



## Evaluating the efficacy of *Regulated 12-Session Matrix Model* in reducing susceptibility in methamphetamine-dependent individuals

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### ABSTRACT

Methamphetamine (ab)use have gained popularity among youth and is increasingly become a part of mainstream culture. Methamphetamine(ab)use is dangerous because of its wide range adverse outcomes and hazardous sustaining side effects. Its dependence is hardly withdrawn by routine therapeutic methods. This study is devoted to evaluate the efficacy of *Regulated 12-Session Matrix Model* in outpatient methamphetamine-dependent individuals. 24 individuals were chosen according to inclusion/exclusion criteria of the study and randomly assigned to equal experimental (age range 19-41; mean age: 46.9) and control groups (age range: 21-42; mean age: 27.8). Experimental group members partook *Regulated 12-Session Matrix Model* once a week in 12 consecutive weeks, while control group members remained at waitlist. Independent *t*-test in 12<sup>th</sup> week showed that experimental group had lower methamphetamine use, comparing to control group ( $p < .05$ ). *Phillai's Trace*, *Wilk's Lambda*, *Hotelling-Lawley's trace*, and *Roy's largest root* showed that there are significant association between experimental and control groups in reduction of methamphetamine-use lapse ( $p < .05$ ). Within-subject *F* ratio revealed that "methamphetamine use" was significantly reduced in experimental group after clinical intervention ( $p < .001$ ). Findings of the study indicate the efficacy of *Regulated 12-Session Matrix Model* in craving management and control as well as reduction of lapse and substance (ab)use in methamphetamine-dependent patients. It appears that the *Regulated 12-Session Matrix Model* would be a new reliable solution to treat methamphetamine-dependence in Iran and other alike cultural and social atmospheres. Limitations and future implications are discussed.

**Keywords:** Methamphetamine, substance abuse, substance use disorders (SUD), substance use disorders (SUD) relapse, Matrix model for SUD treatment, *Regulated 12-Session Matrix Model*, craving, lapse, susceptibility.

### INTRODUCTION

Nowadays, Substance abuse become a major risk in psychological and social debates. Substance abuse is accompanied by a wide range of psychological, social, and economic adverse outcomes and damages include co-occurring of psychological disorders like attention deficit/hyperactivity spectrum disorders (ADHD), conduct disorder, antisocial personality disorder (APD), affective disorders, anxiety disorders, problematic and high-risk sexual behaviors, educational, familial, and occupational difficulties, school/university dismissal, delinquent behaviors, driving accidents and incidents, high-risk behaviors, suicide, and self-mutilative behaviors(1-7).

The most popular stimulant substances are methamphetamines, which are known as *Shishé* in Iran. Global reports indicate increasing use of methamphetamine among people, especially youth, so that after cannabis the second world rank of substance use is for methamphetamine(8). Unfortunately, methamphetamine use become a cultural mainstream especially among adolescents and young adults(9, 10).

In Iran, along with other parts of the world, methamphetamine is a new drug which is widely used by youth. Usually amphetamine is available in powder type (crystalline hydrochloride salt). Various administration ways include smoking, eating, sniffing, and/or injection which depends on the duration of individual's dependence and routine usage dose(11). The major administration way in Iran, according to formal reports, is smoking. From 2005 ask and

use of methamphetamine has increased in Iran, so that in 2011 Iran reached the world fifth rank country of methamphetamine use. Between 2010 and 2011, the rate of ask and use of methamphetamine raised 400%; compared to 238% rise in Mexico, 166% in Thailand, 153% in USA, and 140% in China, Iran gained the global first rank of increase in ask and use of methamphetamine which has made all country and global responsible institutions deeply concerned. The rate of methamphetamine use in Iran is reported between 6-20% in various population sectors(7, 12, 13). Because of high amount of ask and use of methamphetamine drugs and their huge damages especially on central nervous system (CNS), International institutions of SUD research have announced this group as research priority in substance use in Asian countries and societies(14).

Amphetamine-type stimulant drugs result in dangerous, unwanted, and hazardous outcomes in users. Methamphetamine has a wide range of damaging and debilitating side effects which comprise serious problems in behavioral inhibition and self-control, increase of impulsivity, increase of delay discounting, high increase in risk of Parkinson' disease morbidity, memory decline, increase of mRNA levels of brain-derived neurotrophic factor (BDNF) in prefrontal cortices and amygdala and reduction in the protein levels of BDNF in hippocampus (15-18). Methamphetamine has devastating effects on brain structures, because of inversion of the flow of vesicular neurotransmitters and dopamine transmitters simultaneously. In such situation, methamphetamine acts as dopamine releaser and cause a severe dopamine toxicity in CNS(19).

SUD treatment (especially stimulant) have various problems and obstacles. In addition to financial and structural obstacles (not having insurance, having no economic benefit, no access to treatment professionals, geographical problems of accessibility to therapeutic centers), one major cause of low rate of SUD treatment is inexistence of perceived need to treat SUD(20-22). One important point in treatment of SUD is that the people with SUD, if come to search for treatment, refer to mental health services instead of treating SUD (23). Moreover, sensitivity and concerns about surrounding people's negative viewpoint to the patient, negative problems in workplace, and therapeutic inconveniences which reduce the interest to engage in therapeutic process in SUD patients. In general, all strategies of SUD treatment depending on duration, type, and way of administration of individual may implement medications, and/or inpatient/outpatient therapies. Afterwards, patient's psychiatric disorders shall be investigated and treated by a professional clinician in the domain of SUD treatment and simultaneously family education, primary remission skills, and prevention of relapse as well as behavioral therapies should be administered(23-25). In the phase of SUD treatment, Influential factors on relapse (substance re(ab)use) which shall be noticed by all therapeutic staff could be classified in three main domains of personal, interpersonal, and situational (Table 1).

**Table 1. Influential factors on SUD relapse**

domain	Influential factors
Personal(26, 27)	Individual characteristics, personality traits, attitudes, social skills, life skills, psychological coping styles, social coping styles, etc.
Interpersonal(28, 29)	Social environment, family, family of origin, spouse, close friends, dominant culture, dominant sub-culture, neighborhood, workplace atmosphere, eligibility to recruitment, internship facilities, and global view point of society to ex-substance-dependent individuals, etc.
Situational(30)	Satiation in which ex-substance-dependent individual would be instigated to lapse and re(ab)use, e.g., substance-dependent friends, places in which substances are being (ab)used, etc.

Craving is one the most difficult symptoms of SUD and as important as being one the major diagnostic criteria of SUD(31). Craving is described as a pressing and insuppressible desire to addictive behavior and most of the time results in loss of control (32, 33). Despite long periods of full abstinence, craving can suddenly appear and highly increase the probability of lapse and relapse(34). Therefore, it is necessary to pay special attention to craving management and control of patients in SUD treatment programs. Various neuro-circuits of reward and motivation are activated during the phase of craving. These neuro-circuits comprisethe nucleus accumbens, dorsal striatum, orbitofrontal cortex, anterior cingulate cortex, dorsolateral prefrontal cortex (DLPFC), amygdala, hippocampus and insula(35, 36).

One of the newly established methods of methamphetamine-dependence treatment is Matrix Model for condense and outpatient treatment of patients. Matrix Model is composed of a set of complementary therapeutic strategies which are mixed together to make an integrated therapeutic experience for outpatient patients. Matrix Model is a set of evidence-based medicine (EBM) methods which is designed as a program for people with SUD. This model is based on clinical studies in the domains of behavioral therapy, relapse prevention research, motivational interview strategies, psycho-education information, and partaking in 12-steps programs(37-39). Matrix model has been administered in varied studies to treat methamphetamine dependence and reducing craving and lapse (40, 41).

Several studies has been conducted to evaluate the application and feasibility of matrix model on treatment of methamphetamine dependence(40, 42-45). However, there are just a few studies on the efficacy of matrix model on treatment of craving, and lapse in the therapeutic process of methamphetamine-dependence withdrawal (46-49). According to such issues and with respect to the authors' suggestions that craving is the most important factor to anticipate the success of the therapy and/or relapse of SUD, the aim of the present study was determining efficacy of matrix model on reduction of susceptibility, lapse frequencies and use of methamphetamine in methamphetamine-dependent patients. Due to the high rate of abuse and dependence to methamphetamine and the importance of treatment as well as various evidence of clinical efficacy of matrix cognitive-behavioral mode to reduce laps in such individuals, the designed to evaluate the matrix model usefulness in methamphetamine-dependent individuals. However, because most of such people have cannot afford financial costs of the therapeutic procedures in 24 and 36 sessions of original matrix model, and according to high rate of outflow from therapeutic process, The *Regulated 12-Session Matrix Model* was applied.

## MATERIALS AND METHODS

### 2.1. Design

The present study was a randomized clinical trial and based on quasi-experimental design with repeated measures. The study was conducted in *Tehran Addiction Withdrawal Center*, Tehran, Iran in the year 2012.

### 2.2. Participants

Population of the study comprised all male individuals with methamphetamine dependence which referred to a SUD treatment center, Tehran, Iran in the year 2012. Sampling method was nonrandom accidental. After screening according to inclusion and exclusion criteria of study, 24 individuals were chosen and randomly assigned to equal experimental (age range 19-41; mean age: 46.9) and control groups (age range: 21-42; mean age: 27.8).

Inclusion criteria included methamphetamine dependence according to DSM-IV-TR(50), having the motive to withdraw (coming to SUD treatment center and asking for help to withdraw), confirmation of administration of all procedures of the therapeutic intervention (participation in all 12 sessions once a week for experimental group members, acceptance to remain in waitlist in the time of administration of the intervention for control group members).

Exclusion criteria were having history of past and/or present major psychiatric disorder such as psychosis, major depressive disorder (MDD), severe anxiety disorder, SUD other than methamphetamine, cognitive developmental disorder (IQ 30 points below society's average), severe physical and/or cognitive disorder which intervene the therapeutic phase, and using drugs such as methadone or naltrexone.

### 2.3. Intervention

The process of intervention comprised 12 sessions of mixed varied CBT techniques aimed on craving management and control in 12 once-a-week consecutive sessions (*Regulated 12-Session Matrix Model*). The design of the study was quasi-experimental with repeated measures in which the therapeutic outcomes of *Regulated 12-Session Matrix Model* are evaluated through all the procedure. All the participants of experimental group undergone *Regulated 12-Session Matrix Model* once a week (Table 1). Inclusion criteria were administration method methamphetamine use (smoking), and having no history of past or present severe psychotic, depressive, and/or anxious signs/symptoms which need treatment.

Table 1. sessions of *Regulated 12-Session Matrix Model*

Session	Topic
1	Why I withdraw substance? (Justice balance)
2	Starters and their types
3	Major problems in remission: Family mistrust/ Enegry reduction/ Drug misuse
4	Lapse and ways of coping with it
5	Thoughts, feelings, and precedent behaviors
6	Impatience and depression
7-8	Preventive and susceptible activities to relapse/ sexual relations
9	Occupation and remission/ getting involved
10	Shame and guilt/ Honesty
11	Motive to remission/ full abstinence
12	Anticipation of relapse

Follow-up index (dependent variable) included weekly use of methamphetamine in gram.

### 4.2. Instruments

1. Primary screening from comprised inclusion/exclusion criteria of the study.
2. DSM-IV-TR criteria for diagnosis of SUD/methamphetamine dependence(50).
3. Patients' information registration form, which include, patients code, age, gender, marital status, educations, wages, history of methamphetamine use, daily usage dose of methamphetamine (gram/day), administration type, etc.
4. Follow-up form, in which (non)occurrence of lapses, amount of methamphetamine use (number of times of use during last week and dose of usage (gram/day) in each time) were registered.
5. Self-report form, in which daily use of methamphetamine were reported twice a week by participants.

## 2.5. Data analysis

according to the study design, in addition to descriptive indices, T-test for independent groups, multivariate tests of Phillai's Trace, Wilk's Lambda, Hotelling-Lawley's trace, and Roy's largest root as well as analysis of variance were administered.

## 2.6. Ethics

Before starting the intervention, the procedure was fully explained orally for all participants and they have filled out written consent in which the general trend and aims of the study was discussed. In order to meet the criteria of confidentiality, identity of all participants were kept secret and the individual evaluations and results of participants were restricted from access. Considering research and medical ethics in the study and avoiding deprivation of methamphetamine dependent patients from *Regulated 12-Session Matrix Model*, all the control group participants have undergone the therapeutic plan after the intervention phase accomplished.

## RESULTS

Results of the step-by-step gradual assessments of methamphetamine use in both experimental and control groups are presented in table 2. According to the data, the highest methamphetamine use in experimental group was in first week, at initial session (mean: 2.04 grams/day), while the highest methamphetamine use in control group was in second week (mean: 2.01 grams/day). Independent t-test calculation for first week shows no significant differences between experimental and control groups. However, independent t-test in 12<sup>th</sup> week showed that experimental group on which *Regulated 12-Session Matrix Model* was administered, had lower methamphetamine use, comparing to control group ( $p < .05$ ).

Table 2: Statistical indices of methamphetamine use (gram/day) during study

Step	Group	Central tendency indices			Variance indices				Distribution indices	
		Mode	Median	Mean	Range	variance	SD	SEM	Skewness	Skewness coefficient
Screening	Experiment	1.50	1.50	2.04	7	6.61	2.57	.74	.30	.65
	Control	3.50	2	2	3.50	2.17	1.47	.42	-.14	-.90
Week 1	Experiment	1.29	1.29	1.29	7	6.47	2.54	.73	.80	.90
	Control	3.50	2/25	.40	3.50	1.96	1.40	.40	-.43	-.49
Week 2	Experiment	.85	.85	.85	7	4.47	2.11	.61	.71	.35
	Control	3	2.50	2.01	3.50	2.01	1.42	.41	-.36	-.73
Week 3	Experiment	.62	.62	.62	3.50	1.46	1.20	.34	.78	.07
	Control	2	2	1.68	3.50	2.32	1.52	.43	-.10	-.05
Week 4	Experiment	.50	.50	.50	3.50	1.40	1.18	.34	.20	.71
	Control	2	2	1.65	3.50	2.02	1.42	.41	.01	-.79
Week 5	Experiment	.33	.33	.33	3.50	1.01	1.01	.29	.34	.36
	Control	1.35	1.35	1.40	3.50	2.11	1.45	.41	.12	-.14
Week 6	Experiment	.34	.34	.34	2.10	.50	.70	.20	.04	.18
	Control	.66	.66	.66	3.50	1.18	1.09	.31	.94	.64
Week 7	Experiment	.26	.26	.26	2.10	.37	.61	.17	.82	.44
	Control	.10	.10	.45	2.50	.55	.74	.21	.23	.27
Week 8	Experiment	.020	.020	.020	2.10	.36	.60	.17	.26	.88
	Control	.95	.95	1.09	3.50	1.33	1.15	.33	.71	-.27
Week 9	Experiment	.17	.17	.17	2.10	.36	.60	.17	.46	.01
	Control	.43	.43	.43	3.50	1.01	1.01	.29	.03	.54
Week 10	Experiment	.12	.12	.12	1.50	.18	.43	.12	.46	.01
	Control	.54	.54	.54	3.50	1.24	1.11	.32	.16	.25
Week 11	Experiment	.07	.07	.07	.90	.06	.25	.07	.46	.01
	Control	.29	.29	.29	2	.32	.57	.16	.78	.38
Week 12	Experiment	.07	.07	.07	.90	.06	.25	.07	.46	.01
	Control	2	2	1.41	3	1.33	1.15	.33	-.20	-.86
<b>Independent t-test</b>										
		Independent t			df		α			
First week		.04			22		.962			
12 <sup>th</sup> week		11.61			22		.001			

Using four multivariate tests of Phillai's Trace, Wilk's Lambda, Hotelling-Lawley's trace, and Roy's largest root

showed that there are significant association between experimental and control groups in reduction of methamphetamine-use lapse ( $p < .05$ ). *Regulated 12-Session Matrix Model* with emphasis on “craving management and control skill” reduced amount of methamphetamine use (in experimental group) more than just the regular assessment of methamphetamine use (in control group; Table 3).

**Table 3: Multivariate tests to evaluate associations between dependent variables of levels of methamphetamine-use lapse**

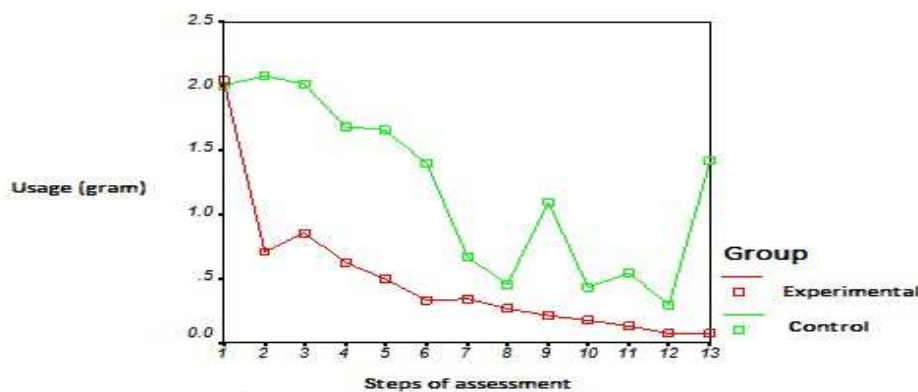
	Multivariate test	F ratio	df
Index	Philla's Trace	3.56	.045
	Wilk's Lambda	3.56	.045
	Hotelling's Trace	3.56	.045
	Roy's Largest Root	3.56	.045

Change in groups were investigated in two levels of within- and inter-subject via analysis of variance. Within-subject F ratio calculation for different assessment levels with emphasis on administration of “craving management and control skills” revealed that there are significant differences in 13 levels of assessment of “methamphetamine use” in experimental group ( $p < .001$ ). The highest usage amount in experimental group was in initial session (mean: 2.04 grams/day) and the usage amount decreased gradually from session one to twelve. Therefore, “craving management and control skills” training was efficient and reduced lapses in methamphetamine-dependent individuals (effect size: .28). In addition, F ratio test administration in experimental group was significant ( $p < .05$ ; table 4).

**Table 4: F test to investigate the significance of *Regulated 12-Session Matrix Model* in methamphetamine-use craving reduction**

		Sum of squares	df	Mean of squares	F ratio	$\alpha$	Effect size
Within subjects	Index	85.66	5.89	14.52	8/72	.001	.28
	Error	216.02	129.75	1.66			
Inter subjects	Index	40.56	1	40.56	4.33	.049	.16
	Error	206.07	22	9.36			

Graph 1 illustrates the effect size of *Regulated 12-Session Matrix Model* in reduction of methamphetamine-use craving in both experimental and control groups within 13 sessions of assessment.



**Graph 1: Trend of methamphetamine-use craving reduction in the process of *Regulated 12-Session Matrix Model*.**

## DISCUSSION AND CONCLUSION

Methamphetamine is a stimulant substance which its use is bursting increased during recent decade globally. This substance causes diverse acute and chronic negative effects and side effects in individuals. Wide-range physiological as well as psychological damages and impairments of Methamphetamine use has been resulted in therapeutic sensitivity to put effort on prevention and treatment of its use. Evidence-based practices (EBP) and scientifically controlled studies has shown no efficacy of pharmacotherapy on reduction of methamphetamine craving in users yet, and still the best and preferred intervention is psychotherapy(2, 12, 13).

One of such beneficial psychotherapies in methamphetamine-use treatment is Matrix Model. As statistical results and observational records showed, craving to use methamphetamine was gradually reduced by progression of *Regulated 12-Session Matrix Model* in experimental group. Hallow effect was neutralized by administration of same monitoring process on both experimental and control groups. All statistical results indicate positive efficacy of

treatment with *Regulated 12-Session Matrix Model* on reduction of amphetamine-use craving in dependent individuals. Findings of the present study are in line with previous studies in the domain of implementation of CBT in SUD treatments, especially on craving control.

Authors have found that management strategies on providing SUD patients with modern therapeutic methods have an important role of development and spreading of treatments of such disorders within varied society sectors as well as increasing the therapeutic motivation in SUD patients. SUD treatment centers which offer modern therapies and therapeutic approaches, in addition to increase the coming sessions of varied patients during the time, would retain patients more in therapeutic process and therefore, have more efficacy on reducing SUD in the society(51). In a recent study in USA, 600 SUD patients were undergone various psychotherapies. Results revealed that psychotherapy, especially when modified and regulated with each individual and her/his SUD, and implementing CBT methods along with 12-step paradigm, are most effective in reduction of craving and substance use(52).

Most of the studies about SUD treatment emphasize on the importance of therapeutic process on the therapeutic results. In a study on veterans with SUD, it has been revealed that issues such as impulsivity, low self-efficacy, unplannedness, and having poor coping strategies would result in inability to follow therapeutic process of SUD. Furthermore, Helping patients in planning therapeutic process and collaboration of therapists with them in therapeutic plans, especially paying attention to the way of expressing impulsivity [important indices of *Regulated 12-Session Matrix Model*], can significantly improve therapeutic outcomes(53).

Comparative studies about different therapeutic approaches in SUD treatment suggest that varied psychotherapies if accompanied with psychological support of patients, proper administration by therapists, and their collaboration with patients, would have positive effects on reduction of substance use craving. Moreover, it has been indicated that the most important factor is involving the individual in therapeutic process and follow-up her/his treatment by therapeutic team. The latter issue was found constant in all SUD treatment methods(54).

Studies on craving management and lapse reduction in people with SUD showed that psychotherapies which reinforce processes such as acceptance, awareness, and non-judgment in SUD patients can significantly reduce substance use craving, and prolong abstinence periods as well as stability of treatment(55). It appears that *Regulated 12-Session Matrix Model*, which is an evolved and enriched version of 12-step method, would have the potential of becoming an effective method of treatment in the domain of SUDs.

Studies about craving management in methamphetamine-use treatment showed that building up a metacognition in psychotherapy about beliefs of craving in methamphetamine-dependent individuals can change mental interpretations about perceived coping potential against craving and lapse. This would gradually increase the will and decision-making in methamphetamine-dependent individual to manage craving and increase the amount of abstinence and hence, reducing the probability of relapse(56). *Matrix Model* has notable efficacy in treatment of SUDs, especially methamphetamine dependence, so that longitudinal studies has proven enhancement of ability to abstinence, resistance to lapse, and management and reducing craving in patients whom undergone this model (37, 40, 41, 44, 57). The underlying logic of Matrix model in treatment is implementing a set of preventive methods to reduce the craving and lapse in people with SUD, so that they more frequently get involved in commitment to therapeutic goals and resist against use lapse(58).

Administration of sessions once a week has its own cons and pros. First benefit is that many of methamphetamine-dependent patients have financial problems and sometimes the therapeutic costs are provided by their families. Therefore, administration of *Regulated 12-Session Matrix Model*, would reduce treatment costs considerably and therefore, both probability of acceptance of treatment and probability of remain in the treatment would increase. The second benefit is that methamphetamine-dependent patients usually have degrees of depression and are low motivation and energy which may not allow patient to have proper capability to attend in therapeutic sessions twice a week and hence, one session a week would be more acceptable.

It shall be noted that according to neuropsychological studies, methamphetamine abusers encounter structural and cognitive impairments which have adverse effects on therapeutic outcome. Damages to cingulate and insular cortices along with decline in functional integrity of hippocampus would confront these individuals with serious problems (59). Hence, successful therapeutic methods in methamphetamine abuse treatment (like Matrix Model) have special value to communities and societies.

Finding of the present study are considered as a new step towards adaptation and naturalization of *Regulated 12-Session Matrix Model* to SUD treatment in Iran, especially stimulant drugs and methamphetamine. It appears that with continuation of replication of such plan in various population sectors of the society, *Regulated 12-Session*

*Matrix Model* would reach a brilliant situation in the process of secondary and tertiary prevention of SUD treatments. Moreover, implementation of modifications to the original Matrix treatment package, have made *Regulated 12-Session Matrix Model* to a flexible therapeutic method to be administered by formal and informal institutions, as well as NGOs which provide individuals with SUD and their families.

Therefore, in addition to revision and improvement of formal and standard therapeutic processes, results of such groups would be coordinated and adjusted which in medium-term increase prosocial behavior, and social solidarity, and in long-term would facilitate the accumulation of social capital and incorporation of productivity of re-engaged ex-SUD patients in labor force. It shall be noted that the main scope of the SUD treatments, especially *Regulated 12-Session Matrix Model*, in addition to helping SUD patients, is helping and supporting their families to enhance life satisfaction and quality of life, reduction of drug abuse surcharges to individuals, families and communities, as well as proliferation of national gross domestic product (GDP).

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