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Enhancing contrast to noise ratio of hippocampi affected with mesial temporal sclerosis: A case-control study in children undergoing epilepsy surgeries

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ABSTRACT

Objective: Detection of mesial temporal sclerosis (MTS) in children with epilepsy is important. We assessed whether an image-processing algorithm (Correlative Image Enhancement, CIE) could facilitate recognition of hippocampal signal abnormality in the presence of MTS by increasing contrast to noise ratio between affected hippocampus and normal gray matter.

Patients and Methods: Baseline coronal FLAIR images from brain MRIs of 27 children with epilepsy who underwent hippocampal resection were processed using CIE. These included 19 hippocampi with biopsy proven MTS and 8 biopsy proven normal hippocampi resected in conjunction with hemispherotomy. We assessed the effect of processing on contrast to noise ratio (CNR) between hippocampus and normal insular gray matter, and on assessment of hippocampal signal abnormality by two masked neuroradiologists.

Results: Processing resulted in a significant increase in mean CNR (from 3.9 ± 5.3 to 25.3 ± 25.8; $P < 0.01$) for hippocampi with MTS, with a substantial (> 100%) increase from baseline seen in 15/19 (78.9%) cases. Baseline CNR of 1.7 ± 5.3 for normal hippocampi did not change significantly after processing (1.8 ± 5.3; $P = 1.00$). For one reader, baseline sensitivity (14/19; 73.6%) was unaffected but the specificity improved from 62.5% (5/8) to 100%. An increase in both sensitivity (from 73.6% to 78.9%) and specificity (from 62.5% to 75%) was seen for the second reader.

Conclusion: By enhancing CNR for diseased hippocampi while leaving normal hippocampi relatively unaffected, CIE may improve the diagnostic accuracies of radiologists in detecting MTS-related signal alteration within the affected hippocampus.

1. Introduction

Mesial temporal sclerosis (MTS) is the second most common histopathologic diagnosis in pediatric patients with drug-resident focal epilepsy. [1] The characteristic histologic features of MTS are hippocampal volume loss and gliosis [2,3]. Surgical resection of the hippocampus in patients with MTS and refractory medial temporal lobe epilepsy can be curative [4]. Pre-operative detection is therefore crucial for treatment planning and optimal patient management [5].

In conjunction with epileptiform electroencephalography, many qualitative and quantitative imaging modalities exist to facilitate MTS detection including Magnetic Resonance Imaging (MRI), Positron Emission Tomography, single-photo emission computerized tomography, and volumetry. [6,7] Structural findings of MTS on MRI include decreased hippocampal volume and distorted hippocampal architecture. Affected hippocampi also demonstrate increased T2 and FLAIR signal relative to normal gray matter [8–11].

Although advanced MTS may be easily identified on MRI in unilateral disease with obvious asymmetry, subtle and difficult cases can be overlooked even by experienced neuroradiologists [12,13]. Detection of aberrant signal within the affected hippocampus is particularly important when hippocampal volumes are preserved, patients with

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bilateral disease, and those with generalized cerebral atrophy [14–19]. A mean duration of symptoms of 22.5 years at the time of diagnosis may reflect these challenges in diagnosing MTS on routine MRI and may contribute to delayed diagnosis and potential cure [1].

Correlative Image Enhancement (CIE) is an algorithm based on a patented image-processing method that aims to improve conspicuity of details of interest within digital images [20]. It has been shown to improve gray-white matter differentiation in head CT images, with a potential to improve detection of signs of early ischemic infarction [21]. (Sharma A, Goyal M, Miller-Thomas M, Jain R, McEachern J, Hildebolt CF: Feasibility Of Improving Detection Of Early Ischemic Infarction on Head CT Using Continuity-Based Correlative Enhancement. Paper presented at the Radiological Society of North America Scientific Assembly and Annual Meeting, Chicago, IL, November 29 - December 4, 2015) A previous preliminary investigation also found that when the algorithm is applied to patients with MTS, the contrast-to-noise ratio (CNR) of the abnormal hippocampus could be enhanced, increasing the conspicuity of abnormal hippocampal signal. (Parsons M, Sharma A, Mhapsekar R, Hildebolt C.: Image Processing to Improve Visualization of Mesial Temporal Sclerosis on MRI. Radiological Society of North America Scientific Assembly and Annual Meeting, Chicago, IL, November 27 - December 2, 2016) This study was, however, limited by absence of controls, making the effect of such processing on sensitivity and specificity difficult to assess. We aimed to further test this algorithm in a case-control study design using MRIs of hippocampi proven on histologic evaluation as being diseased or normal.

2. Materials and methods

The Institutional review board and Washington University in Saint Louis approved this retrospective study with waiver of consent for use of existing imaging data.

2.1. Patient selection

Patients were selected from a database of epilepsy surgeries performed by a pediatric neurosurgeon over a period of 10 years. Inclusion criteria were availability of preoperative coronal FLAIR images through the hippocampi and histopathologic categorization of resected hippocampi as either MTS (cases) or normal (controls). Patients with equivocal histopathology were excluded. A total of 27 patients (19 cases and 8 controls) qualified for the study.

2.2. Image processing

Coronal FLAIR images from qualified patients were processed by one of the co-authors who did not participate in patient selection and who was masked to the case vs. control status of the hippocampi. Images were processed within Osirix-Lite using a custom plug-in that facilitated application of CIE directly to the DICOM images. The algorithm was designed to markedly increase the signal intensity of those regions within hippocampi or insular cortices, whose objective inherent signal intensity was significantly higher than that of normal appearing insular gray matter selected by the user (Figs. 1 and 2). The processed images were saved as a new DICOM series.

2.3. Quantitative image analysis

Using Osirix-Lite's inbuilt tools, signal intensity of each hippocampus was sampled at three locations along hippocampal length, making sure to include any images with obviously abnormal signal. The average of these three measurements provided a measure of the hippocampal signal intensity(H). ROIs varied in size but were placed to include most of hippocampus in a given image, while avoiding adjacent structures. Signal intensity of normal appearing insular cortex (GM) was sampled as a measure of normal gray matter. The standard deviation of intensity measurement in air around the scalp was noted as a measure of noise (N). Baseline and processed images were sampled at equivalent locations by copying and pasting ROIs across the corresponding images.

CNR (H-GM/N) between each hippocampus and normal gray matter was then calculated for baseline(CNR) and processed (CIE_CNR) images.

2.4. Masked image review

Two neuroradiologists with < 1 and > 10 years of subspecialty experience respectively viewed the images within Osirix-Lite and rated each hippocampus for its signal intensity and for presence of MTS on a 5-point scale (1: definitely normal; 2: probably normal; 3: possibly normal; 4: probably abnormal; 5: definitely abnormal). Baseline and processed images were assessed > 1 week apart to prevent recall bias. Both baseline and processed images were presented at similar display settings with option to change these settings left at the discretion of the readers.

2.5. Statistical analysis

For cases and controls, the distributions of differences in CNR between processed and baseline images (CIE_CNR minus baseline CNR) were tested for normality with the Shapiro-Wilk W test. Because both distributions were non-normal (Shapiro-Wilk W test, $p < 0.01$), the Wilcoxon signed rank test was used to test the null hypothesis that the difference was equal to 0.0.

To assess the effect of processing on confidence of detection of signal alteration, differences between the signal intensity ratings for processed and baseline images were calculated. Because ratings were ordinal data, differences were assessed with the Wilcoxon test for paired samples. The expectation is that for disease cases the number of positive differences will be higher than the number of negative differences and for control cases the number of negative differences will be higher than the number of positive differences.

For assessing diagnostic performance of two readers, signal intensity and MTS ratings were converted into binary responses with rating of 4 or 5 signifying a positive response indicating presence of abnormality. Sensitivities, specificities, and accuracies along with 95% confidence intervals were calculated for each reader for baseline and processed images.

3. Results

Baseline CNR for diseased hippocampi was 3.9 ± 5.3. Corresponding CIE-CNR for processed images was 25.3 ± 25.8, representing significant increases from baseline ($P < 0.01$). Baseline CNR for control hippocampi was 1.7 ± 5.3. The corresponding CIE_CNR for control hippocampi was 1.8 ± 5.3, which was not significantly different from baseline ($P = 1$).

An increase in CNR was seen in 16/19 cases, with an increase of $> 100\%$ from baseline in 15 cases (78.9%) (Fig. 3). For one reader, this was associated with an improved confidence of identifying hippocampal signal alteration in 5 cases, decreased confidence in 1, and unchanged confidence in 10. The second reader had increased confidence in 5 cases, decreased confidence in 3, and unchanged confidence in 8. In 3 cases, CNR of the diseased hippocampus remained unchanged following processing (Fig. 3). Despite these 3 images remaining unaffected, there was a change in confidence ratings, with decreased confidence (2 for reader1, 3 for reader 2). Overall, there was no significant change in the confidence of signal intensity rating ($P = 0.97$ and $P = 0.65$) for diseased cases.

CNR remained unaffected following processing in 7/8 (87.5%) control hippocampi and showed minimal change in one (12.5%) (Fig. 4). For 7 normal hippocampi in which processing the left