10.14456/dmhjournal.2011.18

วารสารสุขภาพจิตแห่งประเทศไทย ปีที่ ๒๐ ฉบับที่ ๑ ปี ๒๕๕๕

ความบกพร่องด้านความจำและการทำงานของสมองระดับสูงในผู้ที่เคยป่วยด้วยโรคจิตจากเมทแอมเฟตามีน

แคทเธอรีน โดเมอร์ คานามาร์, ปร.ด.[1]
วอลเตอร์ ลิง, พ.บ.[1]
พันธุ์นภา กิตติรัตนไพบูลย์, พ.บ.[2]
ธิดารัตน์ ศรีสุโข, วท.ม.[3]

บทคัดย่อ

วัตถุประสงค์ เพื่อทดสอบสมรรถนะของสมองและจิตใจ (neuropsychological profile) ในผู้ที่มีประวัติโรคจิตจากเมทแอมเฟตามีนที่หยุดเสพแล้ว

วัสดุและวิธีการ ผู้ป่วยที่เคยรับการรักษาแบบผู้ป่วยในที่โรงพยาบาลสวนปรุง ด้วยโรคจิตจากเมทแอมเฟตามีนในปี พ.ศ. ๒๕๔๓-๒๕๔๔ จำนวน 90 คน ได้รับการติดตาม ซ้ำอีกครั้งหลังจากนั้น 6 ปี เพื่อประเมินด้วยชุดแบบทดสอบสมองและจิตใจ (neuropsychological battery tests) ซึ่งเป็นชุดเครื่องมือทดสอบความใส่ใจ (cognitive battery) ที่ประกอบด้วยการประเมินการทำงานของสมองระดับสูง (executive function) สมาธิ (attention) ความจำ (memory) และความเร็วในการตอบสนอง (psychomotor speed)

ผล พบว่าผู้ป่วยกลุ่มนี้ยังแสดงความผิดปกติของการคงสติ และสมรรถนะความจำอย่างรุนแรงนานหลายปีหลังจากวินิจฉัยและรับการรักษาครั้งแรก ทั้งๆ ที่หยุดเสพเมทแอมเฟตามีนแล้วก็ตาม

สรุป การศึกษานี้แสดงสมรรถนะทางสมองและจิตใจในผู้ป่วยที่เคยได้รับการวินิจฉัยโรคจิตจากเมทแอมเฟตามีน การศึกษาเพื่อหาลักษณะความสามารถเชิงความคิดความเข้าใจในผู้ป่วยโรคจิตจากเมทแอมเฟตามีนทั่วโลกจะช่วยให้เข้าใจเหตุของโรคจิตจากเมทแอมเฟตามีนและให้ข้อมูลแก่แพทย์เพื่อการรักษาได้

คำสำคัญ : เมทแอมเฟตามีน ความจำ การทำงานของสมองระดับสูง โรคจิต

[1]สถาบันประสาทวิทยาและพฤติกรรมมนุษย์ซีมิลล์ มหาวิทยาลัยแคลิฟอร์เนีย ลอสแองเจลิส สหรัฐอเมริกา
[2]กลุ่มที่ปรึกษา กรมสุขภาพจิต
[3]โรงพยาบาลสวนปรุง

Impairment of current memory and executive function in former methamphetamine-induced psychotic patients

Catherine Domier Canamar, Ph.D.[1]
Walter Ling, M.D.[1]
Phunnapa Kittirattanapaiboon, M.D.[2]
Thidarat Srisukho, M.Sc.[3]

Abstract

Objective The goals were to describe the neuropsychological profile of abstinent methamphetamine users with a history of MAP.

Materials and methods Participants (n=90) were admitted to Suan Prung Hospital in Chiang Mai, Thailand for methamphetamine-induced psychosis in 2000-2001 and were re-contacted 6 years later to complete a battery of neuropsychological tests. The cognitive battery consisted of tests assessing executive function, attention, memory and psychomotor speed.

Results Results indicate that this group exhibited severe impairment in executive function and memory performance several years after their initial diagnosis and hospitalization, despite abstaining from MA use.

Conclusions This study characterizes the neuropsychological performance of individuals diagnosed with methamphetamine-induced psychosis. Continuing to investigate cognitive performance in MAP patients worldwide can assist with understanding the etiology of MAP and inform clinicians treating this disorder.

Key words : methamphetamine, psychosis, executive function, memory

[1]Semel Institute for Neuroscience and Human Behavior, University of California, Los Angeles, USA
[2]Advisory Office, Department of Mental Health
[3]Suan Prung Psychiatric Hospital

Introduction

Methamphetamine abuse can elicit methamphetamine psychosis (MAP), a psychiatric syndrome that shares common features and a common neural substrate with schizophrenia. While the neurophysiological and neuropsychological symptoms of schizophrenia are well documented, they have yet to be determined in MAP[1]. Studies indicate that over 50% of dependent amphetamine users experience psychotic symptoms and in some countries, the prevalence of psychosis in methamphetamine users is 11 times higher than in the general population[2,3].

Research indicates that MAP is chronic and persistent, with frequent relapses requiring rehospitalization[4]. Particularly troublesome is that MAP can persist even with sustained abstinence from methamphetamine. An additional complexity of the disorder is that neurobiological changes associated with chronic methamphetamine use appear to promote susceptibility to symptom recurrence[5,6]. The availability and functioning of dopamine influences brain functioning, exhibiting modulatory effects on many cognitive functions[7]. Research demonstrates that methamphetamine-dependent individuals exhibit deficits compared to non-drug using participants, most consistently in the areas of executive function; working memory, attention[8,9], and decision-making[10,11], learning, memory, and motor ability[9,12].

Data on the neuropsychology of MAP patients is inadequate to provide meaningful information to clinicians dealing with MAP patients and assist with understanding the etiology of MAP. Over the past two decades, Thailand has experienced a tremendous increase in methamphetamine abusers, many of whom become psychotic and require hospitalization. Because MAP affects a large proportion of methamphetamine users, and the cognitive consequences of such episodes are unknown, this project examined the cognitive capabilities and deficits within this population.

Method

Participants

This research is a follow-up to a parent investigation of MAP patients in Chiang Mai, Thailand which reviewed the database of Suan Prung Psychiatric Hospital to identify MAP inpatients who were first hospitalized between January 1, 2000 and December 31, 2001. Eligibility criteria included: (i) located in Chiang Mai or nearby provinces; and (ii) being at least 18 years of age. Participants were interviewed approximately 6 years after the initial hospitalization. The aim of the current study was to characterize the neuropsychological performance of the former inpatients diagnosed with MAP. The Institutional Review Boards (IRB) at the University of California, Los Angeles, and the Department of Mental Health, Ministry of Public Health in Thailand approved the research. One hundred and

one participants completed the test battery but 11 reported using methamphetamine in the month prior to testing. Thus, the data analysis included the 90 participants who provided a negative urine test for all drugs at the time of testing and who reported no drug use in the past month.

Procedures

Research staff contacted potential participants who were involved in the parent study. Those who provided written informed consent scheduled an interview with staff at a location near or at the participants' residence, or at Suan Prung Hospital. Participants completed the neurocognitive battery in 20 minutes. Completion of the urine test, psychological and drug use assessments took an additional hour. Participants received 200 baht (~5 $US) for their time.

Neuropsychological Assessments

Trail Making A and B[13]. Trail Making requires that participants draw lines connecting numbers or numbers and letters in order, as quickly as possible. It is a test of visual attention, perceptual tracking, and motor ability. Longer response times (ms) reflect poorer performance.

Color Trails Test (CTT). The test is a culturally fair analogue of the Trail Making Test that uses colors and does not have a language component. It is a test of visual attention, perceptual tracking, and motor ability. Longer response times (ms) reflect poorer performance.

Digit Symbol. Participants must quickly match ten digits with corresponding symbols. It is a test of psychomotor performance, selective attention, and working memory; fewer correct matches reflect poorer functioning.

Stroop[14]. Participants must suppress the word reading response in favor of naming the ink color of the presented target. It is a test of executive function involving cognitive inhibition and selective attention. Fewer correct responses reflect poorer performance.

Repeated Memory Task. Participants briefly view a series of words and pictures[15], complete distractor tasks, and then take recall and recognition tests. This task measures memory. A low number of correctly recalled or recognized words reflect poorer memory.

d2 test of Attention. Participants must scan a page of stimuli and cross out every target letter randomly dispersed throughout the page. This is a test of sustained and selective attention. Fewer correctly identified targets reflect poorer performance. A low Continuous Performance score reflects poor speed-accuracy tradeoff, d2 total and d2 CP show fewer items processed and correct scores.

There are no published normative data for these cognitive tests with Thai samples. Thus, for illustrative purposes, we discuss the results by looking at normative data from non-drug users in China and Viet Nam. Norms for the d2 test

were only available from Germany for the low age and education levels of the current sample.

Additional Measures

Urine test. Staff directly observed the urine samples collected and complied with the procedures required by the Thai Ministry of Public Health. Staff analyzed each sample immediately on site for qualitative results of methamphetamines and other major drugs of abuse: cocaine, opiates, and benzodiazepines.

Results

The average age of the sample was 33.5 (SD=7.5) and 86% were male. Fifty percent of the sample completed a 6th grade level of education. The age at which individuals first used methamphetamine ranged from 13-57, with a mode of 17. Participants had used MA between 0 and 15 years prior to the first hospitalization for MAP, with a mode of 3 years. Eighty-three percent preferred smoking as their route of administration. After the first admission, 49% had one or more repeat hospitalizations for MAP during 6 years period. (Table 1)

Table 1 Participant characteristics.

Characteristic		value[a]
Age (yrs)		33.50 (7.5)
Age 1st MA Use (yrs)		Range 13-57; mode 17
Hospitalized (days)		19 (12)
male (%)		86
education (%)	6th grade	50
	12th grade	41
	15th grade	9
Route (%)	Smoking	83
	Oral	17
Repeat Hospitalizations (%)		49

Note: a = values are means (standard deviations) unless otherwise noted.

MA: methamphetamine

The means of the Color Trails 1, Color Trails 2, Trail Making A, and Trail Making B of the sample show longer response times (54.89, 132.99, 62.63 and 258.33, respectively). The means of Stroop Word, Stroop Color and Stroop Color-Word show fewer correct scores (69.97, 51.38 and 26.34) as well as the d2 Total (331.94) and d2 CP (90.28). The neurocognitive performance of the sample was presented in Table 2.

Table 2 Performance of MAP participants (n = 90) on a neuropsychological battery and comparison data from MAP and non-drug users.

	Thai MAP(n=90)	Non-drug Use Norms
	Mean (SD)	Mean (SD)
executive function		
Digit Symbol	34.93 (12.23)	47.43[a] (8.77)
Color Trails 1	58.49 (28.88)	42.05[b] (15.69)
Color Trails 2	132.99 (77.46)	89.95[b] (37.47)
Trail Making A	62.63 (34.00)	26.17[a] (7.19)
Trail Making B	258.38 (214.54)	67.94[a] (41.36)
Stroop Word	69.97 (19.73)	103.85[d] (18.68)
Stroop Color	51.38 (2.86)	72.10[d] (18.06)
Stroop Color-Word	26.34 (12.27)	43.20[d] (14.27)
d2 Total	331.94 (108.95)	381[c]
d2 CP	90.28 (46.30)	153[c]
memory		
Word Recall - # Correct	1.26 (1.40)	*n/a*
Picture Recall - # Correct	3.45 (2.60)	*n/a*
Word Recognition - # Correct	8.72 (5.12)	*n/a*
Picture Recognition - # Correct	13.44 (5.40)	*n/a*

SD = standard deviation;

n/a = data not available;

a = age and education adjusted normative data from Chinese non-drug users[18];

b = age adjusted normative data from Chinese non-drug users[19];

c = age adjusted averages from a German sample[20];

d = age adjusted normative data from a Vietnamese sample[21].

Discussion

The data presented characterize the neuropsychological performance of individuals diagnosed with methamphetamine-induced psychosis. The results indicate impairment in several abilities related to executive function and memory. Given that testing occurred many years after the initial MAP diagnosis, the findings suggest that methamphetamine users who experienced at least one prior psychotic episode have lasting cognitive impairments that may reflect brain damage. Nearly half of the sample was re-hospitalized for MAP but analyses confirmed that their cognitive performance did not differ from those who were not re-hospitalized. Likewise, there was no effect of route of administration on cognitive impairment. Cognitive dysfunction can limit adherence to treatment and negatively influence outcomes and results of neurocognitive assessments can shed light on the neurological underpinnings of methamphetamine-induced psychosis and related psychoses. As mentioned, methamphetamine is a moderator, influencing the relationship between dopamine functioning and cognitive performance. The cognitive dysfunction exhibited by these MAP patients involves brain regions such as the prefrontal cortex, which has dopaminergic systems vital to the formation of attentional sets and switching behavior[16]. Results support the assumption that MAP patients, like methamphetamine users, have altered dopamine function.

These data are distinctive from an earlier study of Thai MAP patients who completed neurocognitive testing. It appears that the two samples of patients vary in their patterns of cognitive ability; performance scores of the current sample on Trail Making A/B appear poorer while Stroop scores are nearly equivalent[17]. A notable distinction between these two groups of Thai MAP patients is that the prior sample completed testing at their first hospitalization for MAP while for the current sample; approximately six years passed since their first hospitalization for MAP. This evokes the question of whether what we are seeing in the current sample is progressive cognitive impairment from the time of the initial diagnosis. A comparative analysis of a subset of patients who participated in both studies is underway to answer this question.

As one would anticipate, the MAP patients' scores were considerably poorer than those of the normative samples. Executive function, attention, inhibition, visuoperceptual processing, and working memory components all appear impaired in the patients with psychosis compared to the normative control samples.

Future research comparing neuropsychological performance of MA-dependent samples with and without methamphetamine-induced psychosis is warranted to understand the cognitive impairment, if any, that psychosis contributes above and beyond the impairment seen with chronic MA

use. Another line of research that awaits evaluation is the comparison of cognitive performance of MAP patients by country, which would provide information about cultural, educational, and ethnic differences and their potential influences on MAP etiology, prognoses, and treatment. Assessment of the relationship and the potential progression of cognitive decline with duration of methamphetamine use and emergence of MAP symptoms warrant future study. *Limitations.* When interpreting these data one should take into account that this study was limited because of its cross-sectional design. While this prohibited evaluation of cognitive functioning prior to the onset of MAP symptoms, future analyses will assess a subset of MAP participants who completed repeated neurocognitive testing over several years. A second limitation is the lack of objective verification of sustained abstinence over the course of the follow-up timeframe. This may be a minor factor however, as all participants provided urine negative for methamphetamine at the time of testing, implying no use in at least a few days. The lack of Thai norms made it impossible to calculate statistical significance of the cognitive impairment.

Conclusion

This descriptive study characterizes the neuropsychological performance of individuals with methamphetamine-induced psychosis. Continuing to investigate cognitive performance in MAP patients in Thailand and in other countries will provide a better understanding of the etiology and consequences of MAP. Additionally, neuropsychological testing may be a valid diagnostic tool to distinguish methamphetamine abuse from methamphetamine-induced psychosis, or to inform clinicians trying to treat individuals with MAP.

Acknowledgments

Support for this research provided by the National Institute on Drug Abuse grant # U01 DA017394.

References

1. Hermens DF, Lubman DI, Ward PB, Naismith SL, Hickie IB. Amphetamine psychosis: a model for studying the onset and course of psychosis. Med J Australia 2009;190 (4 Suppl): S22-5.
2. Smith MJ, Thirthalli J, Abdallah AB, Murray RM, Cottler LB. Prevalence of psychotic symptoms in substance users: a comparison across substances. Compr Psychiatry 2009;50:245-50.
3. McKetin R, McLaren J, Lubman DI, Hides L. The prevalence of psychotic symptoms among methamphetamine users. Addiction 2006;101:1473-8.
4. Kittirattanapaiboon P. Methamphetamine psychosis: Thailand perspectives. Nonthaburi: Department of Mental Health, Ministry of Public Health; 2008.
5. Sato M. A lasting vulnerability to psychosis in patients with previous methamphetamine psychosis. Ann NY Acad Sci 1992;654:160-70.
6. Yui K, Ikemoto S, Ishiguro T, Goto K. Studies of amphetamine or methamphetamine psychosis in Japan: relation of methamphetamine psychosis to schizophrenia. Ann NY Acad Sci 2000;914:1-12.

7. Backman L, Nyberg L, Lindenberger U, Li SC, Farde L. The correlative triad among aging, dopamine, and cognition: current status and future prospects. Neurosci Biobehav Rev 2006;30:791-807.
8. Simon SL, Domier CP, Sim T, Richardson K, Rawson RA, Ling W. Cognitive performance of current methamphetamine and cocaine abusers. J Addict Dis 2002;21:61-74.
9. Simon SL, Domier C, Carnell J, Brethen P, Rawson R, Ling W. Cognitive impairment in individuals currently using methamphetamine. Am J Addictions 2000;9:222-31.
10. Monterosso JR, Ainslie G, Xu J, Cordova X, Domier CP, London ED. Frontoparietal cortical activity of methamphetamine-dependent and comparison subjects performing a delay discounting task. Hum Brain Mapp 2007;28:383-93.
11. Paulus MP, Hozack N, Frank L, Brown GG, Schuckit MA. Decision making by methamphetamine-dependent subjects is associated with error-rate-independent decrease in prefrontal and parietal activation. Biol Psychiatry 2003;53:65-74.
12. Scott JC, Woods SP, Matt GE, Meyer RA, Heaton RK, Atkinson JH, Grant I. Neurocognitive effects of methamphetamine: a critical review and meta-analysis. Neuropsychol Rev 2007;17:275-97.
13. Reitan R M, Wolfson D. The Halstead-Reitan Neuropsychological Test Battery: Theory and Clinical Interpretation. Tucson, Arizona: Neuropsychology Press; 1985.
14. Golden CJ. Stroop color and word test: a manual for clinical and experimental uses. Wood Dale, Illinois : Stoelting Company; 1978.
15. Snodgrass JG, Vanderwart M. A standardized set of 260 pictures: norms for name agreement, image agreement, familiarity, and visual complexity. J Exp Psychol Hum Learn 1980;6:174-215.
16. Rogers RD, Everitt BJ, Baldacchino A, Blackshaw AJ, Swainson R, Wynne K et al. Dissociable deficits in the decision-making cognition of chronic amphetamine abusers, opiate abusers, patients with focal damage to prefrontal cortex, and tryptophan-depleted normal volunteers: evidence for monoaminergic mechanisms. Neuropsychopharmacol 1999;20:322-39.
17. Srisukho T, Kwankong T, Popairoj J, Thomthitchong KWT, Harindech J. Cognitive performance of methamphetamine psychosis. J Suanprung Psychiatr Hosp 2003;9:24-34.
18. Lee T, Yuen K, Chan C. Normative data for neuropsychological measures of fluency, attention, and memory measures for Hong Kong Chinese. J Clin Exp Neuropsyc 2002;24:615-32.
19. Hseih S, Riley N. Neuropsychological performance in the People's Rebuplic of China: Age and education norms for four attention tasks. Presented at the National Academy of Neuropsychology, Las Vegas, NV; 2009.
20. Brickenkamp R, Zillmer E. The d2 test of attention. Seattle, WA Hogrefe & Huber; 1998.
21. Doan QT, Swerdlow NR. Preliminary findings with a new Vietnamese Stroop test. Percept Mot Skills 1999;89:173-82.