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Comparison of Executive Function of Brain between Drug-dependent, in Abstinences and Normal Individuals in Tehran

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Authors' contributions

This work was carried out in collaboration among all authors. Author ANT designed the study and monitored research process, Author ZS performed the statistical analysis, review litreacher, and wrote the first draft of the manuscript. Author SG managed the analyses of the study. Author AAA read and edited paper in English language. All authors read and approved the final manuscript.

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ABSTRACT

Aim: Drug addiction causes many of brain dysfunctions and intellectual abnormalities so that its problem should be addressed. Hence, this study is aimed at comparing executive functions among drug-dependent, in abstinence, and normal individuals in Tehran.
Methodology: Research method is descriptive-comparative. Studied samples consisted of men chosen from addiction treatment centers in Tehran, using random sampling method. Members of normal groups consisted of 25 normal people without any experience of opiates use; drug user

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group consisted of 25 drug-dependent patients; and group of in abstinence individuals consisted of 25 members who had been drug abusers before but were under treatment during this study. To compare executive functions of the brain of these three groups, Letter-Number Sequence Test and Wisconsin Card Sorting Test were used.

Results: Drug users had lower function compared with normal but had a better function compared with in-abstinence groups in Wisconsin Card Sorting Test. in Letters-Digits Sequence Test, normal group have better performance than two other groups significantly; whereas, among two drug user and in-abstinence groups, drug users significantly performed better than in-abstinence group. Also. this current study showed that there is a relationship between substance use duration and low executive functions of brain ($P<0.01$).

Conclusion: Drug users have lower function compared with normal and in-abstinence groups in Wisconsin Card Sorting and Letters-Digits Sequence test. Moreover, short-term deprivation from drugs correlate with lower executive function of brain in cognitive tasks.

Keywords: Drugs; abstinence; executive functions; brain; addiction; dependency.

1. INTRODUCTION

Drug abuse is associated with neurophysiological and neuroanatomical changes. Neurocognitive impairment tends to effect on cognitive functioning [1], with prevalence estimates varying between 20% and 80% among treatment-seeking abusers of alcohol and drugs [2].

Opiates and opioid compounds have considerable effects on dopaminergic and noradrenergic neurotransmitter systems. Various data imply that addictive and rewarding features of opiate and opioid compounds are applied through activation of dopaminergic neurons of ventrotegmental area that are transferred to cerebral cortex and limbic system [3]. In addition to heavy costs of opioid substance use in society, there are considerable psychological and neurological consequences of substance use on brain and behavioral system of persons [3].

Contemporary models of human drug addiction emphasize neuropsychological and neurobiological dysfunction of complex processes within the brain [4].

Results of several studies showed that long-term drug dependence has a destructive effect on intellectual function [5]. Several studies showed poor executive function of brain, poor impulse control, poor planning and decision-making in drug-dependent individuals [6-8]. Pau et al. (2002) examined the impact of heroin on frontal executive functioning in three cognitive domains, namely attention, impulse control, and mental flexibility and abstract reasoning. The findings showed that heroin addiction has a negative effect on impulse control, while attention and mental flexibility/abstract reasoning ability were not affected by it [9].

Some studies showed cognitive functioning in people with a current or past history of opiate abuse using a range of neuropsychological tests. These findings suggest impulse control and cognitive deficiencies in these patients as a result of 5 years of heroin and Cocaine use [10]. heroin addicts usually demonstrate impairment on psychomotor speed and attention ability in attention test [7,11].

Studies have indicated that psychoactive substance use would severely harm executive control functions, in particular areas related to response inhibition and decision-making [12,13]. The mentioned harms are along with dysfunction of anterior cingulate and prefrontal cortex [8,14]. The current models of Neuroscience consider the vital role of Prefrontal cortex in additive behavior. The Prefrontal cortex circuit is affected by various substances through different methods [14]. Cannabis use would lower inner control leading to cognitive damages such as memory and attention disorders [5]. Cannabis use intensity is along with damages to visual-verbal memory, psychomotor and movement speed, executive functions, and decision-making [15]. chronic Marijuana users are at risk within cognitive-behavioral processes such as poor reaction, adaptability, and decision-making compared with normal individuals so that the low function of them in Wisconsin test might be due to the damage to frontal lobe [13,16].

It seems that executive functions are generally related to PreFrontal Cortex. Conducted researched show that patients with damaged

PreFrontal Cortex have a low function in neuropsychological tests such as Wisconsin Card Sorting Test [17,18]. Although there have been numerous studies in field of psychological effects of opioids, a few number of these studies have addressed the effect of these substances on executive function of brain that is one of the most important abilities of brain. The reason might be attributed to rare clinical samples that opioid is the only drug abused by them. In this regard, the present study examines executive functions of brain among drug-dependent, in-abstinence, and normal individuals in Iran.

2. METHODS

This is a descriptive-comparative study. Statistical population consisted of all persons who were drug dependent or in abstinence during the study based on Diagnostic and Statistical Manual of Mental Disorders (DSM-5). Sample members were chosen through cluster sampling method. In this case, two regions were randomly chosen from Tehran Regions and then a list of Methadone treatment and rehabilitation centers was prepared and 5 centers were randomly chosen from them. The drug-dependent individuals in these centers were selected based on inclusion criteria including male, rang age of 20-40, having at least secondary education degrees, being only drug addicted, lack of severe psychiatric problems. Sample members were interviewed to diagnose if they had psychiatric problems. To select in-abstinence individuals, 25 members who had inclusion conditions were randomly chosen from anonymous groups and permitted camps in Tehran. Normal persons were those who had no experience of drug abuse living in Tehran. Normal members were selected from employees of addiction treatment centers and other persons. After obtaining patients' consent, a summary of tests was described and it was promised to patients that the results of their tests would be confidential. In this regard, abbreviations were used to register identity of participants. Tests were taken from in-abstinence samples in order to make sure about lack of drug abuse. Tests were implemented after obtaining demographic information. To assess executive functions, Wisconsin Card Sorting Test, and Letters-Digits Span Test were employed.

2.1 Data Analysis Methods

To analyze research data, descriptive statistics and one-way ANCOVA were applied.

2.2 Research Instruments

2.2.1 Demographic inventory

This inventory was designed to determine demographic features of participants such as age, gender, education, marital status, job status, substance use experience, the used dose, drug use duration, etc.

2.2.2 Wisconsin card sorting test

This test consists of 64 cards there are different in terms of color (red, yellow, blue, or green), shape (×, circle, triangle, or star), and number (one to four numbers). 64 different states will be created when these variables are matched with each other. This test can be scored based on several methods that the highest used scores are allocated to obtained number of classifications and errors. The obtained classifications are equal to the number of filled out cards during test that varies from 6 to 0 indicating progress level of person during test and discovery of 6 rules. Insisting error is related to selections in which, the previous role is applied again despite that change in test (after 10 correct responses) and these errors show lack of cognitive flexibility [18]. Wechsler et al. (1992) conducted a study on 30 mentally ill patients and results indicated that intra-score reliability (repetition error) of this test was equal to 0.92 and inter-score reliability was equal to 0.94 [9].Lezak (1995) has obtained validity of this test above 0.86 to measure cognitive impairment after traumatic brain injury. Reliability of this test reported equal to 0.83 based on the assessors' agreement coefficient in study conducted by Spreen and Strauss in 1998[18]. Naderi (1994) obtained reliability of this test to 0.85 among Iranian population after retest [19].

2.2.3 Digits' sequence test

This test includes 20 items, each item consists of a number of letters and digits, and respondent should sort them. The examiner asks the participant to read these letters and digits as they are and then asks to sort digits and letters based on the alphabets and numbers order and read them. Since this test requires familiarity of participant with alphabets and their order, participant should have a minimum educational level. The test is ended after three failures. This test has been designed to assess active memory. In this research, the sub-test of letters-digits span existing in Wechsler Memory Scale has been used to measure this variable. In a

national study in USA conducted by a Psychiatric Firm (1997), Wechsler Memory Scale was done for a 1250-member sample at age of 13 to normalize the tests and the mean of Cronbach's alpha of all age groups obtained to 0.82 (for subtest of letters-digits sequence) and reliability of this test obtained to 0.74 using test-retest method [18,20,21]. Wechsler Memory Scale was normalized in this study and reliability of this subtest obtained to 0.74 using Cronbach's method and obtained to 0.75.

3. RESULTS

There was no significant difference between age (significance level of 0.94) and educational (sig level of 0.59) properties of three groups (at significance level>0.01) and it means that these groups were similar in terms of age and educational properties. There was no significant difference between scores of subtests of vocabulary ranges (Sig level of 0.84) of groups (Sig level>0.01). Therefore, groups were similar in terms of intelligence level. There was no significant difference between drug users and in-abstinence groups in terms of substance abuse duration (Sig level of 0.41). There was no significant difference between drug user and in-abstinence groups based on the substance use experience including smoking (91%), opium (85%), Heroin (75%), opium resin (58%), Methadone (16%) and Crack (18%) among drug user group; the mentioned information among in-abstinence group was as follows: smoking (88%), opium (87%), Heroin (68%), opium resin (42%), Methadone (38%) and Crack (31%). There was a significant difference between three groups, with Chi-Square of 14.47 at significance level of 0.001, in terms of job status; accordingly, employment percentage in normal group (68%) was more than two other groups of drug users (36%) and in-abstinence group (12%). The reason for such finding is that most of the people who are in abstinence, had not any job during study because of participating in addiction treatment programs and concentrating on treatment, drug users had lost their job due to substance use and low percentage of them could keep their jobs.

Mean of groups in relation with repetition error (Wisconsin Test) was equal to 22.24 for drug user group, to 29.32 for in-abstinence group, and to 18.12 in normal group; accordingly, men scores of in-abstinence group was more than two other groups in terms of repetition error index. According to the completed classifications, mean of drug user group was equal to 4.40, in abstinence group (3.12), normal group (5.041); it means that mean score of normal group was more than two other groups. In case of repetition error in Wisconsin test, mean of drug user group was equal to 13.62, in-abstinence group (19.51), and normal group (13.12); accordingly, mean score of in-abstinence group was more than two other groups in terms of repetition error index.

As can be seen in Table 1, there is a significant difference between mean scores of three groups obtained from Wisconsin Card Sorting Test and such significant difference can be seen in all three indices of this test including repetition error, number of completed classifications, and non-repetition errors (P<0.01). Tukey post hoc test was used in this research to compare mean scores of participants in accordance with the number of participants in each group.

Table 1. Results of one-way ANCOVA in Wisconsin card sorting test

P	F ratio	Mean squares	df	Sum of squares	Change sources
0/000	8/84	802/25	2	1604/50	repetition error between groups in groups total
		90/73	72	6532/64	
			74	8137/14	
0/001	8/45	23/89	2	47/78	number of classes between groups in groups total
		2/82	72	203/60	
			74	251/38	
0/000	6/33	467/54	2	921/85	repetition error between groups in groups total
		14/04	72	4856/22	
			74	5706/78	

Table 2. Tukey post hoc test for Wisconsin card sorting test

P	mean standard error	mean difference	Groups compositions
0/28	2/69	4/12	drug user normal
0/02	2/69	-7/08	drug user in-abstinence
0/000	2/69	-11/20	Normal in-abstinence

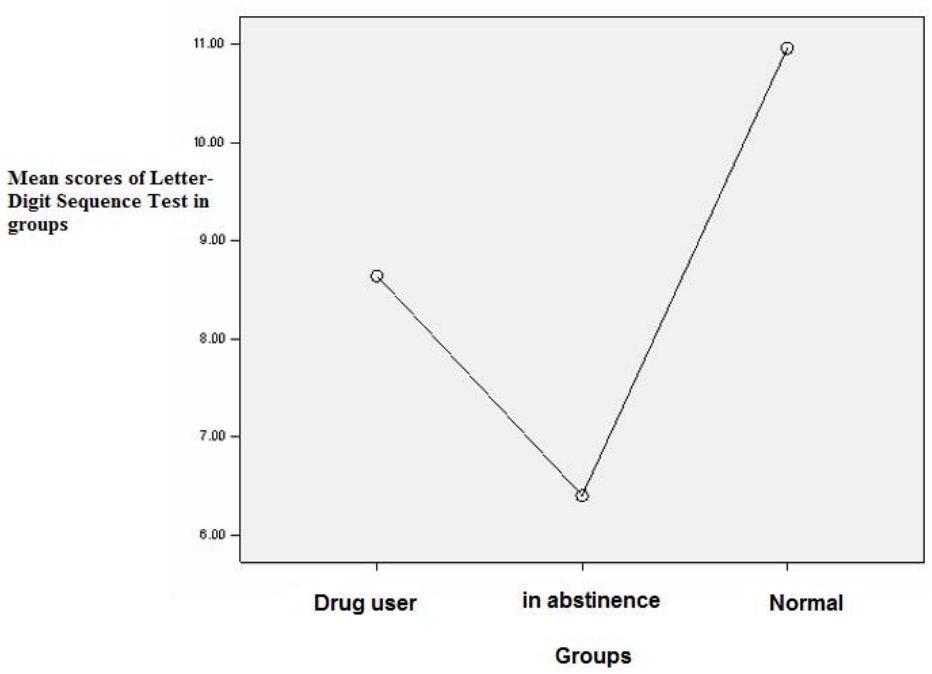

Fig. 1. Mean scores of letter-digit sequence test in groups

According to the results obtained from Table 2, there is a significant difference between means of drug user group and in-abstinence, between group between normal group and in-abstinence group in terms of all three studied indexes, but there was not any significant difference between normal and drug user groups. In other words, members of in-abstinence group have had a weaker function in this test compared with two other groups.

Fig. 1 indicates that mean scores of normal group and drug user group have had the highest scores, respectively and the function score of in-abstinence group has been lower than two other groups. To examine significance of such differences, one-way ANCOVA was used.

According to Table 3, there is a significant difference between mean scores obtained from Letter-Digit Sequence Test in groups ($P<0.01$). Tukey post hoc test was used to test research hypotheses considering the significant difference between scores of three groups.

According to data of Table 4, there is a significant difference between mean of groups within all three compositions of drug user-normal, drug user-in abstinence, and normal- in abstinence showing that participants in normal group have better functions than other two groups in Letter-Digit Sequence Test and drug-user group members have better functions than in-abstinence group. The last research hypothesis has been related to effect of substance use duration on executive functions of brain. The obtained results indicated a relationship between these two variables.

Table 3. Results obtained from one-way ANCOVA in letter-digit sequence test in groups

P	F ratio	Mean squares	df	Sum of squares	Change sources
0/000	27/46	129/97	2	259/94	repetition error
		4/73	72	340/72	between groups
			74	600/66	in groups
					total

Table 4. Tukey post hoc test for letter-digit sequence test

P	mean standard error	mean difference	Groups compositions
0/001	0/61	-2/32	drug user normal
0/001	0/61	2/24	drug user in-abstinence
0/001	0/61	4/56	Normal in-abstinence

Table 5. Correlation between substance use duriation and tests related to executive functions

Letter-Digit Sequence Test	Classification numbers	Repetition error	Pearson Correlation
-0/12	*-0/ 01	0/09	Duration

According to Table 5, there is negative correlation between substance use duration and number of classifications in Wisconsin Card Sorting Test and this correlation is significant at level 0.01. In this regard, the increase in substance use duration would lead to reduction in success level of participants in two drug user and in-abstinence groups.

4. DISCUSSION

The results of current study showed that Drug effect on neurological and psychological functions of human. In the following, the obtained results and research hypotheses were examined.

Hypothesis 1

Drug users had lower function compared with normal but had a better function compared with in-abstinence groups in Wisconsin Card Sorting Test. group. In other words, in-abstinence group had lower function in tests. These findings have been matched with results obtained from studies conducted by Simon et al. (2005), Rotter Hom-Faller et al. (2004) about the relationship between executive function disorder of brain and opiates use [22,23]; whereas, these findings are not in line with results obtained from studies conducted by Pou, Lee and Chan (2001) as well as Grant et al. [9,17].This study indicated that drug abuse has not a considerable effect on results Wisconsin Card Sorting Test, but it could effect on impulse control of drug addicted persons.

In-abstinence group had lower function compared with drug users and normal groups in Wisconsin Card Sorting Test. To explain this finding, some factors should be noted: this study had a small sample size; there was a factor that might create problem in generalization of results; groups were not similar in terms of demographic variables, job is a variable that might affect cognitive abilities; only 12% of in-abstinence group members had job; the other effective factor is drug withdrawal duration. Also,People who have quitted drugs might experience more distress because of deprivation and it might effect on their performances.

Hypothesis 2

There is a significant difference between functions of drug users, in-abstinence group, and normal group in Letters-Digits Sequence Test. In fact, normal group members performed better than two other groups significantly; whereas, among two drug user and in-abstinence groups, drug user group significantly performed better than in-abstinence group. These results are in line with findings of several studies conducted by Minteser and Stitzer (2002), Rogers and Robins (2003), and Hester & Garavan (2004) about difference between two groups in cognitive functions.They showed that there is a significant difference between drug user group and control group in terms of active memory function [6,22-24]. According to present study, in-abstinence group had lower function compared to drug users within Letter-Digits Sequence Test. This finding

is not in line with results obtained from studies conducted by Rogers and Robins [22]. Nowadays, Locus coeruleus and noradrenergic system activity as the main reason for emergence of withdrawal symptoms in drug-dependent individuals and some of symptoms of this system activity include excitability, palpitations, sweating and pain. Therefore, deprivation might lead to lower function in these patients. Alo, The results of current study showed that during dependence intensity control, methadone patients who in abstinence had more repetition errors and responses compared with patient who received daily methadone dose within Wisconsin Card Sorting Test. These finding indicates the relative destructive effect of such deprivation on function of frontal lobe. Therefore, research data of present study about better performance of normal group compared with drug user group was not approved, but better performance of normal group compared with in-abstinence group was approved.

In general, in-abstinence group had a lower function than two groups. Possible level of anxiety and depression is one another factor with a prominent role among in-abstinence group; however, this factor was not examined in this research. As we know, depression effects on motivation as well as cognitive functions. Moreover, such findings might be due to of drug withdrawal with intense deprivation symptoms effecting cognitive function of person. Also, two cognitive tasks were used at this study to examine cognitive functions and this might indicate necessity of other cognitive tasks to identify cognitive dysfunctions in addiction.

Hypothesis 3

There is a relationship between substance use duration and low executive functions of brain. This hypothesis was accepted. Accordingly, the longer the substance use duration, the more harm to executive function of brain might be. This finding is not matched with results of study conducted by Pou et al. [9] in which, they showed that substance use for 5 years might not have a destructive effect on executive function of brain except for inability to impulse control; this finding is in line with result of studies conducted by Vordjou-Garsia [13,22-25] indicated a strong relationship between substance use duration and low function within Wisconsin Card Sorting Test. They stated that opiates dependence intensity is along with more repetition errors in this test. These relations might reflect destructive effects of long-term drug abuse on frontal lobe. These results could be explained in the way that in-abstinence group was affected by withdrawal and deprivation symptoms and members of this group were not similar in terms of substance use duration.

5. CONCLUSION

Drug users had lower function compared with normal but had a better function compared with in-abstinence groups in Wisconsin Card Sorting Test. in Letters-Digits Sequence Test, normal group members performed better than two other groups significantly; whereas, among two drug user and in-abstinence groups, drug user group significantly performed better than in-abstinence group. Also. this current study showed that there is a relationship between substance use duration and low executive functions of brain.

SUGGESTIONS

We suggest psychological intervention for improvement of brain function in Drug-dependent and in Abstinences persons.

CONSENT

As per international standard or university standard, patient's written consent has been collected and preserved by the authors.

ETHICAL APPROVAL

As per international standard or university standard, written approval of Ethics committee has been collected and preserved by the authors.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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