学位論文の要旨

氏名　林　貴史

学位論文名　Enlargement of the Hippocampal Angle:

A New Index of Alzheimer Disease

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著者名　Takafumi Hayashi, Akihiko Wada, Nobue Uchida, Hajime Kitagaki

論文内容の要旨

INTRODUCTION

On routine coronal magnetic resonance (MR) images, progressive hippocampal atrophy appears to increase rotation of the hippocampus. To our knowledge, this hippocampal deformity has not been reported in *in vivo* MR coronal images. We assume this alteration may be related to disease process of Alzheimer disease (AD). We defined the hippocampal angle (HA) and evaluated its enlargement in patients with AD to elucidate whether hippocampal rotation was associated with AD.

MATERIALS AND METHODS

Eleven patients were clinically diagnosed with AD according to the criteria of the National Institute of Neurological and Communicative Disorders and

Stroke/Alzheimer's Disease and Related Disorders Association. The mean Revised Hasegawa Dementia Scale (HDS-R) score was 18.7 (range 12 to 24; SD ± 4.3). Control subjects were 2 men and 9 women, aged 62 to 81 years (mean 71 years; SD ± 5.5) who had no past neurological or psychiatric history and no abnormal findings on MR images. MR imaging was performed with a 1.5-tesla MR unit. Thin-slice coronal images were obtained with 3-D spoiled gradient recalled acquisition in the steady state. The HA is the angle between a horizontal line orthogonal to the falx cerebri and the uncal sulcus line between the deepest point of the uncal sulcus and the point nearest to the side of the ambient cistern in the uncal gyrus facing the uncal sulcus. The HA is measured on the most rostral slice in which the uncal sulcus can be identified and increases with hippocampal rotation. All volume measurements were performed using the automated volumetric method with the IBASPM (Individual Brain Atlases using Statistical Parametric Mapping) software toolbox. Hippocampal volume (HV) was standardized. In brief, HV × 1000 was divided by the calculated total intracranial volume in each subject. HA and HV were measured in the left temporal lobe.

We employed Pearson's correlation coefficient analysis and simple regression analysis to assess the relation between the standardized HV and the HA or the HDS-R score. $P < .05$ was statistically significant. Receiver operating characteristic (ROC) curves were determined using the ROCKIT 0.9β and PlotROC program of Metz's group (http.bsd.uchicago.edu/krl). These programs calculate the area under a ROC curve (Az), as well as sensitivity, specificity, and accuracy.

RESULTS AND DISCUSSION

HA ranged from 30.07° to 43.22° (mean ± SD: 38.24° ± 4.79°) in the AD group and from 15.34° to 35.73° (26.64° ± 6.22°) in controls. The standardized HV was 0.68 to 1.88 (1.27 ± 0.32) for the AD group and 1.08 to 1.86 (1.60 ± 0.26) for controls. In the AD group, we recognized a positive correlation between the standardized HV and the HDS-R score ($r = .686$, $P = .02$) and a negative correlation between the standardized HV and the HA ($r = -.677$, $P = .02$), but there were no significant correlations in controls. In the AD group, the HDS-R score and the HA also correlated ($r = -.623$, $P = .04$) by Pearson's correlation coefficient analysis. The Az value was 0.93 for the HA and 0.75 for the HV. The HA was 34.4° at the point of the curve nearest to the top left corner. Specificity was 88.7%; sensitivity 80.8% and accuracy 86.4%.

We found a correlation between HV and results of cognitive function tests and between HA and both HV and cognitive function. ROC analysis indicated that HA was superior to HV in the diagnostic separation of the AD group and controls. HV measurement is time-consuming, labor-intensive, and unlikely suited to a clinical environment because no fast and robust method for direct hippocampal volumetric quantification is available. On the other hand, HA measurement is fast and easy and suitable to clinical practice as a surrogate marker of volume loss in hippocampal formation.

CONCLUSION

In patients with AD, the HA is affected by hippocampal atrophy and serves as a new marker of AD that could be useful in the routine clinical setting.