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Investigating Cognitive Functions in Methadone Users in Comparison with Methadone and Methamphetamine Users and Control Group

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Original Article

Abstract

Background: Cognitive impairment in drug users is a marker for predicting recurrence and poorer adherence to treatment. The purpose of this study was to compare the cognitive function in three groups of methadone users methadone maintenance treatment (MMT), compared to methadone and methamphetamine (MAMP) users (MMT + MAMP) and healthy people (control group).

Methods: Three groups of 90 people including 30 users of MMT, 30 users of MMT + MAMP, and 30 healthy persons participated in this cross-sectional and purposeful study. The study was performed on outpatients of MMT Clinic of Psychiatric Hospital in Kerman, Iran. The demographic and related data questionnaire was filled out. In addition, Persian version of the Brief Assessment of Cognition in Schizophrenia (BACS) was used to assess cognitive function.

Findings: The mean of total number of scores and all BACS subscales were significantly better in control group than the other two groups of patients. Moreover, not only the mean of total number of BACS was significantly different between two substance abuser groups, but also there was a significant difference between them on verbal memory, digit sequencing, and token motor test, with MMT + MAMP group performing worse than MMT group.

Conclusion: Concomitant use of opioids and stimulant substance such as MAMP results in cumulative toxic effect of them on brain and cognitive functions.

Keywords: Methadone; Methamphetamine; Cognition; Substance-related disorders

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Introduction

There is a long history of inappropriate substance abuse due to their psychoactive effects. Substance abuse creates mood, behavior, and cognitive impairments and is associated with serious impairments in the physical, social, and cognitive functions of individuals. Impairment in these functions is caused by brain damage resulted from substance abuse.[1]

According to a systematic review by Wang et al., individuals on methadone maintenance treatment (MMT) program experience a variety of cognitive dysfunctions.[2] Davis et al. examined a wide range of neuropsychological functions in individuals with current or previous substance abuse. They showed that the scores of 60% of recent opiate abusers in two or more neuropsychological tests were different at least two standard deviations (2-SD) in comparison with the control group with no history of drug abuse. In addition, the risk of neuropsychological impairment was greater in opiate abusers, and recovery might occur during abstinence.[3]

Stimulants, particularly methamphetamines (MAMP), are among the most widely-used and abused illegal substance worldwide. Southeast and East Asia has become a global hub for MAMP production and trafficking over the last decade. MAMP stimulates the central nervous system (CNS), resulting in increased alertness and physical activity.[1,4] Many studies have shown structural and functional changes in the brain of MAMP abusers. Moreover, systematic reviews have shown that MAMP consumption is associated with a wide range of cognitive dysfunctions in attention, executive functioning, language, verbal fluency, learning, and visual and working memory.[5,6] It should be noted that MAMP use is associated with structural and functional changes in the brain structures such as the prefrontal cortex (PFC) and anterior cingulate cortex (ACC) which are involved in majority of cognitive functions.[5,7]

Roohi et al. compared cognitive functions including attention and working memory in two groups of opioid-dependent and MAMP-dependent patients in comparison with the control group, using the Paced Visual Serial Addition Test (PVSAT). They found that while the two groups performed significantly worse than controls, there were no significant differences between opioid-dependent and MAMP-dependent groups.[8] Mazhari et al. found that methadone users had significantly lower scores in measures of executive function, verbal memory, and working memory compared to the control group.[9]

Cognitive impairment is a marker for predicting relapse and poorer adherence to treatment and has a significant impact on different aspects of personal, occupational, and social life. This study aimed to compare the cognitive function of methadone users with that of the methadone combined with MAMP users and the control group, using a battery of tests named the Brief Assessment of Cognition in Schizophrenia (BACS).

Methods

Study participants and sampling: The study was cross-sectional and based on previous studies,[8,10] 30 people in each group were included in the study. It was performed on individuals undergoing MMT at MMT Clinic of Psychiatric Hospital of Kerman University of Medical Sciences, Kerman, Iran, from October 2017 to October 2018 by using a purposeful sampling method. MAMP and methadone dependence was diagnosed according to Diagnostic and Statistical Manual of Mental Disorders-5th Edition (DSM-5) criteria[11] by a trained psychiatric assistant with a clinical interview. People in both abuser groups consumed methadone prior to the study or were receiving outpatient methadone treatment. Moreover, people in MMT + MAMP group abused MAMP, too. Research sample had to fulfill the inclusion criteria (in addition to the diagnosis of methadone dependence or abuse as well as MAMP based on DSM-5 criteria) including: age of 18 to 55 years with at least five years of education, and undergoing MMT.

The control group was matched for age, sex, and education, with no substance abuse. Exclusion criteria for all three groups included: 1) a history of major psychiatric disorders including mental retardation, psychotic, mood, and cognitive disorders, 2) major neurological disorders such as brain injury, convulsion, and head trauma, 3) physical abnormalities affecting cognitive abilities such as visual and hearing impairment, and 4) current dependence on other substances such as cannabis, hallucinogens, and so on, affecting cognitive ability. For ensuring MAMP

use, urine test was obtained at the time of referral.

The study was approved by the Ethics Committee of Kerman University of Medical Sciences with the ethical code number: IR.KMU.AH.REC.071.1397. All participants provided written informed consent before participation and were informed that they were free to leave the study whenever they wished.

Measures

1- The Persian version of the BACS was applied to assess cognitive impairment which has enough reliability and validity in Persian language.[9,12] This test has been designed for a quick and easy assessment in approximately 30 minutes and is available in two versions that are not significantly different. The BACS test was used to assess cognitive performance in schizophrenic patients, for the first time. The BACS consists of six distinct test subsets (verbal memory, digit sequencing, verbal fluency, token motor task, Tower of London instruction, and symbol coding task). The final overall score is obtained from the sum of each subset score.
2- Urine test was conducted in order to ensure drug and MAMP use.

Descriptive statistics were applied to explore the characteristics of the study sample in the control group and two other main groups. In the current study, data were analyzed by SPSS software (version 19, SPSS Inc., Chicago, IL, USA) using one-way analysis of variance (ANOVA) and Pearson's correlation test. Differences were considered significant if $P < 0.05$.

Results

Table 1 shows the demographic characteristics of the study participants. There was no significant difference between the three groups in terms of age, sex, and education.

Table 2 shows mean of scores and SDs achieved for the BACS in the three groups. The results showed statistically significant differences between the three groups on the verbal fluency, symbol coding, and Tower of London test (all $P < 0.01$). Post-hoc test showed that the differences were between control group and both MMT and MMT + MAMP groups for the three measures, and control group performed better than the two other groups. However, MMT and MMT + MAMP groups were not significantly different and performed similarly on verbal fluency, symbol coding, and Tower of London measures.

On the verbal memory, digit sequencing, token motor test, and the BACS total score, the results showed that the three groups were significantly different (all Ps < 001). Post-hoc analyses showed that the differences were between control group and both MMT and MMT + MAMP groups for the three measures. Moreover, the MMT and MMT + MAMP groups were significantly different and MMT group performed better than MMT + MAMP group.

Discussion

In this study, 90 individuals were studied in three groups of MMT, MMT + MAMP, and control for assessing their cognitive functions, using the BACS. The most important findings of our study were significant differences in all areas of cognitive functioning in MMT group and MMT + MAMP group compared to controls, indicating that the controls were significantly better than other two groups. In addition, MMT + MAMP group was significantly worse than MMT group on the BACS composite score, verbal memory, working memory, and motor speed.

Our findings indicate that the control group performed significantly better than MMT group, that is similar to the previous studies which showed the impaired neuropsychological functioning in opioid abusers.[3,6,9,13,14] Davis et al. showed that the scores of neuropsychological tests in 60% of recent opioid abusers differed, at least 2-SD, with the control group.[3] In the Mazhari et al. study, cognitive functioning in methadone users was significantly different from the control group on executive functioning, verbal memory, verbal fluency, and working memory,[9] which was consistent with the present study.

Table 1. Demographic and clinical characteristics of the groups

Variables	MMT	MMT + MAMP	Control	P
Gender (men) [n (%)]	22 (73.3)	25 (83.3)	25 (83.3)	0.50
Age (year) (mean ± SD)	35.33 ± 10.00	34.90 ± 9.50	35.10 ± 9.70	0.90
Education level (year) (mean ± SD)	11.10 ± 2.60	10.40 ± 2.60	11.90 ± 1.90	0.07

MMT: Methadone maintenance treatment; MAMP: Methamphetamine; SD: Standard deviation

Table 2. Means and standard deviations (SDs) of the Brief Assessment of Cognition in Schizophrenia (BACS) for the study participants

Variables	MMT (mean ± SD)	MMT + MAMP (mean ± SD)	Control (mean ± SD)	Comparison
Verbal memory	36.97 ± 11.56	31.87 ± 11.62	43.10 ± 12.49	C* > M** > Mm***
Digit sequencing	15.27 ± 5.23	13.30 ± 4.23	17.40 ± 5.51	C > M > Mm
Token motor	70.27 ± 15.65	59.37 ± 18.28	75.70 ± 15.72	C > M > Mm
Verbal fluency	15.68 ± 6.43	15.07 ± 6.88	19.95 ± 5.19	C > M = Mm
Symbol coding	26.37 ± 10.12	21.93 ± 8.30	35.14 ± 10.95	C > M = Mm
Tower of London	5.87 ± 3.55	4.57 ± 2.48	12.93 ± 5.76	C > M = Mm
BACS composite	28.40 ± 6.16	24.35 ± 6.72	33.82 ± 6.56	C > M > Mm

*Control group; **Methadone maintenance treatment (MMT) group; ***MMT + methamphetamine (MAMP) group

MMT: Methadone maintenance treatment; MAMP: Methamphetamine; BACS: Brief Assessment of Cognition in Schizophrenia; SD: Standard deviation

The finding that MMT + MAMP group obtained the least score compared to MMT and controls indicates cumulative toxic effect of concomitant use of methadone and MAMP. Previous studies have demonstrated that various substances, particularly stimulants such as MAMP, cause impaired cognitive functions through changes in metabolism and oxygenation in the brain areas including the PFC, ACC, striatum, and insula.[5,7] This is consistent with the results of the current study suggesting that the combined use of substances resulted in greater impairment of cognitive function, especially those related to the activity of different parts of the frontal lobe, including verbal memory, working memory, and motor speed. Chronic stimulant and opioid use makes deficits in brain processes and circuitry that are linked to responsivity to drug cues over natural rewards as well as suboptimal goal-directed decision-making.[15]

Substance abuse induces brain plasticity mechanisms and long-lasting changes in neural circuitry as well as ultimate behaviour[16] and also induces lasting neuroadaptations in learning-related brain regions,18 given that cognitive dysfunction is a marker for predicting recurrence and poorer adherence to treatment[4,10,17] and worse treatment outcome.[18]

It seems that it is important to focus on improving cognitive abilities in the pharmacological and non-pharmacological treatment programs of substance abusers. In other words, in rehabilitation and relapse prevention policies, it is useful to evaluate the cognitive function of substance abusers and consider it as a measure of response to the treatment in order to reduce treatment costs and increase adherence to the therapy in substance dependence.

Conclusion

MAMP and opioid abuse epidemic is a critical health concern.[15] Concomitant use of methadone and stimulants such as MAMP affects the cognitive function of consumers more than each other alone. Since the prevalence of substance abuse and following mental disorders is one of the major problems in medical systems with imposing a lot of costs on the family and society, attention to the cognitive function and its impact on patient's performance (occupational, social, and interpersonal) is important.

Conflict of Interests

The Authors have no conflict of interest.

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Authors' Contribution

Supervisor: MES; Co-author assistant: DB and AA; Advisor: NP; Corresponding author: EZ; Data analyst: AS.

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بررسی عملکرد شناختی در مصرف‌کنندگان اپیوئیدها در مقایسه با مصرف‌کنندگان اپیوئیدها توأم با مت‌آمفتامین و گروه شاهد

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مقاله پژوهشی

چکیده

مقدمه: اختلال شناختی در مصرف‌کنندگان مواد، به عنوان نشانگری برای پیش‌بینی عود و پایبندی ضعیف‌تر به ماندن در درمان است. پژوهش حاضر با هدف مقایسه عملکرد شناختی در سه گروه مصرف‌کنندگان اپیوئیدها به تنهایی در مقایسه با مصرف‌کنندگان اپیوئیدها توأم با مت‌آمفتامین و افراد سالم در گروه شاهد صورت گرفت.

روش‌ها: در این مطالعه مقطعی و هدفمند، سه گروه۹۰ نفره شامل ۳۰ نفر مصرف‌کننده متادون (Methadone maintenance treatment یا MMT)، ۳۰ نفر مصرف‌کننده متادون و مت‌آمفتامین (MMT + MTMA) از بین بیماران مراجعه‌کننده به کلینیک سرپایی درمان با آگونیست‌های اپیوئید بیمارستان روان‌پزشکی شهید بهشتی کرمان انتخاب شدند و به همراه ۳۰ نفر گروه شاهد سالم از نظر عملکرد شناختی مورد بررسی قرار گرفتند. پرسش‌نامه اطلاعات دموگرافیک و عوامل مرتبط تکمیل گردید و جهت بررسی اختلال شناختی، نسخه فارسی ابزار ارزیابی کوتاه شناخت در اسکیزوفرنیا (Brief Assessment of Cognition in Schizophrenia یا BACS) مورد استفاده قرار گرفت.

یافته‌ها: میانگین نمره عملکرد کلی و تمام زیرمجموعه‌های عملکرد شناختی آزمون BACS در گروه شاهد از دو گروه بیمار به طور معنی‌داری بهتر بود مگر در سرعت موتور که در گروه شاهد و مصرف‌کنندگان اپیوئید به تنهایی تا حدودی مشابه بود. علاوه بر این، نه تنها نمره کلی BACS بین دو گروه مصرف‌کننده مواد تفاوت معنی‌داری را نشان داد، بلکه در زیرمجموعه‌های حافظه کلامی، توالی اعداد و Token-motor نیز این تفاوت معنی‌دار گزارش گردید و در گروه MMT + MTMA بدتر از گروه MMT مشاهده شد.

نتیجه‌گیری: مصرف توأم مواد اپیوئیدی و محرک‌هایی مانند مت‌آمفتامین، اثر تخریبی تجمعی بر مغز و عملکرد شناختی دارد.

واژگان کلیدی: اپیوئید؛ مت‌آمفتامین؛ عملکرد شناختی؛ اختلالات مرتبط با مصرف مواد

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