Participants

Recruitment Sources

Treatment-seeking iCUD were referred from three drug treatment facilities located in the New York Tri-State area: Phoenix House (n = 7), Samaritan Village (n = 5) and Yale Cocaine Research Clinic (n = 7). Phoenix House and Samaritan Village are residential substance abuse treatment facilities where clients undertake increasingly responsible roles in the community as they progress through treatment levels. They both use a "community as method" approach, where all those in treatment ("the community") are responsible for keeping the community safe from outside drugs, alcohol, and other distractions. Only approved visitors are allowed to enter the facility, preventing access to alcohol or drugs. Additionally, both centers conduct drug testing regularly (randomly and at least weekly) to ensure continued abstinence. In contrast, participants from the Yale Cocaine Research Clinic remain in the facility for one month as inpatients and have no access to drugs or alcohol. The seven participants from the Yale Clinic were studied immediately after discharge (at least four days later to ensure clearance of any experimental drug therapy). Note that comparing the efficacy of different treatment facilities/modalities was not a focus of this study. The HC were recruited through advertisements in local newspapers and by word-of-mouth, and were matched on demographics (**Table 1**) with the iCUD.

Passive Picture Viewing

On each visit, participants underwent electroencephalogram (EEG) recordings as they passively viewed a set of 120 pictures. These pictures were selected from the International Affective Picture System (1), and included 30 pleasant (e.g., smiling babies: mean normative valence of 7.6±1.6; mean normative arousal of 5.7±2.4), 30 unpleasant (e.g., violent images: mean normative valence of 2.4±1.5; mean normative arousal of 5.9±2.2) and 30 neutral (e.g., household objects: mean normative valence of 5.3±1.3; mean normative arousal of 2.8±1.9) pictures (1). The fourth picture category (30 pictures) depicted drugs and individuals preparing, using or simulating use of cocaine as previously described (2-5). Each picture was viewed for 2000 msec, with 2,500 msec inter-trial intervals while continuous EEG data was recorded.

EEG recordings and signal preprocessing

Continuous EEG (Neuroscan Inc., Sterling USA) and electro-oculogram recordings were obtained using a 64 silver–silver chloride electrode cap (Compumedics Neuromedical Supplies Inc.) positioned according to the International 10/20 System (6). All recordings were performed using a fronto-central electrode as ground and a central electrode (between Cz and CPz) as reference. Electrodes were placed above and below the left eye to record vertical eye movements, and placed on the outer canthi of both eyes to record horizontal eye movements. The EEG was digitized at a rate of 500Hz and amplified with a gain of 250, and a band-pass filter of 0–70Hz. The amplifiers were calibrated prior to each recording. Electrode impedances did not exceed 10kΩ for any electrodes used in the analysis.

All bioelectric signals were analyzed off-line using Statistical Parametric Mapping (SPM8) for magnetoencephalography/electroencephalography (MEG/EEG) (Wellcome Department of Cognitive Neurology, London, UK; www.fil.ion.ucl.ac.uk/spm/) and custom

MATLAB code (The MathWorks). Data were filtered with low and high cut-offs of 0.01 and 30Hz, respectively, and were then re-referenced to the averaged electrical activity from all 64-scalp sites. Eye-blink and ocular corrections were performed using the partial signal space projection (pSSP) method proposed by Nolte and Hämäläinen (7), such that the contribution to the estimated spatial structure of eye-blink artifact was removed only from the artifact-ridden epochs, leaving as much information as possible in the data. A subsequent artifact rejection procedure identified a voltage step of $\pm75\mu V$ between sample points and a peak-to-peak voltage difference of $100\mu V$ within an epoch. Additional artifacts were identified through visual inspection and subsequently rejected. Robust averaging was then used to minimize the effect of artifacts (8). After data preprocessing, the event-related potentials (ERPs) were constructed by separately averaging trials based on picture category: pleasant, unpleasant, neutral and drug pictures. Because previous findings have indicated that drug-specific LPPs are maximal at central recording sites (9, 10), the LPPs for each picture type were defined as the average activity at the C1, Cz, C2, CP1, CPz and CP2 electrodes. The average activity in the 200 msec window prior to picture onset served as the baseline.

Results

Longitudinal LPP Comparison in Neutral Condition

The paired t-test in iCUD revealed that the LPP amplitude in response to neutral pictures did not change significantly between baseline and follow-up assessments [$t(18)=1.41$, $p=0.175$]. This finding highlights that the attention to neutral cues did not change longitudinally/as a function of practice and/or habituation.

Effects of Confounding Factors

The 2 (Pictures: pleasant, drug) x 2 (Time: baseline, follow-up) x 2 (Lapse: lapsed, abstinent) mixed ANOVA for all iCUD revealed that there was a significant Pictures × Time interaction [$F(1,17)=7.293$, $p=0.015$], similar to our main results. Neither Lapse (in abstinence) main effect nor Lapse-related interactions reached significance ($p>0.05$), suggesting that the lapse status of iCUD did not affect the change in attention-bias between baseline and follow-up.

Further, an independent t-test to ascertain the impact of cigarette smoking on LPP amplitudes and subjective ratings did not reveal significant differences between current and past/never smokers ($p>0.5$), suggesting that smoking history is unlikely to influence the current results.

Supplementary Table 1: The number of trials used to produced averaged ERP for each condition in HC and iCUD (baseline and follow-up).

	HC	iCUD_B	iCUD_F
Pleasant	23.00 ± 4.91	21.56 ± 2.81	22.05 ± 2.78
Drug	23.28 ± 3.01	23.38 ± 3.49	24.21 ± 4.55
Neutral	24.39 ± 4.15	21.75 ± 3.79	24.00 ± 2.04

Values are means ± standard deviation (S.D.). iCUD_B refers to iCUD at baseline; iCUD_F refers to iCUD at follow-up.

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