On the Comparison of Cognitive Function in Substance Abusers and Addicts under Methadone Treatment with Normal Individuals

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Abstract

Objective: This study was an attempt to compare cognitive functioning in substance abusers and addicts under methadone treatment with normal individuals. **Method:** The current study was a causal-comparative one. The statistical population of this research consisted of all male substance abusers who had referred to addiction treatment centers of Khoy city in 2013. The total of 40 addicts under methadone treatment, 40 active drug users, and 40 non-addicts were selected as the participants of this study via convenience sampling method. Wisconsin Card Sorting Test and Wechsler Memory Scale were administered to the three groups for data collection purposes. **Results:** The results showed that the substance abusers' scores in Wisconsin card sorting test and Wechsler memory scale were significantly different from those of addicts under methadone treatment and normal individuals. In the same way, there was a significant difference between addicts under methadone treatment and normal individuals in terms of cognitive function; however, there was no significant difference between these two groups in terms of perseveration error. **Conclusion:** It can be concluded that chronic use of psychoactive substances causes damage to multiple brain regions such as prefrontal cortex and hippocampus and, thereby, it leads to cognitive malfunctioning in these areas.

Keywords: Cognitive Function, Executive Functions, Memory, Substance Abuse

Introduction

Drug addiction is a mental, relapsing, and chronic illness that is followed by intense motivational disorders and loss of behavioral control (Dallas, David & Julie, 2010). Diagnostic and Statistical Manual of Mental Disorders Fifth Edition (DSM-V, 2013) regards the existence of one of the cognitive, behavioral and physiological symptoms as the important feature of substance abuse disorder that people still persist in taking drugs despite the significant problems related to drug abuse. DSM-V also suggests that substance abuse disorder creates a fundamental change in brain circuits (especially in people with severe disorders) that may remain after detoxification (Diagnostic and Statistical Manual of Mental Disorders, 2013). Thus, clinical observations, common sense, and theoretical mechanisms suggest that acute and chronic use of psychoactive drugs impairs one's cognitive function (Lundqvist, 2005). In this regard, executive function is considered one of the most effective cognitive function whose significant role in addiction to substance abuse has been emphasized (Lyvers, Leggio, Abenavoli & Gasbarini, 2005). Executive functions refer to a set of organized and integrated superior capabilities that are neuro-anatomically connected with different paths of neural interactions such as prefrontal cortex (Robert, Robbins & Weiskrantz, 1998) and include forecast and goal establishment, planning, self-regulation and goal monitoring, implementation, effective feedback of programs, and working memory (Lezak, 1995). Long-term use of drugs succeeds high levels of neuro-psychological defects (Grant, Adams, Carlin & Rennick, 1977). Darke, Sims, Mcdonald & Wicks (2000) compared cognitive deficits between addicts under methadone treatment and normal people. They reported that people treated with methadone showed weaker performance in Wisconsin Card Sorting Test and Wechsler Memory Scale. Omstesin et al (2000) found that both stimulant abusers and opioid abusers had lower performance in Wisconsin Card Sorting Test compared to normal individuals. In consistency with this finding, several studies have shown that the use of stimulants (amphetamines) can affect cognitive function. In this regard Von Geusau, Stalenhoef, Huizing, Snel & Ridderinkhof (2004) and Reneman, et al. (2001) have shown that cognitive flexibility gets impaired in drug abusers and brings about increased preservative behavior in them. Thus, it has been assumed that preservation results from failure to control one's attention to the inhibition of irrelevant information (Salo, et al., 2005). Kalechstein, Newton & Green (2003) and Lundqvist (2005) compared morphine-abstinent people, patients under methadone maintenance treatment, and normal individuals and found that methadone receiving group significantly suffered from cognitive function disorder and the first and third groups were placed in the next ranks, respectively. In this regard, memory is one of the important cognitive functions in one's activities in addition to executive function deficits in individuals with substance abuse (Eysenck, 2000). In general, memory is a mechanism for encoding, storage, and recall of the stored information (Millner, Squire & Kandel, 1998).

Memory is divided into short-term and long-term memory based on the duration of data storage. Short-term memory can hold data for a short time, but long-term memory is concerned with the data that are maintained in memory from several minutes to the whole lifetime and can have different types such as explicit, semantic, event, implicit, etc. memory (Hergenhan & Olson, 2001; translated by Seif, 1995). In this area, various studies have reported defect and reduction in memory, verbal learning, response control, concentration, attention, and recall among drug-taking patients (Mccann & Ricaurte, 2004; Dark, et al., 2000). Yan et al. (2013) suggested that addicts dependent on heroin showed low performance on working memory tasks compared with the control group. Mcketin & Marric (1997) also found that there is a significant relationship between the severity of dependence on amphetamines and poor performance in tasks of Wechsler Memory Scale. In this regard, Miller (1985) conducted a study and compared chronic morphine and heroin users with ordinary people in terms of functional memory, spatial memory, planning, and production sequences and found that both groups of morphine and heroin users are significantly different from the normal group in various aspects, although the type of disorder varied in the two groups of patients. In the same way, several studies have provided support for the incidence of abnormal cognitive function after heavy and prolonged use of cannabis. This abnormal function is reflected in cognitive-motor malfunctions, particularly memory and learning (Curran, Brignell, Fletcher, Middleton & Henry, 2002; O'leary, et al., 2002). In line with the aforementioned points, several studies have indicated the effectiveness of addictive drugs on the brain and cognitive abilities. On the other hand, attention to physical and psychological effects of drug use is necessary particularly to the cognitive domains that are useful for healthy performance in appropriate interpersonal relationships and social behavior. Thus, motivated by the above findings and in line with the development of harm reduction approaches, the present study compares cognitive function (executive function and types of memory) between substance abusers, addicts treated with methadone, and normal individuals.

Method

Population, sample, and sampling method

This was a causal-comparative study. The statistical population of this research consisted of all male substance abusers who had referred to addiction treatment centers of Khoy city in 2013. Among this population, a total of 40 addicts under methadone treatment who were ready to cooperate in this research project were selected via convenience sampling method. In addition, among those who had referred to addiction treatment centers for the first time, the number of 40 participants was selected after being interviewed and announcing their consensus for participating in this study. It is noteworthy that this group had not received any kind of treatment in rehab centers before referring to these centers. Finally, among the individuals without any history of drug abuse, the number of 40 participants who was similar to the other two groups in terms of demographic characteristics was selected via purposive sampling. It is worth mentioning that the three groups were matched together in terms of age ($P>.05$, $F=2.357$), education ($P>.05$, $x^2=.867$), and marital status ($P>.05$, $x^2=.808$). The criteria for the inclusion of the participants in this study were as follows: male, aged from 25 to 40 years, suffering from no acute and chronic psychological disorders other than addiction, suffering from no significant physical illness, treatment with methadone and no drug-use in the methadone group, no dependence on non-opioids (such as crystal or other narcotic substances) in drug user group, and no history of drug use for the normal group. Moreover the exclusion criteria also included: being female and outside the age range 25 to 40 years, the presence of clinically significant acute and chronic psychological disorders other than addiction, suffering a significant physical illness, drug use in the group treated with methadone, consumption of non-opiate drugs in the drug using group, and a history of substance use for the normal group.

Instrument

1- Wisconsin Card Sorting Test (WCST): This test was constructed by Grant & Berg (1948) and evaluates the ability to abstract and change cognitive strategies in response to the stimuli from the environment (Cavallaro, et al., 2003). This test consists of 64 dissimilar cards with different shapes (triangles, stars, crosses and circles) and different colors. For the administration of the test, 4 cards are first placed in front of participants. The tester considers color as the sorting principle without notifying this to the participants and wants them to place the rest of the cards one by one under the four cards. After each attempt, the participants will be announced about the correctness of their placement. If the participant is able to correctly place 10 consecutive categories, the principle sorting changes. Then, shape is considered as the sorting criterion. The norm change is only allowed by changing the yes/no pattern of feedback. In this way, the previous correct answers will be regarded false based on the new norm. The next norm will be Number and these three norms will be repeated. When the participant correctly sorts six categories, the test will be stopped. Sorting Test Wisconsin can be scored in several ways. The most common method is to record the number of categories and preservative error. An obtained category refers to the correct responses or 10 consecutive correct placements. The number of these categories is placed in the range of zero to six wherein the test naturally stops. This test will be one of the main indicators of frontal lobe function when the participants continue the sorting according to the previous successful classification norm and/or when the participants insist on one wrong guess in the first series of categorizing and there is preservative error (Nyhus & Barcel, 2009). The reliability of this test for cognitive deficits after brain injuries has been reported above .86 (Lezak, 1995). Moreover, the reliability of this test based on the agreed-upon coefficient of assessors has been reported .83 (Spreen & Strauss, 1991).

2- Wechsler Clinical Memory Scale Form-I: This test was developed in 1945 by David Wechsler (Ryan, Morris, Yaffa & Peterson, 1981). This test is the result of 10 years of research in the field of memory and provides some information about the separation of organic and functional disorders of memory. Fast administration of this test in 15 minutes, satisfactory standardization of the test, and attention to the differences in memory at different ages are among the advantages of this scale. The scale consists of 7 subscales, including: personal information, orientation, mental control, logical memory, digit span, visual memory, and associate learning. The total score of the scale is obtained from the sum of the subscales' scores. According to the original form of this test, the constant modified score presented in the table pertaining to different age groups can be added to the sum of these raw scores. Then, the total score of memory score is obtained by adding up these two scores. Looking at the table, one can obtain memory quotient which is presented besides the weighted scores (Orangi, 2002). The test retest reliability of the total scale was obtained .89 while this coefficient has been reported equal to .75, .67, .80, .62, .68, .80, and .68 for the subscales personal information, orientation, mental control, logical memory, digit span, visual memory, and associate learning, respectively (Ryan et al., 1981).

Results

Descriptive statistics of the variables under study are presented in the table below for each group.

Table 1: Descriptive statistics of the variables under study for each group

Group		***Drug users***		***Under methadone treatment***		***Normal***	
Variable		***Mean***	***SD***	***Mean***	***SD***	***Mean***	***SD***
Wisconsin test	Preservative error	7.15	4.42	4.40	4.40	2.15	2.93
	Total error	12.33	5.93	8.87	5.160	5.68	2.55
Wechsler Memory	Personal information	4.10	1.31	5.62	1.25	6.70	2.99
	Orientation	3.48	1.84	4.85	1.62	7.43	2.91
	Mental control	4.60	1.89	6.53	1.82	8.88	2.04
	Logical memory	8.43	3.15	14.08	2.93	12.77	4.53
	Digit span	3.55	1.51	5.68	2.64	8.20	3.12
	Visual memory	5.78	1.73	8.77	1.64	10.43	2.12
	Associate learning	7.07	2.60	9.45	3.17	11.42	3.88
	Total memory quotient	67.60	7.67	96.37	8.16	117.15	21.54

Multivariate analysis of variance should be used to examine the difference between the three groups. The normal distribution of variables is one of the assumptions of using this analysis. Kolmogorov-Smirnov test results are provided in the table below.

Table 2: Kolmogorov-Smirnov test results for Wisconsin Card Test and Wechsler Memory Scale

Group	*Drug users*		*Under methadone treatment*		*Normal*	
Variable	*z*	*Sig.*	*z*	*Sig.*	*z*	*Sig.*
Preservative error	.124	.200	.130	.158	.143	.06
Total error	.127	.154	.138	.08	.136	.09
Total memory quotient	.129	.163	.132	.166	.135	1.03

The equality of error variances is another assumption for using this test which is investigated by Leven's test. The results of this test are representative of the presence of this assumption for the total error of Wisconsin test (P>.05, F=.832) and memory quotient (P>.05, F=2.114) and its components in the three groups. Then, MANOVA was conducted and the results indicated the existence of a significant difference (P<.001, F=32.004, Wilks' Lambda=.064). Univariate analysis of variance was used to examine differences in patterns as follows.

Table 3: Univariate analysis of variance representing differences in patterns

Eta squared	*Mean square*	*F*	*Sig.*
Preservative error	250.83	16.980	.0005
Total error	442.43	19.400	.0005
Personal information	68.27	16.660	.0005
Orientation	160.82	33.190	.0005
Mental control	183.35	49.660	.0005
Logical memory	350.23	26.810	.0005
Digit span	216.75	34.129	.0005
Visual memory	222.30	65.390	.0005
Associate learning	189.75	17.840	.0005
Total memory quotient	24765.35	509.760	.0005

As it is observed in the above table, there is a significant difference between the groups in all the components. Post-hoc Tukey test was used to investigate the difference between the three groups. The results indicated that drug users were significantly different from the other two groups in terms of preservative error and logical memory; however, no significant difference was between the normal group and patients under methadone treatment in the mentioned components. In terms of total error, there was no significant difference between drug users and the other two groups. In addition, there was a significant difference between the normal group and patients under methadone treatment in total error. Moreover, there was a significant difference between the drug users and the other two groups (the normal group and patients under methadone treatment) in terms of the components personal information, orientation, mental control, digit span, visual memory, associate learning, and total memory quotient. In the same way, there was a significant difference between the normal group and patients under methadone treatment in these components.

Discussion and Conclusion

The present study was conducted to compare cognitive function (memory and executive functions) between substance abusers, addicts treated with methadone, and normal subjects. The results of executive function assessment by Wisconsin test showed that substance abusers compared to the group treated with methadone and normal subjects had lower performance in total error of Wisconsin test and the same happened to the group under methadone treatment in comparison with the normal group. This finding is consistent with those of the studies done by Darke, et al. (2000), Omstesin, et al. (2000), Von Geusa, et al. (2004), Reneman, et al. (2001), and Lundqvist, et al. (2005). People with substance abuse disorders showed higher perseverative errors in changing the sets of Wisconsin Card Sorting Test compared with normal individuals (Goldstein et al., 2004; Salo, et al., 2005). Existing deficits in executive functions of substance abusers result from damage in frontal cortex of the brain. For example, animal and human studies have shown some defects in ventrolateral prefrontal cortex of the brain (Hampshire & Owen, 2006). Some studies have suggested that the inferior frontal gyrus and its connections with basal ganglia are associated with the relocation of tasks of Wisconsin test (Aron, Monsell, Sahakian & Robbins, 2004; Duncan & Owen, 2000). Therefore, these areas have been generally proposed for better performance on Wisconsin Card Sorting Test and dopamine has been suggested as a regulator of the connections in these areas (Nagano – Saito, et al., 2008). In this regard, Joyce & Meador-Woodruff (1997) suggest that cortical distribution of Dopaminergic and neural receptors may lead to different patterns of cognitive disorders among substance abusers.

For example, the dopamine D1 receptor is mainly present in anterior neocortex, particularly in the prefrontal cortex. Although addictive drugs have distinct effects on brain areas, these effects are common in some activities, such as increasing the metabolism of dopamine system (Koob & Lemoal, 1997; Wise & Bozarath, 1984). In this study, preservative error of Wisconsin test was not significantly different between the group treated with methadone and normal group. To justify this finding, one may assert that withdrawal of psychoactive drugs and regular use of methadone along with other therapies may effectively improve preservative behaviors and reduce them among the patients treated with methadone.

Another finding of this study suggested that drug abusers performed more weakly in Wechsler memory tasks compared to the other two groups. This finding is consistent with the findings of other studies conducted by Mccann, et al. (2004), Darke, et al. (2000), Yan, et al. (2013), Mcketin & Mattick (1997), and Miller (1985). In justification of this finding, it is possible to mention that the chronic use of drugs affects the brain regions involved in memory and learning, including frontal cortex (Yang, et al., 2009) and hippocampus (Lu, et al., 2010). This means that narcotic drugs may increase apoptosis process (programmed cell death) and inhibition of neurogenesis (formation of neural tissue) considering the cognitive processes that are impaired by drug use and its effects on hippocampus and prefrontal cortex (Nyberg, 2012). In this regard, the weakening of the neurogenesis resulting from drug use has already been seen in the hippocampus of the rats exposed to morphine (Eisch, Barrot, Schad & Self & Nestler, 2000). It seems that opioids (e.g. morphine) reduce the process of neurogenesis in sub-granular zone (part of the dentate gyrus) and this neurogenesis inhibition contributes to the defects in cognitive functions such as memory tasks as a result of substance abuse (Arguello, et al., 2008). The process of apoptosis is associated with morphine-induced tolerance and apoptotic effect of morphine is blocked by naloxone (opioid receptor antagonist) (Hu, Sheng, Lokensgard & Peterson, 2002). No comparison of neuropsychological indices in different types of drugs, ignorance of gender differences, limitation of participants to males, and convenience sampling were among the limitations of this study. Further research is recommended to be conducted on different groups of drug users in future.

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