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ORIGINAL REPORT

Hippocampal sclerosis: Volumetric evaluation of the substructures of the hippocampus by magnetic resonance imaging☆

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KEYWORDS
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Abstract
Objective: The pathological classification of hippocampal sclerosis is based on the loss of neurons in the substructures of the hippocampus. This study aimed to evaluate these substructures in patients with hippocampal sclerosis by magnetic resonance imaging and to compare the usefulness of this morphological analysis compared to that of volumetric analysis of the entire hippocampus.
Material and methods: We included 25 controls and 25 patients with hippocampal sclerosis whose diagnosis was extracted from the institutional epilepsy board. We used FreeSurfer to process the studies and to obtain the volumetric data. We evaluated overall volume and volume by substructure: fimbria, subiculum, presubiculum, hippocampal sulcus, CA1, CA2–CA3, CA4, and dentate gyrus (DG). We considered $p < 0.05$ statistically significant.
Results: We observed statistically significant decreases in the volume of the hippocampus ipsilateral to the epileptogenic focus in 19 (76.0%) of the 25 cases. With the exception of the hippocampal sulcus, we observed a decrease in all ipsilateral hippocampal substructures in patients with right hippocampal sclerosis (CA1, $p = 0.0223$; CA2–CA3, $p = 0.0066$; CA4–GD, $p = 0.0066$; fimbria, $p = 0.0046$; presubiculum, $p = 0.0087$; subiculum, $p = 0.0017$) and in those with left hippocampal sclerosis (CA1, $p < 0.0001$; CA2–CA3, $p < 0.0001$; CA4–GD, $p < 0.0001$; fimbria, $p = 0.0183$; presubiculum, $p < 0.0001$; subiculum, $p < 0.0001$). In four patients with left hippocampal sclerosis, none of the substructures had statistically significant alterations, although a trend toward atrophy was observed, mainly in CA2–CA3 and CA4–GD.
Conclusion: The findings suggest that it can be useful to assess the substructures of the hippocampus to improve the performance of diagnostic imaging in patients with hippocampal sclerosis.

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PALABRAS CLAVE
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Esclerosis hipocampal: evaluación volumétrica de las subestructuras del hipocampo utilizando resonancia magnética

Resumen
Objetivo: Evaluar las subestructuras hipocampales utilizando resonancia magnética en pacientes con esclerosis hipocampal (EH), comparando los resultados con el análisis morfológico y la volumetría global del hipocampo.
Método: Se incluyeron 25 controles y 25 pacientes con EH, cuyo diagnóstico fue extraído del informe de la junta institucional de epilepsia. Se utilizó FreeSurfer para el procesamiento de los estudios y la obtención de los datos volumétricos. El volumen fue valorado de manera global y por subestructura: fimbria, *subiculum*, *presubiculum*, fisura hipocampal, CA1, CA2-CA3, CA4 y giro dentado (GD). Se consideró $p < 0,05$ como estadísticamente significativo.
Resultados: Se observó una disminución estadísticamente significativa en el hipocampo homolateral al foco epileptógeno en 19 de los 25 casos (76,0%). A excepción de la fisura hipocampal, se observó una disminución en todas las subestructuras hipocampales homolaterales en la EH derecha (CA1, $p = 0,0223$; CA2−CA3, $p = 0,0066$; CA4−GD, $p = 0,0066$; fimbria, $p = 0,0046$; *presubiculum*, $p = 0,0087$; *subiculum*, $p = 0,0017$) y la EH izquierda (CA1, $p < 0,0001$; CA2−CA3, $p < 0,0001$; CA4−GD, $p < 0,0001$; fimbria, $p = 0,0183$; *presubiculum*, $p < 0,0001$; *subiculum*, $p < 0,0001$). En cuatro casos de EH izquierda, ninguna de las subestructuras presentó alteración estadísticamente significativa; sin embargo, se observó una tendencia de atrofia, principalmente en CA2−CA3 y CA4−GD.
Conclusión: Los hallazgos sugieren la utilidad de la evaluación de las subestructuras hipocampales para mejorar el desempeño de la imagen en el diagnóstico de la EH.

Introduction

Epilepsy is one of the most common neurological disorders and is characterized by involuntary movements, whether partial or generalized, that are sometimes accompanied by loss of consciousness and sphincter control. Back in 2013, the Pan-American Health Organization estimated that nearly 50 million people around the world suffer from epilepsy and that over 2 million new cases are diagnosed each year.[1,2] Although the standard medical therapy for epilepsy is based on the administration of drugs to control the epileptic seizures, 30% of the cases are refractory to medical therapy, being surgery an alternative with healing results and minimal morbidity.[3]

Hippocampal sclerosis (HS) is the most common form of epilepsy of the temporal lobe and in the imaging diagnosis it is characterized by an alteration of signal intensity in the T2-weighted sequences and a reduced size of the affected hippocampi—findings that have been associated with neuronal loss, atrophy, and gliosis of such structures.[4–9] Qualitative assessment through conventional magnetic resonance imaging (MRI) studies has shown low predictive values in the identification of hippocampal atrophy, being more critical in cases with head rotation, alteration of signal intensity, and mild or bilateral atrophy, and a high risk of false-negatives in qualitative assessments even for the most experienced professionals.[10,11]

Compared to qualitative analyses and other quantitative techniques such as spectroscopy and relaxometry, the quantitative assessments of the hippocampal volume have shown superior predictive values in the identification of unilateral and bilateral HS.[6,9,10] Also, the reduced hippocampal volume in this condition has been associated with a reduced neuronal density, frequency, and duration of the seizures, with the postoperative prognosis, and with neuropsychological functions.[12,13] However, outlining these structures manually requires time which is liable to inter- and intraobserver measurement error variability. It is for this reason that automatic methods for the assessment of brain volume were developed during the past decade, and their findings have been compared to manual techniques showing high rates of reliability, sensitivity, and reproducibility of information.[14,15] For the last few years, complementary tools have been developed in order to conduct deeper segmentations of structures of great clinical and research interest such as hippocampal formation.

The hippocampal complex that is part of the so-called limbic system is made up of the temporal lobe allocortex and is found along the floor of the lateral ventricle forming an S. This complex is made up of the *subiculum*, the dentate gyrus (DG), the fimbria (origin of the fornix), and the hippocampus, which is, in turn, divided into four areas known as *cornu ammonis* (CA) (Fig. 1). The pathological classification of HS is based on the neuronal loss of such hippocampal structures, which in clinical–pathological studies has been associated with the duration of the disease and the patient's postoperative prognosis.[16] On the other hand, numerous authors have studied changes in the hippocampal formation homolateral to the epileptogenic region using electroencephalograms, observing a progressive reduction both of the hippocampal volume and the focal concentration of *N*-acetylaspartate in patients diagnosed with HS,[17–20] while Chan et al.[21] showed that this atrophy does not occur uniformly, but originates at the DG and in the CA1, CA4 and,