Arq Neuropsiquiatr 2003;61(4):942-945

# CORPORA AMYLACEA IN TEMPORAL LOBE EPILEPSY ASSOCIATED WITH HIPPOCAMPAL SCLEROSIS

*Marlise de Castro Ribeiro, Lígia Barbosa-Coutinho, Fabiana Mugnol, Arlete Hilbig, André Palmini, Jaderson Costa da Costa, Eliseu Paglioli Neto, Eduardo Paglioli*

ABSTRACT - Hippocampal sclerosis (HS) is the commonest pathology in epileptic patients undergoing temporal lobe epilepsy surgery. Beside, there are an increased density of *corpora amylacea* (CA) founded in 6 to 63% of those cases. *Objective*: verify the presence of CA and the clinical correlates of their occurrence in a consective series of patients undergoing temporal surgery with diagnosis of HS. *Method*: We reviewed 72 hippocampus specimens from January 1997 to July 2000. Student's t test for independent, samples, ANOVA and Tukey test were performed for statistical analysis. *Results*: CA were found in 35 patients (49%), whose mean epilepsy duration (28.7 years) was significantly longer than that group of patients without CA (19.5 years, p= 0.001). Besides, when CA were found, duration was also significantly correlated with distribution within hippocampus: 28.7 years with diffuse distribution of CA, 15.4 with exclusively subpial and 17.4 years with distribution subpial plus perivascular (p= 0.001). *Conclusion*: Our findings corroborate the presence of CA in patients with HS and suggest that a longer duration of epilepsy correlate with a more distribution of CA in hippocampus.

KEY WORDS: hippocampal sclerosis, corpora amylacea, temporal lobe epilepsy.

**Corpos amiláceos associados à esclerose hipocampal na epilepsia do lobo temporal**

RESUMO - A esclerose hipocampal (EH) é a patologia mais observada em lobectomias temporais de pacientes com epilepsia intratável. Além dos achados histopatológicos clássicos existe a presença de corpos amiláceos (CA) em até 60% dos hipocampos ressecados. *Objetivo:* Verificar a presença de corpos amiláceos em hipocampos de pacientes submetidos a cirurgia para tratamento de epilepsia e verificar se havia diferenças clínicas entre pacientes que apresentavam CA e aqueles em que eles não foram encontrados. *Método*: Foram revisados 80 hipocampos ressecados entre janeiro de 1997 a dezembro de 2000 e, posteriormente, os prontuários de 72 dos pacientes. Foi realizado o teste t de Student para amostras independentes, ANOVA e posteriormente o teste de Tukey. *Resultados*: Dos setenta e dois pacientes estudados, 40 eram homens (55,6%) e trinta e dois mulheres (44,4%). Trinta e cinco (48,6%) apresentavam CA e em trinta e sete (51,4%) não foram encontrados. Houve diferença estatisticamente significativa entre a média de tempo de evolução da epilepsia: o grupo com CA apresentava tempo maior de evolução (28,97 anos) em relação ao grupo que não apresentava CA (19,54 anos), com p= 0,001. Também observou-se diferença significativa quando foi comparada a localização de corpos amiláceos com o tempo de evolução da epilepsia: os pacientes com CA presentes difusamente no hipocampo apresentavam maior tempo de epilepsia (p= 0,001). *Conclusão*: Observamos que o nosso estudo confirma a presença de corpos amiláceos em hipocampos de pacientes com EH e sugerimos que quanto maior o período de epilepsia maior é a distribuição de CA no hipocampo

PALAVRAS-CHAVE: esclerose hipocampal, corpora amylacea, epilepsia de lobo temporal.

Hippocampal sclerosis (HS) is the commonest histopathological substrate in epileptic patients undergoing temporal lobe epilepsy (TLE) surgery[1]. Characteristic features include neuronal loss in Ammon's horn fields CA1, CA3 and CA4, with relative sparing of neurons in CA2 and in the subiculum[2], associated with axodendritic reorganization. In addition, hippocampal tissue resected in patients with TLE have an increased density of *corpora amylacea* (CA), reported to be found in 6 to 63% of the cases[3-6]. These are spherical, basophilic structures which normally accumulate in perivascular and subpial regions of the central nervous system as a result of aging[7-9]. However, although CA are seen in the context of neurodegenerative disorders[2,3,8], their pathogenic mechanisms and other factors related to their occurrence are still largely ignored[6,8-10].

Porto Alegre Epilepsy Surgery Program, Hospital São Lucas da Pontificia Universidade Católica (PUC), Porto Alegre RS, Brazil.

Received 26 February 2003, received in final form 7 July 2003. Accepted 18 July 2003.

*Dra. Arlete Hilbig - Rua Quintino Bocaiuva 283 / 401 - 90440-051 Porto Alegre RS - Brasil.*

We have been systematically examining hippocampal tissue of epileptic patients undergoing surgery for TLE in the last 10 years[11]. Thus, we decided to study both the presence of CA and the clinical correlates of their occurrence in a consecutive series of patient undergoing temporal lobe surgery with hippocampal resection in more recent years.

## METHOD

We reviewed the histopathological findings for the presence of CA in 88 consecutive hippocampal specimens in which a diagnosis of HS had been previously established[11]. Tissue was resected as part of the surgical treatment of patients with refractory TLE, from January 1997 to July 2000. All patients underwent comprehensive preoperative evaluation as previously reported[12]. We excluded 16 patients with dual pathology (5 patients), from those with more than 60 years of age (3 patients) and also incomplete medical records (8 patients). Histopathological analysis of 72 hippocampal specimens consisted of neuronal loss and gliosis for diagnosis of HS at least in CA1 and CA were characterizaded morphologically: spherical, laminated,

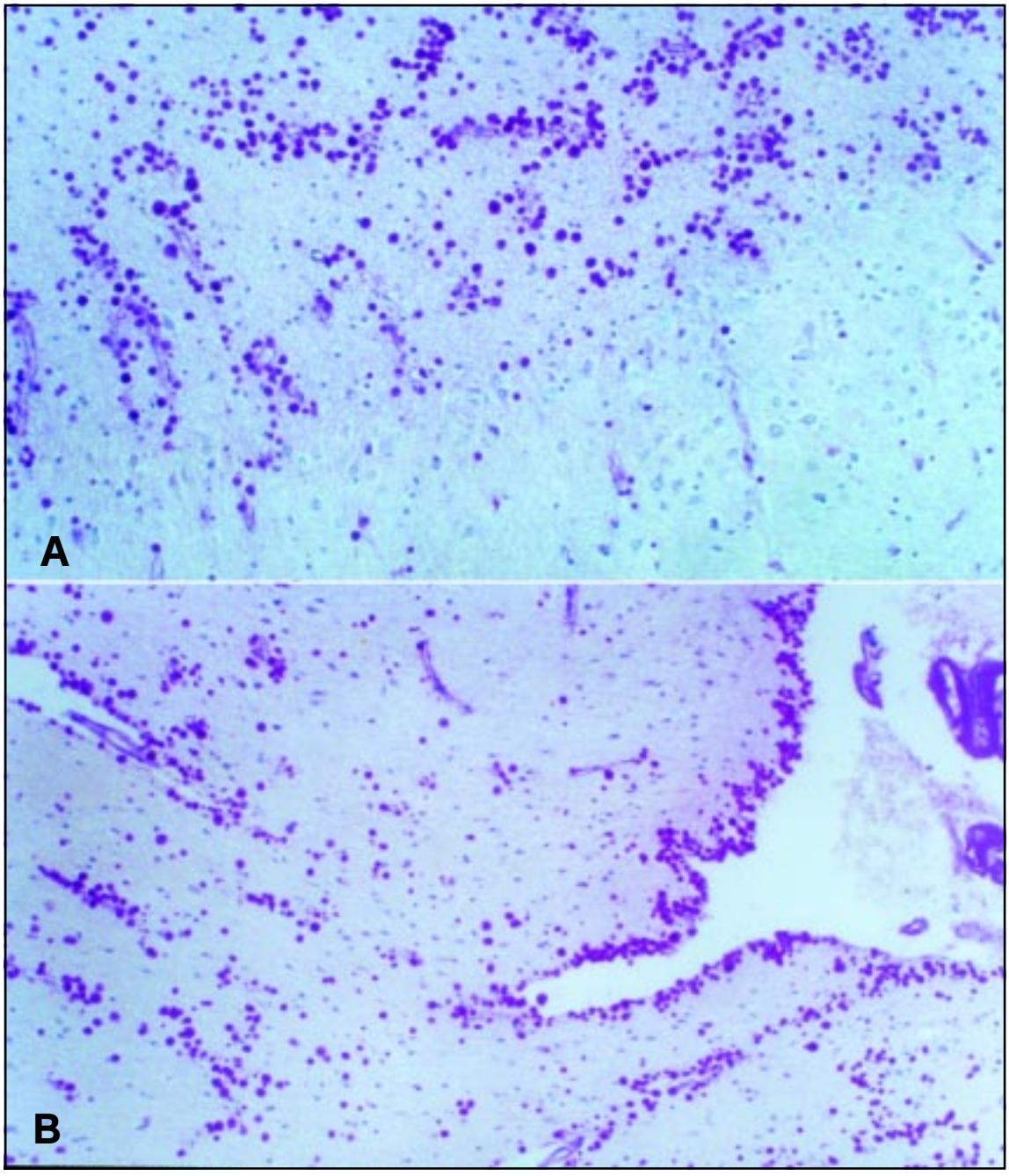


*Fig 1. a) Diffuse distribution of CA in hippocampus (PAS, objective 20X). b) CA in subpial and perivascular through PAS stain (obj 20X).*

*Table 1. Mean epilepsy duration was significantly longer on the group of patients with CA and the demonstration of others studied variables.*

| Variables | Total | With CA | Without CA |
|---|---|---|---|
| Total | 72 | 35 | 37 |
| Men | 40 | 18 | 22 |
| Women | 32 | 17 | 15 |
| Age at seizure onset (mean) | 6,71 | 6,04 | 7,34 |
| Age at operation (mean) | 32,81 | 35,42 | 28,01 |
| Duration of epilepsy (years)* | 24,13 | 28,97 | 19,54 |
| Seizure frequency/annual (mean) | 464,63 | 490,85 | 425,72 |
| Previous Status | 0 | 0 | 0 |
| Generalization secondary | 12 | 7 | 5 |

* p= 0,001

hyaline bodies, stained with periodic-acid-Shiff (PAS) and Groccot (Fig 1a and 1b).

Following the analysis of the histopathological material, the medical records were reviewed to collect data on sex, age at seizure onset, age at operation, preoperative duration of the epileptic disorder, approximate annual preoperative seizure frequency, previous episodes of status epilepticus, and the occurrence of secondary generalization of the complex partial seizures (Table 1). For analysis of the data, the patients were then grouped on the basis of the presence or absence of CA. The group of patients whose hippocampi displayed CA was further subdivided according to their intrahippocampal localization into those in whom CA were observed (i) diffusely in the hippocampus, (ii) only in the subpial region, (iii) and in both the subpial and perivascular regions (Table 2). A SPSS software package (SPSS Inc, Chicago, IL, USA) was used to perform statistical calculations. Student's t test for independent samples were applied to compare possible differences between groups. In addition, the three subgroups of patients harboring CA were compared through analysis of variance (ANOVA) and the Tukey test.

## RESULTS

Forty of the 72 patients (56%) were male. Age at recurrent seizure onset ranged from 1 to 30 years (mean, 6.7) and preoperative epilepsy duration varied between 3 and 58 years (mean, 24.1). CA were found in 35 patients (49%), whose mean epilepsy duration (28.9 years) was significantly longer than that from the group of patients without CA in the hippocampus (19. 5 years, p = 0.001). Furthermore, when CA were found, epilepsy duration was also significantly correlated with their distribution within the hippocampus. Mean duration of epilepsy was 22.7 years in patients with a diffuse distribution of the CA, while those with exclusively subpial or subpial plus perivascular distribution had seizures for a mean of 15.4 and 17.4 years before operation (p=0.001, Table 2). In contrast, gender, age at seizure onset, age at operation, seizure frequency, history of status epilepticus and occurrence of secondary generalization did not significantly differ between the groups (Table 1).

*Table 2. Distribuition of CA within the hippocampus subdivided in three groups,its frequences and mean epilepsy duration.*

| Distribuition of CA | Frequence | Mean epilepsy duration (years) |
|---|---|---|
| Total | 35 | 28,97 |
| Hippocampus | 16 (22,2%) | 22,7 |
| Subpial | 9 (12,5%) | 15,4 |
| Subpial And Perivascular | 10 (13,9%) | 17,4 |

* p= 0,001

## DISCUSSION

CA are roughly round, laminated, structures composed of glucose polymers and a plethora of different proteins, including heat shock proteins (HSP). They usually originate within astrocytic processes, although neuronal and oligodendroglial origins have occasionally been reported[13,14]. The presence of CA in the resected hippocampus of patients with TLE undergoing surgery has been recently reported by different groups[2,4,9,15]. Likewise, Loiseau and

colleagues[5] reported abundant CA in the subcortical white matter of a woman operated for refractory CA in similar series of patients, all showing that about half the patients have these structures in the resected sclerotic hippocampus[4,6] . Furthermore, the lack of correlation between the presence of CA and most epileptic variables like age of seizure or age at operation was also previously reported[16]. In contrast with the latter study from Belgium however, we actually found that epilepsy duration was significantly related to the presence of CA, which may be a pathogenically relevant finding.

Despite their common occurrence in sclerotic hippocampi, the pathogenesis of CA is largely ignored, despite reports suggesting that HSP[9,17] or some proteins of the S100 family may be involved[18]. Erdamar and colleagues[9] reported a significant increase of an HSP subtype in tissue resected form patients with TLE, but the abnormal protein accumulated outside the CA. Studying non-epileptic tissue, Botez et al.[8] found abundant CA in the hippocampi and dentate gyri of patients with a history of recurrent episodes of cerebral hypoxemic insults. They suggested that the genesis of CA may be part of a tissue reaction to buffer the accumulation of free radicals and other potentially damaging elements resulting from metabolic derangements secondary to repeated cellular stresses during life. Our finding of a significantly higher occurrence of CA in the hippocampus of exactly those patients who experienced recurrent seizures for longer periods before surgery support this metabolic hypothesis of the genesis of CA. In addition, we showed that a longer duration of epilepsy significantly correlated with a more diffuse distribution of CA in the resected hippocampi, which also suggest that repeated insults may play a role in the generation of these structures. If our findings are independently confirmed, they add another potential metabolic reason to the growing body of evidence suggesting that early rather than late surgery for medically refractory TLE may achieve better overall results.

**Acknowledgements -** To statistic Alan Birck.

## REFERENCES

1. Babb TL, Brown WJ. Pathological findings in epilepsy. In Engel J Jr (ed), Surgical treatment of the epilepsies. New York: Raven Press, 1986,511-540.
2. Shingrao SK, Neal JW, Newman GR. Corpora amylacea could be indicator of degeneration. Neuropathol Appl Neurobiol 1993;19:269-276.
3. Cavanagh JB. Corpora amylacea and the family of polyglucosan diseases. Brain Res Rev 1999;29:265-295.
4. Chung MH, Horoupian DS. Corpora amylacea: a marker for mesial temporal sclerosis. J Neuropathol Exp Neurol 1996;55:403.
5. Loiseau H, Marchal C, Vital A, et al. Ocurrence of polyglucosan bodies in temporal lobe epilepsy. J Neurol Neurosurg psychiatry 1992;55:1092-1093.
6. Nishio S, Takato M, Tadao K, Kimiko F, Hiroki N, Matsushima M. Corpora amylacea replace the hipocampal pyramidal cell leyer in patient with temporal lobe epilepsy. Epilepsia 2001;42:960-962.
7. Graham D, Lantos P. Greenfield's neuropathology. 6.Ed., New York: Arnold 1997:1:124.
8. Botez G, Rami A. Imunorreactivity for Bcl-2 and C- Jun / AP1 in hipocampal corpora amylacea after ischaemia in humans. Neuropathol Appl Neurobiol 2001;27:474-478.
9. Erdamar S, Zhu ZQ, Hamilton WJ, et al. Corpora amylacea and heat shock protein 27 in Ammon's horn sclerosis. J Neuropathol Exp Neurol 2002;59:698-706.
10. Radhakrishnan VV. Bhaskara R, Radhakrishnan SV, et al. Pathology of temporal lobe epilepsy: an analysis of 100 consecutive surgical specimens from patients with medically refractory epilepsy. Neurology India 1999;47:1150-1157.
11. Barbosa-Coutinho LM, Hilbig A, Calcagnotto ME, et al. Neuropatologia das epilepsies de difícil controle: estudo de 300 casos consecutivos. Arq Neuropsiquiatr 1999;57:405-414.
12. Palmini A, da Costa JC, Paglioli- Neto E. How to select the best surgical strategy for patients with temporal lobe epilepsy. In Lüders H, Comair Y (eds). Epilepsy surgery 2.Ed. New York: Lippincott Raven, 2000:675-687.
13. Shingrao KSK, Morgan BP, Neal JW, Newman GR. A functional role for corpora amylacea based on evidence from complementary studies. Neurodegeneration 1995;4:335-345.
14. Shingrao SK, Neal JW, Piddleslen SJ, Newman GR. New immmunocytochemical evidence for a neuronal / oligodendroglial origin for corpora amylacea. Neuropathol Appl Neurobiol 1994;20:66-73.
15. Leal Õssyl. Corpora amylacea in hipocampal sclerosis (correspondence). J Neurol Neurosurg Psychiatry 1998;65:614.
16. Van Paesscchen W, Revesz T, Duncan JS. Corpora amylacea in hipocampal sclerosis. J Neurol Neurosurg Psychiatry 1997;63:513-515.
17. Gati I, Leel-Ossy L. Heat shock protein 60 in corpora amylacea. Pathol Oncol Res 2001;7:140-144.
18. Hoyaux D, Decaestecker C, Heizmann CW,et al. S100 proteins in corpora amylacea from normal human brain. Brain Res 2000;867:280-288.