Short Communication

Cerebrovascular Responsiveness to Hypercapnia in Alzheimer's Dementia and Vascular Dementia of the Binswanger Type

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Background and Purpose: Alzheimer's dementia is thought to be a primary degenerative dementia, whereas vascular dementia of the Binswanger type is an entity of vascular dementia. We evaluated the cerebrovascular responsiveness to hypercapnia to clarify the differences in the cerebral hemodynamics between two groups of patients. The subjects were eight younger control subjects, five age-matched control subjects, five Alzheimer's patients, and five patients with vascular dementia of the Binswanger type.

Summary of Report: In the resting state, the regional cerebral blood flow was low in both Alzheimer's dementia and vascular dementia of the Binswanger type. The responsiveness to hypercapnia was preserved in Alzheimer's dementia, whereas it was impaired in vascular dementia of the Binswanger type in the cerebral cortices and in the deep white matter.

Conclusions: These results suggest that small vascular lesions exist in vascular dementia of the Binswanger type but not in Alzheimer's dementia, even though regional cerebral blood flow was thought to decrease by hypometabolism in both types of dementia. (Stroke 1992;23:594–598)

KEY WORDS • cerebral blood flow • dementia • hypercapnia • tomography, emission computed

Alzheimer's dementia and vascular dementia are important causes of dementia in elderly patients. Alzheimer's dementia is a primary degenerative dementia, but recent studies using magnetic resonance imaging (MRI) have demonstrated mild-to-moderate periventricular abnormalities and deep white matter lesions. Vascular dementia of the Binswanger type is thought to be an entity of vascular dementia, and it is characterized by diffuse white matter lesions due to small-artery disease. To clarify the differences of cerebral hemodynamics in these conditions, we measured the regional cerebral blood flow (rCBF) using positron emission tomography (PET) in the resting state and during inhalation of 5% CO₂, and compared the responsiveness of the cerebral arteries to hypercapnia between Alzheimer's dementia and vascular dementia of the Binswanger type.

Subjects and Methods

The subjects were eight normal younger controls (all male subjects, 21–40 years of age), five age-matched controls (three male and two female subjects, 45–68 years of age), and 10 patients, including five (two male and three female patients, 56–68 years of age) with Alzheimer's dementia and five (all male patients, 41–76 years of age) with vascular dementia of the Binswanger type. Alzheimer's dementia and vascular dementia of the Binswanger type were diagnosed according to the DSM-III-R criteria. All patients with Alzheimer's dementia had cognitive and memory disturbance. Four of five patients with Alzheimer's dementia had mild-to-moderate white matter lesions on MRI. All patients with vascular dementia of the Binswanger type had a history of long-standing hypertension and diffuse white matter lesions on MRI but no stenosis or obstruction of main cerebral arteries on digital subtraction angiography. The eight younger normal control subjects consisted of medical doctor volunteers in our university hospital. The five age-matched control subjects selected for this study had minimal neurological symptoms, such as transient ischemic attacks, with or without small lesions on MRI, but no significant abnormalities on digital subtraction angiography. The age, blood pressure, hemoglobin, Hasegawa dementia rating score, Wechsler adult intelligence score, and Hachinski's ischemic score in each group are shown in Table 1. There was no significant difference between age-matched control subjects and patients in arterial blood gases and hemoglobin. Maximum and minimum blood pressure in patients with vascular dementia of the Binswanger type was significantly higher than that in patients with Alzheimer's dementia.

The PET study was performed with HEADTOME-III (Shimadzu Corp., Kyoto, and Research Institute for Brain and Blood Vessels--Akita, Japan), which had a spatial resolution of 8.2 mm in full-width at half-maximum and simultaneously obtained five contiguous...
## TABLE 1. Clinical Features of Patients and Control Subjects by Group

<table>
<thead>
<tr>
<th>Clinical feature</th>
<th>Younger control subjects (n=8)</th>
<th>Age-matched control subjects (n=5)</th>
<th>Alzheimer's dementia patients (n=5)</th>
<th>Vascular dementia of the Binswanger type patients (n=5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>28.1±7.1</td>
<td>54.8±10.2</td>
<td>59.8±4.7</td>
<td>61.0±15.2</td>
</tr>
<tr>
<td>Blood pressure (maximum) (mm Hg)</td>
<td>128±12</td>
<td>142±25</td>
<td>112±15</td>
<td>164±41*</td>
</tr>
<tr>
<td>Blood pressure (minimum) (mm Hg)</td>
<td>70±6</td>
<td>88±15</td>
<td>72±10</td>
<td>110±25*</td>
</tr>
<tr>
<td>Hemoglobin (g/dl)</td>
<td>15.5±1.8</td>
<td>13.7±2.9</td>
<td>12.1±2.0</td>
<td>14.2±2.1</td>
</tr>
<tr>
<td>Hasegawa Dementia Rating Scale score</td>
<td>...</td>
<td>30.0±2.2</td>
<td>7.0±9.3</td>
<td>14.8±7.6</td>
</tr>
<tr>
<td>Wechsler Adult Intelligence Scale score</td>
<td>...</td>
<td>...</td>
<td>0.5±0.6</td>
<td>8.8±2.3</td>
</tr>
<tr>
<td>Hachinski's Ischemic Scale score</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Paco2 (mm Hg)</td>
<td>43.8±2.2</td>
<td>37.1±5.7</td>
<td>38.4±3.8</td>
<td>39.1±5.0</td>
</tr>
<tr>
<td>Paco2f (mm Hg)</td>
<td>50.3±2.3</td>
<td>45.0±4.1</td>
<td>44.5±2.7</td>
<td>45.1±5.0</td>
</tr>
</tbody>
</table>

Values are mean±SD. Ellipses indicate tests not performed.
*P<0.05. Values were significantly higher in vascular dementia of the Binswanger type group compared with Alzheimer's dementia group.
†During inhalation of 5% CO2.

slices 15 mm apart. Regional CBF was measured by the oxygen-15 H2O bolus injection method. The subjects were placed in a supine position on a bed in a semidark room. A small canula was placed in the femoral artery for arterial blood sampling. A transmission scan with a germanium-68/gallium-68 ring source was obtained for each patient for attenuation correction. In the PET study, 740 mBq H15O was infused as a bolus, and the scan was started when the radioactivity appeared on a monitor for the head. Five cross-sectional planes were scanned simultaneously for 75 seconds at levels of 20, 35, 50, 65, and 80 mm above the orbitomeatal line. During the scan, arterial blood was drawn continuously at a rate of 15 ml/min for 2 minutes, and radioactivity was monitored by a beta-ray detector using a plastic scintillator (1.1 cm thick and 5.1 cm in diameter). Paco2, Pao2, and pH were measured at the beginning and end of the scan. The first scan was performed in the resting state. A second scan following inhalation of 5% CO2 was started 12 minutes after completion of the first scan. Inhalation of CO2 started 2 minutes before the scan. Regional CBF was calculated by referring to a previously published method.10 Informed consent was obtained from the patients or their families before the PET study.

The rCBF values were obtained using 18x14-mm or 14x14-mm regions of interest placed in the frontal, temporal, parietal, occipital, and primary motor cortices; striatum and thalamus; centrum semiovale; frontal and posterior periventricular white matter; and cerebellum on both sides; and then averaged (Figure 1). Responsiveness to hypercapnia was represented as the percent change of the rCBF per 1 mm Hg change of Paco2.11 Statistical analyses were carried out using

![Figure 1. Location of regions of interest.](http://stroke.ahajournals.org/)

1. 1: CEREBELLUM
2. 2: TEMPORAL CX
3. 3: HIPPOCAMPUS
4. 4: FRONTAL CX
5. 5: POSTERIOR PVW
6. 6: OCCIPITAL CX
7. 7: PRIMARY MOTOR
8. 8: CENTRUM SEMIOVALE
either Student’s t test or Welch’s t test with unequal variance.

Results

Arterial blood gases on PET study are also shown in Table 1. Paco₂ was increased by 6–7 mm Hg during inhalation of 5% CO₂.

The values of rCBF at the resting state are shown in Table 2. There were no significant differences between the younger normal control subjects and age-matched control subjects. In patients with Alzheimer’s dementia, the rCBF was significantly lower in the frontal, temporal, and parietal cortices and in the periventricular white matter compared with age-matched control subjects; however, the occipital and primary motor cortices were spared. In patients with vascular dementia of the Binswanger type, the rCBF was low more diffusely in the cerebral cortices, and it was very low in the white matter.

Responsiveness to hypercapnia is represented as a percent change of rCBF per 1 mm Hg increase of Paco₂ in Table 3. Regional CBF increased by approximately 5% in younger normal control subjects and age-matched control subjects. There were no significant differences between younger normal control subjects and age-matched control subjects. The responsiveness to hypercapnia was not significantly different between patients with Alzheimer’s dementia and age-matched control subjects. However, in vascular dementia of the Binswanger type, responsiveness to hypercapnia was severely impaired in the cerebral cortices as well as in the white matter. There was no
apparent difference in responsiveness to hypercapnia between the anatomic regions in vascular dementia of the Binswanger type.

**Discussion**

Many studies on cerebral hemodynamics in dementia have been done using the xenon-133 clearance method,12-15 single-photon emission computed tomography,18,19 and PET.20 Among them, however, there have been few reports on cerebral vasoreactivity.13-15 Simard et al13 and Hachinski et al14 reported normal vasoreactivity in dementia using the intra-arterial 133Xe clearance method. However, there was no description on responsiveness to hypercapnia in either study, although two cases with dementia were examined using a vasodilator drug in the former study. Yamaguchi et al15 reported that responsiveness to hypercapnia was preserved in Alzheimer's dementia while using the 133Xe inhalation method, but it was impaired in multi-infarct dementia. However, these studies were carried out when MRI was not yet widely available and white matter lesions had not yet been fully examined. In addition, it was difficult to measure rCBF in deep white matter due to methodological problems. Therefore, we carefully selected five age-matched control subjects and 10 patients with dementia based on clinical and MRI findings and measured cerebrovascular responsiveness to hypercapnia using PET and bolus injections of H218O. Because we did not have completely normal age-matched control subjects, we used as age-matched controls patients with minimal neurological symptoms whose rCBF and responsiveness to hypercapnia were not significantly different from those in younger normal control subjects. This is the first study to our knowledge comparing responsiveness to hypercapnia in Alzheimer's dementia and vascular dementia of the Binswanger type by means of PET.

In the present study, the responsiveness to hypercapnia was preserved or slightly excessive in Alzheimer's dementia both in the cortices where MRI signal abnormalities at 1.5 T in Alzheimer's dementia and normal aging. AJNR 1987;8:421-426. Roman GC. Senile dementia of the Binswanger type: A vascular form of dementia in the elderly. JAMA 1987;258:1782-1788. Fisher CM. Binswanger's encephalopathy: A review. Neurology 1989;39:65-79

As mentioned above, there was an apparent difference in responsiveness to hypercapnia between patients with Alzheimer's dementia and those with vascular dementia of the Binswanger type, although the rCBF was low in both pathological conditions. Our results, therefore, support the pathological findings related to the nature of the lesions.

**References**


4. Roman GC. Senile dementia of the Binswanger type: A vascular form of dementia in the elderly. JAMA 1987;258:1782-1788


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