[9] E.S. Bandstra, C.E. Morrow, J.C. Anthony, V.H. Accornero, P.A. Fried, Longitudinal investigation of task persistence and sustained attention in children with prenatal cocaine exposure, Neurotoxicology & Teratology 23 (2001) 545–559.
[10] R. Baron, D. Kenny, The moderator–mediator variable distinction in social psychological research: conceptual, strategic, and statistical considerations, Journal of Personality and Social Psychology 51 (1986) 1173–1182.
[11] L.O. Bauer, V.M. Hesselbrock, Brain maturation and subtypes of conduct disorder: interactive effects on P300 amplitude and topography in male adolescents, Journal of the American Academy of Child & Adolescent Psychiatry 42 (1) (2003) 106–115.
[12] A. Beauducel, S. Debener, Misallocation of variance in event-related potentials: simulation studies on the effects of test power, topography, and baseline-to-peak versus principal component quantifications, Journal of Neuroscience Methods 124 (2003) 103–112.
[13] M. Bendersky, G. Gambini, A. Lastella, D.S. Bennett, M. Lewis, Inhibitory motor control at five years as a function of prenatal cocaine exposure, Journal of Developmental & Behavioral Pediatrics 24 (5) (2003) 345–351.
[14] M. Bendersky, M. Lewis, Prenatal cocaine exposure and impulse control at two years, Annals of the New York Academy of Science 846 (1998) 365–367.
[15] P.J. Bilitzke, M.W. Church, Prenatal cocaine and alcohol exposures affect rat behavior in a stress test (the Porsolt swim test), Neurotoxicology & Teratology 14 (5) (1992) 359–364.
[16] M. Black, M. Schuler, P. Nair, Prenatal drug exposure: neurodevelopmental outcome and parenting environment, Journal of Pediatric Psychology 18 (1993) 605–620.
[17] L.M. Bland-Stewart, H.N. Seymour, M. Beeghley, D.A. Frank, Semantic development of African-American children prenatally exposed to cocaine, Seminars in Speech and Language 19 (1998) 167–187.
[18] J. Brooks-Gunn, C. McCarton, T. Hawley, Effects of in utero drug exposure on children's development. Review and recommendations, Archives of Pediatrics & Adolescent Medicine 148 (1) (1994) 33–39.
[19] J.V. Brown, R. Bakeman, C.D. Coles, W.R. Sexson, A.S. Demi, Maternal drug use during pregnancy: are preterms and full-terms affected differently? Developmental Psychology 34 (1998) 540–554.
[20] W.S. Brown, J.T. Marsh, J.C. Smith, Principal component analysis of ERP differences related to the meaning of an ambiguous word, Journal of Electroencephalography and Clinical Neurophysiology 46 (1979) 706–714.
[21] D.H. Brunzell, J.J.B. Ayres, J.S. Meyer, Effects of prenatal cocaine exposure on latent inhibition in 1-year-old female rats, Pharmacology, Biochemistry & Behavior 72 (4) (2002) 795–802.
[22] D.H. Brunzell, A.E. Coy, J.J.B. Ayres, J.S. Meyer, Prenatal cocaine effects on fear conditioning: exaggeration of sex-dependent context extinction, Neurotoxicology & Teratology 24 (2) (2002) 161–172.
[23] B.J. Casey, M.C. Davidson, Y. Hara, K.M. Thomas, A. Martinez, A. Galvan, J.M. Halperin, C.E. Rodríguez-Aranda, N. Tottenham, Role of caudate in attention switching early development of subcortical regions involved in non-cued attention switching, Developmental Science 7 (5) (2004) 534–542.
[24] R. Chapman, J. McCrary, J. Chapman, H. Bragdon, Brain responses related to semantic meaning, Brain & Language 5 (1978) 195–205.
[25] R.M. Chapman, J.W. McCrary, EP component identification and measurement by principal component analysis, Brain and Cognition 27 (1995) 288–310.
[26] J.J. Chelonis, M.P. Gillam, M.G. Paule, The effects of prenatal cocaine exposure on reversal learning using a simple visual discrimination task in rhesus monkeys, Neurotoxicology & Teratology 25 (4) (2003) 437–446.
[27] C.A. Chiriboga, Neurological correlates of fetal cocaine, Annals of the New York Academy of Sciences 846 (1998) 109–125.
[28] V. Clark, S. Hillyard, Spatial selective attention affects early extrastriate components of the visual evoked potential, Journal of Cognitive Neuroscience 8 (1996) 387–402.
[29] C.D. Coles, K.A. Bard, K.A. Platzman, M.E. Lynch, Attentional responses at eight weeks in prenatally drug-exposed and preterm infants, Neurotoxicology & Teratology 21 (1999) 527–537.
[30] C.D. Coles, K.A. Platzman, M.E. Lynch, D. Freides, Auditory and visual sustained attention in adolescents prenatally exposed to alcohol, Alcoholism: Clinical & Experimental Research 26 (2) (2002) 263–271.
[31] C.D. Coles, K.A. Platzman, I. Smith, M.E. James, A. Falek, Effects of cocaine and alcohol use in pregnancy on neonatal growth and neurobehavioral status, Neurotoxicology & Teratology 14 (1) (1992) 23–33.
[32] M.G.H. Coles, G. Gratton, A. Kramer, G.A. Miller, Principles of Signal Acquisition, in: M.G.H. Coles, E. Donchin, S.W. Porges (Eds.), Psychophysiology: Systems, Processes and Applications—A Handbook, New York, Guildford, 1986, pp. 183–221.
[33] K. Cronise, M.D. Marino, T.D. Tran, S.J. Kelly, Critical periods for the effects of alcohol exposure on learning in rats, Behavioral Neuroscience 115 (1) (2001) 138–145.

[34] T. Curran, The electrophysiology of incidental and intentional retrieval: ERP old/new effect in lexical decision and recognition memory, Neuropsychologia 37 (1999) 771–785.
[35] A. Diamond, Normal Development of Prefrontal Cortex from Birth to Young Adulthood: Cognitive Functions, Anatomy, and Biochemistry, in: D.T. Stuss, R.T. Knight (Eds.), Principles of Frontal Lobe Function, Oxford University Press, London, 2002, pp. 466–503.
[36] J.A. DiPietro, P.E. Suess, J.S. Wheeler, P.H. Smouse, D.B. Newlin, Reactivity and regulation in cocaine-exposed neonates, Infant Behavior and Development 18 (1995) 407–414.
[37] E. Donchin, E.F. Heffley, Multivariate Analysis of Event-Related Potential Data: A Tutorial Review, in: D. Otto (Ed.), Multidisciplinary Perspectives in Event-Related Brain Potentials Research, Environmental Protection Agency, Washington, DC, 1978, pp. 555–572.
[38] E. Donchin, P. Tueting, W. Ritter, M. Kutas, E. Heffley, On the independence of the CNV and the P300 components of the human averaged evoked potential, Electroencephalography & Clinical Neurophysiology 38 (1975) 449–461.
[39] C. Duncan-Johnson, B. Kopell, The Stroop effect: brain potentials localize the source of interference, Science 214 (1981) 938–940.
[40] S. Durston, K.M. Thomas, Y. Yang, A.M. Ulug, R.D. Zimmerman, B.J. Casey, A neural basis for the development of inhibitory control, Developmental Science 5 (4) (2002) 9–16.
[41] B. Eghbalieh, F.M. Crinella, L.E. Hunt, J.M. Swanson, Prenatal stimulant exposure affects alerting and executive control in six- and seven-year-olds, Journal of Attention Disorders 4 (2000) 5–13.
[42] B. Eghbalieh, L.E.H. Crinella, J.M. Swanson, Prenatal stimulant exposure affects alerting and executive control in six- and seven-year-olds, Journal of Attention Disorders 4 (2000) 5–13.
[43] M. Ernst, E.T. Moolchan, M.L. Robinson, Behavioral and neural consequences of prenatal exposure to nicotine, Journal of the American Academy of Child & Adolescent Psychiatry 40 (6) (2001) 630–641.
[44] K.A. Espy, P.M. Kaufmann, M.L. Glisky, Neuropsychologic function in toddler exposed to cocaine in utero: a preliminary study, Developmental Neuropsychology 15 (1999) 447–460.
[45] D.A. Frank, M. Augustyn, W.G. Knight, T. Pell, B. Zuckerman, Growth, development, and behavior in early childhood following prenatal cocaine exposure: a systematic review, Journal of the American Medical Association 285 (2001) 1613–1625.
[46] M. Gabriel, C. Taylor, Prenatal exposure to cocaine impairs neuronal coding of attention and discrimination learning, Annals of the New York Academy of Sciences 846 (1998) 194–212.
[47] M. Gabriel, C. Taylor, L. Burhans, In utero cocaine, discriminative avoidance learning with low-salient stimuli and learning-related neuronal activity in rabbits (*Oryctolagus cuniculus*), Behavioral Neuroscience 117 (5) (2003) 912–926.
[48] H. Garavan, R.E. Morgan, C.F. Mactutus, D.A. Levitsky, R.M. Booze, Prenatal cocaine exposure impairs selective attention: evidence from serial reversal and extradimensional shift tasks, Behavioral Neuroscience 114 (2000) 725–738.
[49] M. Gelfer, An AER study of stop-consonant discrimination, Perception & Psychophysics 42 (1987) 318–327.
[50] M.H. Gendle, T.L. White, M. Strawderman, C.F. Mactutus, R.M. Booze, D.A. Levitsky, B.J. Strupp, Enduring effects of prenatal cocaine exposure on selective attention and reactivity to errors: evidence from an animal model, Behavioral Neuroscience 118 (2004) 290–297.
[51] A.B. Gilde, D.L. Dow-Edwards, Prenatal Cocaine Exposure Affects Stereotypy Following Acute SKF-38393 Injection in Weanling Rats (abstract), American Psychological Association, 1994.
[52] J.L. Gingras, J. Feibel, B. Dalley, A. Muelenaer, Maternal polydrug use including cocaine and postnatal infant sleep architecture: preliminary observations and implications for respiratory control and behavior, Early Human Development 43 (1995) 197–204.
[53] T.A. Girard, H.C. Xing, G.R. Ward, P.E. Wainwright, Early postnatal ethanol exposure has long-term effects on the performance of male rats in a delayed matching-to-place task in the Morris water maze, Alcoholism: Clinical & Experimental Research 24 (3) (2000) 300–306.
[54] S.J. Glatt, C.A. Bolanos, G.H. Trksak, D. Jackson, Effects of prenatal cocaine exposure on dopamine system development: a meta analysis, Neurotoxicology & Teratology 22 (2000) 617–629.
[55] C. Golden, Stroop Color and Word Test, Stoelting Company, Chicago, 1978.
[56] P. Gressens, F. Gofflot, G. Van Maele-Fabry, J.P. Misson, J.F. Gadisseux, P. Evard, J.J. Picard, Early neurogenesis and teratogenesis in whole mouse embryo cultures. Histochemical, immunocytological, and ultrastructural study of the premigratory neuronal–glial units in mouse embryo influenced by cocaine and retinoic acid, Journal of Neuropathology and Experimental Neurology 51 (1992) 206–219.
[57] P. Gressens, B.E. Kosofsky, P. Evrard, Cocaine-induced disturbances of corticogenesis in the developing murine brain, Neuroscience Letters 140 (1) (1992) 113–116.
[58] D.R. Griffith, S.D. Azuma, I.J. Chasnoff, Three-year outcome of children exposed prenatally to drugs. Special section: cocaine babies, Journal of the American Academy of Child and Adolescent Psychiatry 33 (1) (1994) 20–27.
[59] R.L. Hansen, J.M. Struthers, S.M. Gospe Jr., Visual evoked potentials and visual processing in stimulant drug-exposed infants, Developmental Medicine and Child Neurology 35 (9) (1993) 798–805.
[60] N. He, J. Bai, M. Champoux, S.J. Suomi, M.S. Lidow, Neurobehavioral deficits in neonatal rhesus monkeys exposed to cocaine in utero, Neurotoxicology & Teratology 26 (1) (2004) 13–21.
[61] A. Heffelfinger, S. Craft, J. Shyken, Visual attention in children with prenatal cocaine exposure, Journal of the International Neuropsychological Society (1997) 237–245.
[62] A.K. Heffelfinger, S. Craft, D.A. White, J. Shyken, Visual attention in preschool children prenatally exposed to cocaine: implications for behavioral regulation, Journal of the International Neuropsychological Society 8 (1) (2002) 12–21.
[63] J.R. Held, M.L. Riggs, C. Dorman, The effect of prenatal cocaine exposure on neurobehavioral outcome: a meta-analysis, Neurotoxicology & Teratology 21 (1999) 619–625.
[64] C. Heyser, W. Chen, J. Miller, N. Spear, L. Spear, Prenatal cocaine exposure induces deficits in Pavlovian conditioning and sensory preconditioning among infant rat pups, Behavioral Neuroscience 104 (1990) 955–963.
[65] C. Heyser, N. Spear, L. Spear, The effects of prenatal exposure to cocaine on conditional discrimination learning in adult rats, Behavioral Neuroscience 106 (1992) 841–849.
[66] C.J. Heyser, D.L. McKinzie, F. Athalie, N.E. Spear, L.P. Spear, Effects of prenatal exposure to cocaine on heart rate and nonassociative learning and retention in infant rats, Teratology 49 (6) (1994) 470–478.
[67] K. Hugdahl, Psychophysiology: The Mind–Body Perspective, Harvard University Press, Cambridge, 1995.
[68] J.L. Jacobson, S.W. Jacobson, Effects of prenatal alcohol exposure on child development, Alcohol Research & Health 26 (4) (2002) 282–286.
[69] S.W. Jacobson, J.T. Bihun, L.M. Chiodo, Effects of prenatal alcohol and cocaine exposure on infant cortisol levels, Development and Psychopathology 11 (1999) 195–208.
[70] S.W. Jacobson, J.L. Jacobson, R.J. Sokol, S.S. Martier, L.M. Chiodo, New evidence for neurobehavioral effects of in utero cocaine exposure, Journal of Pediatrics 129 (4) (1996) 581–590.
[71] J.M. Johns, M.J. Means, D.R. Anderson, L.W. Means, B.A. McMillen, Prenatal exposure to cocaine. II: effects on open-field activity and cognitive behavior in Sprague–Dawley rats, Neurotoxicology & Teratology 14 (5) (1992) 343–349.
[72] N.A. Jones, T. Field, M. Davalos, S. Hart, Greater right frontal EEG asymmetry and nonemphatic behavior are observed in children

prenatally exposed to cocaine, International Journal of Neuroscience 114 (4) (2004) 459–480.
[73] M. Junghoefer, T. Elbert, D. Tucker, C. Braun, The polar effect of average reference: a bias in estimating the head surface integral in EEG recording, Electroencephalography and Clinical Neurophysiology 110 (1999) 1149–1155.
[74] B.Z. Karmel, J.M. Gardner, Prenatal cocaine exposure effects on arousal-modulated attention during the neonatal period, Developmental Psychobiology 29 (1996) 463–480.
[75] A. Kaufman, N. Kaufman, Kaufman Assessment Battery for Children: Administration and Scoring Manual, American Guidance Service, Circle Pines, MN, 1984.
[76] M. Korkman, S. Kettunen, I. Autti-Ramo, Neurocognitive impairment in early adolescence following prenatal alcohol exposure of varying duration, Child Neuropsychology 9 (2) (2003) 117–128.
[77] B.E. Kosofsky, A.S. Wilkins, A mouse model of transplacental cocaine exposure: clinical implications for exposed infants and children, Annals of the New York Academy of Sciences 846 (1998) 248–261.
[78] D. Kurtzberg, Event related potentials in the evaluation of high risk infants, Annals of the New York Academy of Sciences 388 (1982) 557–571.
[79] L.L. LaGasse, R. Seifer, B.M. Lester, Interpreting research on prenatal substance exposure in the context of multiple confounding factors, Clinics in Perinatology 26 (1999) 39–54.
[80] B.M. Lester, K. Freier, L. LaGasse, Prenatal Cocaine Exposure and Child Outcome: What do we really know? in: M. Lewis, M. Bendersky (Eds.), Mothers, Babies, and Cocaine: The Role of Toxins in Development, Lawrence Erlbaum Associates, Hillsdale, NJ, 1995, pp. 19–40.
[81] M. Lidow, Prenatal cocaine exposure adversely affects development of the primate cerebral cortex, Synapse 21 (1995) 332–341.
[82] M. Lidow, P. Rakic, Unique deployment of adrenergic receptor subtypes during development of the primate cerebral cortex including transient subplate and proliferative zones, Journal of Neuroscience 14 (1994) 4064–4078.
[83] M.S. Lidow, Consequences of prenatal cocaine exposure in nonhuman primates, Developmental Brain Research 147 (1–2) (2003) 23–36.
[84] M.S. Lidow, P. Rakic, Neurotransmitter receptors in the proliferative zones of the developing primate occipital lobe, Journal of Comparative Neurology 360 (1995) 393–402.
[85] M.S. Lidow, Z.-M. Song, Effect of cocaine on cell proliferation in the cerebral wall of monkey fetuses, Cerebral Cortex 11 (6) (2001) 545–551.
[86] M. Liotti, M.G. Woldorff, R. Perez, H.S. Mayberg, An ERP study of the temporal course of the Stroop color–word interference effect, Neuropsychologia 38 (5) (2000) 701–711.
[87] S. Luck, Multiple mechanisms of visual–spatial attention: recent evidence from human electrophysiology, Behavioural Brain Research 71 (1995) 113–123.
[88] B. Lutiger, K. Graham, T.R. Einarson, G. Koren, Relationship between gestational cocaine use and pregnancy outcome: a meta-analysis, Teratology 44 (4) (1991) 405–414.
[89] M.E. Malakoff, L.C. Mayes, R. Schottenfeld, S. Howell, Language production in 24-month-old inner-city children of cocaine-and-other-drug-using mothers, Journal of Applied Developmental Psychology 20 (1999) 159–180.
[90] C. Mangano, J. Gardner, B. Karmel, Differences in salivary cortisol levels in cocaine-exposed and noncocaine-exposed NICU infants, Developmetal Psychobiology 25 (1992) 93–103.
[91] J. Markela-Lerenc, N. Ille, S. Kaiser, P. Fiedler, C. Mundt, M. Weisbrod, Prefrontal-cingulate activation during executive control: which comes first? Brain Research & Cognitive Brain Research 18 (3) (2004) 278–287.
[92] N.A. Martin (Ed.), Effects of prenatal drug exposure on cognitive development and ERPs in 5 to 7 year old children. Dissertation Abstracts International: Section B: the Sciences and Engineering. U.S., Univ Microfilms International (2000) 60(8-B) 3773.
[93] L.C. Mayes, Substance Abuse and Parenting, in: M. Bornstein (Ed.), The Handbook of Parenting, Erlbaum, Hillsdale, NJ, 1995, pp. 101–125.
[94] L.C. Mayes, M.H. Bornstein, K. Chawarska, R.H. Granger, Information processing and developmental assessments in 3-month-old infants exposed prenatally to cocaine, Pediatrics 95 (4) (1995) 539–545.
[95] L.C. Mayes, M.H. Bornstein, K. Chawarska, O.M. Haynes, R.H. Granger, Impaired regulation of arousal in three-month-old infants exposed prenatally to cocaine and other drugs, Development and Psychopathology 8 (1996) 29–42.
[96] L.C. Mayes, T. Fahy, Prenatal Drug Exposure and Cognitive Development, in: R.J. Sternberg, E.L. Grigorenko (Eds.), Environmental Effects on Cognitive Abilities, Lawrence Erlbaum Associates, Mahwah, NJ, 2001, pp. 189–220.
[97] L.C. Mayes, C. Grillon, R. Granger, R. Schottenfeld, Regulation of arousal and attention in preschool children exposed to cocaine prenatally, Annals of the New York Academy of Sciences 846 (1998) 126–143.
[98] B. McMillen, J. Johns, E. Bass, L. Means, Learning and behavior of rats exposed to cocaine throughout gestation, Teratology 43 (1991) 495.
[99] L.A. Mead, A.R. Mayer, J.A. Bobholz, S.J. Woodley, J.M. Cunningham, T.A. Hammeke, S.M. Rao, Neural basis of the Stroop interference task: response competition or selective attention? Journal of the International Neuropsychological Society 8 (6) (2002) 735–742.
[100] P. Metosky, J. Vondra, Prenatal drug exposure and play and coping in toddlers: a comparative study, Infant Behavior and Development 18 (1995) 15–25.
[101] D.L. Molfese, Event related potentials and language processes, in: A.W.K. Gaillard, W. Ritter (Eds.), Tutorials in ERP Research: Endogenous Components, North Holland Publishing Co, The Netherlands, 1983, pp. 345–368.
[102] D.L. Molfese, Left and right hemisphere involvement in speech perception: electro-physiological correlates, Perception and Psychophysics 23 (1978) 237–243.
[103] D.L. Molfese, Left hemisphere sensitivity to consonant sounds not displayed by the right hemisphere: electrophysiological correlates, Brain and Language 22 (1984) 109–127.
[104] D.L. Molfese, Neuroelectrical correlates of categorical speech perception in adults, Brain and Language 5 (1978) 25–35.
[105] D.L. Molfese, The phoneme and the engram: electrophysiological evidence for the acoustic invariant in stop consonants, Brain and Language 9 (1980) 372–376.
[106] D.L. Molfese, R. Freeman, D. Palermo, The ontogeny of lateralization for speech and nonspeech stimuli, Brain and Language 2 (1975) 356–368.
[107] D.L. Molfese, V. Molfese, Cortical responses of preterm infants to phonetic and nonphonetic speech stimuli, Developmental Psychology 16 (1980) 574–581.
[108] D.L. Molfese, V. Molfese, Hemisphere and stimulus differences as reflected in the cortical responses of newborn infants to speech stimuli, Developmental Psychology 15 (1979) 505–511.
[109] D.L. Molfese, V.J. Molfese, Electrophysiological indices of auditory discrimination in newborn infants: the basis for predicting later language development, Infant Behavior and Development 8 (1985) 197–211.
[110] D.L. Molfese, A.L. Schmidt, An auditory evoked potential study of consonant perception, Brain and Language 18 (1983) 57–70.
[111] V.A. Molina, J.M. Wagner, L.P. Spear, The behavioral response to stress is altered in adult rats exposed prenatally to cocaine, Physiology & Behavior 55 (5) (1994) 941–945.
[112] R.E. Morgan, H.P. Garavan, C.F. Mactutus, D.A. Levitsky, R.M. Booze, B.J. Strupp, Enduring effects of prenatal cocaine exposure on

attention and reaction to errors, Behavioral Neuroscience 116 (4) (2002) 624–633.
[113] B.A. Morrow, J.D. Elsworth, R.H. Roth, Prenatal cocaine exposure disrupts non-spatial, short-term memory in adolescent and adult male rats, Behavioural Brain Research 129 (1–2) (2002) 217–223.
[114] C.A. Nelson, P. Salapatek, Electrophysiological correlates of infant recognition memory, Child Development 57 (1986) 1483–1497.
[115] D.R. Neuspiel, The Problem of Confounding in Research on Prenatal Cocaine Effects on Behavior and Development, in: M. Lewis, M. Bendersky (Eds.), Mothers, Babies, and Cocaine: The Role of Toxins in Development, Lawrence Erlbaum Associates, Hillsdale, NJ, 1995, pp. 95–110.
[116] J.S. Noland, L.T. Singer, R.E. Arendt, S. Minnes, E.J. Short, C.F. Bearer, Executive functioning in preschool-age children prenatally exposed to alcohol, cocaine, and marijuana, Alcoholism: Clinical & Experimental Research 27 (4) (2003) 647–656.
[117] J.S. Noland, L.T. Singer, S.K. Mehta, D.M. Super, Prenatal cocaine/polydrug exposure and infant performance on an executive functioning task, Developmental Neuropsychology 24 (1) (2003) 499–517.
[118] R.C. Oldfield, The assessment and analysis of handedness: the Edinburgh inventory, Neuropsychologia 9 (1971) 97–113.
[119] H.C. Olson, S.K. Toth, Samples in research on prenatal cocaine exposure: vexing problems and practical solutions, Journal of Drug Issues 29 (1999) 237–253.
[120] C.C. Overtoom, J.L. Kenemans, M.N. Verbaten, C. Kemner, M.W. van der Molen, H. van Engeland, J.K. Buitelaar, H.S. Koelega, Inhibition in children with attention-deficit/hyperactivity disorder: a psychophysiological study of the stop task, Biological Psychiatry 51 (8) (2002) 668–676.
[121] M.G. Paule, M.P. Gillam, R.R. Allen, J.J. Chelonis, Effects of chronic in utero exposure to cocaine on behavioral adaptability in rhesus monkey offspring when examined in adulthood, Annals of the New York Academy of Sciences 914 (2000) 412–417.
[122] A. Poklis, Evaluation of TDx cocaine metabolite assay, Journal of Analytical Toxicology 11 (1987) 228–230.
[123] P. Rakic, Specification of cerebral cortical areas, Science 241 (1988) 170–176.
[124] M. Regaldo, V. Schechtman, A. Del Angel, X. Bean, Sleep disorganization in cocaine-exposed neonates, Infant Behavior and Development 18 (1995) 319–327.
[125] M.G. Regaldo, V.L. Schechtman, A.P. Del Angel, X.D. Bean, Cardiac and respiratory patterns during sleep in cocaine-exposed neonates, Early Human Development 44 (1996) 187–200.
[126] G. Richardson, Prenatal cocaine exposure: a longitudinal study of development, Annals of the New York Academy of Sciences 846 (1998) 144–152.
[127] G. Richardson, M. Conroy, N. Day, Prenatal cocaine exposure: effects on the development of school-age children, Neurotoxicology & Teratology 18 (1996) 627–634.
[128] G.A. Richardson, C. Ryan, J. Willford, N.L. Day, L. Goldschmidt, Prenatal alcohol and marijuana exposure: effects on neuropsychological outcomes at 10 years, Neurotoxicology & Teratology 24 (3) (2002) 311–320.
[129] A.G. Romano, J.A. Harvey, Prenatal cocaine exposure: long term deficits in learning and motor performance, Annals of the New York Academy of Sciences 846 (1998) 89–108.
[130] D. Ruchkin, S. Sutton, R. Munson, K. Silver, F. Macar, P300 and feedback provided by absence of the stimulus, Psychophysiology 18 (1981) 271–282.
[131] J. Savage, N.L. Brodsky, E. Malmud, J.M. Giannetta, H. Hurt, Attentional functioning and impulse control in cocaine-exposed and control children at age ten years, Journal of Developmental & Behavioral Pediatrics 26 (1) (2005) 42–47.
[132] M.S. Scher, G.A. Richardson, N.L. Day, Effects of prenatal cocaine/crack and other drug exposure on electroencephalographic sleep studies at birth and one year, Pediatrics 105 (2000) 39–48.
[133] M.L. Schneider, C.F. Moore, G.W. Kraemer, Moderate level alcohol during pregnancy, prenatal stress, or both and limbic–hypothalamic–pituitary–adrenocortical axis response to stress in rhesus monkeys, Child Development 75 (1) (2004) 96–109.
[134] M.D. Schroder, P.J. Snyder, I. Sielski, L. Mayes, Impaired performance of children exposed in utero to cocaine on a novel test of visuospatial working memory, Brain and Cognition 55 (2) (2004) 409–412.
[135] J.K. Seamans, S.B. Floresco, A.G. Phillips, D1 receptor modulation of hippocampal–prefrontal cortical circuits integrating spatial memory with executive functions in the rat, Journal of Neuroscience 18 (1998) 1613–1621.
[136] S. Segalowitz, H. Cohen, Right hemisphere EEG sensitivity to speech, Brain and Language 37 (1989) 220–231.
[137] F.J. Seidler, S.W. Temple, E.C. McCook, T.A. Slotkin, Cocaine inhibits central noradrenergic and dopaminergic activity during the critical developmental period in which catecholamines influence cell development, Brain Research & Developmental Brain Research 85 (1) (1995) 48–53.
[138] R.W. Simmons, T. Wass, J.D. Thomas, E.P. Riley, Fractionated simple and choice reaction time in children with prenatal exposure to alcohol, Alcoholism: Clinical & Experimental Research 26 (9) (2002) 1412–1419.
[139] L. Singer, R. Arendt, K. Farkas, S. Minnes, J. Huang, T. Yamashita, Relationship of prenatal cocaine exposure and maternal postpartum psychological distress to child developmental outcome, Development and Psychopathology 1997 (1997) 473–489.
[140] T.A. Slotkin, F.J. Seidler, D. Qiao, J.E. Aldridge, C.A. Tate, M.M. Cousins, B.J. Proskocil, H.S. Sekhon, J.A. Clark, S.L. Lupo, E.R. Spindel, Effects of prenatal nicotine exposure on primate brain development and attempted amelioration with supplemental choline or vitamin C: neurotransmitter receptors, cell signaling and cell development biomarkers in fetal brain regions of rhesus monkeys, Neuropsychopharmacology 30 (1) (2005) 129–144.
[141] A.M. Smith, P.A. Fried, M.J. Hogan, I. Cameron, Effects of prenatal marijuana on response inhibition: an fMRI study of young adults, Neurotoxicology & Teratology 26 (4) (2004) 533–542.
[142] R.F. Smith, K.M. Mattran, M.F. Kurkjian, S.L. Kurtz, Alterations in offspring behavior induced by chronic prenatal cocaine dosing, Neurotoxicology & Teratology 11 (1) (1989) 35–38.
[143] A.M. Snyder-Keller, R.W. Keller Jr., Prenatal cocaine increases striatal serotonin innervation without altering the patch/matrix organization of intrinsic cell types, Developmental Brain Research 74 (2) (1993) 261–267.
[144] R.J.M. Somsen, P.C.M. Molenaar, M.W. van der Molen, NB-LA: a neurometric test battery for learning disabled/attention deficit disordered children, in: L.J.M. Mulder, F.J. Maarse (Eds.), Computers in psychology: Applications in education, research and psychodiagnostics, Swets and Zeitlinger, Amsterdam, Netherlands, 1991, pp. 160–165.
[145] C.A. Sorenson, L.A. Raskin, Y. Suh, The effects of prenatal nicotine on radial-arm maze performance in rats, Pharmacology, Biochemistry & Behavior 40 (4) (1991) 991–993.
[146] L. Spear, N. Frambes, C. Kirstein, Fetal and maternal brain and plasma levels of cocaine and benzoylecgonine following chronic SC administration of cocaine during gestation in rats, Psychopharmacology 97 (1989) 427–431.
[147] L.P. Spear, J. Campbell, K. Snyder, M. Silveri, N. Katovic, Animal behavior models. Increased sensitivity to stressors and other environmental experiences after prenatal cocaine exposure, Annals of the New York Academy of Sciences 846 (1998) 76–88.
[148] L.P. Spear, C.L. Kirstein, J. Bell, V. Yoottanasumpun, R. Greenbaum, J. O'shea, H. Hoffmann, N.E. Spear, Effects of prenatal cocaine exposure on behavior during the early postnatal period, Neurotoxicology & Teratology 11 (1) (1989) 57–63.
[149] G.D. Stanwood, R.A. Washington, P. Levitt, Identification of a sensitive period of prenatal cocaine exposure that alters the develop-

ment of the anterior cingulate cortex, Cerebral Cortex 111 (2001) 430–440.
[150] A. Streissguth, H. Barr, P. Sampson, J. Parrish-Johnson, G. Kirchner, D. Martin, Attention, distraction, and reaction time at age 7 years and prenatal alcohol exposure, Neurobehavioral Toxicology and Teratology 8 (1986) 717–725.
[151] A. Streissguth, H. Barr, B. Sandman, B. Kirchner, B. Darby, Intrauterine alcohol and nicotine exposure: attention and reaction time in 4-year-old children, Developmental Psychology 20 (1984) 533–541.
[152] J.R. Stroop, Studies of interference in serial verbal reactions, Journal of Experimental Psychology: Human Perception and Performance 18 (1935) 643–662.
[153] J.M. Struthers, R.L. Hansen, Visual recognition memory in drug-exposed infants, Journal of Developmental and Behavioral Pediatrics 13 (2) (1992) 108–111.
[154] M.W. Swanson, A.P. Streissguth, P.D. Sampson, H.C. Olson, Prenatal cocaine and neuromotor outcome at four months: effect of duration of exposure, Journal of Developmental and Behavioral Pediatrics 20 (1999) 325–334.
[155] J.D. Thomas, M.E. Garrison, C.J. Slawecki, C.L. Ehlers, E.P. Riley, Nicotine exposure during the neonatal brain growth spurt produces hyperactivity in preweanling rats, Neurotoxicology & Teratology 22 (5) (2000) 695–701.
[156] E.Z. Tronick, M. Beeghley, Prenatal cocaine exposure, child development, and the compromising effects of cumulative risk, Clínicas de Perinatología 26 (1999) 151–171.
[157] J. Vaglenova, S. Birru, N.M. Pandiella, C.R. Breese, An assessment of the long-term developmental and behavioral teratogenicity of prenatal nicotine exposure, Behavioural Brain Research 150 (1–2) (2004) 159–170.
[158] E.K. Vogel, S.J. Luck, The visual N1 component as an index of a discrimination process, Psychophysiology 37 (2000) 190–203.
[159] G. Vogel, Cocaine wrecks subtle damage on developing brains, Science 278 (1997) 38–39.
[160] C.V. Vorhees, T.M. Reed, K.D. Acuff-Smith, M.A. Schilling, G.D. Cappon, J.E. Fisher, C. Pu, Long-term learning deficits and changes in unlearned behaviors following in utero exposure to multiple daily doses of cocaine during different exposure periods and maternal plasma cocaine concentrations, Neurotoxicology & Teratology 17 (3) (1995) 253–264.
[161] H.-Y. Wang, S. Runyan, E. Yadin, E. Friedman, Prenatal exposure to cocaine selectively reduces D1 dopamine receptor-mediated activation of striatal G proteins, Journal of Pharmacology and Experimental Therapeutics 273 (1995) 492–498.
[162] D.E. Weese-Mayer, J.M. Silvestri, D. Lin, C.M. Buhrfiend, E.S. Lo, P.M. Carvey, Effect of cocaine in early gestation on striatal dopamine and neurotrophic activity, Pediatric Research 34 (3) (1993) 389–392.
[163] R. West, C. Alain, Event-related neural activity associated with the Stroop task, Brain Research & Cognitive Brain Research 8 (2) (1999) 157–164.
[164] J.A. Willford, G.A. Richardson, S.L. Leech, N.L. Day, Verbal and visuospatial learning and memory function in children with moderate prenatal alcohol exposure, Alcoholism: Clinical & Experimental Research 28 (3) (2004) 497–507.
[165] C.C. Wood, G. McCarthy, Principal component analysis of event-related potentials: simulation studies demonstrate misallocation of variance across components, Journal of Electroencephalography and Clinical Neurophysiology 59 (1984) 249–260.
[166] B.C. Wright, A. Wanley, Adults' versus children's performance on the Stroop task: interference and facilitation, British Journal of Psychology 94 (2003) 475–485.
[167] E. Yablonsky-Alter, I. Gleser, C. Carter, M. Juvan, Effects of prenatal cocaine treatment on postnatal development of neocortex in white mice: immunocytochemistry of calbindin- and paralbumin-positive populations of gabaergic neurons, Society Neuroscience Abstracts 18 (1992) 367.
[168] S. Zysset, K. Muller, G. Lohmann, D.Y. von Cramon, Color–word matching Stroop task: separating interference and response conflict, Neuroimage 13 (1) (2001) 29–36.