Effect of Methadone Maintenance Treatment on Executive Functions in Drug Users

Vahid Nejati

Abstract

Objective: Methadone maintenance treatment is one of the most common methods of substance abuse treatment. There is conflicting evidence of the effect of methadone on behavior and cognition. The aim of this study was to evaluate the effect of methadone maintenance treatment on executive functions. **Method:** A quasi-experimental research design along with pretest and posttest stages was used for the conduct of this study. A variety of neurological tests, such as Stroop Test, Wisconsin Test, Continuous Performance Test, Verbal Fluency Test, Digit Span Test, and Go/No-Go Test were used to evaluate executive functions. **Results:** The results showed that methadone maintenance treatment did not lead to a significant difference in Wisconsin test, Continuous Performance Test, Verbal Fluency Test, Digit Span Test, and Go/No-Go Test ($P>.05$). However, it brought about a significant difference in the indexes of Stroop test ($P<.05$). **Discussion and Conclusion:** Although methadone treatment does not lead to the improvement of cognitive functions, it exerts no detrimental effect on cognitive functions, as well. Methadone treatment can be used when it is not aimed to improve substance users' cognitive functions.

Keywords: Methadone Treatment, Maintenance Treatment, Executive Functions

Vahid Nejati
Associate Professor of Cognitive Neuroscience
University of Shahid Beheshti
Tehran
Iran
E-mail: v_nejati@sbu.ac.ir

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Introduction

Methadone maintenance treatment is one of the most well-known methods of medical treatment for drug users (White & Lopatko, 2007). Methadone use as a treatment approach for opioid addicts began in 1964 in New York after the epidemic of heroin abuse after World War II. At that time, studies showed that the use of methadone would lead to the reduction of heroin use and decline the rate of death resulting from substance abuse (Herman, 2000). Among the drug users under methadone treatment, the secret use of drugs (Clausen, Anchersen & Waal, 1994), crime (Hall, 1996) and mortality (Degenhardt, et al., 2009) are reduced. Longitudinal studies have shown that the drug users who are treated with an alternative therapy, cannot avoid taking drugs for a long period. Indeed, they may use drugs at the same time or turn to drug use after the treatment. For many substance abusers, methadone use is an appropriate treatment alternative because they can bring some changes in their lives using this medication and can return to their social activities. Reports and studies have shown that methadone dependence and long-term use of methadone lead to the incidence of cognitive disorders in drug users and these cognitive disorders will lead to the decline of individual, familial, and social efficiency of drug users (Bell, Burrell & Indig, 2006; Hser, Longshore & Anglin, 2007). Today, disorders in brain structure and cognitive processes derived from them are among the main issues in the field of substance dependency and abuse (Bava, Jacobus, Mahmood, Yang & Tapert, 2010).

Based on the findings of cognitive neuroscience, the cognitive disorders resulting from drug use are prevalent in the realm of executive functions. In fact, there is a close relationship between executive function deficits and drug dependence that has been proved in numerous studies conducted in laboratory scale. Researchers in this area assume that functional changes in the mesencephalon dopamine system resulting from chronic use of drugs make the individuals vulnerable to disorders in executive functions. Impairment in executive functions such as inhibitory control and inability in preventing recurrent thoughts of drug-driven stimuli leads to the incidence of drug seeking behaviours and increases the possibility of relapse in drug use (Zhao, Fan, Du, Jiang, Chen & Sun, 2012).

Many studies have shown that the use of opiates leads to disorder in attention, concentration, abstraction, problem solving skills, executive functions, and perceptual/motor skills (Teichner, Horner, Roitzsch, Herron, & Thevos, 2002). Nowadays, little information is available about cognitive disorders in substance abusers after withdrawal. Scientific information and evidence on cognitive disorders after chronic addiction can help with more effective clinical treatment (Aharonovic, Nunes & Hasin, 2003). In the review of several studies focused on neuropsychological tests to assess cognitive disorders among the addicts treated with methadone, conflicting results have been reported about the effects of methadone treatment on cognitive functions. Some recent studies have shown

that drug-dependent individuals who do not consume opium, compared to the individuals using methadone maintenance treatment, suffer from slower processing speed and response inhibition (in Five Finger Test), slower visuospatial memory, lower cognitive flexibility (Verbal Fluency Test), and weaker reasoning abilities (Wechsler Test, third version) (Verdejo, Toribio, Orozco, Puente Perez-Garcia, 2005; Davis, Liddiard & McMiian, 2002; Mintzer, Copersino & Stitzer, 2005). Davis et al (2002) demonstrated that the patients under methadone treatment are at least two standard deviations below the norm of the community as well as the groups prohibited from taking heroin. In fact, the risk of neuropsychological dysfunction in the patients under methadone treatment was higher than that in opiate users; therefore, the rehabilitation and reconstruction of drug dependent persons must be done by drug use abstinence (Davis, 2002). Mintzer, et al. (2005) showed that the efficacy of patients treated with methadone was reported to be lower than the individuals stopping drug use in Digit Symbol Substitution Test and Trial Making Test. In addition, both groups obtained lower efficiency scores in these two tests than the control group. Accordingly, methadone use leads to chronic cognitive disorder. Thus, the main research question in this study was formulated as: Can methadone treatment influence cognitive functions?

Method

Population, sample, and sampling method

A quasi-experimental research design along with pretest and posttest stages was used for the conduct of this study. The number of 16 drug-dependent persons referring to medical centers in Tehran for drug use abstinence in 2013 was included in this study.

Instrument

1. Verbal Fluency Test (Semantic Phonetic): two subscales, including animal and fruit names were used to investigate semantic-verbal fluency. Thus, the participants were asked to recite animal names they would recall on a 60-second interval and also recite all the fruit names they could remember within 60 seconds. Then, the number of animals and fruits they could recall was recorded as the participant's score. In the phonetic fluency section of the test, the participants were requested to name the words that begin with letters "F" and "J" in two separate 60-second intervals and the number was recorded as participants' test scores. Amy (2006) examined the psychometric properties and internal consistency of both parts of the test (Cronbach's alpha = .82). In the same way, the retest reliability coefficients of the test were obtained equal to .77 and .87 for phonetic verbal fluency and semantic verbal fluency, respectively.

2. Digit Span Test (forward-backward): In this test, a string of digits is presented to the participants and they are asked to repeat the numbers. This string

starts from 3-number sets to 9-number sets. There are two major lists of number strings with different numbers and the same number of items in each string while the participant's scores will equal the length of the longest list that the participant has been able to repeat back in one of the lists of the numbers. In other words, the test will be stopped when the participant could not repeat the string of numbers in any of the lists. In the other form of the test, the participant should repeat the digits in the reverse order. This test is to measure working memory capacity. Working memory components include central executive section, aural loop, and visual-spatial loop. The central executive section is regarded the attentional part consisting of back dorsal structure and ventromedial prefrontal cortex (Awh, et al., 1996).

3. Stroop Test: In this test, a color name (e.g., green) is written in another ink (e.g., red) and the participant is asked to tell the color of that word instead of reading the color name. In this research, computer-based type of the test was used. In this way, the participant pressed the same color of the word on the computer screen. Stroop test is used to measure selective attention (Coderre, Conklin & Heuven, 2011).

4. Wisconsin Card Sorting Test (WCST): In this test, four cards are placed on top of the screen as samples. These cards are different from each other in terms of the shapes on them (triangles, stars, crosses and circles), the number of shapes (from one to four), and color (green, blue, red, and yellow). A 64-card string also lies at the bottom of the screen, one of which is only visible to the examinee. Each of the cards in this string has its unique characteristics based on the same three rules (4 colors × four types of shapes × number of four shapes = 64 cards). In fact, each card represents a unique state which will not be repeated.

In this test, participants should place the first card whose shape can be seen in one of the card samples based on their guesses (by pressing the number written below the sample one the keyboard). Then, they discover the categorization rule based on feedback "true" or "false" on the screen. The rule changes after the right placement of cards in a sample and the participants should induce the new law based on the feedback they receive. The final score of each participant equals the number of 10-item categories that have been successfully classified. If the participant resumes categorizing based on the previous law despite the change of the classification law by the examiner, s/he has committed preservative error. Preservative error is generally referred to as the repetition of a learned response against the new law. This test is one of the main indicators of frontal lobe (Nyhus & Barcelaa, 2009).

5. Continuous Performance Test (CPT): This test was designed in 1956 by Rosvold and colleagues and has been used as one of the most common and powerful instruments in evaluating patients with attention deficit and hyperactivity. This test requires response control and continuous monitoring of target responses. In this test, the examinee should click the mouse (press the key) when presented with the target stimulus within target and non-target stimuli. The

outputs of this test include the correct response to target stimuli, mean duration of correct responses, wrong response to non-target stimuli, and no response to target stimuli (preservative error). In the test used in the study, two digits were displayed on either side of the screen and the examinee was asked to press the space bar on the keyboard as carefully and quickly as possible if the two numbers appearing on the screen were the same. This task allows the continuous monitoring of the stimuli and the frequent change of the target stimulus (Riccio, Reynolds & Lowe, 2001).

6. Go/No-Go Test: In this test, the participant in a situation (Go step, run or move) is presented with a stimulus and should respond in line with the stimulus as soon as possible. On the other hand, in No-go condition (No-go step, inhibit or stop motion), the examinee is presented with another stimulus and should refrain from providing any response with the advent of the second stimulus. These two conditions are randomly assigned to a task. The examinee's ability to inhibit response in the second situation is an index of his/her inhibitory control. In the version of the test that was used in this study, the number of 100 aircrafts was displayed in the middle of the screen and the examinees were required to immediately push the cursor key in the same direction with each aircraft. In half of the stimuli, a beep (as the inhibit stimulus) was sounded after the emergence of the stimulus target (aircraft) and the examinee was told to inhibit any response in such situations. In this test, the number of correct and the wrong responses in each condition and average response time were recorded in software. Since Barrett and Go/No-Go Tests are not culturally loaded and have a neurological basis, the mention of validity and reliability of other papers is verifiable in this case (Janette, et al., 2012).

Results

This study was conducted on a sample size of 16 male drug users under methadone treatment both before taking methadone and 45 days after taking methadone. The mean score and the standard deviation for the participants' age were 31.23 and 9.20, respectively. These values for the participants' education (years of education) were 10.52 and 3.72, respectively. In terms of the years of addiction, these values were respectively 11.46 and 4.8. The descriptive statistics of the variables under study and the dependent t test results are presented in the following table.

Table1: Descriptive statistics and t-test results before and after methadone treatment

Test		*Pretest*		*Posttest*		*t*	*Sig.*
		Mean	*SD*	*Mean*	*SD*		
Verbal fluency	Phonetic task	4	1.4	4.6	1.6	1.54	.143
	Semantic task	15.29	3.82	41.15	3	.156	.878
Digit span	Forward task	5.76	.43	5.52	.51	1.46	.163
	Backward task	5.35	.49	5.35	.49	.000	1.000
Stroop	Accuracy of 1st task	48.5	3.05	48.85	3.05	.939	.000
	Time of 1st task	1.16	.29	1.12	.22	2.012	.028
	Accuracy of 2nd task	49.25	1.74	49.55	.97	.302	.238
	Time of 2nd task	1.08	.19	1.05	.17	.908	.0005
	Accuracy of 3rd task	1.36	.30	1.28	.28	.703	.003
	Time of 3rd task	46.6	6.77	47.4	9.15	2.102	.020
Continuous Performance	Commission error	.25	.44	.43	.64	.472	.644
	Omission error	49.87	3.7	49.43	3.30	.899	.383
	Reaction time	.479	.049	.487	.063	.473	.643
Wisconsin	Categories achieved	3.85	.86	4.21	.80	1.43	.174
	Preservative error	8.64	3.22	10	4.16	.921	.374
	Correct responses	42.92	7.65	45.92	7.82	1.199	.252
Go/ No-go	Accuracy of Go condition	34.29	1.10	33.94	1.98	.728	.477
	Speed of Go condition	.978	.16	.991	.16	1.714	.106
	Accuracy of No-go condition	.88	.92	.94	1.14	.368	.718
	Speed of No-go condition	.582	.57	.619	.60	.982	.341

As it is indicated in the above table, there is no significant difference in any of the sub-scales of Verbal Fluency Test, Digit Span Test, Continuous Performance Test, Wisconsin Test, And Go/ No-Go Test before and after methadone use. In contrast, a significant difference was found between the two stages, I.e. before and after the intervention terms of accuracy and speed of the Stroop Test.

Discussion and Conclusion

The findings of the present study showed that the use of methadone treatment method does not lead to the improvement of any of the cognitive functions except selective attention. It is indicative of the fact that methadone treatment does not relegate cognitive functions. It was also supported that methadone maintenance treatment has no effect on verbal fluency. Prosser, et al (2008) conducted a cross sectional study in this filed and showed that the patients under methadone treatment were less efficient than their counterparts in linguistic functions (using Verbal Fluency Test). Prosser, et al. (2008) suggested methadone as the root of these disorders and stated that cognitive disorders will

be tackled after methadone detoxification. Davis, et al. (2002) used Verbal Fluency Test and verbal intelligence of Wechsler Test and showed that the people with drug use abstinence were less efficient than their healthy counterparts. From the two aforementioned studies and relevant results, it can be concluded that both methadone and substance use can occasion the impairment of verbal fluency function. The present study shows that although methadone use does not improve verbal fluency, it does not lead to the incidence and/or intensification of disorders in verbal functions among the people under methadone treatment. The results of Digit Span Test suggested the absence of any significant difference between pretest scores and posttest scores. In their cross-sectional study, Prosser, et al. (2008) showed that patients treated with methadone are less efficient in memory and visuospatial analysis in comparison with their counterparts. Rapeli, et al. (2007) found that the patients under methadone and naloxone treatment were less efficient than their counterparts in working memory. Miriam (2002) showed that patients treated with methadone suffer from some deficits in working memory compared to the control group.

Based on the findings, there was no significant difference between the pretest scores and posttest scores of the participants in terms of Continuous Performance Test, which is indicative of the presence of sustained attention. Appel & Gordon (1998) compared the individuals under methadone treatment with drug-dependent individuals and concluded that simple reaction time and reaction time with preparation were not significantly different. Darke, Sims, McDonald & Wicke (2000) showed that the patients treated with methadone obtained lower scores than the control group in all the functional tests, including psychomotor, information processing, attention, and short-term memory. Specka, et al. (2000) showed that patients treated with methadone acted faster than the control group in choice reaction time, but they committed a greater number of errors. Miriam, Mintzer, Maxine & Stitzer (2002) showed that patients treated with methadone are deficient compared to the control group in cognitive functions, such as psychomotor speed, working memory, decision-making, meta-memory, and inhibitory mechanisms. The findings of their study indicate that the use of methadone maintenance treatment has no effect on sustained attention in the participants.

Based on the research findings, a significant difference was found in the efficiency scores of Wisconsin Test before and after methadone treatment usage, which shows decision-making abilities. Using Wisconsin Card Sorting Test, Pirastu, et al. (2006) showed that patients treated with buprenorphine outperformed the patients treated with methadone in decision-making. It was shown that there is a higher preservative error in the patients treated with methadone compared to the other two groups.

Results showed the absence of a significant difference before and after methadone treatment in the efficiency scores of Go-go Test that is indicative of the impulsivity rate. Rapeli, et al. (2007) demonstrated that patients treated with

methadone had better performance than the patients treated with Buprenorphine/naloxone in Go-go test.

The findings of the current study showed that Stroop Test performance has been improved after methadone maintenance treatment, which indicates the improvement of selective attention function in drug-dependent individuals under methadone maintenance treatment. Rapeli, et al. (2007) demonstrated that patients treated with methadone and naloxone were less efficient in simple reaction time. It is noteworthy that Rapeli, et al. (2007) also compared the patients undergoing methadone treatment with two different doses and observed that individuals with a lower dose (40 mg) outperformed those with a higher dose (67 mg); therefore, they concluded that methadone would lead to disorder in psychomotor speed or simple reaction time. Indeed, the first part of Stroop Test represents the simple reaction time. Accordingly, the findings of the current study do not support the findings of the study undertaken by Rapeli, et al. (2007). In the present study, it was shown that methadone maintenance treatment improves simple reaction time.

As common in other studies on addiction, one of the limitations of the study was lack of knowledge about the cognitive functions of people before addiction. However, this limitation does not strongly affect the results since it was an intervention-based study and participants' scores were compared together before treatment and after treatment while this limitation is more evident in other cross-sectional comparative studies that examine addicted people against their normal counterparts. The short follow-up period of the current study was another limitation of the study. Thus, it is recommended that methadone treatment effect be examined in longer time periods.

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