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Texture Analysis of Hippocampal Sclerosis

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Summary: Mesial temporal lobe epilepsy (MTLE) is frequently associated with refractory seizures and pathologic features of hippocampal sclerosis (HS). Quantitative magnetic resonance imaging (MRI) techniques can improve the detection and quantification of HS. The objective of this study was to evaluate whether MRI texture analysis can detect hippocampal abnormalities in patients with pathologically proven HS.

Methods: Nineteen consecutive patients who underwent surgery for refractory unilateral MTLE and had HS diagnosed on histopathology (12 right and seven left) had their preoperative MRIs evaluated. We performed texture analysis in 3-mm coronal T_1-IR MRIs, focusing on the hippocampal head, by using the software MAZDA. Data were compared with those of a group of 78 normal hippocampi from 39 healthy adult volunteers through multivariate analysis of variance and selection of the most significant texture parameters.

Results: Overall, almost all parameters of texture could discriminate the group of hippocampi with HS and the group of contralateral hippocampi from the group of normal hippocampi, but the post hoc comparison showed no differences between HS and contralateral hippocampi.

Conclusions: These results provide evidence of texture alteration in MRIs of hippocampi with HS and corroborate the hypothesis of bilaterality of hippocampal damage in patients with MTLE, but further studies are needed to investigate the lateralization power of texture analysis. **Key Words:** Epilepsy—MRI—Texture—Hippocampal sclerosis.

Hippocampal sclerosis (HS) is the most common underlying pathology in adult patients with mesial temporal lobe epilepsy (MTLE). Neuronal loss also may extend to amygdala and parahippocampal gyrus, characterizing the typical pattern of mesial temporal sclerosis (MTS). MTS is found in most surgical specimens from operated-on patients with refractory MTLE and is associated with an excellent surgical prognosis (1–3).

Magnetic resonance imaging (MRI) hallmarks of HS are reduced volume and increased T_2 internal signal of the hippocampal structure (4). These findings have prompted application of more sensitive quantitative techniques, such as hippocampal volumetry and T_2 relaxometry, for detection of subtle HS (5–7).

Texture analysis of MR images is a quantitative method that can be used to detect and quantify structural abnormalities in different tissues (8,9). It makes it possible to assess the degree of gray-tone modifications and the alterations of gray-tone spatial distribution in a given anatomic region of interest. This gray-tone variation is thought to correspond to underlying functional and anatomic changes (10). In this setting, texture analysis may be sensitive to detect subtle changes in MRI and to extract more information than does visual assessment.

Texture analysis has recently been performed to evaluate hippocampal formation in T_2-weighted images acquired in a 0.28-T scan, and 6-mm axial slices (11). However, no previous studies evaluated the texture MRI features of pathologically proven HS.

The purpose of this study was to evaluate whether texture analysis can detect pathologically proven HS in preoperative MRI from patients with refractory MTLE.

PATIENTS AND METHODS

Patients and control group

We selected 19 consecutive adult patients (11 women) with a mean age of 36.6 years (range, 18–58 years) who underwent temporal lobectomy associated with amygdalohippocampectomy due to unilateral refractory MTLE (defined by visual MRI assessment and interictal or ictal EEG), with histologic confirmation of HS. Twelve patients had pathologically proven right HS, and seven had left HS.

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The control group consisted of 38 healthy adults without remarkable medical history, and without history of neurologic or psychiatric disorders.

MRI acquisition

Diagnostic preoperative MRI was acquired on a 2-T MR system (Elscint Prestige, Haifa, Israel) with our standard protocol, which included 6-mm-thick sagittal T_1, 3-mm-thick coronal IR-T_1 and T_2 (perpendicular to hippocampus axis), 3-mm-thick axial T_1, 5-mm-thick axial fluid-attenuated inversion recovery (FLAIR), and 3D volumetric T_1 with 1-mm isotropic voxel. Patients and controls had the same MRI protocol acquired in an interleaved fashion around the same period.

Texture analysis was performed on 3-mm-thick coronal IR-T_1 slices (TR = 2,800 ms, TE = 14 ms, TI = 840 ms, matrix = 130×256, FOV = 16×18 cm, flip angle = 200°) in DICOM format. We obtained texture parameters from a section of the hippocampal head, defined in the first slice in which the hippocampus could be undoubtedly separated from the amygdala and the temporal horn of the lateral ventricle, and which contained its classic appearance such as the diamond shape and indentations in patients with normal Hippocampi (12), or the atrophy or loss of internal structure in patients with HS.

Texture analyses

We used the software Mazda (http://www.eletel.p.lodz.pl/cost/soft/ware.html) for texture analysis of hippocampus (13–15). The process consisted of manual outlining of hippocampal head internal boundaries, using different color labels for the right and left hippocampus in each individual. After the segmentation of regions of interest (ROIs), the software generated texture features of the labeled region. Texture parameters are determined according to the spatial dependence between gray tones of the image, and they are quantified throughout:

1. "Co-occurrence matrix" represents the probability of occurrence of a pixel pair, with a given gray-tone difference, separated by a predefined distance taken in a predefined orientation.
2. "Histogram" represents the frequency of occurrence of a gray tone in an investigated ROI.
3. "Gradients" represent the neighboring pixel gray-tone variation.
4. "Run-length matrix" represents frequency of runs of defined length and gray tone.

Run-length matrix and co-occurrence matrix are calculated in four orientations: horizontal, vertical, and the two diagonals.

From these definitions, note that the histogram texture features are derived from the distribution of single-pixel gray-level tones within a given ROI, whereas the co-occurrence, run-length, and gradient texture parameters account for the relative (within pairs or groups of pixels) distribution of gray-level tones. Because variation in the overall gray-level tones can be due to external factors such as the MRI acquisition process, we decided to exclude the histogram parameters from further analysis to prevent false conclusions from possibly contaminated data.

Statistical analysis

Group differences for age were evaluated by using one-way analysis of variance (ANOVA), and gender distribution was evaluated by using the χ^2 test. Data were evaluated by using Systat (9.0) software. We grouped the hippocampi with proven HS in one group, the contralateral hippocampi from patients with HS in another group, and all hippocampi from normal subjects in a third group. Group differences of texture parameters were evaluated with MANOVA with one between-subjects grouping factor (groups: controls, HS, and contralateral) and one within-subject grouping factor (all texture parameters). The eight texture parameters that most significantly discriminated the groups were chosen according to the value of λ and were submitted to Tukey HSD post hoc comparisons.

RESULTS

The level of significance was set at $p < 0.05$. No significant difference of age or sex distribution was found between controls and patients with MTLE.

We excluded texture parameters derived from histogram features of the image because the distribution of gray levels within the image can show variation between images because of eventual differences in the MRI processing. All parameters, except those derived from the computation of the skewness of the texture features, proved to be significantly different among the groups (Fig. 1). The most significantly different parameters are shown in Table 1.

DISCUSSION

MRI quantitative postprocessing techniques are useful tools for partial epilepsy investigation. Texture analysis involves computing a large number of different parameters, to be able to account for the different features encountered in MRI, ranging from noise (which produces a visual impression of roughness) to uniformity (which produces a visual impression of smoothness). The gray-tone variation also is influenced by the size of the structure analyzed and the patterns of distribution of the gray tone within the region of interest (Fig. 2). Therefore texture analysis refers to the mathematical evaluation of the variations of gray tone that occur between pixels within the considered region.

A significant difference was found in almost all texture parameters of hippocampi with histologically proven sclerosis and hippocampi contralateral to the side of sclerosis,

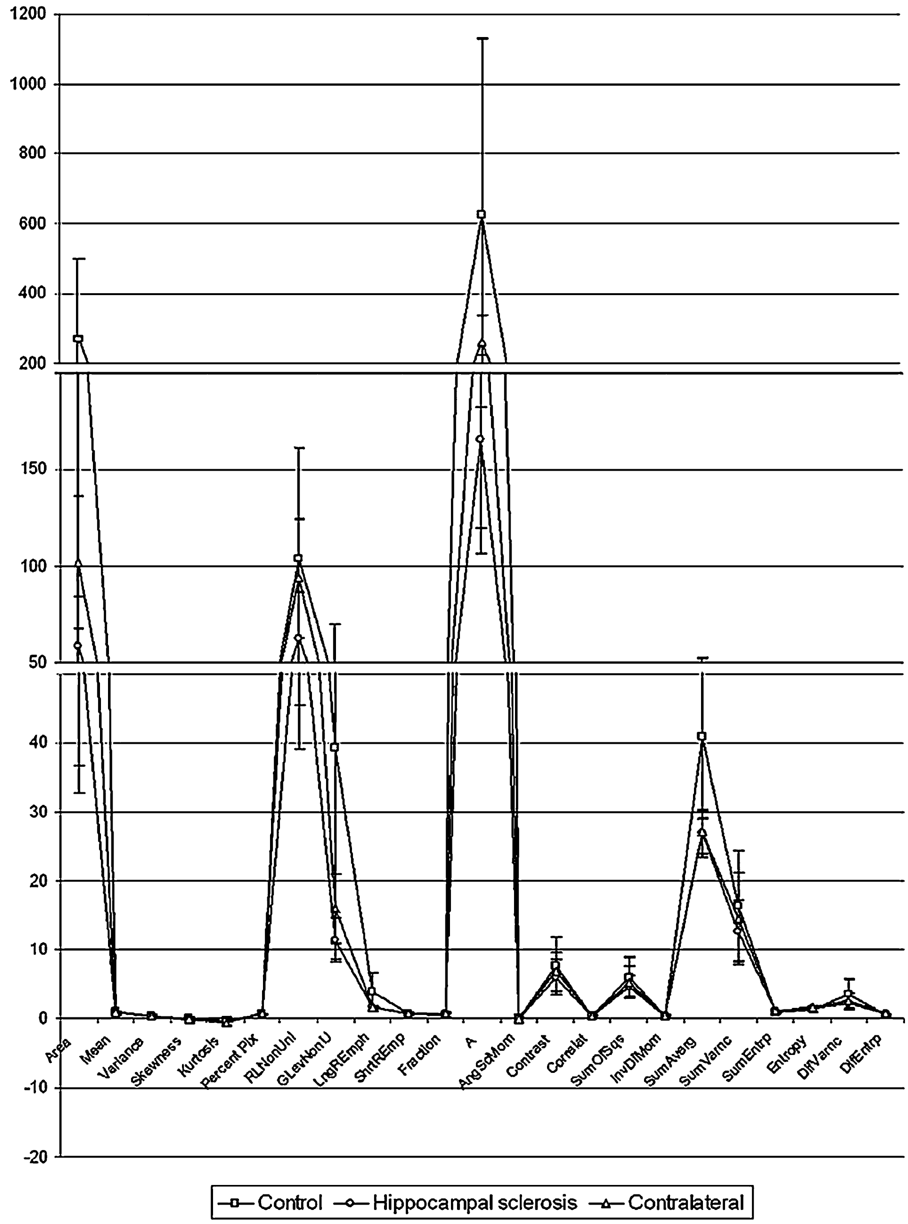

FIG. 1. Overview of the distribution of the mean of the absolute values of all texture parameters among control subjects, hippocampi with hippocampal sclerosis (HS), and hippocampi contralateral to hippocampi with HS. The figure shows absolute gradient parameters (Area, Mean, Variance, Skewness, Kurtosis, and Percentage of pixels with nonzero gradient), run-length matrix parameters (RLNonU, Run length nonuniformity; GLevNonU, Gray level nonuniformity; LngREmph, Long run emphasis; ShrtREmp, Short run emphasis; Fraction of image in runs) and co-occurrence matrix parameters (A, angular moment; AngScMom, angular second moment; Contrast; Correlation; SumOfSqs, sum of squares; InvDfMom, inverse difference moment; SumAverg, sum average; SumVarnc, sum variance; SumEntrp, sum entropy; Entropy; DifVarnc, difference variance; Dif Entrp, difference entropy). The results from the co-occurrence matrix parameters analysis are shown only with the evaluation performed with 1 pixel distance, because the results from 1 to 5 pixels distance follow the same pattern.

compared with the control group. We did not observe, however, a difference between the hippocampi with HS and the contralateral hippocampi. Even using the most significant features of the texture, the contralateral hippocampi was similar to that of HS, meaning that the pathology was bilateral. The observation of bilateral hippocampal abnormalities is concordant with the knowledge that hippocampal pathology results in different bilateral texture alterations (11).

We may have not been able to detect the lateralization power of texture analysis because we analyzed the data with simple comparison of the mean between groups through MANOVA. Possibly the texture alterations may weigh together in different groups, and further techniques for data reduction and discriminant analysis can be useful for this investigation. Nonetheless, we observed a clear difference of texture parameters between HS and normal hippocampi. This is probably a result of the simplification of the structure of hippocampi with HS, in which the cell loss observed in HS results in a less complex image. The simpler image of hippocampi with cell loss embeds reduction of variation of pixels with different gray levels, and this can be detected and quantified through texture parameters. The possibility of detection of subtle texture variations not possibly discriminated by human visual inspection may render the texture analysis a promising tool for the in vivo search for texture features corresponding to hippocampal sclerosis.

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TABLE 1. *The most significantly different texture parameters encountered during the comparison of hippocampi with hippocampal sclerosis, normal hippocampi and hippocampi contralateral to hippocampal sclerosis*

Parameter	λ value $df = (2, 113)$	p Value	Tukey post hoc comparison (mean ± SD)
Short-run emphasis	14.373	$p < 0.001$	HS = contralateral > control (0.88 ± 0.4) (0.88 ± 0.3) (0.72 ± 0.18)
Fraction of image in runs	14.297	$p < 0.001$	HS = contralateral > control (0.85 ± 0.05) (0.84 ± 0.04) (0.69 ± 0.18)
Sum of entropy obtained by the analysis of groups of 1 pixel	5.995	$p < 0.01$	HS = contralateral > control (1.11 ± 0.07) (1.13 ± 0.1) (0.98 ± 0.27)
Difference of entropy from groups of 1 pixel	6.651	$p < 0.01$	HS = contralateral > control (0.72 ± 0.07) (0.73 ± 0.08) (0.62 ± 0.16)
Sum of entropy from groups of 2 pixels	5.694	$p < 0.01$	HS = contralateral > control (1.06 ± 0.06) (1.08 ± 0.09) (0.94 ± 0.26)
Difference of entropy from groups of 2 pixels	6.171	$p < 0.01$	HS = contralateral > control (0.79 ± 0.08) (0.81 ± 0.08) (0.69 ± 0.18)
Sum of entropy from groups of 3 pixels	5.896	$p < 0.01$	HS = contralateral > control (1.05 ± 0.7) (1.05 ± 0.1) (0.92 ± 0.22)
Difference of entropy from groups of 3 pixels	6.537	$p < 0.01$	HS = contralateral > control (0.80 ± 0.08) (0.83 ± 0.08) (0.70 ± 0.19)

APPENDIX 1.

The text shows the formulae of the moments computed for each type of feature, which correspond to the "feature parameters." A brief explanation follows the formulae and explains the meaning of each parameter.

Appendix 1. *The texture parameters that most significantly discriminated among hippocampal sclerosis, contralateral hippocampi, and normal hippocampi*

A. Fraction of image in runs

$$fraction = \sum_{i-1}^{Ng}\sum_{j-1}^{Nr} p(i, j) \bigg/ \sum_{i-1}^{Ng}\sum_{j-1}^{Nr} jp(i, j)$$

B. Short-run emphasis

$$short\_run\_emphasis = \left(\sum_{i-1}^{Ng}\sum_{j-1}^{Nr}\frac{p(i, j)}{j^2}\right) \bigg/ C$$

Fraction of image in runs and short-run emphasis are run-length matrix-based parameters, calculated according to the formulae, where $p(i, j)$ is the number of times there is a run of length j having gray level i (N_g is the number of gray levels and N_r is the number of runs). Therefore $p(i, j)$ represents an element of a matrix that has N_g lines and N_r columns. Note that N_r is limited by the size of the image [or region of interest (ROI)] considered. In the case of the Mazda software, four run-length matrices are computed, by considering runs in the directions horizontal, vertical, and the two diagonals. The fraction of image in runs is thus a measure of the percentage of image pixels that are part of any of the runs considered, and the short-run emphasis is a measure of the proportion of runs occurring in the image which have short length.

C. Sum entropy

$$Sum\_entropy = -\sum_{i-1}^{2Ng} p_{x+y}(i)\log(p_{x+y}(i))$$

$$p_{x+y}(k) = \frac{1}{A}\sum_{\substack{i-1\\ i+j=k}}^{Ng}\sum_{j-1}^{Ng} p(i, j) \quad k = 2, 3, \ldots, 2N_g$$

D. Difference Entropy

$$Difference\_entropy = -\sum_{i-1}^{Ng} p_{x-y}(i)\log(p_{x-y}(i))$$

$$p_{x-y}(k) = \frac{1}{R}\sum_{\substack{i-1\\ |i-j|=k}}^{Ng}\sum_{j-1}^{Ng} p(i, j) \quad k = 0, 1, \ldots, N_g - 1$$

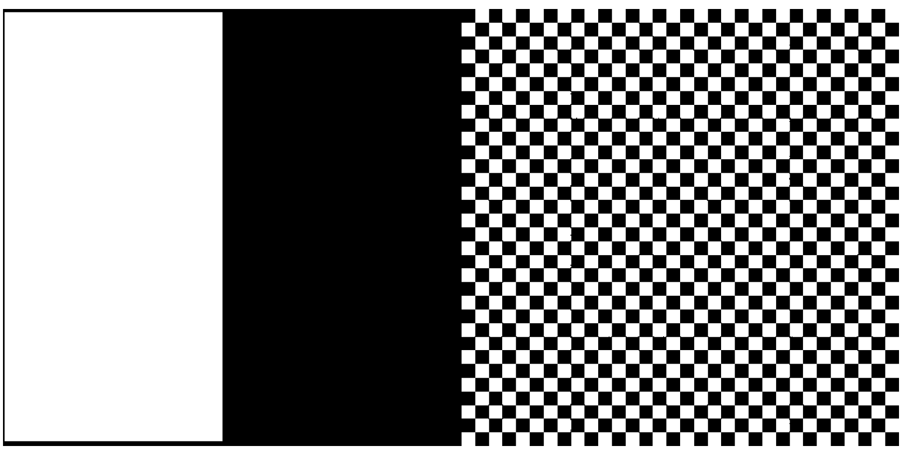

FIG. 2. Texture parameter corresponds to the frequency and spatial distribution of the gray tone. Both figures have the same number of pixels in gray tone 0 (white) and in gray tone 256 (black). However, the distribution of these pixels is different, yielding different texture characteristics.

Sum entropy and difference entropy are co-occurrence matrix-derived parameters, calculated according to the formulae, where $p(i, j)$ is an element of the co-occurrence matrix, giving the joint probability of occurrence of two pixels with gray-level intensities i and j, separated by a given distance, in a given direction; and N_g is the number of gray levels in the image. This means that for each given distance and direction, we have an $N_g \times N_g$ square matrix. Again, the Mazda software considers only distances from 1 to 5 pixels, and four directions (horizontal, vertical, and the two diagonals), giving 20 such matrices. Given thus the co-occurrence matrix of probabilities $p(i, j)$, $p_{x+y}(k)$ represents a distribution obtained from $p(i, j)$ by adding the probabilities where $i + j$ equals a constant; conversely, $p_{x-y}(k)$ represents a distribution obtained from $p(i, j)$ by adding the probabilities where $|i - j|$ equals a constant. The sum and difference entropy parameters are thus obtained by computing the entropy of $p_{x+y}(k)$ and $p_{x-y}(k)$ respectively. (Note: the entropy of a probability distribution $p(i)$, $\mathrm{I} = 1, \ldots, \mathrm{N}$, is given by $\mathrm{E} = -\sum_1^N p(i) \log[p(i)]$.)

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