MRI Volumetric Analysis Techniques, Including Hippocampus Extraction, Based on Data from the Honolulu Asia Aging Study (HAAS)

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Purpose: The purpose of this study is to develop and apply methods for volumetric analyses of magnetic resonance imaging (MRI) data for future comparisons with autopsy findings from the same subjects.

Methods: HAAS MRI data analysis was run using the Oxford Centre for Functional Magnetic Resonance Imaging of the Brain's (FMRIB) Software Library (FSL). The Brain Extraction Tool (BET) performed brain extraction and nonlinear noise reduction with FMRIB's Smallest Univalue Segment Assimilating Nucleus (SUSAN), and extraction of hippocampus data was performed with FMRIB's Integrated Registration and Segmentation Tool (FIRST).

Results: Scull stripping and the extraction of the hippocampus data created a computerized model.

Discussion: MRI analysis techniques can be applied when comparing MRI data to autopsy results. Using the combination of this autopsy and MRI data, this study will make it possible to estimate *in vivo* states. (*Ethn Dis*. 2010; 20[Suppl 1]:S1-104–S1-106)

Key Words: MRI, Hippocampus Extraction, Honolulu Asia Aging Study

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Introduction

The Honolulu Asia Aging Study (HAAS), which has followed Japanese American men since 1965, has collected magnetic resonance imaging (MRI) scans on 600 subjects between 1994 and 1996.[1–4] HAAS also includes autopsy data detailing neurofibrillary tangles, amyloid plaques, infarcts, atrophies, other Alzheimer's-related lesions, the Cognitive Abilities Screening Instrument (CASI), dementia evaluations, and various neurological tests.[5–7]

Segmentation and extraction of brain parts have been explored but were limited to the putamen, thalamus, hippocampus in Alzheimer's brains.[1,8,9] There also had been an effort to compare the various MRI quantification software such as FSL, Freesurfer, and SPM.[10] However, in these studies, the very old brain was not the focus of the studies. Thus, our research focused on the very old brain in normal- aging subjects and our purpose was to develop and apply methods for volumetric analyses of MRI data for future comparisons with autopsy findings from the same subjects.

Methods

Study Subjects and MRI Data

The study participants originated from the HAAS cohort. The range of ages at the time of MRI scan was between ages 75 and 94 years, with average age of 81.37 (SD=5.06 years, median= 80.00). A GE Signa 1.5T MRI machine (GE Healthcare, Piscataway, NJ) was used for acquiring coronal slice images, Sagittal T1 images, and PD and T2 axial images. The native genesis files were converted to Analyze 7.5 format with 8-bit .tif image and 16-bit .img file with corresponding header (hdr) file. The original genesis file names were truncated to comply with the "8.3" file naming convention in ISO-9660 format on the CD-ROM.

Procedure

To investigate cross-disciplinary associations, the MRIs were studied alongside data from the behavioral and cognitive tests as well as autopsy observations from HAAS. As a first step, HAAS MRI data were preprocessed with several MRI software programs: the Brain Extraction Tool (BET)[11] and Smallest Univalue Segment Assimilating Nucleus (SUSAN),[12] from the Oxford Centre for Functional Magnetic Resonance Imaging of the Brain's (FMRIB) Software Library (FSL).[13,14] Second, the preprocessed MRI data were analyzed with: a) FMRIB's Automated Segmentation Tool (FAST)[14,15] to separate gray matter from white matter; b) Structural Image Evaluation Using Normalization of Atrophy Cross-Sectional (SIENAX)[13,16] to estimate brain volumes; and c) FMRIB's Integrated Registration and Segmentation Tool (FIRST)[14,17] to extract the hippocampus.

Brain extraction was performed with FMRIB's BET. Nonlinear noise reduction was performed by FMRIB's SUSAN, to distinguish between noise and signal without blurring the underlying image. (Figure 1).

Results

Volumetric Analysis

The whole brain was segmented into 17 brain parts: left lateral ventricle, left thalamus proper, left caudate, left putamen, left pallidum, brainstem, left hippocampus, left amygdala, left ac-

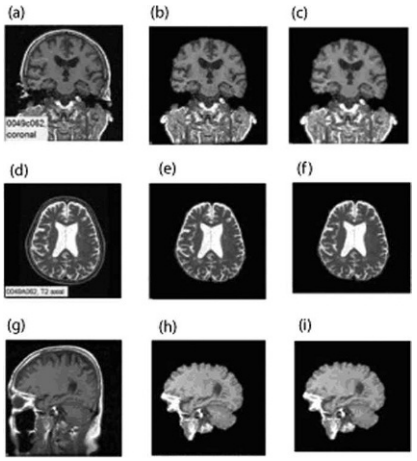

Fig 1. BET and SUSAN image processing. Coronal, proton density, and sagittal images first processed by BET, then by SUSAN. (a) coronal image before skull stripping, (b) coronal image after BET with fractional intensity threshold of 0.40, (c) coronal image after BET and SUSAN with bright threshold of 2000 and mask half-width of 2mm, (d) axial T2 image before skull stripping, (e) axial image after BET with fractional intensity threshold of 0.52, (f) axial image after BET and SUSAN with bright threshold of 79.39 and mask half-width of 2mm, (g) sagittal image before skull stripping, (h) sagittal image after BET with fractional intensity threshold of 0.85, (i) sagittal image after BET and SUSAN with bright threshold of 43.84 and mask half-width of 2mm

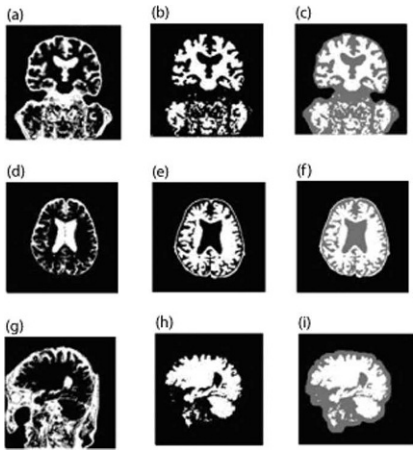

Fig 2. Brain segmentation with bias field correction. (a) coronal image with CSF, (b) coronal image with gray and white matter, (c) coronal image with CSF, gray, and white matter, (d) axial image with CSF , (e) axial image with gray and white matter, (f) axial image with CSF, gray, and white matter, (g) sagittal image with CSF, (h) sagittal image with gray and white matter, (i) sagittal image with CSF, gray, and white matter

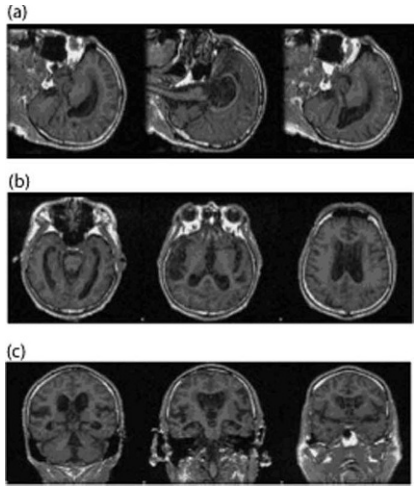

Fig 3. Whole brain segmentation by SIENAX. (a) sagittal images, (b) axial images, (c) coronal images

cumbens area, right lateral ventricle, right thalamus proper, right caudate, right putamen, right pallidum, right hippocampus, right amygdala, and right accumbens area. Figure 2 shows the bias field correction results. After the segmentation, the left hippocampal volume was calculated with FIRST in FSL.

Structural Brain Change Analysis

The SIENAX procedure yielded the volume of the whole brain. By estimating the intracranial volume, it was then possible to estimate the atrophy (Figure 3). Slightly fewer than half of the subjects were cognitively normal and had no substantial risk factors for dementia. The others were diagnosed with dementia, mild cognitive impairment, or stroke at the time of the scan, or had been identified as carrying the epsilon 4 allele of the apolipoprotein E gene (the only gene definitively linked to late-onset Alzheimer's disease). Approximately 20% of the scanned subjects who were unimpaired at the time of their scans subsequently developed dementia or mild cognitive impairment. Nearly 100% of the scanned subjects subsequently died and came to autopsy.

DISCUSSION

The scope of this study was to report the success of volumetric analyses of HAAS MRI scans despite the severe atrophy of the very old brain. Older brains and neonatal brains are very difficult cases of parcellation due to the small size and the variation of the signals in tissues.[17]

This study confirmed that the FAST procedure could find general white matter volume, gray matter volume, CSF volume, and intracranial volume. Since HAAS has intracranial volume estimation from autopsy, this MRI FAST procedure could be used as a confirmatory tool for very old brains in future studies. Also, this study found that hippocampal extraction was possible in the very old brain. The volumetric comparisons between MRI analyses and autopsy data would be possible as another validating tool for the very old brain although hippocampal shape analysis had been conducted.[6]

One limitation of this study is the fact that matching data, which would be produced in the future on intracranial volume and on hippocampal volume between MRI analysis and autopsy data, would not guarantee the accuracy of the other data analyses from an MRI. Another limitation is that this study's scope is limited to the methodological validation on the very old brain.

While confirmation between MRI and autopsy data has been extensively explored by other researchers,[18] the implications of this study are on the combined strengths of MRI, epidemiology, and autopsy study for the very

old brain. MRI data give the current volumetric information; epidemiological studies provide the information on the clinical courses the patients have taken; and, autopsy studies provide ultimate verdict of the brain pathology. In order to merge these principles for utilization with the very old brain, this study confirms the link between MRI volumetric analyses and autopsy data. This study is the first step of a confirmation project that will report volumetric MRI analyses in the very old brain were possible. The methods presented here will be applied to the 600 MRI brain scans obtained on HAAS participants to generate volumetric estimates for gray and white matter in both the entire brain and specifically defined regions. In the near future, analyses of the accuracy of MRI analyses from the autopsy point of view will be processed. Subsequently, we will conduct analyses to assess relationships between total and regional brain volumes and clinical diagnoses, and neuropsychological test performance, based on our epidemiological data. Autopsy-based neuropathological observations will be used as a confirmatory tool while MRI volumetric analyses would provide predicting measures.

ACKNOWLEDGMENTS

This paper was supported by a Research Centers in Minority Institutions award, P20 RR11091, 1 R25 RR019321, ''Clinical Research Education and Career Development (CRECD) in Minority Institutions.'', from the National Center for Research Resources, National Institution of Health and by Grant U01AG019349-08 NIA, NIH Grant: Brain Aging in the Very Old.

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