

## REVIEW ARTICLE

# Craving by imagery cue reactivity in opiate dependence following detoxification

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### ABSTRACT

**Background:** Frequent relapses in opioid addiction may be a result of abstinence-emergent craving. Exposure to various stimuli associated with drug use (drug cues) may trigger craving as a conditioned response to 'drug cues'.

**Aims:** The present study explored the effects of imagery cue exposure on psychophysiological mechanisms of craving, viz. autonomic arousal, in detoxified opiate addicts.

**Methodology:** Opiate dependent subjects (N=38) following detoxification underwent imagery cue reactivity trials. The subjects were asked to describe verbally and then imagine their craving experiences.

**Results:** Craving was measured subjectively by using Visual Analogue Scale and autonomic parameters of galvanic skin resistance (GSR), pulse rate (PR), and skin temperature (ST) was taken during cue imagery. Spearman's *r* and Wilcoxon signed ranks test were employed in analysis. Multivariate repeated measurement analysis (Wilks' Lambda) was employed wherever appropriate. Subjective measures of craving, GSR and PR increased significantly whereas ST decreased significantly during drug related cue imagery as compared to neutral cues.

**Conclusions:** The results support that cue imagery is a powerful tool in eliciting craving. Hence, it can be used as a screening manoeuvre for detecting individuals with high cue reactivity, as well as for extinction of craving.

**Key words:** cue reactivity, imagery, opiate addiction, craving.

### INTRODUCTION

Drug addiction is a major public health problem having multiple dimensions, disrupts many aspects of social life. It is a complex illness, which runs a chronic course with frequent relapses (Gossop et al, 1989). Drug craving related to various opioid related environmental cues is one of the most important predictors of high-risk behavior or relapse in opioid dependence (Powell et al, 1993). Craving has been defined as a strong, and almost overpowering urge for opiates that is experienced by opiate addicts during acute withdrawal. Craving can be elicited by various external and internal opioid related cues such as sight, smell of the opioid or sensation of an opioid entering stomach. Cue exposure at its most basic refers to a general process in classical

conditioning theory, in which a cue (or stimulus) when presented to an animal, the response of the animal is dependent on the previous experience that the animal has had with cue. A cue that has been repeatedly paired with opioid administration can be viewed as conditional stimulus which, when the animal is exposed to cue alone, can elicit a conditioned response. Craving can also be associated with vivid imagery of drug taking behavior (Bradley and Moorey, 1998). When the individual is exposed to opioid related imagery, it results in autonomic arousal, symbolic expressive and behavioral reactivity (Niaura et al, 1988; Drummond et al, 1990). The present study was undertaken with the objectives of measuring the intensity of craving by providing imagery cues to patients of opioid dependence following successful detoxification. This may have the practical

utility in screening those individuals who are reactive to drug cues and are consequently at a high risk of relapse. This can be exploited as an important tool in the relapse prevention programs.

### METHOD

#### Settings and Participants

Thirty-eight male subjects, aged 15 to 60 years, mostly inpatients, meeting the diagnostic criteria of opioid dependence according to Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) (APA, 1994) were included in the study. Most were in the second week of deaddiction program following one week of detoxification. A written informed consent was obtained from all.

The average daily consumption of opiate substances was 1.2 gm and majorities were used for 5 or more years. Participants having medical or Psychiatric illness, significantly limiting their capacity to participate in the study, not willing to participate, withdrew consent (dropouts), relapsed following detoxification, expressed their inability to imagine the cue, and needed other drug(s) apart from standard regimen to control withdrawal symptoms were excluded from the study.

#### Procedure

After 5 minutes relaxation, the baseline parameters of galvanic skin resistance (GSR), skin temperature (ST), and pulse rate (PR) were recorded. These recordings were done during the last one-minute of relaxation. Subjects were then asked to describe a pleasurable situation they experienced in the past (e.g. about a picnic, travel etc) for 2 minutes. After completing the description, patient was asked to imagine the same by closing the eyes (Imagery) for another two minutes. During the last half minute, all the parameters were measured again. Then 2-minute rest was given and the subjects were asked to relax during that time. Subjects were then asked to describe a drug-craving situation verbally for 2 minutes. Here most patients described situations when there was difficulty in getting drug, subsequent problems of withdrawal and intense craving.

After verbally describing for two minutes, subjects were asked to imagine the same for another two minutes with their eyes closed. During the last half-minute of the experiment all the parameters were measured and documented. Then the recording device was removed, and subject were made to sit comfortably.

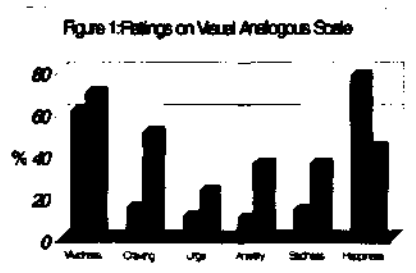
**Measurement of craving**

Subjects then rated their verbal descriptions on a Visual Analogue Scale (VAS) (ratings 0-100) on measures of vividness, craving, urges, anxiety, sadness, and happiness, during both pleasurable and craving imagery.

**RESULTS**

Ratings on VAS for all six descriptions in detoxifying subjects were compared between craving and pleasurable (neutral) descriptions by using paired *t* test. Highly significant difference was found between the ratings of vividness, craving, urge, anxiety, sadness, and happiness during recollections of craving imagery as compared to neutral imagery ( $p < 0.001$ ). Similar significant difference ( $p < 0.001$ ) was also found when all descriptions were compared for craving and neutral imagery by using multivariate repeated measurement analysis (Wilks Lambda) (Fig. 1).

FIG. 1 shows ratings on visual analogue scales (VAS) all descriptions in detoxifying subjects after pleasurable and drug related cue imagery.



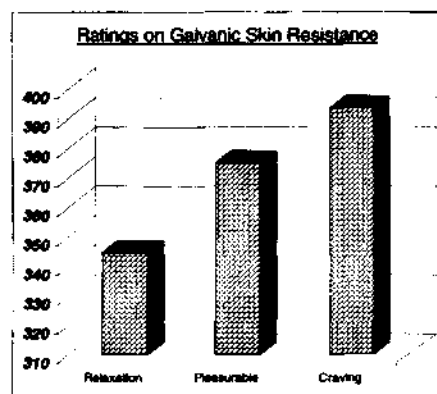
**Behavioral measures**

Repeated measures ANOVA (RM-ANOVA) to determine the significance of magnitude of change from the neutral to

drug related imagery was not appropriate with a fixed order of pleasurable verbal descriptions and imagery first and craving talking and imagery afterwards. Previous talking and imagery of positive and neutral experiences would confound factors such as talking and imagery of craving, but this would not be problematic for the within-subject analysis. Hence the measures were compared by means of a Paired Wilcoxon test and Multivariate Repeated Measurement Analysis.

Subjects showed a significant increase in GSR during drug related imagery compared with neutral imagery (20 units) when compared by means of a Wilcoxon signed ranks test ( $p < 0.005$ ) (Fig. 2).

**FIGURE 2:** Showing galvanic skin resistance (GSR) with exposure to neutral, pleasurable and craving-eliciting cue imagery.



Because of wide individual variations (high variance) of GSR, we carried out the percentage increase or decrease in GSR from relax to neutral imagery, from neutral to craving imagery, and from relax to craving imagery (Table 1).

Using multivariate repeated measurement

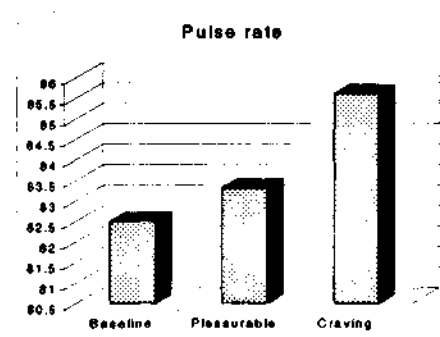
**TABLE I :** Showing significant change (neutral to craving delta) the mean values of percentage change of GSR during imagery cue.

	*RLX->PLS (RP)	*PLS->CRV (PC)	*RLX->CRV (RC)
GSR	10.4	6.9	17.7

analysis; significant change were found between them (Wilks Lambda  $r = 1.055$ ;  $p < 0.05$ ). When compared with wilcoxon signed ranks test between GSR (Relaxation to craving) and GSR (Pleasurable to craving) significant changes were found based on negative ranks ( $z = 3.130$ ;  $p < 0.005$ ).

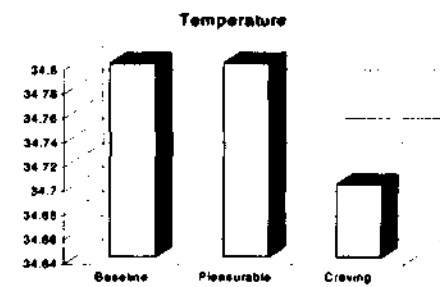
Subjects showed a significant increase in pulse rate indicative of physiological arousal during drug related imagery cue compared with pleasurable cue (2.3 beats) when compared by means of a paired Wilcoxon test ( $p < 0.005$ ) (Fig. 3).

**FIGURE 3:** Showing pulse rate (PR) with exposure to neutral, pleasurable and craving-eliciting cue imagery.



Furthermore, the test subjects showed a significant decrease in skin temperature during drug related imagery compared with neutral imagery, on comparing the data using Wilcoxon signed ranks test ( $z = 2.838$ ;  $p < 0.005$ ) (Fig. 4).

**FIGURE 4:** Showing temperature in all the experimentally delivered cue-determined conditions, respectively.



(\*RLX -> relaxation; \*PLS-> pleasurable; \*CRV -> craving).  $\bar{\eta}^2$  ( $p < 0.05$ )

**TABLE. 2 :** shows galvanic skin resistance, skin temperature, and pulse rate during both drug related cue and pleasurable cue imagery over 2 min recording.

	Baseline	Pleasurable	Craving
GSR	344.4 (170.9)	374.7 (192.7)	393.3 (209.8)
Skin Temp.	34.8 (1.1)	34.8 (1.1)	34.7 (1.1)
Pulse rate	82.5 (12.8)	83.3 (12.1)	85.6 (11)

When all three situations viz. relax (baseline), pleasurable, and craving imagery were compared by multivariate repeated measurement analysis for skin temperature, it showed significant decrease ( $p < 0.05$ ) from neutral to drug related cue. These physiological results indicate greater arousal in subjects while imagining drug craving as compared to imagining pleasurable verbal descriptions.

## DISCUSSION

In a subject, acute opiate administration results in decreased arousal, increased peripheral skin temperature, and pupillary constriction whereas opiate withdrawal causes decreased skin temperature, tachycardia, and pupillary dilation. By contiguous pairing of various environmental and internal drug related paraphernalia (stimuli) with periods of withdrawal-induced distress, the withdrawal syndrome can become a conditioned response (CR). This in turn leads to withdrawal response (CR), whenever the individual encounters with any stimuli associated with withdrawal (Wikler, 1948; Siegel, 1975). Negative reinforcements are not the only culprits that compel an individual for compulsive drug ingestion, rather positive incentive values of the drug, in the absence of aversive states associated with withdrawal state, sometimes act as an appetitive motivational force behind this habit (Stewart et al, 1984).

The results of the study throw light on the imagery technique as a strong indicator of craving in opioid dependent individuals post detoxification. This is indicated by both the subjective ratings on the VAS as well as by autonomic measures. It has

been suggested that opioid related visual stimuli in the form of exteroceptive cues are powerful autonomic conditioned response elicitors (Childress et al, 1988). In this experiment interoceptive cues such as subjects own images were used as stimuli to elicit the conditioned responses. Tiffany and Hakenwerth (1991) reported increase in heart rate in the smokers during urge imagery verbal descriptions as compared to neutral imagery verbal descriptions suggestive of autonomic arousal by manipulating affective states in an individual. Weinstein et al (1997) in a similar experiment studied craving through imagery in opiate addicts undergoing detoxification, and observed a significant increase in heart rate during drug talk and a significant increase in systolic blood pressure during the drug related imagery. The most consistent responses to drug related stimuli across a series of studies include decrease in galvanic skin resistance (Childress et al, 1988, 1986; McCaul et al, 1989; Newlin et al, 1985) and decrease in skin temperature (Childress et al, 1986). A few studies reported significant increase in skin conductance as a response to drug related cues (Glaulier and Drummond, 1994; Sideroff and Jarvic, 1980). In the current experiment too, decrease in skin temperature, increase in both heart rate and galvanic skin resistance were found during the drug imagery.

During the imagery of drug related descriptions significant increase in craving, urge, anxiety, and sadness as compared to significant decrease in happiness in the VAS suggested that negative affective states rather than positive appetitive forces played a role in conditioned responses keeping in with the classical conditioned model (Wikler, 1948; Siegel, 1975).

The significant change in the GSR, skin temp, and pulse rate while imagery craving of drug paraphernalia provides a preliminary evidence of eliciting craving which among the major factors playing role in relapse. If could be successfully used, the same procedure might be used for extinction of craving as was carried out by Tiffany and Drobos, 1990; Tiffany and Heckenwerth, 1991; and Elash et al, 1995.

The advantages of using imagery procedure are many, as it can be generalised to many drug related extero- and interoceptive cues, which might have been very difficult producing in vivo.

Finally, the imagery paradigm may have the practical utility in screening those individuals at risk (reactive to cue exposure) for relapse. It is well established that, relapse is a key problem in the drug addiction and most studies reveal high rate of relapse to drug use after treatment (Gossop et al, 1989).

In our study, we tried to find out the cue reactivity by imagery in opiate addicts and this reactivity might cause them more vulnerable to relapse. Imagery can therefore be a useful tool in addressing individual's reactivity to various drug craving cues and may give an objective measure of their potential risk of relapse to drug use.

Given the current uncertainty concerning the usefulness of cue exposure in the treatment of opiate addiction, this procedure may therefore play an important role as a part of relapse prevention treatment.

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