

## Selective Attention and Drug Related Attention Bias in Methadone Maintenance Patients

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Received: 17 Jan. 2011; Received in revised form: 30 Jul. 2011; Accepted: 6 Sep. 2011

**Abstract-** One of the main problems of the drug abusers is drug related attention bias, which causes craving, and as a result drive the drug abusers to take narcotics. Methadone is used as a maintenance treatment for drug abusers. The purpose of this study is evaluation of the effect of Methadone maintenance therapy (MMT) on selective attention and drug related attention bias. This study investigated drug cue-related attention bias and selective attention in 16 methadone-maintained patients before and 45 days after methadone therapy period. Stroop color-word test and addiction Stroop test were used as measurement methods. Results show less reaction time and higher accuracy in Color-Word Stroop Test after MMT and less delay for addict related word in addiction Stroop test. It is concluded that methadone can improve selective attention capability and reduce drug related attention bias.

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*Acta Medica Iranica*, 2011; 49(12): 814-817.

**Keywords:** Methadone maintenance therapy; Selective attention; Attention bias; Addiction Stroop Test; Stroop Color-Word Test

### Introduction

Methadone maintenance therapy (MMT) is used for preventing withdrawal symptoms and reducing craving for street opioids. Methadone is a synthetic mu opioid agonist with good oral bioavailability and a long duration of action. Methadone is used in the treatment of opioid dependence, because it helps preventing opioid withdrawal symptoms, reduces cravings for opioids, and blocks the euphoric effects of shorter acting opioids (1,2). Methadone has some side effects on attention and memory in healthy subjects (3) and drug dependent subjects during methadone maintenance therapy (4-8).

Selective attention is one of the most important factors in cognitive abilities but some time it is problematic (9). For example addicts have selective attention to drug related stimuli so that detect them quickly and process them more than normal individuals. In addicts substance-related attention bias (AB), an information processing bias for substance-related stimuli is found that caused craving and substance use. Some gaps are faced in literature about attention bias in

opioid-dependent patient. On one hand, using street opioids could impair attention processing of patient (9). On the other hand, the reduction of selective attention to drug related stimuli can be considered as a main goal of MMT (2). The main question of the current research is evaluation of MMT effect on selective attention and drug related attention bias.

### Materials and Methods

#### Participants

Sixty opium addict males with  $31.2 \pm 9.2$  years old participated in study with available sampling. Participants were naive to the purpose of the study before testing.

#### Procedures

The Participants were evaluated with neuropsychological test before and 45 days after MMT. Participants receive methadone with 30-40 mg per day. Stroop color-word test and addiction Stroop test were used orderly for selective attention and attention bias evaluation.

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### Stroop color-word test

Stroop Color-Word Test has been used extensively in studies of selective attention and response inhibition. The Stroop procedure has been called “the gold standard of research in attention” This test has three stages that assess simple reaction time in the first one, cued reaction time in the second one and inhibitory control in third one (10,11).

### Addiction stroop test

As with the Stroop task (12), participants performing a modified emotional Stroop task are asked to view words presented in various colors (usually on a computer screen) and name the color while attempting to ignore reading and discerning the meaning of the word. The tendency to attend to (i.e., read and, in the case of the emotional Stroop task, be affected by the emotional significance) the word is referred to as attention bias. This study used two word sets designed as related or unrelated word to addictive behaviors.

During the experiment, those in the blocked conditions completed two blocks: A block of neutral words and a block of active (drug dependent) words. Participants in the unblocked condition viewed one long block of randomly ordered active and neutral words. The colors of the words consisted of blue, red, green, and yellow. There were 72 words in each block (4 colors x 18 items) and 144 words for the unblocked group.

The words were presented once at a time in the center of a 15 inch, laptop computer screen. The words were visible until the participant made an appropriate key stroke, indicating one of the four possible color choices. The computer recorded the latency of response and the number of correct responses.

Participants were instructed to name the word color as quickly as possible and to ignore the meaning of the word. They were also asked to finish the entire block without giving it up.

### Analysis

Paired sample t-test is used for comparing variables before and after methadone maintenance therapy.

### Results

Demographic data such as age, education and gender were shown in table 1 for the subjects.

Table 2 shows performance of Stroop color-word test as a measurement of selective attention before and after MMT. Dependent sample t-test is used for comparing two groups of data. As the following table shows, reaction time is reduced in all stages of Stroop test after MMT. Subjects were more accurate in stage one and three of the task. The main stage of Stroop task is stage 3 as the incongruent stage. It could be inferred that subjects were more accurate after MMT.

Performance of addiction Stroop test as a measurement of drug related attention bias before and after MMT shows that MMT can reduce attention bias to drug related stimuli (Table 3).

**Table 1.** Demographic Data

	Mean	SD
Age (year)	31.23	9.20
Education (year)	10.35	3.46
Addiction Period (year)	6.30	2.10
Gender (Male: Female)	16: 0	

**Table 2.** Findings of color-word test

Variable	Before MMT Mean (SD)	After MMT Mean (SD)	T	P-Value
Stroop Test Stages				
Stage I				
Reaction Time (ms)	1.16 (0.29)	1.12 (0.22)	0.533	0.028
Accuracy	48.5 (3.05)	48.85 (3.05)	0.939	0.000
Stage II				
Reaction Time (ms)	1.08 (0.19)	1.05 (0.17)	0.908	0.000
Accuracy	49.25 (1.74)	49.55 (0.97)	0.302	0.238
Stage III				
Reaction Time (ms)	1.36 (0.30)	1.28 (0.28)	0.703	0.003
Accuracy	46.6 (6.77)	47.4 (9.15)	0.556	0.020

ms: mili second, SD: Standard deviation

Table 3. Findings of addiction stroop test

Variable	Before MMT Mean (SD)	After MMT Mean (SD)	t	P-Value
Reaction Time (ms)				
Addict Related Word	1.112 (0.214)	1.032 (0.184)	0.829	0.000
Neutral word	1.148 (0.236)	1.038 (0.199)	0.760	0.000
Correct Response Percent				
Addict Related Word	40.11 (4.31)	40.64 (3.92)	0.864	0.000
Neutral word	39.58 (3.57)	38.88 (4.18)	0.305	0.234

Discussion

The findings show that MMT can increase selective attention performance in methadone maintenance patient (MMP). Many researchers report that chronic use of psychoactive substances is associated with widespread deficits in neuropsychological function (13-15). Deficits are pronounced in the executive domain including decision-making (16-19), response inhibition (20-22), planning (23), and working memory (6,15). These deficits may be associated with prefrontal cortex dysfunction and, their extent and nature is likely to depend on the substance of abuse.

Methadone has been used for years as a substitution treatment for opiate addiction (24). Despite the amply documented advantages of methadone maintenance programs, there are some side effect and complain with MMT. Darke *et al.*, compared performance of MMP relative to controls matched with respect to age, gender, and years of education, on a standardized neuropsychological battery and show worse psychomotor performance, information processing, attention, short term memory, long term memory, and problem solving in MMP (1). Specka *et al.*, showed that MMP were impaired relative to controls on measures of attention and tachistoscopic perception. On a choice RT task, that subject should response to stimuli as soon as possible MMP were faster but produced more errors. On two tasks requiring visual tracking, results suggested that MMP were more accurate but slower (2).

In other hand, Prosser *et al.*, found no correlation between neuropsychological performance and either opiate use or methadone treatment (8).

Darke *et al.*, have suggested that other factors indirectly related to opioid abuse, such as greater exposure to overdoses and concurrent alcohol dependence may be linked to the presence of cognitive impairments in MMP (1), however, some other researchers suggest that methadone consumption by itself may be associated with the cognitive deficits present in this population (6). One great limitation of

this study is comparing MMP with normal healthy people in cross-sectional study. The result is based on one interventional study that cognitive performance of each case is compared to itself before and after MMT. Another finding of present study is reducing attention bias to drug related stimuli after MMT. Attention bias to drug related stimuli drive addicts to taking drugs. When abusers are exposed to addiction-related stimuli, automatic cognitive processes drive them to stimuli and this factor motivate them for substance use (25). Based on the results in this research, methadone can reduce this motivation and therefore, the findings here can be considered as a beneficial effect of MMT. Similarly Walter *et al.*, found a decrease in cortisol level, craving and negative effects of addiction after the daily methadone medication (26). The findings of present research confirm Kreek *et al.* findings that methadone attenuates heroin craving (27). Furthermore, some researches show methadone maintenance tends to normalize many aspects of the hormonal disruptions found in compulsive heroin users (28-30). Several potential limitations of this study should be considered and addressed by future research, including the limited sample size and the lack of measures related to other relevant domains.

Acknowledgment

The Authors wish to thank to all participant and Dr. M. R. Naghavi for assistance on the data provided. This work was supported by Psychiatry and Psychology Research Center, University of Tehran.

References

1. Darke S, Sims J, McDonald S, Wickes W. Cognitive impairment among methadone maintenance patients. *Addiction* 2000;95(5):687-95.

2. Specka M, Finkbeiner T, Lodemann E, Leifert K, Kluwig J, Gastpar M. Cognitive-motor performance of methadone-maintained patients. *Eur Addict Res* 2000;6(1):8-19.

3. Rapeli P, Fabritius C, Alho H, Salaspuro M, Wahlbeck K, Kalska H. Methadone vs. buprenorphine/naloxone during early opioid substitution treatment: a naturalistic comparison of cognitive performance relative to healthy controls. *BMC Clin Pharmacol* 2007;7:5.
4. Verdejo A, Toribio I, Orozco C, Puente KL, Pérez-García M. Neuropsychological functioning in methadone maintenance patients versus abstinent heroin abusers. *Drug Alcohol Depend* 2005;78(3):283-8.
5. Davis PE, Liddiard H, McMillan TM. Neuropsychological deficits and opiate abuse. *Drug Alcohol Depend* 2002;67(1):105-8.
6. Mintzer MZ, Stitzer ML. Cognitive impairment in methadone maintenance patients. *Drug Alcohol Depend* 2002;67(1):41-51.
7. Mintzer MZ, Copersino ML, Stitzer ML. Opioid abuse and cognitive performance. *Drug Alcohol Depend* 2005;78(2):225-30.
8. Prosser JM, Eisenberg D, Davey EE, Steinfeld M, Cohen LJ, London ED, Galynker II. Character pathology and neuropsychological test performance in remitted opiate dependence. *Subst Abuse Treat Prev Policy* 2008;3:23.
9. Bruce G, Jones BT. Methods that measure attentional bias. In: Wiers RW, Stacy AW, editors. *Handbook on Implicit Cognition and Addiction*. Thousand Oaks, CA: SAGE Publishers; 2006. p. 135-49.
10. Freudenreich O, Deckersbach T, Goff DC. Insight into current symptoms of schizophrenia. Association with frontal cortical function and affect. *Acta Psychiatr Scand* 2004;110(1):14-20.
11. Marks KA, Fastenau PS, Lysaker PH, Bond GR. Self-Appraisal of Illness Questionnaire (SAIQ): relationship to researcher-rated insight and neuropsychological function in schizophrenia. *Schizophr Res* 2000;45(3):203-11.
12. Stroop JR. Studies of interference in serial verbal reactions. *J Exp Psychol* 1935;18:643-62.
13. Rogers RD, Robbins TW. Investigating the neurocognitive deficits associated with chronic drug misuse. *Curr Opin Neurobiol* 2001;11(2):250-7.
14. Rogers RD, Robbins TW. The neuropsychology of chronic drug abuse. In: Ron MA, Robbins TW, editors. *Disorders of Brain and Mind*. Cambridge, UK: Cambridge University Press; 2003.
15. Verdejo A, Toribio I, Orozco C, Puente KL, Pérez-García M. Neuropsychological functioning in methadone maintenance patients versus abstinent heroin abusers. *Drug Alcohol Depend* 2005;78(3):283-8.
16. Bechara A, Damasio H. Decision-making and addiction (part I): impaired activation of somatic states in substance dependent individuals when pondering decisions with negative future consequences. *Neuropsychologia* 2002;40(10):1675-89.
17. Bechara A, Dolan S, Denburg N, Hindes A, Anderson SW, Nathan PE. Decision-making deficits, linked to a dysfunctional ventromedial prefrontal cortex, revealed in alcohol and stimulant abusers. *Neuropsychologia* 2001;39(4):376-89.
18. Bechara A, Dolan S, Hindes A. Decision-making and addiction (part II): myopia for the future or hypersensitivity to reward? *Neuropsychologia* 2002;40(10):1690-705.
19. Grant S, Contoreggi C, London ED. Drug abusers show impaired performance in a laboratory test of decision making. *Neuropsychologia* 2000;38(8):1180-7.
20. Fillmore MT. Drug abuse as a problem of impaired control: current approaches and findings. *Behav Cogn Neurosci Rev* 2003;2(3):179-97.
21. Hester R, Garavan H. Executive dysfunction in cocaine addiction: evidence for discordant frontal, cingulate, and cerebellar activity. *J Neurosci* 2004;24(49):11017-22.
22. Kaufman JN, Ross TJ, Stein EA, Garavan H. Cingulate hypoactivity in cocaine users during a GO-NOGO task as revealed by event-related functional magnetic resonance imaging. *J Neurosci* 2003;23(21):7839-43.
23. Ornstein TJ, Iddon JL, Baldacchino AM, Sahakian BJ, London M, Everitt BJ, Robbins TW. Profiles of cognitive dysfunction in chronic amphetamine and heroin abusers. *Neuropsychopharmacology* 2000;23(2):113-26.
24. Kreek MJ. Rationale for maintenance pharmacotherapy of opiate dependence. *Res Publ Assoc Res Nerv Ment Dis* 1992;70:205-30.
25. Tiffany ST. Cognitive concepts of craving. *Alcohol Res Health* 1999;23(3):215-24.
26. Walter M, Wiesbeck GA, Bloch N, Aeschbach S, Olbrich HM, Seifritz E, Dürsteler-MacFarland KM. Psychobiological responses to drug cues before and after methadone intake in heroin-dependent patients: a pilot study. *Eur Neuropsychopharmacol* 2008;18(5):390-3.
27. Kreek MJ, LaForge KS, Butelman E. Pharmacotherapy of addictions. *Nat Rev Drug Discov* 2002;1(9):710-26.
28. Kling MA, Carson RE, Borg L, Zametkin A, Matochik JA, Schluger J, Herscovitch P, Rice KC, Ho A, Eckelman WC, Kreek MJ. Opioid receptor imaging with positron emission tomography and [(18)F]cyclofoxy in long-term, methadone-treated former heroin addicts. *J Pharmacol Exp Ther* 2000;295(3):1070-6.
29. Schluger JH, Bart G, Green M, Ho A, Kreek MJ. Corticotropin-releasing factor testing reveals a dose-dependent difference in methadone maintained vs control subjects. *Neuropsychopharmacology* 2003;28(5):985-94.
30. Schluger JH, Borg L, Ho A, Kreek MJ. Altered HPA axis responsivity to metyrapone testing in methadone maintained former heroin addicts with ongoing cocaine addiction. *Neuropsychopharmacology* 2001;24(5):568-75.