

## Regional cerebral blood flow and oxygen metabolism in a patient with Korsakoff syndrome

Kant MATSUDA,\* Shigeru YAMAJI,\* Kazunari ISHII,\* Masahiro SASAKI,\* Setsu SAKAMOTO,\*\*  
Hajime KITAGAKI,\* Toru IMAMURA\*\*\* and Etsuro MORI\*\*\*

*Divisions of \*Neuroimaging Research and \*\*\*Clinical Neurosciences, Hyogo Institute  
for Aging Brain and Cognitive Disorders (HI-ABCD)*

*\*\*Department of Radiology, Kobe University School of Medicine*

We report a functional neuroimaging study of a patient clinically diagnosed with Korsakoff syndrome. Positron emission tomography (PET) with the  $^{15}\text{O}$  inhalation method showed decreased regional cerebral blood flow (rCBF) and decreased regional cerebral metabolic ratio for oxygen ( $\text{rCMRO}_2$ ) in the bilateral fronto-temporal areas and in the left thalamus. These results suggest that dysfunction of the frontal-thalamic neural network plays a role in the disturbance of Korsakoff syndrome.

**Key words:** Korsakoff syndrome, positron emission tomography (PET), cerebral blood flow, cerebral oxygen metabolism

### INTRODUCTION

KORSAKOFF SYNDROME is a neurobehavioral disorder which consists of severe amnesia (deficits in both anterograde and retrograde memory systems), disorientation, and confabulation, but with preserved intelligence. This syndrome is usually preceded by Wernicke encephalopathy, subarachnoid hemorrhage from an anterior commissure artery aneurysm, or frontal brain contusion.

In patients with Wernicke encephalopathy, magnetic resonance (MR) imaging shows an increased T2 signal intensity in the medial thalamus, mammillary bodies and the areas surrounding the aqueduct and third ventricle.<sup>1,2</sup> One report described atrophic mammillary bodies in patients with Korsakoff syndrome after Wernicke encephalopathy.<sup>3</sup> On the other hand, several reports have assessed the cerebral perfusion in Korsakoff syndrome with single photon emission computed tomography (SPECT), but the results have been controversial.<sup>4,5</sup>

We report here a patient with Korsakoff syndrome who underwent a study with  $^{15}\text{O}$ -labeled gas and positron emission tomography (PET).

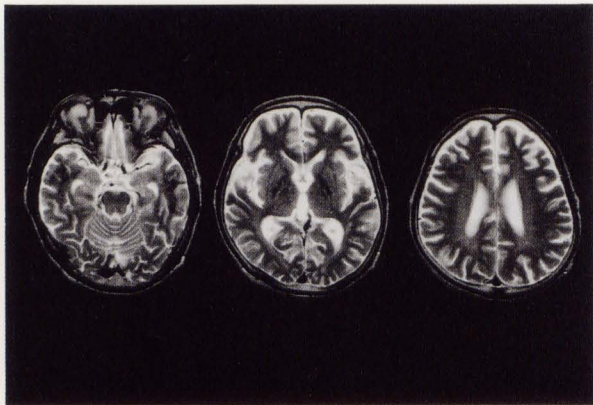
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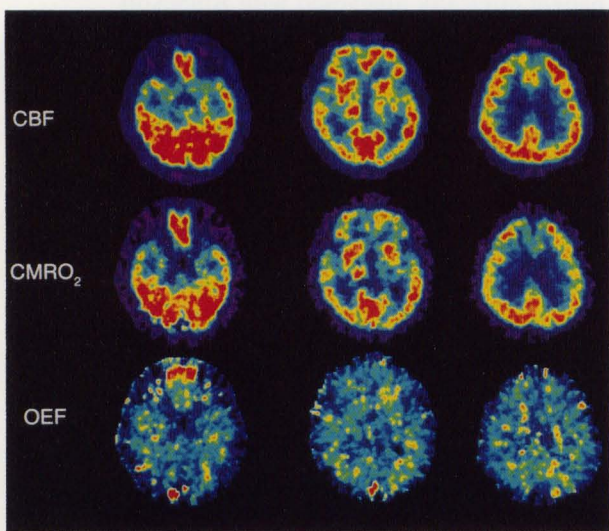
For reprint contact: Kazunari Ishii, Hyogo Institute for Aging Brain and Cognitive Disorders, 520 Saisho-Ko, Himeji, Hyogo 670, JAPAN.

### CASE REPORT

A 55-year-old factory worker, with a history of heavy alcohol drinking for more than 30 years, was referred to us because of severe amnesia. Six months earlier, he suddenly developed an episode of confusional state and convulsions. Before admission to our hospital the convulsions disappeared after treatment by his family physician, and the confusion gradually subsided. The levels of serum vitamin B<sub>1</sub> and the transketolase activity in red blood cells were not measured at that time, but severe amnesia, disorientation and confabulation persisted. On admission to our hospital, he was alert, but severe amnesia and disorientation were apparent. Neurological examination revealed decreased tendon reflexes of the distal lower extremities. Diplopia and cerebellar ataxia were negative. On neuropsychological examination, he was cooperative and had no signs of aphasia, apraxia or agnosia. Frontal lobe examinations including a fist-edge-palm task, a Red-green test, and color-form sorting were normal. He scored 24 on the Mini Mental State Examination. His verbal IQ was 84 and his performance IQ was 88 on the Wechsler Adult Intelligence Scale-Revised. On the other hand, his memory index was 56 on verbal subtests and 52 on visual subtests on the Wechsler Memory Scale-Revised (WMS-R). The delayed recall index on the WMS-R was decreased.



**Fig. 1** T2-weighted MR images demonstrate a mild atrophy, which was dominant in the frontal lobe. There was no abnormal intensity in cortical and subcortical structures including the bilateral thalamus.



**Fig. 2** CBF images show a mild reduction of the medial temporal and frontal perfusion and a moderate decrease in rCBF in the left thalamus. The deficits in these areas are more obviously delineated in rCMRO<sub>2</sub> images.

The MR images showed mild cerebral atrophy predominantly in the frontal lobe, but no abnormal signal intensity was detected (Fig. 1). The volume of mammillary bodies was also normal. Regional cerebral blood flow (rCBF), regional oxygen extraction fraction (rOEF) and regional cerebral metabolic ratio for oxygen (rCMRO<sub>2</sub>) were measured by PET and the <sup>15</sup>O-labeled gas (C<sup>15</sup>O<sub>2</sub>, <sup>15</sup>O<sub>2</sub>, C<sup>15</sup>O) inhalation steady state method. Details of the PET procedures have been reported elsewhere.<sup>6</sup> The PET study showed a mild decrease in rCBF and moderate decrease in rCMRO<sub>2</sub> in the bilateral frontal lobes, especially in the medial region. Decreases in rCBF and rCMRO<sub>2</sub> were also apparent in the temporal lobes including the hippocampus and the left thalamus (Fig. 2).

## DISCUSSION

This patient's neurocognitive disturbances were identical to those of Korsakoff syndrome. The etiology was uncertain, but the neuroimaging studies ruled out the possibility of a previous episode of subarachnoid hemorrhage or brain contusion. On the other hand, the patient's history of heavy drinking suggested that the initial confusion was a sign of Wernicke encephalopathy, though the neurological findings in the acute stage were not revealed. Some patients with Wernicke encephalopathy show only confusion and amnesia. We therefore believe this patient had Wernicke-Korsakoff syndrome (Korsakoff syndrome after Wernicke encephalopathy). The present study with <sup>15</sup>O-labeled gas and PET confirmed the decreased rCBF and rCMRO<sub>2</sub> in the bilateral medial frontal, temporal and thalamic areas.

Hunter et al.<sup>4</sup> assessed patients with Korsakoff syndrome with <sup>99m</sup>Tc-hexamethyl propyleneamine oxime (<sup>99m</sup>Tc-HMPAO) and SPECT and found decreased rCBF in the frontal lobe, but another study that used <sup>123</sup>I-isopropylamphetamine (<sup>123</sup>I-IMP) and SPECT demonstrated no remarkable decrease in rCBF in this syndrome.<sup>5</sup> In chronic alcoholism, <sup>18</sup>F-fluorodeoxyglucose (FDG) PET showed reduced glucose metabolism in the medial frontal area.<sup>7</sup> Fazio et al.<sup>8</sup> reported on a FDG PET study of patients with amnesia including patients with Korsakoff syndrome. They demonstrated decreased glucose metabolism in the basal cortex, cingulate gyrus, hippocampus and thalamus in patients with amnesia compared with normal controls.

Microscopic necrotic changes in Wernicke-Korsakoff syndrome involve the dorso-medial thalamus and mammillary bodies. These two lesions are considered to be responsible for the amnesia of Korsakoff syndrome because the Papez circuit, one of the neuroanatomical structures in the human memory system, includes anterior thalamic nuclei and mammillary bodies. In our case the decreased rCBF and rCMRO<sub>2</sub> in the left thalamus suggest a dysfunction of the Papez circuit. The decreased rCBF and rCMRO<sub>2</sub> in the fronto-temporal area, a finding which is consistent with that of Fazio et al., might be a remote effect of the dysfunction of the Papez circuit.

Previous SPECT reports did not describe the perfusion deficits in the medial temporal region including the hippocampus in patients with Korsakoff syndrome, because of the limited spatial resolution of SPECT. We previously reported the usefulness of measuring rCMRO<sub>2</sub> for detecting medial temporal involvement in Alzheimer's disease.<sup>6</sup> This case with Korsakoff syndrome also showed signs of decreased medial temporal rCMRO<sub>2</sub>. This finding may appear not only in Alzheimer's disease but also in other pathological states with memory disturbance associated with dysfunction of the Papez circuit.

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