Cocaine Transiently Constricts Human Spleen and Alters Hemoglobin Levels and Hematocrit

Marc J. Kaufman, Arthur J. Siegel, Jack H. Mendelson, Stephanie L. Rose, Thellea J. Kukes, Michelle B. Sholar, Scott E. Lukas and Perry F. Renshaw

Brain Imaging Center, Alcohol & Drug Abuse Research Ctr., & Behavioral Psychopharmacology Res. Program, McLean Hospital, Belmont, MA 02478, USA

Introduction

Although much work has focused on cocaine's effects in the heart and brain, cocaine may have important effects in other organs including the spleen. Cocaine abuse has been associated with splenic infarction (1) and with abnormal spleen hemodynamics (2). Additionally, human cocaine administration is associated with elevated hemoglobin levels and hematocrit (3). Since the spleen is the primary storage site for red blood cells, we hypothesized that cocaine-associated hematologic changes are in part evoked by splenic constriction. In support of this suggestion, cocaine constricts the spleen in animals and cocaine-induced hematologic changes are abolished in splenectomized animals (4, 5). This study used serial magnetic resonance imaging to evaluate human spleen volume after cocaine administration to determine whether any such changes were temporally correlated with hematologic alterations.

Subjects

Spleen imaging was conducted in 5 men aged 32±1 years (mean±SE) weighing 79±2 kg. Venous blood samples were obtained from two of these subjects to determine hematologic parameters during spleen imaging. Venous blood samples were also obtained from an additional 6 men participating in other cocaine-related brain imaging studies. The average age and weight of the subjects in the hematologic study was 30±2 years and 77±3 kg, respectively. All subjects reported occasional cocaine use averaging 13 lifetime exposures, primarily via insufflation, and provided written informed consents with McLean Hospital Institutional Review Board approval. Subjects underwent complete physical and neurological exams, were judged to be in good health, and tested negative for recent alcohol and illicit substance use immediately prior to the study.

A catheter was inserted in the antecubital vein for drug administration. Some subjects had an additional catheter inserted in the opposite arm for blood sampling to determine venous hematologic parameters. Subjects vital signs were continuously monitored with 4 lead ECG, blood pressure cuff, and pulse oximeter (In Vivo Research).

Hematologic Analyses

Samples were analyzed with a Mile/Bayer H2 System by a commercial laboratory (SmithKline Beecham Clinical Laboratories).

Imaging

Serial magnetic resonance imaging was conducted on a 1.5 Tesla General Electric Signa Scanner using the body coil. Subjects were placed feet first in the magnet in the supine position. Abdominal axial SPGR breath-hold images with saturation transfer were obtained with the following parameters: TR = 30 msec, TE = 5 msec, FOV = 32 cm, Flip angle = 35°, 256 x 128 or 192 matrix, 4 excitations, and either 5 mm slice thickness and 2 mm skip or (in 1 subject) 8 mm slice thickness and 2 mm skip. Three baseline and 5 post-cocaine (0.4 mg/kg) image sets were acquired.

Results

Baseline (Figure, D) spleen volume averaged 210±30 ml (mean±SE). The coefficient of variance of within-subject, baseline spleen volume measurements averaged 7%. Post-cocaine (Figure, P1-P5), spleen volume rapidly declined to 80±4% of controls at about 10 minutes post cocaine (Figure, P2). The spleen volume reduction was significant (p < 0.03, repeated measures ANOVA). Spleen volume returned to baseline (100±3% baseline) within 35 minutes (Figure, P5) following cocaine administration, indicating that this effect is transient.

Cocaine increased hematocrit, hemoglobin and red blood cell counts to peak values of 105.6±1.2, 104.5±0.9 and 106.5±1.0% of baseline values, respectively, 10-20 minutes after cocaine administration. These values all decreased toward baseline values within 30 minutes after cocaine, indicating that this effect was transient. Placebo administration did not alter these measures.

Conclusions

These findings document a transient, cocaine-induced constriction of the human spleen that likely contributes to the temporally concordant hematologic changes. Hematologic changes may help to preserve tissue oxygenation in periods of high oxygen demand or increased vascular resistance, and may have profound effects on tissue perfusion, which is in part regulated by hemoglobin (7). Hematologic changes also may complicate interpretation of BOLD fMRI signal changes in cocaine administration studies, since an underlying assumption in those studies is that total hemoglobin concentration remains constant during the experiment (8), and hemoglobin changes on the order of those observed presently have been shown to dramatically alter the BOLD fMRI response to photic stimulation in humans (9).

References


Supported by DA09448, DA04059, DA00329, DA00064 & DA00343.