Intelligence in Children With Moyamoya Disease: Evaluation After Surgical Treatments With Special Reference to Changes in Cerebral Blood Flow

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SUMMARY The effect of surgical treatment upon the intelligence of 20 children with moyamoya disease was evaluated and related to changes in cerebral blood flow (CBF). The patients were treated by various surgical revascularization procedures, mainly by encephalo-myo-synangiosis. Intelligence was tested using the Wechsler intelligence scale for children (WISC) in 19 children and the Wechsler adult intelligence scale (WAIS) in one child. Measurements of regional CBF were performed by a $^{133}$Xe inhalation method.

In the preoperative state, the degree of reduction in the intelligence quotient (IQ) correlated well with the age of the patients; the older patients revealed a more marked reduction of IQ, and the patients with lower Intelligence scores in general showed a tendency for more marked depression of mean CBF.

Postoperatively, most of the patients showed increase in IQ, especially in performance IQ which improved significantly in 10 patients, remained unchanged in 3 and deteriorated in 2. Mean CBF increased by an average of 11.4%, and postoperative changes in mean CBF correlated well with the changes in IQ in most patients. This may show that the postoperative increase in CBF is quite possibly responsible for the changes in IQ.

MOYAMOYA DISEASE is a rare occlusive cerebrovascular disease consisting of progressive narrowing or occlusion of the arteries of the circle of Willis, and is accompanied by abnormal vascular networks of anastomotic vessels. Children with this disease usually present with recurrent episodes of cerebral ischemia but show little tendency to hemorrhagic manifestations. As the disease progresses, it produces a focal neurological deficit characteristic of cerebral infarction, resulting in a poor prognosis. Slowly progressive mental impairment must be one of the most serious problems which influence the outcome, especially after they reach school age and begin to lead more social lives.

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, etc. We have reported the efficacy of EMS for patients with moyamoya disease in previous papers.

The purpose of this paper is to evaluate the effect of these surgical procedures on the intelligence of children with moyamoya disease, with an attempt to relate this to changes in cerebral blood flow (CBF).

Materials and Methods

Patients (table 1)

Twenty children were treated by various surgical revascularization procedures, mainly by EMS. Ten were males and 10 were females. Their ages ranged from 5 to 16 years, with an average of 10 years. The follow-up periods were 6 months to 4 years after operation.

The clinical manifestations were cerebral ischemic symptoms and signs, such as hemi- and monoparesis, mental impairment, involuntary movement of the limbs, epileptic seizures and headache. No intracranial hemorrhage were encountered in these patients. Preoperative computed tomographic scans showed low density areas, which varied in size in all patients except for 2 (case 5, 18).

Operations

The operative methods of STA-MCA anastomosis, EMS and EDAS were identical to those described by several authors. EMS was performed in 34 operations as on 19 patients. Among them STA-MCA anastomosis was added in 3 operations on 2 patients, and the transected frontal branch of STA or the aponeurosis alone was transposed to the cortical surface (EAS) in 13 operations on 7 patients. EDAS was performed in 3 operations on 3 patients.

Evaluation of Mental Function

Intelligence was tested using the Wechsler intelligence scale for children (WISC) in 19 children aged less than 15 years, and the Wechsler adult intelligence scale (WAIS) in one child aged 16 years.

Measurements of Regional CBF

Measurements of regional CBF were performed by a $^{133}$Xe inhalation method, with each patient having 1 to 5 recordings. Eleven regional detectors on each side allowed simultaneous and bilateral flow determinations. CBF was calculated according to Risberg et al, as an initial slope index (ISI), but not corrected for changes in PaCO$_2$. Changes in mean hemispheric values of regional CBF (mean CBF) were analyzed as an indicator.
TABLE 1  Clinical Summary of the Patients

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age</th>
<th>Sex</th>
<th>Clinical manifestations*</th>
<th>Operations† 1st</th>
<th>Preoperative IQ</th>
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<tr>
<td>1</td>
<td>5</td>
<td>F</td>
<td>stroke, TIA</td>
<td>L-EMS</td>
<td>100</td>
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<td>2</td>
<td>6</td>
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<td>TIA, RIND</td>
<td>L-EMS</td>
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<td>3</td>
<td>6</td>
<td>M</td>
<td>TIA</td>
<td>L-EMS, STA transposition</td>
<td>121</td>
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<tr>
<td>4</td>
<td>6</td>
<td>M</td>
<td>stroke, TIA, RIND</td>
<td>R-EMS</td>
<td>86</td>
</tr>
<tr>
<td>5</td>
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<td>L-EMS, STA transposition</td>
<td>102</td>
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<tr>
<td>6</td>
<td>8</td>
<td>M</td>
<td>TIA, stroke</td>
<td>L-EMS, STA-MCA anastomosis</td>
<td>123</td>
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<td>7</td>
<td>8</td>
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<td>L-EMS, STA-MCA anastomosis</td>
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<td>R-EMS</td>
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<td>L-EMS</td>
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<tr>
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<td>10</td>
<td>F</td>
<td>TIA</td>
<td>R-EDAS, EAS</td>
<td>104</td>
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<tr>
<td>12</td>
<td>11</td>
<td>F</td>
<td>TIA, stroke</td>
<td>L-EMS, STA-MCA anastomosis</td>
<td>105</td>
</tr>
<tr>
<td>13</td>
<td>11</td>
<td>M</td>
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<td>L-EMS, STA transposition</td>
<td>100</td>
</tr>
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<td>14</td>
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<td>TIA, RIND, stroke</td>
<td>R-EDAS, EAS</td>
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<td>15</td>
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<td>18</td>
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<td>R-EMS, EAS</td>
<td>106</td>
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<td>20</td>
<td>16</td>
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<td>TIA, RIND, stroke</td>
<td>R-EMS</td>
<td>71</td>
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</table>

* TIA = transient ischemic attack; RIND = reversible ischemic neurological deficit; stroke = completed stroke.
† EMS = encephalo-myo-synangiosis; STA-MCA anastomosis = superficial temporal artery-middle cerebral artery anastomosis; STA transposition = transposition of the transected STA to the cortical surface; EDAS = encephalo-duro-arterio-synangiosis; EAS = encephalo-aponeuro-synangiosis (transposition of the aponeurosis alone to the cortical surface).

Results

Preoperative State

1) Intelligence Quotient (IQ)

The mean scores for verbal, performance and full scale IQs were 95.4 ± 17.8 (n = 19), 97.2 ± 21.4 (n = 19) and 97.2 ± 19.6 (n = 18), respectively, excluding 4 scores which were too low to calculate. There was no significant difference between them.

The degree of reduction in preoperative IQ correlated well with the age of the patients. The older patients revealed a more marked reduction of IQ, as shown in table 2. In fact, most of the patients aged between 13 and 16 years had extremely low IQ scores.

2) CBF

Preoperative mean CBF values were lower in most of the patients than those in healthy young volunteers (fig. 1). The degree of reduction in the preoperative mean CBF was more prominent in the advancing age group. The relationship between the preoperative full scale IQ and mean CBF is shown in figure 2. The patients with lower intelligence scores in general
showed a tendency for more marked depression of mean CBF.

**Postoperative Evaluation**

Postoperative results were excellent in 6 patients who had neither neurological deficits nor TIA's, good in 13 patients, and unchanged in one patient who had diffuse cortical atrophy of the cerebral hemispheres.

Performance IQ showed the most satisfactory increase in the studies which were retested between 2 and 34 months after bilateral operation, with each patient having 1 to 3 tests (fig. 3); improvement was substantial in 10 patients, remained unchanged in 3 and deteriorated in 2. Full scale IQ was improved in 8 patients, remained unchanged in 6, and deteriorated in

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**Table 2: Preoperative Intelligence Scores in Different Age Groups**

<table>
<thead>
<tr>
<th>Intelligenc* quotient</th>
<th>Age on admission (years)</th>
<th>5-8 (n = 8)</th>
<th>9-12 (n = 6)</th>
<th>13-16 (n = 6)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Verbal</td>
<td></td>
<td>106.7 ± 13.1</td>
<td>97.8 ± 13.2</td>
<td>79.8 ± 17.0</td>
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<tr>
<td>Performance</td>
<td></td>
<td>106.9 ± 16.3</td>
<td>95.8 ± 26.6</td>
<td>83.4 ± 16.5</td>
</tr>
<tr>
<td>Full scale</td>
<td></td>
<td>108.0 ± 12.9</td>
<td>96.8 ± 22.6</td>
<td>82.6 ± 16.4</td>
</tr>
</tbody>
</table>

*Values are means ± standard deviation.

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**Figure 1.** Relationship between preoperative mean CBF and age. Preoperative mean CBF values were lower in most of the patients than those in healthy young volunteers (asterisks). The degree of reduction in preoperative mean CBF was more prominent in the advancing age group. Open circles indicate the values on the left side. Closed circles indicate the values on the right side.

**Figure 2.** Relationship between preoperative full scale IQ and mean CBF. Patients with lower intelligence scores in general showed a tendency for more marked depression of mean CBF. The symbols are defined in figure 1.

1. Verbal IQ was improved in 2, remained unchanged in 11 and deteriorated in 2.

Although the mean CBF decreased slightly or remained unchanged within 3 months after operation in several patients, it increased gradually and/or became stationary about 6 to 12 months later in most of the patients (fig. 4). Postoperatively, the mean CBF increased by an average of 11.4%. However, in 3 patients (case 2, 9, 12), mean CBF decreased over 3 months later despite the presence of marked revascularization in the angiograms. In most of the hemispheres with moderate to large low density lesions in the preoperative computed tomographic scans, mean CBF did not increase.

The relationship between the changes in mean CBF and the changes in IQ after operation is shown in figure 5. In most of the patients the postoperative changes in mean CBF correlated well with the changes in IQ; mean CBF increased in 9 of 11 patients who showed an increase in IQ.

**Figure 3.** Postoperative changes in performance IQ, which showed the most satisfactory increase, improved significantly in 10 patients, remained unchanged in 3 and deteriorated in 2.
months after the operation

**FIGURE 4.** Postoperative changes (%) in mean CBF. Though the mean CBF decreased slightly or remained unchanged within 3 months after operation in several patients, it increased gradually and/or became stationary about 6 to 12 months later in most of the patients.

**Discussion**

The studies of children with moyamoya disease have revealed that this disorder shows a progressive course with repeated ischemic episodes frequently resulting in permanent deficits.1,2,10,11 Furthermore, the progression of the disease process with time also occurs in angiographic,12-14 electroencephalographic10,15 and computed tomographic findings.16 Maki et al12 reported on the clinical results in 24 children with onset below the age of 13, and an average follow-up period of 5 years and 9 months. Of their 24 children, 7 had a good prognosis, of which 5 had no symptoms and 2 had slight weakness. On the other hand, 8 children had a poor prognosis including one who died from acute subdural hematoma, 2 who could not learn in school because of motor and mental deficits, and 5 who were learning in a special class. Another 8 cases were not physically handicapped, but the parents complained either of their poor results at school or slow behavior pattern as compared to their peers. From these results it was suggested that the prognosis in moyamoya disease was good in about one third, poor in one third, and borderline in the other one third. Nishimoto11 stated that half of the children are able to lead social lives, one fourth have slight neurological deficits and the other one fourth revealed poor clinical functioning.

Slowly progressive mental impairment is one of the most serious problems affecting the victims. The factors influencing the poor prognosis in mental function were: early onset, repeated transient ischemic attacks followed by residual neurological deficit, symptoms suggesting bilateral or dominant hemispheric lesions, and angiographically widespread occlusions.2 In the present study, it was found that the older patients tended to have more reduction of IQ. Most of the patients aged between 13 and 16 years had extremely low IQ scores. Preoperative mean CBF values were lower in most patients than those in healthy volunteers; the degree of reduction in preoperative mean CBF was more prominent in the advancing age group. As shown in figure 2, patients with lower intelligence scores in general showed a tendency for more marked depression of mean CBF.

Since the pathogenesis of moyamoya disease is still unknown, no effective treatment has been found for this disease. The most reasonable approach for the treatment of this chronic, multiple occlusive cerebrovascular disease appears to be construction of anastomotic channels to increase blood supply to the ischemic brain. EMS and STA-MCA anastomosis appear to be attractive means of carrying blood from the extracranial arteries to the surface of cerebral hemisphere. We prefer EMS, because the procedure of EMS is much easier and safer; STA-MCA anastomosis is not easily applicable because of the diameter of the vessels; furthermore in some cases the MCA is occluded not only at its proximal site but also distally. In the present study, most of the patients showed improvement or increase in IQ postoperatively, especially in performance IQ, which improved significantly in 10 patients, remained unchanged in 3 and deteriorated in 2. Numerous studies have reported lower verbal than performance IQ in patients with unilateral left hemisphere lesions and lower performance than verbal IQ in those with right hemisphere lesions. The lesions in moyamoya disease are bilateral and multiple, so that
the situation is more complex and further studies with long-term follow-ups are required to clarify this point.

Mean CBF increased by an average of 11.4%. This increase was not as great as we had expected. However, it may be due to the reduction of mean CBF with advancing age. The changes of cerebral hemodynamics in moyamoya disease have been reported by several Japanese authors, but its relationship to intelligence has not, to our knowledge, been evaluated. In most patients postoperative changes in mean CBF correlated well with changes in IQ, though there were exceptions in some children. An encouraging finding from our study is that most of the children who had excellent collaterals from the extracranial vessels postoperatively, showed increase in CBF as well as improvement of mental function.

Although it is not easy to compare our operative results with the natural history of the disease, since no controls were utilized, the surgical treatment of moyamoya disease including EMS seems to be an effective procedure for preventing the progression of clinical findings caused by cerebral ischemia and for increasing the cerebral blood flow.

References

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