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Evaluation of cerebral blood flow and metabolism in childhood moyamoya disease: an investigation into "re-build-up" on EEG by positron CT*

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Abstract. The cerebral blood flow and cerebral metabolic rate of oxygen (CBF and $CMRO_2$) of three cases of childhood moyamoya disease were examined by positron-emission-computed tomography for the purpose of investigating the mechanism of the "re-build-up" phenomenon on EEG. Decrease in both CBF and $CMRO_2$ were observed following hyperventilation. However, dissociation between the decrease in CBF and $CMRO_2$ was also observed. Arterial blood-gas analysis disclosed hypocapnea during hyperventilation and hypoxia following hyperventilation. These results clearly indicate that the re-build-up seen on EEG is the manifestation not only of ischemic hypoxia but also of hypoxic hypoxia characteristically seen in moyamoya disease.

Key words: Moyamoya disease – Cerebral blood flow – Cerebral metabolism – Re-build-up – EEG – Positron CT.

The appearance of an abnormal electroencephalogram (EEG) induced by hyperventilation is one of the most specific findings in childhood moyamoya disease. The authors have previously noted that in childhood moyamoya disease the characteristic EEG changes seen after hyperventilation are not merely "build-up", which appears during hyperventilation or its prolongation, but also what we have labeled "re-build-up", which occurs subsequent to the disappearance or attenuation of "build-up." It has been emphasized that the EEG examination is an effective means for screening childhood moyamoya disease [3]. However, the nature of this re-build up phenomenon has been poorly understood. In this paper, our experiences with positron-emission-computed tomography in three cases of moyamoya disease are presented with the primary purpose of clarifying the relationship between the mechanism of re-build-up and brain functions.

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Case studies

Case 1

The patient was a 13-year-old boy who had experienced a paraventricular hemorrhage in February, 1983. The angiographic stage [10] was V on the right side and III in the left. Positron-emission-computed tomography was performed 7 months after the hemorrhage, at which point no neurological deficits were noted.

Case 2

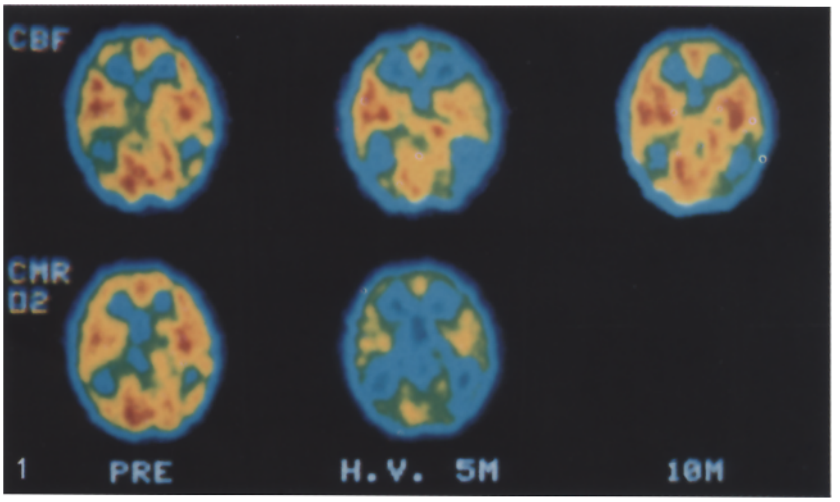
This 17-year-old had had frequent transient ischemic attacks (TIAs) since the age of four. Perivascular sympathectomy and superior cervical ganglionectomy [12] had been performed on both sides 7 years ago. The angiographical stage was VI on both sides.

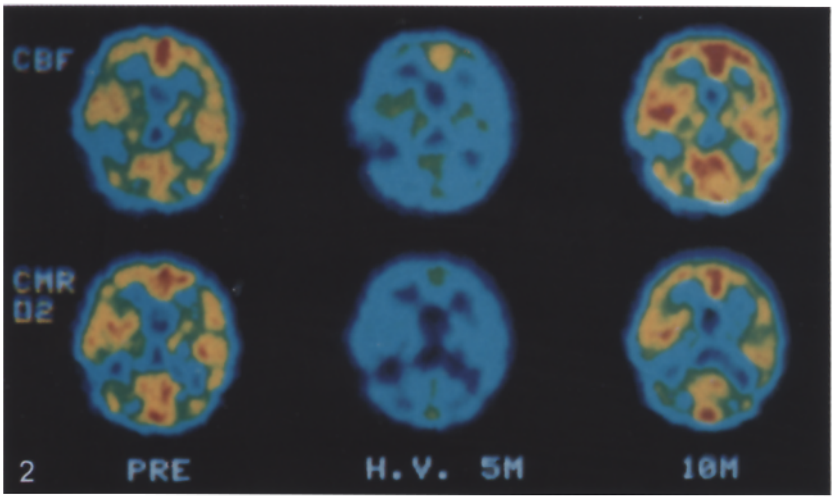
Case 3

This 18-year-old suffered a paraventricular hemorrhage 2 years ago. At the time of our positron-emission-computed tomography examination, however, he did not show any neurological deficits. The angiographical stage was II on the left side and VI on the right.

Positron-emission-computed tomography

Regional cerebral blood flow (CBF) and the cerebral metabolic rate of oxygen ($CMRO_2$) were measured with an ECAT II [8] using the cyclotron-produced $C^{15}O_2$ and $^{15}O_2$ continuous inhalation technique [2]. The patients lay quietly on the ECAT bed with eyes open, essentially seeing and hearing under a dark ambient condition in the laboratory. Patients were asked to hyperventilate for 3 min, and 4-min scannings were performed before and after the hyperventilation. Since the ECAT II is a single slice scanner, scanning was performed in the same single plane parallel to the orbitomeatal line, which includes basal ganglia. During the study, serial arterial blood samples were taken for analysis of ^{15}O radioactivity, PaO_2, and $PaCO_2$. Continuous EEG recordings were also made throughout the study.





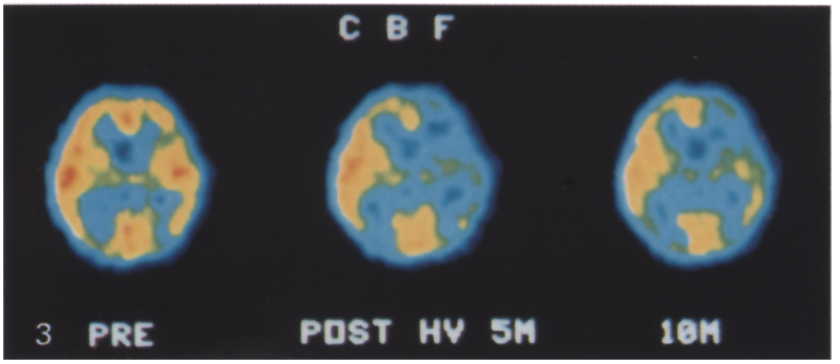


Fig. 1. *Case 1.* Decreased CBF was observed mainly in the right hemisphere, where the angiographical stage was more advanced, at posthyperventilation 5-min scanning. In contrast, the decrease in $CMRO_2$ was much more than CBF in the whole brain region

Fig. 2. *Case 2.* Marked and symmetrical decreases in both CBF and $CMRO_2$ were observed at posthyperventilation 5-min scanning. They almost returned to the prehyperventilation level, however, at posthyperventilation 15-min scanning. Careful comparison of pre- and posthyperventilation 5-min scanning revealed that the decrease in $CMRO_2$ was more than that of CBF

Fig. 3. *Case 3.* Decreased CBF was also observed mainly in the right hemisphere, where the angiographical stage was more advanced than that of the right following hyperventilation

Results

The prehyperventilation values of CBF and $CMRO_2$ revealed no difference between the two hemispheres in any of the three cases, even though angiography showed different right and left stages in cases 1 and 3.

Posthyperventilation 5-min scannings showed remarkable changes in both CBF and $CMRO_2$. In case 1, a decrease in CBF was observed mainly in the right hemisphere where the angiographical stage was more advanced. However, $CMRO_2$ had decreased much more than CBF in all brain regions (Fig. 1). In case 2, where there was no difference in the angiographical stage between the hemispheres, marked decreases in both CBF and $CMRO_2$ were observed, with the decrease in $CMRO_2$ also being more than that of CBF (Fig. 2). In case 3, only a CBF study using $C^{15}O_2$ was performed. A decrease in CBF was also observed mainly in the right hemisphere where the angiographical stage was more advanced (Fig. 3).

Simultaneous EEG recordings revealed typical rebuild-up in all three cases during the posthyperventilation 5-min scanning (Fig. 4). The sequential changes of PaO_2

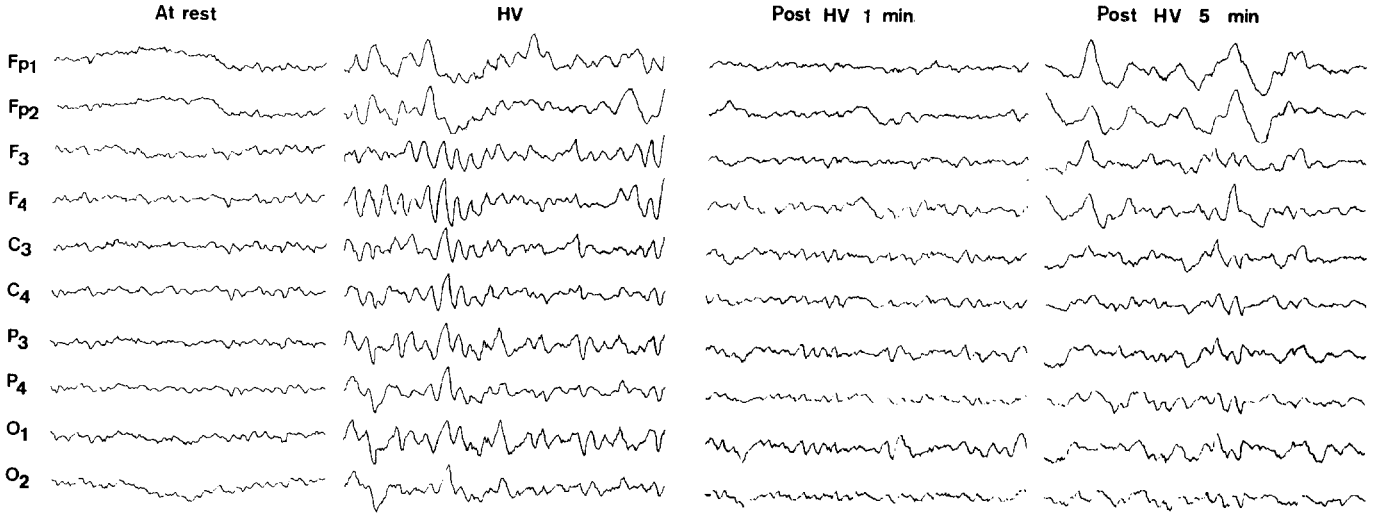


Fig. 4. Simultaneous EEG recordings in case 1 in which re-build-up was seen 5 min after hyperventilation

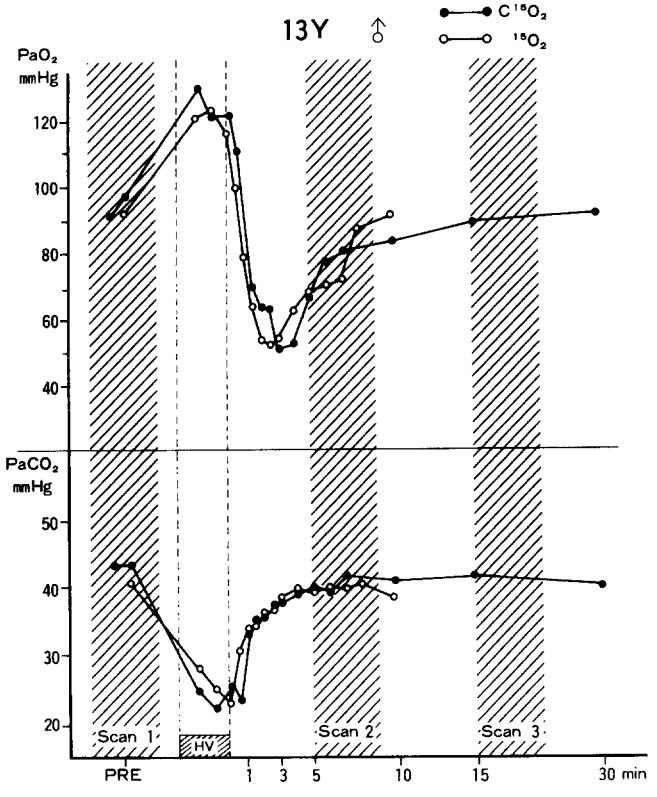


Fig. 5. Sequential changes in PaO_2 and $PaCO_2$ in case 1. At the time of posthyperventilation 5-min scanning, $PaCO_2$ had returned to the normal range, but PaO_2 still remained at a low level due to the decrease in the rate of respiration following hyperventilation

and $PaCO_2$ also showed characteristic findings in all three cases. At first, a gradual decrease in $PaCO_2$ due to hyperventilation was observed. This gradually recovered following the cessation of hyperventilation, and returned to the prehyperventilation level at the time of the post-hyperventilation 5-min scanning. In contrast, the high level of PaO_2 due to hyperventilation fell sharply after the termination of hyperventilation, probably because of the decrease in the rate of respiration. Even though it gradually recovered, it was still at a low level at the time of the posthyperventilation 5-min scanning (Fig. 5).

Discussion

Moyamoya, a Japanese word meaning "something hazy, like a puff of cigarette smoke drifting in the air" is the descriptive term that Suzuki and Takaku [10] applied to a peculiar angiographic picture consisting of abnormal net-like vessels at the base of the brain, together with bilateral occlusion or stenosis of the internal carotid artery at the level of its terminal bifurcation, the anterior and middle cerebral arteries. In 1963, Suzuki and co-workers [11] first suggested that this type of vascular abnormality was a new disease entity. Since then, many cases have been reported and many studies have been done from various aspects.

One of the interesting features of Moyamoya disease is the striking difference in the clinical presentation between children and adults. Children typically present with recurrent episodes of sudden motor disturbances, which are often induced by hyperventilation, such as when crying or playing the harmonica, whereas adults present with evidence of intracranial hemorrhage [9]. It is of great interest that the polymorphous high-voltage slow waves on EEGs seen following the termination of hyperventilation, which have been labeled re-build-up, correlate deeply with these kinds of attacks characteristically in children [3]. Nevertheless, the mechanism of re-build-up has not been well understood.

There have been several reports concerned with the change in cerebral circulation due to hyperventilation in moyamoya disease [1, 4–6]. No studies using positron-emission-computed tomography, which provides three-dimensional images of both CBF and cerebral metabolism simultaneously, have appeared in the literature.

Our observations using positron-emission-computed tomography in the present study suggest that the hemodynamic changes following hyperventilation alone are

unlikely to be responsible for the emergence of re-build-up on the EEG, since dissociations between the decreases in CBF and $CMRO_2$ were observed. On the basis of our results, the mechanism of re-build-up can be explained as follows: cerebral vessel constriction is produced due to the decrease in $PaCO_2$ following hyperventilation, and this appears as a CBF decrease on positron-emission-computed tomography. In addition to this decreased CBF, a delayed decrease in PaO_2 following hyperventilation results in a decrease in $CMRO_2$, which causes cerebral dysfunction and thus appears as re-build-up on the EEG. In other words, re-build-up is the manifestation not only of ischemic hypoxia but also of the hypoxic hypoxia seen characteristically in moyamoya disease.

Recently, the authors found that moyamoya vessels became less visualized and that the diameter of the cortical arteries decreased in size angiographically, together with re-build-up after hyperventilation, but that these changes were suppressed by 8% CO_2 inhalation. Moreover, the emergence of re-build-up on EEG was also suppressed when hyperventilation was performed under 8% CO_2 + 92% O_2 or 100% O_2. Hypocapnea, which causes vessel consticton and CBF decrease, did not appear under CO_2 inhalation, and the delayed decrease in PaO_2 also did not appear under pure oxygen inhalation [7, 13]. These findings strongly support our proposed explanation.

There might be some criticism regarding the methodological feasibility of applying the $C^{15}O_2$ and $^{15}O_2$ continuous inhalation technique in this study, because it cannot be denied that hyperventilation might alter the equilibrium state of ^{15}O in the brain during the scanning. However, our recent study (M. Ito, Y. Abe, H. Fukuda, T. Matsuzawa, M. Kameyama and T. Ido, in preparation) showed that the effect of hyperventilation upon the measurement of CBF and $CMRO_2$ can be minimized by our original program, which carefully takes into account changes in input function, i.e., the arterial blood level of ^{15}O radioactivity. Moreover, scannings were performed before and after hyperventilation, not during hyperventilation, which again reduced the methodological risk in this study.

Further studies must be performed before a definite conclusion can be reached. However, the results of positron-emission-computed tomography clearly give us an important clue regarding the pathophysiology of this disease.

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