

## Hemodynamic Evaluation after Surgical Treatments for Moyamoya Disease

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**ABSTRACT.** Thirty-one patients were treated by various revascularization procedures, mainly by encephalo-myo-synangiosis. A total of 113 rCBF measurements were performed by a  $^{133}\text{Xe}$  inhalation method. Preoperative mCBF values were markedly lower in most of the young patients than in healthy young volunteers, while there is no significant difference between the adult groups. Postoperatively, mCBF increased by an average of 7.1% in the children, while it decreased slightly or remained unchanged in the adults. Postoperative improvement of abnormal distribution of rCBF was demonstrated in approximately two-thirds of the children, as compared with the adults showing little improvement. Pre- and postoperative  $\text{CO}_2$  responses were examined in 4 children, and impaired  $\text{CO}_2$  response was improved in all the operated hemispheres. Our experience suggests that the surgical treatment can be an effective procedure for preventing the progression of clinical findings caused by cerebral ischemia and for improving the cerebral hemodynamics, especially in children with moyamoya disease.

**Key words :** Moyamoya disease — Cerebral blood flow —  
Surgical treatment — Cerebral ischemia —  
Encephalo-myo-synangiosis

Moyamoya disease is a rare occlusive cerebrovascular disease consisting of progressive narrowing or occlusion of the arteries of the circle of willis, starting at the terminal portion of the intracranial internal carotid artery and also at the origin of the anterior cerebral and middle cerebral artery, and is accompanied by abnormal vascular networks of anastomotic vessels in the region of the basal ganglia and several transdural anastomoses. Children with this disease usually present with recurrent episodes of cerebral ischemia. As the disease progresses, it produces focal neurological deficits characteristic of cerebral infarction, frequently resulting in a poor prognosis. In adult patients, on the contrary, hemorrhagic manifestations are more prevalent and fatal outcomes are frequently encountered in cases of massive hemorrhage.

Although no definite and effective treatment was reported, several surgical attempts have been made to increase the blood supply to the ischemic hemispheres. They are superficial temporal artery-middle cerebral artery (STA-MCA) anastomosis, encephalo-myo-synangiosis (EMS), encephalo-duro-arterio-synangiosis (EDAS), omental transplantation etc. The purpose of this paper is to evaluate the effect of these surgical procedures on cerebral hemodynamics in patients with moyamoya disease.

## MATERIALS AND METHODS

### Patients

Thirty-one patients were treated by various surgical revascularization procedures. Thirteen were males and 18 were females. Their ages ranged from 5 to 48 years. Twenty-two patients were less than 16 years of age, and all of them presented with cerebral ischemic symptoms and signs, such as hemi- and monoparesis, mental impairment, involuntary movement of the limbs, cortical blindness, epileptic seizures and headache. No intracranial hemorrhage was encountered in these children. On the other hand, hemorrhagic episodes (intracerebral hemorrhage and/or ventricular hemorrhage) were encountered in 6 of 9 adult patients. A diagnosis was established with bilateral carotid and vertebral angiographies in all patients. One patient whose angiogram showed typical findings of moyamoya disease unilaterally was also included in this study. The follow-up periods were 10 months to 5 and a half years, with an average of 3 years and 4 months, after operation.

### Operations

Fifty-five surgical revascularization procedures were performed on 31 patients, of whom 24 patients underwent operations on both hemispheres. The method of operations was shown in Table 1. EMS was performed in 50 operations as on 30 patients. Among them, STA-MCA anastomosis was added in 8 operations on 6 patients. Encephalo-arterio-synangiosis (EAS) and/or encephalo-galeo-synangiosis (EGS) was also added in 20 operations on 12 patients. EDAS was performed in 7 operations on 6 patients.

The operative methods of STA-MCA anastomosis,<sup>1)</sup> EMS<sup>2)</sup> and EDAS<sup>3)</sup> were identical to those described by several authors. Middle meningeal arteries were preserved as far as possible when performing dural incisions, which looked like dural windows. In patients where marked transdural anastomoses were observed in the preoperative angiograms, the transected and pedicled frontal

TABLE 1. Various surgical procedures for moyamoya disease  
(55 operations for 31 patients)

EMS <sup>1)</sup>	25
EMS + EAS <sup>2)</sup>	10
EMS + EGS <sup>3)</sup>	2
EMS + EAS + EGS	2
EMS + EGS + EDAS <sup>4)</sup>	3
EMS + STA-MCA <sup>5)</sup>	5
EMS + STA-MCA + EGS	3
EGS	1
EAS + EDAS	1
EDAS	3
total	55

- 1) EMS : encephalo-myo-synangiosis
- 2) EAS : encephalo-arterio-synangiosis
- 3) EGS : encephalo-galeo-synangiosis
- 4) EDAS : encephalo-duro-arterio-synangiosis
- 5) STA-MCA : STA-MCA anastomosis

branch of STA or the Galea aponeurotica alone was also transposed to the cortical surface ; EAS or EGS. These two procedures were often used in combination with EMS in order to provide additional circulation to the territory of the anterior cerebral and posterior cerebral arteries or when the patients had spontaneous anastomoses already formed between the intracranial and extracranial arteries (middle meningeal and superficial temporal arteries) and had the risk of injuring them during scalp and dural incision.

A second operation of the revascularization procedures on both sides was performed more than 2 weeks after the first operation.

#### Measurements of regional cerebral blood flow (rCBF)

A total of 113 rCBF measurements were performed by a  $^{133}\text{Xe}$  inhalation method using Meditronic–Novo Cerebrograph, with each patient having 1 to 6 recordings. Eleven regional detectors on each side allowed simultaneous and bilateral flow determinations. CBF was calculated according to Risberg *et al.*<sup>4)</sup> as an initial slope index (ISI), but not corrected for changes in  $\text{PaCO}_2$ . Measurements were performed in the awake and resting state without using sedation or anesthesia. Postoperative changes in mean hemispheric values of rCBF (mCBF) and distribution patterns of rCBF were analyzed.  $\text{CO}_2$  responses were also examined in 4 patients before and after the operations.

### RESULTS

Postoperative results were excellent in 16 patients who had neither neurological deficits nor TIAs, good in 8, unchanged in 4, deteriorated in 2, and dead in 1. The cause of the death was a recurrence of intracerebral hemorrhage which was noticed in an adult patient, in which EDAS+EMS+EGS had been performed on both hemispheres about 1 year previously. In 5 of 9 adult patients, neurologic status was unchanged or deteriorated.

Postoperative complications were encountered as follows : transient neurological deterioration which was partly due to hypocapnia during anesthesia in 5 patients, subdural hematoma without any further neurological deficit in 2, hemorrhagic infarction after anastomosis in 1, and subcutaneous abscess in 1.

#### mCBF

In healthy young volunteers mCBF values were reduced with advancing age, and the reduction is more progressive in younger ones. Preoperative mCBF values were lower in most of the young patients than in healthy young volunteers (Fig. 1). On the other hand, there was no significant difference between both groups in the adults, except for one with extensive infarction. Preoperative mCBF values were markedly low in most of the hemispheres with low density areas in CT scan, and the degree of reduction in the preoperative mCBF correlated well with the severity of clinical manifestations.

Although the mCBF decreased slightly or remained unchanged within 3 months after operation in several patients, it increased gradually and/or became stationary in most of the patients (Fig. 2). Thus, postoperatively, mCBF increased by an average of 7.1% in the children (39 hemispheres), in comparison with 4.2% decrease in the adults (10 hemispheres). In the children, it prominently

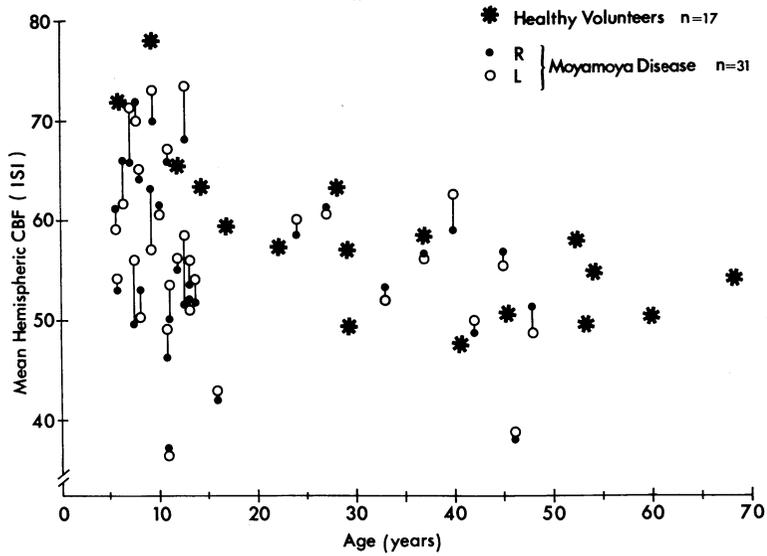


Fig. 1. Correlation between preoperative mCBF values and age in healthy volunteers and in patients with moyamoya disease. Preoperative mCBF values were lower in most of the young patients than in healthy young volunteers.

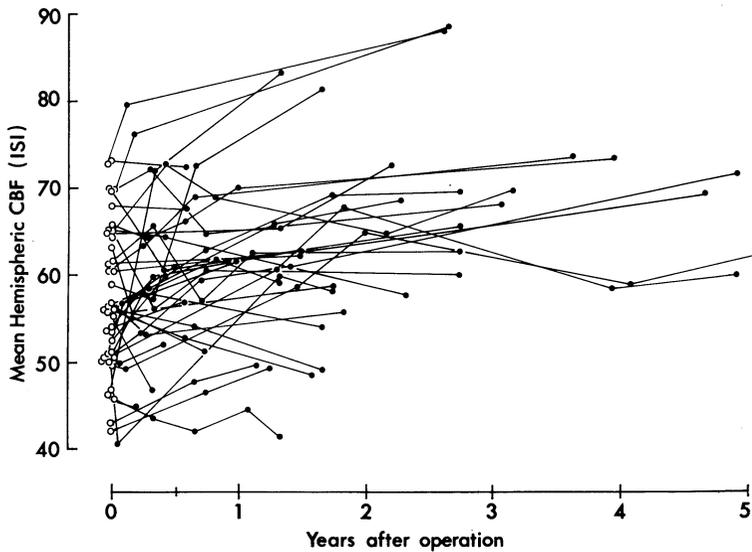


Fig. 2. Postoperative changes in mCBF. Although the mCBF decreased slightly or remained unchanged within 3 months after operation in several patients, it increased gradually and/or became stationary in most of the patients.

increased ( $>15\%$ ) in 12 hemispheres, increased (5–15%) in 9, unchanged in 9 and decreased in 9, while in the adults it was unchanged in 6 hemispheres and decreased in 4. mCBF did not increase in the hemispheres with moderate to large low density areas in the preoperative CT scans, even in the children.

#### Distribution patterns of rCBF

Distribution patterns of rCBF were divided into 3 groups as follows: hypofrontal, hypoparietal and hypoccipital. The hypofrontal pattern was a common type of distribution and found in 54.8% of this series. In the children group, this frequency was prominently high, as seen in 26 of 44 hemispheres (Table 2). Postoperative changes in rCBF patterns of the 51 operated hemispheres are shown in Table 3; prominently improved in 6 hemispheres, improved in 21, unchanged in 22 and exaggerated in 2. Of the 39 operated hemispheres of children, 26 could be demonstrated to have an improvement in the rCBF pattern, that is, in approximately two-thirds of the children, as compared with the adults showing little improvement.

TABLE 2. Distribution patterns of rCBF in 62 hemispheres

rCBF pattern	Children	Adults
hypo-frontal	26	8
hypo-parietal	9	10
hypo-occipital	9	0
total	44	18

TABLE 3. Postoperative changes in rCBF pattern of the operated hemispheres

	Children	Adults
prominently improved	6	0
improved	20	1
unchanged	13	9
exaggerated	0	2
total	39	12

Changes of the rCBF pattern and angiographic findings in the right hemisphere of a 13-year-old girl, who underwent EMS on both sides, is shown in Figure 3. The first rCBF examination showed subnormal mCBF (ISI 51.1) in the right hemisphere with the lowest values in the parietal area (hypoparietal pattern). The second study performed 9 months later showed an improvement of the hypoparietal pattern with a 16.2% increase of mCBF and a marked filling of middle cerebral arteries mainly via the deep temporal and middle meningeal arteries. About 5 years after the operation, an improvement in the hypoparietal pattern still existed and a tendency to the hypofrontal pattern of rCBF distribution was found with a 39.5% increase of mCBF and a marvellously good visualization of middle cerebral arteries.

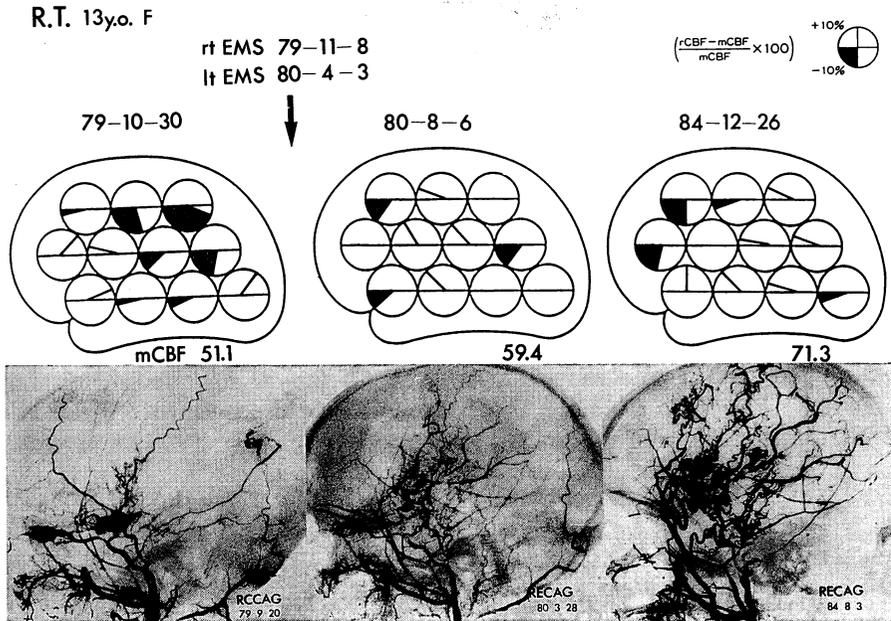


Fig. 3. Changes of the rCBF pattern and angiographic findings in the right hemisphere of a 13-year-old girl, who underwent EMS on both sides.

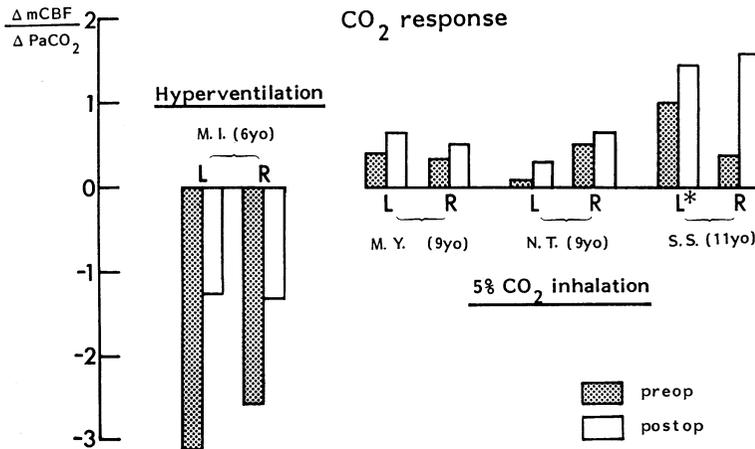


Fig. 4. Changes in CO<sub>2</sub> response. Variations of the mCBF change versus that of PaCO<sub>2</sub> change were calculated before and after operation ( $\Delta mCBF/\Delta PaCO_2$ ). Preoperative mCBF excessively decreased during hyperventilation, while it hardly increased during inhalation of 5% CO<sub>2</sub>. These abnormal CO<sub>2</sub> responses improved after operation in all the operated hemispheres. In one patient with unilateral moyamoya disease, operation was not performed on the healthy hemisphere (asterisk), showing a normal CO<sub>2</sub> response preoperatively.

CO<sub>2</sub> response

Postoperative changes in CO<sub>2</sub> response were examined in 4 patients. CO<sub>2</sub> response was measured by repeating rCBF studies during hyperventilation in 1 patient and inhalation of 5% CO<sub>2</sub> in air in 3 patients. Preoperative mCBF excessively decreased during hyperventilation, while it hardly increased during inhalation of 5% CO<sub>2</sub>. Variations of the mCBF change versus that of PaCO<sub>2</sub> change were calculated before and after operation ( $\Delta mCBF/\Delta PaCO_2$ ). These abnormal CO<sub>2</sub> responses improved after operation in all the operated hemispheres, as shown in Figure 4. This tendency was prominent in the patient having a hyperventilation study. In one patient with unilateral moyamoya disease, operation was not performed on the healthy hemisphere, showing a normal CO<sub>2</sub> response preoperatively.

Paradoxical CO<sub>2</sub> response during hypercapnia was found to be focal in 5 hemispheres of 3 patients, but improved in 4 of 5 hemispheres postoperatively. Pre- and postoperative rCBF patterns at rest and during hypercapnia in a 11-year-old boy, who underwent EMS on the right hemisphere, is shown in Figure 5. Paradoxical CO<sub>2</sub> response which was seen during hypercapnia in the frontal area was improved after operation with a marked filling of the middle cerebral artery via the hypertrophied external carotid system.

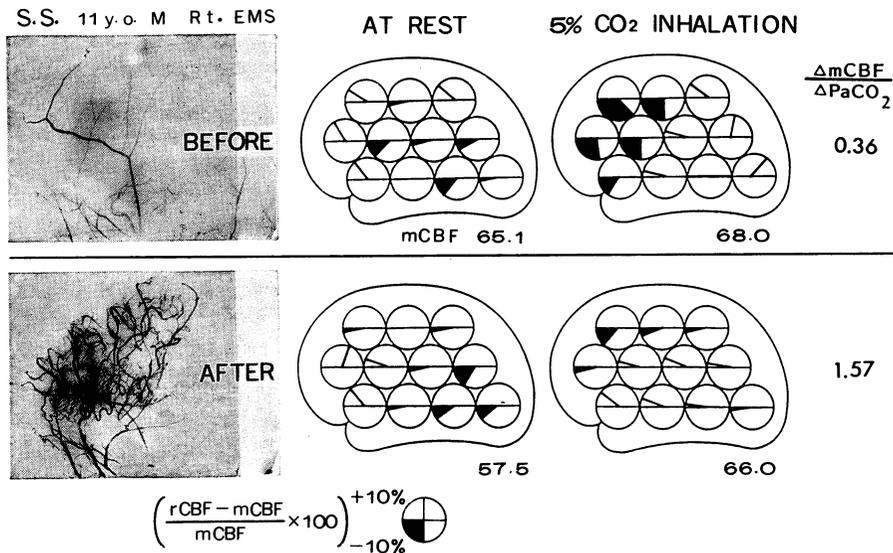


Fig. 5. Pre- and postoperative rCBF patterns at rest and during hypercapnia in a 11-year-old boy, who underwent EMS on the right hemisphere. Paradoxical CO<sub>2</sub> response which was seen during hypercapnia in the frontal area was improved after operation with a marked filling of the middle cerebral artery via the hypertrophied external carotid system.

DISCUSSION

The changes of cerebral hemodynamics in moyamoya disease have been reported by several Japanese authors,<sup>5-10)</sup> but its relationship to revascularization

procedures have not been evaluated in detail. In the present study, rCBF measurements were performed by a  $^{133}\text{Xe}$  inhalation method. The  $^{133}\text{Xe}$  clearance method for measuring rCBF has increasingly been used and led to a greater understanding of newer concepts of pathophysiological and clinical importance. There is no doubt that a  $^{133}\text{Xe}$  intracarotid injection method is one of the most sophisticated methods available to study brain circulation, but it is traumatic and cannot be repeated frequently because it requires carotid artery puncture and catheterization. In order to overcome this problem, a  $^{133}\text{Xe}$  inhalation method is increasingly used. This method can be repeated painlessly and harmlessly, provides bilateral and simultaneous measurements, and yields reproducible quantitative data of cerebral circulation. Another advantage of the inhalation method is the opportunity to acquire normal control data that can be compared with the patient findings, even in the children. There appears to be a rapid fall in mCBF with advancing age until the time of puberty, which continues through adolescence, and afterward there is a more gradual but continuous decline as reported in the literature.<sup>5,11,12)</sup> Therefore, the flow data should be compared with the values obtained in age-matched normal controls.

However, the methodological limitations of this method, which occasionally fails to detect a regional ischemia in the brain tissue, especially in the deep lesions, owing to superimposition of many tissue layers, should be taken into consideration, when evaluating the data of rCBF. In spite of these limitations, the inhalation method can be a useful tool for measuring rCBF in patients with moyamoya disease, because of the two peculiar hemispheric circulations; firstly, the epicerebral microcirculation studied by fluorescein angiography is various in fashion of filling and in circulation time from gyrus to gyrus<sup>13)</sup>; secondly, the multiple collateral pathways are often formed between the intracranial and extracranial arteries.

Since the pathogenesis of moyamoya disease is still unknown, no effective specific treatment has been found for this disease. The most reasonable approach to the treatment of this chronic, multiple occlusive cerebrovascular disease appears to be construction of anastomotic channels to increase blood supply to the ischemic brain. STA-MCA anastomosis, EMS, EDAS, and omental transplantation have been reported to be attractive means of carrying blood from the extracranial arteries to the surface of cerebral hemispheres. We prefer EMS, because its procedure is much easier and safer, and it can extensively vascularize the ischemic hemispheres in which multiple occlusive lesions of cortical arteries as well as occlusion of the circle of willis can be demonstrated in the advanced stage and the peculiar epicerebral microcirculation is observed by fluorescein angiography varying in fashion of filling and in circulation time from gyrus to gyrus or from area to area in a gyrus.<sup>13)</sup>

However, the middle meningeal artery should be preserved as far as possible when performing craniotomy and dural incision. In this study EMS was performed in 51 operations as on 30 patients. Among them, STA-MCA anastomosis was added in 8 operations on 6 patients, EAS and/or EGS in 20 operations on 12 patients, EDAS in 7 operations in 6 patients, as well. In the patients where marked transdural anastomoses were observed in the preoperative angiograms, the transected and pedicled frontal branch of STA or the Galea aponeurotica alone was also transposed to the cortical surface.

Postoperative changes in cerebral blood flow have been reported by several authors.<sup>5,6,8,14)</sup> Yonekawa *et al.* measured rCBF by a  $^{133}\text{Xe}$  inhalation method on the surgically treated patients where most of the surgeries were the STA-MCA anastomosis with or without combination EMS.<sup>14)</sup> Their findings were as follows: 1) A symptomatic side revealed a reduced CBF as compared with an asymptomatic side in 80% of the cases. 2) Decreased cerebral blood flow on the operated side at one week in 60% of the cases. 3) Better distribution of rCBF and increased cerebral blood flow on the operated side at several months in 80% of the cases. In the previous papers,<sup>5)</sup> we reported that the surgical treatments of moyamoya disease including EMS seem to be effective procedures for preventing the progression of clinical findings caused by cerebral ischemia and for increasing the cerebral blood flow. The results of the present study point to an improvement of rCBF distribution and abnormal  $\text{CO}_2$  response as well as an increase of mCBF after operation, and a striking difference of the preoperative and postoperative cerebral hemodynamics between in children and adults. Those are as follows: 1) Preoperative mCBF values were markedly lower in most of the young patients than in healthy young volunteers, while there is no significant difference between both adult groups. 2) Postoperatively, mCBF increased by an average of 7.1% in the children: prominently increased in 12 patients, increased in 9, unchanged in 9 and decreased in 9, while it decreased by an average of 4.2% in the adults: unchanged in 6 patients and decreased in 4. 3) A postoperative improvement of abnormal distribution of rCBF was demonstrated in approximately two-thirds of the children, as compared with the adults showing little improvement. These findings suggest that the surgical revascularization procedures, mainly EMS in this series, can be effective tools to give additional collateral flow to the ischemic brain, especially in children with moyamoya disease. The difference in the clinical presentation between children and adults is another interesting feature of this disease; cerebral ischemia is common in the children, while cerebral hemorrhage is more prevalent in the adults. Six of our 9 adult patients had hemorrhagic episodes in their clinical courses, and preoperative mCBF values were within normal limits in all patients except for one with an extensive infarction. This seems to be related to the good collaterals which had developed spontaneously, resulting in no increase of mCBF nor improvement of the circulatory pattern in the adult patients.

In the present study, postoperative changes in  $\text{CO}_2$  response were examined in 4 children; preoperative mCBF excessively decreased during hyperventilation, while it hardly increased during inhalation of 5%  $\text{CO}_2$  in air. The cause of the impaired  $\text{CO}_2$  response may lie in the fact that the cortical and pial arteries are in the state of full dilatation, so that they are unable to dilate furthermore during hypercapnia, but under such condition they may excessively contract during hypocapnia induced by hyperventilation. Postoperatively, impaired  $\text{CO}_2$  responses improved in all the operated hemispheres, more prominently in the patient having a hyperventilation study. This fact is well interpreted that these postoperative improvements of  $\text{CO}_2$  response can result in no occurrence of ischemic attack provoked by some condition of hyperventilation such as blowing or crying. Furthermore, a paradoxical  $\text{CO}_2$  response (steal phenomenon) was found during hypercapnia in 5 hemispheres of 3 patients, but improved in 4

of 5 hemispheres postoperatively.

Although it is not easy to compare our operative results with the natural history of the disease, the surgical treatment of moyamoya disease seems to be an effective procedure for preventing the progression of clinical findings caused by cerebral ischemia and for increasing the cerebral blood flow, especially in the children. As the permanent complication rate was quite low, EMS or EDAS, in combination with EGS and/or EAS, appears to be quite safe and effective. In addition, a postoperative reduction of abnormal vascular networks of anastomotic vessels has also been reported.<sup>1)</sup> However, whether these procedures could reduce the chance of bleeding remains to be studied.

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