EEG and Cerebral Blood Flow Velocity Abnormalities in Chronic Cocaine Users

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Key Words
Cerebral Blood Flow Velocity
Cocaine
Electroencephalography
Pulsatility Index
Transcranial Doppler Sonography

ABSTRACT
EEG and cerebral blood flow abnormalities have been documented in chronic cocaine abusers. To identify possible relationships between EEG and blood flow changes and their relationship to the intensity of cocaine use, we recorded the resting eyes-closed EEG and anterior (ACA) and middle (MCA) cerebral artery blood flow velocity during systole (Vs) and diastole (Vd) by transcranial Doppler (TCD) sonography of 99 (76 male, 23 female; mean [SD] age 34.3 [5.2] years, 8.6 [5.5] years of cocaine use, 17.8 [7.7] days of cocaine use in month prior to screening) cocaine users within 5 days of admission to a closed research unit. Forty-two non-drug-using, age-matched control subjects (22 male, 20 female) were tested as outpatients. A 3-minute period of resting EEG was recorded from 16 standard scalp electrodes. Artifact-free EEG was converted to six frequency bands (delta, theta, alpha1, alpha2, beta1 and beta2) using a Fast Fourier Transform. Pulsatility index (PI) was calculated as a measure of small vessel resistance.

Cocaine users had decreased Vs and increased PI in the MCA, with no difference in Vs2, and reduced EEG theta, beta1 and beta2 absolute power in posterior brain regions. Recent cocaine use was positively associated with MCA PI (r = 0.27, p < 0.001) and negatively associated with low frequency EEG power (delta power: r = -0.25, p < 0.002; theta power: r = -0.29, p < 0.001). EEG beta1 (r = -0.211, p < 0.05) and beta2 (r = -0.176, p < 0.05) power measures were correlated with PI. These observations suggest that EEG and TCD changes reflect related physiological processes during early cocaine abstinence.

INTRODUCTION
Neurological complications of cocaine use include strokes, seizures, and headache. Cerebrovascular perfusion deficits have been observed in chronic cocaine users with the techniques of single photon emission computed tomography (SPECT) and magnetic resonance imaging (MRI), primarily in frontal, central and temporal cortices. These perfusion deficits have been found after 6 months of monitored abstinence from cocaine. We have previously reported cerebrovascular deficits detected by transcranial Doppler (TCD) sonography over 4 weeks of monitored cocaine abstinence, including lower systolic and diastolic blood flow velocities and increased pulsatility index in the anterior and middle cerebral arteries.

Prolonged use of cocaine is also associated with EEG changes, including decreases in delta and theta and/or increases in alpha and beta frequency band power. These EEG changes have not been clearly associated with specific neurological or cognitive deficits. Alper suggested that the decrease in EEG delta activity observed in cocaine abusers is associated with cognitive deficits, while increases in EEG delta activity have been traditionally associated with impaired cognitive function in other disorders.

The increased EEG alpha activity observed in cocaine users might have resulted from cocaine users with co-morbid depression, since these studies included depressed cocaine abusers. Aper and associates tested seven depressed cocaine users and found increased absolute and relative alpha power. Roemer and associates attributed the increase in relative alpha power to the decrease in power in other bands. Increases in EEG beta observed in cocaine abusers might be linked to increased risk alcohol dependence, conduct disorder and a family history of alcoholism.

The relationship between the cerebrovascular perfusion deficits and the resting EEG changes both observed early in cocaine abstinence remains unclear. The goals of the present study were to (1) examine the relationship between EEG and cerebrovascular changes in chronic cocaine users, and (2) examine the relationship between these changes and history of cocaine use.

METHODS

Subjects
Participants were 99 adult (76 male, 23 female; mean [SD] age 34.3 [5.2] years), chronic cocaine users and 42 adult (22 male, 20 female) non-drug using, age-matched controls recruited from the community. The study was approved by the Institutional Review Board of the National Institute on Drug Abuse (NIDA) Intramural Research Program (IRP). Subjects gave written informed consent and were paid for their research participation. All subjects were physically healthy, based on medical history, physical examination, clinical laboratory tests, and 12-lead ECG. Psychiatric and substance use histories were assessed with the Diagnostic Interview Schedule, Addiction Severity Index (ASI), and urine drug testing.

Both groups were primarily African-American. The cocaine users were slightly older, less educated, and more likely male than the controls (Table 1). Cocaine users averaged 8.6 [5.0] years of cocaine use and 17.8 [7.7] days of use in the month prior to screening (Table 2). They were not currently dependent on any substances other than nicotine (and cocaine). Cocaine users were more likely than controls to smoke cigarettes (90.1% vs. 31.0%, χ² = 56.8, df = 1, p < 0.001), but did differ in prevalence of alcohol use (88.8% vs. 76.2%, χ² = 74.5, df = 1, p < 0.001).
Log Power

Delta
Theta
Alpha1
Alpha2
Beta1
Beta2

Control
Cocaine
p value

0.8
1.0
0.99

Figure 1.
Visual representation of log transformed absolute EEG power in each of the six frequency bands for the control group (1st column) and cocaine-using group (2nd column). The 3rd column shows the statistical significance of the difference between the two groups (see text for description of statistical methods). Vertical bar at lower right shows color code for EEG power (left side) and p value (with Bonferroni correction) of group difference (right side). In comparison to controls, cocaine users showed decreased power in posterior regions in theta, beta1, and beta2 frequency bands.

Table 3
Effect of cocaine use on transcranial doppler measures

<table>
<thead>
<tr>
<th></th>
<th>Control (n = 42)</th>
<th>Cocaine Users (n = 99)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean SD</td>
<td>Mean SD</td>
</tr>
<tr>
<td>Middle Cerebral Artery</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diastolic Velocity (cm/s)</td>
<td>42.3 9.5</td>
<td>37.3 7.4</td>
</tr>
<tr>
<td>Systolic Velocity (cm/s)</td>
<td>97.8 20.7</td>
<td>91.3 18.5</td>
</tr>
<tr>
<td>Mean Velocity (cm/s)</td>
<td>60.8 12.8</td>
<td>55.3 11.2</td>
</tr>
<tr>
<td>Pulsatility Index (PI)</td>
<td>0.89 0.12</td>
<td>0.96 0.11</td>
</tr>
<tr>
<td>Anterior Cerebral Artery</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diastolic Velocity (cm/s)</td>
<td>39.8 7.8</td>
<td>34.0 9.0</td>
</tr>
<tr>
<td>Systolic Velocity (cm/s)</td>
<td>92.8 19.4</td>
<td>81.4 14.7</td>
</tr>
<tr>
<td>Mean Velocity (cm/s)</td>
<td>56.7 11.0</td>
<td>49.5 9.3</td>
</tr>
<tr>
<td>Pulsatility Index (PI)</td>
<td>0.90 0.16</td>
<td>0.93 0.12</td>
</tr>
</tbody>
</table>

Table 4
Correlation between transcranial doppler measures and EEG power

<table>
<thead>
<tr>
<th>EEG Frequency Band</th>
<th>Diastolic Velocity</th>
<th>Systolic Velocity</th>
<th>Mean Velocity</th>
<th>Pulsatility Index</th>
</tr>
</thead>
<tbody>
<tr>
<td>Delta</td>
<td>0.71</td>
<td>0.05</td>
<td>0.09</td>
<td>-0.11</td>
</tr>
<tr>
<td>Theta</td>
<td>-0.001</td>
<td>-0.008</td>
<td>-0.001</td>
<td>-0.13</td>
</tr>
<tr>
<td>Alpha1</td>
<td>0.005</td>
<td>-0.005</td>
<td>0.005</td>
<td>-0.13</td>
</tr>
<tr>
<td>Alpha2</td>
<td>0.029</td>
<td>0.016</td>
<td>0.048</td>
<td>-0.11</td>
</tr>
<tr>
<td>Beta1</td>
<td>0.100</td>
<td>0.030</td>
<td>0.088</td>
<td>-0.21*</td>
</tr>
<tr>
<td>Beta2</td>
<td>0.090</td>
<td>0.038</td>
<td>0.098</td>
<td>-0.176*</td>
</tr>
</tbody>
</table>

*p < 0.05, df =139, controlled for age.

In previous EEG studies of cocaine abusers, by this laboratory and others, relative EEG beta power was increased in cocaine users as compared to control subjects. Costa and Bauer were the only group of researchers to observe an increase in absolute EEG beta power in cocaine abusers compared to control subjects. The present study found a decrease in both beta1 and beta2 power in cocaine users, which was correlated with an increase in cerebral small vessel resistance as measured by TCD sonography. In studies of ischemic stroke, increases in delta and theta EEG activity have been associated with deficits in cerebral perfusion, while decreases in beta activity have been associated with subtle decreases in brain perfusion.

The present study has several strengths and was performed on a large sample of well characterized control subjects and cocaine users. Both EEG and cerebral perfusion were measured at the same time in the same subjects, allowing for direct comparison of the two measures. This study has several limitations. The two groups were not age or sex matched, although age was statistically controlled by using an analysis of covariance or partial correlation analyses. While one would not expect to see gender differences in the EEGs of healthy adults, resting EEG is relatively stable throughout healthy adult life and TCD changes start above age 50, or in post-menopausal women, age was used as a statistical control throughout the present study.

In conclusion, these TCD findings are consistent with those from SPECT and IMRI showing abnormal brain perfusion in cocaine users. EEG findings are also consistent with those observed in abstinent cocaine users in other studies. Our study shows a relationship between the cerebral perfusion and EEG in abstinent cocaine abusers suggesting the probability of using these parameters as potential markers of treatment response.
ACKNOWLEDGMENT
This work was supported by the National Institutes of Health, National Institute on Drug Abuse. Intramural Research Program.

REFERENCES