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IV. 2. Decreased Striatal Dopa Uptake Correlated with Fronto-Temporal Glucose Utilization in Alzheimer's Disease

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Previously we used [^{18}F]6-fluoro-L-dopa (FDOPA) and PET (positron emission tomography) and found that FDOPA uptake into the striatum (the Ki value) in Alzheimer's disease (AD) correlated with cognitive function. Decreased cerebral glucose utilization (CMRglc) in the parietal and temporo-parieto-occipital region were well-known PET finding in AD. We investigated the relationship between the Ki value and regional CMRglc (rCMRglc), with reference to cognitive impairment and wandering behavior. Ten AD with moderate severity of dementia were studied. Using PET and FDOPA and [^{18}F]-fluoro-deoxyglucose techniques, the Ki value and rCMRglc in the frontal, temporal, parietal, temporo-parietal, and occipital lobes were measured. There were significant Spearman correlation between the Ki value and mean cortical CMRglc. For rCMRglc, those of the frontal and temporal lobe significantly correlated with the Ki value. There could be a functional neural network between the striatum and the frontal and temporal lobes in AD.

Introduction

There were many neuroimaging studies using [^{18}F]6-fluoro-L-dopa (FDOPA)[1] as a presynaptic indicator of dopaminergic neurons in the striatum of Parkinson disease[2]. For Alzheimer's disease (AD), we noted[3] that the rate of FDOPA uptake into the striatum (the Ki value) correlated with cognitive function as shown by MMS (Mini-Mental State[4]). Using an antagonist to D_2 receptor, we reported[5] an intercorrelation between level of dopa uptake and D_2 receptor level: the data variability could support heterogeneity of AD, and that the PET-assessment of dopamine function could predict outcome of neuroleptic treatments for dementia symptoms. Subsequently we noted[6] that psychiatric wandering behavior of AD correlated with increased D_2 receptors.

On the other hand, decreased regional CMRglc in the temporal, parietal, and temporo-parieto-occipital (TPO) region in its early stage, and that in the frontal lobe in its late stage, were well-known PET finding in AD[7-9]. In this study, we investigated the relationship

between the Ki value and rCMRglc, with reference to their cognitive impairment as well as an abnormal psychiatric wandering behavior.

Methods

Patients

Ten probable AD patients with moderate severity of dementia with the NINCDS-ADRDA criteria[10] were studied. All were within 5 years of onset. All received MMS and WAIS-R[11] for their cognitive assessment.

MRI

MRI used was a 0.5T MRVectra (GE-YMS, Japan). An axial T_1-weighted MRI (TR/TE 300/15) parallel to the OM (orbito-meatal) line was examined at the same head position as in the PET study, and an axial T_2-weighted (TR/TE 2000/100) MRI was performed to exclude patietns with infarctions out of the subjects. Using the OM +40, 50, 60, 70 mm T_1-weighted planes, the % brain volume to the cranial cavity was calculated. Also, using the OM + 40 mm T_1-weighted plane, the striatum was outlined to calculate the volume by a digitizer system[12].

CMRglc Measurement

The PET study was performed with a model PT-931 scanner (CTI Inc., USA), according to the [^{18}F]-fluoro-deoxyglucose (FDG) method[13,14]. A short cannula was placed in a radial artery for blood sampling. A cross of light was projected onto marks on the subject's head, which were set at the standard points of 30 and 77 mm above and parallel to the OM line. A 20-min transmission scan using a ^{68}Ge/^{68}Ga external ring source was performed. Thirty to 45 min after the 5-12 mCi FDG injection, a series of two emission scans was performed. Twenty blood samples were collected. The plasma glucose were measured every 10 min. The analysis for CMRglc was the same as previously[12]. The rCMRGlc in the following regions were measured: upper frontal, anterior frontal, inferior frontal, primary auditory, temporal, parietal, TPO, primary visual, occipital, basal ganglia.

FDOPA Uptake Measurement

General condition including the transmission scan was the same as the FDG study. Dynamic data acquisition was performed after i.v. administration of the ligand: 6 scans of 60 sec., 8 scans of 3 min., 6 scans of 5 min., and 3 scans of 10 min. Tissue time-activity curves of the bilateral striatum were obtained using the OM +40 mm plane or the adjacent plane which had suitable striatum images. The elliptical regions of interest (ROIs) of the bilateral striatum (3.6 ± 0.6 cm^2) were set. The measurement of the Ki value was the same as previously described[3].

Statistical Analysis

We used each unilateral value of the Ki (i.e., two values for each subject) as well as rCMRglc (i.e., two values for the same ROI for each subject, 10 values for the same ROI for each group). Spearman rank correlation coefficients were calculated between the Ki value and rCMRglc in each ROI. After finding significant correlations, the effects of age, duration of the disease, and educational level were patialled out by covariance.

Results

There was no significant relationship between the Ki value and the % brain volume nor did the striatum measured by MRI (data not shown), indicating that the results described below was not due to an effect of atrophy. The Ki value and mean cortical CMRglc were significantly correlated ($p<0.01$). For rCMRglc, those in the frontal (anterior and inferior) and in the temporal (upper and lower) lobes were significantly ($p<0.01$) correlated with the Ki value.. The rCMRglc in the basal ganglia region was mildly correlated ($p<0.05$).

Discussion

We found that the striatal dopa uptake correlated with fronto-temporal glucose utilization in AD. Although the Ki value mildly correlated with rCMRglc in the basal ganglia, there was no correlation between rCMRglc in the region and those in the frontal, temporal, or parietal lobe. It meant that the finding of the Ki value - rCMRglc relation was not due to the relationship between rCMRglc in both areas. Also, since there was no significant relationship between the Ki value and the % brain or the striatum volume, the results was not due to an atrophy. The AD-pathologic changes are evident in the hippocampal area and the association neocortices[15,16]. And hippocampal atrophy and decreased rCMRglc in the parietal lobe or TPO region are well-known neuroimaging findings. We think there is a functional neural network between the striatum and the fronto-temporal lobe. It is important in AD, not only the neural network between the hippocampus and the temporo-parietal cortex[12] related to cognitive function, but also a possible network between the striatum and the fronto-temporal lobes.

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