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Existence of contralateral abnormalities revealed by texture analysis in unilateral intractable hippocampal epilepsy

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Abstract

We selected 23 patients with unilateral temporal lobe epilepsy characterized by ipsilateral hippocampal sclerosis and an apparently normal contralateral hippocampus on MR imaging. Images were acquired on a 0.28 T MR scanner using a conventional Carr-Purcell Meiboom Gill sequence in all patients and in 9 healthy subjects. Texture analysis was applied to axial MR images of the first and tenth echoes. Texture analysis detects macroscopic lesions and microscopic abnormalities that can not be observed visually. The presence of texture differences in the between normal (controls) and sclerotic hippocampi was ascertained by statistical discriminant analysis. The apparently normal contralateral hippocampi can be classified into three categories in terms of texture: 4 apparently healthy, 8 similar to sclerosis, and 11 different from either healthy or sclerosis. These findings are related to a certain degree of hippocampal alteration, which further investigation might help better characterize.

Keywords: Temporal lobe epilepsy; Hippocampal sclerosis; MR imaging; Texture analysis; Discriminant analysis

1. Introduction

Hippocampal sclerosis (HS), characterized by selective neuronal loss and reactive gliosis in the hippocampus and other mesial temporal structures, is a common pathologic finding in temporal lobe epilepsy. With magnetic resonance (MR) imaging, the detection rate for HS has been found to vary largely and such substantial variations in the detection rate have been primarily attributed to the subjective nature of the assessment of scans. These assessments rely on image contrast, itself totally conditioned by the MR systems and/or the imaging methodology used. Since the detection of unilateral HS plays an important role in the management of patients, by encouraging a possible surgical approach as a therapy, the quantitative MR techniques (volumetry, T_2 relaxation time measurement, proton MR spectroscopy) are of great interest because they provide a more objective alternative for the evaluation of HS. It is generally admitted that MR imaging can detect hippocampal sclerosis only when at least 50% cell loss has occurred in the hippocampus [1,2], and that the quantitative MR techniques detect HS earlier than MR imaging [3,4].

Texture is a visual attribute of an object or of its image dependent on its structure. Intuitively, texture in an image refers to the distribution of brightness and darkness within the image and to concepts such as coarseness, linearity, and regularity. Texture analysis is the term used for methods developed to quantify image texture. Texture analysis methods evaluate the spatial location and signal intensity characteristics of the fundamental structure elements (pixels) of digital images. The texture features are, in other words, statistical parameters, calculated from the pixel distribution which characterize the texture variety and consequently the structure of the tissues depicted by their image. For some authors, the brain proceeds in a similar manner in order to construct a mental image of an object [5]. Medical images contain much clinically relevant texture information. Texture analysis has been applied with success to the classification of pathologic tissue in liver, thyroid, breast, kidney, prostate, heart and brain [6–11].

The aim of this study is to examine the diagnostic potential of computerized statistical texture analysis, in a homogeneous group of patients presenting unilateral temporal lobe epilepsy and ipsilateral hippocampal sclerosis on MR imaging, focusing on two aspects, i.e., (i) how sensitive is

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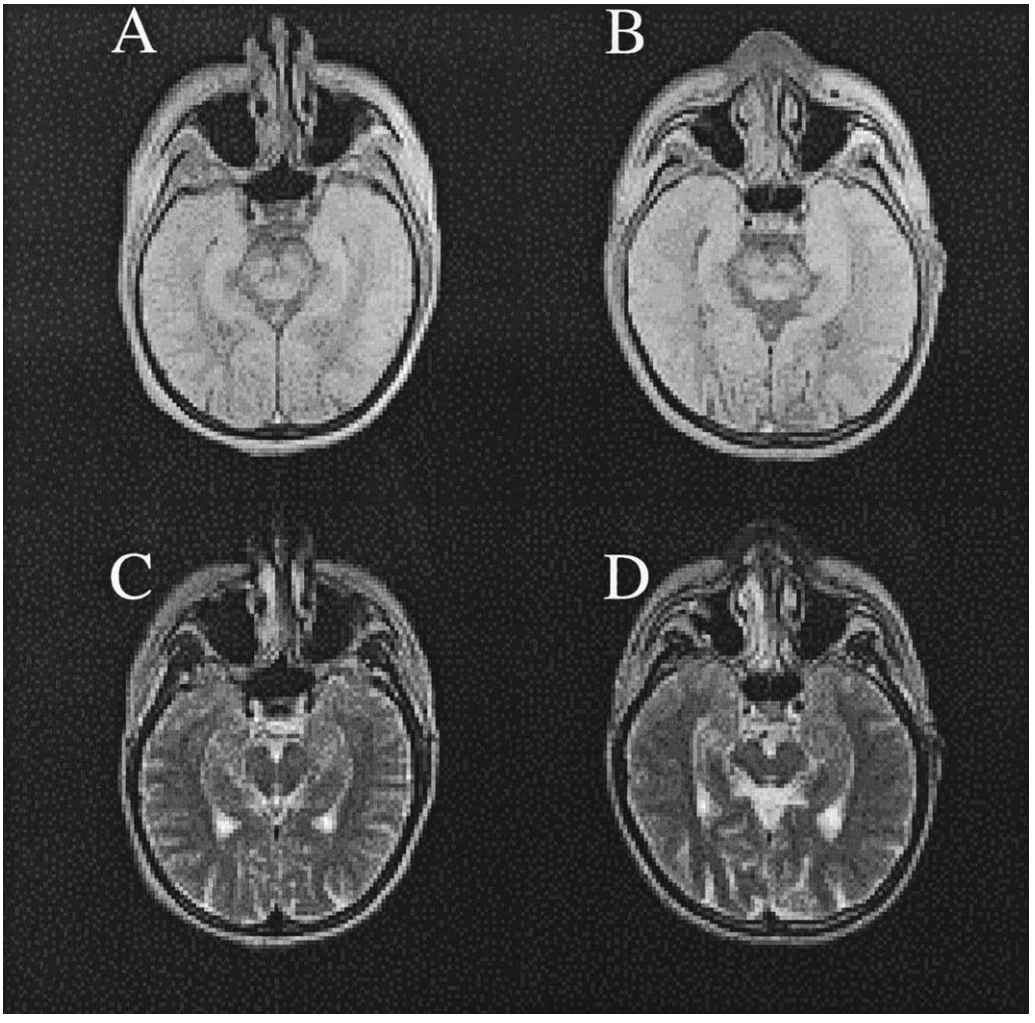

Fig. 1. Examples of MR images in a control subject (first echo A; tenth echo C) and an epileptic patient with right hippocampal sclerosis (first echo B; tenth echo D).

this approach in the assessment of the apparently normal contralateral hippocampus, and (ii) do the results correlate with MR spectroscopy and T_2 relaxation time measurements.

2. Materials and methods

2.1. Subjects

A total of 9 healthy volunteers (age 27.0 ± 5.7 y) served as controls.

A total of 23 patients (age 34.7 ± 10.2 y) with pharmacoresistant temporal lobe epilepsy included in previous studies [12,13], were studied. All patients underwent a neurologic examination, repeated and prolonged video-EEG monitoring, neuropsychological investigations, MR imaging, single-photon emission computed tomography (SPECT) imaging. The patients were selected on the following criteria:

- clinical and EEG evidence of unilateral temporal lobe epilepsy;
- signs of ipsilateral hippocampal sclerosis on MR imaging and absence of visually detectable contralateral abnormality;
- presence of perfusion abnormalities in the ipsilateral temporal lobe on SPECT imaging.

The seizures were characterized clinically by epigastric, autonomic or psychic aura, behavioral arrest, staring, automatism and/or unilateral dystonic posture and by the detection of a unilateral interictal temporal focus (9 left and 14 right) on prolonged video-EEG monitoring, confirmed in 19 cases by ictal recordings. The patients presenting occasionally bilateralization of interictal EEG abnormalities during the very active period of epilepsy, were not excluded from this study.

2.2. MR imaging

The MR images used in this study were obtained on a 0.28 T imaging system (Bruker) using 6-mm slice, orientated in an axial plane parallel to the long axis of the

hippocampi, which was slightly tilted so as to pass through the amygdala. The following imaging parameters were used: a 25.6-cm field of view and 128^2 matrix, defining a voxel volume of 24 mm^3. A conventional Carr-Purcell-Meiboom-Gill multiple spin-echo pulse sequence with a repetition time of 2000 ms, an echo time of 15 ms and 48 echoes was applied. Only the proton density-weighted images for the 1^{st} echo and T_2-weighted images for the 10^{th} echo were evaluated in our study (Fig. 1).

All MR imaging measurements were performed in seizure-free periods. The time of the last seizure, as reported by the patients, was in all cases at least 38 h before the MR measurement.

2.3. Texture analysis

Texture analysis was performed by using statistical techniques, mostly of the first order, involving only single pixels, and second-order features which also take into account the spatial arrangement of pixels such as the co-occurrence matrix (which describes the spatial gray level dependencies) or runlength matrix which is the matrix of the runlength frequency occurring in the image for a certain angle of sight (lines of the same pixel level). This method has been fully described by Haralick [14].

The whole hippocampus was taken as one region of interest. Statistical treatment was made on the results of MAZDA [15], a software program for the calculation of texture parameters in digitised images within a region of interest which gives 200 texture parameters (see appendix). The options used by default were 4 bits by pixel, distances 1–4, gradient 4 bits by pixel.

2.4. Statistical analysis

Using stepwise discriminant analysis, (Statistica, Statsoft Inc.), we checked the ability of each texture parameter to discriminate between hippocampal sclerosis or not. The software considered the parameter(s) that were selected in previous steps in order to obtain the best discrimination. Discriminant analysis (DA) was used for multigroup classification to determine if the groups (sclerosis or normal) could be distinguished on the basis of the set of texture features. In the last step, the results obtained with three MR analysis methods (quantitative T_2, NMR spectroscopy, and texture) were compared using Cohen-Kappa's test of concordance.

3. Results

Three groups of hippocampal scans were studied; 18 hippocampi of healthy volunteers (HH), 23 ipsilateral hippocampi showing increased signal classified as sclerosis (HS) and 23 contralateral hippocampi without apparent abnormalities in visual inspection (HA). Texture analysis using the software MAZDA yielded 200 parameters for each hippocampus. In other words, one hippocampus is defined by 200 texture parameters for the first echo image and by 200 texture parameters for the tenth echo image. DA was used to determine which parameters yielded the best discrimination between sclerosis and normal hippocampi. The classification functions in DA are determined by a linear combination of texture parameters. The classification functions compute directly a classification score for a given hippocampus. The hippocampus is classified as belonging to the group for which it has the highest classification score.

With the first echo hippocampal images, we obtained a correct classification with the two parameters: vertical entropy (ENT04) and correlation for 45 degree (COR33). The two classification functions for the hippocampi respectively called F(HH) (healthy hippocampi) and F(HS) (hippocampi with sclerosis) were the following:

$$F(HH) = 78.1*ENT04 - 10.2*COR33\text{-}29.6$$

and (1)

$$F(HS) = 100*ENT04 - 7.3*COR33\text{-}46.6.$$

With the tenth echo hippocampal images, the functions included 9 texture parameters, the classification functions were the following:

$$F(HH) = 433*DENT04 + 88.9*DVAR40 + 21.4*SAV44 - 10.7*CON4\_4 + 43.7*CON03 - 14.5*SVA22 + 495*COR01 + 184*COR33 - 67.8*DENT44 - 634$$

and (2)

$$F(HS) = 425*DENT04 + 80.4*DVAR40 + 20.2*SAV44 - 10.0*CON4\_4 + 42.3*CON03 - 13.4*SVA22 + 469*COR01 + 169*COR33 - 51.3*DENT44 - 578$$

3.1. Classification of the ipsilateral hippocampus

Using functions [1] for the first echo hippocampal images, we correctly classified all the hippocampi of the HH group. However two hippocampi of the HS group were incorrectly classified as normal (Table 1A).

Similarly, using functions [2], we confirm all the hippocampi in both the HH and the HS group were correctly classified (Table 1B).

3.2. Classification of the contralateral hippocampus

Applying functions [1] to the first echoes images, 13 hippocampi were considered as sclerotic, and the other 10 were classified as normal (Table 1C).

Table 1
Comparison of the clinical or texture analysis classification of the hippocampi of epileptic patients and control subjects

Ipsilateral hippocampi							
1st echo (A)				10th echo (B)			
		Clinical analysis				Clinical analysis	
		Sclerosis	Normal			Sclerosis	Normal
Texture Analysis	Abnormal	20	0	Texture Analysis	Abnormal	23	0
	Normal	3	18*		Normal	0	18*
Contralateral hippocampi of the patients							
1st echo (C)				10th echo (D)			
		Clinical analysis				Clinical analysis	
		Sclerosis	Normal			Sclerosis	Normal
Texture Analysis	Abnormal	—	13	Texture Analysis	Abnormal	—	14
	Normal	—	10		Normal	—	9

*Both the left and right hippocampi of the 9 normal subjects were taken into account in the discriminant procedures.

Sensitivity S = 20/23 = 86.9%
Specificity F = 18/18 = 100%
Accuracy A = 38/41 = 92.7%

Sensitivity S = 23/23 = 100%
Specificity F = 18/18 = 100%
Accuracy A = 41/41 = 100%

Applying functions [2] to the tenth echoes images, 14 hippocampi were considered as sclerotic, the other nine being classified as normal (Table 1D).

4. Discussion

On visual inspection of MR imaging scans, HS is often associated with noticeable hippocampal atrophy and increased T_2 signal intensity. MR imaging analysis can help detecting abnormalities by three quantitative measurements of the hippocampus:

1. Increased T_2 relaxation time reflecting mainly gliosis [16,17];
2. Decreased NAA/(Cho+Cr) ratio in proton MR spectroscopy indicating that the neuronal integrity is not maintained, implying at least neuronal loss and/or dysfunction [12];
3. A decreased volume reflecting hippocampal atrophy [18].

Our method combines texture analysis of raw images (first echo, tenth echo) with a classification by discriminant analysis as an additional method, in order to characterize other structural abnormalities in the contralateral hippocampus of epileptic patients.

We have taken the ipsilateral hippocampus to test our method, and extended the procedure to the contralateral hippocampus. The high sensitivity and specificity of the classification of the ipsilateral hippocampi underlines the robustness of this method. The sensitivity of the tenth echo image analysis is maximum and slightly higher than the sensitivity of the first echo image analysis (Table 1A, 1B) for which 2 out of 23 ipsilateral hippocampi were wrongly classified as normal. These results depend on the type of MR contrast: the tenth echo image is T_2-weighted, while the first echo image is proton density-weighted. These two types of contrast reflect different (sclerotic or non sclerotic) tissue structures, which can be picked-up by the classification functions used in DA, which relies on only two or nine texture features for the analysis of first and tenth echo images respectively. Only texture parameters extracted from the co-occurrence matrix were selected in the classification function.

In Tables 2 and 3 are reported the comparison between texture analysis and proton MR spectroscopy and/or T_2 relaxation time measurements in 23 patients. The values of the two parameters are very distinct and their spreading range very small. Hence, they are different from those of the healthy subjects, and a conclusion about the hippocampal status can be easily reached. Table 3 shows that there exists no correlation between the classification of the patients on the basis of MR spectroscopic data, T_2 relaxation times and texture analysis results, as confirmed by the concordance test [19]. Cohen-Kappa's test of concordance yielded a value of −0.0733. This value, very close to 0, is highly non significant and indicates a discordance between the results obtained with the 3 methods. This may be interpreted in the same way as Meiners et al.'s statement [20] that no relationship has been found between the (NAA/(Cho+Cr)) ratio and histopathology of the sclerosis of the hippocampus. This characterization is done either at the pixel level, calculating the parameters in the neighborhood, or in a ROI which was the whole hippocampus in our study. This analysis contributes additional information, not evident

Table 2
Comparison of the classification of the controlateral hippocampi of the epileptic patients between texture analysis and proton MR spectroscopy or T_2 relaxation time measurements

1st echo (A)				10th echo (B)			
		MR spectroscopy				MR spectroscopy	
		Sclerosis	Normal			Sclerosis	Normal
Texture Analysis	Abnormal	7	6	Texture Analysis	Abnormal	8	6
	Normal	7	3		Normal	6	3
1st echo (C)				10th echo (D)			
		T_2 relaxation time				T_2 relaxation time	
		Sclerosis	Normal			Sclerosis	Normal
Texture Analysis	Abnormal	4	9	Texture Analysis	Abnormal	3	11
	Normal	2	8		Normal	3	6

on visual inspection [21,22]. The information obtained on the hippocampus by texture analysis demonstrates the complexity of the structure of this organ, as underlined also by histologic anatomic observations. A recent study on neurons from the temporal lobe of epileptic patients with mesial sclerosis evidenced not only important modification of dentate granular cells but also decreased dentate spine density. All these hippocampal modifications could result in a modification of the structure of MR images of this organ [23,24].

Judging from the clinical classification, all the contralateral hippocampi were expected to be normal. However, we detected from first- and tenth-echo images, abnormalities to some degree, in some patients. Considering the structure of the contralateral hippocampus of each patient, they could be classified into 3 groups: i) patients with contralateral abnormalities on both first and tenth echo images, ii) patients with contralateral abnormalities either on first or tenth echo images, and iii) patients without anomalies. It is likely that the subjects presenting no anomalies (iii) could benefit from surgery.

5. Conclusion

This preliminary study has provided evidence that texture analysis can characterize new structural abnormalities on MR images of apparently normal contralateral hippocampi in patients with temporal lobe epilepsy. In the present state of art, we cannot give further explanations, and questions remain unanswered relative to the biologic origin of the discrepancies observed. This study is not closed and we are seeking to obtain information on the evolution of the disease in these patients in order to refine our findings. However, we have shown that texture can detect alterations not seen by the conventional MRI measurements.

Table 3
Comparison of the classification of the controlateral hippocampi of the epileptic patients between texture analysis (first plus tenth echoes) and proton MR spectroscopy plus T_2 relaxation time measurements

		MR spectroscopy plus T_2 relaxation time		
		Sclerosis	?	Normal
Texture Analysis	Abnormal	1	3	4
	?	2	5	4
	Normal	0	3	1

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Appendix

Texture parameters

As we explained in the body of the paper, there are more than 200 texture parameters. We present only the most relevant ones.

We define the *first-order parameters* depending only on a sample of *one* pixel as

Histogram-based parameters

1. mean, (mean)
2. variance, (VAR)
3. skewness, (SKE)
4. kurtosis, (KUR)

We define the *second-order parameters* depending on sample of *two* pixels (i, j) as

gradient-based parameters

1. absolute gradient mean, (GRM)
2. absolute gradient variance, (GRV)
3. absolute gradient skewness, (GRS)
4. absolute gradient kurtosis, (GRK)

Run length matrix-based parameters (computed four times for each ROI-for 90 degree, 0 degree, 45 degree and 135 degree directions)

1. run length nonuniformity, (RL)
2. gray level nonuniformity, (GL)
3. long run emphasis, (SR)
4. short run emphasis, (SH)
5. fraction of image in run. (FR)

for example FR90 i.e., fraction of image in run for 90°

Co-occurrence matrix-based parameters (computed up to 20 times, for (d, 0), (0, d), (d, d), (d, -d) where the distance d can take values of 1,2,3,4 in our case)

1. angular second moment, (ASM)
2. contrast, (CON)
3. correlation, (COR)
4. sum of squares, (SOS)
5. inverse difference moment, (IDM)
6. sum average, (SAV)
7. sum variance, (SVA)
8. sum entropy, (SEN)
9. entropy, (ENT)
10. difference variance, (DVAR)
11. difference entropy. (DENT)

For example CON03 i.e., contrast for (0, d) where d = 3.

The definition and discussion of the above parameters are provided in Haralick's article [14].

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