Brain & Language 120 (2012) 209–216

Contents lists available at SciVerse ScienceDirect

Brain & Language

journal homepage: www.elsevier.com/locate/b&l

Deviant ERP response to spoken non-words among adolescents exposed to cocaine in utero

Nicole Landi [a,b,*,1], Michael J. Crowley [a,1], Jia Wu [a], Christopher A. Bailey [a], Linda C. Mayes [a]

[a] Yale Child Study Center, Yale School of Medicine, New Haven, CT, United States
[b] Haskins Laboratories, New Haven, CT, United States

ARTICLE INFO

Article history:
Accepted 1 September 2011
Available online 5 October 2011

Keywords:
Prenatal cocaine exposure
Adolescence
Risk
Event-related potential

ABSTRACT

Concern for the impact of prenatal cocaine exposure (PCE) on human language development is based on observations of impaired performance on assessments of language skills in these children relative to non-exposed children. We investigated the effects of PCE on speech processing ability using event-related potentials (ERPs) among a sample of adolescents followed prospectively since birth. This study presents findings regarding cortical functioning in 107 prenatally cocaine-exposed (PCE) and 46 non-drug-exposed (NDE) 13-year-old adolescents.

PCE and NDE groups differed in processing of auditorily presented non-words at very early sensory/phonemic processing components (N1/P2), in somewhat higher-level phonological processing components (N2), and in late high-level linguistic/memory components (P600).

These findings suggest that children with PCE have atypical neural responses to spoken language stimuli during low-level phonological processing and at a later stage of processing of spoken stimuli.

1. Introduction

Evidence from both human and animal research indicates that exposure to cocaine during gestation alters the development of neural systems, particularly the monoaminergic systems (dopamine, norepinepherine and serotonin) involved in cortical development (Bhide, 2009; Lester & Padbury, 2009; Mayes, Granger, Frank, & Bornstein, 1993). In addition, a significant body of research has now identified impaired performance in PCE relative to NDE children across a number of cognitive tasks at multiple age points. Deficits have been identified in attentional processing, executive function, spatial learning and reaction times (Alessandri et al., 1993; Heffelinger, Craft, & Shyken, 1997; Savage Brodsky, Malmud, Giannetta, & Hurt, 2005; Schroder Snyder, Sielski, & Mayes, 2004). One of the most consistent findings in the literature on prenatal cocaine exposure (PCE) is impairment across a variety of language tasks, suggesting that cocaine alters development of neurobiological systems responsible for language processing. Specific language deficits that have been linked to PCE include: deficits in speech processing, deficits in expressive language ability and semantic processing, and general language delay (e.g., Cone-Wesson, 2005; Delaney-Black et al., 2000; Malakoff, Mayes, Schottenfeld, & Howell, 1999; Singer, Arendt, Minnes, Farka, & Salvator, 2001; Bandstra, Vogel, Morrow, Xue, & Anthony, 2004; Bandstra et al., 2002). Despite this often-identified relationship between PCE and impaired language function, the specific locus of these deficits has not been identified. Moreover, not all studies find significant differences between exposed and unexposed children; Frank, Augustyn, Grant Knight, Pell, and Zuckerman (2001) performed a meta analysis of 36 studies of physical and cognitive development and did not find evidence of deficits in expressive or receptive language skills (or any cognitive skills measured) in children 6 years and younger after other variables such as SES and other substance exposure were taken into account. More recent studies, however, have found significant effects of cocaine exposure after controlling for these additional variables (e.g., Bandstra et al., 2004).

One limitation of the majority of the existing research on language function in PCE children and adolescents is that it is almost entirely limited to performance on standardized tests, which assess broadly defined cognitive skills but do not necessarily permit assessment of the underlying component processes supporting cognition. Reliance on standardized tests alone may be particularly problematic when evaluating individuals from low SES backgrounds (the majority of exposed children) because these tests are often normed on higher SES populations. Direct measures of

Abbreviations: ERP, event related potential; PCE, prenatally cocaine-exposed; NDE, non-drug-exposed.

* Corresponding author. Address: Yale Child Study Center, 230 South Frontage Rd., New Haven, CT 06473, United States.
E-mail address: nicole.landi@yale.edu (N. Landi).

[1] This is a shared first authorship.

0093-934X/$ - see front matter © 2011 Elsevier Inc. All rights reserved.
doi:10.1016/j.bandl.2011.09.002

neurocognitive functioning are likely to be more effective for identifying cognitive processes affected by disease or exposure to neurotoxins. Specifically, cognitive neuroscience methods such as fMRI and EEG/ERP can identify where and when (respectively) in the brain a specific cognitive skill is impacted. To date, no studies have examined language function in PCE children or adolescents at the level of neural activity. Behavioral findings may be mixed because they are not sensitive enough to underlying subtle differences in linguistic processing. To this end, we examined auditory non-word processing among adolescents exposed to cocaine prenatally with an event related potential (ERP) design.

Auditory non-word processing was chosen because it allows for examination of the sensitivity to the building blocks (phoneme combinations) of word learning and vocabulary development that are not already linked to semantic representations (e.g., Saffran, Johnson, Aslin, & Newport, 1999). Moreover, examination of these relatively low-level non-word processing skills are not confounded with language experience, which may be impoverished in low SES children independent of PCE. Abnormality in processing of auditory non-words could indicate residual deficits in phonological processing, which may be responsible for the observed poorer performance in some speech and language tasks observed in PCE children. We also chose to use an old/new paradigm (presenting one series of non-words in the first block and then adding a second non-word to the second block, intermixing the two); this was chosen to allow for an examination of phonological memory processes, which are also critical in the formation of lexical representations.

ERPs have been widely used to study spoken language and printed language processing and have well defined components associated with particular aspects of speech and language processing. Early components including the N1/P2 complex are sensitive to basic auditory processing (such as tone frequency and pitch) as well as phonemic and phonological processing (such as phoneme category and rhyme). Later components have been shown to be sensitive to higher level processing demands, such as semantics (N400) and syntax/ pragmatics (P600 ELAN), (see Kutas & Van Petten, 1994; Kutas, Van Petten, & Kluender, 2006 for an in-depth review of language processing components). In addition to these "classic" language components, additional task specific components that may be sensitive to speech and language processing depending on the study design have also been identified (e.g., the mismatch negativity or MMN).

In the current investigation we examined neural response to repeated and non-repeated spoken non-words using a task modeled after (Molfese, Morse, & Peters, 1990). Specifically, we auditorily presented two rhyming non-words ("bidu" and "gibu") in an old/new design, presenting a block of bidu trials followed by a mixed block of randomly presented bidu and gibu trials (as described below). We were interested in both "lower-level" phonemic/phonological processing, associated with the N1/P2 complex and the P200 and N200 as well as "higher-level" components that would be sensitive to repetition of non-words (comparing old/new), such as the repetition sensitive P600-like component identified by Curran (1999). We predicted that if PCE children have deficits in the lowest-level aspects of speech perception, then we would observe reduced N1/P2 complex amplitudes in this group compared to NDE children (for both old and new items). However, if exposed children do not have difficulty with the lowest-level perceptual aspects of speech processing, but instead have difficulty with somewhat higher level representation of linguistic units (phonology, rhyme), we would only expect altered responses to repeated relative to unrepeated items later in processing (possibly reflecting differences in phonological encoding or retrieval). A deficit in both high-level and low-level aspects of language processing in this task would be evidenced as abnormal early and late component response to stimuli, for both repeated and unrepeated items.

2. Material and methods

2.1. Participants

Participants were a sub-sample of a larger sample of adolescents involved in a 16 year longitudinal study on the effects of fetal cocaine exposure on physical, cognitive, emotional, and social development. The full sample consists of 523 children, including both exposed children and non-exposed controls who were recruited at birth and returned for at least one visit in their first year, with children and families seen biannually thereafter. The two groups were initially selected to be of similar SES and racial background. Families were initially recruited when they sought prenatal care at the Yale-New Haven Hospital or when they were admitted to the postpartum ward in the case of no prenatal care. Prenatal cocaine exposure was determined by a combination of maternal report, urine toxicology in the prenatal or postpartum period, and meconium toxicology. We have maintained contact with 78% of the originally recruited cohort with no selective attrition between the cocaine-exposed (21.4% lost) and non-drug-exposed (24.4% lost).

The sub-sample that completed our ERP study consisted of 107 adolescents (51 females and 56 males) who were exposed to cocaine and other drugs prenatally (PCE group) and 46 non-drug exposed adolescents who were not exposed to cocaine or other drugs prenatally (NDE group, 19 females and 27 males). These participants were randomly selected from the longitudinal cohort, PCE participants were oversampled to ensure stable results given the potential for more subject to subject variability in many clinical populations (e.g., Dhar, Been, Minderaa, & Althaus, 2010). The PCE group includes 90.6% African American participants, 0.9% Latino participants, 2.8% Pacific Islander participants and 5.70% Caucasian participants. The NDE group includes 67.4% African American participants 8.7% Pacific Islander participants and 23.9% Caucasian participants. Most participants were right handed ($N = 130$) and a few participants were left–landed ($N = 16$) (with left handed participants distributed in equal proportion across the groups). All participants participated in the EEG experiment and took an IQ assessment within 3 months of their 13th birthdays. The two groups that participated in the ERP study did not differ on the verbal or performance IQ composites (measured by the Kaufman Brief Intelligence Test, KBIT), but they did differ on the mathematical reasoning subtest ($t = 2.83$, $p < .01$), with exposed children performing more poorly on this subtest. All participants had normal hearing (−20 dB to +20 dB) as measured by an audiometer. At the time of ERP testing, all children were fluent in English with no evidence of serious mental illness (e.g., psychosis), head injury (based on parental report, participant report and medical records if available) or substance use. See Appendix A for additional birth variables available on this sample.

2.1.1. Maternal education

The number of mothers in the non-exposed group that completed high school was higher than in the PCE group $X^2 = 8.49$, $p < .005$ (non using mothers who completed high school $N = 40$, non using mothers who did not complete high school $N = 6$; using mothers who completed high school $N = 69$, using moms who did not complete high school = 38).

2.1.2. Maternal drug use for PCE cohort

As mentioned above, prenatal cocaine exposure was determined by a combination of maternal report, urine toxicology in the prenatal or postpartum period, and meconium toxicology. In addition to cocaine use, which rarely occurs in isolation, 75% of mothers reported using tobacco (e.g., smoked cigarettes), 71% also