Published in final edited form as:

Psychiatry Res. 2008 August 15; 160(2): 145–154. doi:10.1016/j.psychres.2007.11.019.

Attentional deficits in Cocaine-dependent patients: Converging behavioral and electrophysiological evidence

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Abstract

Although there are several reports of patients with cocaine dependence displaying cognitive deficits, the nature of their information processing deficits is not well characterized. In the present study, the attentional performance of cocaine-dependent patients ($n = 14$) was examined and compared with that of healthy control individuals ($n = 15$). Attention was assessed using an auditory oddball event-related task as well as the Continuous Performance Test (CPT; Identical Pairs version). The cocaine-dependent group displayed P300 amplitude reduction compared to controls. The group difference in P300 response latency did not reach significance. On the CPT, the cocaine-dependent patients displayed significantly poorer discriminability and greater errors of commission than the controls. There was a positive correlation between performance on the oddball event-related task and performance on the CPT. This investigation provides converging behavioral and electrophysiological evidence of attentional deficits in cocaine-dependent patients.

Keywords

event-related potentials; Continuous Performance Test; psychosis

1. Introduction

Elicited in response to an infrequent stimulus, the amplitude of the P300 component reflects capacity allocation, selective attention, and updating of working memory (Donchin & Coles, 1988; Johnstone & Barry, 1996; Johnstone et al, 2001). Reduced P300 amplitude has been observed in various patient groups, including individuals with schizophrenia (cf. Bramon et al. 2004 for a recent review; Davenport et al., 2006;), alcoholism (Chen et al., 2007; Hesselbrock et al., 2001), cocaine dependence (Bauer 1996, 1997) and conduct disorder (cf. Bauer & Hesselbrock, 1999). P300 abnormalities have also been reported in first-degree relatives of schizophrenia patients (Turetsky & Cannon, 2000; Sponheim et al., 2006; Davenport et al., 2006). In addition, several research findings indicate that P300 amplitude may be associated with risk for substance use disorders. Offspring of alcoholic fathers produce reduced P300 amplitude (Begleiter et al., 1984; Polich, Pollock, & Bloom, 1994; Hill, 1995;

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Hesselbrock et al., 2001). Brigham, Herning, and Moss (1995) demonstrated that offspring of fathers with other forms of psychoactive substance dependence also display P300 amplitude reduction. Longitudinal studies indicate that reduced P3 amplitude at ages 11 to 14 are associated with the later development of substance-related disorders (Iacono, 1998). Furthermore, results from a longitudinal twin study of 17-year-old males at genetic risk for substance use disorders (Iacono, 1998; Carlson, Iacono & McGue, 2004) support the notion that P300 amplitude reduction may serve as an endophenotype indicating risk for the development of substance use disorders.

1.1 Prior studies of P300 in Cocaine dependent patients

Although the P300 ERP is a useful measure for studying cognitive capacity in drug-dependent populations (c.f. Amass, 1989), relatively little is known regarding the effects of cocaine dependence and/or chronic cocaine use on cognitive functioning. Studies of ERPs in cocaine dependent patients reveal reduced frontal P300 amplitude (Bauer, 1996; Bauer, 1997; Biggins et al., 1997; Bauer, 2001). In a classic 'oddball paradigm', Moeller et al. (2004) observed that the cocaine-dependent patients displayed significantly smaller P300 amplitudes than the controls. Moeller et al. (2004) found a significant inverse relationship between P300 amplitude and years of cocaine use, as well as an inverse relationship between the patients' impulsivity measures and their P300 amplitude.

The latency of the P300, operationally defined as the time from stimulus onset to the point of maximum positive amplitude within the latency window, is an index of the timing of stimulus evaluation processes (Courchesne et al., 1977; Kutas et al., 1977; Polich et al., 1997). Additionally, P300 latency is thought to reflect cognitive performance, with shorter latencies associated with superior performance (Polich, 1998). Findings regarding cocaine-dependent patients' P300 response latency have been equivocal (Bauer, 1996; Biggins et al., 1997; Bauer, 2001).

1.2 Sustained attention and Cocaine use

Some studies (such as Berry et al., 1993, Strickland et al., 1993) suggest that cocaine use is associated with sustained attention deficits. However, a review by Horner (1999) indicates that there is insufficient evidence of impaired sustained attention deficits among cocaine abusers. As Horner pointed out, the range of attentional tests used in past studies is limited, and the measures used may not have been sufficiently challenging and/or unconfounded measures of sustained attention. Moreover, there were several methodological limitations, such as including individuals with comorbid psychiatric disorders, comparing patients with published norms rather than with control subjects, and relying upon heterogeneous samples of cocaine-abusing patients with concurrent alcohol dependence, despite evidence that there are neurocognitive impairments associated with chronic alcohol abuse. Also, the apparent discrepancy in findings may reflect the possibility that factors such as extent and severity of use (i.e., cocaine use vs. cocaine dependence) may affect the relationship between cocaine use and effect on attentional performance.

Cocaine use may be associated with enhanced performance on measures of sustained attention. Johnson et al. (1998) observed that controlled intravenous administration to eight cocaine-dependent individuals was associated with improved performance on the Rapid Visual Information Processing Task. Using a co-twin control research design, Toomey et al. (2003) observed that in their sample of 50 twin pairs discordant for abuse of cocaine and/or amphetamines, the drug-abusing co-twin displayed significantly better performance on the CPT, though impaired performance on other attentional measures. On the other hand, two more recent investigations (Moeller et al., 2004; Moeller et al., 2005) suggest that cocaine dependence may be associated with attentional impairments. In a comparison of 17 individuals

with current cocaine-dependence and 14 controls, the cocaine-dependent subjects had significantly higher behavioral laboratory scores of impulsivity, operationally defined as proportion of hit-corrected false alarms, than controls (Moeller et al., 2004). In a later study (Moeller et al., 2005) 18 cocaine-dependent patients and 18 normal controls were administered a questionnaire measure of impulsivity, namely, the Barratt Impulsivity Scale-11 (BIS-11), and the Immediate and Delayed Memory Task, and underwent diffusion tensor imaging (DTI). Compared to the controls, the cocaine-dependent patients displayed significantly fewer hits and greater commission errors on the continuous performance test, as well as greater impulsivity on the questionnaire measure. The cocaine-dependent subjects were distinguishable from the controls in terms of reduced integrity of anterior corpus callosum white matter. The cocaine-dependent patients' white matter pathology was associated with increased behavioral laboratory measured impulsivity and reduced discriminability.

1.3 The present study

The goal of the present study was to assess cocaine-dependent patients' attentional performance. The majority of the individuals in our patient group (71%) had cocaine-induced psychosis. Estimates of the frequency of Cocaine-induced psychosis (CIP) range from 15% (Schuckit, 2006) to over 50% (Brady et al., 1991). Affected individuals report behavioral sensitization, in which psychotic symptoms become more frequent over time and occur with the use of less drug (Brady et al., 1991). The development of a cocaine-induced chronic psychosis is rare (Thirithalli & Benegal, 2006), relative to that of cannabis- and amphetamine-induced psychoses. We wanted to replicate the findings of Moeller et al. (2004), namely, an association between P300 amplitude and a behavioral measure using a different subgroup of cocaine-dependent patients. We attempted to overcome some limitations of previous studies by using a well-validated measure of sustained attention, namely, the Continuous Performance Test-Identical Pairs Version (CPT-IP), assessing subjects for a childhood history of ADHD, obtaining an objective verification of abstinence from drug use, and including a normal control group.

Based on prior findings, we expected that the cocaine dependent patients would display reduced P300 amplitude. Because both the P300 and the Continuous Performance Test are reflective of attention and information processing, we predicted that there would be a significant relationship between P300 amplitude and CPT performance. More specifically, we hypothesized that there would be a strong association between P300 amplitude and discrimination sensitivity and an inverse association between impulsivity on the CPT and P300 amplitude. Given the equivocal nature of the prior findings, we had no hypotheses regarding whether there would be group differences in latency. However, we predicted that P300 latency would be associated with participants' reaction times to correct detections on the CPT.

2. Methods

2.1 Subjects

The sample consisted of 18 cocaine-dependent patients and 16 control participants with no history of cocaine use. The cocaine-dependent sample consisted of participants who met DSM-IV (APA, 1994) criteria for cocaine dependence during the past year and who had been free of cocaine use for at least 3 weeks (documented by toxicology screens). All cocaine-dependent subjects were recruited from drug-rehabilitation or residential drug-treatment facilities where random urine screening for drugs of abuse is routinely performed.

Use of alcohol within the context of moderating the effects of cocaine was permitted. Moreover, all of the cocaine-dependent patients denied use of alcohol during the three weeks preceding recording of the event-related potentials. This history was verified by the subjects' primary

clinician. Toxicology screens confirmed that all subjects were free of cocaine, marijuana, opiates, PCP, and benzodiazepines at the time of the study. None were receiving psychotropic medications at the time of the study. None of the participants met criteria for another Axis I disorder that was judged to be independent of cocaine use.

Sixteen healthy control participants were also examined. The control participants were drawn from a sample of volunteer participants recruited via posted fliers and by word of mouth. All potential participants had to be between the ages of 18 and 65 years. The goal was to match the control and cocaine-dependent groups in terms of age range and gender; it was especially important to ensure a similar age range across groups. The groups were not matched for ethnic backgrounds or education. All study participants had completed at least 10 years of formal education. The control group also had to have negative urine screening results for study inclusion. For both groups, exclusion criteria included any first-degree relatives with major psychiatric disorders (other than drug and alcohol abuse).

After the study was explained and all questions were answered, participants signed a written informed consent form. The study was approved by the Human Investigations Committees of the VA-Connecticut Healthcare System and Yale University School of Medicine, and the Institutional Review Board of the University of Wisconsin-Madison. Subjects were allowed to smoke until they arrived at the laboratory. At least 1 hour was spent in the laboratory before event-related potential recording began.

2.2 Event-related potentials(ERP) recording

The ERP recording was performed while participants were seated with their eyes closed in a sound-attenuated room. The ERPs were elicited during an oddball paradigm. In the oddball paradigm, two types of stimuli are delivered at random every 2 seconds binaurally through earphones with an ISI of 1.25s. The stimuli consisted of a random sequence of two tones: a frequent, 1,000Hz tone and an infrequent, 1,500 Hz tone. These tones were presented at a ratio of 85/15. Each run therefore consisted of 340 frequent tones and 45 infrequent tones. Subjects were asked to silently count the infrequent tones.

Monopolar recordings were made from silver/silver chloride disk electrodes applied to midline locations and referenced to linked ears. One channel was devoted to detecting eye movement artifacts recorded from a supraorbital electrode to the outer canthus. On-line EEG artifact rejection allowed for trial rejection when activity in any channel exceeded 75 μ V (Neuroscan Software, Herndon, Virginia).

Electrical signals were amplified 20,000 by Grass amplifier. The EEG were digitally filtered with a bandpass of 0.05 Hz to 300 Hz at 1000 Hz prior to peak detection. The variables of interest were the amplitude and latency of the P300 component. The period 100msec from pre-response to 500msec post response served as baseline. The largest positive deflection in that window was identified as the P300. P300 measurements were made from the Pz electrode. The components were identified and measured by one of the authors (SB) who was naïve to the subject group. All ERPs were subsequently checked by one of the senior investigators (NB). After baseline correction, EEG epochs were subsequently averaged together..

2.3 Wender Utah Rating Scale

Given that the Continuous Performance Test provides a measure of sustained attention and the P300 component is frequently used as an index of information processing, it was necessary to screen out any individuals with a history of Attention Deficit Hyperactivity Disorder. Prior research (Carroll & Rounsaville, 1993) suggests that a disproportionate number of cocaine-dependent individuals may meet criteria for ADHD. The Wender Utah Rating Scale (WURS;

Ward, 1985) was developed to aid in the retrospective diagnosis of childhood behavioral symptoms associated with Attention Deficit Hyperactivity Disorder (ADHD). Respondents are asked to rate each item of this 61-item self-rating scale on a 5-point scale (0, not at all, to 4, very much). The WURS was scored by an investigator (DCG) who was naïve to group membership.

2.4 Continuous Performance Test

The CPT-IP is a high processing load version of the continuous performance task paradigm. During the CPT-IP, stimuli are visually presented in relatively rapid succession, and participants are required to respond when the same stimulus appears twice in a row (i.e., an identical pair). In this study, there were two subtasks that were matched in difficulty: the digit subtask and the shapes subtask. In the digits subtask, a series of four digit stimuli are presented on a computer screen. In the shapes subtask, a series of four nonsense shapes are presented. The nonsense shapes are complex patterns that were specifically designed to resist verbal labeling. Numbers and shapes were presented in separate conditions. For both conditions, the stimuli were presented at the rate of 1 per second, and the stimulus duration was 50 msec, with an ITI of 950 msec.

The tasks were administered on computers equipped with a mouse so that the participants could respond with a finger lift connected to a reaction time key. Participants were instructed to respond as fast as possible. The task was made more difficult by including not only target trials but also including catch trials, in which, for example, the consecutive four digit numbers differed by one digit only. After a practice session, in which participants were given feedback for correct and incorrect responses, the tasks were administered. A total of 600 trials, 20% of them targets and 20% of them catch trials, were divided into four successive blocks.

The CPT was scored using the program provided (Biobehavioral Technologies, Inc., 1997). Correct responses, responses made to the second of two identical stimuli presented in a row, were scored as hits. Errors of commission in which responses were made to the catch trials were scored as false alarms. Performance on the CPT was scored in terms of: proportion of hits, reaction time (in milliseconds) of hits, and proportion of false alarms, as well as two signal detection indices. The two signal detection indices were: d' (the index of discriminability), which measures decline in sensitivity or attentional capacity, and beta (b)(transformed to the natural log scale, $\ln b$), an index of response bias, or tendency to overrespond or under-respond. Both the d' and $\ln b$ indices were computed using the hit rate and false alarm rate data. The d' value provides an index of sensitivity, with higher d' values indicating better attentional performance. The $\ln b$ value reflects the participant's response bias, with higher values indicating a more conservative response criterion. In order to allow comparisons with prior work by Moeller et al. (2004), we also calculated an impulsivity index for each of the task conditions. The impulsivity index, intended to provide a more accurate rate of impulsive errors, was calculated by dividing the false alarm rate by the rate of correct detections. The Continuous Performance Test data were scored independently of the event-related potential data and the clinical data.

2.5 Cocaine Experiences Questionnaire

In order to further characterize the cocaine-dependent sample, we administered the 58-item Cocaine Experience Questionnaire (CEQ; Satel & Edell, 1991). This scale can be used to determine whether a subject experiences paranoid symptoms during cocaine use as well as assess the nature of the experience.

The CEQ score has a range of 0 to 16 with three subscales, namely, paranoia, severity, and insight. The paranoia scale assessed the nature of the experience of paranoia during cocaine

use to differentiate between suspiciousness and apprehension and psychotic experiences including delusions and hallucinations. Patients were instructed to distinguish between adaptive hypervigilance or anxiety in high-risk situations (e.g., making drug deals, engaging in illicit activities) and completely irrational beliefs. An analog scale then assessed the severity of the experience, ranging from minimally distressing (score of 0) to intolerable and terrifying (score of 6). Scores of 5 or 6 on this subscale indicate a frankly psychotic experience. The behavioral severity subscale assessed the behavior associated with paranoid ideation and ranges from simple feelings of fear (score of 1) to attacking others in perceived need for self-defense in the absence of any real danger (score of 6). The insight subscale assessed subjects' insight during cocaine intoxication, and ranges from 0 (full insight) to 3 (total lack of insight).

2.6 Statistical analyses

Independent-samples T-tests were performed to compare the two participant groups in terms of their P300 amplitude and latencies. Following the recommended method of analysis (Cornblatt et al., 1988, 1989), we performed a 2 (group: patient vs. control) by 2 (stimulus: numbers vs. shapes) repeated measures analysis of variance for the two CPT performance indices, namely, d' and $\ln b$. In addition to the primary outcome measures for the CPT, reaction time data for the correct responses, number of commission errors (false alarms), and impulsivity indices were also analysed. The association between the ERP measures, the CPT performance indices, and the self-report measures (e.g., WURS, CEQ) was analyzed by Pearson product moment correlations. The correlations of ERP measures with behavioral and clinical measures were considered exploratory and were not corrected for multiple comparisons.

3. Results

3.1 Demographics

Individuals whose scores were indicative of definite ADHD were excluded from further analyses. This resulted in four out of 18 (22.2%) of the eligible cocaine-dependent individuals and one of 16 (6.25%) of the healthy controls being excluded. The final sample consisted of 29 participants (namely, 14 cocaine-dependent patients and 15 healthy controls). Table 1 provides demographic characteristics of the cocaine-dependent sample (7 males and 7 females; a mean age of 39.00 years) and the healthy control participants (7 males and 8 females; a mean age of 34.27 years).

The groups did not differ significantly in terms of their proportion of males, $\chi(1) = 0.03$, n.s. The two groups did not differ significantly in terms of age at the time of testing, $t(27) = 1.98$, n.s. The groups did not differ significantly in terms of ethnicity, $\chi(3) = 6.57$, n.s. Subjects were considered smokers if they reported smoking either regularly or socially. The patient group was more likely to include smokers, $\chi(3) = 12.71$, $p < .01$. The groups were also compared in terms of their scores on the WURS. They did not differ in terms of their mean scores on the scale, $t(27) = 1.51$, n.s.

3.2 Cocaine use

The mean age when these patients first used cocaine was 20 (range, 13 to 31) years. Their average age when they began regular use of cocaine was 23 (range, 14 to 35) years. Mean duration of use was 19 (range, 1 to 25) years. The CEQ was administered to the cocaine-dependent patients. Although none of the patients reported experiencing psychotic symptoms prior to their illicit drug use, most (71%, or 10 of 14) of the cocaine-dependent individuals reported experiencing paranoid symptoms during their use.

3.3 Electrophysiological measures of attention and information processing

Grand averaged ERPs for the cocaine dependent patients and the healthy controls are shown in Figure 1. The amplitudes and latencies are summarized in Table 2. Analyses revealed a significant group difference between cocaine-dependent subjects and healthy controls in P300 amplitude, with the cocaine-dependent subjects having reduced amplitude compared to the controls, $t(27) = 4.04$, $p < .001$. Cocaine dependence resulted in an average decrease of 63% compared to controls. However, the difference between groups in terms of P300 latency failed to reach statistical significance, $t(21) = 2.06$, n.s. To determine whether there was an association between duration of cocaine use and the P300 indices, we computed Pearson product-moment correlations. There was no significant relationship between duration of cocaine use and either P300 amplitude or latency, r 's = $-.32$ and $-.04$, n.s., respectively.

3.4 Continuous Performance Test

We examined the association between patients' duration of cocaine use and performance on the CPT. Duration of cocaine was not significantly associated with any of the CPT performance indices, r 's ranged from $-.28$ to $.24$, n.s. Table 2 provides the means and standard deviations on the CPT-IP indices for both groups. Analysis of the discrimination sensitivity (d') data revealed that there was a main effect of group, $F(1, 27) = 10.33$, $p < 0.01$. However, there was no effect of stimulus type (digits vs. figures), $F(1,27) = 0.17$, n.s., nor was there a group by stimulus interaction, $F(1,27) = 0.84$, n.s.

In terms of the groups' response criteria ($\ln b$), the between-factor analysis failed to yield a significant main effect of group, $F(1,27) = 0.91$, n.s. Within-subject analysis did not reveal a significant effect of either stimulus type [$F(1,27) = 0.00$, n.s.] or stimulus $\times$ group interaction [$F(1,27) = 0.26$, n.s.]. Taken together, these findings indicate that the two groups differed in terms of their task performance, with the patient group having a significantly lower mean d' than the controls. However, the two groups did not differ in terms of their response criterion.

The latency for correct responses (hits) was also analyzed. We observed a significant effect of stimulus, $F(1,27) = 5.60$, $p < .05$, whereby participants displayed a significantly longer reaction time on the digits condition relative to the shapes condition. However, the two groups did not differ in terms of their latency for correct hits, $F(1,27) = 1.88$, n.s., nor was there a significant group $\times$ stimulus type effect, $F(1,27) = 0.38$, n.s. The cocaine-dependent group made more commission errors than the control group, $F(1,27) = 8.53$, $p < .01$. However, there was no effect of stimulus type [$F(1,27) = 0.26$, n.s.], nor was there a significant group by stimulus interaction [$F(1,27) = 2.36$, n.s.].

Finally, we compared the two groups on an index of impulsivity, operationally defined as the ratio of false alarms to correct detections. There was a significant group effect, $F(1,27) = 9.57$, $p < .01$, though there was no effect of stimulus type [$F(1,27) = 0.01$, n.s.]. The group $\times$ stimulus interaction failed to reach significance, $F(1,27) = 3.37$, n.s.

3.5 Associations between the electrophysiological measures and behavioral and clinical measures

With the exception of RTs for correct responses, there were no significant differences between the CPT-digits condition and the CPT-shapes condition. Thus, for the remainder of the analyses, the data for the two stimulus types were combined. In the entire sample, we observed a significant association between P300 amplitude and discrimination sensitivity (d'), $r = 0.43$, $p = .019$. Overall, participants with larger P300 amplitudes displayed better CPT performance, as measured by d' . Behavioral impulsivity, operationalized as the ratio of false alarms to hits, was inversely related to P300 amplitude, $r = -0.41$, $p = .026$. Contrary to expectations, P300 latency was not significantly associated with reaction time to correct detections, $r = 0.11$, n.s.

In fact, none of the correlations between P300 latency and the CPT performance indices were significant.

Scores on the Wender-Utah Rating Scale were not significantly correlated with P300 amplitude for the entire sample, healthy controls, or cocaine-dependent patients ($r = -.20$, $.07$, and $-.19$, n.s., respectively). Similarly, the WURS scores were not significantly associated with P300 latency for the groups separately or pooled (r 's ranged from $-.35$ to $-.18$, n.s.). We observed a trend, whereby WURS scores were negatively associated with the number of correct responses (hits) on the CPT, $r = -.36$, $p = .056$. None of the other correlations between WURS scores and CPT performance indices approached statistical significance.

3.6 Cocaine-Induced Psychosis

All of the cocaine-dependent patients who experienced cocaine-induced psychosis had no history of psychosis prior to their drug use. The patients reported a varying amount of time that elapsed before paranoia set in (within an episode of drug use), ranging from less than 5 minutes to more than 120 minutes following use. The CEQ total score was significantly correlated with scores on the distress subscale, $r = .79$, $p < .01$. The mean score on the CEQ paranoia distress subscale was 4.2 ($SD = 1.55$), with half (5 of 10) of the patients with cocaine-induced paranoia reporting frankly psychotic experiences. The patients displayed a considerable range of behaviors associated with their paranoid ideation, ranging from simple fears to needing to attack others in perceived albeit delusional need for self defense (mean behavioral severity subscale rating = 2.60, $SD = 1.3$). CEQ insight scores ranged from 1 to 3 (mean = 1.70, $SD = .68$), with 60% of the patients indicating a lack of full insight regarding their paranoia. Scores on the insight subscale were not correlated to CEQ total score, $r = .40$, n.s.

Among the cocaine-dependent patients who experienced psychosis, P300 amplitude was inversely related to CEQ paranoid distress scores, $r = -.66$, $p < .05$. Thus, the greater the self-reported distress during cocaine-induced paranoia, the smaller the patients' P300 amplitudes. Similarly, CEQ total scores were inversely related to P300 amplitude, $r = -.62$, $p = .05$. No other significant associations between the CEQ scores and any of the behavioral measures were significant.

4. Discussion

In this investigation, we assessed cocaine-dependent patients in terms of their selective attention using the 'oddball' paradigm, and their sustained attention, via the CPT-IP. The patients displayed attentional deficits on both types of tasks. Compared to the control group, the cocaine-dependent patients had smaller P300 amplitudes in response to the infrequent stimuli. However, the two groups did not differ significantly in terms of P300 latency. Thus, our results provide a partial replication of the Moeller et al. (2004) investigation. In both studies, there was evidence of a moderately strong association between indices of impulsivity and P300 amplitude. For the entire group of subjects, we observed that P300 amplitude was inversely correlated with behavioral impulsivity on the Continuous Performance Test and positively correlated with discrimination sensitivity.

Our study extends the literature by providing further insight into the nature of cocaine-dependent patients' information processing deficits. The cocaine-dependent patients made more errors of commission (i.e., false positive errors). The patients' increased frequency of errors of commission could reflect greater impulsivity, poorer discriminatory ability, or both processes. Using the CPT-IP, we observed that the cocaine-dependent group was significantly less able to detect the difference between the target and nontarget than the controls, though the groups did not differ in terms of their response criterion. Thus, the present findings suggest

that cocaine-dependent patients show poorer discriminatory ability as well as greater impulsivity.

Some reports (e.g. Franken et al., 2007) indicate that cocaine-dependent patients show reduced error processing and impaired behavioral correction after an error is made. An alternative explanation of our present findings is that they reflect cocaine patients' general insensitivity to behavioral errors. However, this is a less tenable account given that we observed significant group differences not only in the CPT performance but also in terms of P300 amplitude. A parsimonious account of the patients' performance is that it reflect deficits in attentional processes. This latter interpretation is supported by the significant differences between the patients and controls in terms of the stimulus-locked P300 amplitudes, and the correlation between subjects' CPT performance and P300 amplitude.

It is noteworthy that both the patient and the control groups were screened for premorbid and current history of ADHD. The rate of reported childhood ADHD among our patient group (22%) falls within the reported range 12 to 34% (cf. Rounsaville et al., 1991). Thus, it is likely that our sample of cocaine-dependent participants was derived from a group that is representative of the larger population of those in treatment for cocaine dependence (c.f. Horner, Scheibe, & Stine, 1996).

There is a growing interest in whether time of abstinence from drug modifies its effects on event-related potentials. However, information regarding length of abstinence from cocaine has not been consistently provided in some reports and/or the investigators relied upon drug users' self-report (Horner, 1999). A strength of our study includes quantification of the length of abstinence from drug use and objective verification of the abstinence. The Moeller et al. (2004) sample had current cocaine dependence and were not currently undergoing treatment, whereas our sample was enrolled in a treatment program and was abstinent at the time of testing. Additionally, most of our sample (71%) of cocaine-dependent patients had cocaine-induced psychosis. Thus, the present study also extends the literature, by providing clinical characterization of another subgroup of cocaine-dependent individuals. Among the patients, P300 amplitude was inversely related to self-reported paranoid distress scores as well as total CEQ scores. This finding, while particularly intriguing, is based on a small group and awaits replication.

Study limitations include the small size of our sample. Despite the small size of our sample, we had sufficient power to able to detect significant group differences. It is noteworthy that the cocaine-dependent subjects and controls were matched for gender and age. One other limitation of the present study is that we did not assess the presence or extent of conduct disorder symptoms. Past research (c.f. Bauer, 1997; Bauer, 2001) has indicated that P300 amplitude in drug-dependent patients may be negatively correlated with the number of conduct disorder criterion behaviors exhibited prior to age 15.

The relationship between idiopathic psychosis and the psychoses that fall within the schizophrenia-spectrum is unclear. Several investigators (cf. Iacono et al. 2002, Moeller et al. 2004) have suggested that reduced P300 amplitude may be related to a latent trait associated with risk for both substance abuse and disinhibitory psychiatric disorder. Our finding of both P300 amplitude reduction and CPT-IP performance deficits in cocaine-dependent patients, many of whom displayed cocaine-induced psychosis, is consistent with this notion. However, because the groups with and without psychosis are not compared directly in the present study, the role of psychosis can only be done in an explorative fashion. Further study of cocaine-dependent patients with cocaine-induced psychosis using putative endophenotypes of risk for psychoses may yield insights regarding the relationship between cocaine-induced psychosis

and the schizophrenia spectrum. These data could then be used to support or refute the concept that psychosis exists on a continuum (cf. Thirithalli & Benegal, 2006).

Acknowledgment

This work was supported by a NARSAD Independent Investigator Award and K24 DA00520 and partially by R01DA019055.

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Figure 1. Grand Averaged Response to the Infrequent Stimuli

Grand averaged event-related potential waveform at Pz for the cocaine-dependent patient group (in red) and healthy control group (in blue) where the X-axis depicts the time in msec and Y-axis depicts μV .

Table 1

Demographic characteristics of the subject groups

	<u>Cocaine-Dependent</u> (n = 14)	<u>Healthy Control</u> (n = 15)
Age (years)	39.00 ± 5.52	34.27 ± 7.20
Gender (M/F)	7/7	7/8
Ethnicity		
Caucasian	5	10
African-American	8	2
Latino	0	1
Other	1	2
Smoking status		
Smoker	10	3
Nonsmoker	4	12

Table 2

Attention and Information Processing in Cocaine-Dependent Subjects and Controls

	<u>Cocaine-Dependent</u>	<u>Healthy Control</u>
P300 ^a		
Amplitude	3.93 ± 3.4	10.63 ± 5.2
Latency	331.00 ± 40.87	304.97 ± 24.88
CPT-IP indices ^b		
Numbers		
d'	1.37 0.57	2.05 0.84
ln b	0.18 0.78	0.30 0.63
Hits	0.69 0.19	0.79 0.16
RT hits	544.67 80.84	568.51 43.66
False alarms	0.23 0.14	0.15 0.08
Impulsivity index	0.34 0.22	0.20 0.13
Shapes		
d'	1.23 0.55	2.10 0.80
ln b	0.10 0.56	0.36 0.59
Hits	0.66 0.18	0.76 0.18
RT hits	517.38 77.49	552.51 41.24
False alarms	0.24 0.12	0.11 0.06
Impulsivity index	0.38 0.20	0.16 0.09

^a Means ± standard deviations for P300 amplitude and latency at electrode Pz in cocaine-dependent subjects and controls.

^b Means ± standard deviations for Continuous Performance Test, Identical Pairs version (CPT-IP) indices: d' is a measure of discriminability; ln β is a measure of response bias or decision criterion; hits is the proportion of correct responses to target trials; RT hits is reaction time for the correct responses; false alarms is the proportion of commission errors; impulsivity index = false alarm rate/rate of correct detections.