Cocaine Abusers Have Reduced Auditory P50 Amplitude and Suppression Compared to Both Normal Controls and Alcoholics

George Fein, Christie Biggins, and Shane MacKay

The auditory P50 evoked response to click stimuli was recorded from 10 2-week abstinent African-American chronic cocaine abusers and 10 African-American non-substance-abusing controls. Stimuli consisted of pairs of clicks with a 500-msec interval between clicks in a pair, and a 7–8 sec interval between pairs of clicks. After averaging responses to 100 pairs of clicks and digital bandpass filtering between 10 and 50 Hz, P50 amplitude to the first and the second click was measured. The conditioning/testing (C/T) ratio, an index of P50 suppression, was computed as the ratio of P50 amplitude to the second compared to the first click. Chronic cocaine abusers had markedly diminished P50 amplitudes and increased C/T ratios (indicating decreased P50 suppression) in comparison to the controls. These P50 abnormalities were not seen in additional Caucasian gay/bisexual comparison groups of active alcoholics (n = 15) and non-substance-abusing controls (n = 10). Thus, decrements in P50 amplitude and P50 suppression appear to be specific to cocaine abuse, and to differentiate cocaine abuse from alcohol abuse. A response analogous to P50 can be measured in animals, facilitating the development of animal models of this cocaine effect.

Key Words: Cocaine, P50, auditory ERP, sensory gating, alcoholism.


Introduction

Human clinical studies of cocaine effects on brain function are confounded by concurrent alcohol and polydrug abuse in the vast majority of cocaine abusers. If cocaine has direct pharmacologic effects on the brain that are distinct from the effects of alcohol, measures of central nervous system (CNS) function that distinguish cocaine abusers not only from normal controls, but also from alcoholics, should exist. We report here an investigation of the P50 component of the auditory event-related potential (ERP) as a candidate measure for distinguishing cocaine effects on the CNS from those of alcohol.

The auditory P50 is a brain electrical response in humans that occurs about 50 msec after brief auditory stimuli (usually clicks) and has maximal amplitude in recordings at or near the vertex when referenced to earlobe or mastoid. P50 amplitude is decreased when trains of stimuli are presented, with this decrease becoming larger as the interval between consecutive stimuli decreases, a phenomenon known as P50 suppression or P50 gating.
P50 is usually studied using either a repetitive stimulus paradigm where responses to a continuous train of stimuli (e.g., 1/sec) are recorded, or in a conditioning/testing paradigm where responses to pairs of stimuli are recorded, with long intervals between stimulus pairs (e.g., > 7 sec) and shorter intervals within stimulus pairs (e.g., 5 sec). The conditioning/testing paradigm allows separate measurement of P50 generation and P50 gating, and has been fruitful in elucidating different neural mechanisms underlying these two phenomena. Animal models of P50 generation and gating have been developed for the cat (wave A) (Dickerson and Buchwald 1991; Erwin and Buchwald 1987; Harrison et al 1990) and the rat (the N40 response) (Adler et al 1986, 1988; Bickford-Wimer et al 1990). Human (Buchwald et al 1991), cat, and rat studies agree in implicating nicotinic cholinergic neurons in P50 generation, and noradrenergic and dopaminergic neurons in P50 modulation.

In clinical research, the auditory P50 has been primarily used in the study of schizophrenia, where there are two distinct P50 abnormalities: a) reduced P50 amplitude; and b) reduced P50 suppression (Freedman et al 1983, 1987a; Nagamoto et al 1989). The model developed by Freedman’s group is that two different brain neurotransmitter system disturbances are involved in the two types of P50 abnormalities in schizophrenics, with hyperactivity of the dopamine neurotransmitter system resulting in reduced P50 amplitude, and hyperactivity of the noradrenergic neurotransmitter system resulting in reduced P50 gating. The idea that dopaminergic hyperactivity causes reduced P50 amplitude in unmedicated schizophrenic patients is supported by the normalization of P50 amplitude by neuroleptic manipulation of dopamine, with this normalization associated with a fall toward normal values in serum levels of the dopamine metabolite, plasma-free homovanillic acid (Adler et al 1990; Straunis et al 1982). Additional studies in the rat and human support this model (Adler et al 1988; Johnson and Adler 1993; Stevens et al 1993) wherein the dopaminergic system modulates P50 amplitude while the noradrenergic system modulates P50 suppression.

Catecholaminergic and dopaminergic mediated effects on the N40 (analog of the P50) response in rats have been demonstrated secondary to acute administration of amphetamine (Stevens et al 1991) and PCP (Miller et al 1992); however, the human P50 component has received relatively little attention in the drug and alcohol abuse literature. Acute low-dose alcohol reduces P50 amplitude and suppression (Freedman et al 1986; 1987b), whereas chronic alcohol abuse does not affect P50 except in a subset of alcoholics where there is a P50 suppression reduction during a brief hypomanic period associated with early abstinence (Adler, personal communication). In this article, we report comparisons between cocaine abusers, alcoholics, and nonabusing controls on measures of P50 amplitude and P50 suppression.

Methods

Subjects

Ten male African-American chronic heavy cocaine users (mean age ± SD = 41.4 ± 7.4 years) were studied. Subjects were screened to exclude those with any major psychiatric or neurologic disorder except those secondary to chronic substance abuse. Subjects were not excluded for episodes of substance-abuse-associated head trauma with loss of consciousness if these episodes were not serious enough to require hospitalization. All cocaine-abusing subjects were inpatients on the Substance Abuse Inpatient Unit (SAIU) at the San Francisco Department of Veterans Affairs Medical Center. By self-report, recent cocaine use in the substance-abusing group averaged 10.85 (± 4.7) grams of crystalline cocaine per week with a range of 3–17.5 g. Mean duration of use was 11.23 (± 8.1) years with a range of 3–23 years. Mean alcohol use was 5.3 (± 5.5) drinks per day. Six of the 10 cocaine-abusing subjects met DSM-III-R criteria for alcohol abuse and dependence (APA 1987). Marijuana use was common; needle use was rare. One subject had a past history of regular LSD use. Only one subject reported experiencing head trauma with loss of consciousness. For all SAIU patients, recordings were obtained in the second week after cessation of cocaine and/or alcohol use.

Ten African-American non-substance-abusing men served as control subjects (mean age = 37.6 ± 6.5 years). The groups did not differ significantly on age (t = 1.22, p = .24). Control subjects were recruited from the community, and met all psychiatric and neurologic exclusionary criteria. Alcohol use varied from 0 to 40 drinks per month (mean 10.3 ± 14.2).

In addition to the primary study samples of African-American men delineated above, P50 data from two samples of HIV-seronegative [established by polymerase chain reaction (PCR) testing] gay/bisexual Caucasian males were available for comparison to assess the specificity of findings. These samples had been recruited into HIV-seronegative control groups for a study of the effects of chronic alcohol abuse on the CNS morbidity of HIV and also met the above exclusionary criteria. One sample consisted of non-substance-abusing controls (n = 10, mean age = 35.7 ± 11.1 years, mean alcohol use = 12.6 ± 9.8 drinks per month), and the other sample consisted of currently drinking alcohol abusers (n = 15, mean age = 38.3 ± 9.4 years). By self-report, the alcohol abusers drank at least 120 drinks per month (avg. 195 drinks/
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Figure 1. The two electrode montages used to gather the data. The electrodes common to both montages are in italicized bold.

EP Recording

Data were recorded from either 14 or 30 electroencephalogram (EEG) channels using an electrode cap with tin disk electrodes (Electro-Cap International, Eaton, OH) referenced to a tin electrode clipped to the left earlobe. For the analyses reported here, either the vertex channel alone, or a common set of 11 electrodes was used. Figure 1 displays the two electrode montages, with the common set of electrodes in bold. Vertical eye movements were monitored via gold cup electrodes placed above and below the right eye, and horizontal eye movements were monitored via electrodes placed at the lateral canthi. All impedances were below 5000 Ω and signals were amplified 50,000 times by a Grass Model 12 Neurodata Acquisition System with analog filters at 1 and 1000 Hz. Stimulus presentations were controlled and data were collected by ERP SYSTEM Software (Neurobehavioral Laboratory Software) and an Analog Devices RTI 800-815/F laboratory interface card on a 20-MHz Intel 80386-based personal computer. Data were sampled for 200 msec at a 2000-Hz within-channel resolution beginning 20 msec prior to stimulus presentation for each click. Individual trials were rejected if activity on either eye movement channel exceeded ± 75 microvolts. Data were collected until there were 100 single trials that did not meet the eye movement channel rejection criteria.

Auditory Stimulation

Click stimuli were created by amplification of a 0.05-msec square wave generated by the Analog Devices D/A converter. The square waves were passed through a Hewlett-Packard 350D Attenuator, amplified by a Pioneer SX-2300 stereo receiver/amplifier and delivered to the subject over Realistic NOVA’20 headphones (Tandy Corporation, Houston, TX). Stimulation was binaural with the same monaural signal delivered to each ear of the headphones. After each subject’s threshold for detecting the click stimuli was established using a method of limits procedure, stimuli were presented at 55 dB above threshold. Each trial consisted of the presentation of two clicks, 500 msec apart. The time from the beginning of one trial to the beginning of the next trial varied randomly between 7 and 8 sec.
Figure 2. Average EPs before and after filtering for an African-American control subject (top) and for a cocaine addict (bottom). The 10–50-Hz bandpass filter removes nearly all influence of the N100 and P200 components, while passing the P50 response.

Procedure

During the session, the subjects were relaxed, awake, and seated upright in a room that was quiet but not acoustically isolated. They were instructed to sit quietly, listen to the clicks, and try to keep their eyes still.

Evoked Potential Waveform Analysis

All data were analyzed blind with respect to subject's group membership. Average waveforms for each subject were constructed from the single trial data after elimination of trials with eye movement artifact. To further diminish the effects of those eye movements that were below the rejection criterion, the data were submitted to a frequency domain eye movement correction procedure (Gasser et al 1985). The data were then digitally filtered between 10 and 50 Hz prior to measurement of P50 amplitude using a sharp digital bandpass filter we previously developed and validated for analysis of P50 (Cardenas et al 1993; Jerger et al 1992). Finally, P50 amplitudes were measured both by 1) picking peaks in the 40–70-msec poststimulus interval on vertex channel recordings; and 2) using topographic maps at each timepoint in the same poststimulus interval to help identify the presence or absence and topographic maximal amplitude of the P50 component.

For the vertex recording analyses, a computer-assisted procedure was used to measure the P50 peak amplitude from the subject's average Cz channel recording following each of the two clicks. The P50 peak was defined as the greatest amplitude between 40 and 70 msec after stimulus presentation. Because the P50 often overlaps in time with the beginning of the N100 component, the absolute amplitude of the P50 peak can be confounded by the occurrence of the N100. As we have demonstrated previously (Jerger et al 1992), this effect is markedly reduced by the very sharp 10–50-Hz bandpass filter. Figure 2 presents an average evoked potential (EP) before and after filtering for a representative subject from the cocaine and African-American control groups. (Notice that the 10–50-Hz bandpass filter removes nearly all influence of the N100 and P200 components while passing the P50 response.) To further minimize this effect, P50 amplitude was measured from the preceding negativity.
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Figure 3. Grand average waveforms to the first and second click for the cocaine addicts and the African-American controls. Individual averages were latency-adjusted to a P50 latency of 50 msec before grand averaging.

The presence of a P50 component on the topographic maps was indicated by a vertex (or close to vertex) peak distribution occurring within the 40–70-msec time window after the first click. If a P50 was identified in the topographic maps, the averages were transformed to the average reference using just the 11 electrodes that were common to the two electrode montages (to eliminate differences in amplitude due to differences in the number and location of channels contributing to the average reference). A computer-assisted procedure was used to pick P50 peak amplitude following each of the two clicks from the subject’s average waveform at the channel most closely corresponding to the location of the peak in the topographic map of the first click. Topographic analysis has two advantages over peak picking: 1) identification of the component is performed using all data channels and is therefore more resistant to the effects of noise; and 2) peak location is not constrained to fall at a specific site, such that the slight differences between subjects in the orientation of the component generators are not ignored.

Results

Analysis of Vertex Waveforms

The P50 component to the first click was readily apparent in all waveforms. A P50 to the second click could be identified in all subjects except one Caucasian control subject. A priori comparisons between African-American cocaine abusers and controls revealed cocaine-abuse-associated reductions in P50 amplitude to the first click ($t_{18} = 3.02, p = .007$) and increases in the C/T ratio ($t_{18} = 2.58, p = .024$). Figure 3 illustrates these effects in the grand average waveforms for the these two samples. P50 amplitudes and C/T ratios for all samples are presented in Table 1 and Figure 4. In Figure 4, the data for the African-American cocaine abusers are displayed as empty or filled circles depending on whether the subject did or did not also meet DSM-III-R criteria for alcoholism. Although the

Table 1. Vertex Analyses: Means and Standard Deviations for P50 Amplitude and Latency to the First Click, Second Click, and C/T Ratio

<table>
<thead>
<tr>
<th></th>
<th>Click 1 Mean</th>
<th>Click 1 SD</th>
<th>Click 2 Mean</th>
<th>Click 2 SD</th>
<th>C/T Ratio Mean</th>
<th>C/T Ratio SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cocaine addicts</td>
<td>1.23</td>
<td>0.66</td>
<td>1.02</td>
<td>0.71</td>
<td>0.97</td>
<td>0.71</td>
</tr>
<tr>
<td>African-American controls</td>
<td>2.55*</td>
<td>1.21</td>
<td>0.74</td>
<td>0.51</td>
<td>0.33*</td>
<td>0.32</td>
</tr>
<tr>
<td>Caucasian controls</td>
<td>3.03*</td>
<td>1.51</td>
<td>1.01</td>
<td>0.81</td>
<td>0.32*</td>
<td>0.24</td>
</tr>
<tr>
<td>Active alcoholics</td>
<td>2.72*</td>
<td>1.75</td>
<td>1.26</td>
<td>0.89</td>
<td>0.55</td>
<td>0.38</td>
</tr>
</tbody>
</table>

Notes: Differences among the African-American controls, Caucasian controls, and active alcoholics for click amplitudes and the C/T ratio: all $n < 1.71, all ps > .10$.

* Different from cocaine addicts, $p < .01$.

* Different from cocaine addicts, $p < .05$. 

Figure 3 illustrates these effects in the grand average waveforms for the these two samples. P50 amplitudes and C/T ratios for all samples are presented in Table 1 and Figure 4. In Figure 4, the data for the African-American cocaine abusers are displayed as empty or filled circles depending on whether the subject did or did not also meet DSM-III-R criteria for alcoholism. Although the
Figure 4. Vertex analyses P50 amplitude distributions for each of the subject groups. The group median is indicated by the horizontal line through each distribution.
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4 4 4

-2.0

1.5

Cocaine Addict

African American Control

Caucasian Control

Active Alcoholic

Abstinent Alcoholic

Figure 5. Topographical maps from a representative subject in each group.

numbers are very small, that display suggests that the P50 abnormalities are similar in African-American cocaine abusers with or without concomitant alcoholism. Post hoc comparisons between the primary study groups and the gay/bisexual male Caucasian samples of HIV-negative active chronic alcohol abusers and nondrinkers showed the reductions in P50 amplitude to the first click and increases in the C/T ratio to be present only in the African-American cocaine abusers (see Table 1 and Figure 4). Although there were too few subjects to warrant statistical comparisons, the data from the three SAIU 2-week-abstinent alcoholic subjects were similar to those of the actively drinking alcoholics in not showing evidence of either reduced P50 amplitude or increased C/T ratios.

Analysis of Topographic Data

The P50 component was identified in the topographic maps to the first click for all subjects. The peak location of the P50 component occurred at the various electrode locations with the following frequencies: C3: 1; C4: 3; Cz: 31; F3: 1; Fz: 10; and Pz: 2, with Figure 5 presenting

Table 2. Topographical Analyses: Means and Standard Deviations for P50 Amplitude and Latency to the First Click, Second Click, and C/T Ratio

<table>
<thead>
<tr>
<th>N</th>
<th>Click 1 Mean</th>
<th>SD</th>
<th>Click 2 Mean</th>
<th>SD</th>
<th>C/T Ratio Mean</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cocaine addicts</td>
<td>10</td>
<td>0.91</td>
<td>0.38</td>
<td>0.86</td>
<td>0.34</td>
<td>1.02</td>
</tr>
<tr>
<td>African-American controls</td>
<td>10</td>
<td>1.78*</td>
<td>0.63</td>
<td>0.58*</td>
<td>0.24</td>
<td>0.36*</td>
</tr>
<tr>
<td>Caucasian controls</td>
<td>10</td>
<td>1.88*</td>
<td>0.78</td>
<td>0.79</td>
<td>0.55</td>
<td>0.44*</td>
</tr>
<tr>
<td>Active alcoholics</td>
<td>15</td>
<td>1.92*</td>
<td>1.11</td>
<td>0.90</td>
<td>0.70</td>
<td>0.43*</td>
</tr>
</tbody>
</table>

Notes. Differences among the African-American controls, Caucasian controls, and active alcoholics for click amplitudes and the C/T ratio: all r < 1.41, all ps > .17.

* Different from cocaine addicts, p < .01.

* Different from cocaine addicts, p < .05.

* Different from cocaine addicts, p < .001.
Figure 6. Topographical analyses P50 amplitude distributions for each of the subject groups. The group median is indicated by the horizontal line through each distribution.

topographic maps from a representative subject in each group. The results of group comparisons on the P50 measures derived from the topographic analyses were almost identical to those from the analysis of the vertex waveforms, with the topographic analyses proving more powerful in detecting group differences. P50 amplitudes and C/T ratios for all groups are presented in Table 2 and Figure 6. As above, Figure 6 suggests that the P50 abnormalities are similar in African-American cocaine abusers with or without concomitant alcoholism. A priori comparisons reveal that, compared to the African-American controls, the African-American cocaine abusers had lower P50 amplitudes to the first click ($t_{18} = 3.78, p = .002$) and greater C/T ratios ($t_{18} = 4.54, p = .0002$). Post hoc comparisons revealed that the reductions in P50 amplitude to the first click and increases in the C/T ratio were present only in the African-American cocaine abusers (see Table 2 and Figure 6). Finally, the data from the three 2-week-abstinent alcoholic subjects did not evidence either reduced P50 amplitude to the first click or an increased C/T ratio, both consistent with the data from the actively drinking alcoholics and non-substance-abusing controls.

Discussion

The major finding of this study is that P50 amplitude and suppression are dramatically decreased in chronic cocaine abusers compared to both normal controls and chronic alcoholics. To our knowledge, this is the first clinically applicable neurophysiological measure that differentiates cocaine abusers not only from normal controls, but also from chronic alcoholics. We have recently shown that the auditory P50 is unaffected by powerful attentional manipulations (Jerger et al 1992) and thus reflects basic neurophysiological processing of auditory information. This work, together with the literature reviewed earlier regarding neurotransmitter system effects on the P50, supports the hypothesis that the P50 effects we observed are a consequence of differences in the status of neuronal and/or neurotransmitter systems in the cocaine abusers versus the normal controls and chronic alcoholic controls.

We do not know whether these P50 disturbances reflect damage to neuronal systems and/or pathways, or direct effects of cocaine on neurotransmitter system function. Based on the P50 neurotransmitter studies in animals and schizophrenics, the findings reported here would indicate increased dopaminergic and noradrenergic activity in 2-week-abstinent cocaine abusers. The literature suggests increased dopamine levels with acute cocaine use, and depletion of this neurotransmitter with chronic cocaine abuse (Karoum et al 1990). Animal models suggest that repeated exposure to cocaine leads to D2 autoreceptor subsensitivity in the ventral tegmental area, which results in increased spontaneous firing rates of dopaminergic neurons during early cocaine withdrawal (Henry and White 1992). Depletion of dopamine in target regions leads to D1 receptor supersensitivity during withdrawal as demonstrated by increased firing rates during stimulant or dopamine challenge. Postsynaptic receptor supersensitivity is also seen in the noradrenergic neurotransmitter system following chronic cocaine use (Banerjee et al
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1979). Clinically, this may correspond to the increased anxiety levels and susceptibility to panic attacks observed in withdrawing cocaine abusers (McDougle et al. 1994). Studies of the persistence of these P50 disturbances with continued abstinence could help determine whether neurotoxic changes or neurotransmitter system disturbances underlie the phenomena. If the disturbances reflect damage to neuronal system and/or pathways, they should be relatively permanent, while if they reflect neurotransmitter system disturbance, they should resolve with progressive abstinence. Moreover, if these disturbances reflect neurotransmitter system disturbance, they should be markedly affected by dopamine and/or stimulant challenges.

An important uncontrolled difference between the cocaine abuser and alcoholic groups was that the alcoholics were still active drinkers while the cocaine abusers had all been abstinent for about 2 weeks. This raises the crucial question of whether the P50 changes in the cocaine abusers are permanent (or very slowly diminishing) effects of their chronic cocaine abuse, or are part of their cocaine withdrawal response. We have recently begun studying the P50 in short-term abstinent alcoholics. The preliminary data on three such subjects presented above suggests that P50 differences exist between short-term abstinent cocaine abusers and short-term abstinent alcoholics. Studies examining the auditory P50 in active abusers, and in short-term through long-term abstinence from cocaine, are needed to further elucidate the P50 findings. Given that there are animal analogs of the human P50 (Dickerson and Buchwald 1991; Adler et al. 1986, 1988), which have been shown to be sensitive to modulation by drugs of abuse (Stevens et al 1991; Miller et al. 1992), corresponding studies could be carried out in animals to develop an animal model of the cocaine-induced reduction in P50 amplitude. Animal studies could also be developed to determine which neurotransmitter and/or neuronal systems are responsible for the P50 effects of chronic cocaine administration.

The cocaine abusers studied were all African-Americans. Although there are no examples in any ERP literature of differentiation of racial groups on exogenous ERP measures, we compared the results from the cocaine addicts to both African-American and Caucasian control groups. The similarity of the measures for both control groups indicates no racial differences in the P50 measures. The samples studied here are small. The a priori comparison between African-American cocaine abusers and African-American controls revealed large effects and did not need to be interpreted in the context of multiple statistical comparisons. In contrast, the comparisons with and between the other samples were performed post hoc. The negative findings in those comparison groups need to be interpreted with caution. In particular, given the wide range of P50 gating found in the alcoholic samples, it is possible that a subset of alcoholics may exhibit impaired gating. Such a finding would be consistent with the results of Baker et al (1987); however, if such findings exist, they are likely to be small in comparison to the findings in recently abstinent cocaine abusers reported here.

When cocaine and alcohol are used together, the resulting metabolite, cocaethylene, more specifically affects the dopaminergic system than does cocaine itself. Cocaethylene is formed in the presence of ethanol by the activity of liver enzymes. It inhibits uptake of dopamine, with greater specificity of effects on the dopaminergic compared to noradrenergic and serotonergic neurotransmitter systems, and can reach high plasma concentrations following combined cocaine and ethanol use (Heam et al 1991; Jatlow et al 1991). To the degree that 1) the P50 abnormalities in cocaine abusers reflect neurotransmitter system abnormalities, and 2) cocaethylene effects predominate over cocaine effects in cocaine–alcohol coabusers, then 3) cocaine–alcohol coabusers will evidence greater P50 amplitude abnormalities and reduced (or absent) P50 gating abnormalities compared to cocaine-only abusers. This prediction is based on a model that, similar to the situation in schizophrenia, the P50 amplitude and gating deficits in cocaine abusers reflect abnormalities of the dopaminergic and noradrenergic neurotransmitter systems, respectively. The very preliminary data pertinent to this issue from the present study does not support the hypothesis that cocaine–alcohol coabusers evidence greater P50 abnormalities than cocaine-only abusers; however, given the very small number of subjects in that comparison, the question remains worthy of further study.

Two recent studies demonstrate that an acute dose of nicotine normalizes the P50 suppression deficit for about 10–20 min in schizophrenics (Adler et al. 1993) and in their relatives (Adler et al. 1992). The authors suggest that an acute dose of nicotine may transiently treat the P50 deficit in schizophrenia; whether this phenomenon is related to the very high rates and severity of cigarette addiction in schizophrenics is unknown. Given the very high rates of cigarette–cocaine coaddiction, it is worthwhile to pose the question of whether the effect of acute nicotine on the P50 gating abnormality in schizophrenics also applies to the gating abnormality in cocaine abusers. For the data reported here, we did not control for cigarette use. All the SAIU patients smoked cigarettes, but we did not ask about smoking in any of the other groups. We do not know when smokers had their last cigarette before the recording session, but we do know that no one smoked for at least an hour and a half before the P50 recordings were obtained. That was the period during which electrodes were applied and other recordings were obtained, all in a smoke-free building. To address the issue of potential
nicotine modulation of P50 in cocaine abusers in our ongoing studies, we are recording P50 twice in cigarette smokers: once 12 hours cigarette abinent, and once within 5 min of smoking a cigarette.

The analysis of vertex recordings is the most common method of analyzing P50. In addition, we verified the presence of the P50 response through examination of topographical maps. This analysis illustrates one advantage of using multichannel topographic maps in the identification and measurement of EP components. Using topographic maps helps in choosing the best channel for P50 amplitude measurement because, as is apparent in Figure 5, the topography of the component is not always maximal at Cz. To be identified as a P50, a component had to conform to our definition of the required P50 topography (vertex, or close to vertex maximum). This made it highly unlikely that the TP41 [another positive component described by Cacace et al (1990) maximal at temporal sites, and occurring slightly earlier than the P50] would be misclassified as a P50. Picking P50 peaks from the channel at which it is maximal improves the power to detect group differences, as illustrated by the smaller p values from the topographical analysis results. Although the results from the vertex and topographical analyses were virtually identical in this study, improved power to detect differences could be of importance in a study where the group differences are not as strong.

In summary, we have demonstrated large reductions in P50 amplitude and suppression in 2-week-abstinent chronic African-American cocaine abusers in comparison to both African-American and Caucasian controls and in comparison to actively drinking chronic alcohol-abusing Caucasian controls. Further research is needed to determine whether these findings reflect neurotransmitter system effects that will resolve over time with abstinence or reflect relatively permanent neurotoxic effects. The specificity of these effects also needs to be determined, especially given the incidence of P50 abnormalities in psychiatric disorders (Baker et al 1987) and the high comorbidity of psychiatric disturbance and drug abuse.

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