IV. 1 Dementia in Positron Emission Tomography

Matsuzawa T., Takeda S., Hatazawa J. and Yamada K.
Department of Radiology and Nuclear Medicine, Research Institute for Tuberculosis and Cancer, Tohoku University

Summary

In case of primary dementia (Alzheimer's disease), atrophy of the brain was slight in the initial stage, but severe in the late stage. Using PET it was made clear that there was a marked decrease in permeability of glucose through the blood-brain barrier, causing a decline in glucose consumption in the brain.

In case of secondary dementia (vascular dementia), mental deterioration was caused by loss of brain tissues, but was not always found in patients with severe atrophy of the brain. These results indicate the existence of critical sites in brain tissues closely related to intelligence.

Introduction

In the developed societies of the world, there are increasing numbers of aged people who survive. Senile dementias, associated with atrophy of the brain, impair mental performance, causing social problems. In the present study, pathogenesis of Alzheimer's disease (primary dementia) and vascular dementia (secondary dementia) was studied using x-ray computerized tomography (CT), magnetic resonance imaging (MRI), and positron emission computerized tomography (PET).

Subjects and Methods

Thirty to forty thousand subjects were screened for neurological abnormalities by means of CT and MRI. Both of the volumes of cerebrospinal fluid (CSF) space and cranial cavity were measured in neurologically normal subjects using CT. Brain atrophy index (100% × CSF space volume / cranial cavity volume) was calculated as an indicator of brain atrophy. Epidemiological and clinical examinations were performed in order to elucidate the mechanism of brain atrophy during aging. PET was performed to measure cerebral blood flow, consumptions of oxygen and glucose, and rate constants for glucose passing through the blood-brain barrier (k1, inflow; k2, outflow; k3, phosphorylation) in order to study the pathogenesis of primary dementia (Alzheimer's disease) and secondary dementia (vascular dementia).
Results

(1) Brain atrophy during aging

The brain developed maximally until the thirties, and then decreased in volume exponentially with advancing age. Patients with vascular dementia were seen among those with severe atrophy of the brain (Fig. 1). There was a close correlation between brain atrophy and deterioration of intelligence: IQ in Wechsler Adult Intelligence Scale (performance subtest) declined with atrophy of the brain (Fig. 2). Factors promoting brain atrophy included heart disease, hypertension, hypotention, arteriosclerosis (Fig. 3), diabetes mellitus, heavy smoking and drinking. Prospective epidemiological studies (Fig. 4) indicated that progress of brain atrophy was rapid in people with low cerebral blood flow, and slow in those with high cerebral blood flow (Fig. 5). These results indicate that brain atrophy can be predicted and prevented.

(2) Brain atrophy in vascular dementia and Alzheimer's disease

Figure 6 shows brain CT images of a patient with vascular dementia (upper row) and those of a control subject (lower row). The brain was more atrophied in the former than in the latter. Although brain atrophy was always severe in vascular dementia, patients with severe brain atrophy did not always show dementia. Therefore, there might be target sites in the brain involved in the incidence of vascular dementia. In Alzheimer's disease, brain atrophy was slight in the initial stage, but very severe in the late stage as shown in Fig. 7.

(3) Vascular dementia and Alzheimer's disease in PET study

Using PET we can quantitatively study in vivo biochemistry of the brain in patients with vascular dementia and Alzheimer's disease. In both dementias, there were significant decreases in the volumes of the vascular bed, cerebral blood flow, and consumption of glucose, but slight decreases in oxygen consumption when compared with normal elderly (70 years and older).

In case of vascular dementia, there were decreases in consumptions of oxygen and glucose in parallel with decreases in cerebral blood flow. In case of Alzheimer's disease, on the other hand, there were more decreases in glucose consumption than in cerebral blood flow (Fig. 8). In both vascular dementia and Alzheimer's disease, significant reduction of oxygen and glucose consumptions was found in the parietal and temporal lobes, but slightly in the occipital lobe and basal ganglia, showing a characteristic image like a snowman. Table 1 shows the differences in the rate constants (k1, k2 and k3) obtained by the model of Sokoloff, as well as glucose consumption in the normal aged control, patients with vascular dementia and those with Alzheimer's disease. Glucose consumption in patients with Alzheimer's disease was one-half of that in the normal aged control, while that in vascular dementia showed a drop about half way between these two. Since the decrease
in glucose consumption in Alzheimer's disease was clearly based on decreases in rate constants, the abnormal decrease in glucose consumption appeared to be caused by the decline in glucose intake through the blood-brain barrier.

Conclusion and Discussion

Atrophy of the brain is thought to be a background of vascular dementia.\(^1\) Since brain atrophy is promoted by various factors causing circulatory disturbances in the brain, it is possible to prevent brain atrophy by the elimination of such factors.\(^2,3\) In Alzheimer's disease, brain atrophy was slight in the initial stages and severe in the late stages.\(^4\) Reduction of cerebral blood flow and consumptions of oxygen and glucose were seen in both Alzheimer's disease and vascular dementia.\(^5,6\) There were decreases in oxygen and glucose consumptions in parallel with decrease in cerebral blood flow in vascular dementia, while decreases in glucose consumption was much more marked than that in oxygen consumption in Alzheimer's disease. The cause of decrease in glucose consumption appeared to be the decrease in the permeability of glucose through the blood-brain barrier and the decrease in hexokinase activity. Decreases in the intake and metabolism of glucose in Alzheimer's disease appeared to be caused by an abnormal aging of the neural cell walls.

References

Table 1. Rate constants of glucose and CMRGlucose in normal aged control, patients with vascular dementia and those with Alzheimer's disease.

<table>
<thead>
<tr>
<th></th>
<th>$k_1$</th>
<th>$k_2$</th>
<th>$k_3$</th>
<th>CMRGlucose (mg/100ml/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control (n=6)</td>
<td>0.088±0.022</td>
<td>0.120±0.012</td>
<td>0.051±0.009</td>
<td>7.0±1.2</td>
</tr>
<tr>
<td>Vascular dementia (n=5)</td>
<td>0.076±0.028</td>
<td>0.128±0.015</td>
<td>0.060±0.011</td>
<td>4.9±1.0</td>
</tr>
<tr>
<td>Alzheimer's disease (n=5)</td>
<td>0.057±0.009</td>
<td>0.086±0.011</td>
<td>0.031±0.006</td>
<td>3.7±0.9</td>
</tr>
</tbody>
</table>

Fig. 1. Age-related change in brain atrophy index in men and women.

Fig. 2. Relationship between atrophy index of the brain and intelligence index (Wechsler Adult Intelligence Scale, performance subtest).
Fig. 3. Age-related change in brain atrophy index (BAI) in atherosclerotic (●) and non-atherosclerotic (○) patients.

Fig. 4. Age-related change in progress of brain atrophy index.
Fig. 5. Relationship between annual brain atrophy index (increase in brain atrophy index per year) and cerebral blood flow (ISI) values in men (●) and women (○).

Fig. 6. CT images of the brain of a patient with vascular dementia (upper row) and a control subject (lower row).
Fig. 7. MRI images of the brain of a patient with Alzheimer's disease (A, coronal; B, sagital section).
Fig. 8. Cerebral blood volume (CBV), cerebral blood flow (CBF), oxygen extraction fraction (OEF), cerebral metabolic rate for oxygen (CMRO₂) and of glucose (CMRGl), and CMRO₂/CMRGl in normal aged (N), multi-infarct dementia (M), and Alzheimer’s disease (A).