



Comparison of Continuous Performance Test Results of Former Morphine and Methamphetamine Users During the Early Abstinence Phase

Mehdi Tehrani-Doost¹, Maryam Soleimannejad^{2,*}, Anahita Khorrami³ and Sadegh Yoosefee⁴

¹Psychiatry Department, Medical School, Tehran University of Medical Sciences, Tehran, Iran

²Psychiatry Department, Medical School, Qazvin University of Medical Sciences, Qazvin, Iran

³Cognitive Neuroscience, Youtop Clinic, Tehran, Iran

⁴Ph.D of Neuroscience, Neuroscience Research Center, Qom University of Medical Sciences, Qom, Iran

*Corresponding author: Maryam Soleimannejad, Psychiatry Department, Medical School, Qazvin University of Medical Sciences, Postal Code: 3414917633, Qazvin, Iran. Tel: +98-9122815917, Fax: +98-2833657606, Email: m.soleimannejad@qums.ac.ir.

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Abstract

Background: Chronic abuse of methamphetamine and morphine may result in cognitive impairment with negative consequences for patients' treatment and rehabilitation.

Objectives: We applied Conner's CPT II (continuous performance test) to determine the effect of methamphetamine and morphine use on patient performance in terms of type of substance use.

Methods: The research was performed at the Tehran University of Medical Sciences, Iran, during the autumn and winter of 2014. Twenty-two male patients previously dependent on morphine, twenty-one former methamphetamine abusers, and nineteen healthy controls were assessed by Conner's CPT II. The patients groups were pure consumers of their drug of choice in the last six months before treatment, and were in their abstinence period without intoxication or withdrawal symptoms. Initially, the potential depression and anxiety levels of volunteers were evaluated with the Hamilton questionnaire, and then a computerized CPT test was performed.

Results: Omission errors ($P = 0.008$) and variability ($P = 0.02$) in the methamphetamine group and variability in ex-morphine users were significantly higher in comparison with healthy controls ($P = 0.004$).

Conclusions: Significant differences in CPT performance were observed between the methamphetamine group and the healthy control group.

Keywords: Abstinence, Impulsivity, Substance Use, Vigilance

1. Background

Although Iran has an advanced healthcare system and complete supervision on prevention and treatment of substance use (1) methamphetamine consumption, which leads to high risk and hazardous behaviors, has become a major health concern (2, 3). According to psychological and neurological perspectives, addiction leads to cognitive changes in the field of attention deficits (4), mental processing speed (5), cognitive flexibility (6), and executive function (7). Defects in behavioral inhibition control, in some instances, have been created, maintained, and continued even after an individual refrains from substance use (8). In one study, CPT was used to evaluate changes in sustained attention in stimulant abusers. The results showed an increase in omission errors and variability (9). A simi-

lar study conducted on morphine users showed decreased discrimination ability between target and non-target stimuli (10). Preliminary findings from the Cambridge Neuropsychological Test Automated Battery revealed the inability of morphine and methamphetamine users' attention while performing the task (11). It is established that different substances, despite their diverse initial actions, produce some common effects on the ventral tegmental area and nucleus accumbens (12, 13), but show distinct structural changes of the brain owing to their intensity and quality (14). In contrast, one study showed no difference in executive function between the abuse and abstinence periods in either opioid or stimulant abusers (9), while other results showed longer visual attention during early attention between former morphine and methamphetamine abusers (15).

2. Objectives

In light of elevated methamphetamine consumption in Iran, we conducted this study to evaluate impulsivity and attention in consideration of the abused substance (morphine or methamphetamine).

3. Materials and Methods

3.1. Study Design and Setting

The current descriptive study was conducted on patients referred to the addiction cessation centers in Tehran, Iran, and matched drug naive control volunteers. The data collection lasted from May to December in 2014.

3.2. Participants

A total of 72 male volunteers aged 18 years or above participated in our study. They signed a written informed consent form. Ultimately, 62 volunteers remained in our study, in which 22 participants were former morphine abusers (age 36 ± 9.9 years), 21 were former methamphetamine abusers (31 ± 6.8 years), and 19 were healthy participants (30.6 ± 3.7 years). The healthy control group had matched demographic criteria and was selected from a general population.

3.2.1. Inclusion Criteria

- Participants used either of the drugs (morphine or methamphetamine without using another drug) in the last six months
- Absence of signs or symptoms of withdrawal or intoxication, screened by expert psychologist
- Negative result on a urinary test for substance use

3.2.2. Exclusion Criteria

- Polydrug abuse
- Cigarette smokers

3.2.3. Exceptions

Eight former morphine abusers were under treatment with methadone, and one participant from the healthy control group had used fluoxetine for his depression symptoms. On moral grounds, the participants continued taking their medication during the study.

3.3. Questionnaire

3.3.1. Anxiety and Depression Questionnaire of Hamilton

None of the participants had significant symptoms or signs of depression or anxiety. To rule out any effect of depression and anxiety on impulsivity or attention (16), we used the Hamilton questionnaire (17). All participants were evaluated with Hamilton questionnaires adapted for the Iranian population (18).

3.4. Study Procedure

3.4.1. Conners' Continuous Performance Test II

Conners' CPT II is a computerized test, lasting approximately 14 minutes. Stimuli appear in letter form. The display time for each letter on the monitor is held constant for 250 milliseconds (19). The room was dim, and had no environmental disturbances. We evaluated seven variables of the CPT II, which consisted of signs of inattention, impulsivity, or disturbed vigilance in participants, and scored them accordingly.

1. Hit reaction time: The mean average speed of all correct responses in test performance (20).
2. Omission error: High scores of this error are an indicator of insufficient attention or sluggish response towards a stimulus (21).
3. Commission error: Fast reaction times with high scores of commission errors suggest impulsivity. In contrast, high errors in omission and commission accompanied by slow reaction time suggest inattention as a general principle (22).
4. Response style (β): This shows an individual's tendency for answering the test. Sometimes participants prefer to answer correctly despite the longer time resulting in higher β scores (23).

5. Perseveration: Any reaction time of less than 100 milliseconds represents a perseverative response (19).

6. Detectability: This value represents the mean of every individual's discrimination power. Higher scores suggest greater discrimination ability (23).

7. Variability: A measure of the response speed consistency (24).

3.5. Statistical Analysis

The data was statistically analyzed using SPSS version 20.0. We performed a data analysis using the Kruskal-Wallis analysis and Mann-Whitney U test.

4. Results

Evaluated variables comprised CPT II variables; depression and anxiety scores of Hamilton tests; and demographic data. In the groups with a history of substance abuse, characteristics such as quantity of drug consumption, duration of abuse, and number of days of abstinence were evaluated. The frequency of marital status varied between groups. With respect to occupation and income, the highest frequency of employment was observed in the control group (73.3%) and higher frequency of unemployment was found in former methamphetamine abusers (28.6%). Demographic and clinical data are presented in Table 1.

Table 1. Demographic and Clinical Data's of Three Groups; (Ex-Morphine Abusers, Former Methamphetamine Abusers and Healthy Control)

Parameters	Morphine, (n = 22) ^a	Methamphetamine, (n = 21) ^a	Healthy Control, (n = 19) ^a	df	X ²	P Value
Age (y)	36 ± 9.9	31 ± 6.8	30.6 ± 3.7	2	3.35	0.18
Education (y)	10.7 ± 1.9	11.9 ± 2.2	14.9 ± 1.8	2	28.86	0.001 ^b
Duration of abstinence (days)	20.1 ± 8.4	20.8 ± 9.6	-	1	0.0	1
Duration of abuse (month)	96.2 ± 71.8	48.3 ± 35.1	-	1	4.94	0.026 ^b
Amount of abuse (gr)	1.9 ± 1.6	0.9 ± 0.7	-	1	4.90	0.027 ^b
HAM-D ^c	4.3 ± 6.1	4.7 ± 5.2	1.2 ± 1.5	2	6.01	0.04 ^b
HAM-A ^d	2.6 ± 4.3	1.5 ± 1.8	1.3 ± 2.2	2	3.12	0.2

^aValues are expressed as mean ± SD.

^bP values are significant.

^cHamilton questionnaire for depression.

^dHamilton questionnaire for anxiety.

We considered depression score and education level as covariates and eliminated their effect by using ANCOVA analysis. After correction, CPT measurements were compared again between groups. The only variable that had a small effect on omission error was education level with partial eta squared = 0.09, P value = 0.01, F(1) = 6.15. Correction of depression score and education level did not have any significant effect on other CPT variables.

The analyses of the CPT II variables are shown in [Table 2](#).

Paired groups comparison performed with the Mann-Whitney U test showed higher measures of omission error in the former methamphetamine abusers group in comparison with the control group (U = 103, Z = 0.007, P = 0.008, r = 0.0). Variability was significantly different between the three groups, significantly higher in the former methamphetamine abusers in comparison with control group (U = 114, Z = -2.31, P = 0.02, r = 0.36), and higher in former morphine abusers compared with the control group (U = 99, Z = -2.87, P = 0.004, r = 0.44).

We conducted our analysis again with exclusion of eight morphine users with methadone consumption to avoid cognitive differences which may affect their performance. When controlling for methadone use, the differences were not significantly different. The second set of results are presented in [Table 3](#).

Lastly, we entered a few other variables (level of education, drug dosage, duration of abuse and Hamilton depression scores) in Spearman's correlation analysis to assess their relationship with CPT II variables. A summary of these results is presented in [Table 4](#).

5. Discussion

The results of our study showed that there are differences in the CPT II performance between the two former

abuser groups and the control group, with no significant differences in executive functions between former morphine and methamphetamine abusers in their abstinence period. This emphasizes the executive function changes that take place after long durations of substance use. Former morphine abusers had higher measures in variability compared to the control group. The performance of former methamphetamine abusers showed a significant increase in the number of omission errors and variability that is similar to the results from another study in which the participants were evaluated using Conners' CPT II and represented increased omission errors and variability (9). One difference was that the participants of the other study were in the abuse phase, while our study participants were in the abstinence period. These results suggest that disturbances that are observed in the early abstinence phase of the former methamphetamine abusers group are similar to the abuse period. In addition to these results, sustained and divided attention in the abstinence phase of former methamphetamine abusers in the Price study showed lower measures in comparison with the control group (25). Cognitive disturbance found in former methamphetamine abusers in comparison with the healthy control group was confirmed by other studies in which impaired vigilance was detected by an auditory vigilance CPT II in participants with 4 - 7 days of abstinence (26) and significant impulsivity in the delay discounting task found in participants with 2 - 24 weeks of abstinence from methamphetamine (27).

Considerable executive dysfunction and attention disturbances in addiction are documented by numerous studies (28), but the persistence of them after overcoming the addiction, based on type of substance used is only partially discussed. In a comprehensive study performed using the frontal systems behavior scale (FrSBe), executive dysfunction in multi-drug addicted participants, even in

Table 2. CPT Variables in Three Groups; (Ex-Morphine Abusers, Former Methamphetamine Abusers and Healthy Control)

Group	Morphine, (n = 22) ^a	Methamphetamine, (n = 21) ^a	Healthy Control, (n = 19) ^a	df	X ²	P Value
Omission	10.4 ± 23.6	2.2 ± 2.2	0.7 ± 0.8	2	6.4	0.03 ^b
Commission	11.3 ± 7.7	9.7 ± 5.3	10 ± 5.9	2	0.33	0.84
Hit reaction time	453.3 ± 99.2	421.6 ± 79.7	397.4 ± 65.9	2	3.36	0.18
Detectability	0.7 ± 0.4	0.8 ± 0.4	0.8 ± 0.3	2	0.33	0.84
Variability	12.4 ± 11.5	8.5 ± 4.1	5.9 ± 2.3	2	9.56	0.008 ^b
Response style	0.8 ± 0.6	1.1 ± 1.7	0.8 ± 1.1	2	2	0.36
Perseveration	1.3 ± 3.8	0.6 ± 1.3	0.5 ± 0.2	2	5.44	0.06

^aValues are expressed as mean ± SD.^bP values are significant.**Table 3.** CPT Variables in Three Groups; (Ex-Morphine Abusers without Methadone Treatment, Former Methamphetamine Abusers and Healthy Control)

Group	Morphine, (n = 14) ^a	Methamphetamine, (n = 21) ^a	Healthy Control, (n = 19) ^a	df	X ²	P Value
Omission	12.2 ± 16.9	2.2 ± 2.2	0.7 ± 0.8	2	7.2	0.023 ^b
Commission	10.5 ± 7.2	9.7 ± 5.3	10 ± 5.9	2	0.31	0.77
Hit reaction time	466 ± 83.1	421.6 ± 79.7	397.4 ± 65.9	2	4.51	0.15
Detectability	0.7 ± 0.2	0.8 ± 0.4	0.8 ± 0.3	2	0.33	0.79
Variability	15.2 ± 8.3	8.5 ± 4.1	5.9 ± 2.3	2	8.68	0.0001 ^b
Response style	0.8 ± 0.7	1.1 ± 1.7	0.8 ± 1.1	2	2	0.4
Perseveration	1.2 ± 2.9	0.6 ± 1.3	0.5 ± 0.2	2	5.4	0.06

^aValues are expressed as mean ± SD.^bP values are significant.**Table 4.** Spearman's rho Correlation Between CPT Variables and Hamilton Depression Score, Education Years, Amount and Duration of Drug Abuse

CPT Variables	Hamilton Depression Score	Education (Y)	Amount of Drug Abuse	Duration of Drug Abuse
Omission errors	0.19	-0.39 ^a	0.06	-0.01
Commission errors	-0.15	0.04	-0.45	0.10
Hit RT	0.26 ^a	-0.32 ^a	0.11	0.005
Variability of standard error	0.26 ^a	-0.32 ^a	0.30	0.095
Detectability	0.06	-0.06	0.094	-0.16
Perseveration	0.30 ^a	-0.20	0.099	-0.03
Response style	0.22	-0.30 ^a	0.11	0.14

^aCorrelations are significant in P > 0.05

the abstinence period, have been reported to be greater than that in a healthy control group (29). Researchers have tried to select specific participants and develop more precise measures of neurocognitive and neuropsychological investigations to avoid confounding effects of the drugs themselves. Similarly, one study reported weak performance of opium abusers with a mean of 9.6 days of abstinence in the Ruff figural fluency test (RFFT) assessment (30). This suggests the existence and/or persistence of executive dysfunction in the abstinence phase of morphine

abusers similar to other substances.

Multiple studies have revealed that many cerebral regions and brain circuits are affected during the addiction process that leads to changes in cognitive and emotional functions of addicted people, and strongly impacts the development of drug dependence (31). Structural abnormalities identified in the brain of psychostimulant users are more specific and affect the prefrontal and medial temporal lobe areas (32-34). In contrast, non-specific ventricular and cortical volume loss has been reported in opiate users

(35, 36). Increased central monoamine neurotransmission is an outcome of acute pharmacological effects of methamphetamines (37). In contrast, opiates act mainly through μ -opioid receptors (38).

The different chronic effects of prolonged use of amphetamines and opiates probably explain the differences in intensity and quality of neuropathological disturbances (14) and different measures of CPT II variables that have been achieved in our results from these two groups of patients. The purity of drugs purchased from the streets differ; enormous differences in the concentrations of main components are typically observed. In a report by the UNODC (39), the most popular material used in the Middle East as methamphetamine is called "Captagon", whose psychoactive ingredients are not fully clear. This variability presents difficulties in assessing the true effects of methamphetamine use in Iranian users. Besides, acute withdrawal signs for both opioids and amphetamines may last for several weeks following abstinence. We propose a long term abstinence CPT performance evaluation for elimination some biases which would affect short term abstinence results.

5.1. Conclusion

Our study showed a significant discrepancy in CPT performance by substance abusers in comparison with healthy controls, even in their abstinence period. This discrepancy would have undesirable influence on their treatment maintenance. Thus, we suggest a long period of abstinence follow up for a more precise comparison of executive and cognitive changes which may follow substance use.

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Footnotes

Authors' Contribution: Mehdi Tehrani-doost and Maryam Soleimannejad conceived and designed the study, Maryam Soleimannejad and Anahita Khorrami performed the evaluation of data and drafting of the manuscript, Mehdi Tehrani-doost, Maryam Soleimannejad and Sadegh Yoosefee revised the manuscript for important intellectual content, Maryam Soleimannejad and Anahita Khorrami reanalyzed the clinical and statistical data.

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