Psychiatria Danubina, 2011; Vol. 23, No. 1, pp 53-59 *Original paper*

THE EFFECT OF HEROIN ON VERBAL MEMORY

Sladjana Martinović Mitrović, Aleksandra Dickov, Nikola Vučković, Dragan Mitrović & Danijela Budiša

Institute of Psychiatry, Clinical Centre „Vojvodina", Novi Sad, Serbia

received: 22.04.2009; revised: 15.05.2010; accepted: 28.10.2010

SUMMARY

Background: *As a result of long-term heroin abuse we can see impairment of cerebral structures, that leads to specific psychopathological and neuro - physiological deficits in the cognitive and connative areas. There is a positive correlation between the mentioned deficits and the duration of heroin abuse. The memory is a cognitive function highly sensitive to toxic effects of opiates. The aim of this study was to establish the psychiatric and psychological consequences of heroin abuse, in the sense of verbal memory deficits, and the specific relation between mentioned deficits with the duration of abuse.*

Subjects and methods: *The research was devised as a prospective study, including ninety heroin addicts, divided into three groups, based on the abuse duration. The following instruments were used for data collecting: questionnaire, with basic social-demographic and addictive characteristics of subjects and Rey Test of Verbal Learning, a neuropsychological test for verbal memory estimation.*

Results: *Only the examinees who have abused heroin for less than a year obtained scores within the domain of the expected performances within the part of the test which relates to the direct verbal memory, as well as, the part of the test that relates to delayed verbal memory. With regard to the mentioned criteria, the difference between examinees with different length of opiates abuse is statistically important (direct memory: F=2.706; p=0.063, delayed memory: F=2.538; p=0.045). With the increase of heroin abuse length the number of examinees with a rising learning curve is decreased significantly, and the number of examinees with a flat learning curve is increased (Chi-square=19.589; p=0.003).*

Conclusion*: Heroin abuse, lasting longer than one year, is connected with impairment of short-term and delayed verbal memory. The intensity of the mentioned effects is higher with addicts who use a higher daily dose of heroin.*

Key words: *verbal memory – heroin - substance related disorders*

* * * * *

INTRODUCTION

The consumption of heroin over a long time can lead to organic damage of various cerebral structures which results in psychopathological and neuro-physiological consequences which become apparent through cognitive, connative and affective spheres of mental functioning (Lacković 2007). Cognitive functions which are in most cases affected by the toxic influence of opiates are: attention, concentration, memory and perceptual-motor speed / coordination.

Among factors which contribute to the creation and severity of neuropsychological consequences the long term abuse and high daily dose of heroin is an outstanding factor. Ahmad and Bindra (1989) state that addicts who have been taking heroin for more than two years, demonstrate deficits in psychological tests which measure intelligence, attention and concentration, memory and perceptual – motor coordination. Davis et al. (2002) confirm the fact that heroin abuse leads to cognitive deficits and behaviour disorders, but they emphasize the fact that for these effects of opiates it is necessary that they are used for five years at least.

Davis et al. (2002) point to the necessity of differentiating transitory changes from permanent personality changes, emphasizing that the recovery of cognitive deficits is possible during a period of abstinence. Latest research confirm these findings, with the addition that the partial improvement of cognitive functioning appears in the very early stage of abstinence, after the withdrawal symptoms reach their peak, and take note of the fact that cognitive deficits during early abstinence are connected with the withdrawal syndrome induced by neural dysregulation in the prefrontal cortex, so that they are partially of transitory character (Rapeli et al. 2006).

Memory belongs to the category of cognitive functions which are sensitive to toxic effects of opiates, but it is important to mention that mnestic deficits do not occur as a result of heroin influence on the central nervous system. Mild damage of verbal memory, appearing due to the long term abuse of high doses of opiates, were described in the end of eighties (Strang & Gurling 1989). In literature one can always find papers describing damage of short-term, which is, working memory (Ornstein et al. 2000, Darke et al. 2000, Rodriguez 1994). Wang et al. (2008) established the damage of verbal working memory capacity in former drug addicts, while the system of long-term verbal memory remained intact. Regarding the fact that the multicomponent system of working memory is inseparably connected with the attention system, the deficits of the two previously mentioned functions are usually described together.

Numerous papers from the field of neuropsychology point out that the most vulnerable neurons to the effects of heroin are frontal and prefrontal cortex neurons (Weinstein & Shaffer 1993, Lyvers & Yakimoff 2003), phylogenetically the youngest brain structures, responsible for the control, planning and programming of all higher psychological and motor functions (Colb & Whishaw 1985). It is indisputable that the patients with prefrontal cortex damage demonstrate completely specific memory disorders. Increased sensitivity to the influence of interferential stimuli, hindered memory of the time sequence of recent events and the impossibility of liberation from proactive inhibition are the main features of frontal amnestic syndrome (Colb & Whishaw 1985). Additionally, there is the dissociation between the capability to freely recall the thought word list, which is lowered and the recognition of the same material, which is relatively preserved (Shimamura et al 1991).

The aim of the study was to estimate verbal memory function in heroin addicts and establish the specific relationship between eventual deficits of verbal memory and the length of substance abuse.

SUBJECTS AND METHODS

Subjects

Ninety examinees were includes in the sample, chosen by clearly defined inclusion and exclusion criteria. Inclusion criteria were the following: opiates addiction diagnosis according to the ICD-10, abstinence in relation to the opiates longer than three weeks, male sex, age from 19 to 28 years. In order to exclude all other factors, which can cause the verbal memory disorder, while selecting the sample, the following exclusion factors were defined: experienced craniocerebral trauma, the presence of intracranial tumour, diagnosed temporal epilepsy, the presence of psychotic disorder, current presence of affective disorders, the existence of mental deficit syndrome, diagnosis for other substance addiction illnesses, the existence of neurological and neuromuscular damage, established abstinence in relation to opiates longer than 1/6 of the time of abusing the same, serious liver damage.

Examinees were divided into three groups of 30 examinees, according to the length of drug abuse:

1. group- examinees who have abused heroin up to 1 year;
2. group- examinees who have abused heroin for a 1-5 year period;
3. group- examinees who have abused heroin for more than 5 years.

Study procedure

The paper is a prospective two years study. The research was conducted at the Institute of Psychiatry at the Clinical Centre in Novi Sad. All the examinees were processed by a standardised method which comprised of a questionnaire adjusted to the needs of the research and psychological and neuropsychological tests for estimation of verbal memory.

Measures

1. QUESTIONNAIRE

The questionnaire is specially devised to suit the needs of this research; it is related to the basic sociodemographic and addictological characteristics of the examinees and contains the following points: age of examinees, length of substance abuse, average daily dose of heroin in the last three months, types of heroin abuse in the last three months, age at the time of the first contact with whatever psychoactive substance of whatever kind, age at the time of the first contact with heroin, frequency of the break in heroin abuse, presence of addiction in the family. For each individual variable, the level at which it could influence of the effect of heroin abuse on verbal memory was determined.

2. PSYCHOLOGICAL EXPLORATION

VITI (Wechsler Individual Test of Inteligence) a standard version of **Wechsler Adult Intelligence Scale (WAIS),** was the primary clinical instrument used to measure adult and adolescent intelligence. VITI is a combination of WAIS and WAIS/R (revised version) forms. WAIS is the basis, while the test is given in the manner taken from WAIS/R. The instrument estimates different aspects of intellectual functioning. Three different scores are obtained: total intelligence quotient (TIQ) or intelligence quotient of the whole scale, verbal intelligence quotient (VIQ) and performance intelligence quotient (PIQ). Verbal and performance IQ scores are based on the means of a larger number of different functions. A table of weighted scores corresponding to age groups is used for the calculation of normative values for the examinee in question.

Indicators of intellectual functioning of examinees have been introduced into the research as confounding variables, which are believed to have potential to significantly influence the examinees' achievement on the test for verbal memory assessment. General intelligence is the foundation of memory and a requirement for an individual to solve different tasks at more or less the same level of efficiency. Memorizing of verbal material is in direct and positive relation to the "verbal aspect" of intellectual abilities.

Potential impact of both verbal and practical IQ scores on the verbal memory function has been considered in the analysis of the results, since the basic VITI partition to the verbal and non-verbal parts only partially corresponds to the subtests' factorial determinateness, and significant functional overlapping of the two scales is hence believed to be inevitable.

3. NEUROPSYCHOLOGICAL EXPLORATION

The Rey Test of Verbal Learning is a test of verbal memory, which can estimate at the same time: direct remembering, learning process, and the relation

between the reproduction ability and recognition. As supplementary elements retroactive and proactive interferences are introduced. The damage of certain elements of the mnestic process, is directly connected with the type of brain dysfunction.

Statistical analyses

The analysis of covariance is used in the cases of dependent achievement variables such as the psychological/neuropsychological test; categorical group variable (length of abuse), and controlling (interfering) variables: age of examinees, age at the first contact with the heroin and psychoactive substances, average daily dose of heroin, type of abuse and the number of breaks in the heroin use, as well as the measurements of intellectual efficiency, where it is necessary. Variables followed a normal distribution, thus meeting the conditions for conducting this analysis. This method enabled us to establish the significance of the overall method in the multivariate analysis, and afterwards in univariate analysis, to establish the importance of the effect of the independent factor (group) on all dependent variables, whereas the covariables are kept under control. Scheffe's comparison tests the significance of the differences among arithmetic means of dependent variables in the subgroups based on the independent factors which proved themselves important in the former analysis.

RESULTS

Sociodemographic and addictological traits of examinees

The sample included examinees aging 19-24. At the overall sample level, average age of examinees was 24.5 (M=24.51, SD=3.05). With the analysis of variance, it was identified that examinees with different heroin abuse duration differ significantly with regard of their current age as well (F=27.919; df=2; p=0.000).

Examinees in this research have had the first contact with any of psychoactive substances at, averagely, 15 years (M=15.57; SD=1.88). Relative to the stated criterion, the difference between examines with different duration of addiction is at the marginal level of significance (F=2.637; df=0.078).

Examinees report that their first contact with heroin was around the age 19 (M=18.9; SD=2.49). Examinees with longer duration of addiction started with heroin abuse at a younger age (F4.716; df=0.012).

Average heroin dose that examinees take daily was, on the level of the total sample, approximately 1.5 grams (M=1.40; SD=0.87). Analysis of variance shows that it can be claimed with high reliability that examinees from different groups systematically differ in respect to the average daily dose of heroin intake (F=2.631; p= 0.000).

There is a statistically significant connection between the duration of heroin abuse and the way of administration. Addicts with longer abuse duration tend to use heroin intravenously considerably more often ($\chi 2$=18.086; df=2; p=0.000).

It was determined by analysis of variance that addicts who use heroin for a longer period of time also have more discontinuations in drug abuse (F=9.550; df=2; p=0.000). Results of multiple comparisons tested with Scheffe's test show that the systemic difference is maintainable between the first and the second (p=0.002) and the first and the third group (p=0.001), while the difference between the first and the third group (p=0.994) is not maintained.

Indicators of intellectual functioning

Intellectual abilities of examinees in this research are within the range of average values for their age. Analysis of variance has not identified any statistically significant difference between examinees with different heroin abuse durations (F=6.024; df=0.12).

Rey Test of Verbal Learning

The difference in attainment of examinees with different lengths of heroin abuse, at Rey Test of Verbal Learning, observed as a whole, was found to be at the marginal significance level. Poor results by the examinees can be connected with a higher daily dose of abused substance (Table 1).

Table 1. Multivariant analysis of covariance for the Rey verbal learning test as overall model

	RTVL - F	RTVL - df	RTVL - p
Age	0.671	5	0.647
Dose	3.013	5	0.016
Type of abuse	0.342	5	0.886
Age- PAS	2.023	5	0.085
Age- heroin	0.905	5	0.482
Number of breaks	1.373	5	0.244
VIQ	1.807	5	0.122
TIQ	1.065	5	0.386
Group	1.723	10	0.080

Direct and delayed verbal memory

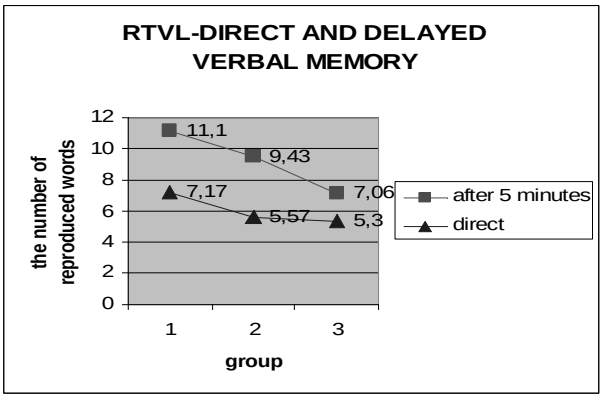

Figure 1. Averaged number of reproduced words immediately after the presentation and after 5 minutes

In figure 1 we can see that after first presentation of a 15 word list, examinees who abuse heroin for less than a year were capable of reproducing more than 7 words on average, whereas the examinees with a length of addiction to heroin of longer than one year were able to reproduce less than 6 words. The difference among the three groups of examinees was found to be on the marginal significance level (Table 2). Multiple comparisons using Scheffe's test show that the difference is of high statistical importance between the first and the second (p=0.000), and between the first and the third (p=0.000), while between the examinees of the second and the third group the difference loses its importance (p=0.737 The age of examinees at the time of first contact with psychoactive substances and the number of breaks during the abuse are important variables. Examinees who start with heroin consumption at an early age and have a greater number of breaks, reproduce less words at the first test series (Table 2).

The number of reproduced words 5 minutes after the last presentation of the given list decreases almost linearly with the function of the length of heroin abuse (Figure 1). In relation to the mentioned criterion, the difference between examinees with different length of abuse experience was found to be at the marginal significance level (Table 2). At the level of single pairs in groups, the differences remain statistically important (Table 3).

Learning curve

With the increase of heroin abuse length the number of examinees with rising learning curve is decreased and the number of examinees with a flat learning curve is increased. The difference between the groups is of high statistical importance (Chi-square=19.589; df=6; p=0.003) (Figure 2).

Examinees in all three groups can recognize 14 out of 15 presented words on average (Figure 3), and the difference among the groups is not statistically important (Table 4).

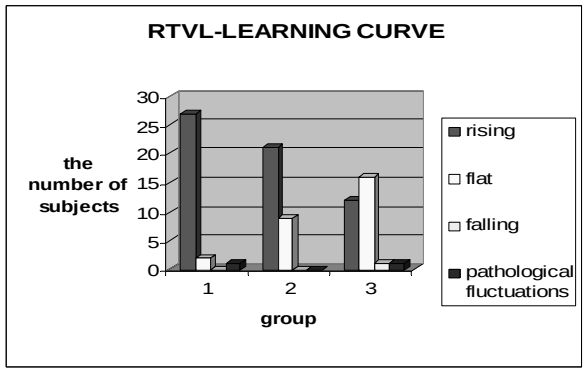

Figure 2. Examinees distribution with regard to learning curve

Table 3. Multivolume comparison of group pairs at variables direct and delayed verbal memory

Groups	Direct m. - p	Delayed m. - p
1-2	0.000	0.023
1-3	0.000	0.000
2-3	0.737	0.045

Recognition and retaining of remembered verbal material

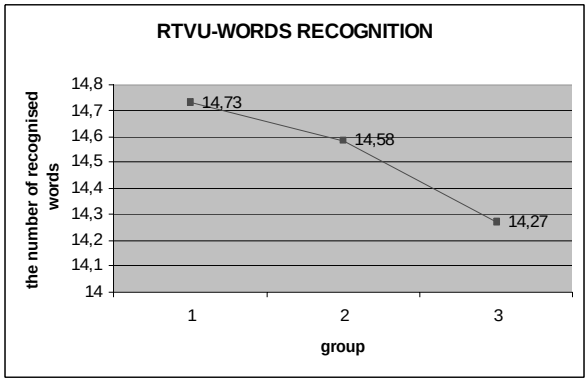

Figure 3. Averaged number of recognized words according to examinees groups

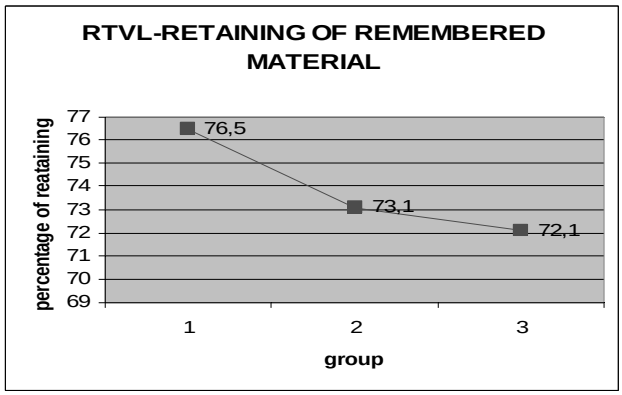

Figure 4. Percent of retained verbal material according to examinees groups

Examinees retain more than 70% of remembered verbal material on average (Figure 4), and statistically significant difference is not registered among groups (Table 4).

Table 2. Univariant analysis of covariance with indicators of direct and delayed verbal memory as dependent variables

	df	Direct memory		Delayed memory after 5'	
		F	p	F	p
Age	1	0.020	0.892	0.192	0.663
Dose	1	0.070	0.789	0.127	0.722
Type of abuse	1	0.093	0.761	0.122	0.728
Age- PAS	1	7.345	0.008	0.007	0.933
Age- heroin	1	3.182	0.078	0.002	0.961
Number of breaks	1	3.888	0.050	1.306	0.257
VIQ	1	0.097	0.757	0.996	0.321
TIQ	1	2.290	0.134	0.177	0.675
Group	2	2.706	0.063	2.538	0.075

Table 4. Univariant analysis of covariance with indicators of retaining and recognition of remembered verbal material as dependent variables

	df	Recognition		Retaining of remembered material	
		F	p	F	p
Age	1	0.272	2.636	0.376	0.541
Dose	1	0.005	4.752	3.316	0.072
Type of abuse	1	0.163	0.187	0.057	0.812
Age- PAS	1	1.407	0.318	0.459	0.500
Age- heroin	1	0.998	0.001	0.479	0.491
Number of breaks	1	0.064	0.315	0.001	0.980
VIQ	1	0.625	4.183	1.413	0.238
TIQ	1	1.802	2.457	0.032	0.858
Group	2	2.959	0.257	0.049	0.952

Confabulations

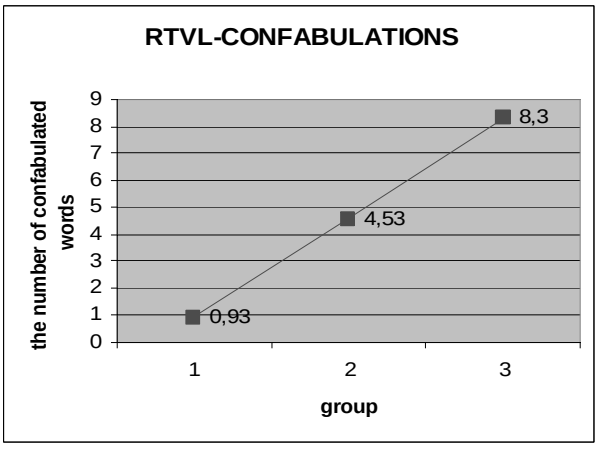

Figure 5. Averaged number of confabulated words according to examinees groups

The average number of confabulated words on Rey's test grows linearly with the increase of heroin abuse length (Figure 5). The difference among examinees is of high statistical importance (table 5), and remains the same after the multivolume comparison of group pairs (in all three combinations p=0.000).

The daily dose of heroin and verbal coefficient of intelligence are important among the set of interfering variables.

Table 5. Univariant analysis of covariance with the number of confabulations as dependent variables

	df	Confabulations	
		F	p
Age	1	2.636	0.108
Dose	1	4.752	0.032
Abuse type	1	0.187	0.666
Age- PAS	1	0.318	0.574
Age- heroin	1	0.001	0.978
Number of breaks	1	0.315	0.576
VIQ	1	4.183	0.044
TIQ	1	2.457	0.121
Group	2	5.257	0.007

DISCUSSION

The results show that with the first repetition of the presented 15 words list at Rey test of verbal learning only the examinees who abuse heroin for less than a year reached scores within the domain of expected results (7.27 reproduced words), while the examinees who abuse heroin for more than a year, that it to say, five years, reproduce less than the expected performance (5.57 words). The first repetition of words at Rey's test is a direct measure of the scope of short-term verbal memory, and the reported results show that

heroin abuse for more than a year leads to damage of short-term verbal memory. The poorer result of the initial reproduction can be connected with the damage of focusing and flexibility of attention, with initial immobility, excitement, and then reaction to overrating the difficulty of the task. The exclusion of all the above mentioned factors would be possible only with the qualitative analysis of the reproduced words.

The reported results are in accordance with the papers by many authors who present the thesis about the existence of direct verbal memory damage in heroin addicts (Ornstein et al. 2000, Darke et al. 2000, Fishbein et al. 2007). Rapelli et al. (2006) speak about the damage of the multicomponent system of working memory under the influence of drugs, emphasising the fact that the damage is inseparably connected with the damage of attention systems. Apart from this, they establish a significant correlation between short-term memory deficit, overall heroin abuse length and total length of psychoactive substances abuse. The results of this research point to the connection between damage of short-term verbal memory and the early beginning of abuse of whatever psychoactive substance, as well as heroin abuse at an early age. The more serious damage of short-term verbal memory can occur with examinees who have a greater number of breaks in their addict experience, and this underlines the possible influence of the withdrawal syndrome, that is, the neural cortex dysregulation induced by it, on cognitive damage.

The reproduction of the presented word list with a five minutes latency period is an indicator of *delayed verbal memory*. By analysing the results it was established that the examinees who abuse heroin for less than a year do not satisfy the prescribed standard for the number of reproduced words, more exactly, that they have damage of delayed verbal memory. The degree of deficit is increased with longer substance abuse.

The results show that the percentage of examinees with a flat learning curve increases significantly with the increase of abuse length (6.67% with the examinees in the first, 30% with the examinees in the second and 53.3% with the examinees in the third group). The learning process is based on the two important aspects of long-term memory: creating the trace and consolidation of the received information. A flat learning curve indicates the deficits of the above mentioned processes.

On the other hand, one can see that the average number of recognised words in all three groups of examinees is around 14, which matches the prescribed standard for the given population. The preserved recognition of the presented verbal material demonstrates an intact function of evoking stored information, which represents the third aspect of long-term memory. Mintzer & Stitzer (2002) give data about the damage of verbal recognition function in former heroin addicts, who are still in a methadone maintenance programme.

Dissociation between recognition process and the learning process is one of the characteristics of frontal mnestic syndromes. The fact that with examinees in this research the damage of learning function is registered along with preserved recognition, suggests that the verbal memory deficits with heroin addicts are probably of frontal type, which is in accordance with the thesis that the frontal brain structures brain are the most sensitive to heroin abuse (Weinstein & Shaffer 1993).

The percentage of *retaining* remembered verbal material with examinees from all three groups exceeds 70%, which matches with percentage scores of retaining healthy subjects, which means that the process of forgetting (information loss) with heroin addicts does not reach a pathological level and is not connected to the length of addict intership.

With high statistical significance one can claim that the number of confabulated words in Rey's test grows with the length of heroin abuse (from 0.93 with examinees in the first group to 4.53 with examinees in the second group, up to 8.3 with examinees in the third group). A typical psychiatric attitude is that confabulations are indicators of organicity. For such a claim in this case, a qualitative analysis would be necessary, which would establish the associative origin of the confabulation, regarding the fact that the occurrence of confabulated words can be the consequence of weaker focusing of attention, the influence of present perception, lack of insight into self behaviour, tiredness, and deficient ability of correlation. Among possible interfering factors, an important connection was established between the number of confabulations and the daily dose of heroin ($p=0.032$) and the verbal coefficient of intelligence ($p=0.044$), in the sense that the examinees who take more opiates on a daily basis and who have lower intelligence coefficient tend to confabulate more.

CONCLUSION

The abuse of heroin for more than a year leads to short-term verbal memory damage. The degree of short-term verbal memory damage is connected in a statistically significant way with the beginning of heroin consumption at an early age and with the greater number of breaks in the abuse of substances.

The damage to long-term verbal memory occurs with examinees who use heroin for more than a year.

REFERENCES

1. *Ahmad S, Ahmad H & Bindra G: Cognitive impairment in chronic heroin addicts. Journal of Personality Clinical Studies 1989; 5:237-240.*
2. *Colb B & Whishaw I: Fundamentals of Human Neuropsychology, New York: W.H. Freeman and company, 1985.*
3. *Darke S, Sims J, McDonald S & Wickes W: Cognitive impairment among methadone maintenance patients. Addiction 2000; 95:687-95.*
4. *Davis PE, Liddiard H & McMillan TM: Neuropsychological deficits in opiate abuse. Drug and Alcohol Dependence 2002; 67:105-8.*
5. *Fischbein DH, Krupitsky E, Flannery BA, Langevin DJ, Bobashev G & Verbitskaya E: Neurocognitive characteri-*

zations of Russian heroin addicts without a significant history of other drug abuse. Drug and Alcohol Dependance 2007; 90:25-38.

6. *Lacković Z: Psychoactive drugs and neuroplasticity. Psychiatria Danubina 2007; 19:202-5.*
7. *Lyvers M & Yakimoff M: Neuropsychological correlates of opioid dependence and withdrawal. Addictive Behaviors 2003; 28:605-11.*
8. *Mintzer MZ & Stitzer ML: Cognitive impairment in methadone maintenance patients. Drug and Alcohol Dependence 2002; 67:41-51.*
9. *Ornstein TJ, Iddon JL & Balacchino AM: Profiles of cognitive dysfunction in chronic amphetamine and heroin abusers. Neuropsychopharmacology 2000; 23:113-26.*
10. *Rapeli P, Kivisaari R & Autti T: Cognitive function during early abstinence from opioid dependence: a comparison to age, gender, and verbal intelligence matched controls. BMC Psychiatry 2006; 6:9.*
11. *Rodriguez M: Influence of sex and family history of alcoholism on cognitive functioning in heroin users. European Journal of Psychiatry 1994; 8:29-36.*
12. *Shimamura JS, Janowsky JS & Squire LR: What is the Role of Frontal Lobe Damage in Memory Disorders. In Levin HS, Eisenberg HM & Benton AL (eds): Frontal Lobe Function and Dysfunction. Oxford University Press, New York, 1991.*
13. *Strang J & Gurling H: Computerized tomography and neuropsychological assessment in long-term high-dose heroin addicts. British Journal of Addiction 1989; 84:1011-19.*
14. *Wang ZX, Xiao ZW, Zhang DR, Liang CY & Zhang JX: Verbal working memory in abstinent heroin abusers. Acta Neuropsychiatrica 2008; 20:265-8.*
15. *Weistein C & Shaffer H: Neurocognitive aspects of substance abuse treatment: a psychotherapist's primer. Psychoterapy 1993; 30:317-33.*

Correspondence:

Slađana Martinović Mitrović
Clinic for Drug Addiction, Institute of Psychiatry, Clinical Centre "Vojvodina"
Hajduk Veljkova 1, 21 000 Novi Sad, Serbia
E-mail: damit@sbb.co.yu