

SYMPTOMATIC EPILEPTOGENIC LESIONS

Tatjana Chepreganova-Changovska¹, Dragana Petrovska-Cvetkovska¹,
Marija Srceva-Jovanovski², Venko Filipce³

¹ University Clinic of Neurology, Faculty of Medicine, Ss. Cyril and Methodius University, Skopje, R. Macedonia

² University Clinic for Anesthesia, Reanimation and Intensive Care, Faculty of Medicine, Ss. Cyril and Methodius University, Skopje, R. Macedonia

³ University Clinic of Neurosurgery, Faculty of Medicine, Ss. Cyril and Methodius University, Skopje, R. Macedonia

Corresponding Author: Tatjana Chepreganova-Changovska, ul. Jurij Gagarin br. 25/3 1000 Skopje, Tel. +389 (0)2 3 08 02 60, E-mail: tcepreganova@yahoo.com

Abstract

Background and objectives: The main aim of this study is to prove the association of seizure types with the MRI findings of the brain (etiological factor). Also, to prove which type of lesion is mostly represented in which age-group, and with which type of seizure.

Methods: A total of 100 patients with symptomatic epilepsy, aged from 16 to 80 years, were hospitalized at the Neurology Clinic or in its Outpatient Unit, in the period from 2009 to 2012. They were neurologically examined and the seizure type registered. All patients underwent MRI of the brain.

Results: (56%) men and 44 (44%) women were examined. The represented type of epileptic seizures were 41.0% with SPC + CPC, followed by 15.0% GTCC, and 14.0% CPC with secondary generalization, 12.0% CPC, 10.0% SPC and 8.0% with absences. The epileptic lesions of 25.0% were hippocampal sclerosis, 20.0% post-traumatic injuries, 19.0%, post-vascular and brain tumours, and the lowest percentage of 17.0% with post-infectious lesions.

Conclusions: Post-traumatic lesions occur more frequently in the elderly population with the accent on the male, while hippocampal sclerosis occurs in the adolescent and younger population with higher frequency in the female.

Key words: symptomatic epilepsy, epileptic seizures, epileptic lesions.

Introduction

The term "symptomatic epilepsy" refers to epilepsy that is a symptom of an underlying problem, such as an injury, an infection, a congenital brain malformation, a tumour, or a metabolic disorder.

Brain imaging has improved over the last several decades, so that doctors can detect smaller lesions and structural problems. As a result, many cases of epilepsy that would once have been called idiopathic or cryptogenic are now known to be symptomatic.

Anything causing structural or functional derangement of the cortical physiology may lead to seizures and different conditions may express themselves solely by recurrent seizures and thus be labelled "epilepsy". The semiology of seizures and the consequences for the sufferers are, however, similar and therefore epilepsy could be better described as a symptom complex or a condition rather than a disease in its own right [1].

Each patient, having at least one certain epileptic seizure, has to undergo neurological,

and radiological investigation on computerized tomography or magnetic resonance imaging (MRI) of the brain as well as an electroencephalographic investigation.

In the context of symptomatic epilepsies, MRI is the most objective method for discovering the etiological factor, or the epileptogenesis of the lesion, respectively.

Epileptogenic lesions could be posttraumatic injuries, post-vascular accidents, vascular malformations, infections, demyelinations, cortical dysplasia, hippocampal sclerosis, etc.

The range of risk factors for the development of epilepsy varies with age and geographical location [1]. Congenital, developmental and genetic conditions are mostly associated with the development of epilepsy in childhood, adolescence and early adulthood.

Clinical expression of symptomatic epilepsy varies, the seizures could be simple partial, complex partial with or without secondary generalization, generalized tonic-clonic seizures and absences.

Aim of the study

The main aim of this study is to prove the association of the seizure types with the MRI findings of the brain (etiological factor).

Also, to prove which type of lesion is most represented in which age group, and with which type of seizure.

Material and method

A total of 100 patients with symptomatic epilepsy, aged from 16 to 80 years, were hospitalized at the Neurology Clinic or in its Outpatient Unit, in the period from 2009 to 2012. They were neurologically examined and the seizure type registered. All patients underwent MRI of the brain and electroencephalography; the latter has not been a part of this investigation.

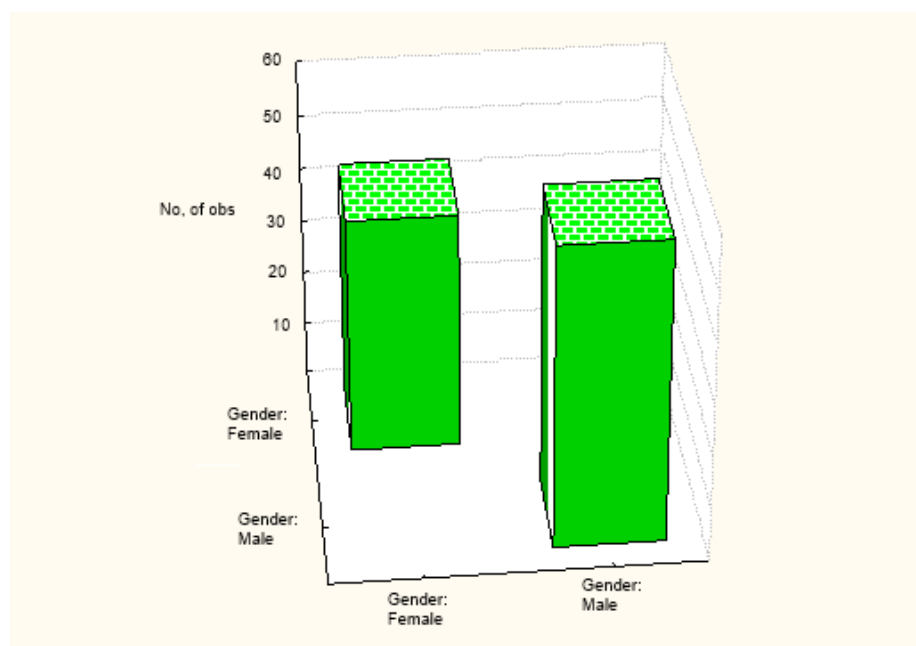
Results

Patients aged from 16 to 80 years were included in this study, 56 (56%) men and 44 (44%) women, the percent difference has been statistically non-significant for $p > 0.05$. It was a homogenous group according to gender (Table 1 and Graph 1).

Table 1

Distribution of patients according to gender

| Gender | No | % |
|--------|----|------|
| Men | 56 | 56.0 |
| Women | 44 | 44.0 |



Graph 1 – Graphical drawing of the number of patients according to gender

There was no statistically significant dependence among the types of the epileptogenic

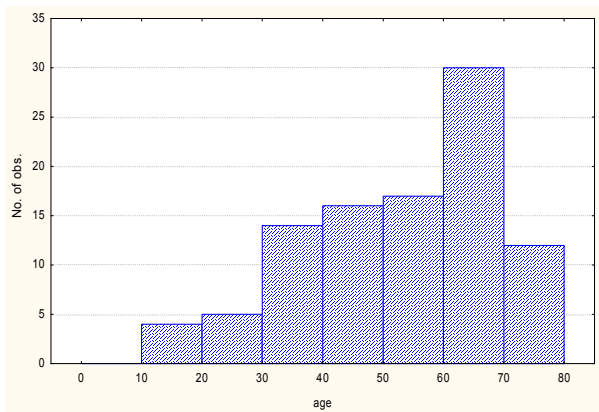
seizures upon the gender of the patients (Pearson Chi-square: 0.868205, $p = 0.972480$).

The mean age of the patients ranged from 53.8 ± 15.9 . The greatest number of patients, 30, belonged to the age group ranging from 61 to 70 years, followed by 17 patients from 51 to 60, 16 patients from 41 to 50, and 14 patients aged from 31 to 40, etc. (Table 2 and Graph 2A).

Table 2

Mean age of the patients

| Valid N | Mean | Minimum | Maximum | SD. |
|---------|----------|---------|---------|------|
| 98 | 53.80612 | 16.0 | 80.0 | 15.9 |



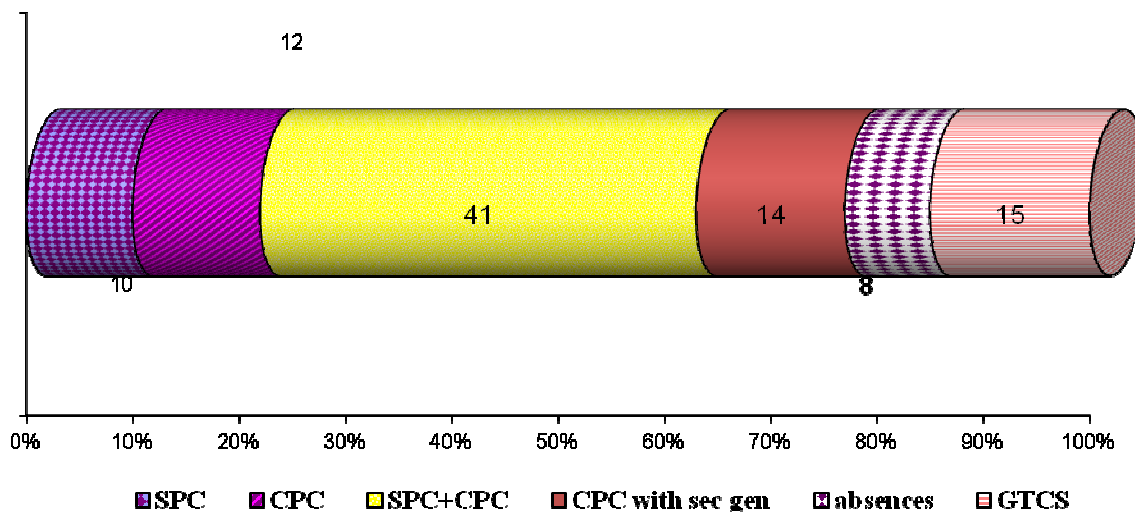
Graph 2A – Histogram of patients' age

The greatest percentage in the investigated group, the represented type of the epileptic seizures (crises), were 41.0% with SPC+CPC, followed by 15.0% GTCC, 14.0% CPC with secondary generalization, 12.0% CPC, 10.0% SPC and 8.0% absences (Table and Graph 3). The percentage difference being registered between SPC + CPC versus other modalities was statistically significant for $p = 0.000$.

Table 3

Distribution of the examinees according to the type of epileptic seizures (crises)

| Crisis | No | % |
|-----------------------------------|----|----|
| Simple partial crises (SPC) | 10 | 10 |
| Complex partial crises (CPC) | 12 | 12 |
| SPC + CPC | 41 | 41 |
| CPC with secondary generalization | 14 | 14 |
| Absences | 8 | 8 |
| GTCC | 15 | 15 |



Graph 3 – Graphic drawing of the examinees according to the type of epileptic seizures (crises)

In the greatest percentage of the investigated group, the epileptic lesions of 25.0% were hippocampal sclerosis; the other epileptogenic lesions found were with 20.0% post-traumatic injuries, 19.0% with post-vascular and brain tumours with and the lowest percentage of 17.0% were the post-infectious (Table 4 and Graph

4A). The percentage difference being registered among all modalities of epileptogenic lesions was statistically non-significant for $p > 0.05$.

There was no statistically significant dependence among the epileptogenic lesions upon the type of epileptic seizures (Pearson Chi-square: 30,7911, $p = 0.058037$).

Brain tumors as epileptogenic lesions were present in SPC + CPC in greatest per cent with 31.6, with the lowest per cent of 5.3% were in GTCS.

Post-traumatic injuries as epileptogenic lesions were present with the greatest per cent of 35.0% and 30.0% in SPC + CPC and GTCS, and in the lowest per cent of 5% in SPC.

Post-vascular injuries as epileptogenic lesions were present with the greatest per cent of 36.8% in SPC + CPC, the least per cent of 5.3% in absences and SPC.

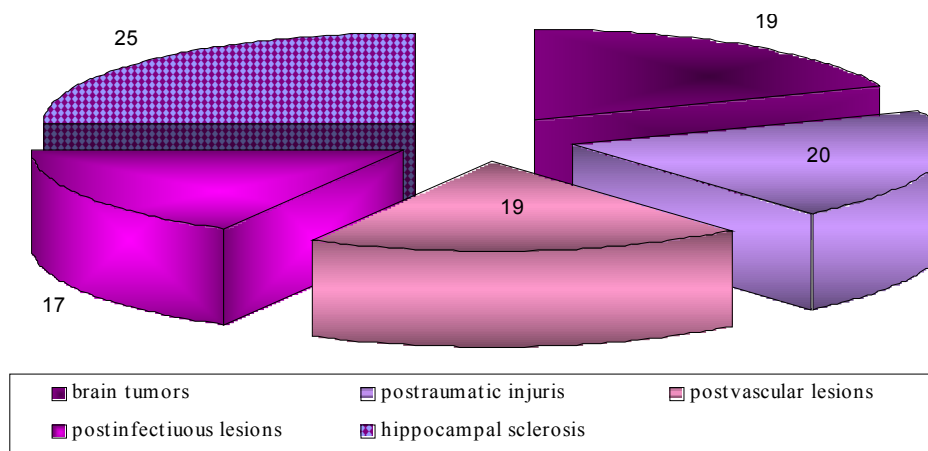
Post-infectious lesions as epileptogenic lesions in the greatest percent of 52.9% were present in SPC + CPC, and in the least percent

of 5.9% SPC and CPC with secondary generalization.

Table 4

Distribution of patients according to present epileptogenic lesions

| Epileptogenic lesions-present | No | % |
|-------------------------------|----|----|
| Brain tumors | 19 | 19 |
| Post-traumatic injuries | 20 | 20 |
| Post-vascular | 19 | 19 |
| Post-infectious | 17 | 17 |
| Hippocampal sclerosis | 25 | 25 |



Graph 4A – Graphical drawing of the examinees according to epileptogenic lesions

Hippocampal sclerosis as epileptogenic lesions was represented with the greatest per

cent of 48.0% in SPC+CPC and in the least per cent of 4.0% in GTCS (Table 5).

Table 5

Percentual distribution of the epileptogenic lesions in types of epileptogenic seizures

| Epileptogenic zones | Brain tumors | | Post-traumatic injuries | | Post-vascular | | Post-infectious | | Hippocampal sclerosis | |
|-----------------------------------|--------------|-------|-------------------------|-------|---------------|-------|-----------------|-------|-----------------------|-------|
| | No | % | No | % | No | % | No | % | No | % |
| Epileptic seizures types | | | | | | | | | | |
| Simple partial crises (SPC) | 3 | 15.8 | 1 | 5.0 | 1 | 5.3 | 1 | 5.9 | 4 | 16.0 |
| Complex partial crises (CPC) | 0 | | 2 | 10.0 | 2 | 10.5 | 3 | 15.8 | 5 | 20.0 |
| SPC+CPC | 6 | 31.6 | 7 | 35.0 | 7 | 36.8 | 9 | 52.9 | 12 | 48.0 |
| CPC with secondary generalization | 4 | 21.0 | 4 | 20.0 | 4 | 21.0 | 1 | 5.9 | 1 | 4.0 |
| Absences | 5 | 26.3 | 0 | | 1 | 5.3 | 0 | | 2 | 8.0 |
| GTCS | 1 | 5.3 | 6 | 30.0 | 4 | 21.0 | 3 | 15.8 | 1 | 4.0 |
| Total | 19 | 100.0 | 20 | 100.0 | 19 | 100.0 | 17 | 100.0 | 25 | 100.0 |

There was no statistically significant dependence among the epileptogenic lesions upon the age of the patients (Pearson Chi-square: 58.2962, df = 24, p = 0.000111).

Brain tumours as epileptogenic lesions were registered in the greatest per cent of 57.9% at the age of above 61 years of age.

Post-traumatic injuries as epileptogenic lesions were registered in the greatest per cent of 70.0% at the age of above 51 years of age.

Post-vascular injuries as epileptogenic lesions were registered in the greatest per cent of 94.7% at the age of above 61 years of age.

Post-infectious lesions as epileptogenic lesions were registered in the greatest per cent of 52.9% at the age of above 51 years of age.

Hippocampal sclerosis as epileptogenic lesions was registered in the greatest per cent of 53% at the age of under 40 years of age (Table 6).

Table 6

Distribution of patients according to age and epileptogenic lesions

| Epileptogenic lesions Age | <= 20 | 21-30yr | 31-40yr | 41-50yr | 51-60yr | 61-70yr | >= 71 | Total |
|------------------------------|-------|---------|---------|---------|---------|---------|-------|-------|
| Tumors | 1 | 0 | 2 | 1 | 4 | 9 | 2 | 19 |
| Post-traumatic | 0 | 1 | 2 | 3 | 5 | 5 | 4 | 20 |
| Post-vascular | 0 | 0 | 0 | 0 | 2 | 13 | 5 | 20 |
| Post-infectious | 1 | 1 | 3 | 3 | 5 | 3 | 1 | 17 |
| Hippocampal sclerosis | 2 | 3 | 8 | 9 | 2 | 0 | 0 | 24 |
| Total | 4 | 5 | 14 | 16 | 17 | 30 | 12 | 100 |

Simple partial crises were found in both genders in 50%.

Complex partial crises were found in male gender in 58.3%, while 41.7% were found in females; the percentage difference was statistically non-significant.

SPC + CPC were found in the male gender in 53.7%, and in 46.3% of female gender; the percentage difference was statistically non-significant.

CPC with secondary generalization was present in 64.3% males, and in 35.7% females; the percentage difference was statistically non-significant.

Absences were found in 50.0% in both genders.

GTCS were found in 60.0% of the male gender, and in 40.0% of the females; the percentage difference was statistically non-significant.

The greatest percentage of 39.9% fell to SPC + CPC in males, with 43.2% in the female gender (Table 7).

Table 7

Distribution of patients according to gender and type of epileptic seizures

| Epileptic seizures – types | Men | Women | Total |
|-----------------------------------|-----|-------|-------|
| Simple partial crises (SPC) | 5 | 5 | 10 |
| Complex partial crises (CPC) | 7 | 5 | 12 |
| SPC + CPC | 22 | 19 | 41 |
| CPC with secondary generalization | 9 | 5 | 14 |
| Absences | 4 | 4 | 8 |
| GTCS | 9 | 6 | 15 |
| Total | 56 | 44 | 100 |

There was no statistically significant dependence among the epileptogenic lesions upon the gender of the patients (Pearson Chi-square: 4.82640, $p = 0.305585$).

Brain tumors as epileptogenic lesions were registered in the greater percent of 52.6% of the males, and 47.4% of females.

Post-traumatic injuries as epileptogenic lesions were registered in the greater percent of 70.0% of the males, and 30.0% of females.

Post-vascular lesions as epileptogenic lesions were registered in the greater percent of 57.9% of the males, and 42.1% of females.

Post-infectious lesions as epileptogenic lesions were registered in the greater percent of 64.7% of the males, and 35.3% of females.

Hippocampal sclerosis as epileptogenic lesions was registered in the greater percent of 60.0% of the females, and 40.0% of males.

The greatest percentage of 25.0% fell to post-traumatic epileptogenic lesions, and 60.0% fell to hippocampal sclerosis as epileptogenic lesion in the female gender (Table 8).

Table 8

Distribution of patients according to gender and epileptogenic lesions

| Lesions/gender | Males | Females | Total |
|-----------------------|-------|---------|-------|
| Tumors | 10 | 9 | 19 |
| Post-traumatic | 14 | 6 | 20 |
| Post-vascular | 11 | 8 | 19 |
| Post-infectious | 11 | 6 | 17 |
| Hippocampal sclerosis | 10 | 15 | 25 |
| Total | 56 | 44 | 100 |

Discussion

The analysis of the results showed that the most frequent form of epileptic seizures in symptomatic epilepsies are simple partial seizures and complex partial seizures, while the least represented are absences as a type of seizure in this type of epilepsy.

Concerning the epileptogenicity, hippocampal sclerosis as the most epileptogenic was represented in the greatest percentage in relation to other lesions.

Hippocampal sclerosis is a very common feature of temporal lobe epilepsy (complex partial seizures or limbic epilepsy). It is found in approximately 50–75% of temporal lobe resections made for medically intractable limbic epilepsy [2].

The other lesions, such as the post-traumatic lesions, are found in approximately 20% while the infectious lesions (17%) were represented as epileptogenic in the lowest percentage.

Post-traumatic seizures often occur after severe head injury. The more severe the head injury, the more likely it is that post-traumatic seizures will occur.

Significant risk factors for the development of seizures within the first week are acute intra-cerebral haematoma (especially subdural haematoma), brain contusion, increased injury severity, and age > 65 years at the time of injury [3, 4].

Infections are a frequent cause for the occurrence of seizures. Different types of infections can cause epileptic seizures at all ages. The prevalence of the infection's development is lower in developed countries compared with poor ones.

There was no statistically significant dependence between the epileptogenic lesions and the type of the seizures.

Concerning the type of seizure in each lesion, it was found that SPS + CPS were mostly represented as a type of seizure: in brain tumours 31.6% had SPC + CPS, while in the least percent GTCS, in the post-traumatic lesions, 35% presented SPS + CPS, 30% GTCS (generalized tonic-clonic seizures) and in the least percent SPS. Post-vascular lesion of 36,8% had SPS + CPS and absences in the least percent.

Post-infectious lesions were found in the greatest percentage in SPC + CPS and in the least percentage with secondary generalization, in hippocampal sclerosis SPS + CPS were found in 48%, and only 4% had GTCS.

Seizure is often the first clinical symptom of a brain neoplasm, especially in cases of low-grade neoplasms. Seizures caused by brain tumours, as with any focal lesion, will be of partial or focal onset. As such, they can cause a variety of symptoms for the patient. The symptoms and behaviour of the patient during the seizures is determined by the area of cortex involved [5, 6].

Cerebrovascular disease is the most common cause of seizures in the elderly, and partial and complex partial seizures (CPS) are the most common seizure type in this age group [7].

The mean age of the patients was 53.8 ± 15.9, 56 (56%) were men and 44 (44%) women, the percentage difference was statistically non-significant for $p > 0.05$, it was a homogenous group according to gender.

There was statistically a non-significant dependence among the epileptogenic lesions with the age of the patients (Pearson Chi-square: 58.2962, $df = 24$, $p = 0.000111$).

The most common tumours found to produce seizures in later life are gliomas, meningioma and metastases [8, 9]. Older people with cerebral tumours are less likely than younger patients to present with seizures, but age is a risk factor for increased mortality in people who do develop seizures [10].

Trauma is common in old age. Older people are more likely than younger patients to develop post-traumatic epilepsy.

Underlying abnormalities such as infarctions, neoplasms and vascular malformations can be identified in 80% of causes with magnetic resonance imaging [11].

Brain tumours as epileptogenic lesions were found in the greatest percentage of 57.9% at an age above 61.

Post-traumatic injuries as epileptogenic lesions were found in the greatest percentage of 70.0% at an age above 51.

Post-vascular lesions as epileptogenic lesions were found in the greatest percentage of

94.7% at an age above 61. Post-infectious lesions as epileptogenic lesions were found in the greatest percentage of 52.9% at an age above 51.

Head trauma, infections of the central nervous system and tumours may occur at any age and may lead to the development of epilepsy. Infections of the central nervous system have one of the highest risks for causing epilepsy [12, 13]. For instance, over three-quarters of the survivors of cerebral abscess develop severe epilepsy and survivors of viral encephalitis have an odds ratio of 16 : 2 for the development of epilepsy [13].

Cerebrovascular disease is the single most common pathological factor underlying epilepsy in elderly patients [14, 15].

Hippocampal sclerosis as epileptogenic lesions were found in the greatest percentage of 53% at an age under 51.

The 65% prevalence of hippocampal sclerosis arose from mesial temporal epilepsy, and developed in late childhood, equally in the male and female genders [16].

There was a statistically non-significant dependence among the epileptogenic lesions with the gender of the patients (Pearson Chi-square: 0.868205, $p = 0.972480$), as well as a statistically non-significant dependence between the epileptogenic lesions upon the gender of the patients (Pearson Chi-square: 4.82640, $p = 0.305585$).

Conclusion

Association of the seizure type with the MRI finding detects the epileptogenic focus in symptomatic epilepsies which should be the leading factor for its further regular management.

Post-traumatic lesions occur more frequent in the elderly population with the accent on the male, while hippocampal sclerosis occurs in the adolescent and younger population with the accent on the female.

As to the seizures, simple partial seizures and complex partial seizures were more frequently represented.

This investigation will enable an initial pre-surgical evaluation of symptomatic epilepsies for their further regular therapeutic stra-

tegy, and, at the same time, prevention of psycho-social inability in refractory epilepsies.

REFERENCES

1. Sander JW. The epidemiology of epilepsy revisited. *Current Opinion in Neurology*. 2003; 16: 165–170.
2. Honavar M, Meldrum BS. Epilepsy. In: Graham DI, Lantos PL, editors. *Greenfield's Neuropathology*. 6th ed. London: Arnold. 1997; pp. 931–71.
3. Frey LC. Epidemiology of posttraumatic epilepsy: a critical review. *Epilepsia*. 2003; 44 Suppl 10: 11–7.
4. Temkin NR. Causes, prevention, and treatment of post-traumatic epilepsy. *New Horiz*. 1995; 3: 518–22.
5. Hesdorffer DC, Chapter 6: Risk Factors in Epilepsy: A Comprehensive Textbook, Vol. 1, J. Engel and T.A. Pedley, eds. 2008; 57–63.
6. Recht JD, and Glantz M. Chapter 264: Neoplastic Diseases in Epilepsy: A Comprehensive Textbook, Vol. 2, J. Engel and T.A. Pedley, eds. 2008; 2637–42.
7. Cepreganova Cangovska T, Lazarova S, Tarvari A, Stojcev S. Symptomatic epilepsy in the elderly. *Acta Morphologica*. 2011; Vol. 8(1): 86–89.
8. Roberts M, Godfrey J. Epileptic seizures in the elderly: etiology and type of seizure. *Age Ageing*. 1982; 11: 24–28.
9. Sundaram MB. Etiology and patterns of seizures in the elderly. *Neuroepidemiology*. 1989; 8: 234–38.
10. Smith D, Hutton J, Sandemann D, et al. The prognosis of primary intracerebral tumors presenting with epilepsy: the outcome of medical and surgical management. *J Neurol*. 1991; 54: 915–20.
11. Thomas R. Seizures and epilepsy in the elderly. *Arch Intern Med*. 1997; 157: 605–17.
12. Hauser WA, Annegers JF. Risk factors for epilepsy. *Epilepsy Research Supplement*. 1991; 4: 45–52.
13. Annegers JF, Rocca WA, Hauser WA. Causes of epilepsy: contributions of the Rochester epidemiology project. *Mayo Clinic Proceedings*. 1996; 71: 570–575.
14. Sander JW, Hart YM, Johnson AI, Shovron SD. National general practice study of epilepsy: newly diagnosed epileptic seizures in a general population. *Lancet*. 1990; 336: 1267–71.
15. Roberts M, Godfrey J. Epileptic seizures in the elderly: etiology and type of seizure. *Age Ageing*. 1982; 11: 24–28.
16. Panayiotopoulos CP, MD, PhD, FRCP. Mesial temporal lobe epilepsy with hippocampal sclerosis. The educational kit on epilepsies. In: *The epileptic syndromes*. 2008; Originally published by MEDICINAE 21 Cave Street, Oxford OX4 1BA

Резиме

СИМПТОМАТСКИ ЕПИЛЕПТОГЕНИ ЛЕЗИИ

Татјана Чепреганова-Чанговска¹,
Драгана Петровска-Цветковска¹,
Марија Јовановски-Срцева², Венко Филипче³

¹ Универзитетска клиника за неврологија,
Медицински факултет, Универзитет
„Св. Кирил и Методиј“, Скопје,
Р. Македонија

² Универзитетска клиника
за анестезиологија, реанимација
и интензивна нега, Медицински факултет,
Универзитет „Св. Кирил и Методиј“, Скопје, Р.
Македонија

³ Универзитетска клиника за неврохирургија,
Медицински факултет, Универзитет
„Св. Кирил и Методиј“, Скопје, Р. Македонија

Цел: Главна цел на ова испитување е да се докаже поврзаноста на видот на нападите со наодот од нуклеарна магнетна резонанција на мозокот (етиолошкиот фактор). Исто така и да се докаже во која старосна група кој тип лезија е најзастапена и со каков вид напади.

Материјал и методи: Евалуирани се 100 пациенти со симптоматска епилепсија на

возраст од 16 до 80 години, хоспитализирани или амбулантски водени на Клиниката за неврологија. Пациентите се невролошки испитани и се регистрирани типовите напади. Кај сите пациенти е реализирана НМР на мозокот.

Резултати: Беа испитувани 56 мажи (56%) и 44 жени (44%). Испитувани се видовите епилептични напади (кризи): кај 41,0% ЕПК + КПК, потоа следува со 15,0% ГТКН, со 14,0% КПК со секундарна генерализација, со 12,0% КПК, со 10,0% ЕПК и со 8,0% апсанси.

Во испитуваната група се застапени епилептогени лезии со 25,0% хипокампадна склероза, останатите епилептогени лезии се застапени со 20,0% посттравматски повреди, со 19,0% постваскуларни и тумори на мозокот и со најмал процент 17,0% постинфективни лезии.

Заклучок: Посттравматските лезии се најчести епилептогени симптоматски лезии кај постарата машка популација, додека кај помладата популација (доцно детство) и адолесцентите е застапена хипокампадна склероза како епилептоген фактор. Едноставните парцијални напади и комплексните парцијални напади се најчести типови напади кај симптоматската епилепсија.

Клучни зборови: симптоматска епилепсија, епилептични напади, епилептогени лезии.