IV. 7. Cerebral Blood Flow and Oxygen Metabolism Disturbances in Children with Craniosynostosis

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Introduction
Mental developmental retardation is one of the most serious complication of craniosynostosis. It may be caused by distorted brain growth, increased intracranial pressure, or primary brain malformation\textsuperscript{2,5}). But the direct effect of maldeveloped cranial vault on the brain was not studied yet. In the present study, cerebral blood flow and oxygen metabolism in children with craniosynostosis were investigated by positron emission tomography.

Materials and Methods
Subjects were six girls and five boys, ages ranged from 3 months to 7 years. Types of craniosynostosis were scaphocephaly, plagiocephaly, brachycephaly, oxycephaly, Crouzon's disease, and trigonocephaly. No patients presented severe neurological deficit or distinctive developmental retardation. Mild mental retardation was seen in one case of scaphocephaly (Table). By positron emission tomography with O-15 CO\textsubscript{2}, O\textsubscript{2}, CO inhalation method, regional cerebral blood flow (rCBF), regional oxygen extraction fraction (rOEF), regional cerebral metabolic rate of oxygen (rCMRO\textsubscript{2}), regional cerebral blood volume (rCBV) were measured. PT-931(CTI, Knoxville, Tennessee) was employed. The spatial resolution was 8mm(FWHM) and seven slices were obtained simultaneously. All PET studies were performed in accordance with the policies of the Committee for Clinical PET study of Tohoku University. Informed consents were obtained from the parents. All subjects were scanned at the axial tomographic level from the thalamus up to the centrum semiovale. The PET images were reconstructed using a measured attenuation correction. Venous and arterial catheters were inserted in a hand vein and brachial artery respectively, under the administration of local anesthesia. Thiopental sodium was administered intravenously 20 minutes prior to the emission scan in order to anesthetize the patient during the examination. Measurements of rCBF, rOEF, rCMRO\textsubscript{2} and rCBV were carried with steady state inhalation of tracer amounts of C\textsuperscript{15}O\textsubscript{2}, 15O\textsubscript{2} and C\textsuperscript{15}O, respectively\textsuperscript{4}). The content of radioactivity in the inhalation air was approximately 10% of those of adults content for the study of infants.
Results

Disturbances of cerebral circulation and metabolism were observed in eight cases. In two cases of plagiocephaly caused by closure of unilateral coronal suture, lower values of rCBF and rCMRO\textsubscript{2} were observed in the affected side of cerebral cortex (Fig. 1). However, the cranial vault was hypoplastic, intracranial hypertension was not observed. In a case with brachicephaly caused by early closure of bilateral lambda sutures, low values of rCBF and rCMRO\textsubscript{2} was observed in the posterior half of cerebral cortex and cerebellum, which was covered by hypoplastic vault (Fig. 2). The same finding was seen in a case with oxycephaly. In those four cases, regional increase or decrease was not observed in rOEF and rCBV.

Three out of four cases of scaphocephaly were associated with ventriculomegaly in our series. Very low rCBF and rCMRO\textsubscript{2} was observed in the cerebral cortex except the sensorimotor and the visual cortices (Fig. 3). No disturbance in circulation and metabolism was recognized in the case of scaphocephaly without ventriculomegaly.

In the case of Crouzon's disease with intracranial hypertension, high rOEF values of whole cerebral cortex was observed, but focal disturbance of cerebral blood flow and metabolism was not seen.

In a present series, signs or symptoms of intracranial hypertension was obvious in five cases. Three cases younger than 5 months of age with disturbances of cerebral blood flow and metabolism were not involved in them.

Discussion

The immature skull enlarges in response to the growth of the underlying brain. This is permitted by expansion of the calvarial bones which are joined by the sutures consisted by elastic connective tissue. During the first six months of life, the brain of a neonate doubles in weight. By two years of age, the weight of the brain exceeds three times and is approximately 80 percents of its adult weight. The growth of the brain continues thereafter until 10 to 12 years of age.

As a consequence of the rapid growth of the brain during the first year of life. New osseous tissue is continuously added the calvarial bones, increasing their size and thickness. With the cessation of brain growth at 10 to 12 years of age, the skull ceases to enlarge and the cranial sutures become obliterated by firm fibrous tissue.

Neurological abnormalities accompanying craniosynostosis are to be expected, since dramatic changes in skull shape must be accompanied by changes in brain shape. To what extent this disturbance in brain shape affects function is uncertain. Furthermore, increased intracranial pressure resulting from brain growth in a rigid skull and/or from hydrocephalus may have deteriorative effects. Whatever the mechanisms, the most devastating effect on brain function is mental retardation, which affects a substantial number of craniosynostosis patients 7). The results of present study clearly demonstrated disturbances of cerebral
circulation and metabolism in the compressed or maldeveloped brain under the hypoplastic cranial vault. Furthermore, mild ventriculomegaly caused remarkable decrease of circulation and metabolism in the cerebral cortex.

Mental developmental retardation was not always distinctive in younger children. Careful neurological examination may fail to disclose the symptoms from craniosynostosis. In the treatment of craniosynostosis, patients with mild craniosynostosis and/or mild ventriculomegaly may not always come to medical attention \(^1\), but the results of this study strongly indicates a necessity of early surgical decompression of the developing brain. Thus measurements of cerebral blood flow and metabolism may detect an influence of craniosynostosis on the brain before developmental retardation or neurological deficit appears\(^6\).

**References**


**Table 1.**

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Fig. 1. PET images of five-month-old girl with plagiocephaly. The upper left image is rCBF, upper right is rCMRO₂, lower left is rOEF, and lower right is rCBF.

Fig. 2. PET images of five-month-old girl with brachicephaly. The upper left image is rCBF, upper right is rCMRO₂, lower left is rOEF, and lower right is rCBF.
Fig. 3. PET images of two-year-old boy with scaphocephaly and hydorccephalus. The upper left image is rCBF, upper right is rCMRO$_2$, lower left is rOEF, and lower right is rCBF.