

Cognitive and Neuropsychological Assessments for Co-Occurring Opioid and Amphetamine-Type stimulant (COATS) Dependent Patients

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Abstract

Introduction: Several studies have shown that individuals with drug dependence have poorer cognitive functioning in the domain of executive functions. Studies investigating cognitive impairments in people with poly-drug use are limited. This study is designed to assess executive functions of patients with dual drug dependence (DDD) on opioid and (Amphetamine-Type Stimulants) ATS entering medication-assisted-treatment at Hospital Universiti Sains Malaysia.

Methodology: A total of $n=96$ male respondents ($n=56$ patients, and $n=40$ control group) were recruited for this cross-sectional study. Six neuropsychological tests (Rey-Osterrieth Complex Figure, Trail Making Test, Raven's Progressive Matrices, Digit Span Test, Digit Symbol Test, and Stroop Test) were administered.

Findings: Results showed patients performed significantly worse in perceptual motor speed, and visual scanning measured by Trail Making Test Part A, cognitive flexibility measured by Trail Making Test Part B, mental processing speed measured by Digit Symbol Test, and response inhibition measured by Stroop Test, compared to those in the control group.

Conclusion: Results suggests that perceptual motor speed, visual scanning, cognitive flexibility, mental processing speed, and response inhibition may be impaired in patients with dual drug dependence. Proper prevention and treatment interventions should consider addressing cognitive deficits for patients with dual dependence

Keywords: *Cognitive functions; Opioid; Amphetamine-Type-Stimulants; medication-assisted treatment*

1. Introduction

A large body evidence shows that with the use of psychoactive substance may lead to various cognitive impairments (Verdejo-Garcia et al, 2007; Ornstein et al, 2000). Although much research has been conducted in drug addiction in Malaysia, the cognitive and neuropsychological aspects of this phenomenon still remain scarce (Zamani, et al. 2014).

A new trend of dual dependence (Opioid and ATS) will provide a clear picture about the need to implement the effective treatment approach (Singh et al, 2013). Since the use of opioid and ATS are frequently co-occur (COATS), thus, this study aim to measure cognitive impairment that may affect this dual dependence drug users Since this trend is on the rise, it is important to know what cognitive functions may have been affected in this group of individuals.

Studies have showed that addiction to heroin may lead to the slow performance in the domain of executive functions such as attention, learning and pattern recognition (Fishbein et. al., 2007). Hekmat et. al., (2011) reported impairments in cognitive flexibility, attention, and speed of

mental processing in individuals dependent on amphetamine and opioid in Iran. It is important to identifying cognitive impairment observed in dual dependent patient compare to impairment found in those with only opioid and ATS dependence to tailoring effectiveness in treatment programmed.

Although there are evidence and link between this both drug heroin (opioid) and ATS in executive function, research on cognitive function between the uses of this drug still undeveloped in Malaysia. Thus, this study was carried out to investigate some domain in executive functions including visuoconstructional and visuo-perceptual, visual scanning and task switching, nonverbal intelligence, short-term memory, speed of mental processing, and response inhibition in comparison with control healthy subject who free from drug use.

2. Materials and Method

2.1 Subjects

A total of $n=96$ male respondents ($n=56$ patients, and $n=40$ control group) who meet the inclusion criteria were recruited. Inclusion criteria for patients entering treatment were being actively dependent on both drug (opioid and ATS). Exclusion criteria included psychiatric illness such as schizophrenia, bipolar disorder and inability to understand test instructions. Patients were recruited from medication-assisted treatment in Hospital Universiti Sains Malaysia, Kelantan, Malaysia. Participants in the control group were recruited from poster and chain referral method. Efforts were made to match these participants with the patients in terms of age, educational level and employment status. The assessments were conducted 3-4 days after patients were admitted to treatment to make sure they were free from opioid [withdrawal](#) symptoms.

2.2 Test Battery

2.2.1 Rey-Osterrieth Complex Figure (ROCF)

A test provides measures of visuo-constructional, visuo-perceptual ability incidental visual memory and attention (Stern et. al., 1999). Two conditions were administered (Copy and Delayed). Stimulus picture which was printed in A4 paper and blank response A4 paper were placed horizontally on a table in front of respondent and oral instruction are given to them. The Boston Qualitative Scoring System (BQSS) was administered in our study. In this system, the picture is divided into three sets of elements including configural elements, clusters and details.

2.2.2 Trail Test Part A and B

This timed assessment measures perceptual motor speed including visual scanning for part A and task cognitive flexibility in Part B. In set A, there are 25 circles on a sheet of paper numbered 1 to 25. Participants are instructed to connect the circles in ascending order, beginning at number 1. In set B, there are circles numbered 1-13 and letters from A-L. Participants are asked to connect the circles of numbers and letters alternately in the correct order (i.e., 1-A-2-B-3-C...). Time to complete each section was recorded.

2.2.3 Raven's Progressive Matrices

This culture free test evaluates reasoning skills (Ravens et. al., 2000). This test contains of 60 items in five sets A,B,C,D, and E. Each set are made up of 12 problems. Problems in each set become progressively more difficult. Each item contain a target pattern with one part removed and the subjects task is to choose the correct pattern from six to eight response patterns presented below target problem.

2.2.4 Digit Span Test Forward and Backward (DST)

This test is a measure of short-term memory in forward and for backward span, it measures working memory. In this test, a series of random digits of varying lengths are presented to the participant and the participant is asked to repeat the series of numbers in the order presented.

2.2.5 Symbol Digit Test (SDT)

This test measure the speed of mental processing under time pressure (Mathiesen, Ellingsen & Kjuus, 1999). For this test, patient and participant have to match the number and the symbol. The symbol appeared sequentially on the laptop screen and they have to match it quickly as they can.

2.2.6 Stroop test

This test used to measure response inhibition. Participant must response to the color of the word. In this computerized test, the congruent color words, neutral non-color word and incongruent color words are presented one at times and time taken (reaction time) then, are recorded. In the color word part, an individual will respond automatically in the word reading but has to suppressed and prevented from interfere with naming the color of color word. Stroop interference is extended delay in naming the color of incongruent condition relative to naming the color of congruent color word and control non-color word or neutral. (Lansbergen, Kenemans & Engeland, 2007) and this may create greater mental effort.

3. Result

All participants were male and all are Malay ethnic group. The average age of both participants was 34.4 (SD = 7.88). All socio-demographic characteristic are presented in table 1.

Table 3.1: Socio-demographic Characteristic of Study Groups

Demographics	DDD Patients (n=56)		Control Group (n=40)	
	Frequency	%	Frequency	%
Age				
≤ 20	0	(0)	0	(0)
20-25	7	(11.1)	10	(25.0)
26-30	11	(17.5)	3	(7.5)
31-35	12	(19.0)	8	(20.0)
36-40	17	(27.0)	7	(17.5)
41-50	9	(14.3)	12	(30.0)
51-60	0	(0)	0	(0)
Education				
Primary School	5	(7.9)	1	(2.5)
PMR	24	(38.1)	3	(7.5)
SPM	24	(38.1)	34	(85.0)
Certificate	1	(1.6)	2	(5.0)
Diploma	1	(1.6)	0	(0)
Degree	0	(0)	0	(0)
Employment				
Employed	46	(73.0)	36	(90.0)

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Unemployed	8	(12.7)	4	(10.0)
Income (RM)				
≤500	18	(28.6)	6	(15.0)
500-1000	27	(42.9)	9	(22.5)
1000-1500	6	(9.5)	12	(30.0)
1500-2500	2	(3.2)	10	(25.0)
>2500	3	(4.8)	3	(7.5)

	DDD Patient Mean (SD)	Control Group Mean (SD)	<i>t</i> statistics (df)	* <i>p</i> value
Rey-Osterrieth Complex Figure (ROCF)				
Copy Condition	59.2 (9.06)	62.0 (5.66)	t(94) = 92.5	0.08
Delayed Condition	53.0 (8.63)	51.1 (11.9)	t(94) = 0.85	0.39
Trail Making Test (TMT)				
Part A (Sec)	71.7 (26.0)	45.0 (12.2)	t (67.6) = -6.29	*** <i>p</i> <0.001
Part B (sec)	122(50.6)	101(38.5)	t (84) = - 2.08	***0.04
RAVENS Progressive Matrices				
TOTAL SCORE	35.3(9.72)	35.4(8.71)	t (85) = 0.05	0.96
Digit Span Test (DST)				
Digit Span Forward (DS-F)	5.73 (1.19)	5.95 (1.30)	t (83) = 0.80	0.43
Digit Span Backward (DS-B)	4.20 (1.29)	4.55 (1.77)	t (70.6) =1.03	0.31
Symbol Digit Test (SDT)				
Average correct symbol (milliseconds)	3215(810)	2584 (608)	t (83) = -0.40	*** <i>p</i> <0.001
Total error made symbol digit	2.13(2.14)	2.85 (5.48)	t (83) = 0.81	0.42

Stroop Test

Total number of correct response	79.5(4.80)	80.3(5.78)	t (74) = 0.63	0.53
	1421 (756)	1151 (392.5)	**U = 550	**0.07
Congruent latency (milliseconds)	1776 (944)	1419 (425)	t (47.5) = -2.08	*** 0.04
Incongruent Latency (milliseconds)	1508 (810)	1197(495)	t (74) = -2.04	*** 0.04
Control Latency (milliseconds)				

Table 3.2: Summary of Statistical Analysis for all Cognitive Measures

*Independent *t* test, ** Mann-Whitney Test, ***statistically significant with $p < 0.001$, $p < 0.05$

4. Discussion

This is the first study in Malaysia that captured the cognitive functioning in patients with dual drug dependence (DDD) on opioid and ATS. We found that there were significant differences between the control group and dual dependence group in measures of perceptual motor speed, visual scanning, cognitive flexibility, mental processing speed and response inhibition. Patient with dual dependence performed significantly worse compared with control group. Such deficits could affect their daily activities such as remembering scheduled appointments and inhibiting responses related to drug-seeking behavior.

For trail making test part A, our findings were not consistent with the study by Simon and Colleagues (2000) in which they found methamphetamine-using individuals performed significantly worse in Trail Making Test B but not Trail A. Deficit in visual scanning may reduce the speed and accuracy of the reactions and responses. Moreover, perceptual motor speed also seen in patient with their slow performance in this test. For Trail B, cognitive ability are impair in patient with dual dependence on opioid and ATS. It shows that for patients, they having difficulty when the tasks get more complicated. This notion may explain why some of them failed to maintain free from drug use.

For the Symbol Digit Test, Also, there are study also done by McCaffrey and colleagues (1988), comparing patient also from drug abuse treatment facilities and they found that patient (opioid) have impairment in this test. In the other hand, there are study also done by Simon and colleague (2000) by comparing methamphetamine and non-drug user and they found that methamphetamine users impaired in this test. This all finding support that drug addict in opioid and ATS have impairment in their mental processing speed. This notion may explain why some patient still use drug and suffering from several relapse due to the mistakes that done in this test and additionally, the slowing of their mental processing might impair their ability to make the best decision in appropriate time (Bush et. al., 2002).

Another important finding in our study was slower performance of the dual dependence patient on the Stroop test. The patient exhibit impairment in response inhibition more than control group. This study finding also supported by Hekmat et al., (2011). They compared 4 groups which are opium, heroin, methamphetamine and control and it showed impairment in drug using subjects.

This his finding also parallel with the study done by Verdejo-García, and Pérez-García (2007) which comparing two group with abstinent poly substance users (cocaine versus heroin) and control and showed that abstinence poly substance users having impairment on their executive function. Cocaine poly-substance users have worst impairment than heroin users and controls on the measures of inhibition in this Stroop test.

5. Conclusion

As a conclusion, perceptual motor speed, visual scanning, cognitive flexibility, mental processing speed, and response inhibition may be impaired in patients with dual drug dependence. Proper prevention and treatment interventions should consider addressing cognitive deficits for patients with dual dependence. Thus, additional research is needed to look at cognitive function and specific attention should be given during tailoring the treatment program for this group. This cognitive impairment especially in the domain of executive function may lead to less successfully in treatment program and the abstinence of drug use. Thus, it needs special attention in drug use treatment program.

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