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# Neurovascular Deficits in Cocaine Abusers

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*The nature of the neurological and cerebrovascular deficits in cocaine abusers and whether they persist in abstinence is unclear. Blood flow velocity of the anterior and middle cerebral arteries was measured by transcranial Doppler sonography in cocaine abusers ($n = 50$) and control subjects ($n = 25$). Blood flow velocity was measured within 3 days and again after about 28 days after being admitted to an inpatient research ward to determine whether blood flow velocity improved during monitored abstinence conditions. The mean, systolic, and diastolic velocities as well as the pulsatility index in middle and anterior cerebral arteries significantly differed between controls and cocaine abusers ($p < .05$). Cerebrovascular resistance is increased in cocaine abusers and the increase persists for over a month of abstinence. Further research is needed to determine whether cerebrovascular resistance can be improved by pharmacological manipulations and whether improved blood flow relates to improved treatment outcome.*
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The cocaine epidemic has continued unabated in this country causing a myriad of complications for the user as well as for society as a whole (Cornish and O'Brien 1996). No established course of treatment has evolved from two decades of research (Schuckit 1994; Leshner 1996; O'Brien 1996). In the search for a pharmacological treatment, considerable emphasis has been placed on understanding the effects of cocaine on dopaminergic reward systems (Pulvirenti and Koob 1994; Mello and Negus 1996) while recent evidence suggests dopamine was also involved in the regulation of cortical circulation (Krimer et al. 1998). Psychosocial interventions using adjunctive therapies, cue reduction, providing increased treatment services, and simply more intensive treatment have had limited success in treating cocaine dependence (Margolin et al. 1994; Rosenblum et al. 1995; Hoffman et al. 1996). This lack of success might be contributed to by a limited understanding of the clinical neurobiology of drug abuse. A more promising approach might involve a comprehensive assessment of neuropsychiatric deficits in this population. A better understanding of such deficits might aid in the development of more relevant pharmacological and psychosocial treatment approaches (Cadet and Bolla 1996; Herning et al. 1997a).

Cocaine abuse is associated with life-threatening medical complications (Marzuk et al. 1995), including increased risk of neurological complications including strokes, seizures, transient ischemic attacks, and headaches (Mody and Miller 1988; Qureshi et al. 1995; Koppel et al. 1996). With cocaine-related stroke as a neurological complication, it is reasonable to suggest an increased prevalence of subclinical neurovascular deficits in this population. EEG (Alper et al. 1990, 1998; Noldy et al. 1994; Roemer et al. 1995; Prichep et al. 1997; Herning et al. 1997b; Costa and Bauer 1997). PET/SPECT blood flow (Tumeh et al. 1990; Weber et al. 1990; Volkow et al. 1991; Holman et al. 1991; Levin et al. 1994, 1995), and neuropsychological (Herning et al. 1991; O'Malley et al. 1992; Roberts and Bauer 1993; Easton and Bauer 1997) studies have indeed found that prolonged cocaine abuse is associated with subtle, subclinical CNS deficits. Although these subclinical neuropsychiatric deficits may be an indication of increased risk of medi-

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cal complications, they also characterize cocaine dependence as a neuropsychiatric syndrome (Cadet and Bolla 1996). Moreover, reduced cerebral blood flow may be the underlying cause of the EEG and neuropsychological deficits in a manner similar to vascular dementia (Sattel et al. 1996; Starkstein et al. 1996). Thus, reduced cerebral blood flow may have been overlooked as a symptom requiring treatment in cocaine abusers (Herning et al. 1997a).

What is known about cerebral perfusion deficits in cocaine abusers comes from PET/SPECT imaging studies (Tumeh et al. 1990; Weber et al. 1990; Volkow et al. 1991; Holman et al. 1991; Levin et al. 1994, 1995). An alternate approach in studying cerebral hemodynamics is transcranical Doppler sonography (TCD), which has proven useful in assessing abnormal hemodynamics in cerebral arteries (Silvestrini et al. 1996; Howard et al. 1996). A critical difference between TCD and other methodologies is that TCD measures blood flow velocity in large arteries rather than cerebral perfusion in small vessels. Pulsatility which is derived from velocity is also measured by TCD (Arnolds and von Reutern 1986; Czosnyka et al. 1996; Cho et al. 1997). The TCD assessment is noninvasive, quick, and economical. Consequently, TCD allows for repeated assessment of large samples of subjects which are typically not the case in the PET/SPECT imaging studies of cocaine abuses. As a first step toward assessing the status of the cerebral vasculature in a large sample of cocaine abusers, we recorded blood flow velocity and pulsatility from four large cerebral arteries using TCD. We also investigated if a month of monitored abstinence would cause changes in cerebral blood flow parameters in these subjects.

## METHODS

### Subjects

Fifty cocaine abuses and 25 control subjects were studied. Before undergoing blood flow velocity assessment by TCD, all volunteers had undergone comprehensive medical, neurological, psychological, and laboratory evaluations. All cocaine abusers met the DSM-IIIR criteria for cocaine dependence ($n = 40$) or abuse ($n = 10$) using the Diagnostic Interview Schedule (DIS) (Robins et al. 1988). Other Axis-I current diagnoses included were phobia (control subjects $n = 5$; cocaine abusers $n = 9$), post-traumatic stress disorder (control subjects $n = 2$; cocaine abusers $n = 5$), and nicotine dependence (control subjects $n = 5$; cocaine abusers $n = 28$). In addition, some cocaine abusers met the criteria for alcohol ($n = 10$) and heroin ($n = 3$) abuse. Eleven had a diagnosis of antisocial personality disorder. Demographic information and drug use history information were obtained from the Addiction Severity Index (ASI) (McLellan et al. 1986). Psychiatric symptoms were measured during screening and admission procedures using the Symptom Check List 90 Revised (SCL-90R) (Derogatis 1983).

Exclusion criteria which applied to all subjects include: (1) major medical and psychiatric illnesses; (2) head injuries with loss of consciousness for greater than 5 minutes; (3) evidence of any neurological abnormalities by history or examination. The research protocol was approved by the National Institute on Drug Abuse and Johns Hopkins Bayview Medical Center Institutional Review Boards for Human Research. Informed consent was obtained from all subjects.

### Procedures

Blood flow velocity was determined using a temporal window (zygomatic arch) for four arteries: right and left middle (MCA), and right and left anterior (ACA) cerebral arteries using pulsed transcranial Doppler sonography (Nicolet, Model TC2000). Mean velocity (Vm: cm/s), systolic velocity (Vs: cm/s), diastolic velocity (Vd: cm/s), and pulsatility index (PI = (Vs−Vd)/Vm) were determined for each artery.

The inpatient cocaine abusers were tested twice. The first evaluation was within 72 hours of admission to the research ward. The second evaluation was after 26 to 30 days of monitored abstinence on the closed research ward. The control subjects were tested during an outpatient visit.

### Statistical Analysis

A group (cocaine abusers vs. control subject) by gender by side (right vs. left) analysis of covariance (ANCOVA) was used to test for differences in flow velocity parameters between the cocaine abusers and control subjects. Alcohol and nicotine use data from the ASI, systolic blood pressure, and hematocrit were used as covariates in the preliminary analyses because of the possibility that they might account for some of the differences in flow measures. Because only duration (months) of alcohol use was found to be a significant covariate, only this variable was retained as a covariate in the final statistical analyses. A repeated measures analysis of variance with gender as a between-subject factor and time as well as location as within-subject factors were used to determine if any of the blood flow velocity parameters changed during the month of abstinence for the cocaine abusers.

## RESULTS

Demographic and drug use history information from the ASI is presented in Table 1. Mean scores for the nine SCL-90R scales are presented in Table 2. The cocaine

**Table 1.** Demographic Measures and Drug History

| | Control Subjects | | | | | | Cocaine Abusers | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Female | | | Male | | | Female | | | Male | | |
| **Demographic Measures** | **Mean** | **SD** | ***n*** | **Mean** | **SD** | ***n*** | **Mean** | **SD** | ***n*** | **Mean** | **SD** | ***n*** |
| Age (years) | 37.1 | 7.7 | 7 | 30.5 | 8.4 | 18 | 34.5 | 5.9 | 10 | 33.8 | 5.2 | 40 |
| Education (years) | 13.0 | 1.4 | 7 | 12.5 | 1.6 | 18 | 12.5 | 2.2 | 10 | 12.0 | 1.3 | 40 |
| African American (%) | 57% | | | 83% | | | 90% | | | 83% | | |
| **Drug History Measures** | | | | | | | | | | | | |
| Cocaine (days/30) | | | | | | | 18.5 | 7.2 | 10 | 18.2 | 7.6 | 40 |
| Cocaine (years) | | | | | | | 7.3 | 4.3 | 10 | 7.6 | 4.7 | 40 |
| Alcohol (days/30) | 5.7 | 2.2 | 3 | 2.0 | 1.4 | 4 | 8.4 | 7.5 | 9 | 8.6 | 5.5 | 37 |
| Alcohol (years) | 12.7 | 7.1 | 6 | 4.7 | 5.1 | 9 | 14.9 | 9.5 | 8 | 16.4 | 7.0 | 40 |
| Heroin (days/30) | | | | | | | 5.0 | | 1 | 3.9 | 2.4 | 14 |
| Heroin (years) | | | | | | | 7.0 | | 1 | 4.5 | 3.5 | 19 |
| Marijuana (days/30) | | | | | | | 2.0 | 2.1 | 5 | 4.2 | 6.3 | 22 |
| Marijuana (years) | | | | | | | 11.7 | 10.6 | 6 | 12.7 | 6.9 | 34 |
| Cigarettes/day | 18.8 | 11.7 | 5 | 10.7 | 0.7 | 7 | 19.0 | 12.1 | 9 | 17.2 | 10.9 | 39 |
| Cigarettes (years) | 18.3 | 6.6 | 6 | 17.0 | 12.8 | 9 | 16.4 | 12.0 | 9 | 16.5 | 7.1 | 39 |

abusers had elevated mean scores on six of the nine scales. Family history of psychiatric illness, alcoholism, drug abuse, cardiovascular disease, hypertension, and stroke was obtained from the ASI and medical history interviews and is expressed as percentages in Table 3. Chi-square tests on the frequencies underlying the percentages revealed no significant differences between the control subjects and cocaine abusers on family history measures. Resting heart rate and blood pressure were measured in all subjects. Cholesterol, hematocrit, and hemoglobin were obtained from the admission blood sample. Cardiovascular and blood chemistry values are displayed in Table 4. No group differences were found for these measures using a group (control vs. cocaine) by gender analysis of variance on each measure, except for cholesterol. Cholesterol values were significantly higher for the control subjects.

**Table 2.** SCL-90R Scales

| | Control Subjects | | | Cocaine Abusers | | |
|---|---|---|---|---|---|---|
| **Scale** | **Female** | **Male** | **Both** | **Female** | **Male** | **Both** |
| Somatization | 45.6 | 40.0 | 41.9 | 53.1 | 43.1 | 45.1[b] |
| | 8.3[a] | 9.7 | 5.6 | 9.7 | 6.9 | 8.5 |
| Obsessive-compulsive | 49.0 | 46.1 | 46.9 | 59.0 | 51.2 | 52.7[b] |
| | 8.8 | 8.5 | 8.5 | 8.7 | 10.0 | 10.1 |
| Interpersonal sensitivity | 52.3 | 47.4 | 48.8 | 59.6 | 51.9 | 53.4 |
| | 8.9 | 8.0 | 8.3 | 13.6 | 13.6 | 12.1 |
| Depression | 48.6 | 46.3 | 46.9 | 63.8 | 54.1 | 56.1[b] |
| | 8.3 | 10.7 | 10.0 | 6.4 | 13.0 | 12.6 |
| Anxiety | 43.8 | 41.9 | 42.4 | 54.1 | 48.4 | 49.5[b] |
| | 6.9 | 5.8 | 6.1 | 11.2 | 9.8 | 10.2 |
| Hostility | 49.8 | 45.9 | 47.0 | 57.8 | 45.2 | 47.8 |
| | 5.7 | 7.8 | 7.4 | 13.4 | 8.4 | 10.7 |
| Phobic anxiety | 48.7 | 48.8 | 48.8 | 53.8 | 52.0 | 52.4 |
| | 5.9 | 5.1 | 5.2 | 9.8 | 9.0 | 9.0 |
| Paranoid ideation | 52.1 | 48.9 | 49.8 | 63.1 | 52.5 | 54.6[c] |
| | 6.7 | 11.4 | 10.3 | 13.0 | 10.7 | 11.8 |
| Psychoticism | 49.3 | 46.9 | 47.6 | 62.5 | 52.1 | 54.2[b] |
| | 7.4 | 5.6 | 6.1 | 11.5 | 9.7 | 10.8 |

[a]These data represent the mean and standard deviation of the scores.
[b]Group means differ, $p < .001$.
[c]Group means differ, $p < .050$.

## Middle Cerebral Artery

Vm, Vs, and Vd for the MCA were significantly lower for cocaine abusers as compared to those for control subjects (Vm: $F[1,70] = 15.9$, $p < .001$; Vs: $F[1,70] = 8.4$, $p < .005$; Vd: $F[1,70] = 27.0$, $p < .001$). There were no significant group-by-gender or group-by-side interactions for any of these velocity measures. Figure 1 shows the plots of mean velocity measures averaged over both right and left MCAs and both males and females. The cocaine abusers also had significantly higher PI than the control subjects ($F[1,70] = 11.6$, $p < .001$). There were no significant group-by-gender or group-by-side interactions for PI. Figure 2 shows the plots of mean PI.

## Anterior Cerebral Artery

Vm, Vs, and Vd were significantly reduced for cocaine abusers as compared to the control subjects (Vm: $F[1,70] = 8.9$, $p < .005$; Vs: $F[1,70] = 5.4$, $p < .05$; Vd: $F[1,70] = 12.9$, $p < .001$). Figure 1 shows mean velocity measures averaged over both anterior arteries and averaged over males and females. The cocaine abusers also had significantly higher PI values than the control subjects ($F[1,70] = 5.2$, $p < .05$). There were no significant group-by-gender or group-by-side interactions for any anterior cerebral artery measure. Figure 2 shows

**Table 3.** Family History

| Family History Positive for (%) | Control Subjects | | | Cocaine Abusers | | |
|---|---|---|---|---|---|---|
| | Female ($n$ = 7) | Male ($n$ = 18) | Both ($n$ = 25) | Female ($n$ = 10) | Male ($n$ = 40) | Both ($n$ = 50) |
| Alcohol abuse | 57.1 | 33.3 | 40.0 | 80.0 | 42.5 | 50.0 |
| Drug abuse | 42.9 | 27.8 | 32.0 | 80.0 | 37.5 | 46.0 |
| Psychiatric disorders | 0.0 | 5.6 | 4.0 | 10.0 | 0.0 | 2.0 |
| Cardiovascular disease | 14.3 | 16.7 | 16.0 | 30.0 | 15.0 | 18.0 |
| Hypertension | 28.6 | 22.2 | 24.0 | 60.0 | 37.5 | 42.0 |
| Stroke | 42.9 | 22.2 | 29.1 | 20.0 | 12.5 | 14.0 |

the plot of mean PI averaged over both sides and averaged over males and females.

### Effects of Abstinence

Blood flow velocity for the cocaine abusers significantly increased in MCA over the month of abstinence (Vm: $F[1,48] = 6.4$; $p < .05$, vs: $F[1,48] = 4.8$, $p < .05$; and Vd: $F[1,48] = 7.2$, $p < .01$). Middle artery PI did not change during the month of monitored abstinence ($F[1,48] = 1.1$, $p > .25$). Figure 2 shows the plots of flow velocity averaged over both sides and averaged over males and females for the two test times. There were no significant gender-by-time interactions for the above flow measures. There were no significant changes in blood flow in the ACA during the month of abstinence. Figures 2 and 3 show the plots of these data.

## DISCUSSION

This study found that blood flow velocity in the MCA and ACA is reduced and that PI is increased in cocaine abusers as compared to control subjects. The present observations using TCD sonography in this large sample of cocaine abusers may reflect a deficit in cerebral hemodynamics. Although our methods are not directly comparable, SPECT/PET studies with smaller samples find deficits in cerebral perfusion (Tumeh et al. 1990; Weber et al. 1990; Volkow et al. 1991; Holman et al. 1991; Levin et al. 1994, 1995). The elevated PI values with slow velocity values observed in 30- to 40-year-old cocaine abusers in the present study was found for 60-year-old individuals (Martin et al. 1994). Elevated PI values were also observed in patients with multi-infarct dementia (Biedert et al. 1995; Sattel et al. 1996) and in

**Table 4.** Cardiovascular and Blood Chemistry Measures

| | Control Subjects | | | Cocaine Abusers | | |
|---|---|---|---|---|---|---|
| | Female ($n$ = 7) | Male ($n$ = 18) | Both ($n$ = 25) | Female ($n$ = 10) | Male ($n$ = 40) | Both ($n$ = 50) |
| **Cardiovascular** | | | | | | |
| Heart rate | 77.7 | 70.8 | 72.7 | 68.0 | 69.4 | 69.2 |
| | 15.9[b] | 10.1 | 12.0 | 7.4 | 11.2 | 10.5 |
| Systolic BP[a] | 119.3 | 128.3 | 125.8 | 114.4 | 131.8 | 128.3 |
| | 10.9 | 9.6 | 10.8 | 7.2 | 15.6 | 15.9 |
| Diastolic BP | 73.7 | 80.9 | 78.9 | 70.4 | 82.2 | 79.9 |
| | 11.1 | 7.8 | 9.2 | 11.0 | 9.4 | 10.7 |
| **Blood chemistry** | | | | | | |
| Hematocrit | 13.0 | 14.7 | 14.3 | 13.4 | 14.5 | 14.3 |
| | .8 | 1.0 | 1.2 | 1.2 | 1.5 | 1.2 |
| Hemoglobin | 38.3 | 43.0 | 42.8 | 40.1 | 43.6 | 42.9 |
| | 2.2 | 2.9 | 3.4 | 3.7 | 4.4 | 4.5 |
| Cholesterol | 207.6 | 189.6 | 194.6[c] | 165.0 | 179.0 | 176.2 |
| | 43.0 | 48.0 | 46.5 | 19.7 | 32.7 | 30.9 |

[a]Blood pressure.
[b]Mean and Standard Deviation.
[c]The mean for the control group was higher than that of the cocaine abusers, $F[1, 71] = 6.66$, $p < .05$.

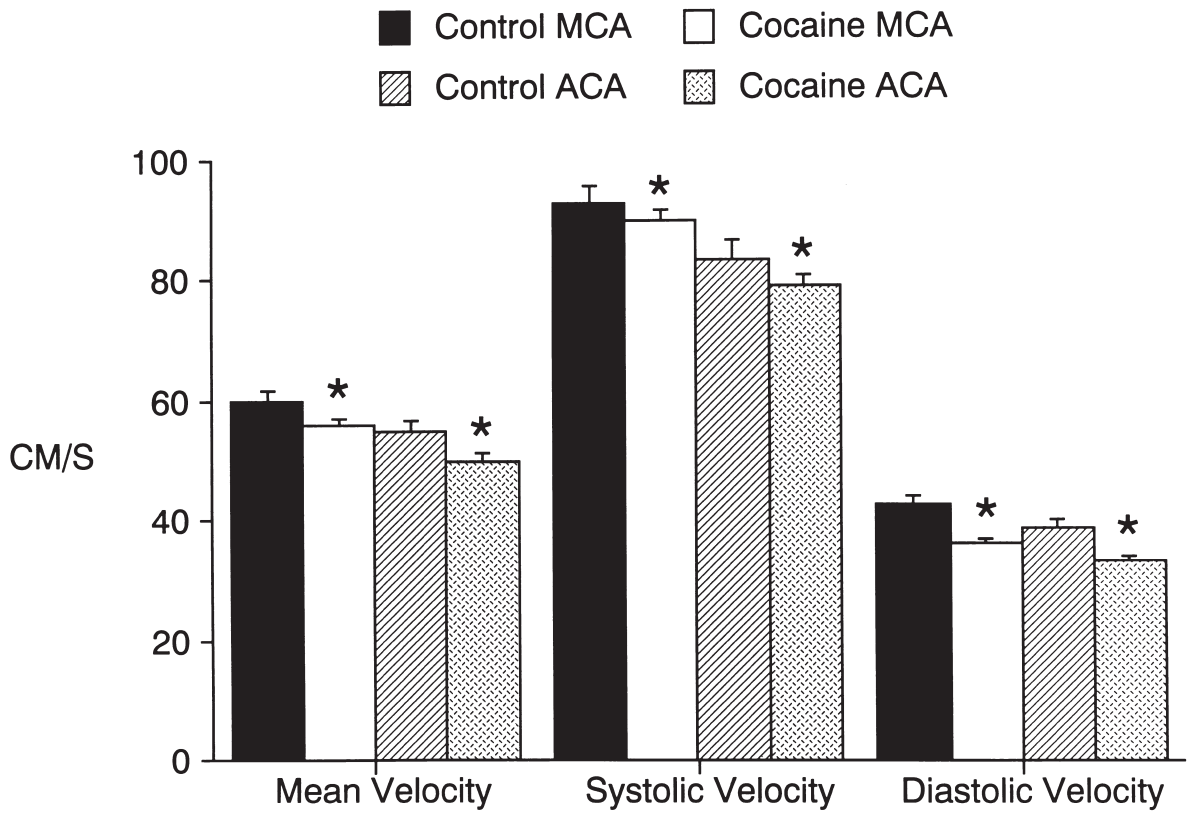


**Figure 1.** Mean, systolic, and diastolic flow for the middle (MCA) and anterior (ACA) arteries are plotted for the control subjects and cocaine abusers. Error bars are standard error of the mean. An asterisk indicates a significant difference between the flow values for the control subjects and cocaine abusers.

hypertensive patients (Cho et al. 1997). It is also possible that the decrease in flow velocity might be secondary to changes in the caliber of large vessels. The non-drug-using individuals in our sample fell within the normative range for both blood flow velocity and PI, thus supporting the absence of measurement error.

Slowed cerebral blood flow velocity with increased pulsatility in certain patient populations indicate increased cerebrovascular resistance was due to vasoconstriction of small cortical vessels (Martin et al. 1994; Biedert et al. 1995; Cho et al. 1997; Schondorf et al. 1977; Grubb et al. 1998). Such an interpretation of pulsatility does not hold in situations where blood pressure differed among groups (Czosnyka et al. 1996). Because the cocaine abusers had similar blood pressure as the control subjects in our study, it is possible that these blood flow velocity changes indicate increased cerebrovascular resistance in the cocaine abusers. While cocaine blocks dopamine reuptake at the synapses throughout the brian, dopaminergic neurons also innervate and produced vasoconstriction in small blood vessels in the cortex (Krimer et al. 1998). Repeated cocaine administration in rabbits constricts pial arterioles by blocking the bradykinin-induced dilation of pial arterioles (Copeland et al. 1996). Thus, prolonged exposure to cocaine may alter cerebrovascular resistance directly as we observed in this study.

Blood flow velocity in the MCA only slightly improved in the cocaine abusers after a month of monitored abstinence. No change in velocity was observed after a month of abstinence in the ACA. Pusatility of both arteries did not change over the month of abstinence for the cocaine abusers. These observations are consistent with the reports of Levin et al. (1995) who found that cocaine/opiate-dependent patients had fewer perfusion deficits after being treated with buprenorphine, but not after 5 days of placebo. Because the subjects in our study were abstinent for only about 1 month, the possibility that these deficits may last for a relatively longer period of time exists and needs to be explored. This suggestion is supported by other reports. Neuropsychological deficits reported in cocaine abusers also failed to improve during a 4-week period of monitored abstinence (Herning et al. 1991). Furthermore, other reports using PET and EEG have also suggested that there might be significant changes in the brains of cocaine abusers for over 6 months of monitored abstinence (Volkow et al. 1991; Alper et al. 1998). Nevertheless, more comprehensive neuropsychological, neurovascular, and imaging studies are needed in

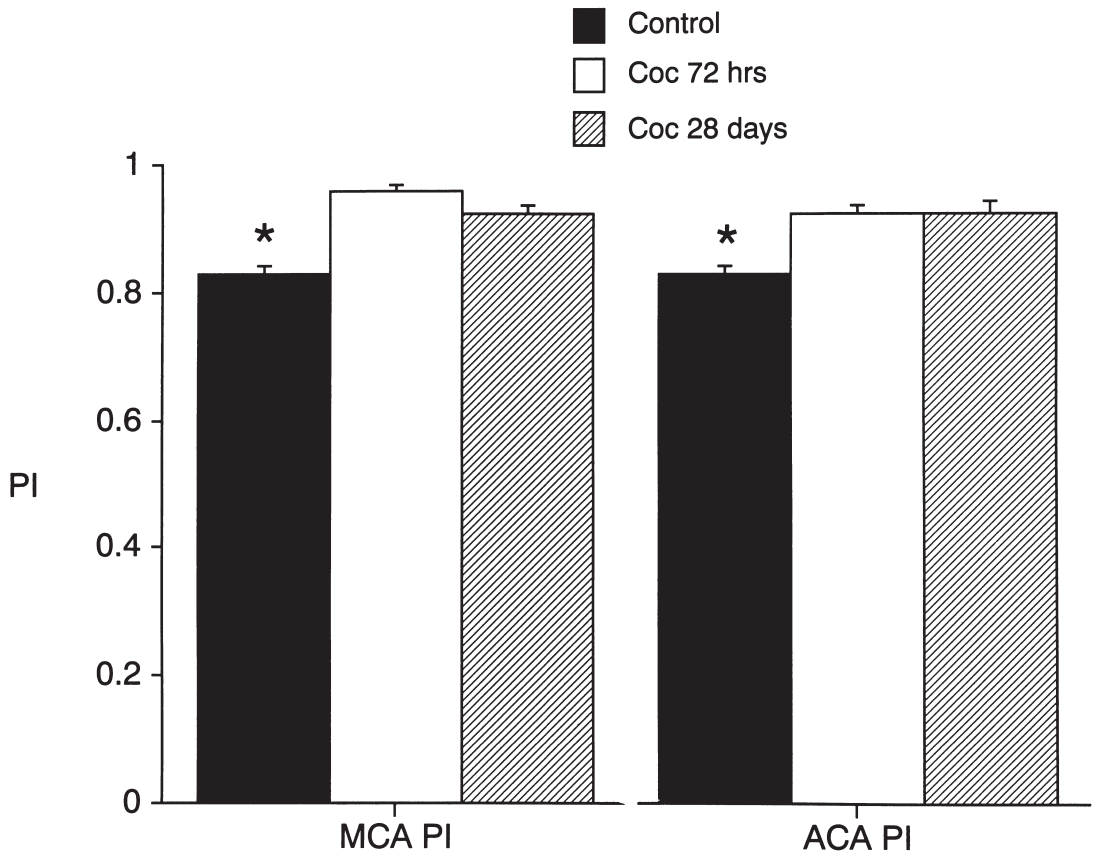


**Figure 2.** PI for the middle (MCA) and anterior (ACA) arteries are plotted for the control subjects and cocaine abusers. Error bars are standard error of the mean. An asterisk indicates a significant difference between the flow values for the control subjects and cocaine abusers. No differences were observed over time for the cocaine abusers.

order to determine if these deficits persist for much longer period of time. The possibility that various therapeutic modalities might cause improvement in these variables also needs to be evaluated.

It is interesting to note that the neuropsychological and EEG deficits previously reported (Herning et al. 1997b; Costa and Bauer 1997) might be related to the reduced blood flow velocity being reported herein. Thus, reduced cerebral blood flow velocity might be associated with neuropsychological deficits in a mechanism similar to changes observed in vascular dementia (Biedert et al. 1995; Sattel et al. 1996; Starkstein et al. 1996). This comparison must be made with caution because reduced cerebral blood flow velocity cannot be directly compared with reduced cerebral perfusion. Studies compared EEG and cerebral perfusion not velocity. A relationship between decreased regional cortical blood flow and increased levels of EEG beta observed in spinocerebellar degeneration has been reported (Nagata et al. 1993). Increased EEG beta has also been reported in patients who suffer from vertebrobasilar artery insufficiency (Niedermeyer 1963). When considered together with these observations, our findings suggest that the repeated use of cocaine may contribute to a state of vascular insufficiency which is associated with subclinical cognitive deficits (Herning et al. 1991; O'Malley et al. 1992; Roberts and Bauer 1993; Easton and Bauer 1997), EEG changes (Alper et al. 1990, 1998; Noldy et al. 1994; Roemer et al. 1995; Prichep et al. 1997; Herning et al. 1997b; Costa and Bauer 1997) and imaging alterations (Tumeh et al. 1990; Weber et al. 1990; Volkow et al. 1991; Holman et al. 1991; Levin et al. 1994, 1995). This idea is supported by the findings that EEG observed in cocaine abusers was normalized by nimodipine (Herning et al. 1995), a drug known to improve blood flow (Godfraind et al. 1990).

Although the discussion so far has focused on the contributory role of cocaine in the present findings, it is important to consider alternative explanations. For example, because alcohol and nicotine use was significantly higher in the cocaine abusers, it is possible that the reduced flow velocity might be due to these drugs. However, the analysis of covariance showed that alcohol, but not nicotine use, accounted for some of the differences in blood flow velocity. Further controlling for alcohol use revealed that blood flow velocity in cocaine abusers was still poorer than that of the control subjects. Factors other than drug use may influence cere-

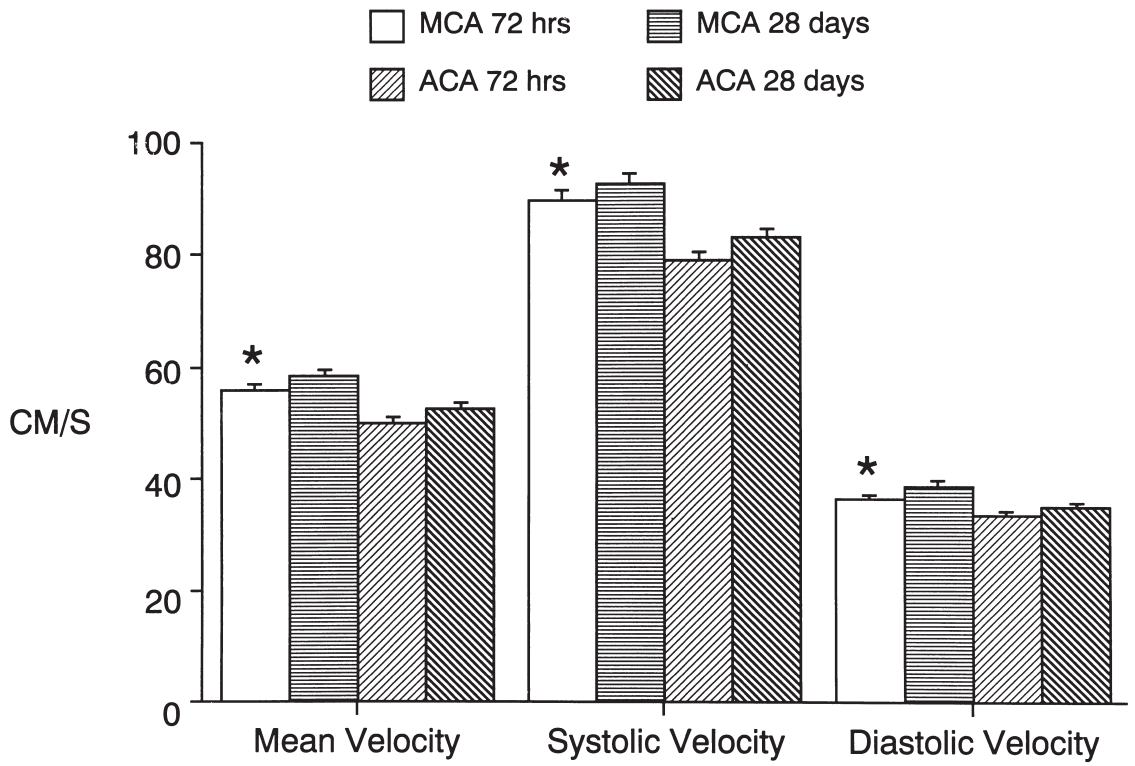


**Figure 3.** Velocities for the middle (MCA) and anterior (ACA) arteries are plotted for the cocaine abusers at the two test times. Error bars are standard error of the mean. An asterisk indicates a significant difference between the flow values at the two times for MCA of the cocaine abusers. No differences were observed over time for the cocaine abusers on ACA velocities.

bral blood flow velocity and impact the interpretation of results for this study. Differences in values of heart rate, blood pressure, hematologic characteristics, and family history of medical and physical disorders might contribute to differences observed in cerebral blood flow velocity. However, these factors were measured in our sample and not found to differ between the cocaine abusers and the control subjects. The only measure found to differ between groups was cholesterol, which might potentially reduce blood flow, but in our sample cholesterol was higher in the control subjects. Finally, increased cerebrovascular resistance in small cortical blood vessels in this study was inferred from blood velocity measures in large arteries. While the latter inference has been previously made in some TCD studies, a direct measure would be ideal.

Acute doses of cocaine changed cortical blood flow (Pearlson et al. 1993; Mathew et al. 1996) and cortical glucose metabolism (London et al. 1990) in humans. While different imagining methods were used, intravenous doses cocaine of 40 mg or more reduced cortical glucose metabolism using FDG PET (London et al. 1990) and cerebral blood flow with HMPAO SPECT (Pearlson et al. 1993), and doses lower than 40 mg appear to increase cortical blood flow using Xenon inhalation (Mathew et al. 1996). In addition, Levin's group (Kaufman et al. 1998) found that cocaine constricted the proximal cerebral arteries using Magnetic Resonance Angiography. These acute and chronic cocaine-induced alterations in cerebrovascular function may be related to the increased incidence of stroke and neuropsychological deficits reported in human cocaine abusers as recently reviewed by Kosten (1998). Because no clearly clinically significant improvement in neurovascular status was noted during monitored abstinence, the neurovascular deficits observed in this population may require a treatment with pharmacological agents which may be effective in reducing the deficits.

In conclusion, this is, to our knowledge, the first study to evaluate cerebral blood flow by TCD in a relatively large population of cocaine users. Although nonhemorrahagic and hemorrhagic stroke (Mody and Miller 1988; Qureshi et al. 1995), as well as blood flow abnormalities by PET and SPECT (Tumeh et al. 1990; Weber et al. 1990; Volkow et al. 1991; Holman et al. 1991; Levin et al. 1994, 1995) have been reported in these patients, the status of cerebral vasculature has not been evaluated previously. Our present finding suggests that the vasculature of 30–40-year old cocaine abusers might be comparable to that of 60-year-olds and may be of clinical relevance because old age is a risk factor for stroke. At another level, these observations further strengthen the view that cocaine use might indeed result in a neurobehavioral syndrome, the treatment of which might

necessitate a more comprehensive, biopsychosocial approach to treatment in this population.

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