Cocaine Increases BOLD fMRI Response to Photic Stimulation

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INTRODUCTION
Acute cocaine administration has been associated with cerebral vasocostriction with reduced cerebral blood flow (CBF) and cerebral blood volume (CBV) (1-3). The blood oxygenation level dependent (BOLD) functional MRI (fMRI) technique relies upon locally increased CBF accompanying focal cerebral activation to provide image contrast. The effect of changes in baseline conditions, such as vascular tone, upon fMRI response to activation are poorly understood. Reduced BOLD response has been seen with vasodilators such as acetazolamide (4), alcohol (5), and heroin (6). In theory, vasocostriction would augment the response, as has been shown with hyperventilation (7). Although a prior study showed no change in BOLD visual activation ~ 25 minutes following cocaine administration (2), cocaine’s peak plasma concentration and physiological effects occur within at 4 – 8 minutes (8). We now examine the time course of possible changes in activation following cocaine, and present a preliminary analysis.

MATERIALS AND METHODS
Subjects
We studied 15 men aged 25.5 ± 3.3 years (mean ± SD) reporting occasional intranasal cocaine use with BOLD fMRI and diffuse flash photic stimulation.

Imaging protocol
Imaging was performed on a 1.5T scanner modified with a whole body echo planar gradient set (Instascan, ANMR). A gradient-echo EPI pulse sequence (TE=40 msec, TR=3 sec, α=66°, 3x3 mm in-plane resolution, slice thickness=6 mm, 3 slices) was used to collect images from an oblique axial plane parallel to the calcarine fissure using a 5 in. surface coil. Images were acquired continually over 30 minutes, with 1 minute periods of 8 Hz photic stimulation via light-proof goggles, alternating with 1 minute periods of darkness. Cocaine or placebo injection
Eight minutes into the acquisition, 0.4 mg/kg cocaine or saline placebo was administered intravenously over one minute in a double-blind fashion.

Image Processing and Analysis
Images from 14 of the 15 subjects were technically adequate for analysis. All image sets were corrected for motion using the DART algorithm (9), and the analyzed for residual motion artifact. Only segments free of significant motion artifact were used for analysis.

MEDx 3.0 was used to produce Z-score maps of photic activation using three discrete 5-minute subsets of the data: at baseline, 5 and 20 minutes following injection. Statistical parameters and thresholding were kept consistent.

Maps were visually inspected by three independent raters blinded to the condition of each case; the 5 and 20 minute post injection maps were rated for change from baseline.

RESULTS
Following cocaine, 5 of 7 subjects showed an increase in activation to photic stimulation; following placebo, all subjects showed either reduction in activation or no change (Fisher’s Exact P-value = 0.02). In most cases, there was greater increase at 5 minutes post-cocaine, with some degree of return to the baseline condition at 20 minutes post-cocaine. No clear correlation with physiological or behavioral response was noted. There was no interrater disagreement with respect to classification.

DISCUSSION AND CONCLUSION
These results suggest that intravenous cocaine administration results in brief, reversible vasocostriction, which can, in and of itself, alter the fMRI response to a focal activation. These findings are consistent with the expected augmented BOLD activation in the face of vasocostriction, and with the known vascular effects of cocaine. Separating the peripheral and central vascular effects of dopaminergic drugs such as cocaine is especially important in light of emerging evidence of dopamine’s critical role in the central regulation of cerebral blood flow (10). These findings demonstrate how rapid, sequential fMRI experiments can address such issues.

REFERENCES

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