

Cognitive Flexibility, Attention and Speed of Mental Processing in Opioid and Methamphetamine Addicts in Comparison with Non-Addicts

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ABSTRACT

Introduction: Many studies have revealed that drug addicted individuals exhibit impaired performance on executive function tests but a few studies have been conducted on executive functions of drug addicts in Iran. To contribute to this understanding, the present study was designed to assess some domains related to executive functions including cognitive flexibility, attention and speed of mental processing in a sample of drug addicts in comparison with a sample of non-drug addicts.

Methods: 155 male addicts between 25 to 35 years of age were selected from outpatient addiction clinics in Karaj, Iran. This group consisted of 3 subgroups of opium (n=40), hydrochloride heroin (n=63), and methamphetamine (n=52) addicts. A control group was selected matching the drug addicts in gender, age, education and socio-economic status and included 130 healthy non-drug taking males. A battery of standardized executive function tests including the Color trail making test, Stroop color word test, and Symbol digit modalities test were administered. Data analysis was conducted by performing Co-variance (MANCOVA) in SPSS.v.16.0.

Results: The study findings indicated that the group of drug addicted subjects performed significantly worse compared with the controls on all executive measures. There were also significant differences among the 3 subgroups. The hydrochloride heroin group had the worst performance compared with the methamphetamine and opium groups respectively. Drug addicted subjects with longer duration of drug addiction were much worse on all measures in comparison with drug addicted subjects with shorter duration of drug addiction.

Discussion: The study results confirmed that the functions of specific brain regions underlying cognitive flexibility, attention and speed of mental processing were significantly impaired in the group of drug addicted subjects. These impairments were also significantly related to type of drug used and duration of drug addiction that may contribute to most of behavioral disturbances found in drug addicts and need specific attention for intervention and treatment programs.

Key Words:

Executive Functions,
Opium,
Hydrochloride Heroin,
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1. Introduction

Chronic abuse of illicit drugs is associated with serious impairments in executive functions (Rogers & Robbins, 2003; Verdejo-Garcia et al., 2004). Some of these impairments include deficiencies in response inhibition (Kaufman et al., 2003; Hester & Garavan, 2004), cognitive flexibility (Verdejo et al., 2005), attention, and speed of mental processing (Al-Zahrani, & Elsayed, 2009).

Studies show that addiction to some opioids such as heroin leads to slow performance in executive functions related to prefrontal lobe such as attention, learning, and pattern of recognition (Fishbein et al., 2007). In addition, addiction to some psychostimulant drugs such as methamphetamine results in slow performance in executive functions related to frontal lobe (Han et al., 2008) and impaired performance on the tests related to perceptual speed, ability to manipulate information, and abstract thinking (Simon et al., 2002).

In recent decades, executive functions of opioid addicts in the domains of cognitive flexibility, attention and speed of mental processing have been investigated and compared with healthy individuals in other countries. For example; McCaffrey and colleagues (1988) studied the performance of a sample of 90 patients from a drug abuse treatment facility and revealed that patients exhibited varying degrees of impairment on the Trail making test, Symbol digit modalities test, and Hooper visual organization test compared with normal subjects.

Verdejo and colleagues (2005) studied some executive functions in a sample of methadone maintenance patients in comparison with a sample of abstinent heroin abusers and revealed that methadone maintenance patients had slower performance on processing speed, visuo-spatial attention, and cognitive flexibility tests respectively.

Al-Zahrani and Elsayed (2009) studied cognitive flexibility, attention and speed of mental processing among 154 opioid, amphetamine and alcohol patients in Saudi Arabia and found that all the 3 drug addicted groups had slower performance on the Color trail making test, Stroop color word test, and Symbol digit modalities test compared with the control group in their study. Their study results also indicated that the group of drug addicted subjects performed significantly slower than the comparison group on all executive measures and alco-

holic group was much slower followed by the amphetamine then the opioids groups on all executive measures.

In contrast, a few studies have been conducted on executive functions of methamphetamine addicts in comparison with studies on opioid addicts. However, Kalechstein and colleagues (2003) studied executive impairments in a sample of 27 methamphetamine addicted subjects who had achieved 5 to 14 days of continuously monitored abstinence and in 18 control subjects and found that methamphetamine addicted subjects performed significantly worse than control subjects on executive function measures sensitive to attention, psychomotor speed and some other executive functions. Although there is growing evidence of a significant link between opioid and methamphetamine addiction with executive functions, research on executive functions of opioid (opium and hydrochloride heroin) and methamphetamine addicts is still undeveloped in Iran. On the other hand, executive dysfunctions would lead to less success in treatment and abstinence from drug use and need special attention in drug use treatment programs.

The present study was designed to investigate some main domains of executive functions including cognitive flexibility, attention and speed of mental processing in a sample of opium, hydrochloride heroin and methamphetamine addicts in comparison with a sample of healthy non-drug taking subjects.

2. Methods

2.1. Subjects

155 male drug addicts (n=40 opium addicts, n=63 hydrochloride heroin addicts, and n=52 methamphetamine addicts) with mean age 29.8 (SD±8.3) years who met Diagnostic and Statistical Manual of Mental Disorders-IV (DSM-IV; American Psychiatric Association, 1994) criteria for drug dependence were selected through poster presentation in outpatient addiction clinics in Karaj, Iran. The opium and hydrochloride heroin groups were in abstinence from opioid use for 14(SD±3.4) days on average, and they were in methadone maintenance treatment program. The methamphetamine group was in abstinence from methamphetamine use for 16(SD±4.1) days on average, and they were in treatment with the Matrix Model at the onset of the study. The 3 subgroups of drug addicts did not differ statistically in level of education and age.

The typical subjects had completed almost 12 years of education, and less than 12 years of education. The majority of subjects identified themselves as unemployed (58%) and single (64%) while the remaining were employed (42%), married (26%) and divorced (10%) respectively.

130 non-addict subjects with mean age 30.1(SD±7.4) years were selected as the control group. The control group was matched with the group of drug addicted subjects in gender, age, education and socio-economic status. The group of drug addicted subjects was also divided into 4 subgroups according to duration of drug use, from 12 months, 13-19 months, 20-24 months and more than 24 months respectively.

Eligibility criteria were: being 18 years of age or older; being an active drug addict within the past 12 months before treatment entry for addiction and route of smoking administration. The exclusion criteria included any significant use of other drugs within the past two years before entry to treatment for drug addiction; lack of normal vision and positive history of physical, neurological and psychiatric disorders that would impact executive functions. The sample did not include poly substance users and intravenous drug users.

All subjects were free of withdrawal symptoms and free of drugs on the test day. Urine drug screening was done for all subjects to confirm the types of drug and exclude other drugs.

Written informed consent was taken from all subjects. The protocol of the study was approved by the institutional review board of Roudhen Azad University in Karaj.

2.2. Measures

2.2.1. The Mini-international neuropsychiatric interview

The Mini-international neuropsychiatric interview which is a short structured diagnostic interview based on the DSM-IV (Sheehan et al., 1998) was administered for assessment of psychiatric and substance use symptoms.

2.2.2. Color Trail Making Test (CTMT)

The Color trail making test is a widely used cognitive test that applies numbered colored circles and symbols related to universal sign language. The circles are printed with vivid pink or yellow backgrounds. The test

involves two forms of application. In the first form, the examinee uses a pencil to rapidly connect circles numbered 1 through 25 in sequence. In the second application, the subject rapidly connects numbered circles in sequence, but alternates between pink and yellow colors. It means that the complexity increased in the second form as there are possibilities of both number and color errors. This test measures some of the frontal lobe functions especially cognitive flexibility, perceptual tracking, and sequencing of events, sustained and divided attention and graphomotor skills (D'Elia et al., 1999).

2.2.3. Stroop Color Word Test (SCWT)

The Stroop color word test (Spreeen & Strauss, 1998) is commonly used as a test of selective attention and cognitive flexibility. This test takes advantage of the ability of the subject to read words more rapidly and automatically than he/she can name colors. If a word is printed or displayed in a color different from the color it actually names, the subject will read the word more readily than he/she can name the color in which it is displayed.

The underlying cognitive mechanism involved in this important test is named selective or directed attention, as the subject has to manage his/her attention, resist interference from irrelevant stimuli, inhibit or stop one response in order to express or do something else. The investigators administered the test in 5 forms gradually increasing in complexity. In the first form, subjects were instructed to recognize colors. In the second form, subjects were instructed to read the words written in black (names of colors). In the third form, subjects were instructed to read the names of the colors printed in different colors. In the fourth form, subjects were instructed to recognize the names of colors. In the last form, subjects were instructed to serially read the words in one row and recognize the color in one row. The time needed to each application and numbers of errors were basically recorded on a separate sheet.

2.2.4. Symbol Digit Modalities Test (SDMT)

The symbol digit modalities test (Smith, 1982) is a simple substitution task that individuals can easily perform. Using a reference key, the subject has 90 seconds to pair specific numbers with given geometric figures. This test measures speed of mental processing, attention and concentration, divided attention, ability to fix and detect errors and learn from them. The scoring ranges from 0-110, with higher scores representing better and more precise performance. It must be noted that the instructions of these measures were translated into

Persian, reviewed by an expert panel of six members to judge their clarity, cultural relevance, and comprehensibility, and then pilot tested.

2.3. Statistical Analysis

The data was analyzed using SPSS version 16.0. Tests for comparisons used included the mean and standard deviation and multivariate analysis of Co-variance (MANCOVA). Level of significance was detected at p value 0.05.

3. Results

The sample was all male between 25 to 35 years of age. The mean age of the group of drug addicted subjects was 29.8(SD±8.3) years and the mean age of the control group was 30.1(SD±7.4) years. There were no significant difference between the level of education and ages of the 2 groups (See details in Table1).

As shown in Table2, there were significant differences between the performance of the group of drug addicted subjects and the performance of the control group on the

Table 1. Level of education and age ranges of subjects (n=285)

Group	≤ 6 years	7-9 years	10-12 years	>12 years	Age	Mean Age
Opium (n=40)	9	11	10	10	25-33	30.1(SD±6.1)
Hydrochloride Heroin (n=63)	11	17	27	8	25-33	31.2(SD±8.1)
Methamphetamine (n=52)	8	10	26	8	26-33	28.3(SD±7.1)
All patients (N=155)	28	38	63	26	25-35	29.8(SD±8.3)
Control Group (N=130)	29	35	43	23	25-34	30.1(SD±7.4)

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Color trail making test. The drug addicted group took longer time in responding to items in forms 1 and 2 on the Color trial making test compared with the control

group. In addition, the drug addicted group had more color sequence errors in the first form and more color and number sequence errors in the second form of Color

Table 2. Results of the Color trial making test, Stroop color word test and Digit span modalities test

Assessment			Drug addicted group	Control group	F	P
CTMT ¹	Form 1	Time	73.61±1.15	64.13±2.21	F(1.16)=3.13	0.01
		Color errors	0.72±0.09	0.25±0.13	F(2.10)=11.82	0.001
	Form 2	Time	116.31±3.02	106.51±3.20	F(1.37)=7.13	0.05
		Number of errors	0.46±0.08	0.18±0.06	F(2.21)=5.21	0.05
SCWT ²		Color errors	0.71±0.06	0.31±0.12	F(3.43)=7.0	0.001
		Time 2	18.12±0.39	17.29±0.34	F(1.13)=3.27	0.05
		Time 3	14.23±0.36	12.17±0.39	F(1.16)=4.30	0.01
		Time 4	26.13±0.48	25.00±0.23	F(1.58)=2.32	0.05
		Time 5	29.15±0.71	25.18±0.36	F(1.12)=12.33	0.01
		Errors 4	2.61±0.13	1.40±0.17	F(1.51)=21.5	0.001
DSMT ³		Errors 5	2.43±0.31	2.29±0.20	F(1.17)=3.12	0.05
			33.90±1.43	53.41±1.34	F(1.10)=118.12	0.000

¹ CTMT: Color trial making test

² SCWT: Stroop color word test

³ DSMT: Digit span modalities test

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trial making test. Higher scores received on this test indicated worse performance. On the Stroop color word test, there was no significant difference in form 1 while in forms 2 and 3, there were statistically significant differences in the time required between the two groups. Also, on Stroop forms 4 and 5, there were significant differences as regard to time required and number of errors. Higher scores received on this test indicated worse performance. In addition, On the Symbol digit modalities test, the control groups had better performance compared with the group of drug addicted subjects. Higher scores received on this test indicated better performance.

The hydrochloride group took longer time in comparison with the methamphetamine and opium groups to achieve the responses in the first and the second forms

of the Color trail making test. In the second form of the test, the number of errors with the hydrochloride group was significantly higher than with the methamphetamine and lastly opium groups. On the Stroop color word test, there were statistically significant differences between the three subgroups of drug addicted subjects as the time needed in all forms of the test was significantly more with the hydrochloride group followed by the methamphetamine then the opium groups. Also, the number of errors was more with the hydrochloride group in form numbers 1 and 2 while it was more with the methamphetamine group in form number 5. In the Symbol digit modalities test, there were statistically significant differences between the groups as the scores were worse among the hydrochloride group in all aspects of the test followed by the other two groups (See Table2).

Table 3. Differences in drug addicted subgroups according to type of drug

Assessment	Opium	Hydrochloride Heroin	Methamphetamine	F	P
CTMT Time 1 ^b	71.6±31.1	83.3±21.09	75.4±15.5	F(2.102)=5.6	0.005
CTMT Time 2 ^b	110.37±4	123.3±33.4	114.6±5.0	F(2.103)=5.0	0.005
CTMT errors 2 ^b	0.18±1.2	0.59±0.84	0.26±1.3	F(2.64)=3.1	0.01
Stroop Time 4 ^b	24.92±6.9	31.9±7.8	25.7±6.1	F(1.10)=14.6	0.005
Stroop Time 5 ^b	29.28±8.0	36.2±9.4	30.9±8.4	F(1.10)=11.5	0.001
Stroop Errors 5 ^b	2.90±2.8	3.9±2.2	2.9±3.2	F(3.38)=2.7	0.05
Digit span test ^a	32.04±10.0	25.8±10.8	26.8±10.1	F(4.42)=5.6	0.001

a. Higher scores indicate better function.

b. Higher scores indicate slower function.

Table 4. Differences between patients according to duration of drug use

Assessment	12 Months	13-19 Months	20-24 Months	>24 Months	F	P
CTMT Time 1 ^b	69.1±22.5	70.33±25.7	75.65±18.6	82.63±22.3	F(3.10)=2.6	0.01
CTMT Color errors1 ^b	1.2±1.3	0.43±0.86	0.33±0.78	0.82±1.2	F(4.38)=3.6	0.01
CTMT Time 2 ^b	113.6±24.0	118.1±29.3	122.3±31.2	133.2±40.7	F(3.81)=2.3	0.05
Stroop Time 4 ^b	24.3±6.2	25.0±6.3	27.6±8.4	29.3± 8.3	F(3.10)=2.1	0.05
Stroop errors 4 ^b	2.6±2.2	2.5±2.1	3.2±1.3	3.7±2.3	F(3.50)=2.6	0.05
Stroop Times 5 ^b	28.0±4.6	29.6±4.1	31.9±10.1	34.3±9.3	F(7.81)=2.0	0.01
SDMT ^a	27.8±11.1	32.8±8.2	31.8±10.5	25.6±10.5	F(4.38)=3.1	0.05

a. Higher scores indicate better function.

b. higher scores indicate poorer function

CTMT: Color trial making test

SCWT: Stroop color word test

SDMT: Digit span modalities test

As shown in Table 4, on the Color trail making test, Stroop color word test, and Symbol digit modalities test, there were statistically significant differences between the different durations of drug addiction. The group of the shortest duration of drug addiction (12 months) was relatively the best group in performance and the group of the longest duration of drug addiction (> 24 months) was the worst. It must be noted that the number of color errors in the Color trail making test was more with the group of the shortest duration of drug addiction.

4. Discussion

The present study examined the executive functions of a sample of Iranian male opioid (e.g. opium and hydrochloride heroin) and methamphetamine addicts in comparison with a sample of healthy non-drug taking subjects within the domains of cognitive flexibility, attention and speed of mental processing and tried to find the relationship between these executive functions with the type of drug of abuse and duration of drug addiction.

We found that the drug addicted group performed significantly worse compared with the control group on all executive measures. The differences between the two groups increased with the increase in the complexities of the tasks presented. This study finding supports previous research studies that have confirmed greater executive impairments in male drug addicts compared with healthy male individuals (Kim et al., 2005; Stout et al., 2005).

We also found significant differences in executive functions that were identified in groups based on type of drug of abuse and duration of addiction.

Drug addicted subjects who reported a shorter duration of drug addiction performed better in comparison with subjects with longer duration of drug addiction. Our study findings confirmed notable impairments in the functions of the frontal and temporal lobes which are mainly engaged in executive functions and could be one of the main reasons behind slower performance of the drug addicted group on the tests of this study. The present study findings support other study findings revealed that different drug addicted groups are less successful on executive function tests compared with healthy individuals (Ersche et al., 2006; King et al., 2010).

We found that drug addicted subjects exhibited impaired performance on the Color trail making test compared with our healthy subjects. Drug addicted subjects exhibited delay in responding to items in forms 1 and 2,

a considerable number of color sequence errors in form 1 and more color and number sequence errors in form 2. This notion reflects impaired cognitive flexibility, problem in perceptual tracking, impairment in sequencing of events, deficiency in sustaining and dividing attention and impairment in graphomotor skills among our drug addicted subjects.

This study finding supports the study finding of McCaffrey and colleagues (1988). They revealed in their study that drug addicted subjects exhibited impairment on the Color trail making test in comparison with healthy subjects.

Moreover, this notion may reveal that the drug addicted subjects had significant impairments in some executive functions related to tracking tasks to the end, arranging events, maintaining attention and resisting irrelevant stimuli. This finding may be one of the important factors behind failure of patients to maintain abstinence from drug use. Deficiency in performing executive items on the Color trial making test may partly reflect dysfunction of lateral temporal lobe which is engaged in receiving stimuli, reducing irrelevant stimuli and conducting relevant messages to brain frontal lobe for further processing (D'Elia et al., 1999).

Another important finding in our study was slower performance of the drug addicts on the Stroop color word test. The drug addicted subjects exhibited impairment in selective attention and cognitive flexibility. Impaired performance on the Stroop color word test showed that the differences increased gradually with the different applications of the test and reached its maximum in the fourth and fifth application. This notion may explain that the group of drug addicted subjects had impaired selective attention, concept formation, and correction of errors, set shifting, behavioral control and modifications according to stimuli, inhibition of irrelevant responses, self-regulation capability and cognitive flexibility more than control group. Some drug addicted subjects had also executive impairment to shift rapidly and adequately from one behavior to another.

Impaired performance on the Stroop color word test may also reflect dysfunction of some brain regions such as the anterior cingulate cortex, dorsolateral prefrontal cortex, parietal lobule, striatum and insula (Brewer et al., 2008).

This study finding supports the study of Verdejo-Garcia and Perez-Garcia (2007). They compared two groups of abstinent poly substance users (cocaine versus heroin)

and controls and showed that abstinent poly substance users exhibited clinically significant impairments on measures assessing executive functions. Moreover, cocaine poly substance users had more severe impairments than heroin users and controls on measures of inhibition on Stroop color word test.

Another important finding in our study was the lower speed of mental processing in the group of drug addicted subjects compared with the control group. Indeed, attention in our drug addicted subjects was significantly impaired as measured by administering the Symbol digit modalities test.

This notion may be related to impairment in concentration, divided attention, ability to fix and detect errors and learn from them. It may partly explain some underlying reasons that why some patients continue to use drug and suffer from several relapses due to the same mistakes in addition to slowing of mental processing that impair their abilities to take the best decisions at the appropriate time (Bush et al., 2002).

In a similar study, Simon and colleagues (2000) compared attention in 65 methamphetamine users with 65 non-users by applying the Digit symbol test and found that methamphetamine users were significantly more impaired on this test.

We also found by comparing the three subgroups of patients, the performance of our hydrochloride heroin group was much slower than the methamphetamine and opium groups on most aspects of the study measures. In a study, researchers found that alcoholics were much slower than amphetamine and heroin users on the Color trial making test, Stroop color word test and Symbol digit modalities test (Al-Zahrani & Elsayed, 2009). However, the current findings are opposing to the study findings of Rounsavillae and colleagues (1982). They reported that executive functions among opiate users were better compared with the healthy controls.

Our study revealed that the duration of drug addiction was an important indicator for severity of executive dysfunctions. In fact, an increase in duration of drug addiction was associated with more deterioration of executive functions. In a similar study, Becker and his colleagues (1983) revealed that some drug addicted patients developed deterioration of cognitive functions compared with other groups.

Interestingly, impairments were found and were different among the groups even with a short duration of

drug addiction (12 months). It may be partly due to the rapid detrimental effects of hydrochloride heroin smoking which influenced neuropsychological functions of the drug addicted subjects even in a short period of time. In a similar study, Al-Zahrani and Elsayed (2009) found that even a short period of drug addiction would be associated with executive dysfunctions.

Impairment in executive functions of patients may be an important factor affecting the outcome of drug use treatment. There is a need to consider those patients who need other treatment programs to improve their cognitive flexibility, attention and speed of mental processing. There is a need for rethinking of the way in which drug addicts are assessed at the onset of any drug use treatment program because it is likely that they need assessment for their executive functions through different neuropsychological tests.

The current study suggests that the functions of specific brain regions underlying executive functions are significantly impaired in patients involved in drug addiction. This impairment was identified in groups based on primary drug of abuse and duration of drug addiction. Executive dysfunctions may contribute to most of behavioral disturbances found in patients with drug use disorders and need specific attention during tailoring of treatment programs for these patients.

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