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Semiautomatic Method to Separate Sulcal and Ventricular CSF Compartments in Alzheimer's Disease: Clinical Correlations

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Introduction

MR is a powerful, high-resolution, non-invasive technique for imaging the brain *in vivo*. Combined with appropriate computer software, it can be used to quantify the volumes of designated brain compartments and regions of interest. In conjunction with neuropsychological measures it can be used to assess brain-behaviour relationships. In this paper we focus on the potential usefulness of measuring the sulcal and ventricular cerebrospinal fluid (CSF) compartments in patients with Alzheimer's Disease (AD).

Methods

Twenty-one patients satisfying NINCDS-ARDA criteria [1] for probable AD and eighteen healthy, age-matched and education-matched controls underwent MR imaging and neuropsychological testing. For volume calculations, a two-spin-echo sequence covering the whole brain was performed in the axial plane. Fifty-eight 3 mm slices were obtained with half-Fourier sampling, 192 phase-encoding steps, TR of 3000 ms, TE of 30/80 ms, and a field-of-view of 20 cm. For hippocampal volume determination, a sagittal T1-weighted 3D volume technique was used. One hundred and twenty-four, 1.3 mm slices were obtained, with TR/TE of 35/5 ms, flip angle of 35°, and field-of-view of 22 cm.

Bifeature segmentation based on the method of Kikinis *et al* [2] was developed [3] to calculate the volume of grey matter, white matter, CSF and white matter lesions. A trained observer outlined an area in each slice which included all CSF within the ventricles. The program then calculated ventricular CSF volume and subtracted it from total CSF to give a separate estimate of sulcal CSF. To obtain accurate lobe demarcation, a brain surface reconstruction was used. Conventional anatomical landmarks were identified by the observer to separate the left and right frontal, parietal, temporal and occipital lobes (Fig 1) and these boundaries were projected orthogonally to define the equivalent brain volumes. This methodology was carefully tested and refined to achieve consistent results. Inter- and intra-operator variation were assessed and repeated analyses of two subjects were performed.

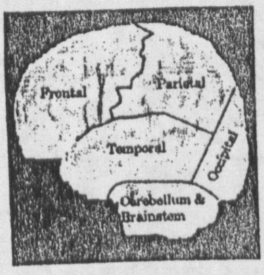

Figure 1. Lobar regions are defined on the lateral surface in each hemisphere.

To segment the hippocampus the sagittal images were used to define the endpoints of the hippocampal structures. Coronal slices perpendicular to the hippocampal endpoints were derived and the hippocampal area in the left and right hemispheres was digitized manually in each coronal image by a neuroradiologist, blind to the subject category.

Results

The method defined brain volumes very reproducibly. The intra-operator correlation coefficient for four lobe segmentation repeated at least two days apart was 0.98, and for separation of sulcal and ventricle CSF was 0.99. Percentage differences in total brain volumetric measures for serial measurements on two normal subjects over a six-month interval were less than 1%.

The neuropsychological data were used to define the range of AD and control subjects. Various models were then investigated to asses the ability of the imaging studies to distinguish between AD and control subjects. Figure 2 shows results for three models where the combination of hippocampal measurements with left parietal ventricular CSF volume provided the best discrimination between AD and the control group.

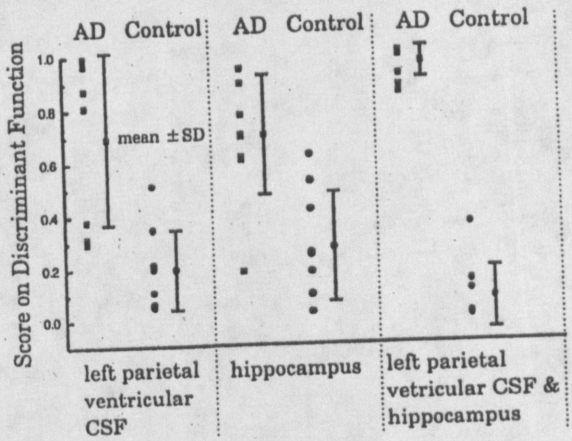

Figure 2. Score on discriminant functions for three different models comparing AD and control groups.

Conclusions

Left parietal ventricle CSF volume combined with hippocampal measurements emerged as a powerful indicator of AD. This morphometric approach offers potential for both diagnosis and quantitative monitoring of biological effects of drug therapies in progressive neurodegenerative disorders such as AD.

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