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HIGHLIGHTING BRAIN ANATOMICAL CHANGES IN ALCOHOL ABUSE AND DEPENDENCE

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The aim of this paper is to study some cases by calculating the different cerebral parameters by which the brain indexes used in radiology for quantification of cortical atrophy were estimated in the context of chronic alcoholism.
Materials and Method: In the descriptive study, six patients aged 60 years or over, known as alcohol addicts and with at least one withdrawal episode in history, with ethanol consumption of over 40–80 grams per day for more than ten years. Information was obtained based on approximately 80 computed tomography images, including those of the case control. To measure the brain diameters underlying index calculation, the Radiant Dicom Viewer program, specific to this type of radiology measurement, was used. To carry out the study, the ethics of medical research were taken into account, the results of tomographic computer imaging being obtained with the consent of the patients and the radiologist.
Results: The presented cases are compared with the results of a single reference index. In the series of cases I have shown, there are noticeable results of framing within the ranges that demonstrate the presence of cortical atrophy. To demonstrate the cortical atrophy and its degree, it is not necessary for all the clues to have the same results concurrently, and they can be corroborated.
Conclusions: From the cases here shown, it appears that cortical atrophy is present and is the consequence of prolonged alcohol consumption in the context of alcohol dependence. It would be useful for a future study to compare a much more significant sample of patients by dividing them into several categories.

Keywords: alcoholism, cortical atrophy, computed tomography, brain diameters.

INTRODUCTION

With the debut of DSM-III, alcoholism splits conceptually into two entities: alcohol abuse and addiction syndrome. Alcohol abuse implies pathological consumption with social and professional maladaptive consequences, but without the tolerance and withdrawal side effects. The dependency syndrome involves the physiopathological existence of tolerance and withdrawal. Only 10–15% transgress from alcohol abuse to addiction. Besides the difficulty of defining alcoholism from a nosological point of view, there is also a great variability in determining the level of alcohol consumed per day considered to be harmful for an individual. A quantitative definition can only be variable, and today's consensus considers harmful a consumption of 40-80grams of pure alcohol/day. Also, genetic predisposition has been incriminated over time to varying degrees. Currently, the risk of becoming a chronic alcoholic is believed to be due to 60% of the genetic predisposition, and the rest is the interaction between the genetic entity and the influences of the environment.[1]

The risk of chronic alcoholism throughout life is 10–15% for men and 2–5% for women, with a prevalence of 6% per year for both categories. The average age associated with the highest risk of developing addiction is between 20 and 40 years of age, and, like other psychiatric disorders, the more a person becomes addicted earlier in his life, the more severe the evolution. The onset of addiction after 40 years of age, although most often with fewer signs and symptoms than in young people, is more likely to develop another pathology correlated with alcoholism as a risk factor.[2]

This paper aims to analyzea series of cases by calculating the different brain parameters, with cerebral indices used in radiology, for quantification of cortical atrophy. The study contains the interpretation and measurement of approximately 80 computer tomography images via *Radiant DicomViewer*. The data obtained has confirmed the presence of cortical atrophy in the context of chronic alcoholism, eliminating as far as possible the influence of age, so that each patient was under 60 years of age. The indices were compared with values obtained on larger samples from external reference studies. It shows that the presence of cortical atrophy is invariably a consequence of chronic alcoholism when age influence is excluded and correlates with specific changes in organs and behaviour.

MATERIALS AND METHODS

In this descriptive study, six patients were known to be alcohol-addicted. Each had at least one withdrawal episode in the past, with a consumption of over 80 grams of ethanol per day for more that ten years. To conduct the study, the ethics of medical research were taken into account, the results of computer tomograph imaging being obtained with the consent of the patients and the radiologist.

The following criteria for patient selection have been met. Inclusion criteria:

– an ethanol consumer without co-morbidity;

– a consumption of over 80 grams of ethanol per day over ten years; aged 40–64; the presence of at least one withdrawal episode in the past. Exclusion criteria: the presence of comorbidities (cardiovascular disease, liver cirrhosis, etc.), age over 64 (age-related cortical atrophy would interfere with the outcome of the results).

Information was obtained based on approximately 80 computed tomography images, including those of the case control. The CT was performed in the "Victor Babeş" Diagnostic and Treatment Center.

To measure the brain diameters underlying the index calculation, the Radiant Dicom Viewer program was used, specific to this type of radiology measurement.

The most critical changes in cerebral structure in chronic alcoholism are those of cortical atrophy, closely related to alcoholic dementia and corpus collosum atrophy. It is a well-known fact that cortical atrophy is closely related to the age of the individual, which makes the changes in brain structure to be best studied in adults under 64 years of age. The pathogenesis of atrophy is multifactorial, and there was a certain reversibility, albeit insignificant, following abstinence. Factors influencing the pathogenesis are cerebral ischemia, changes in vascular structure in the brain, the total amount of inhaled ethanol, smoking, a person's sex, the presence of liver disease, especially liver cirrhosis, and the nutritional status. The following parameters are used to determine the degree of cortical atrophy, as shown in the figure:

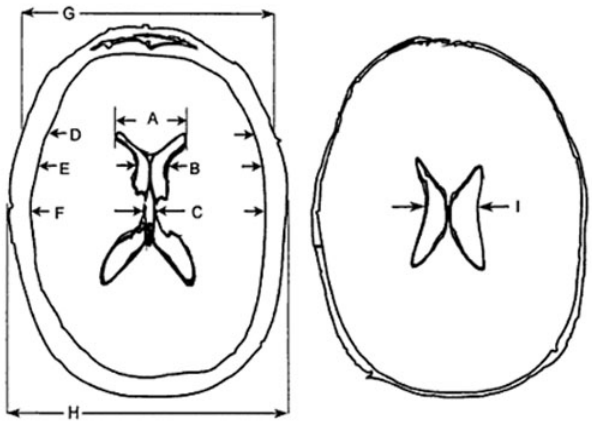

Fig. 1 – Parameters are used to determine the degree of cortical atrophy.
A = the maximum width between the front horns of the lateral ventricles; B = the minimum width of the lateral ventricle at the head of the caudal nucleus; C = maximum ventricular width; D = internal diameter of the skull in the front horns; E = internal diameter of the head at the head of the kernel; F = maximum internal diameter of the skull; G = the external diameter of the skull in the frontal horns; H = the maximum (biparietal) outer diameter of the skull; I = minimum width of lateral septum ventricles (main part - cella media).

Based on the parameters measured by CT, the following indices are calculated:

– the *bifurcate index* (A/D) = the maximum width between the frontal corners of the lateral ventricles relative to the inner diameter of the skull at the same level as the front horns

– the *bicaudate index* (B/E) = minimum width of the lateral ventricle at the head of the kernel nucleus relative to the internal diameter of the skull in the head of the caudal nucleus.

– the cella media (H/I) = maximum external diameter of the skull (biparietal) about the minimum width of lateral septum ventricles (main part - cella media). A normal index is over 4.

– the *Evans index* (A/F) = the maximum width between the front horns of the lateral ventricles relative to the central maximum of the skull.

– the *ventricular index* (B/A) = minimal lateral ventricular width at the head of the core nucleus

relative to the maximum amplitude between the frontal cortices of the lateral ventricles

– the *Huckman number* (B + A) = the minimum width of the lateral ventricle at the head of the caudal nucleus gathered with the maximum amplitude between the frontal cortices of the lateral ventricles

– *cortical atrophy* = the sum of the widths of the farthest four swaths from the last two upper scanning levels relative to the inner maximum of the skull (F).

Data used as a reference for fitting own measurements can be found in Valdecasas-Campelo EG *et al*. These are part of a 2007 study of 36 subjects, chronic ethanol consumers, and the results obtained have statistical significance to allow reporting.[3]

Table 1

Brain antrophy indices in cirrhotics, non-cirrhotics and controls

Brain atrophy indices in cirrhotics, non-cirrhotics and controls

	Evans	Bicauda	Cella	Bifront	Ventric	Huckma	Cortical
Cirrhotics (1)	0.35 ± 0.11	0.17 ± 0.04	4.13 ± 1.07	0.37 ± 0.07	0.46 ± 0.19	0.56 ± 0.11	0.07 ± 0.02
Non-cirrhotics (2)	0.30 ± 0.06	0.20 ± 0.05	3.56 ± 0.59	0.34 ± 0.07	0.60 ± 0.16	0.52 ± 0.13	0.07 ± 0.03
Differences (1,2)	$T = 1.63$, $P = 0.11$	$T = 1.90$, $P = 0.07$	$T = 2.03$, $P = 0.05$	$T = 1.11$, $P = 0.28$	$T = 2.13$, $P = 0.04$	$T = 0.82$, $P = 0.42$	$T = 0.19$, $P = 0.85$
Controls (3)	0.25 ± 0.05	0.13 ± 0.03	4.92 ± 0.75	0.28 ± 0.05	0.48 ± 0.1	0.37 ± 0.07	0.02 ± 0.01
Differences (1,2,3)	$F = 3.42$, $P = 0.042$	$F = 11.26$; $P < 0.001$	$F = 13.44$; $P < 0.001$	$F = 4.48$, $P = 0.017$	$F = 3.98$; $P = 0.026$	$F = 9.19$; $P < 0.001$	$F = 21.68$; $P < 0.001$

Table 2

Brain antrophy indices in pathients with CT scans informed as having or not having cortical antrophy

Brain atrophy indices in patients with CT scans informed as having or not having cortical atrophy

	Evans	Bicauda	Cella	Bifront	Ventric	Huckma	Cortical
Cortical atrophy	0.31 ± 0.05	0.20 ± 0.05	3.58 ± 0.73	0.36 ± 0.06	0.59 ± 0.17	0.54 ± 0.13	0.07 ± 0.02
No cortical atrophy	0.31 ± 0.08	0.19 ± 0.04	3.85 ± 0.91	0.35 ± 0.09	0.53 ± 0.22	0.54 ± 0.12	0.05 ± 0.02
	$T = 0.20$, $P = 0.98$	$T = 0.54$; $P = 0.59$	$T = 0.93$; $P = 0.36$	$T = 0.44$; $P = 0.66$,	$T = 0.80$; $P = 0.43$	$T = 0.03$; $P = 0.98$	$T = 2.40$; $P = 0.023$

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In the case control, we used, at first instance, measurements and parameters from a healthy patient, to serve as a comparison, a 58-year-old man, without cortical atrophy.

Data obtained from CT images for the case control: A = 2.88 cm; B = 0.974 cm; C = 0.674 cm; D = 10.04 cm; E = 10.37 cm; F = 12.77 cm; G = 13.11 cm; H = 15.13 cm; I = 1.572 cm.

From these, the following indices are calculated, based on which a normal size brain is identified without cortical atrophy. Values are compared to those in the study, shown in Table-1 and Table-2.

– the Evans index = 0.255, the bicaudate = 0.093; the cella media index = 9.625; thebifrontal index = 0.286; the ventricular index = 0.338; the Huckman number = 3,854

Compared to this normal baseline case, measurements were obtained for six alcohol-dependent patients.

First case: 55-year-old patient, early alcohol consumption from 17 years old.

Indices: A = 3.5 cm; B = 2.63 cm; D = 11.23 cm; E = 11.48 cm; F = 12.86 cm; G = 13.11 cm; H = 13.79 cm; I = 3.01 cm

And: the Evans index = 0.272; the bicaudate index = 0.229; the cella media index = 4.58; the bifrontal index = 0.311; the ventricular index = 0.751; the Huckman number = 6.13.

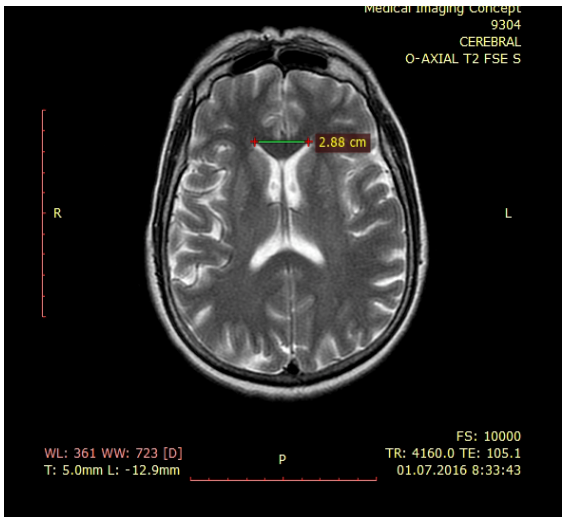

Figure 2. The maximum width between the frontal horns of the lateral ventricles.

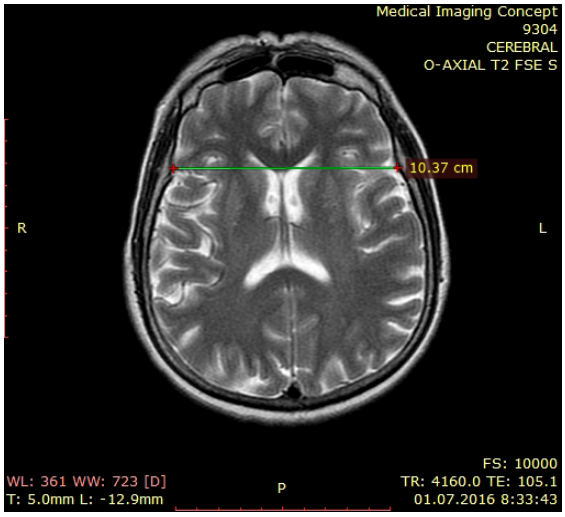

Figure 3. Half the minimum width of the lateral ventricle at the head of the kernel core.

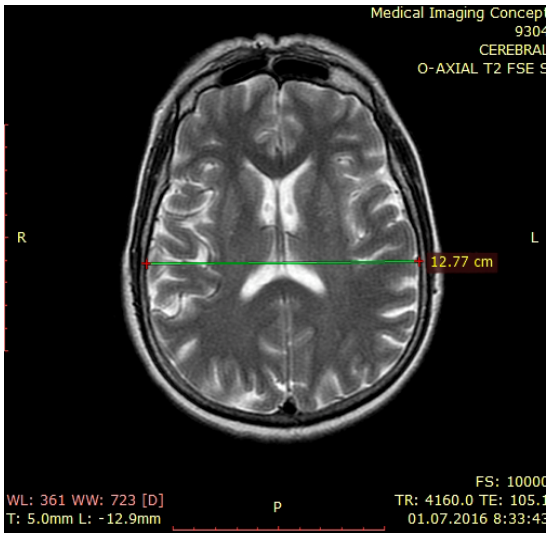

Figure 4. The internal diameter of the skull in the front horns.

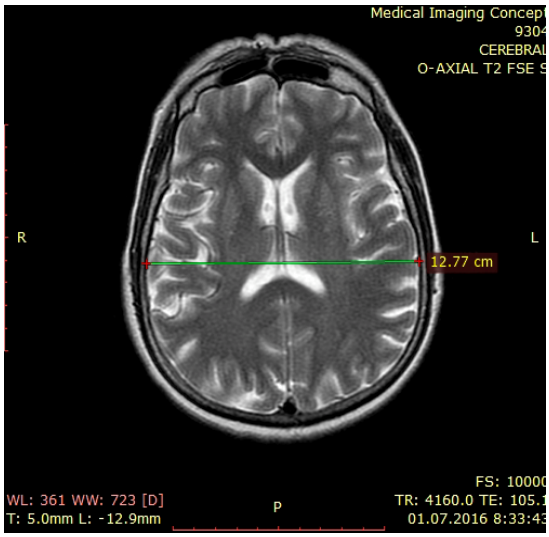

Figure 5. Maximum internal diameter of the skull.

Second case: 60-year-old male, 23-year-old chronically ill: A = 3.75 cm; B = 2.75 cm; D = 10.44 cm; E = 10.96 cm; F = 11.2 cm; G = 12.90 cm; H = 12.13 cm; I = 3.41 cm.

The calculated parameters: the Evans index = 0.334; the bicaudate index = 0.250; the cella media index = 3.557; the bifrontal index = 0.359; the ventricular index = 0.733; theHuckman number = 6.5.

Third case: 59-year-old male, 32-year-old chronically ill: A = 3.39 cm; B = 1.75 cm; D = 10.93 cm; E = 11.41 cm; F = 12.57 cm; G = 12.81 cm; H = 13.71 cm; I = 3.11 cm.

Parameters: the Evans index = 0.269; the bicaudate index = 0.153; the cella media index = 4,408; the bifrontal index = 0.310; the ventricular index = 0.516; the Huckman number = 5.14.

Fourth case: 44-year-old male, 27-year-old chronically ill: A = 3.63 cm; B = 2.91 cm; D = 10.96 cm; E = 11.30 cm; F = 12.05 cm; G = 12.50 cm; H = 13.20 cm; I = 2.80 cm.

Calculations: the Evans index = 0.301; the bicaudate index = 0.257; the cella media index = 4.71; the bifrontal index = 0.331; the ventricular index = 0.801; the Huckman number = 6.5.4

Fifth case: 61-year-old male, 37-year-old male: A = 4.2 cm; B = 3.81 cm; D = 12.4 cm; E = 12.80 cm; F = 14.90 cm; G = 15.30 cm; H = 16 cm; I = 5 cm.

Datacalculations: the Evans index = 0.281; the bicaudate index = 0.297; the cella media index = 3.2; the bifrontal index = 0.338; the ventricular index = 0.907; the Huckman number = 8.01.

Sixth case: 59-year-old female, 21-year-old female.

- A = 3 cm; B = 1.70 cm; D = 10.1 cm; E = 10.90 cm; F = 11.10 cm; G = 11.90 cm; H = 12 cm; I = 2.80 cm

Parameters: the Evans index = 0.270; the bicaudate index = 0.155; the cella media index = 4.28; the bifrontal index = 0.297; the ventricular index = 0.566; the Huckman number = 4.70.

RESULTS

The cases presented are compared with the results of a single index. We used the reference intervals from the article Valdecasas-Campelo EG *et al.* in three situations: cortical atrophy intervals in cirrhosis cases, non- cirrhosis, and cases without cortical atrophy. Although the 6 cases presented here do not take into account the presence of cirrhosis, we have selected this situation as a comparison, because according to the studies mentioned the cortical atrophy is found more actively in the association of this co-morbidity.

For each index, two tables will be given. The first table shows the index in the reference intervals of Valdecasas-Campelo EG *et al.* The second table shows the results of the cases presented here and their classification between the minimum and maximum values of the reference intervals, the minimum and maximum values being vertically displayed as a dotted line interval. On a horizontal level, there is the minimum and maximum presentation for patients without cortical atrophy and the studied cases, including the witness, in a hierarchical numerical order.

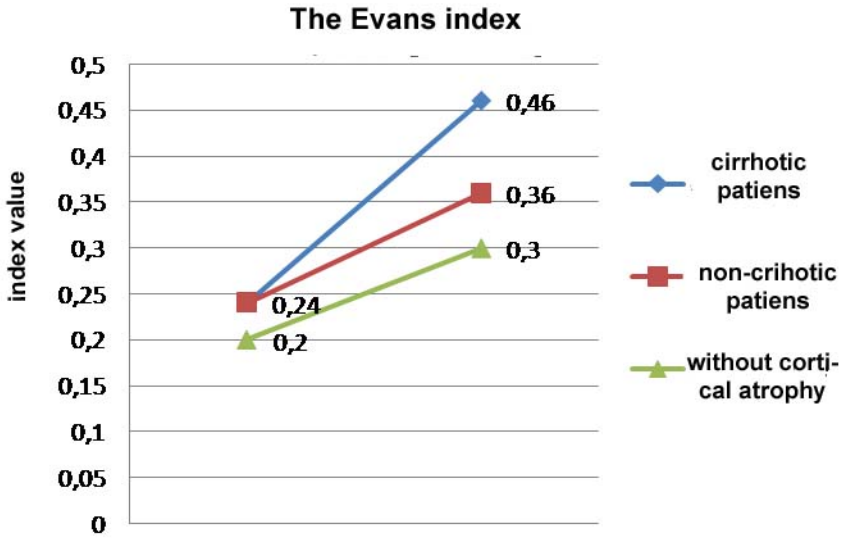

Figure 6. The Evans index reference values.

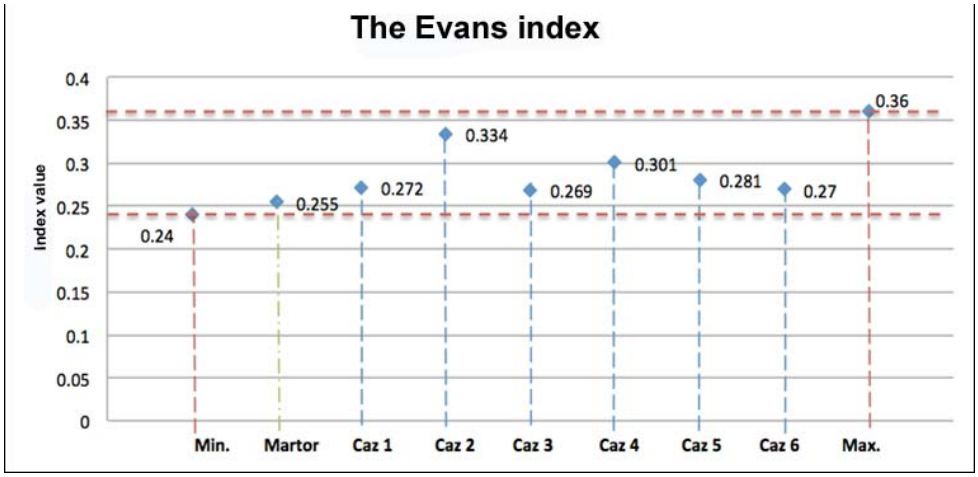

Figure 7. The Evans index obtained in the witness and the 6 cases.

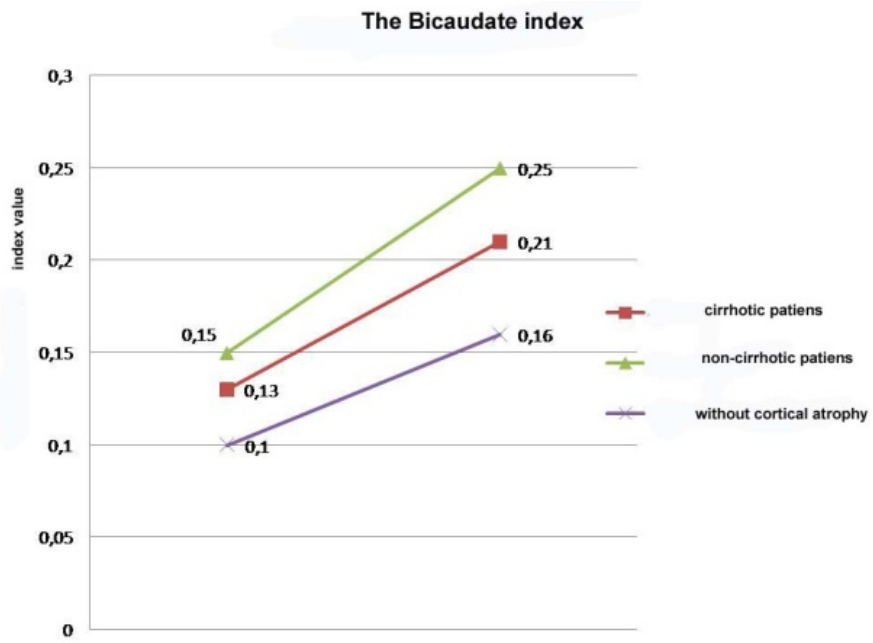

Figure 8. Reference values of the bicaudate index.

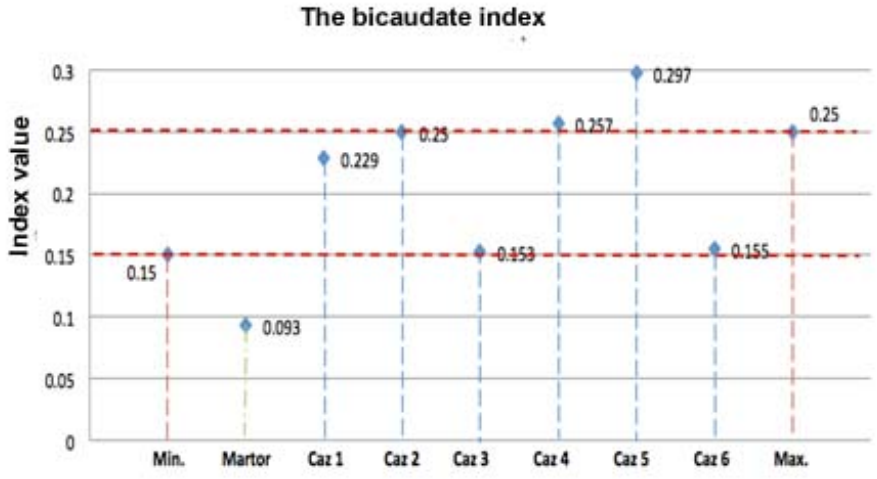

Figure 9. The bicaudate index obtained in the witness and the 6 cases.

As can be seen in Figure 6, the reference values we took into consideration are 0.24-0.46 for patients who have cirrhosis, 0.24-0.36 for non-cirrhosis cases, and 0.2-0.3 in normal cases without cortical atrophy.

According to the results of Figure 7, all 6 cases show cortical atrophy, including the control, within the range of non-cirrhotic patients with cortical atrophy.

In Figure 8 there are the reference values we have took into consideration for the bicaudate index: 0.15–0.25 in cirrhotic patients with cortical atrophy, 0.13–0.21 in non-cirrhotic patients with cortical atrophy, and 0.1–0.16 in patients without cortical atrophy.

The witness is below the lower limit. Cases 1, 2, 3, and 6 fall within the range of interest, that of cortical atrophy in non-cirrhotic patients. Example 4 is at the limit, but can be taken into consideration as it is immediately above the upper limit. Only Case 5 does not match, with a value of 0.297, above the superior threshold of 0.25 (Figure 9).

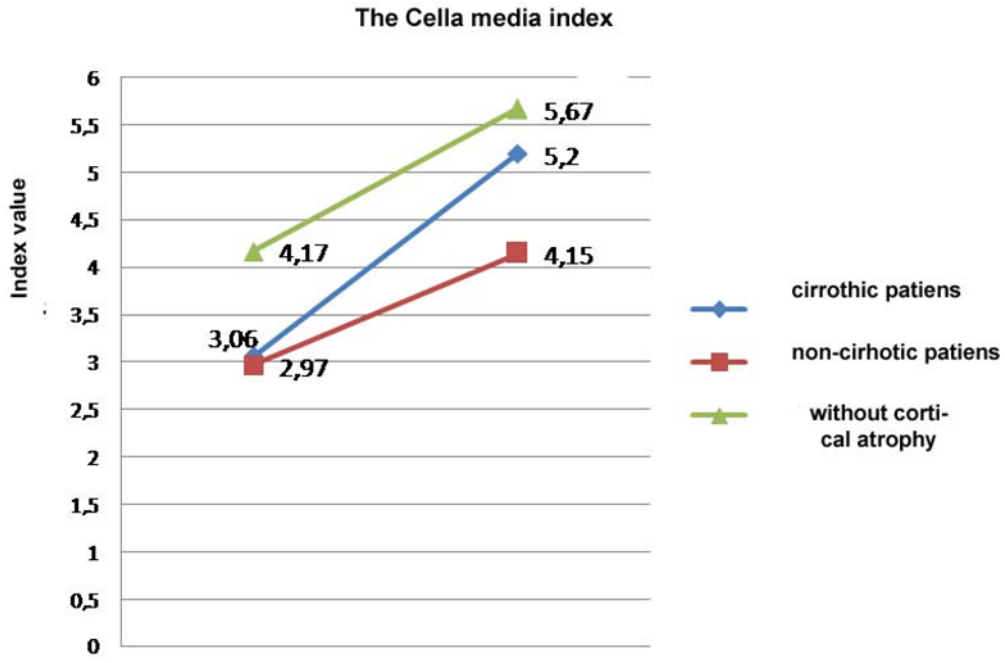

Figure 10. The cella media index reference values.

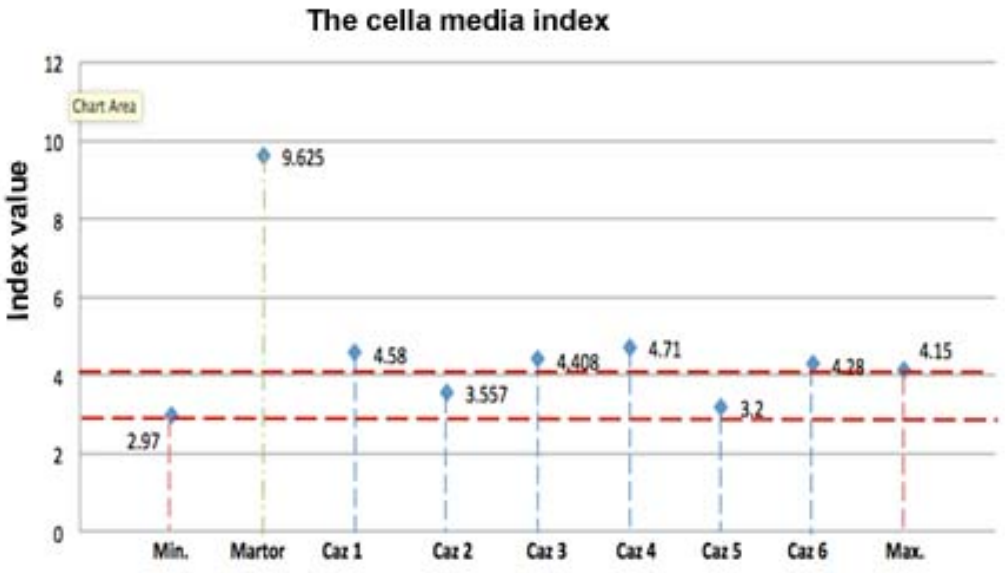

Figure 11. The cella media index obtained at the witness and in the 6 cases.

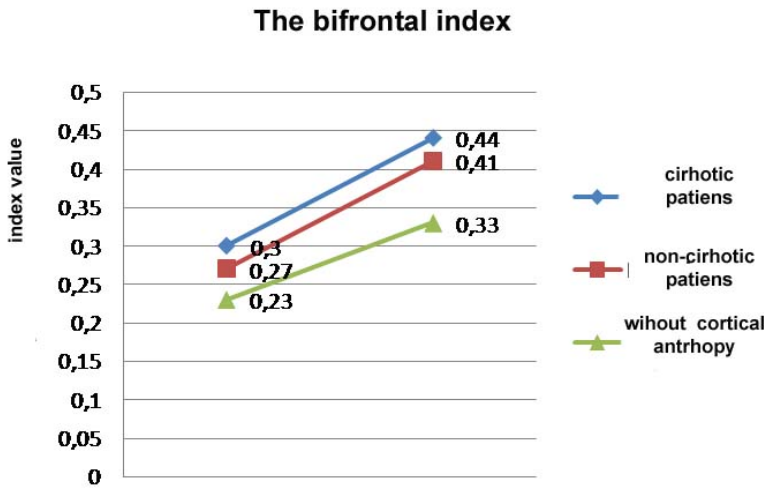

Figure 12. Reference values of the bifrontal index.

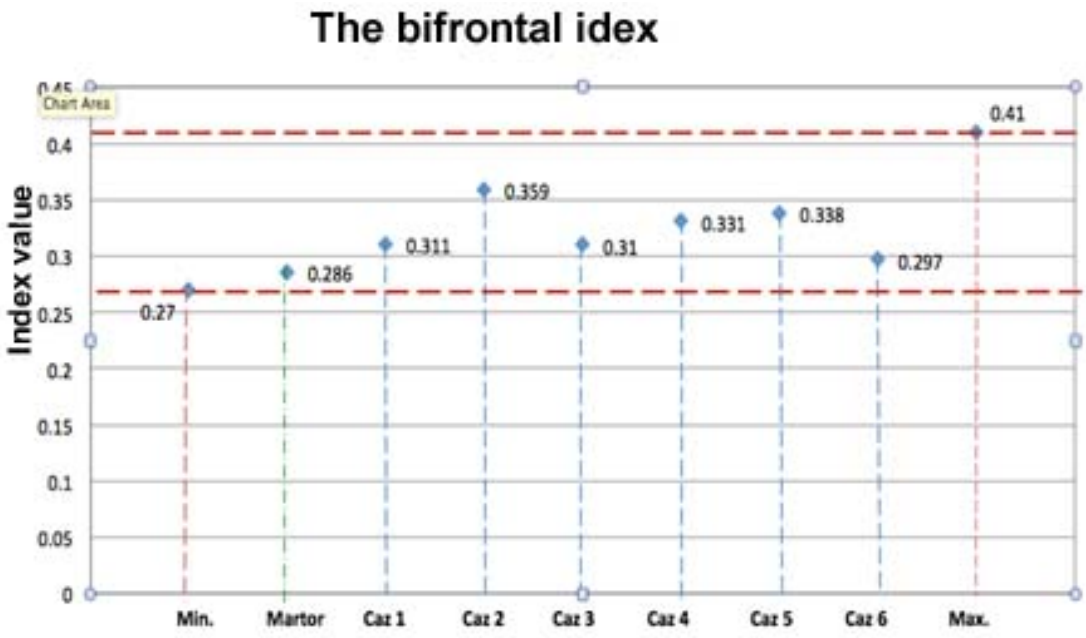

Figure 13. The bifrontal index obtained in the blank and the 6 cases.

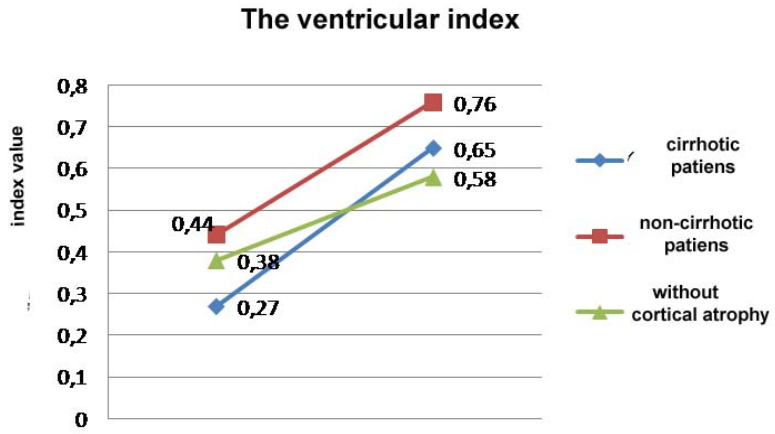

Figure 14. The ventricular index reference values.

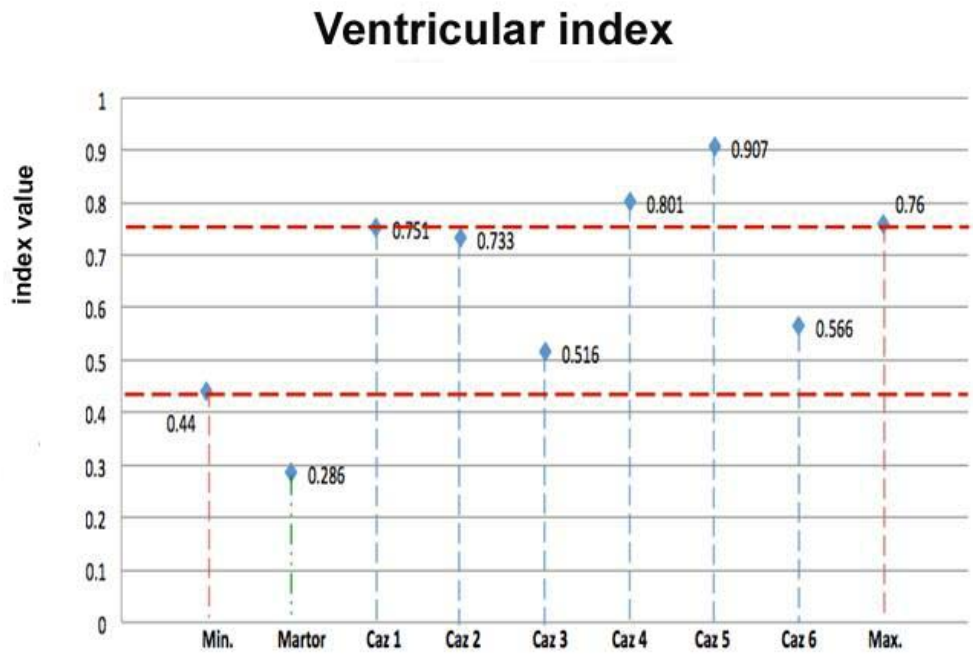

Figure 15. The ventricular index obtained in control case and the 6 cases.

The mean cella media index, as shown in Figure 10, has the following baseline values: the range 3.06–5.2 in cortical patients with cortical atrophy, 2.97–4.15 in non-cirrhotic patients without cortical atrophy, and 4.17–5.67 at patients without cortical atrophy.

Only cases 2 and 5 respect the range. Although examples 1, 3, 4 and 6 are not within the reference range, the values are immediately above the upper limit. Unlike the witness, which is well above the range, at 9.625 (figure 11).

Figure 12 shows the following reference intervals for the bifrontal index: in cirrhotic patients with cortical atrophy 0.3–0.44, in non-cirrhotic patients with cortical atrophy 0.24–0.41 and those without cortical atrophy 0.23–0 33. For the reporting interval, Figure 13, that of non-cirrhotic cortical atrophy, all 6 cases discussed match, including the witness, immediately above the lower limit.

In Figure 14, we have the reference ranges for the ventricular index: cirrhotic patients with cortical atrophy 0.44–0.76, non-cirrhotic patients with cortical atrophy 0.27–0.65 and patients without cortical atrophy 0.38–0.58.

The witness, with the value of 0.286, does not respect the rank, being well below the lower limit. Also, cases 4 and 5 exceed the upper limit and do not fall.Cases 1, 2, 3 and six falls within the range of cortical atrophy without other comorbidities (Figure 15).

DISCUSSIONS

Cortical atrophy tends to become a physiological process with age, but alcohol consumption intensifies this process in those who consume it excessively, a fact that is discordant in those who drink moderately and, have physiological cortical atrophy. In the study of Kubota M *et al. alcohol consumption and frontal lobe shrinkage: survey of 1432 non-alcoholic subjects* demonstrated that cortical atrophy depends mostly on age, but heavydrinkers had a 1.8-fold increased risk of cortical atrophy than those who did not drink alcohol. Also, those in the age group of 30–60 years were at highest risk in comparison with those of 60, with almost no risk, despite alcohol consumption. In the same study, it is stated that nearly one-tenth of the cases of cortical atrophy encountered in the healthy population is caused by excessive use of alcohol. The risk of atrophy occurs at over 350 grams of ethanol per week.[4]

In the article of Valdecassas-Campelo *et al. - Brain atrophy in alcoholics: relationship with alcohol intake; liver disease; nutritional status, and inflammation*, the patients under study were observed according to the comorbidity they presented and according to numerous biochemical parameters. Besides the relationship age-cortical atrophy and alcohol consumption- cortical atrophy, this study revealed that those who associated

cirrhosis had higher cerebral changes of cortical atrophy, consistently observable in this group, compared to non-cirrhotic patients.

In the series of cases here presented in this paper, we have tried to select patients who have had no other significant comorbidities, excluding hypertension(not a risk factor for cortical atrophy). Both the case control and the six cases do not have cirrhosis present. Therefore, the degrees of cortical atrophy in these heavy drinkers were compared with the results of the *Valdecassas-Campelo EG et all* study in patients with cortical and non-cirrhotic atrophy. Within this topic, there are relatively few studies conducted over time, and fewer studies still have statistical significance. We used this last mentioned study as a reference as it has a well-split sample according to many other parameters and obtained data with significant statistical correlation. A study such as *Harper C, Jillian K, Brain Atrophy in Chronic Alcoholic Patients: A quantitative pathological study* demonstrates the presence of cortical atrophy in chronic patients, but with the post-mortem analysis at necropsy, there were too many variables related to the precision method of analysis.[5]

In the series of cases presented here, there are noticeable results of framing within the ranges that demonstrate the presence of cortical atrophy. To show the cortical atrophy and its degree, it is not necessary for all the data to have the same results concurrently, and they can be corroborated. In the calculation of the Evans index, all 6 cases are within the interval limits for cortical atrophy. In the computation of the bicaudate index, examples 1, 2, 3 and six match clearly, as well as case 4 in the limit, but case 5 does not fit. From the cella media index analysis, only cases 2 and 5 clearly follow the range, the others being immediately at the upper limit. Taking the example of Case 5, it exhibits cortical atrophy only by corroborating two indices, so not every single measurement has to be met. Calculation of the bifrontal index indicates the obvious atrophy of the six cases. And the biventricular index shows the framing of cases 1, 2, 3 and 6.

In calculating these indices, there are variables that influence the results and can not be excluded, regardless of the method of study adopted. Undoubtedly, what can not be quantified is the individual, genetic and phenotypic constitution of the patient concerned. To this is added the alcohol consumption period and the age at which the examination is performed. It is possible to try to "idealize" one study claiming that each patient has the same sex, age and the same period of consumption, but the results will be influenced all the time by individual variability.

It is also possible to observe the small values of the intervals used to compare the indices, as well as the fact that some indices have intervals that coincide in some cases in patients with cortical atrophy and without cortical atrophy. This makes it necessary to corroborate the results obtained with several indices. It can also be considered if a single index indicates the presence of cortical atrophy. In such a situation, the values of the index would instead be related to the particularities of the anatomy of the brain of that person. This is evident in the case of the witness, which in two instances falls within the cortical atrophy ranges, but this is not correlated with alcohol consumption. The witness is attributable to age or due to anatomic particularity.

CONCLUSIONS

From the cases presented, it appears that cortical atrophy is present and is the consequence of prolonged alcohol consumption in the context of alcohol dependence. Such results must be demonstrated by analytical scale studies, as the current study is a descriptive observation. This study does not provide information on the frequency of the phenomenon and does not unduly prove the causal relationship in the absence of statistical confirmation. It would be useful for a future study to compare a much more extensive sample of patients by dividing them into several categories. In this study, only alcohol dependence or moderate or abstinent dependence was used. Future research could more accurately take into account the number of years of alcohol consumption and daily intake, the nutritional status of the patient, and the relationship between malnutrition and cortical atrophy, the presence of inflammation, and the study of the influence on cortical atrophy. Also, the presence of liver cirrhosis and the risk of cortical atrophy associated with this comorbidity.

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