

Comparison of Executive Function of Brain between Drug-dependent , in Abstinences and normal individuals in Tehran

Abstract

Objective: drug addiction causes many of brain dysfunctions and intellectual abnormalities so that is problem should be addressed; hence, this study aimed at comparing executive functions among drug-dependent , in abstinence , and normal individuals in Iran.

Method: research method is descriptive-comparative. Studied sample consisted of men chosen from addiction treatment centers in Tehran, Iran using random sampling method. Members of normal groups consisted of 25 normal people without any experience of opiates use; drug user 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: results obtained from Wisconsin Card Sorting Test indicated that there was not any significant difference between normal and drug-user individuals; while, in-abstinence group members had a weaker function compared with two other groups. Also, results obtained from Letter-Number Sequence Test showed that in-abstinence group had weaker function than two other groups and drug users also performed badly compared to normal group. Moreover, there was a negative correlation between drug abuse duration and weaker executive functions of brain. Accordingly, the longer the substance use time, the more harmed the function of person will be during conducted tests ($P < 0.01$).

Conclusion: long-term drug abuse negatively affects the executive functions of brain and drug abusers would perform weaker within active memory tests. Moreover, short-term deprivation from drugs would weaken the function of person within tests measuring executive function of brain.

Keywords: drugs, abstinence, executive functions of brain

Introduction

Opioids have been using as opiates or alcohol solution of opium over the centuries (at least for 3500 years). Codeine 1802 and Morphine in 1806 were extracted from opiates for first time.

Initial effects of opiates and opioid are taken by opioid receptors. 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 ventro tegmental area that are transferred to cerebral cortex and limbic system [2]. 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. Results obtained from various studies have indicated that long-term drug dependence has a destructive effect on intellectual function [3]. Some of the complications of substance use include poor impulse control, poor planning and decision-making [4]. Results of studies conducted by Petry et al. (1998) and Strang & Gurlin g (1989) indicated weak executive function of brain of drug-dependent individuals [3]. Several research results showed that 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 weak function of them in Wisconsin test might be due to the damage to frontal lobe [4]. “Executive Function” is defined as capabilities of brain that enable the person to create new thinking and behaving patterns as well as thoughts revision and problem solving. These capabilities are highly required in unfamiliar conditions, where the person does not know what to do or in conditions in which, the pre-created behavioral methods are not suitable [5]. Traditionally, test of ability to start, stop, or change the behavior in response to changing driver is a part of evaluation related to inefficiency of frontal area [6]. All of the mentioned abilities are related to executive functions of brain associated with required cognitive abilities to have complicated behaviors subjected to goal and adaptability with a wide range of environmental changes and demands such as planning, anticipation (cognitive flexibility), paying attention to uncommon events and self-care behavior [7]. Studies have indicated that psychoactive substance use would severely harm executive control functions, in particular areas related to response inhibition and decision-making [8,9]. The mentioned harms are along with dysfunction of anterior cingulate and prefrontal cortex [10]. The current models of Neuroscience consider the vital role of Prefrontal cortex in addictive behavior. The Prefrontal cortex circuit is affected by various substances through different methods [11]. Cannabis use would weaken inner control leading to cognitive damages such as memory and attention disorders [12]. Cannabis use intensity is along

with damages to visual-verbal memory, psychomotor and movement speed, executive functions, and decision-making [13].

It seems that executive functions are generally related to Pre frontal Cortex. Conducted researched show that patients with damaged Pre frontal Cortex have a weak function in neuropsychological tests such as Wisconsin Card Sorting Test [14]. 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.

Method

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.

Research Instruments

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.

Wisconsin Card Sorting Test: this test consists of 64 cards there are different in terms of color (red, yellow, blue, or green), shape (\times , 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 [15]. 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 [16]. 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 [17]. Naderi (1994) obtained reliability of this test to 0.85 among Iranian population after retest [18].

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

Results

There was not any 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 not any 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 not any significant difference between drug users and in-abstinence groups in terms of substance abuse duration (Sig level of 0.41). There was not any 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.

Table 1. Results of one-way ANCOVA in Wisconsin Card Sorting Test

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

As can be seen in this table, 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 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

According to the results obtained from Tukey post hoc test for Wisconsin Card Sorting Test, 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.

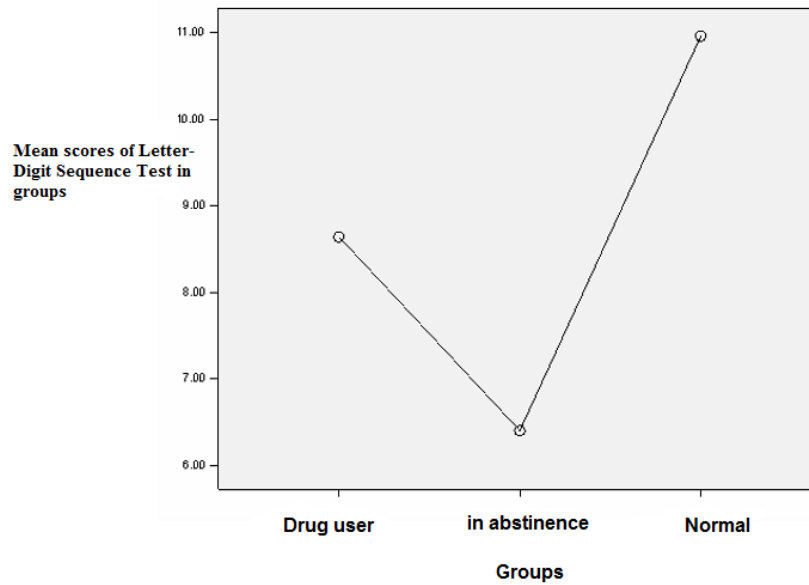


Figure 1. Mean scores of Letter-Digit Sequence Test in groups

Figure 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.

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

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.

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
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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 5. Correlation between substance use duration 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.

Discussion

The results obtained from study indicated that opiates effect on neurological and psychological functions of human. In the following, the obtained results and research hypotheses are examined.

Hypothesis 1: drug users have weaker function compared with normal and in-abstinence groups within Wisconsin Card Sorting Test. in present study, drug users had weaker functions than normal group, but had a better function compared with in-abstinence group. In other words, in-abstinence group had weaker function in tests. The mentioned findings have been matched with results obtained from studies conducted by Simon et al. (2005), Rotter Hom- Faller et al. (2004) about the executive function disorder of brain due to opiates use [19,20]; 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. [16,21]. This study indicated that drug abuse has not a considerable effect on

results obtained from Wisconsin Card Sorting Test, but function of these members would be at risk within tests for impulse control.

In-abstinence group had weaker function compared with drug user and normal groups within 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 employment variable; 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. People who have quitted drugs might experience more distress because of temptation 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 within Letters-Digits Sequence Test. in fact, results indicated as significant difference between three groups within Letters-Digits Sequence Test and 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 unexpectedly. These results are in line with findings obtained from studies conducted by Minteser and Stitzer (2002), Rogers and Robins (2003), and Hester & Garavan (2004) stating that there is a significant difference between drug user group and control group in terms of active memory conditions [6,22-24]. According to present study, in-abstinence group had weaker 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 from substances might lead to weak function among individuals. 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; such 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 worse function than two other 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 affects motivating power of person as well as cognitive functions. Moreover, such findings might be due to of drug withdrawal with intense deprivation symptoms affecting cognitive function of person. Also, two tasks were used at this study to examine cognitive functions and this might indicates necessity of other tasks to identify dysfunctions or cognitive disorders.

Hypothesis 3: there is a relationship between substance use duration and 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 obtained from study conducted by Pou et al. [16] 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 obtained from studies conducted by Vordjou-Garsia [25-28] indicated a strong relationship between substance use duration and weak function within Wisconsin Card Sorting Test. they stated that opiates dependence intensity is along with more repetition errors and responses. These relations might reflect destructive effects of long-term drug abuse on frontal lobe. These results can 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.

Conflict: None

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