



## Original article

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**INFLUENCE OF CERTAIN PARAMETERS  
OF CHRONIC HEROIN ABUSE (AGE,  
BEGINNING AND LENGTH OF ABUSE,  
PSYCHOORGANIC SYNDROME)  
ON DEVELOPMENT OF CEREBRAL  
ATROPHY DIAGNOSED BY  
COMPUTED TOMOGRAPHY**

## SUMMARY

Cerebral atrophy is a morphological brain damage caused by the effects of heterogeneous etiological factors. Loss of neurons and neuroglia, as well as the degree and speed of this deterioration depend on the type, concentration and the length of effect of one or more etiological agents. Cerebral atrophy is clinically accompanied by development of the psychoorganic syndrome. Methods of choice for diagnosing cerebral atrophy are CT (Computed Tomography) and MR (Magnetic Resonance) endocranium examinations. Although the degree of mental deterioration corresponds to the degree of endocranium changes as seen on CT scans, variations within this range are so great that in some patients only the ratio between diagnostic and clinical examinations can point to diagnosis of cerebral atrophy.

The aim of the paper was to establish the correlation between CT-diagnosed cerebral atrophy and the age of the addict, the age of first heroin use, the length of abuse and the psychoorganic syndrome if it has developed.

This paper is a retrospective study carried out from January 2006 till July 2007 among patients at the Psychiatric Clinic of the Clinical Center "Kragujevac". We examined CT scans of endocranium of 38 heroin addicts (7 women and 31 men). The estimate of cerebral atrophy was based on dilatation of cerebral ventricles and outer liquor space (cortical sulci and cisterns). The data related to the age of the addicts, the type of the substance abused, the length of abuse, the age of first heroin use and psychoorganic syndrome, which was estimated by minimental scale (MM), were taken from the addicts' files of the Clinic Methadone Programme.

We found a statistically significant relation between the degree of cerebral atrophy and the age of the subjects ( $r = -0.498$ ,  $p = 0.001$ ) and between the age of first heroin use and the degree of cerebral atrophy ( $r = -0.727$ ,  $p = 0.000$ ). We found a statistically significant relation neither to the length of heroin abuse ( $r = 0.283$ ,  $p = 0.085$ ), nor to the value of MM test. ( $r = 0.156$ ,  $p = 0.350$ ).

CT examination should be performed only in addicts with shorter periods of abuse, because at this stage, atrophy is reversible. The paper has confirmed that cerebral atrophy, from the clinical aspect, does not include only morphological deterioration of the brain tissue if it is not accompanied with a clinical presentation of the psychoorganic syndrome. Its diagnosis implies the obligatory presence of both criteria, since no statistically significant relation was found.

**Key words:** cerebral atrophy, heroin addiction, computed tomography

## INTRODUCTION

Cerebral atrophy is morphological irreversible damage of the brain caused by effects of heterogeneous etiological factors. Its underlying characteristic is the loss of neuron and neuroglial cells, in different ratios, which is accompanied by decrease in volume of the cerebral substance with proportional expansion of inner and outer liquor space. The loss of neurons and neuroglia, as well as the degree and speed of this deterioration depend on the type, concentration and the length of effect of one or more etiological agents. Therefore, the time it takes to develop varies from a few months to a few years (1).

Cerebral atrophy is clinically accompanied by development of the psychoorganic syndrome – low concentration, memory disorder, dementia, confusion, paranoid reactions, while depending on the causes, neurological failures can also occur – paresis, aphasia, ataxia, extrapyramidal disorders and pseudobulbar syndrome. (2)

Methods of choice for diagnosing cerebral atrophy are CT scans (Computed Tomography) and MR scans (Magnetic Resonance), while pneumoencephalography has only a historical significance. Only with introduction of endocranium CT scans into clinical practice, it was noted that cerebral atrophy was correlated with psychoorganic syndromes, thus further investigations were directed towards the etiology of its development. Furthermore, with introduction of MR scans of endocranium in everyday clinical practice, it was accepted that incipient atrophy was reversible, because this sophisticated visualization examination enabled early detection of atrophy caused by effects of different etiological factors (4,5,6,7,8). Although the degree of mental deterioration corresponds to the degree of changes in the structure of endocranium as seen on CT and/or MR scans, variations are so great that in some patients, only the ratio between diagnostic and clinical examinations can point to diagnosis of cerebral atrophy (9,10,11,12,13).

Diagnostic visualization examinations can reveal cerebral atrophy in patients with no apparent psychoorganic syndrome, or the psychoorganic syndrome can be diagnosed although endocranium CT or MR scans are normal (14).

Quantification of cerebral atrophy based on CT scans is difficult due to multicausality of its development, but it is possible when based on measurements of the width of anatomical structures and determination of their relations.

## AIMS

To determine if CT verified cerebral atrophy depends on the following variables: the age of the subjects, age of first heroin use, length of heroin abuse and psychoorganic syndrome.

## MATERIAL AND METHODS

This paper is a retrospective study carried out from January 2006 till July 2007 among patients at the Psychiatric Clinic of the Clinical Center "Kragujevac". We examined CT endocranium scans of 38 heroin addicts (7 women and 31 men).

The patients included in the study had to meet the following criteria:

- Age between 18 and 50 years.
- Absence of gravidity.
- Heroin addiction.
- At least one year of heroin abuse.
- Voluntary participation in the study.
- No chronic diseases.
- Absence of cerebrovascular insufficiency.
- No other addictions.
- Excluded diagnosis of other mental disorders.
- Minimental test performed.

CT endocranium scans were performed on the spiral CT scanner "HI SPEED" produced by "General Electric", without i.v. contrast. Axial skull base sections were 3 mm thick, while for the rest of the endocranium they were 7 mm.

Cerebral atrophy estimation was based on dilatation of the brain ventricles and the outer liquor space (cortical sulci and cisterns), estimated according to the following indices:

1. Coefficient of frontal horns (width of occipital horns / width of frontal horns of lateral brain ventricles).
2. Huckmann's index (width of frontal horns of lateral brain ventricle + width of interpeduncular region).
3. Width of brain ventricle III.
4. Pars centralis index (width of skull / width of lateral parts of both lateral ventricles).
5. Width of frontal interhemispheric fissure.
6. Width of cortical sulci.

The data related to the age of the addicts, type of the substance abused, length of abuse, the age of first heroin use and psychoorganic syndrome, which was estimated by minimental scale (MM), were taken from the addicts' files of the Clinic Methadone Programme.

The obtained values were analyzed by Student's t-test for paired large samples. The values

were considered significant when the p value was less than 0.05 and highly significant when the p value was less than 0.01.

**RESULTS**

At the moment the study began, the youngest addict was 23, and the oldest was 51 years old (SD= ±9.54) There was no statistically significant difference between the mean age of male and female subjects (p=0.721).

Analysis of the CT endocranium scans revealed cerebral atrophy predominantly in the frontal region in 34 addicts, in different degrees: incipient in 14 (36.8%), moderate in 9 (23.7%) and severe in 11 addicts (28.9%) (Figure 1).

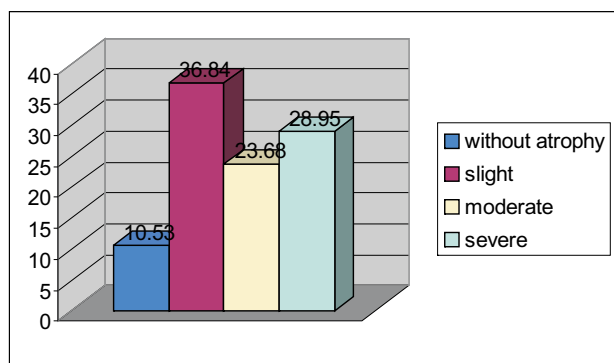


Figure 1- Percentage of cerebral atrophy among examinees

The mean age of the first intravenous use of heroin was 18.7 years. The earliest age was 14, and the latest age was 24. (SD= ±2.96). (Figure 2). The shortest period of narcotic abuse was 6 years, and the longest was 33 years. (SD= ±10.01) (Figure 3) The mean value of MM test was 27.74, the minimal value was 19, and maximal was 31 (SD= ±2.07).

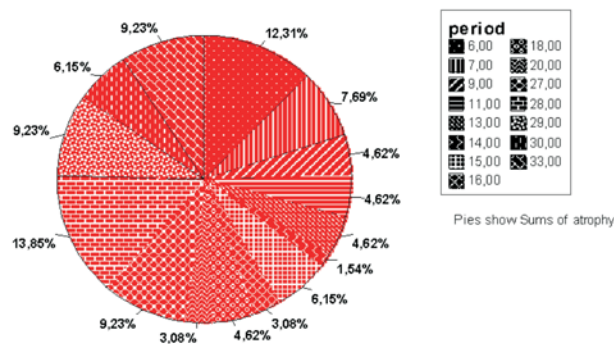


Figure 2. Length of drug abuse among examinees displayed in years

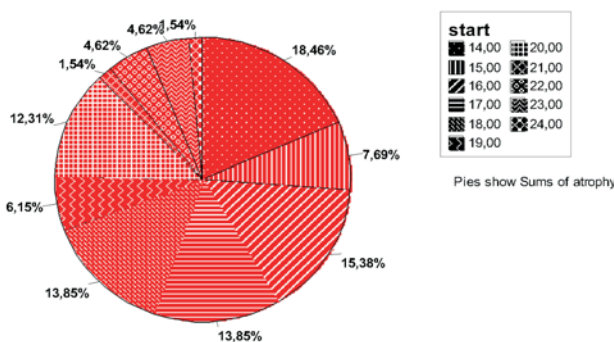


Figure 3. Distribution of age when drug abuse started among examinees displayed in percentage

We found statistically significant relations between the degree of cerebral atrophy and the age of the subjects (r= -0,498, p= 0,001) and between the age of the first heroin use and the stage of cerebral atrophy (r = -0.727, p = 0.000). We found statistically significant relation neither to the length of heroin abuse (r = 0.283, p= 0.085), nor to the value of MM test (r = 0.156, p= 0.350).

**DISCUSSION**

Cerebral atrophy in most of the subjects points to a conclusion that the effects of the studied etiological factor (morphia) contributes to development of atrophy, which can be detected based on the morphological changes in the endocranium structures. In this sense, the results of this study coincide with the results of other studies conducted worldwide (10,11,13). CT-diagnosed cerebral atrophy in 6 patients (except in one of the addicts) was in the frontal region of the cerebrum. This can be explained with cerebral ischemia caused by blood vessel spasm, which is at first gradual and then progredient with longer periods of narcotic abuse. Vasoconstriction of smaller branches of frontal and medium cerebral artery was found when a substantial dose of amphetamines was injected intravenously in experimental animals (monkeys). Amphetamines have an effect equivalent to opiates, which partially explains etiopathogenesis of cerebral atrophy in heroin abusers (14).

The conclusions drawn in this study coincide with the investigators claiming that degenerative changes in this region in heroin abusers can be explained by neurochemical, neuroimmunological and biochemical changes and the decreased metabolism of glucose (15, 16). These changes become irreversible with longer periods of heroin abuse. The incipient form of atrophy was found in the patient with the shortest period of abuse, which is yet another parameter that coincides with other studies conducted in the world. Many authors suggest that

atrophy at this stage is reversible if the patient is by an adequate treatment brought into abstinence (16, 17, 18).

In addicts that started taking heroin at an early age, cerebral atrophy was more severe because during that period the physiological transmission of neurotransmitters was not possible due to opiate-receptor blockade, which brought about a disorder in permeability of the cell membrane. This interfered with glucose transport mechanisms, mitochondria functions and pH values of cytoplasm with tendencies towards acidosis, causing cell hypoxia and its inevitable death. Brain cells of younger addicts are more susceptible to anaerobic glucose metabolism than those in older ones (16).

However, the lack of statistically significant relation between the degree of atrophy and minimal test, used for fast and simple determination of the extent to which cognitive functions are preserved, indicates that morphologically changed cerebrum does not necessarily implies the presence of the psychoorganic syndrome. This syndrome is clinically expressed only under effects of some other factors, which is a conclusion that also coincides with other studies (10, 19, 20, 21, 22).

## CONCLUSION

At the beginning of our investigation, we encountered a problem – a large number of addicts refused to take part in the study. This brought about a fundamental change in the protocol. Given the costs of MR scans, we chose CT instead of the planned MR endocranium scans. We believed that the results obtained from a small sample of addicts can show if this kind of examination is necessary for the treatment of a larger group, which was not motivated to take part in the study. Although we had to change the protocol, the aim of the paper was achieved. The patients' refusal to participate in the study resulted in the fact that the studied population was not representative compared to the existing data on registered number of heroin abusers – the sample was not proportional to the total number and sex of the registered heroin abusers.

Nevertheless, this study, carried out for the first time in the Clinical Center "Kragujevac" remains very important because it pinpoints the variables that should be included in a more comprehensive investigation. Since this population is rather particular and reluctant to cooperate and the costs of CT and MR scans are high, narrowing the field of interest would enable faster gathering of data relevant to the treatment of consequences of this kind of addiction.

To be precise, the fact that there are relations between the atrophy and the age of first heroin use and between the atrophy and the age of the subjects, and that there is no relation between the atrophy and minimal test means that CT scans should be performed only in younger addicts and those with shorter periods of abuse because the timely treatment would prevent psychoorganic syndrome. The diagnostics algorithm of cerebral atrophy in addicts with shorter period of abuse or with those who started before the age of 18 would be the following: endocranium MR scan as an initial examination and then follow-up CT examinations in accordance with the clinical findings. The follow-up examinations could be used for monitoring the effects of treatment and giving a more reliable prognosis for these patients. This way the costs of treatment would decrease without jeopardizing the patients' interests.

The paper has confirmed that cerebral atrophy, from the clinical point of view does not involve only the morphological damage of the brain tissue if it is not accompanied with a clinical presentation of psychoorganic syndrome; its diagnosis requires the presence of both criteria. In view of this finding, the necessary cooperation of a clinical physician and diagnostician in every day practice is confirmed.

The absence of the established medicamentous approach in the treatment of this type of addiction places special emphasis on neurological sequels of chronic heroin abuse. Therefore, cerebral atrophy, especially of frontal regions, must be understood in the light of pathogenesis, which would enable an adequate therapy for any individual addict, since there are no generally accepted protocols.

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**UTICAJ POJEDINIH PARAMETARA HRONIČNE ZLOUPOTREBE HEROINA  
(STAROST, POČETAK I DUŽINA ZLOUPOTREBE, PSIHOORGANSKI SINDROM)  
NA RAZVOJ CEREBRALNE ATROFIJE DIJAGNOSTIKOVANE  
KOMPJUTERIZOVANOM TOMOGRAFIJOM**

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**SAŽETAK**

Cerebralna atrofija je morfološko oštećenje mozga nastalo kao rezultat dejstava heterogenih etioloških činilaca. Odnos gubitka neurona prema nestanku neuroglije, stepen i brzina tog propadanja zavise od vrste, koncentracije i dužine delovanja jednog ili više etioloških agenasa. Cerebralna atrofija je klinički najčešće praćena razvojem psihoorganskog sindroma. Za dijagnozu cerebralne atrofije metode izbora su CT (eng. Computed Tomography) i MR (eng. Magnetic Resonance) pregledi endokranijuma. Iako stepen mentalnih poremećaja odgovara stepenu promena u strukturama endokranijuma na CT tomogramu, varijacije u tom odnosu su toliko velike da kod pojedinih bolesnika, tek stepen odnosa dijagnostičkih i kliničkih pregleda može da ukaže na dijagnozu cerebralne atrofije.

Cilj rada bio je da se utvrdi korelacija između CT-om dijagnostikovane atrofije cerebruma i starosti zavisnika, godine života kada je narkotik prvi put uzet, dužine zloupotrebe i psihoorganskog sindroma, ukoliko se razvio kod ispitanika.

Rad predstavlja retrospektivnu studiju od januara 2006. godine do jula 2007. godine koja je obuhvatila bolesnike Psihijatrijske klinike KC "Kragujevac". Analizirano je 38 CT pregleda endokranijuma narkomana (7 žena i 31 muškarac). Procena cerebralne atrofije zasnivala se na dilataciji cerebralnih komora i spoljašnjeg likvornog prostora (kortikalni sulкуси i cisterne). Podaci vezani za starost zavisnika, vrstu upotrebljivanih narkotika, dužinu zloupotrebe, u kojoj godini je narkotik prvi put uzet i psihoorganski sindrom koji je procenjivan minimalnim (MM) skalom, uzeti su iz dosijea zavisnika metadonskog programa KC "Kragujevac".

Nađena je statistički značajna veza između stepena cerebralne atrofije i godina starosti ispitanika ( $r = -0,498$ ,  $p = 0,001$ ) i godine započinjanja zloupotrebe narkotika u odnosu na stepen razvijene cerebralne atrofije ( $r = -0,727$ ,  $p = 0,000$ ). Statistički značajna veza cerebralne atrofije ne postoji u odnosu na dužinu narkomanskog staža ( $r = 0,283$ ,  $p = 0,085$ ), ni u odnosu na vrednost MM testa ( $r = 0,156$ ,  $p = 0,350$ ).

CT pregled bi trebalo ograničiti samo na zavisnike sa kraćim periodom zloupotrebe, jer je atrofija u ovakvom stepenu reverzibilna. Rad je potvrdio da cerebralna atrofija, s kliničkog aspekta, ne znači samo morfološko propadanje moždane mase ako nije praćena razvojem kliničke slike psihoorganskog sindroma, već je za njenu dijagnozu nužno postojanje oba kriterijuma, s obzirom da statistički značajna veza nije nađena.

***Cljučne reči:*** cerebralna atrofija, heroinska zavisnost, kompjuterizovana tomografija