Heroin Cue-induced neural activation in heroin addicts: An fMRI study

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Introduction: Functional imaging techniques, including PET and fMRI, have been widely used in studying the neurobiological basis of drug craving in human subjects. Most studies focus primarily on cocaine abusers rather than heroin addicts (1, 2). The neural circuitry responsible for heroin craving has not been clearly identified and warrants further investigation. The objective of this fMRI study is to identify the brain regions activated by heroin-related cues in heroin addicts.

Materials and Methods: Fifteen heroin addicts and 12 normal control subjects (all male, age 32.17±3.83 yrs) were recruited for this study. The heroin subjects had at least 2 weeks drug abstinence before the experiment. A consent form was obtained from each subject before scanning. Two scanning runs were performed for each subject, one for the neutral cue another for the heroin cue. Each run lasted 12 min and contained three sections: 3-min black screen, 4-min video cue (neutral or heroin films), 5-min black screen. **fMRI experiments:** The fMRI scans were conducted at a GE 1.5T Signa LX scanner with a birdcage RF head coil. A set of SPGR anatomical images was acquired prior to functional scans. Functional images were obtained by using a single-shot EPI sequence (TE=30 ms, TR=2000 ms, slice thickness=5 mm, Field-of-view=24 cm, matrix size=64×64, 25 sagittal slices). After the scans, subjects completed a self-report form (Likert scale) referencing their subjective responses about the cues. **Data analysis:** The image processing and statistical analysis were conducted with AFNI. Among all subjects, the data from 9 heroin addicts and 9 control subjects were used after motion detection and correction. The voxel time courses were then linearly detrended then low-pass filtered (f < 0.02Hz). After the pre-processing, the voxel time series were fitted to a beta function model with a linear trend baseline. The activity of each voxel was expressed by the percentage of the area-under-the-curve (AUC%) relative to the area-under-the-baseline. The map of AUC% for each subject was then converted to standard Talairach space and spatially smoothed with a FWHM of 4-mm Gaussian kernel before entering the group statistical test. During group analysis, a linear contrast was formed: AUC% for heroin cue versus AUC% for neutral cue. The nonparametric statistical tests are more robust than traditional parametric tests for a small sample size. A two-sample Wilcoxon signed-rank test was used to test the contrast for the heroin group against the nondrug user group. The test results were then thresholded at $P<0.05$ for activated regions, corrected for multiple comparisons.

Results and Discussions: Relative to the neutral cue, the heroin cue elicited significant activation in a variety of brain regions in the heroin addicts, while no significant regions were activated in the control group. The activation comparison is shown in Figure 1. The heroin users have significant activation in BA10 and the inferior frontal cortex, bilateral amygdale, ventral tagmental area (VTA), thalamus, cerebellum, cuneus, precuneus, and fusiform gyrus (BA19). The heroin cue significantly induced region-specific signals in the mesocortical limbic network in heroin addicts, while have no effects on the control subjects. These neural circuits are related to reward, learning and memory functions. Interestingly, no activation in the nucleus accumbens was induced when the heroin users watched the heroin cues. The nucleus accumbens was activated when cocaine users watched cocaine cues. This difference may relate to their different pharmacological functions in the human brain.

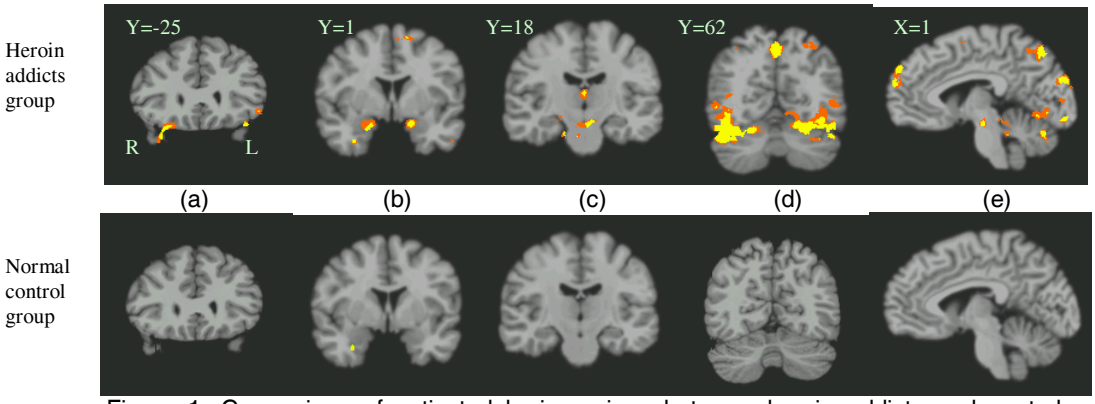

Figure 1. Comparison of activated brain regions between heroin addicts and control subjects. (a) IFC, (b) Amygdale, (c) VTA, (d) Fusiform gyrus (BA19) and Precuneus, (e) BA10

Reference

1. Daglish, M.R. *et al.* Am. J. Psychiatry 2001:158:1680-86. **2**. Xiao Z. *et al.* Drug and Alcohol Dependence 2006:83(2):157-62

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