Proceedings of the Society of Magnetic Resonance in Medicine
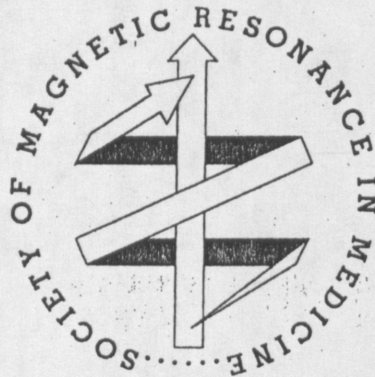## *Volume 3*

Society of Magnetic Resonance in Medicine

Twelfth Annual Scientific Meeting
August 14 - 20, 1993
New York, NY, USA

Regional Brain-Behaviour Correlations with MR Volumetric Measures in Alzheimer's Disease

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Introduction

The diagnosis of Alzheimer's disease (AD) remains a difficult medical problem. Although there are multiple descriptions of neuroimaging findings associated with AD, their relationships to other clinical manifestations of the disease remain undefined. Quantitative MR measures offer some advantage in this context because they should permit data from multiple centres to be pooled and compared. This quantitative MR approach is likely to prove useful both for developing definitive diagnostic criteria for AD and for investigations of the underlying biological basis of the disease.

Methods

Ten subjects with probable AD and ten age- and education-matched control subjects underwent detailed neuropsychological testing and MR imaging. 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 [1] was used to calculate the volume of grey matter (GM), white matter (WM), cerebro-spinal fluid (CSF) and lesions in the whole brain, and in the left and right frontal and parietal/temporal lobes. This methodology was carefully tested and refined to achieve consistent results. In particular, the use of filtering was investigated and rules were developed for choosing the "segmentation slice" which gave the best reproducibility. Inter- and intra-operator variation was assessed, longitudinal analysis was performed on two subjects, and the effect of head coil nonuniformity was assessed.

Automated segmentation of the hippocampal formation proved difficult and we adopted a manual method. The sagittal images were reformatted into coronal slices perpendicular to the hippocampal structure and the hippocampal area in the left and right hemispheres was outlined manually by a neuroradiologist, blind to the subject category.

Results

Use of a nonlinear anisotropic filter [2] with the same training points in filtered and unfiltered images leads to a decrease in GM of 1.9%, an increase in WM of 0.8% and an increase in CSF of 0.4%. This difference was so small that we decided not to use filtering. It was important, however, to choose the same "segmentation slice" in all subjects and the first image in which the anteroposterior continuity of the lateral ventricles was visible gave the best inter-observer reproducibility. Additional rules for selection of points in GM, WM, CSF and background were developed.

Inter-operator variation using these rules is shown in Table I. The inter-operator correlation coefficient was 0.97. For comparison, the intra-operator correlation coefficient for five segmentations repeated at least two days apart was 0.98. Percentage differences in total brain volumetric measures for serial measurements on two normal subjects over a six-month interval were less than 1%.

A significant increase in overall CSF volume was found for AD subjects, as well as in frontal and temporal/parietal regions. Multivariate models using age, years of education, and global measures of cognitive function showed significant correlations of some regional CSF volumes with corresponding neuropsychological tests. For example, left temporal/parietal atrophy accounted for 26% of the variance on semantic fluency (p<0.02) and left hippocampal volume for 24% of the variance on verbal learning (p<0.04). Premorbid intelligence was seen to have a modulating effect; more years of education correlated with less brain atrophy when all other factors were taken into account.

Conclusions

Careful implementation of MR techniques appears to be a good tool for quantitative longitudinal assessment of AD and for evaluating the biological benefits of drug therapies. The diagnostic utility of these MR techniques for individual patients remains to be determined.

References

1. Kikinis, R., Shenton M., Gerig G. et al., *JMRI*, 2:619-629, 1992.
2. Clarke L., Velthuizen R., Phuphanich S. et al., *Magn Reson Imaging*, 11:95-106, 1993.

Volume, cm^3	operator 1	operator 2	operator 3	operator 4	mean ± %SD
GM	596 ± 4	581 ± 3	609 ± 4	567 ± 2	588 ± 3%
WM	500 ± 12	516 ± 4	481 ± 2	537 ± 2	508 ± 4%
CSF	175 ± 1	170 ± 1	176 ± 1	165 ± 1	171 ± 3%

Table I. Segmentation results (whole brain) for the same subject with different operators.

(59.)   Bronskill M., Stanchev P., Black S., Foster J., Buck B., "Regional Brain-Behaviour Correlations with MR Volumetric Measures in Alzheimer's Disease", *Twelfth Annual Scientific Meeting, Society of Magnetic Resonance in Medicine*, New York, NY, August 14-20, 1993, 1438.