Med Sci Monit, 2001; 7(6): 1292-1298

Executive function in abstinent MDMA ('ecstasy') users

Konstantine K. Zakzanis[1], Donald A. Young[2]

[1] Division of Life Sciences, University of Toronto, Toronto, Canada
[2] Archway Clinic, Centre for Addiction and Mental Health, Toronto, Canada

key words: MDMA ('ecstasy'), neuropsychology, executive function

SUMMARY

Background: *Methylenedioxymethamphetamine (MDMA, or 'Ecstasy') is a growingly popular recreational drug of abuse that is known to damage brain serotonergic neurons in animals and possibly humans. Few functional consequences of MDMA-induced serotonin neurotoxicity have been identified, either in animals or humans. This study sought to determine whether individuals with a history of MDMA use showed evidence of executive dysfunction.*
Material and methods: *Two groups of young individuals were compared: 24 abstinent MDMA users who had taken MDMA at least once and 24 controls who had never taken MDMA. Each MDMA user completed a questionnaire regarding the characteristics of their MDMA use and all participants completed a questionnaire regarding other recreational drug experience. The Behavioural Assessment of the Dysexecutive Syndrome (BADS) was used to measure executive function in all participants.*
Results: *Evidence of impairment was found on two subtests of the BADS and in terms of a Total Profile Score. In addition, several significant product moment correlations were found suggesting that increases in MDMA consumption may relate to more pronounced impairment in executive function.*
Conclusion: *Accordingly, MDMA use may be associated with deficits in executive function.*

BACKGROUND

The use of the ring-substituted amphetamine derivative ±3,4-methylenedioxymethamphetamine (MDMA or 'Ecstasy') has escalateed to epidemic proportions in recent years. Several experimental studies indicate that MDMA damages brain serotonin (5-HT) in animals (including nonhuman primates) and possibly humans and that a significant proportion of users may eventually be at risk for long--term neurotoxicological effects, particularly in the hippocampus, a brain region that is believed to play an important role in learning and the consolidation of new memories [1–3]. Accordingly, a neuropsychological literature has begun to emerge where human studies suggest that repeated use of MDMA produces lasting impairments in explicit memory [4–10].

That is, users of MDMA have been found to be impaired on neuropsychological measures of memory that require the conscious recollection of an episode (see [11]). For example, Bolla et al, [4] compared abstinent MDMA users and control subjects on the Rey-Auditory Verbal Learning Test (RAVLT; [12]), the Wechsler Memory Scale-Revised (WMS; [13]) and the Rey-Osterrieth Complex Figure (see [12]). They found that greater use of MDMA (in terms of total milligrams per month) was associated with greater impairments in immediate verbal memory and delayed visual memory. Moreover, Morgan [6] utilized subtests of the Rivermead Behavioral Memory Test (RBMT; [14]) to investigate immediate and delayed recall. He found MDMA users to recall significantly fewer ideas from a short passage of prose that was read out to subjects immediately after its presentation and after a delay. Moreover,

Received: 2001.08.13
Accepted: 2001.08.20

Correspondence address: Dr. Konstantine K. Zakzanis, Division of Life Sciences (Neuroscience), University of Toronto at Scarborough, 1265 Military Trail, Toronto, Ontario, M1C 1A4, Canada, e-mail: zakzanis@utsc.utoronto.ca

Zakzanis and Young [15] examined the neurotoxic potential of continued MDMA use in humans and its functional consequences over the course of 1--year. They also found that continued use of MDMA is associated with progressive decline in terms of immediate and delayed recall on the RBMT. In addition, Parrot et al [8], administered a computerized battery of cognitive tasks and found MDMA users to recall significantly fewer words immediately following presentation and after a delay. Krystal et al [16], also found a pattern of mild-to-moderate impairment in terms of both initial and delayed recall on the Logical Memory subtest of the WMS-R in chronic MDMA users.

Indeed, evidence supporting an impairment of explicit memory in abstinent MDMA users is plentiful. Given that memory is not a unitary system, however, and that many different neuropsychological processes are likely to influence performance on memory measures, researchers have begun to elucidate the specificity memory impairment in this population. For example, Gouzoulis-Mayfrank et al [17], state that although the nature of cognitive disturbance in MDMA users is not clear, an impairment of working memory might be the common denominator underlying or contributing to declines of performance in various tasks. Accordingly, they showed that MDMA users were unimpaired in simple tests of attention and were, however, impaired in more complex tests of attention, in memory and learning tasks, and in tasks reflecting aspects of general intelligence. Moreover, McCann et al [5] found MDMA users to manifest significant performance deficits on a sustained attention task requiring arithmetic calculations, a task requiring complex attention and incidental learning, a task requiring short term memory and a task of semantic recognition and verbal reasoning. Finally, Morgan [6] established the presence of elevated impulsivity with recreational use of MDMA in a series of two studies using a behavioral measure of impulsivity, spatial span, 'Tower of London' tests, and an impulsiveness, venturesomness and empathy questionnaire.

Direct behavioral evidence of this sort in MDMA users prompted researchers to elucidate further the contribution of higher order executive function on the neuropsychological deficits found in abstinent MDMA users. For example, Semple et al [18] used the CANTAB Spatial Working Memory subtest, Trial Making Test (Part B), phonemic word fluency, and the Stroop task to examine executive function in abstinent MDMA users. It was found that larger lifetime doses of MDMA were associated with more errors on the Spatial Working Memory test. As such, it was concluded that this finding might indicate that decreased performance on this particular Spatial Working Memory test may be attributed to the high density of MDMA destroyed serotonin terminals found in the frontal lobes. From this finding, it remains unclear however, how the frontal-executive system can be implicated in keeping with inferences made from a spatial working memory test and the absence of a meaningful difference between MDMA users and non-users on the remaining measures of executive function. That is, while working memory provides temporary storage to hold data on-line for brief periods (up to 10–15 seconds), the temporal integration of behavior entails the ability to organize ones perceptions and actions. The prefrontal cortex acts in a supervisory capacity upon the hippocampal episodic memory system, thereby directing attention in the temporal domain. One may view different episodic memories as being 'called-up' into working memory, as each in turn is made the focus of current attention. Hence, working memory is a multi-component system that loops beyond frontal cortices (see [19]). Thus, the validity of an executive deficit in abstinent MDMA users remains unclear as deficits in working memory do not always implicate deficiencies in executive function, but may reflect disturbances anywhere along the phonological loop in keeping with the working memory model proposed by Baddely and Hitch [20].

To determine the nature of executive function in MDMA users that might further address questions of specificity with regard to the neurotoxic potential of continued MDMA use in humans and its functional consequences, we administered an ecologically valid battery of executive measures to a sample of abstinent MDMA users and a control group of non-MDMA users. Accordingly, the purpose of this investigation was to further explore the nature and pattern of executive function in abstinent MDMA users.

MATERIAL AND METHODS

Participants

Twenty-four MDMA users participated in the study. All participants were recruited by word of mouth and hence, self referred, having learned about ongoing research on the consequences of MDMA use. Subjects were all fluent English speaking individuals. Exclusion from the study was warranted

when subjects reported a past or current history of major medical illness (e.g, neurologic, renal, endocrine, or hematologic), current major psychiatric illness as determined by the Structured Clinical Interview of the Diagnostic Statistical Manual-III-Revised, a positive drug screen for illicit or prescribed psychoactive drugs, or current alcohol dependence. Subjects were also excluded if they reported a current pregnancy, migraine, dyslexia, or eating disorder. Most participants, however, reported erratic, or highly erratic sleep habits typically coinciding with MDMA use. Hence, given that sleep deprivation is a noted finding in MDMA users and affects cognitive performance, we tested participants when they reported at least 7-nights of 7–9 hours of continuous sleep. Moreover, all subjects agreed to abstain from all drugs for at least 2-weeks prior to testing. Their drug free status was confirmed by urine and blood drug screens. Given that the half-life of MDMA in animals is 1 to 2 hours, the 2-week period of abstinence was deemed long enough to rule out any withdrawal effects including sleep deprivation.

Twenty-four non-MDMA users served as a control group. These subjects were also all fluent English speaking individuals without a self-reported past or current history of major medical illness (e.g., neurologic, renal, endocrine, or hematologic), current major psychiatric illness, or alcohol dependence. Control subjects were also excluded if they reported a current pregnancy, migraine, dyslexia, or eating disorder. Both MDMA users and controls were not paid for their time but were reimbursed for travel (i.e., parking) expenses. Informed consent was obtained from all participants.

Sociodemographic data of the participants is presented in Table 1. Most MDMA users were female (67%) and had completed approximately 15 years of education. The modal age of the MDMA users was 23-years. The non-MDMA users were on average 20 years of age and had completed approximately 14 years of education. Sixty-seven percent of the control group was female.

Table 1. Sociodemographic characteristics.

Characteristic	Normal controls (n = 24)	MDMA users (n = 24)
Age in years, mean (range)	19.54 (17–26)	22.96 (18–34)*
Education in years, mean (range)	14.33 (14–17)	14.54 (13–16)
Sex, female/male	16/8	16/8

*p<.001

Age of participants differed significantly between groups. Accordingly, all statistical analyses were carried out with age as a covariate. There were no other statistically significant differences between groups in terms of sociodemographic variables.

Procedure

Participants completed a brief survey to determine their characteristic MDMA use and other recreational drug experience. Participants also completed the Behavioral Assessment of Dysexecutive Syndrome (BADS; 21) Briefly, the BADS is a test battery aimed at predicting everyday problems arising from the 'Dysexecutive Syndrome' which can be characterized by an amorphous, varied group of deficits resulting from diverse aetiologies, different locations, and variable extents of abnormalities [21]. BADS measures included (in the order they were administered):

1. The Rule Shift Cards Test that examines the participants' ability to respond accurately to a rule and to shift from one rule to another. Total time and the number of errors are recorded;

2. The Action Program Test which involves novel problem solving. The participants are to devise a plan of action in order to solve the problem at hand. The number of steps completed on their own is recorded;

3. The Key Search Test which is designed to examine the participants' ability to plan an effective and efficient course of action. The score achieved reflects the efficiency of the search pattern strategy;

4. The Temporal Judgement Test which examines the participants' ability to estimate the time required for four common events;

5. The Zoo Map Test which examines the participants' ability to plan, in advance, how they would visit a series of designated locations on a map of a zoo without breaking a number of rules. The test is scored according to the number of correct locations visited and number of broken rules; and

6. The Modified Six Elements Test which examines the participants' ability to organize themselves, according to certain rules and restrictions, in order to complete at least some of each of the six subtasks at hand. Scores are based on the num-

Table 2. Characteristics of MDMA Use.

Characteristic	Mean (range)
Number of times used	31.21 (1.0–150.0)
Duration of use (years)	1.99 (0.25–6.0)
Usual dose (tablets)	1.21 (0.5–2.5)
Frequency of use (month)	1.91 (0.5–6.0)
Time since last dose (week)	16.96 (2.0–156.0)

ber of tasks attempted, whether the rule was broken, and the maximum amount of time spent on any one subtask.

Once the scoring of each test was completed, raw scores were converted to profile scores that ranged from 0–4. The six profile scores were then added together, resulting in a Total Profile Score.

RESULTS

MDMA and other drug use

To provide an estimate of the intensity, frequency, and duration of MDMA use, detailed information about prior MDMA use was obtained from a structured interview that ascertained the number of milligrams per capsule of MDMA generally taken at one time (each capsule was assumed to equal 100 mg based on previously published estimates; see Bolla et al. [4]), the number of times that MDMA was taken per month, and the total number of months of MDMA use. A dose variable – a combination of intensity and frequency – was also calculated by multiplying the self-reported milligrams ingested in a single MDMA session (which could last hours and involve several separate doses of MDMA) by the number of MDMA sessions per month [4]. Table 2 summarizes the characteristics of MDMA use in the user group. Table 3 illustrates the other recreational drug exposure in the MDMA user and non-user groups.

Statistical analyses between groups

Using age as a covariate, between group differences on the BADS was examined using ANCOVA. Additionally, the magnitude of effect was articulated using Cohen's [22] effect size statistic and associated overlap distribution percentages (see [23]). Briefly, an effect size was used to describe the magnitude of difference between group means, rather than the mere chance probability of the difference. That is, statistical significance testing does not reveal the strength of effect, whereas an effect size is a direct measure of magnitude where an effect size of:

- 0.0 reflects no difference in mean scores;
- an effect size of about 0.2 represents a small effect;
- 0.5 a medium effect, and,
- 0.8 a large effect;

in keeping with Cohen's [22] rule of thumb. Moreover, Cohen's effect size can be easily transformed into overlap percentages that illustrate the degree to which test scores overlap between groups. For example, if an effect size of 0.5 is found, approximately 67% of the two groups being compared share the same test scores. Only 33% differ in terms of performance on the measure. Hence, the less overlap, the greater the effect size, or more po-

Table 3. Other recreational drug experience.

Drug	Normal controls (n = 24)*	MDMA users (n = 24)*
Cigarettes	8 (33)	20 (83)
Alcohol	15 (63)	23 (96)
Non-MDMA amphetamines	1 (4)	12 (50)
Cocaine	0 (0)	6 (25)
Anti-depressants	1 (4)	1 (4)
Sedative hypnotics	1 (4)	1 (4)
LSD	1 (4)	8 (33)
Cannabis	9 (38)	23 (96)
Organic solvents/inhalants	0 (0)	0 (0)
Opiates	0 (0)	0 (0)
PCP and related drugs	0 (0)	4 (17)

* Values are numbers and percentage of individuals within each group who reported any prior use.

Table 4. Performance of abstinent MDMA users and normal controls on the behavioural. Assessment of the dysexecutive syndrome (BADS)

BADS variable	MDMA users N=24 M (sd)	Normal controls N=24 M (sd)	d (OL%)	F
Rule shift cards	3.04 (0.69)	3.38 (0.58)	-0.53 (64)	1.67
Action program	3.75 (0.44)	3.58 (0.58)	0.33 (77)	0.62
Key search	1.92 (0.83)	2.13 (1.26)	-0.20 (85)	1.00
Temporal judgment	0.88 (0.61)	1.33 (0.64)	-0.72 (56)	4.41*
Zoo map	2.25 (1.07)	2.46 (1.10)	-0.19 (78)	0.24
Modified six elements	2.75 (1.19)	3.71 (0.46)	-1.06 (42)	8.01**
Total profile score	14.58 (2.81)	16.58 (2.10)	-0.81 (52)	3.97*

*p< 0.05; **p<0.001

ignantly, the bigger the difference between groups on the variable of interest.

Significant differences between groups emerged on the Temporal Judgment Test, Modified Six Elements Test, and Total Profile Score (see Table 4). The associated effect sizes on these particular subtests ranged from medium to large in keeping with Cohen's [22] heuristic benchmark. Moreover, the most discriminatory measure was the Modified Six Elements Test, as approximately 58% of MDMA user scores fell below the lowest score obtained by a non-user (i.e., 42% overlap in test score distribution).

Significant moderators of effect

Pearson product moment correlations were calculated between MDMA user sociodemographic characteristics and each BADS component. A number of sociodemographic variables correlated significantly with BADS subtest scores. Table 5 includes Pearson's r along with a calculated coefficient of determination. It can be seen clearly from the table that increases in MDMA usage, duration, dosage, and frequency associated with lower scores on many subtests of the BADS.

Table 5. Significant moderators of effect.

Characteristic	Pearson correlation r (p-value)	Coefficient of determination r^2
Number of times used / Rule shift cards	-0.65 (<0.001)	0.42
Number of times used / Action program	-0.52 (<0.01)	0.27
Number of times used / Modified six elements	-0.45 (<0.05)	0.20
Number of times used / Total profile score	-0.64 (<0.001)	0.41
Duration of use / Rule shift cards	-0.57 (<0.005)	0.32
Duration of use / Action program	-0.57 (<0.005)	0.32
Duration of use / Modified six elements	-0.68 (<0.001)	0.46
Duration of use / Total profile score	-0.67 (<0.001)	0.45
Usual dose / Rule shift cards	-0.50 (<0.05)	0.25
Usual dose / Total profile score	-0.61 (<0.005)	0.37
Frequency of use / Rule shift cards	-0.45 (<0.05)	0.20
Frequency of use / Temporal judgment	-0.44 (<0.05)	0.19

DISCUSSION

The purpose of this investigation was to determine the nature of executive function in MDMA users that might further address questions of specificity with regard to the neurotoxic potential of continued MDMA use in humans and its functional consequences. Our results indicate that for this sample of users, MDMA may be associated with deficits in terms of executive function. That is, we found evidence of impairment on the Temporal Judgment and Modified Six Elements subtests of the BADS, and more convincingly, depressed scores on all but one subtest of the BADS in MDMA users, resulting in a significant Total Profile Score between groups. Additionally, an effect size analysis revealed a large difference between the groups on the Modified Six Elements Test and Total Profile Score in terms of test score discriminability. In addition, several significant product moment correlations were found suggesting that increases in MDMA consumption may relate to more pronounced impairment in executive function.

Together, the results basically implicate the alteration of serotonin, or 5-hydroxytryptamine (5-HT) transmission in frontal cortices following MDMA use. This finding underscores evidence that has found neurons that synthesize and release 5-HT to participate in the control of many central cognitive functions, and that alterations of serotoninergic transmission are associated with various neuropsychiatric conditions such as major depressive disorder, anxiety, schizophrenia, and behavioral disorders in dementias, all of which are sometimes marked by executive dysfunction [23–24]. Indeed, behaviors related to frontal lobe disorders and serotoninergic (5-HT) system abnormalities include impulsivity, depression, obsessive-compulsive characteristics, and retardation, all of which may have contributed to the difference in BADS performance between the two groups in the present investigation.

There were important limitations to the study however. Additional research will have to resolve limitations that impede the validity of most human MDMA research. For instance, given that there is little quality control in street drugs, most investigations provide only an estimate at best when calculating each subjects MDMA intake. As such, for le-

gal and ethical reasons, there was no control over MDMA administration nor was there objective confirmation of the dose or purity of MDMA taken. In keeping with published reports of 'ecstasy' content [25], however, we were able to deduce that all of our participants had indeed used MDMA in various amounts given the 'type of ecstasy' that was reportedly used. Moreover, published reports (e.g., [25]) have noted that tablets sold as 'ecstasy' can contain MDA (3,4-methylenedioxy-amphetamine), MDEA (3,4-methylenedioxy-ethylamphetamine), or mixtures of a range of other compounds (e.g., caffeine, ephedrine, selegiline, amphetmaine, ketamine, LSD-9). Although some tablets sold as 'ecstasy' contain little or no MDMA, however, the majority does contain MDMA, or the related compound MDEA [6].

Another issue concerns the drug history of the participant sample. That is, self-report of drug taking behavior in drug users is notoriously unreliable. As such, it remains unclear whether the reported use of MDMA and other drug exposures are gross under/over estimates of actual drug use. Given that this was a self-referred sample of users with an invested interest in its outcome, it is believed that the self-reported drug taking behaviors of the participants can be loosely described as reliable. It is possible, however, that the executive disturbance may be secondary to polydrug use and not MDMA itself. Indeed, executive type deficits have been found in college students with heavy drinking (e.g. [26]), marijuana (e.g. [27]), cocaine (e.g. [28]), and cocaine/alcohol (e.g. [29]) histories. Although we excluded MDMA users with a positive drug screen for illicit or prescribed psychoactive drug or current alcohol dependence, the use, but not dependence, of polydrugs use in the MDMA group and its effect on executive function remains quantitatively unresolved and requires further examination. Accordingly, we should emphasize the difficulty of drawing conclusions about the effects of MDMA in poly--drug users. Although we would like to be able to draw neurochemical conclusions based on our observations between groups, given the contamination of the group through use of other substances, and the relative paucity of information regarding the neurochemical effects of MDMA, our desire to relate MDMA use and executive dysfunction should not be taken well beyond what can be foreseeably derived from our preliminary investigation.

Finally, premorbid personality characteristics may also make difficult interpretation of the present findings. That is, poor decision-making and planning, and difficulties in terms of volition and purposive action, might both contribute to substance abuse habit. Accordingly, a person premorbidly marked by poor executive function may be more inclined to abuse MDMA, thus making any cause-effect speculations imperceptible. It will be important for future research to keep these limitations in mind while trying to untangle the neuropsychology of MDMA.

CONCLUSIONS

We have shown here that MDMA use may be associated with deficits in executive function. In keeping with recent neuropsychological investigations of MDMA and its effects on memory, it is possible to reformulate the hypothesized primary consequence of MDMA use in the human brain. That is, it has been speculated that MDMA has an affinity to hippocampal structures based on early investigations of MDMA in rat brains (e.g., [1–2]). This led researchers to tentatively conclude that memory impairments in human MDMA users also suffered neuronal damage to hippocampal cortices. We have seen however, a number of MDMA users in our laboratory who do not exhibit a typical mesial-temporal-hippocampal amnestic syndrome following MDMA use. That is, these users do not exhibit the type of memory consolidation deficit found in patients with dementia of the Alzheimer's type, or focal amnesia following stroke. Our users have shown varying deficits in memory that include both prospective and encoding/retrieval difficulties, but not difficulties in the consolidation of new memories. Hence, these types of memory deficits would further support our finding of executive dysfunction in MDMA users in the present study, as it has been found that both prospective memory and encoding/retrieval are negotiated by the frontal lobes (see [30–31]. Moreover, it is not uncommon to find depressive symptomatology in MDMA users following extensive use [32]. This finding would lend further support to altered executive function in MDMA users as it has been found that the dorsolateral prefrontal cortex, particularly in the right hemisphere, is a key brain structure in emotion/cognition interactions in negative mood states [33]. Hence, what seems to be evolving in the neuropsychology of MDMA, is the consequential role of the frontal--executive system following MDMA use. Future research might want to direct effort toward these cortices to further understand the consequences of MDMA use.

REFERENCES:

1. *Aquirre N, Frechilla D, Garcia-Osta A et al: Differential regulation by methylenedioxy-methamphetamine of 5-hydroxytryptamine 1A receptor density and mRNA expression in rat hippocampus, frontal cortex, and brainstem. Journal of Neurochemistry, 1997; 68: 1099-1105*
2. *Fischer C, Hatzidimitriou G, Wlos J et al: Reorganization of ascending 5-HT axon projections in animals previously exposed to the recreational drug 3, 4-methylenedioxymethamphetamine (MDMA, „Ecstasy"). Journal of Neuroscience, 1995; 15: 5476-5485*
3. *Schmidt CJ: Neurotoxicity of the psychedelic amphetamine methylenedioxymeth-amphetamine. Journal of Pharmacology and Experimental Therapy, 1987; 240: 1-7*
4. *Bolla KI, McCann UD, Ricaurte GA: Memory impairment in abstinent MDMA („Ecstasy") users. Neurology, 1998; 51: 1532-1537*
5. *McCann UD, Mertl M, Eligulashvili V, Ricaurte GA: Cognitive performance in (() 3, 4-methylenedioxymethamphetamine (MDMA, „ecstasy") users: a controlled study. Psychopharmacology, 1999; 143: 417-425*
6. *Morgan MJ. Memory deficits associated with recreational use of „ecstasy" (MDMA). Psychopharmacology, 1999; 141: 30-36*
7. *Parrott AC, Lasky J: Ecstasy (MDMA) effects upon mood and cognition: before, during and after a Saturday night dance. Psychopharmacology, 1998; 139: 261-268*
8. *Parrott AC, Lees A, Garnham NJ et al: Cognitive performance in recreational users of MDMA of 'ecstasy': Evidence for memory deficits. Journal of Psychopharmacology, 1998; 12: 79-83*
9. *Reneman L, Booij J, Schmand B et al: Memory disturbances in „Ecstasy" users are correlated with an altered brain serotonin neurotransmission. Psychopharmacology, 2000; 148: 322-32412*
10. *Ricaurte GA, Markowska AL, Wenk GL et al: Journal of Pharmacology and Experimental Therapy, 1993; 266: 1097-1105*
11. *Tulving E, Markowitsch HJ: Episodic and declarative memory: Role of the hippocampus. Hippocampus, 1998; 8: 198-204*
12. *Lezak MD: Neuropsychological assessment (3rd Ed.). New York: Oxford University Press, 1995*
13. *Wechsler D: Wechsler Memory Scale- Revised. San Antonio: The Psychological Corporation, 1987*
14. *Wilson BA, Cockburn J, Baddeley AD: The Rivermead Behavioral Memory Test. Bury Saint Edmunds: Thames Valley Test Co, 1985*
15. *Zakzanis KK, Young DA: Memory impairment in abstinent MDMA („Ecstasy") users: A longitudinal investigation. Neurology in press;*
16. *Krystal JH, Price LH, Opsahl C et al: Chronic 3, 4-methylenedioxymethamphetamine (MDMA) use: Effects on mood and neuropsychological function? American Journal of Drug and Alcohol Abuse, 1992; 18: 331-341*
17. *Gouzoulis-Mayfrank E, Daumann J, Tuchtenhagen F et al: Impaired cognitive performance in drug free users of recreational ecstasy. Journal of Neurology, Neurosurgery, and Psychiatry, 2000; 68: 719-725*
18. *Semple DM, Ebmeier KP, Glabus MF et al: Reduced in vivo binding to the serotonin transporter in the cerebral cortex of MDMA ('ecstasy') users. The British Journal of Psychiatry, 1999; 175(7): 63-69*
19. *Baddeley A: Short term and working memory. In E Tulving & FIM Craik (Eds.) The handbook of memory. New York: Oxford University Press, 2000; 77-92*
20. *Baddely A, Hitch GJ: Working memory. In GA Bower (Ed.), The psychology of learning and motivation. New York: Academic Press, 1974; 205-217*
21. *Wilson BA: Behavioural Assessment of Dysexecutive Syndrome. Bury Saint Edmunds: Thames Valley Test Co, 1995*
22. *Cohen J: Statistical power analysis for the behavioral sciences. New York: Lawrence Earlbaum and Associates; 1988*
23. *Zakzanis KK, Leach L, Kaplan E: Neuropsychological differential diagnosis. Lisse, The Netherlands: Swets and Zeitlinger; 1999*
24. *Taylor MA: The fundamental of clinical neuropsychiatry. New York: Oxford University Press; 1999*
25. *Wolff K, Hay AWM, Sherlock K, Conner M: Contents of „ecstasy. „ Lancet, 1995; 346: 1100-1101*
26. *Blume AW, Marlatt GA, Schmaling KB: Executive cognitive function and heavy drinking behavior among college students. Psychology of Addictive Behaviors, 2000; 14: 299-302*
27. *Pope HG, Yurgelun-Todd D: The residual cognitive effects of heavy marijuana use in college students. Journal of the American Medical Association, 1996; 275: 521-527*
28. *Bolla KI, Cadet JL, London ED: The neuropsychiatry of chronic cocaine abuse. Journal of Neuropsychiatry and Clinical Neurosciences, 1998; 10: 280-290*
29. *Bolla KI, Funderburk FR, Cadet JL: Differential effects of cocaine and cocaine alcohol on neurocognitive performance. Neurology, 2000; 54: 2285-2292*
30. *Fletcher PC, Henson RN. Frontal lobes and human memory: insights from functional neuroimaging. Brain, 2001; 24: 849-881*
31. *Burgess PW, Quayle A, Frith CD: Brain regions involved in prospective memory as determined by positron emission tomography. Neuropsychologia, 2001; 39: 545-555*
32. *Parrott AC, Lasky J: Ecstasy (MDMA) effects upon mood and cognition: before, during and after a Saturday night dance. Psychopharmacology, 1998; 139: 261-268*
33. *Liotti M, Maybeg HS: The role of functional neuroimaging in the neuropsychology of depression. Journal of Clinical and Experimental Neuropsychology, 2001; 23: 121-136*