EEG and Evoked Potentials Alterations in Cocaine-Dependent Individuals

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INTRODUCTION

After two decades of epidemic cocaine use and extensive animal research, what is known about the effects of prolonged exposure to cocaine on the central nervous system (CNS) comes from human findings. Reports of neurological and cerebrovascular infarcts attributed to cocaine abuse and studies investigating CNS function of abstinent cocaine-dependent patients provide important insights into prolonged effects of cocaine on the human brain. The neurological and cerebrovascular infarcts investi-gated include strokes (Sloan and Mattioni 1992), seizures (Holand et al. 1992), transient ischemic attacks (Spivey and Euerle 1990), and headaches (Dhopesh et al. 1990). The studies of abstinent cocaine-dependent patients used neuropsychological evaluations, electroencephalogram (EEG), single photon emission computed tomography (SPECT), and positron emission tomography (PET) methodologies. The neurological infarcts appear to be at the one end of a continuum with subtle, but not trivial, CNS alterations at the other. These alterations, whether residual or permanent, may complicate treatment for cocaine dependence. The importance of treating these alterations needs to be addressed.

This chapter reviews EEG and event-related potential (ERP) data from cocaine-dependent subjects who are not seeking treatment. This research is ongoing at the National Institute on Drug Abuse (NIDA) Intramural Research Program (IRP). The results are compared to other published studies. Some of the data are in the process of being published elsewhere, and some of the data are very preliminary.

There are some problems in studying CNS alterations in abstinent cocaine abusers. First, cocaine use is often linked to other substance abuse, comorbidity with other psychiatric disorders is often present, and it is possible that the deficits observed predated cocaine abuse. Although these difficulties exist, it is possible to remove the confounds of polysubstance abuse and comorbidity statistically or by the use of appropriate experimental and control groups. If the

deficits predated substance abuse, they may be similar to those observed in populations at risk for substance abuse. If the deficits are different from those seen in at-risk populations, they may be due to prolonged drug abuse. Certainly, prospective research is needed to clarify this issue.

The EEG and ERP changes examined here do not parallel the dysphoric mood effects observed in abstinence. Dysphoric mood symptoms occur in abstinent cocaine-dependent patients and dissipate after 1 to 2 weeks (Satel et al. 1991; Weddington et al. 1990). The CNS alterations appear to persist beyond the dysphoric mood state and may be linked to relapse. The cocaine craving, which also persists, may be related to these CNS alterations.

BACKGROUND: PET, SPECT, AND EEG STUDIES

Changes in the cerebral glucose metabolism of cocaine abusers have been observed, and are reviewed elsewhere (London et al. and Volkow et al., this volume). SPECT studies of blood flow show areas of reduced cortical blood flow in cocaine abusers (Holman et al. 1991; Mena et al. 1990; Tumeh et al. 1990; Volkow et al. 1988; Weber et al. 1990). In these studies the sample size was often small, and the cocaine abuser may not have meet the criteria for cocaine dependence. The subjects also abused drugs other than cocaine. However, these studies do suggest the possibility of cortical perfusion deficits in cocaine abusers; further research with larger sample sizes and more clearly defined populations of cocaine-dependent patients are needed.

EEG studies in cocaine-dependent individuals appear to paint an inconsistent picture. In terms of the resting EEG, Alper and colleagues (1990) found increased EEG alpha and to a lesser extent increased EEG beta in cocaine abusers, while Bauer (1994) found no baseline differences in EEG between cocaine-dependent subjects and control subjects. Roemer and colleagues (1994) reported decreases in EEG delta activity. The present authors found increased EEG beta in cocaine-dependent subjects relative to established norms, and the percentage of EEG beta was corre-lated to self-reported cocaine drug history measures (Herning et al., under review). Thus, the four groups appear to have different findings.

EEG hyperactivity to modulated sensory stimuli was reported by Bauer (1993). The EEG studies suffer from the same problems as the

PET and SPECT studies. That is, the subjects are polysubstance abusers and the sample sizes are also small, but not as small as in PET and SPECT studies. The differences in EEG findings observed in cocaine-dependent subjects can possibly be explained in part by differences in EEG recor-ding and analysis procedures, but they may also be due to the heterogeneity of cocaine-dependent patients.

The neuropsychological investigations of cocaine-dependent patients suggest a possible underlying deficit in information processing (Herning et al. 1990; O'Malley et al. 1992; Roberts and Bauer 1993). Thus, the authors examined the ERPs of cocaine-dependent patients and compared them to control subjects. Bauer (this volume) also used the ERP metho-dology to study brain processing deficits in cocaine-dependent patients.

No attempt has been made in previous EEG studies to relate the magni-tude of the observed CNS alterations to the specific amount of cocaine used or the duration of cocaine abuse. The authors studied the EEG and cognitive ERPs of cocaine-dependent individuals, not currently depen-dent on other illicit drugs or alcohol, during monitored abstinence on a closed research ward. The hospitalized cocaine-dependent patients were tested at about 8 days of abstinence. The subjects' EEG and ERP findings were compared with that of control subjects or normative data and corre-lated with their self-reported drug histories.

METHOD

Subjects

The subjects (N = 37) were cocaine-dependent by "Diagnostic and Statistical Manual of Mental Disorders," 3d ed. rev. (DSM-III-R) criteria and were studied after about 9 days of monitored abstinence. An addi-tional sample of 31 subjects who abused cocaine but did not have a struc-tured psychiatric interview were included in the resting EEG tests. The cocaine-dependent subjects resided on a closed residential research unit. Abstinence was monitored by testing randomly obtained urine samples. The control subjects (N = 17) who had no substance use disorders except nicotine dependence and no other psychiatric disorders using DSM-III-R criteria were tested as outpatients. The nondrug-using status of the out-patient control subjects was verified by urine toxicology. The drug his-tory was obtained using the Addiction Severity Index (ASI). The ASI drug

history for cocaine-using subjects is presented in tables 1 to 3. All subjects were seronegative for human immunodeficiency virus (HIV).

EEG Recording Procedures

The EEG was collected during a resting recording session with the eyes closed. The EEG was recorded from the following International 10/20 scalp sites: F3, C3, P3, O1, F4, C4, P4, and O2. The ERPs were recorded from the following International 10/20 scalp sites: F3, Fz, P3, F4, Cz, P4, and Pz. The EEG recording was monopolar with the reference ipsilateral site at A1 or A2. Silver-silver chloride electrodes were used at all loca-tions. The EEG was amplified using a signal conditioning unit with 1 to 50 hertz (Hz) half-amplitude bandpass. The output from the amplifier was recorded on a personal computer with an analog-to-digital convertor. The EEG was displayed on the computer monitor as it was collected and the raw EEG data were saved on the computer disk. The EEG during the ERP tasks was amplified with 0.1 Hz to 100 Hz half-amplitude bandpass amplifiers and 60 Hz notch filter. Monitoring of EEG artifact was per-formed during both on-line collection and off-line processing.

During the recording of the EEG and ERPs, subjects sat in a reclining chair located in a sound-attenuated electronically shielded chamber. A minimum of 3 minutes of EEG was recorded during the eyes-closed

TABLE 1. ASI drug history: Number of days used in the last 30 days.

Drug	Substance abusers Mean and SD		Cocaine dependent Mean and SD	
Cocaine	5.7	6.6	20.2	7.6
Alcohol	8.7	7.3	9.6	8.1
Heroin	3.9	7.1	2.6	3.8
Marijuana	5.6	7.7	1.7	3.8
Amphetamines	0.6	2.9	0.1	0.2
Barbiturates	0.1	0.4	0.3	1.8
Benzodiazapines	0.3	1.9	0.3	1.2

TABLE 2. ASI drug history: Drug of use (number of months).

Drug	Substance abusers Mean and SD		Cocaine dependent Mean and SD	
Cocaine	87.0	75.8	93.0	75.8
Alcohol	168.9	89.9	121.9	102.2
Heroin	90.7	158.0	52.1	90.6
Marijuana	143.8	106.4	93.1	88.0
Amphetamines	34.4	78.1	12.0	43.8
Barbiturates	32.8	71.1	12.4	47.2
Benzodiazapines	21.8	61.8	13.2	38.4

TABLE 3. ASI drug history: Cocaine use.

Cocaine Measure	Substance abusers Mean and SD		Cocaine dependent Mean and SD	
g/week	0.61	0.99	3.66	5.40
g/month	2.38	3.91	12.40	14.36
Day/30 days	5.73	6.64	20.30	7.57
Months used	87.40	75.82	92.96	76.81

condition. During these 3-minute recordings, the percentage of EEG activity was determined for delta (1.3-3.5 Hz), theta (3.6-7.5 Hz), alpha (7.6-13.5 Hz), and beta (13.6-50.0 Hz) EEG bands using the clinical zero-cross method.

The EEG for the ERP collection was recorded on a personal computer with an analog-to-digital convertor. Each channel was sampled at 5.0-millisecond (ms) intervals using software developed by NIDA's IRP for this purpose. The sampling interval began 150 ms before stimulus onset and ended 850 ms after onset. An average ERP was calculated separately for the target and nontarget stimuli. The amplitude and latency for N1, P2, and P3 were measured for the target and nontarget ERPs.

ERP Tasks

During the auditory rare event monitoring (AREM) task, the subject was asked to count the number of rare tones in a series of rare and frequent tones. At the end of the series the researcher obtained the

subject's count of the rare tones. The tones were presented at the rate of one every 2seconds using the Neurological Workload Test Battery (NWTP). The task lasted about 4 minutes. Rare tone frequency was 1000 Hz, and the frequent tone frequency was 2000 Hz. Twenty percent of the tones were of the rare type. Both tones were 70 decibels (dB) standard pressure level (SPL) and 100 ms long. The tones were presented to the subject through a headset.

For the continuous performance task (CPT) and Sternberg Memory Task, event-related responses were elicited visually using letters presented on aTV monitor by the NWTB system. For the CPT task, the subject monitored a series of letters displayed on the screen, one at a time, and was required to press a button with the preferred hand when any letter repeated itself. For the Sternberg Memory Task, three or six letters were shown for 30 seconds and the subject was required to monitor a series of letters. When a letter from the test set appeared, the subject was to press a button with the preferred hand. When any other letter appeared, the subject was required to press another button with the nonpreferred hand. Each task lasted about 5 minutes. The letters subtended 100 of visual angle, were on the screen for 600 ms, and were presented at a rate of one every 2 seconds. The mean luminance of the screen was 40 candela per square meter (cd/m2). The TV monitor was 30 centimeters (cm) from the subject's eyes.

RESULTS

The mean percentage for the EEG beta band for the resting eyes-closed session is shown in table 4. The mean data for cocaine-dependent individuals (Herning et al., under review) and 31 additional substance abusers is compared with 30- and 40-year-old male norms. A description of the sample from which the norms were obtained is included elsewhere (Herning et al., under review). The mean percentages for both the

TABLE 4. Percentage of activity in beta band.

Electrode	30-year-old norms1		40-year-old norms1		Sustance abusers and cocaine-dependent subjects (N = 68)	
	Mean	1 SD	Mean	1 SD	Mean	1 SD
F3	23.0	2.3	23.0	3.0	38.4*	12.9
F4	21.0	2.0	22.0	2.9	37.0*	13.4
C3	22.0	2.3	23.0	2.9	39.0*	12.4
C4	23.0	2.3	24.0	3.0	39.2*	11.7
P3	21.0	2.3	20.0	2.0	34.8*	10.7
P4	22.0	2.3	21.0	2.9	34.2*	11.1
O1	20.0	2.3	20.0	2.9	35.3*	13.1
O2	20.0	2.3	20.0	2.9	32.4*	10.9

KEY: 1 = Commercial norms are from HZI Research Center (see Herning et al. 1994 for demographic information on this sample); * = indicates value is more than 3 SD above norms.

substance abusers and the cocaine-dependent patients were greater than the age-matched norms. The percentage of EEG beta was elevated at all electrode sites.

The authors tested whether the increased percentage of EEG beta was correlated with drug history variables from the ASI. If these increases in EEG beta were indeed due to cocaine use, a strong positive correlation with cocaine drug history measures should be present in the data. Since 13 drug history measures were used, the Bonferroni corrected probability was used to preserve a 0.05 confidence level for each electrode site ($p<-0.05/13$ or 0.0042). Table 5 lists these correlations for the cocaine drug history measures for all the subjects (N = 68). The increase in EEG beta at F3 and F4 was significantly correlated with the number of grams of cocaine these subjects used the week before admission to the research study. Correlations with other cocaine drug history measures approached significance. EEG alpha was correlated with months of cocaine use for

TABLE 5. Correlation between EEG beta and self-reported cocaine use: All subjects (N = 68).

	Electrode							
Self-report measure	F3	C3	P3	O1	F4	C4	P4	O2
Day/30 days	0.25	0.16	0.06	0.02	0.26	0.06	0.08	-0.02
Months of use	-0.13	0.06	0.00	-0.04	-0.06	0.03	0.01	-0.11
g/week	0.46*	0.31	0.07	0.07	0.45*	0.09	0.03	-0.03
g/month	0.30	0.13	-0.05	-0.08	0.28	-0.03	-0.09	-0.11
Age	0.05	0.04	0.12	-0.07	0.07	-0.07	0.10	0.00

KEY: * = $p < 0.05$ (13 drug history measures) = 0.0042.

C4 and P4 electrode sites. However, none of the other substances used by these subjects was correlated with EEG beta.

The grand means waveforms are plotted for the AREM, CPT, and Sternberg tasks for both the cocaine-dependent subjects and control sub-jects in figures 1-4. The cocaine-dependent individuals had longer N1 (group by electrode: $F(2,82) = 9.24$, $p < 0.005$) and P2 (group: $F(1,38)=3.96$, $p < 0.05$) latencies in the AREM task and reduced P2 amplitudes in the CPT (group: $F(1,38) = 11.75$, $p < 0.005$) and Sternberg Memory Tasks (group by electrode interaction: $F(2,84) = 4.95$, $p<0.01$). The cocaine-dependent subjects had reduced P3 amplitudes in all tasks (AREM group by electrode interaction: $F(2,82) = 3.12$, $p < 0.05$; CPT group: $F(1,38)= 24.13$, $p < 0.001$; Sternberg group: $F(1,38) = 3.42$, $p<0.07$). These differences can be observed in the grand averages. The ERP measures that significantly differed between groups were correlated with drug history measures (see table 6). The N1 latency delay in the AREM task was correlated with the number of days alcohol was used in the last 30days, and the P2 latency delay was correlated with self-reports of the number of months of cocaine and alcohol use. The reduction in P3 amplitude was modestly, but not significantly, correlated with self-reported alcohol, marijuana, and opiate use, but not with cocaine use. Perhaps as the sample size in this study increases, these latter correlations will become significant.

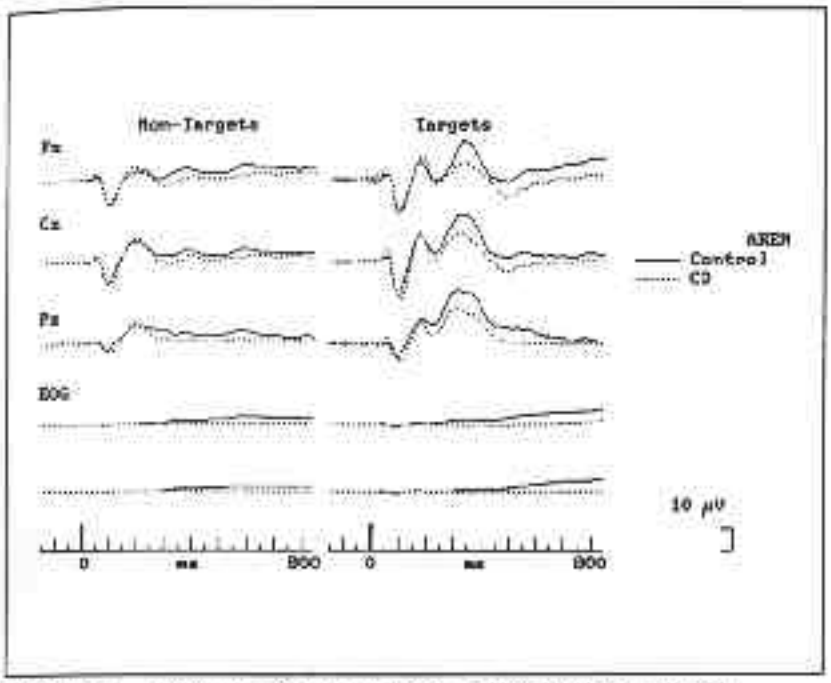

FIGURE 1. *The grand average ERPs are plotted for control subjects (N = 17) and cocaine-dependent subjects (CD)(N = 27) for the AREM task. The left column presents the ERP for the nontargets and the right column presents the ERP for the targets. The N1 is the negative-going component (down) at about 100 ms, the P2 is the positive-going (up) component at about 200 ms, and P3 the postive-going component at about 350 ms. The bottom two waveforms in each column are eye movements (EOG) recorded from above to the side of the left eye and from above the left eye to A$_1$.*

KEY: Fz = frontal scalp position; Cz = central scalp position; Pz = parietal scalp position.

DISCUSSION

The amount of beta activity in the resting EEG was elevated, and the N1, P2, or P3 component of the ERP to task-relevant stimuli was reduced or delayed in this sample of abstinent cocaine abusers. The percentage of

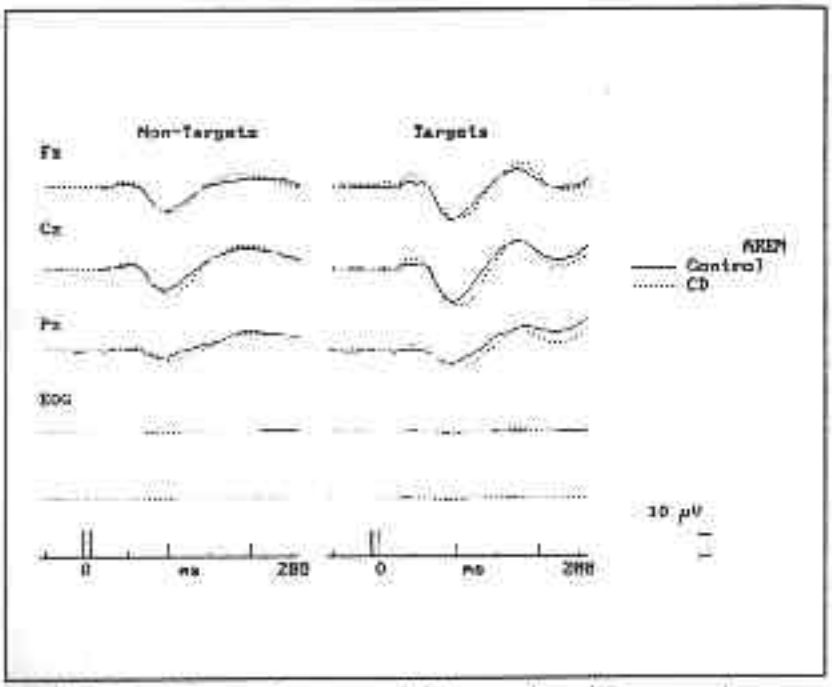

FIGURE 2. *The grand average ERPs are plotted for control subjects (N = 17) and cocaine-dependent subjects (CD)(N = 27) for the AREM task. The first 200 ms after the onset of the stimuli is shown so that the latency delays in N1 and P2 can be observed. The left column presents the ERP for the nontargets, and the right column presents the ERP for the targets. The N1 is the negative-going component (down) at about 100 ms, and the P2 is the positive-going (up) component at about 200 ms. The bottom two waveforms in each column are eye movements (EOG) recorded from above to the side of the left eye and from above the left eye to A$_1$.*

KEY: Fz = frontal scalp position; Cz = central scalp position; Pz = parietal scalp position.

beta in the EEG of the sample exceeded age-matched norms. The N1 and P2 components, as well as the P3 component of the ERPs elicited in several cognitive tasks, were altered when compared to a sample of control subjects. The percentage of EEG beta and P2 latency was correlated with the self-reported amount of cocaine use. The amount of cocaine used in the last week before admission was correlated with EEG

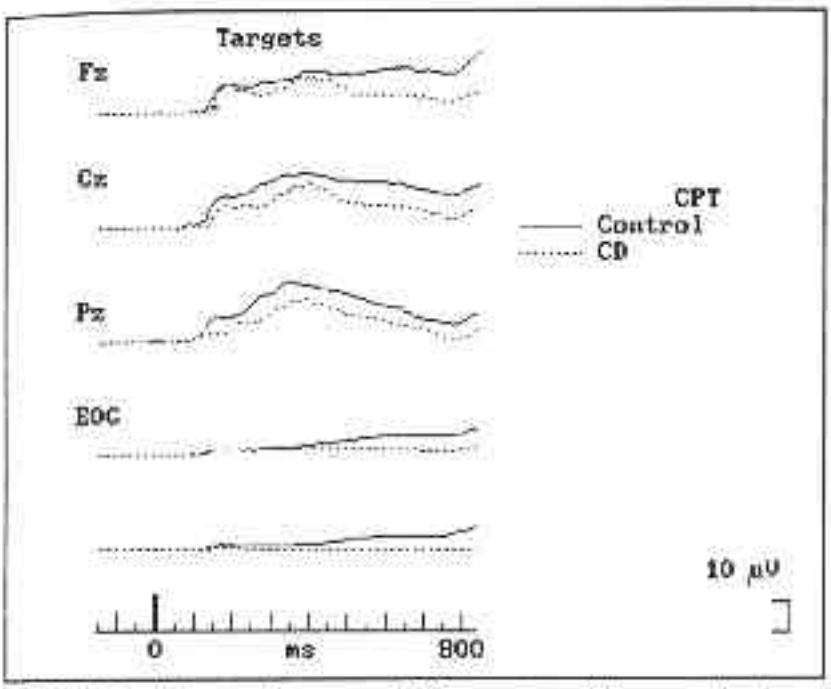

FIGURE 3. *The grand average ERPs are plotted for control subjects (N = 17) and cocaine-dependent subjects (CD) (N = 27) for the CPT. Only the targets are shown. The P2 is the positive-going (up) component at about 200 ms, and P3 is the positive-going component at about 350 ms. The bottom two waveforms in each column are eye movements (EOG) recorded from above to the side of the left eye and from above the left eye to A$_1$.*

KEY: Fz = frontal scalp position; Cz = central scalp position; Pz = parietal scalp position

activity in the beta band at both frontal electrode sites. P2 latency was correlated with the number of months of cocaine and alcohol use. P3 amplitude was only weakly correlated with self-reported drug history measures.

The EEG findings agree in part with those of Alper and colleagues (1990) and Roemer and colleagues (1994), but not with Bauer (1993, 1994, this volume). In the Alper study, the EEG of the cocaine-dependent indi-viduals was also compared to age-matched norms. Those researchers

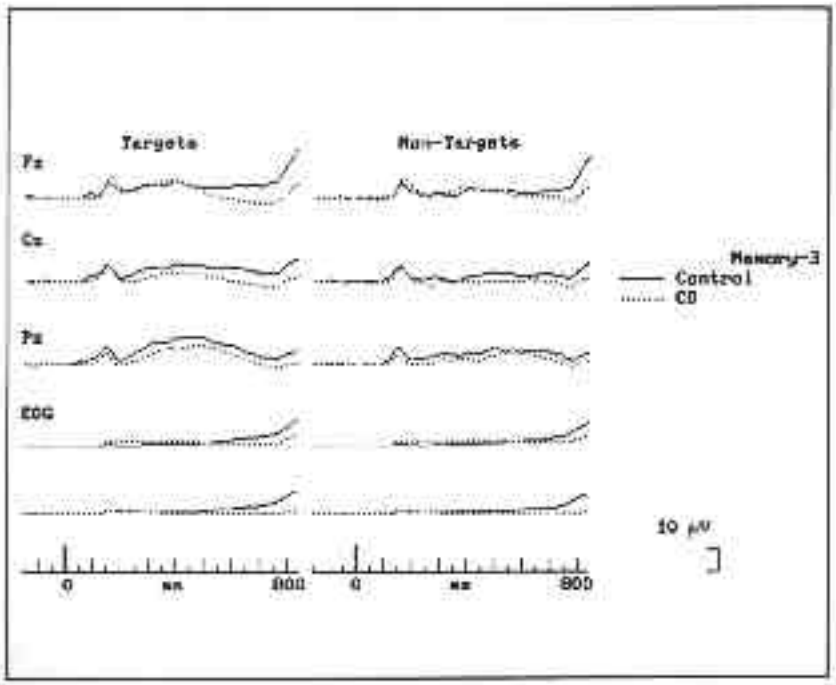

FIGURE 4. *The grand average ERPs are plotted for control subjects (N = 17) and cocaine-dependent subjects (CD) (N = 27) for the Sternberg Memory Task with a 3-letter set size. The left column presents the ERP for the targets, and the right column presents the ERP for the nontargets. The P2 is the positive-going (up) component at about 200 ms, and P3 is the postive-going component at about 350 ms. The bottom two waveforms in each column are eye movements (EOG) recorded from above to the side of the left eye and from above the left eye to A$_1$*

KEY: Pz = frontal scalp position; Cz = central scalp position; Pz = parietal scalp position.

found elevated levels of beta at frontal electrode sites and increased EEG alpha over the cortex in seven cocaine-dependent crack users. The time of recording relative to the self-reported last use of cocaine varied considerably. Roemer reported reduced EEG delta and theta. The authors found increased EEG beta with reduced delta and theta, but the self-reported use measures were correlated with the increase in beta and not

TABLE 6. Correlation between ERP measures and self-reported drug use: Cocaine-dependent subjects (N = 27).

	Task and ERP measure						
Self-report measure	Oddball			Paired CPT		Sternberg Memory	
	N1L	P2L	P3A	P2A	P3A	P2A	P3A
Cocaine							
Days/30 days	0.20	0.24	-0.11	0.01	0.07	-0.38	-0.13
Months of use	-0.10	0.57*	0.13	-0.05	0.31	0.32	0.08
g/week	0.32	-0.12	-0.08	-0.18	-0.26	-0.22	-0.27
g/month	0.43	-0.15	0.04	-0.11	-0.15	-0.23	-0.19
Alcohol							
Days/30 days	0.62*	-0.25	-0.24	0.01	-0.36	-0.25	-0.38
Months of use	-0.18	0.53*	0.15	0.11	0.35	-0.10	0.04
Marijuana							
Days/30 days	0.11	0.04	0.20	-0.06	0.14	-0.22	0.42
Months of use	-0.25	0.47	0.22	-0.12	0.42	0.35	0.12
Heroin	0.04	0.31	-0.39	-0.25	-0.08	-0.34	-0.37
Days/30 days	0.04	0.31	-0.39	-0.25	-0.08	-0.34	-0.37
Months of use	-0.10	0.41	-0.31	-0.12	-0.07	-0.15	-0.16

KEY: * = $p < 0.005$ or 0.05 for 10 drug history measures; N1L=-N1latency; P2L = P2 latency; P2A = P2 amplitude; P3A=P3-amplitude.

with the decreases in delta and theta (Herning et al., under review). Bauer reported no difference in the resting EEG activity in a sample of cocaine-dependent patients when they were compared to control subjects. Bauer reported EEG hyperactivity to modulated sine, but not square, wave sensory stimuli in cocaine-dependent patients. In the present sample of cocaine-dependent individuals, the authors found higher levels of beta activity in the resting EEG after about 10 days of monitored abstinence on a closed research ward.

Several factors may have contributed to the differences in results. First, a major difference among the studies was the frequency range of the EEG beta band. Alper used 12.5 to 25.0 Hz beta band and Bauer used 12.5 to 30.0 Hz band, while the authors used 13.6 to 50.0 Hz. Roemer may have also used a small EEG beta band, but these details were not reported. The peak frequency in the authors' subjects' individual beta bands was about 26 Hz. With the smaller beta band,

the Alper group and Bauer eliminated an important part of the EEG beta activity in their samples. Second, the subjects in the Alper, Bauer, and Roemer studies were seeking treatment; the majority of the authors'subjects were not. It is unclear how this may have contributed to the difference in results. As the authors continue to monitor the EEG of larger samples of cocaine-dependent subjects, the differences may be resolved or explained.

Bauer (this volume) and Amass and colleagues (1990) reported a reduced P3 component in cocaine-dependent subjects. P3 or P300 is an electro-physiological measure related to the intensity of stimulus evaluation observed during the updating of working memory (Donchin and Coles 1988; Johnson 1993). In this preliminary study, the P3 was reduced in cocaine-dependent subjects as compared with control subjects. However, the magnitude of the reduction was not correlated with self-reported cocaine drug history measures. The reduction in P3 may have predated the cocaine abuse. A reduced P3 amplitude was also observed in adoles-cent boys who used cocaine or heroin (Herning et al. 1989). Reduced P3 amplitudes were observed in young sons of alcoholic fathers (Polish et al. 1994), children diagnosed as having attention deficit-hyperactivity disorder (Holcomb et al. 1986; Klorman et al. 1979, 1990; Loiselle et al. 1980; Satterfield et al. 1988; Taylor and Keenan 1990), and in antisocial boys (Raine and Venables 1987). These groups of children are at increased risk for substance abuse (Kofoed and MacMillan 1986; Lewis 1984; Mannuzza et al. 1993; Sutker 1984; Weiss et al. 1985). Thus, the reduction in P3 amplitude may have predated substance abuse.

N1 and P2 alterations in cocaine-dependent individuals have not previously been reported. In the AREM task, both N1 and P2 components were delayed in the cocaine-dependent subjects. These delays were correlated with cocaine and alcohol use. While visual P2 amplitudes in the CPT and Sternberg Memory Tasks were reduced, these decreases were not correlated with drug history measures. Reduced visual P2 components were observed in children diagnosed with attention deficit-hyperactivity disorder (Halliday et al. 1976; Klorman et al. 1979, 1990; Prichep et al. 1976), sons of opiate-abusing mothers (Guo et al. 1994), and sons of alcoholic fathers (Begleiter et al. 1987). Thus, only the delays in the auditory P2 components may be related to prolonged cocaine abuse, but the reduction of visual P2 observed in this study may have predated the subjects' drug abuse.

Excess EEG beta activity appears to be a sign of cocaine dependence (Herning et al., under review). The authors' study extends these findings using a much larger sample. Both the EEG alpha and beta activity in these cocaine abusers were correlated with self-reported recent cocaine use. The abundance of EEG alpha and beta was not correlated with depression as measured by the Beck Depression Inventory. These EEG alterations in cocaine abusers are due to prolonged effects of cocaine on the brain, and they may be related to the reduced blood flow in frontal, central, and temporal cortical areas reported in cocaine abusers (Holman et al. 1991; Mena et al. 1990; Tumeh et al. 1990; Volkow et al. 1988; Weber et al. 1990).

Niedermeyer (1963) first reported that vertebrobasilar artery insufficiency was associated with increased EEG beta. This interpretation is supported by reported correlations between decreases in regional cortical blood flow and increased levels of EEG beta observed in patients with spinocerebellar degeneration (Nagata et al. 1993). The reductions in cortical perfusion may lead to neuron death, and the increased EEG beta may be related to this neuron loss. Chronic use of cocaine was associated with cortical atrophy (Pascual-Leone et al. 1991). Increases in EEG beta were reported to increase with age and to be related to neuron loss (Iyma et al. 1992; Shearer et al. 1989).

Further support for the notion that the increases in EEG beta and, perhaps, the information processing alterations are due to reductions in cortical perfusion come from the authors' work with nimodipine (Herning et al., in press-a, in press-b.). Nimodipine is a dihydropyridine calcium channel blocker used in the treatment of cerebrovascular vasospasm associated with subarachnoid hemorrhage. Nimodipine increased cerebral blood flow by dilatation of cortical arterioles (Godfraind et al. 1990; Oliver et al. 1993) and reduced vasospasm (Fleckenstien-Gruin and Fleckenstien 1990). The EEG of elderly patients was normalized after chronic nimodipine treatment (Ulrich and Stieglitz 1988). Acute doses of nimodipine reduced EEG beta and increased EEG alpha in substance abusers (Herning et al., under review). Nimodipine also blocked the decline of the P3 component with repeated testing of auditory and visual ERP in two cognitive tasks (Herning et al., under review). The relation-ship between normalizing CNS function and reducing craving needs to be investigated. The authors' data provide a strong rationale for treatment of cocaine dependence with nimodipine at doses that produced changes in EEG and ERP measures.

Cocaine-induced euphoria is associated with the reduction of cortical activity and perhaps with the loss of cortical inhibition in subcortical areas (Herning et al. 1994). Given the cortical perfusion deficits and neurophysiological alterations observed in abstinent cocaine-dependent patients, it is tempting to suggest that cocaine craving is the result of reduced cortical inhibition in subcortical areas. With reduced cortical regulation of these areas, subcortical areas may be more responsive to cocaine-related cues. Improving cortical perfusion and restoring neural functioning to borderline neurons may reduce craving.

In conclusion, the relative abundance of EEG beta is increased and ERP information processing components are delayed in cocaine-dependent individuals. These alterations in CNS function may be related to the reduced cortical blood flow observed in cocaine abusers using SPECT and PET methodologies. These observations suggest that the repeated use of cocaine may be associated with abnormal brain functioning, resulting in cognitive deficits. Further studies are needed to assess whether these changes are associated with craving for cocaine and the implications they have for treatment.

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