Designing and Evaluation of Reliability and Validity of Visual Cue-Induced Craving Assessment Task for Methamphetamine Smokers

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Article info:
Received: 10 April 2009
First Revision: 5 May 2009
Accepted: 20 June 2009

ABSTRACT

Introduction: Craving to methamphetamine is a significant health concern and exposure to methamphetamine cues in laboratory can induce craving. In this study, a task designing procedure for evaluating methamphetamine cue-induced craving in laboratory conditions is examined.

Methods: First a series of visual cues which could induce craving was identified by 5 discussion sessions between expert clinicians and 10 methamphetamine smokers. Cues were categorized in 4 main clusters and photos were taken for each cue in studio, then 60 most evocative photos were selected and 10 neutral photos were added. In this phase, 50 subjects with methamphetamine dependence, had exposure to cues and rated craving intensity induced by the 72 cues (60 active evocative photos + 10 neutral photos) on self report Visual Analogue Scale (ranging from 0-100). In this way, 50 photos with high levels of evocative potency (CICT 50) and 10 photos with the most evocative potency (CICT 10) were obtained and subsequently, the task was designed.

Results: The task reliability (internal consistency) was measured by Cronbach's alpha which was 91% for (CICT 50) and 71% for (CICT 10). The most craving induced was reported for category Drug use procedure (66.27±30.32) and least report for category Cues associated with drug use (31.38±32.96). Difference in cue-induced craving in (CICT 50) and (CICT 10) were not associated with age, education, income, marital status, employment and sexual activity in the past 30 days prior to study entry. Family living condition was marginally correlated with higher scores in (CICT 50). Age of onset for (opioids, cocaine and methamphetamine) was negatively correlated with (CICT 50) and (CICT 10) and age of first opiate use was negatively correlated with (CICT 50).

Discussion: Cue-induced craving for methamphetamine may be reliably measured by tasks designed in laboratory and designed assessment tasks can be used in cue reactivity paradigm, and imaging studies related to methamphetamine dependence.

Key Words:
Craving,
Cue Reactivity,
Methamphetamine,
Visual Task

1.Introduction

Methamphetamine abuse is a serious health problem in Iran and the world (UNODC, 2009). Methamphetamine is a stimulant drug with high abuse and dependence potential. There is no approved pharmacological treatment for the treatment of methamphetamine abuse, the rates of relapse are high and psychological interventions are the main modality of treatment (Elkashef et al., 2008).

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Craving is understood as an urge to use drug in dependent individuals with multiple biological, psychological and environmental aspects (Ekhtiari et al., 2006). Although an accurate universally acceptable definition of craving is though (Tiffany et al., 2000 & Abrams, 2000), it is commonly defined as an intense, irresistible and pathological urge to use the favorite drug (Sayette et al., 2000). This is often considered by most clinicians as a crucial feature in contributing to relapse (Elkashef et al., 2008).

One of the early pioneers who studied cue reactivity, Wikler (1948) suggested that cues related to the drug play a critical role in the pathogenesis of drug dependence in human and animal subjects. Cues associated with drug use can evoke cue reactivity which has symbolic (such as craving and enjoyment), physiological (such as withdrawal signs similar to drug) and behavioral signs (drug-seeking and using behavior) (Drummond, 2000). On the other hand, cue-reactivity, which is based on classical conditioning response, is a predictor of relapse and can facilitate reinstatement of dependence (Drummond, 2000 & Kuntze et al., 2001). Cue reactivity is a universal phenomenon applicable to all drugs. Some studies have shown that cue exposure among methamphetamine users could induce severe craving (Tolliver et al., 2010).

In recent years, several major theoretical models e.g. phenomenological models, cognitive theories and conditioning models have tried to explain craving and it relationship to cue-reactivity (Drummond, 2001). Although no single model can comprehensively explain all aspects of drug craving, the classical conditioning model proposed by the Russian scientist Ivan Pavlov delicately explains cue-induced craving (Van Gucht et al., 2008). Such theoretical and methodological approaches have provided definitions and also principles for reliable measurement of drug craving (Sayette et al., 2000).

Based on Ludwig's theory (1988), craving originates from two sources: withdrawal craving (baseline craving) and cue-elicited craving, which are correlated to each other but cue-elicited craving is more likely to provoke intense craving and predict relapse phenomenon. Whereas in baseline craving, withdrawal symptoms can provoke reactivity and enhance cue-reactivity craving (Drummond, 2000).

Drug craving may be induced and elicited by diverse approaches in controlled laboratory conditions and settings such as drug use imagery, drug using paraphernalia and its instruments, and pictorial or verbal drug cue exposure associated to users (Sayette et al., 2000) or some very recently emergent techniques such as virtual reality technology (Kuntze et al., 2001; Lee et al., 2004 & Ryan et al., 2009). Craving induction may also be used in functional magnetic resonance imaging studies on neuro-circuits of craving (Bauman et al., 2003) or in clinical settings for desensitizing cue exposure treatment (Franken et al., 1999).

Several studies have examined the role of different cues in inducing drug craving in cocaine (Fox et al., 2005 & Saladin et al., 2006), heroin and other opiate users (Franken et al., 2004; Yu et al., 2007; Ekhtiari, et al., 2006, 2008 & Yu Ren et al., 2009), alcohol (Tiffany et al., 2000 & Heinze et al., 2007), nicotine (Chiamulera, 2005 & Tong et al., 2007) and tobacco (Heishman et al., 2006). But we found only very few studies (only 3 studies so far) which have investigated the significant role of methamphetamine craving (Hartz et al., 2001; Newton et al., 2006 & Tolliver et al., 2010) in human subjects.

Hartz and his colleagues (2001) conducted a study assessing the relationship between the severity of craving and relapse among 31 male and female methamphetamine dependent patients in treatment and found that craving can significantly predict continued use of methamphetamine in methamphetamine patients in treatment. Newton and his colleagues (2006) in their research on the role of bupropoin in reducing induced subjective effects and cue-induced craving among 20 methamphetamine subjects found that bupropion could reduce cue-induced craving in methamphetamine dependent subjects. Tolliver and his colleagues (2010) in their study on cue-induced craving and physiological reactivity among 43 methamphetamine abusers found that compared with baseline craving, craving was dramatically increased after methamphetamine cue-exposure. No meaningful correlation was found between physiological reactivity and cue-induced craving but baseline craving was strongly correlated with cue-induced craving.

The present study is aimed to develop a series of visual cues which induce drug craving among methamphetamine smokers in the controlled experimental conditions and provide a task for valid and reliable induction and measurement of methamphetamine craving.

2. Methods

2.1. Subjects

Men aged 18-55 who met DSM-IV.TR criteria for methamphetamine dependence with the past six months prior to study entry were eligible to participate. Only treatment seekers who were recruited from the waiting

lists of outpatient stimulant use treatment clinic of INCAS and from 4 other local private drug use treatment clinics in the capital city of Tehran, Iran were selected as the sample. Subjects were required to meet physician' medical approval on positive methamphetamine urine screening test for entry in to study. Subjects with current psychiatric disorders, affective disorders, and current dependence on any other drug except nicotine, using medication other than sedatives or failing to meet mental health requirements were also excluded. The study was approved by the institutional review board of Tehran University of Medical Sciences (TUMS) and Research Committee of INCAS. All subjects were given oral and written consent forms prior to study entry.

2.2. Study Design

All study procedure was conducted in the neurocognitive laboratory of the Iranian National Center for Addiction Studies (INCAS), Tehran University of Medical Sciences (TUMS) between 2008 and 2009. Potential participants were screened using a short structured diagnostic interview based on DSM.IV.TR criteria to assess psychiatric and substance use symptoms. After strictly following the inclusion and exclusion criteria, 50 eligible subjects were included in the study.

2.3. Study Procedure

Before beginning the study, the task was required to design and it was done in four consecutive phases as follow:

First Phase: Visual Cue Selection and Task Design

To develop a list of effective visual cues for craving induction among methamphetamine subjects, five focus group discussions (FGDs) were held with voluntary participation of 10 active non-treatment seeking methamphetamine smokers in the neurocognitive laboratory of INCAS. The focus groups were conducted by an INCAS expert psychologist in the field of drug addiction, to discuss possible imagery evocative scripts which may induce subjective craving based on brain-storming, their personal memories of methamphetamine smoking and their experiences on craving inducing situations.

Each participant identified a series of craving inducing situations that included methamphetamine-related cues (e.g. viewing methamphetamine, pack, lighter, pipe, methamphetamine smoking, meeting a drug-using peer, watching others preparing and smoking). The cues were developed from specific descriptions of each situation and were used as an example of a trigger for subsequent methamphetamine smoking. In the fifth FGD session, the list of proposed evocative cues reached an acceptable saturated level. The cues that had been proposed at least twice in FGD sessions were selected for the final list to avoid including cues related to unique personal experiences.

Then, an expert committee consisting of INCAS physicians, psychiatrists and psychologists who were all experts in the field of craving and addiction research, classified evocative visual signs into 4 main categories (Drug, Instruments, Accompanying cues, and act of abuse). Subsequently, the INCAS laboratory professional photography team provided the required photos of real situations of methamphetamine smoking in a private studio. All the pictures were taken with a black background for two main reasons: first, to avoid interfering background elements, and second, to make it possible to use these pictures in tight pictures-matched (active vs. neutral) task design for functional magnetic resonance imaging (fMRI) or stimulus-response behavioral studies. Sixty active pictures were selected, 12 pictures for each category, except "act of abuse" category with 24 pictures, to be assessed in the next step.

For designing the visual cue-induced craving task, a list of neutral cues was also developed by the expert team with similar visual patterns to craving inducing pictures such as taking a pen in hand, a battery on a flat surface and keeping sugar lumps in hand. Three volunteer participants were asked if these scenes were neutral methamphetamine-free situations, and no participant endorsed these scenes as triggers. Then 12 neutral photos were taken and added to methamphetamine- craving inductive photos in a printed 72 picture task, all with black backgrounds and with the size of 33× 23 cm.

To minimize the carry over effects of craving during cue exposure process and having more intensive craving report for the last pictures, we applied a numbering order with 6 blocks of 10 evocative cues and 2 control (neutral) photos in a sequential way from number 1 to 72. Then, each subject received a random number from 1 to 72 (selected number was excluded from number list), and the cue exposure sessions began with the picture that had the allocated number and terminated with the previous picture in the list.

Second Phase: Inclusion of Subjects for Assessment of Craving Cues

The 50 male subjects were included in the study as described in subject section. Consent forms were signed. Demographics, details of substance use and risky behaviors were collected using the Addiction Severity Index (fifth edition) (Mclellan, et al., 1992) before cue

exposure, by the laboratory interviewer and cue exposure session began as follow.

Third Phase: Evaluation of Cues by Methamphetamine Abusers

Participants were asked to rate the intensity of their craving and their subjective urge for methamphetamine induced by each picture on self report VAS from 0 to 100. The time interval of each cue exposure in the task was between 15 - 20 seconds.

Physical examination and clinical interview were done before and after cue exposure. Subjects who reported craving during the cue exposure or physiological reactions such as dizziness, severe heartbeat and flushing, remained in the laboratory until the levels of craving retuned to baseline level. All the participants received a brief psychological intervention for craving reduction before leaving the laboratory.

Fourth Phase: Selection of Cues for Long and Short Craving Induction Tasks

In the final phase, two less evocative pictures were omitted from each category of the 12 active or neutral cues, to reach a task with 50 evocative and 10 neutral pictures in following main categories (See details of each category in figure.1):

1. Methamphetamine outside or inside package without instruments (5 pictures)
2. Methamphetamine with instruments (5 pictures)
3. Instruments (10 pictures)
4. Cues accompanied with drug use, such as candies beverages, cigarette, money and etc. (10 pictures)
5. Act of abuse without a seen instrument (5 pictures)
6. Act of abuse with pipe (5 pictures)
7. Act of abuse with used lamps (5 pictures)
8. Act of abuse with foil (5 pictures)

Furthermore, 10 most evocative cues (one or two pictures in each category of the task) and 2 neutral pictures (battery and sugar lumps in hand) were selected as the format of short pictorial task which has been marked by sign (*) in figure.1.

2.4. Statistical Analysis:

Mean scores of the 50 active cues (Long Version of Cue Induced Craving Assessment Task or CICT 50), the 10 most provocative cues (Short Version of Cue Induced Craving Assessment Task or CICT 10) and the mean scores of each category of cues were calculated, all by descriptive methods. Demographics, profile of substance abuse and risky behaviors of the subjects were also analyzed by descriptive statistical methods. Pearson correlation coefficient was calculated to determine the relationship between demographic characteristics e.g. age, years of education, monthly income and sexual activity with spouse and non-spouse with scores of CICT 50 and CICT 10 (Pearson's correlation was applied for non normally distributed variables determined by KS test). Independent-sample T-test was used to determine the relationship between living condition, substance abuse profile, risky behaviors and first type of drug use (in the past 30 days and entire life-time) with CICT 50 and CICT 10. ANOVA was also used to determine the relation between marital and employment status with CICT 50 and CICT10. To measure the reliability of the task, Alpha Cronbach's test was used for each category of the task, CICT 50 and CICT 10 respectively. All data were analyzed by using the SPSS-16 version.

3. Results

The subjects were all male. The mean age of the sample was 28.40 and the mean years of education were 11.32. The majority of the sample (88%) was living with family, single (46%) and approximately half of them were without employment (42%) at the time of participation in the study (See some demographic keys in Table 1).

Table 1. Details of demographics in participants (n=50).

Gender (male)		50(100.0%)
Age		28.40±7.63
Education (years)		11.32±3.10
Living Conditions	With family	44(88.0%)
	With friends/colleagues	1(.2%)
	Alone	5(10.0%)
Marital Status	Married	18(36.0%)
	Single	23(46.0%)
	Separated	1(2.0%)
	Divorcee	8(16.0%)
Employment	Full time	15(30.0%)
	Student	2(4.0%)
	Part time	12(24.0%)
	Out of work	21(42.0%)
	Monthly income (last month)(dollars)	416.83 (±212.220)

Subjects had initiated methamphetamine use at mean age of 25.34, with 19.6 days of methamphetamine use in the past 30 days prior to study entry and 3.9 years methamphetamine dependence. Majority of the sample (76%) initiated serious drug use with opiates (e.g. opium, heroin and crystalline heroin) while some of subjects (24%) initiated with methamphetamine. Participants also had a history of using other drugs e.g. opium (76%), heroin (32.7%), crystalline heroin (59.2%), cocaine (16%), hashish (56%), alcohol (76%), tramadol (48%), ecstasy (34%), sedatives (30%) and also nicotine (96%) (See the details in Table 2).

Table 2. Substance use details among participants (n=50).

Methamphetamine (Main type of drug)	Abuse History (life-time)	50(100.0%)
	Age of onset	50(25.34±8.5)
	No. of abuse days (in the past 30 days)	50(19.6±10.1)
	Duration of dependence (years)	50(3.9±9.5)
	Route of abuse Smoking	50(100.0%)
	Cost of methamphetamine abuse (last month)(dollars)	416.50(±262.94)
First Hard Drug at Onset	Opiates	38(76.0%)
	Methamphetamine	12(24.0%)
Opium	Abuse History (life-time)	38(76.0%)
	Age of onset	38(19.7±4.9)
	Duration of dependence (years)	28 (5.81±5.31)
	Route of abuse Injection	5(13.2%)
	Route of abuse Smoking	33(86.8%)
Heroin	Abuse History (life-time)	16(32.7%
	Age of onset	16(21.7±5.1)
	Duration of dependence (year)	7(3.07±2.3)
	Route of abuse Smoking	11(68.7%)
	Route of abuse Sniffing	2(12.5%)
	Route of abuse Injection	3(18.7%)
Crystalline Heroin	Abuse History (life-time)	29(59.2%)
	Age of onset	29(24.9±7.7)
	Duration of dependence (years)	21(2.81±2.27)
	Route of abuse Smoking	27(98.8%)
	Route of abuse Injection	2(1.2%)
Cocaine	Abuse History (life-time)	8(16.0%)
	Age of onset	8(21.5±4.8)
	Duration of dependence (years)	1(1.5±0.0)
	Route of abuse Sniffing	3(37.5%)
	Route of abuse Smoking	4(50.0%)
	Route of abuse Sniffing/smoking	1(12.5%)
Cannabis (Hashish)	Abuse History (life-time)	28(56.0%)
	Age of onset	28(17.6±5.9)
	Duration of dependence (year)	9(3.4±4.4)
	Route of abuse Smoking	28(56.0%)
Alcohol	Abuse History (life-time)	38(76.0%)
	Age of onset	38(16.5±5.0)
	Duration of dependence (year)	5(9.0±3.0)
	Route of abuse Ingestive	38(100.0%)
Tramadol Tablet	Abuse History (life-time)	24(48.0%)
	Age of onset	24(22.9±6.3)
	Duration of dependence (years)	4(9.1±16.16)
	Route of abuse Ingestive	24(100.0%)
Ecstasy	Abuse History (life-time)	17(34.0%)
	Age of onset	17(20.5±3.4)
	Duration of dependence (years)	4(1.9±2.1)
	Route of abuse Ingestive	17(34.0%)

Table 2. Cont.

Sedatives	Abuse History (life-time)	15(30.0%)
	Age of onset	15(23.9±6.9)
	Duration of dependence (years)	4(3.0±1.6)
	Route of abuse Ingestive	15(100.0%)
Cigarette	Abuse History (life-time)	48(96.0%)
	Age of onset Age of onset	48(17.21±5.5)
	Duration of dependence (years)	48(9.9±7.3)
	Route of abuse Smoking	48(100.0%)

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A few subjects (16%) had history of injecting drug and very few (2%) reported sharing injecting syringes. History of jailing/arrest (20%) and drug dealing (38%) were also common among subjects. The majority (90%) reported positive life time history of sexual experiences. Nearly half the sample (44%) reported extra marital sexual activity in the past 30 days prior to study entry and the number of condom users (16%) was small but they did not report any positive result in HIV and HCV tests (See the details in Table 3).

Table 3. Details of risky behaviors among participants (n=50).

Drug Injection (life-time)		8(16.0%)
Shared Injecting Needles (Life-time)		1(2.0%)
Jailing/Arrest	**Life-time**	10(20.0%)
	Last year	5(10%)
Drug Dealing	**Life-time**	19(38.0%)
	Last year	3(6.0%)
Positive History of Sex (entire –life time)		45(90.0%)
Number o Sexual Activity (last month)		1.86± 2.83
Number of extra Marital Sexual Activity (last month)		1.30 ± 1.81
Extra Marital Sexual Activity (last month)		22(44.0%)
Condom Use in extra Marital Sexual Activity (last month)		8(16.0%)
Medical Examination of HIV Test (Positive result)		0(0.0%)
Medical Examination of HCV Test (Positive result)		0(0.0%)

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Table 4 shows the relationship between some demographic characteristics with scores in CICT 50 and CICT 10. Pearson correlation coefficients shows no meaningful correlation between demographics e.g. age, education years and monthly income with scores of CICT 50 and CICT 10 respectively.

Table 4. Correlations between demographics, score of cue induced craving task with 50 cues (CICT 50) and 10 cues (CICT 10) (n=50).

		Age	Education	Monthly Income
CICT 50 Scores	**Coefficient**	-.092	.001	.153
	P Value	.527	.994	.340
CICT 10 Scores	**Coefficient**	.019	-.212	.057
	P Value	.898	.139	.725

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Furthermore, ANOVA analysis, indicated no relationship between marital and employment status with scores of CICT50 and CICT10 respectively. We should mention that we divided the subjects in 3 marital groups e.g. married, single and separated and in 3 employment groups e.g. full-wok, part-time and jobless for ANOVA analysis. In contrast, Living with family was associated with higher scores of CICT50 in T-test analysis with marginal significance (p value=0.057). We should also mention that we divided the subjects in 2 family groups e.g. living with family and not living with family for statistical T-test analysis.

Table 5 shows negative relation between age of first hard drug use (opioid or stimulant) with CICT50 and CICT 10 and age of first opiate use with CICT50.

Table 5. Correlations between substance use details and score of cue induced craving task with 50 cues (CICT 50) and 10 cues (CICT 10) (n=50).

		Age of first sub-stance	Age of first Soft drug use	Age of first hard drug use	Age of first opiate use	Onset age of metham-phetamine use	Duration of metham-phetamine dependence /Year	No. of metham-phetamine use in last 3o Days	Cost of metham-phetamine use /Last Month.$
CICT 50	Coefficient	-.089	-.105	-.338	-.328*	-.107	.210	-.302	-.013
	P Value	.540	.475	.016	.039	.460	.144	.082	.931
CICT 10	Coefficient	.028	.024	-.391	-.240	-.058	.014	-.233	-.001
	P Value	.846	.873	.005	.135	.689	.923	.185	.994

**. Correlation is significant at the 0.01 level (2-tailed).
*. Correlation is significant at the 0.05 level (2-tailed).
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Table 6 shows the relationship between some risky behaviors in the past 30 days prior to study entry and scores of CICT 50 and CICT 10. Pearson correlation coefficients show no meaningful correlation between risky behaviors e.g. number of extra marital sex and number of condom use in extra marital sex with scores of CICT 50 and CICT 10 respectively. All data in this section relate to the past 30 days prior to study entry.

Table 6. Correlations between sexual activities and score of cue induced craving task with 50 cues (CICT 50) and 10 cues (CICT 10) (n=50).

		No. of Extra Marital Sex Last Month	No. of Sex with Spouse Last Month	No. of Sex Last Month	No. of condom use Last Month
CICT 50 Scores	Coefficient	-.210	.120	-.074	-.164
	P Value	.143	.408	.611	.256
CICT 10 Scores	Coefficient	-.152	.023	-.101	-.100
	P Value	.292	.875	.486	.490

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Table 7 shows the relationship between the substances used in the past 30 days prior to study entry and the intensity of cue-induced craving in CICT 50 and CICT 10. The statistical analysis (independent sample T-test) indicates, no meaning relationship between the substances used (crystalline heroin, hashish and sedatives) in the past 30 days and the cue-induced craving scores (See the details in table 7).

Table 7. Comparison between score of cue induced craving task with 50 cues (CICT 50) and 10 cues (CICT 10) (n=50) among those who used other drugs or not in last month.

Abuse in last 30 days	Negative (CICT50)	Positive (CICT10)	P Value
Crystalline Heroin	44(45.55)	6(37.83)	.299
Cannnabis (Hashish)	44(44.35)	6(46.65)	.759
Sedatives	46(44.19)	4(49.63)	.543
Abuse in last 30 days	**Negative (CICT10)**	**Positive (CICT10)**	**P Value**
Crystalline Heroin	44(67.04)	6(61.83)	.451
Cannnabis (Hashish)	44(65.98)	6(69.67)	.594
Sedatives	46(66.17)	4(69.28)	.708

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Table 8 shows the relationship between the substances used, risky behaviors (e.g. jailing/arrest, drug injection, history of sex and history of extra marital sex activity) and the first type of drug used in entire life-time and the intensity of cue-induced craving in CICT 50 and CICT 10. The statistical results (independent sample T-test) indicates, no meaning relationship between the uses of opium , heroin, crystalline heroin, hashish, sedatives in entire life-time, risky behaviors and first type of drug used in entire life time with the cue-induced craving scores of CICT 50 and CICT 10 respectively (See details in Table 8).

Table 8. Comparison between score of cue induced craving task with 50 cues (CICT 50) and 10 cues (CICT 10) among the subjects who used other drugs or not in entire life (n=50).

Abuse in entire life	Negative (CICT50)	Positive (CICT50)	P Value
Opium Abuse	12(38.7937)	38(46.4657)	.174
Heroin Abuse	34 (45.7187)	16(42.2990)	.511
Crystalline Heroin	21(45.3067)	29(44.1304)	.811
Hashish	21(44.3595)	29(44.8162)	.926
Sedatives	35(45.1489)	15(43.4006)	.742
Drug Injection	42(45.8346)	8(38.2708)	.251
History of sex	5(56.7815)	45(43.2736)	.091
History of Extra Marital Sex	27(46.1164)	23(42.8730)	.505
First Type of Drug Use	12(38.7937)	38(46.4657)	.174
	Negative (CICT10)	**Positive (CICT10)**	
Opium Abuse	12(57.92)	38(69.10)	.030
Heroin Abuse	34(65.07)	16(69.29)	.380
Crystalline Heroin	21(64.53)	29(67.79)	.474
Hashish	21(67.14)	29(65.89)	.784
Sedatives	35(66.61)	15(65.97)	.897
Drug Injection	42(67.25)	8(62.08)	.398
History of sex	5(73.54)	45(65.63)	.289
History of Extra Marital Sex	27(66.57)	23(66.24)	.942
First Type of Drug Use	12(57.92)	38(69.10)	.030

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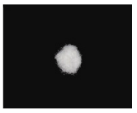
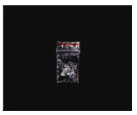
Figure 1. Selected categories of craving induced pictorial cues for methamphetamine abusers. cues were rated by 50 methamphetamine smokers with 0-100 Visual Analogue Scale (VAS). Results were presented in Mean ± Sandard Deviation. Starred pictures have been selected as a Pictorial Cues-Induced Craving Assessment Task for Methamphetamine Abusers (CICT 10)

Main Category		Features	Photo
A. Drug	I. Without Instrument	* 1. Methamphetamine Crystalls 70.79 ± 28.18	
		2. Methamphetamine Powder 67.40 ± 36.11	
		3. Methamphetamine Crystalls inside Pack 46.90 ± 36.02	
		4. Methamphetamine Powder inside Pack 65.40 ± 36.78	
		5. Methamphetamine Lump/ Powder inside/outside Pack 69.40 ± 33.68	
	I. With Instrument	* 6. Methamphetamine in Simple Pipe 70.40 ± 30.16	
		7. Methamphetamine in Spiral Pipe 60.70 ± 37.81	
		8. Methamphetamine on Foil 59.70 ± 36.70	
		9. Methamphetamine in Lamp 36 ± 39.55	
		10. Melted Methamphetamine in Pipe 70.10 ± 32.23	
Mean Score:		61.67 ± 34.72	
Category Reliability (Cronbach`s Alpha):		77%	

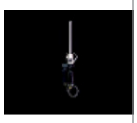
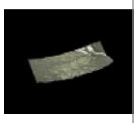
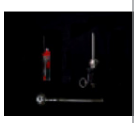
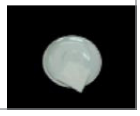
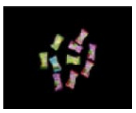
Main Category	Features	Photo
B. Instruments	* 1. Simple Pipe 66.10 ± 33.52	
	2. Spiral Pipe 66.50 ± 32.48	
	3. Torch Lighter 66 ± 35.80	
	4. Lighter with Bar 38.64 ± 37.20	
	5. Lighter with Needle 34 ± 39.84	
	6. Lamp 26.80 ± 34.31	
	7. Foil 14.20 ± 26.65	
	8. Straw 28.50 ± 31.13	
	* 9. A Collection of Lighters/ Pipe 71.70 ± 30.01	
	10. Moisturized Handkerchief 63.30 ± 30.34	
Mean Score:		47.47 ± 33.13
Category Reliability (Cronbach`s Alpha):		68%

Figure 1. Cont.

Main Category	Features	Photo
C. Cues Accompanied with Drug Use	1. Juice/ Beverage 22 ± 21.42	
	2. Chewing Gum 24.58 ± 33.21	
	3. Chocolate/ Candy 14.62 ± 25.88	
	4. Matching Box 6.80 ± 16.34	
	5. Cigarette 53.40 ± 39.19	
	6. A 10,000-Rial Note 32.40 ± 37.55	
	7. Several 10,000-Rial Notes 33.61 ± 36.73	
	8. A 20,000-Rial Note 37.30 ± 39.63	
	9. Several 20,000-Rial Notes 53.90 ± 42.75	
	10. 50,000-Rial Notes 35.28 ± 36.99	
Mean Score:		31.38 ± 32.96
Category Reliability (Cronbach`s Alpha):		79%

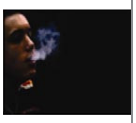
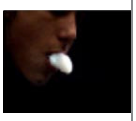
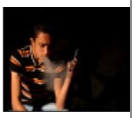
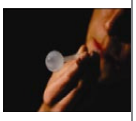
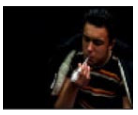
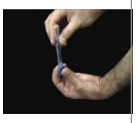
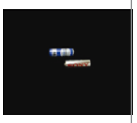
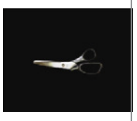
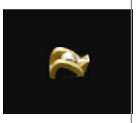
Main Category		Features	Photo
D. Drug Usage Procedures (I)	I. Without Main Instruments	* 1. Taking Methamphetamine by Straw from Pack 65 ± 32.34	
		* 2. Taking White Smoke out of Mouth 63.10 ± 35.78	
		3. Taking Heavy Smoke out of Mouth 59.60 ± 35.51	
		4. Smoking with Lighter 57.60 ± 34.43	
		5. Lighter with Needle and Straw in Hand 57.61 ± 34.44	
	I. With Pipe	6. Inserting Methamphetamine into Pipe Hole by Straw 68.40 ± 29	
		* 7. Taking Lighter with Bar under the Pipe with Methaphetamine 83.50 ± 21.14	
		8. Smoking the Fume from Pipe 77.70 ± 28.94	
		* 9. Taking Torch Lighter on Pipe 85.90 ± 23.07	
		10. Smoking Fume from Pipe Tube 73.74 ± 30.42	
Mean Score:			61.27 ± 30.32
Category Reliability (Cronbach`s Alpha):			82%

Figure 1. Cont.

Main Category		Features	Photo
D. Drug Usage Procedure (II)	III. With Lamp	1. Inserting Methaphetamine with Straw in to Lamp 16.48 ± 31.17	
		* 2. Connecting Straw to Lamp Full of Methamphetamine 62.50 ± 34.37	
		3. Taking Lighter with Bar under Lamp Full of Methamphetamine 66.40 ± 37.06	
		4. Putting Hot Lamp on Moisturized Handkerchief 66.40 ± 37.06	
		5. Smoking White Fume by Straw 57.62 ± 37.03	
	IV. With Foil	6. Folding the Foil 29.02 ± 32.5	
		7. Inserting Methamphetamine with Straw in Foil 54.20 ± 40.17	
		8. Taking Lighter with Needle under Foil Full of Methamphetamine 29.82 ± 35.36	
		* 9. Taking Straw in Mouth and in Foil 59.30 ± 38.83	
		10. Methamphetamine Smoker with a Collection of Instruments 32.54 ± 39.27	
Mean Score:			47.8 ± 36.91
Category Reliability (Cronbach`s Alpha):			82%

Main Category	Features	Photo
E. Neutral Photos	1. Highlight Marker 0	
	2. 3 Pens 0	
	3. Battery in Hand 0	
	4. Pen in Hand 0	
	5. Ballpen 0	
	6. Battery 0	
	7. Scissors 0.21 ± 0.31	
	8. Sugar Lumps in Hand 0	
	9. Glue 0.91 ± 0.33	
	10. Pressing Machine 0	
Mean Score:		0.56 ± 0.32

4. Discussion

Methamphetamine dependence is a crucial health problem with high rates of relapse and intense craving. Although in short term, methamphetamine use increases energy and feeling of wellbeing but in long term, it leads to severe dependence, psychotic symptoms and cognitive problems. There is no effective medical treatment for methamphetamine use or dependence (Elkashef et al, 2008). Induced craving is a crucial intervening factor for drug relapse during abstinence, so evaluation and measurement of parameters associated with methamphetamine craving can be a valuable tool in the management and intervention programs related to methamphetamine use and dependence.

Craving assessment is centered on two main concepts: general baseline craving and responsiveness of the subject to be made to crave by exposure to external or internal cues. Induced craving is even more important as compared to the weaker baseline craving, but it is correlated with it, so those individuals who experience higher levels of baseline craving are more susceptible to craving induction by cues. In real life, pictorial cues are amongst the most efficient cues for craving induction and development of a series of effective visual cues is important for craving assessment in controlled laboratory settings and for better understanding of "craving induction phenomenon".

In this study, we designed and evaluated a visual cue-induced craving task for methamphetamine abusers with visual cues which provoked craving in subjects. The results yielded a reliable task for valid craving induction which demonstrates some main aspects of the diverse nature of craving and that can be used in a wide range of studies related to cue-reactivity.

This study's findings show that cue-elicited craving (cue-reactivity) can be induced by exposing methamphetamine-dependent subjects to a wide range of visual cues related to methamphetamine. This finding is consistent with other empirical findings and research results on the influential role of cues in eliciting cue-reactivity and induction (Bonson et al., 2001; See, 2002; Newton et al., 2006; Tolliver et al., 2010) which demonstrate that cue-related stimuli evokes craving. Our findings indicate that differences in cue-induced craving were not associated with demographic variables e.g. age, sex, education, marital status and employment. This finding is in line with those of Tolliver and colleagues (2010) who showed that methamphetamine craving was significantly increased by cue-exposure but no relationship was found between induced craving and age, gender, education, job status, treatment and days of using methamphetamine in the past 30 days before study entry.

In contrast, Guidalini and colleagues (2006) proposed that age, duration of addiction, lower level of education and daily drug cost are significantly correlated with cocaine use among cocaine users. However Mokri, et al (2008) did not find any correlation between craving intensity and demographic keys among intravenous heroin users but we found that the duration of opiate abuse had a negative effect on craving induction; hence we propose that as addiction progresses along its natural course by shifting from an impulsive reward directed behavior to a compulsive habit, craving responsiveness decreases. But it seems that in our current study, the picture is different in methamphetamine abusers as lower age onset of drug abuse was correlated with higher level of craving responsiveness. Hence the effects of demographic features and substance abuse related variables should be investigated further in future research.

Our study also provides a valuable bank of effective and ecologically validated pictures for methamphetamine for the first time in the Middle-East and Central Asia. Black-back pictures provided, are beneficial for task design for behavioral and fMRI studies on craving. Furthermore, the intensity of cue reactivity reported by subjects could be showed as a treatment outcome predictor in future studies and clinical practice. These cues could be used in cue desensitization studies to evaluate the effectiveness of this treatment paradigm among methamphetamine abusers.

Our visual induced-craving assessment task had the potential to cause relapse among the subjects; so cue exposure and craving assessment could have had serious implications for in-treatment subjects. Because of the possibility of relapse, we had to offer brief psychological intervention to reduce craving and lead it to base-line after cue-exposure sessions. Some of the subjects were not basically cue reactive and this was another challenge we faced, similar to what has been noted in similar studies (Avants et al., 1995). Non reactivity to cues may be due to non - motivational cognitive approaches toward cues (Avants et al., 1995) so it should be regarded as a real phenomenon at least in some cases, not just a denial to response.

Results of this study may raise concern that advertisements which are designed for anti drug campaigns, should be without craving inducing cues for drug abusers. Using drug related cues in the posters to enhance the public

awareness about drugs of abuse and mounting these posters in treatment clinics (the problem that we have now with some of the posters designed and distributed by UN office for drug and crime (UNODC) with Iranian ministry of Health support) could enhance craving among in-treatment patients and potentiate the relapse.

We acknowledge that our study had some limitations. First, the assessment and measurement of craving intensity was based on subjects self reports and it may be subject to denial and unreliable reports although they were highly motivated to report their subjective desires by our professional and trained interviewers. Second, although reliability of the task was accurately measured by psychometric parameters the same was not true of the task validity.

With high reliability, efficiency and feasibility, the proposed assessment task can help to gain a better understanding of the dimensions of methamphetamine craving. Cross validation with other craving assessment measures such as different craving self reports, semantic craving induction tasks by drug related words, or craving induction tasks with imaginary scripts or paraphernalia and/or more objective measures such as addiction modified stoop tasks and dot probe tasks could be useful next steps. Using the prepared visual cues and tasks for neuroimaging studies (fMRI) of methamphetamine craving neurocircuits or craving modification studies through transcranial magnetic stimulation (rTMS) or transcranial direct current stimulation (tDCS) techniques are among our plans for future research.

In conclusion, through this study, we have provided a pictorial task for the evaluation and measurement of subjective craving in a group of current Iranian methamphetamine smokers by using visual cues that induce craving. We also identified a list of most potent visual stimuli for this purpose. The findings let researchers assess cue-induced craving among methamphetamine users with an acceptable reliability and validity.

Acknowledgment

Authors wish to thank Miss. Haleh Ghorbani for her helpful assistance in designing tables and Mr. Alireza Tavosi for his valuable cooperation with the photography team.

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