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Comparison of behavioral activation subscales of Gray's original reinforcement sensitivity theory in opioid and methamphetamine dependent patients

Amir Ghaderi¹; Marjan Alamikhah²; Mohammad-Amin Karimi³;
Negisa Bashkar⁴; Omid Saed⁵; Mostafa Gholami¹; Mohammadreza Davoudi¹;
*Morad Rasouli-Azad⁶

¹Student Research Committee, Kashan University of Medical Sciences, Kashan, Iran.

²MS. in clinical psychology, Islamic Azad University, Branch of Torbat-e-Jam, Torbat-e-Jam, Iran.

³MS. in consultancy, Iran Prisons Organization, Tehran, Iran.

⁴Research Center for Substance Use and Dependence (DARIUS Institute), Welfare and Rehabilitation University, Tehran, Iran.

⁵Assistant professor of clinical psychology, School of Medicine, Zanjan University of Medical Science, Zanjan, Iran.

⁶Assistant professor of clinical psychology, School of Medicine, Kashan University of Medical Science, Kashan, Iran.

Abstract

Introduction: The relationship of behavioral activation subsystems with methamphetamine and opioids dependency, which are the most commonly used illicit substances in Iran, is still unclear. The purpose of this study was to compare the behavioral activation subsystems and behavioral inhibition system of opioid and methamphetamine dependents with those of healthy subjects.

Materials and Methods: In this case-control study, two groups of methamphetamine and opioids dependents (25 cases on each group) were selected through purposeful method from patients admitted to substance rehabilitation centers of Mashhad, Iran, during March to September 2012. A group of 25 healthy cases (non-addict) were also matched as the control group. Data was collected using Carver and White's BAS/BIS scales and analyzed using Chi-square test, one-way analysis of variance, and multivariate analysis of variance.

Results: The methamphetamine-dependents group had a higher BAS-DR subscale score than the opioid dependent group ($P < 0.01$), but in neither group these scores were significantly different from the BAS-DR scores of healthy subjects ($P > 0.05$). The BAS-RR scores of the methamphetamine-dependents group were higher than the other two groups ($P < 0.05$). The scores of BAS-FS subscale of the control group was higher than in the opioid-dependent group ($P < 0.05$), but was no difference from the scores of methamphetamine-dependent patients ($P > 0.05$). There was no difference between the three groups in terms of scores of behavioral inhibition system ($P > 0.05$).

Conclusion: The difference of BAS subscales of patients with different substance dependencies from those of healthy subjects confirms the role of reward deficiency syndrome in the substance use disorder. Also, methamphetamine and opioid dependencies were found to have a duration-dependent impact on the behavioral activation subsystems.

Keywords: Reinforcement sensitivity, Behavioral activation system, Methamphetamine, Opioids

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*Corresponding Author:

Department of clinical psychology, School of Medicine, Kashan University of Medical Science, Kashan, Iran.

rasouliazad-m@kaums.ac.ir

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Introduction

According to Gray's original Reinforcement Sensitivity Theory (o-RST), behavior and emotion are controlled by two basic brain systems corresponding to two motivation systems: 1- aversive system, which corresponds to Behavioral Inhibition System (o-BIS), and 2- appetitive system, which corresponds to Behavioral Approach System (o-BAS) (1,2). In this theory, BIS is activated by the conditioned stimuli associated with punishment and governs the behavior in response to negative events. In contrast, BAS is activated by the conditioned stimuli associated with reward or cease of punishment and governs the behavior in response to positive stimuli such as non-conditional reward or avoiding punishment. O-BIS is associated with avoidance behavior, and o-BAS is associated with approach behavior (2). In addition, Gray hypothesized a third system called Fight/Flight System (o-FFS), which governs the responses to non-conditional aversive stimuli and punishment, i.e. non-conditional defensive aggression (o-Fight) and non-conditional aversion (o-Flight) (3).

BAS is mostly involved with the structures in striatal and frontal regions of the brain that are associated with ascending dopamine projections. BIS is involved with the structures in amygdala, hippocampus, and medial regions of hypothalamus that regulate the neurotransmitters GABA and serotonin (4,5).

BAS plays a decisive role in reward triggered behaviors and their associated pathological behaviors, and has been shown to be a good predictor of high-risk behaviors (6), higher fat intake (7), problem gambling (8), high risk sexual behaviors (9), and substance abuse (10-12). In a review study by Bijttebier, Beck, Claes and Vandereycken (13), they reported that BAS has a definite role in substance-related disorders, but the role of BIS in these disorders is still unclear. Gray (14) argues that the ecstasy experienced by alcohol and drug abusers, which is controlled by the release of dopamine in nucleus accumbens is associated with high levels of BAS. Studies have shown that opioid dependents, smokers and alcoholics have higher BAS scores than normal populations (15-17).

Lately, a growing number of studies have shown interest in BAS subscales of Gray's original theory, namely Drive (BAS-DR), Reward

Responsiveness (BAS-RR), and Fun Seeking (BAS-FS). In a study by Franken et al. (18), which compared these subscales in the groups of substance dependents (cocaine and heroin), alcoholics and normal population, it was found that the group of substance dependents had a higher BAS-DR and BAS-FS scores than the control group. In a study by Abdi, Bakhshipour, and Aliloo (19), where they compared BAS/BIS scales and sensitivity of o-RST systems in substance dependents, smokers, and normal people, it was reported that BAS-RR, BAS-FS, and BAS-DR of substance abusers and BAS-DR of smokers are significantly different from those of normal people. Some researchers have suggested that reward deficiency syndrome may contribute to the development of substance use disorder (20). The role of BIS sensitivity in substance use disorders is still unclear, as about half of the studies on this subject have reported a significant negative relationship between BIS sensitivity and substance use problems (21-23) and other half have not found such relation (24-26).

Biologically, BAS is associated with the changes in the neurotransmitter dopamine (4) and BIS with the neurotransmitters serotonin and GABA. The substances with greatest impact on dopamine are methamphetamine and cocaine, but there is still little knowledge about methamphetamine dependence and o-RST subscales relationship. In the most recent study based on revised Reinforcement Sensitivity Theory (r-RST) on methamphetamine and opiate dependents (27), the parameter with highest impact on three groups (opioid-dependents, methamphetamine dependents, and healthy people) was r-BAS, for which methamphetamine dependents had a higher score than healthy people but lower than opioid dependents. In that study, the group of methamphetamine dependents also had a higher r-BIS score than other two groups.

The r-Fight scores of methamphetamine-dependent group were higher than those of opioid-dependent group, but none of the differences between the r-Fight scores of three groups was statistically significant.

Also, r-freeze score of methamphetamine-dependent group was higher than control group, but was not significantly different from the opioid group, which also showed higher r-freeze score than the control group. The RST system with most

noticeable abnormality in substance-dependent people is r-BAS, and the relationship of o-BAS subscales with methamphetamine, which is the substance with greatest impact on this system, and opiates, which are the most widely consumed illicit substance in Iran (28) and operate differently than methamphetamine, is still unclear. In many parts of Iran, both urban and rural, the use of traditional opiates and heroin has been replaced by the simultaneous consumption of several substances including methamphetamine and condensed heroin (29).

Comparing the o-RST subscales in people with opioid and methamphetamine dependence can be helpful in understanding the pathology of substance use disorders in Iranian clinical population. Therefore, the present research investigated the difference between the o-RST and o-BIS subscales of methamphetamine/opioid dependents and those of a healthy population.

Materials and Methods

This study was carried out with a cross-sectional/case-control design, and in accordance with the ethical principles specified by World Medical Association's Declaration of Helsinki and with the ethical approval of Kashan University of Medical Sciences (authorization code: IR.KAUMS.REC.1396.1).

Accordingly, all subjects were asked to fill a written consent form before enrolling. The study population consisted of the patients diagnosed with dependence on methamphetamine or opioids (opium and its extracts, crystal, condensed heroin) who were admitted to drug rehabilitation centers of Mashhad, Iran, from March to September 2012. In a purposeful sampling, 25 eligible subjects with methamphetamine dependence and 25 eligible subjects with opioid dependence were selected. Patients whom clinic psychiatrists diagnosed as having psychotic disorders and significant signs of axis I and II disorders in the preceding year were excluded.

A group of 25 cases consisting of patients' healthy (non-addict) family members and friends, which was matched with the patient groups in terms of demographic variables, was formed to serve as the control group. Participants were evaluated during the second week of detoxification. The total number of subjects in three groups was 75.

Research instruments

A) *BAS/BIS scale*: The behavioral activation-behavioral inhibition system scale (BAS/BAS Scale) is a self-report questionnaire consisting of 24 items that measure o-BAS and o-BIS subscales (30). The BIS part of the questionnaire consists of seven items that measure the sensitivity of the behavioral inhibition system or the response to threat and anxiety due to negative stimuli. The BAS part of the questionnaire, which measures the sensitivity of the behavioral activation system, consists of 13 items dedicated to three subscales: 4 items dedicated to Drive subscale (BAS-DR), 5 items dedicated to Reward Responsiveness subscale (BAS-RR), and 4 items dedicated to Fun Seeking subscale (BAS-FS). BAS-RR measures the response to reward and the degree to which rewards lead to positive emotions, BAS-DR measures the person's willingness to pursue the desired goals, and BAS-FS measures the person's desire for new rewards and his tendency toward potentially rewarding impulsive stimulation. Carver and White (30) have reported an internal consistency of 0.74 for the BIS subscale and 0.71 for the BAS subscale. The psychometric validity of the Persian version of this scale have been confirmed in a study by Mohammadi on Iranian college students, where test-retest reliability for the BIS and BAS subscales have reported to be 0.71 and 0.68, respectively (31).

B) *Structured Clinical Interview for Diagnostic and Statistical Manual of Mental Disorders (SCID)*: The substance use disorders (including substance dependence and other comorbid disorders) were assessed using the Structured Clinical Interview for Diagnostic and Statistical Manual of Mental Disorders (SCID). SCID is widely used by trained clinicians for diagnosis of Axis I disorders based on DSM-IV criteria, and has been shown to provide reliable diagnoses for most psychiatric disorders (32). In Iran, the Persian version of SCID has been developed by Sharifi et al. (32), who have confirmed its psychometric validity for the Iranian population. In the present study, this instrument was used for diagnosis of substance dependency and comorbid Axis I and II disorders throughout life and in the preceding 12 months. Data analysis was performed with one way analysis of variance (ANOVA), multivariate analysis of variance (MANOVA), Tukey's post

hoc test, Mann-Whitney U test, and Chi-square test. Homogeneity of variances and covariance matrices were investigated with the help of Levene's test and Box's test, respectively. This project was approved and funded by the Student Research Committee of Kashan University of Medical Sciences (IR.KAUMS.REC.1396.1).

Results

As shown in Table 1, the mean age of the methamphetamine-dependent group was 29, that is, 3 years lower than the mean age of the opioid-dependent group (33) and about 1.5 years lower than the mean age of the control group (30.5). By average, the patients in the opioid-dependent and methamphetamine-dependent groups were less educated than the people in the control group. Also, there were more single (unmarried) people in the methamphetamine-dependent group than in the other two groups. However, none of the aforementioned differences was statistically significant. Box's test showed the equality of covariance matrix (Box's $M=23.11$; $F=1.06$; $P>0.05$) and Levene's test showed the equality of variances of all subscales except BAS-FS ($F_{2,72}=3.79$; $P<0.05$) in three groups. The results of these tests and Bartlett's test of correlation between dependent variables confirmed the suitability of

MANOVA for data analysis (with chi-square of about 40.416, degree of freedom of 9, and significance level of 0.001). The results of MANOVA showed a significant difference between the methamphetamine-dependent group, opioid-dependent group, and control group in terms of their scores in Carver-White's BAS/BIS subscales ($P<0.002$; Wilk's $\Lambda=0.716$; Partial $\eta^2=0.154$, $F_{8,138}=3.14$).

According to the correlation matrix of dependent variables (Table 2), all variables had correlation coefficient of more than 0.3, which signified suitability for MANOVA. As shown in Table 2, MANOVA showed significant differences between the methamphetamine-dependent group, opioid-dependent group, and control group in terms of Drive subscale of behavioral activation system ($P<0.006$; Partial $\eta^2=0.134$, $F_{2,72}=5.56$). As indicated in Table 3, the results of the post hoc Tukey's HSD (honest significant difference) test showed that this difference lies between the groups of opioid-dependents and methamphetamine-dependents. In other words, patients with methamphetamine dependency had a higher BAS-DR score than those with opioid dependency, but neither of these groups was significantly different from the control group in this respect (Table 3).

Table 1. Demographic variables in the methamphetamine-dependent, opioid-dependent, and control groups

Variable	Control group	opioid-dependent group	methamphetamine-dependent group	Significance
Age (years)	M (SD)	M (SD)	M (SD)	0.19
	30.2 (5)	31.8 (7.6)	29.9 (3.9)	
Age at consumption onset	-	19.5 (6.66)	16 (2.2)	#0.004
Age at dependence onset	-	22.7 (7.1)	18.9 (3)	#0.013
Education	F(%)	F(%)	F(%)	0.206
Middle school	9 (36)	8 (32)	11 (44)	
High school	9 (36)	13 (52)	13 (52)	
College	7 (28)	4 (16)	1 (4)	
Marital status				*0.272
Married	17 (68)	17 (68)	11 (44)	
Single	7 (28)	8 (32)	12 (48)	
Others	1 (4)	0 (0)	2 (8)	
Job status				0.65
Full time	9 (36)	9 (36)	5 (20)	
Part time	8 (32)	7 (28)	11 (44)	
Unemployed	8 (32)	9 (36)	9 (36)	
History of alcohol consumption				*0.061
Yes		15 (60)	21 (84)	

*Fisher's Exact Test #Mann-Whitney U M: Mean SD: Standard Deviation F: Frequency %: Percent Frequency Group size 25 subjects (per group)

Table 2. Correlation matrix of dependent variables

		BAS-DR	BAS-RR	BAS-FS	BIS
BAS-DR	Pearson correlation	1	0.364	0.261	0.391
	Significance		0.001	0.024	0.001
BAS-RR	Pearson correlation		1	0.319	0.461
	Significance			0.005	0.001
BAS-FS	Pearson correlation			1	0.248
	Significance				0.032
BIS	Pearson correlation				1
	Significance				

Table 3. Mean and standard deviation of Carver-White BAS/BIS scores of the methamphetamine-dependent, opioid-dependent, and control groups

Variable	Control group (1)		Opioid-dependent group (2)		Methamphetamine-dependent group (3)				HSD
	M	SD	M	SD	M	SD	P	η ²	
Scale BAS/BIS									
BAS-DR	11.36	2.49	10.04	2.58	12.32	2.17	0.006	0.134	*2<1, ***2<3
BAS-RR	16.32	2.24	16.48	2.60	18.04	1.51	0.011	0.118	***1<3
BAS-FS	11.84	2.46	9.96	1.96	11.20	3.05	0.034	0.090	**2<1
BIS	18.80	2.32	18.32	2.67	19.16	2.23	0.472	0.021	NS

*P=0.058 borderline significance **P<0.05 ***P<0.01 NS: Not significant M: Mean SD: Standard Deviation

BAS-DR: Behavioral Activation System-Drive subscale

BAS-RR: Behavioral Activation System - Reward Responsiveness subscale

BAS-FS: Behavioral Activation System - Fun Seeking subscale

BIS: Behavioral Inhibition System

The results also showed a significant difference between the methamphetamine-dependent group, opioid-dependent group, and control group in terms of reward responsiveness ($P < 0.011$; Partial $\eta^2 = 0.118$, $F_{2,72} = 4.79$). The results of Tukey’s post hoc test showed that the mean scores of BAS-RR in the methamphetamine-dependent group was significantly higher than both the opioid-dependent group and the control group. In addition, MANOVA showed significant differences between the three groups in terms of Fun Seeking subscale ($P < 0.034$; Partial $\eta^2 = 0.09$, $F_{2,72} = 3.55$) and subsequent Tukey’s post hoc test showed that the mean scores of BAS-FS of the opioid-dependent group was significantly lower than the control group, but was not significantly different from the methamphetamine-dependent group.

The results of statistical analysis showed no significant difference between the methamphetamine-dependent group, opioid-dependent group, and control group in terms of Behavioral Inhibition System (BIS) score ($P > 0.05$; Partial $\eta^2 = 0.472$, $F_{2,72} = 0.76$).

Discussion

The purpose of this study was to measure and compare the o-RST scores of opioid and methamphetamine-dependent patients and a matched group of healthy people. The results concerning the three BAS subscales show the strong association of this system with opioid and methamphetamine dependence, and supports the reports of many other studies that have shown such association for various substances (7,8,17-19,22,23,33,34). Personality traits that are specifically related to substance abuse fully match the two-dimensional factors of Gray’s theory, namely avoidance and approach sensitivity (17). BAS is known to be strongly associated with substance abuse, and this may be able to confirm the presence of reward deficiency syndrome in this clinical population (20). However, we found notable differences in the scores of BAS subscale in the methamphetamine dependents and those scores in the opioid dependents. Our results showed that methamphetamine dependents had a higher BAS-DR score than opioid dependent individuals, which means they have a more active inclination

toward attractive goals but there was no statistically significant difference between the two substance-dependent groups and healthy people in this respect. Also, methamphetamine-dependent individuals had a higher BAS-RR score than the other two groups, meaning that they are more reactive to the effect of rewards and experience more intense emotions and energy in response to such stimuli. The results also showed that opioid-dependents had a lower BAS-FS score than healthy people, which means they have fewer tendencies to seek new stimuli. In this respect, the results of methamphetamine-dependents of opiate-dependents were close if not entirely similar. These results are inconsistent with the findings of Abdi et al. (19), who reported that all of their substance-dependent groups had abnormal scores in all three BAS subscales. As suggested by Bijttebier et al. (13), the disorders comorbid with substance-dependency can alter the scores of RST scales and interfere with the impact of substance use disorder. The difference between our results and Abdi's (19) may support the argument of De Groot, Franken, Van der Meer and Hendriks (35) who hypothesize a duration-dependent change in some RST scores of substance dependents. This difference can be attributed to the role of variables mediating the relationship of reinforcement sensitivity systems and substance abuse. It has been shown that behavioral approach system has a significant positive relationship with substance abuse in highly stressed people (36). The results of a study by Ivory and Kambouropoulos (34) have also shown the significant direct association of BAS and indirect association of r-FFFS with alcohol dependence. According to this study, the relationship between r-FFFS and alcohol consumption is mediated by the avoidance-focused and emotion-focused strategies. Further, the mediating role of the sympathetic system in the relationship of approach behavior and response to potential rewards has also been investigated. The results of a study by Hinnant et al. (37) on this subject show that it is only in the presence of low sympathetic activity that the approach to potential reward may result in exacerbated substance abuse. In a study by Franken (38), BAS-DR scores had a correlation with the strong desire for alcohol and negative reinforcement in exposure to alcohol cues. BAS-

RR also had a significant positive correlation with negative reinforcement aspect of alcohol craving, but BAS-FS had no significant relationship with craving dimensions. In a comparison of o-BAS and o-BIS scales in the alcoholic and substance-dependent groups, it was revealed that substance-dependent subjects had higher total o-BAS scores than controls but BAS-DR and BAS-FS scores of alcoholic group were not significantly different than those of other two groups. The difference in BAS-RR scores of three groups was also insignificant (17). Wills et al. (10) showed that people with higher novelty seeking, lower risk avoidance, and lower reward dependence were more likely to use illicit substances.

In any case, high reward responsiveness and drive scores of methamphetamine dependents can be due to direct toxic effect of methamphetamine on the neurotransmitters dopamine and serotonin in the brain (39). Different effects of opioids and methamphetamine on neurotransmitters and brain pathways can explain the differences of two groups in the o-BAS subscales. As suggested by Verdejo-García and Bechara (40), reinforcing effects of substances can enhance reward sensitivity and encourage continuous consumption by affecting dopamine system. Pharmacologic manipulation of dopamine, serotonin and noradrenaline systems in normal individuals can affect various aspects of emotion experience (41). More specifically, direct and severe impact of methamphetamine on the brain dopaminergic system can reinforce the BAS subsystems as observed in our results. In a review study by Verdejo-García and Bechara, they suggest two hypotheses. One hypothesis is that impulsivity of substance abusers may be due to prolonged consumption of these substances, which have damaging effects on the brain. The alternative hypothesis suggests that impulsivity has triggered the substance abuse and is associated with susceptibility to addiction (40). In the case of BIS scale, our results showed no difference between the three groups. The reports about the relation of BIS with substance abuse are contradictory. In this respect, a consistency can be seen in the findings of Franken et al. (18), Spoon et al. (12) and Kambouropoulos and Staiger (42). Bijttebier et al. (13) reports that there is still no consensus regarding the relation

of BIS with substance abuse, but so far, most studies have found no difference in the BIS scores of drug-dependents and normal people. Nevertheless, Abdi et al. (19) have reported higher than normal o-BIS scores in smokers and opioid dependents and Alemikhah et al. (27) have reported a higher r-BIS score in methamphetamine-dependent individuals.

In a study by Taylor et al. (43), a relationship was found between high BIS sensitivity and substance abuse, which may suggest that extremely high BIS, which is highly correlated with severe negative emotions, triggers the substance abuse (44) as an emotion regulation strategy to deal with severe negative emotions, and can also predict the recurrence of substance abuse after a period of rehabilitation (44).

As suggested by Franken and Muris (18) and Bijttebier et al. (13), substance abuse appears to have a negative and nonlinear relationship with BIS, and is likely to be exacerbated when very low BIS is combined with high BAS. The instruments used in previous studies to measure the indices of reinforcement sensitivity theory and the type of RST theory employed (o-RST or r-RST) can be the causes of contradictory reports regarding the relationship of BIS and substance abuse. The importance of BAS subscales in the choice of psychotherapy highlights the need for further research to determine the impact of prolonged consumption of different substances on the brain systems as theorized by RST. Several studies have shown a relationship between behavioral activation therapy and many

psychological disorders, so the necessity of due attention to personality traits such as BAS sensitivity in the treatment of substance dependence in order to maximize the therapeutic efficacy is quite clear.

Conclusion

The difference of BAS subscales in patients with dependence on different substances from those of healthy subjects confirms the role of reward deficiency syndrome in the substance use disorder. Also, methamphetamine and opioid dependencies were found to have a duration-dependent impact on the behavioral activation subsystems.

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