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MRI volume loss of subcortical structures in unilateral temporal lobe epilepsy

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Abstract

Few studies have examined the relative degree of brain volume loss in both the hippocampi and subcortical structures in unilateral temporal lobe epilepsy (TLE) and their association with clinical seizure correlates. In this study, quantitative MRI volumes were measured in the hippocampus, thalamus, caudate, putamen, and corpus callosum in 48 patients with unilateral TLE (26 right, and 22 left) and compared with the volumes of 29 healthy controls. The ipsilateral hippocampus, corpus callosum, and bilateral thalami exhibited the greatest volume loss, reflected by large to moderate effect size differences compared with controls. Bilaterally, the putamen showed the next highest volume reduction. The contralateral hippocampus and bilateral caudate nuclei showed the least volume reduction, characterized by small effect sizes. Furthermore, clinical seizure characteristics (e.g., duration of epilepsy) exhibited different patterns of association with the volume reductions observed across these structures. Findings suggest that distinct neurodevelopmental features may play a role in the volume abnormality observed in these regions.

Keywords: Temporal lobe epilepsy; Subcortical; Quantitative magnetic resonance imaging

1. Introduction

Quantitative MRI studies have characterized the nature, extent, and clinical seizure correlates of hippocampal atrophy in unilateral temporal lobe epilepsy (TLE) [1–3]. The typical pattern is asymmetric hippocampal volume loss with greater abnormality in the ipsilateral hippocampus compared with the contralateral hippocampus. In addition, both disease course features (e.g., duration) and neurodevelopmental features (e.g., history of complex febrile seizures in childhood) have been implicated in hippocampal atrophy [4–7].

Quantitative MRI studies have confirmed that TLE is also associated with brain volume abnormalities in structures outside the hippocampus. Brain volume loss has been reported for adjacent mesial temporal lobe structures including the amygdala and parahippocampal region, as well as more distal structures within the ipsilateral temporal lobe [8,9]. More recent investigations have provided evidence that regions outside of the temporal lobe, including the thalamus, striatum, and corpus callosum, are also affected [10–14].

To date, there has been limited examination of multiple subcortical structures and the hippocampus in the same study sample. Across studies there is considerable heterogeneity in the composition of TLE groups studied, which may account for the differences in findings reported in the literature. For example, findings are mixed as to the extent of damage evident in the thalamus (ipsilateral or bilateral) and basal ganglia, and there are also differences reported concerning the relationship of potential etiological factors to subcortical brain volume abnormalities [11,13,14].

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The purpose of this study was to examine MRI volume integrity of the hippocampus and multiple subcortical structures in the same cohort of subjects. There are several advantages to examining multiple structures in a single cohort of patients with TLE. First, it ensures that the subject characteristics of the TLE group, clinical seizure characteristics, and MRI measurement characteristics will be the same for all the structures examined. Second, it facilitates quantification of the relative extent of volume abnormality across different structures. Third, it provides an opportunity to examine the influence of both disease course features and early neurodevelopmental features across multiple structures within the same cohort. Recent studies employing this approach have focused on the medial temporal lobe region and have helped to delineate the relative impact of atrophy evident within different parts of this region and its associated clinical seizure correlates [15].

This study examined the hippocampus, thalamus, caudate, putamen, and corpus callosum. Selection of regions of interest (ROIs) was guided by previous findings indicating atrophy in these regions and evidence that these structures are considered important in seizure initiation, modulation, and/or propagation [16]. Specifically, we used quantitative MRI to: (1) measure and compare MRI volumes of the hippocampus, thalamus, corpus callosum, caudate, and putamen; (2) examine the association of age at onset, duration of epilepsy, number of antiepileptic drugs (AEDs), and lifetime number of secondarily generalized seizures with brain volume in these structures; and (3) provide a systematic presentation of the relative volume abnormality (effect size and percent difference) evident in these structures.

2. Methods

2.1. Participants

The study sample consisted of a total of 77 subjects between the ages of 14 and 60: 48 subjects (26 right and 22 left) with unilateral chronic TLE and 29 healthy controls. The institutional review boards at the University of Wisconsin Hospital and Rosalind Franklin University of Medicine and Science approved the study and informed consent was obtained from each study participant. Comprehensive assessment of seizure history, clinical semiology, and neuroimaging findings (e.g., PET) was used for diagnosis of TLE. For all patients, findings from video/EEG telemetry with scalp recordings confirmed evidence of unilateral temporal lobe onset of spontaneous seizures. Patients with independent left and right temporal lobe onset were excluded. All scans were reviewed by a neuroradiologist. Patients with MRI evidence of lesions (e.g., tumor, vascular malformation) other than hippocampal sclerosis were also excluded. Patients with TLE were typically interviewed in the presence of a family member regarding details of their epilepsy history and clinical course. Available medical records concerning previous epilepsy-related hospitalizations and records from treating physicians were reviewed.

Healthy controls were either friends or family members, primarily spouses, of the patients with TLE. Inclusion of friends and spouses helped rule out shared genetic factors that may contribute to cognitive and neural development. They were also between the ages of 14 and 60, with no current substance abuse, no medical conditions, no history of loss of consciousness longer than 5 minutes, and no history of developmental learning disorder.

2.2. MRI acquisition and postprocessing

Images were obtained on a 1.5-T GE Signa MRI scanner. Sequences acquired for each subject included: (1) T1-weighted, three-dimensional SPGR (TE = 5, TR = 24, flip angle = 40, NEX = 2, FOV = 26, slice thickness = 1.5 mm, slice plane = coronal, matrix = 256 × 192), and (2) proton density (PD) and (3) T2-weighted images (TE = 36 m (for PD) or 96 ms (for T2), TR = 3000 ms, NEX = 1, FOV = 26, slice thickness = 3.0 mm, slice plane = coronal, matrix = 256 × 192, echo train length = 8).

MRI scans were acquired at the University of Wisconsin Hospital and were processed using a semiautomated software package, Brain Research: Analysis of Images, Networks, and Systems (BRAINS2) [17]. The T1-weighted images were spatially normalized so that the anterior–posterior axis of the brain was realigned parallel to the anterior commissure–posterior commissure (ACPC) line, and the interhemispheric fissure was aligned on the other two axes. A six-point linear transformation was used to warp the standard Talairach atlas space onto the resampled image. Images from the three pulse sequences were then co-registered using a local adaptation of automated image registration software. Following alignment of the image sets, the PD and T2 images were resampled into 1-mm cubic voxels, following which an automated algorithm classified each voxel as gray matter, white matter, cerebrospinal fluid (CSF), blood, or "other." Neuroimaging analyses were conducted by raters blinded to group status, cognitive functioning, and both clinical and sociodemographic characteristics of the subjects. ROIs included the hippocampus, thalamus, caudate, putamen, and corpus callosum. Fig. 1A–C illustrate prototypical tracings of these ROIs.

2.3. Hippocampus tracing guidelines

An automated neural network application was used to trace the hippocampus using guidelines established and psychometrically validated by the University of Iowa, with manual correction of the traces by a qualified technician [18]. Guide traces were performed in the sagittal view, while the neural net was edited in the coronal view. These tracings included the pes or head of the hippocampus, the body, and the tail. Within the hippocampus, the subic-

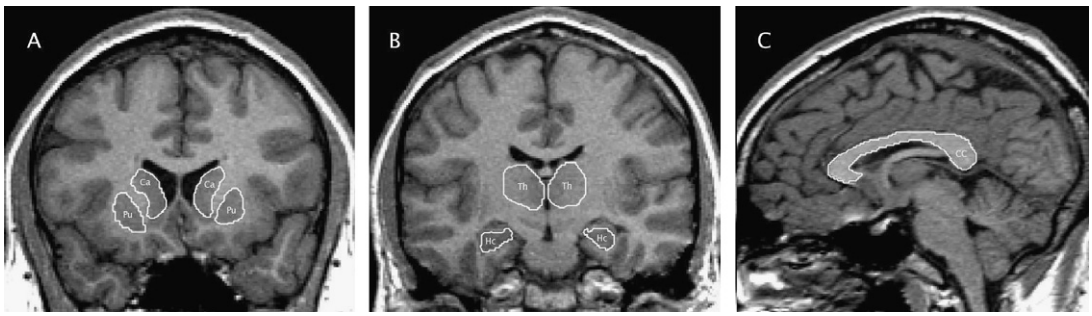

Fig. 1. MRI regions of interest. (A) Caudate (Ca) and putamen (Pu). (B) Thalamus (Th) and hippocampus (Hc). (C) Corpus callosum (CC).