IV. 12. Cerebral Blood Flow and Oxygen Metabolism in Developing Brain

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Introduction

Since glucose and oxygen are the principle substrates for meeting the energy demands of the brain, measurements of the rates at which these substrates are utilized provide an assessment of the level of neuronal function in the brain. Normal values for cerebral blood flow and metabolism in adults are well established\(^1,2\), but not for children except the cerebral metabolic rate for glucose\(^3,4\). Measurement of the rates of regional substrate utilization in the brain during maturation provide a means whereby local functional activity can be related to various stages of behavioral development. This study measured regional cerebral blood flow (rCBF), regional cerebral metabolic rate for oxygen (rCMRO\(_2\)), and regional oxygen extraction fraction (rOEF), using positron emission tomography (PET) in children to clarify human brain functional development.

Subjects and Methods

This study included 24 children (11 males, 13 females), aged from 1 month to 16 years old. All subjects had minor neurosurgical problems, but their motor and mental development were normal. None had neurological deficits.

Twenty-six PET studies were performed using a PT-931 scanner (CTI, Knoxville, Tennessee\(^5\)) in accordance with the policies of the Committee for Clinical PET Study of Tohoku University. Informed consent was obtained from the parents. The spatial resolution of the images were 8mm in FWHM and slice thickness was 7mm. Seven or fourteen images were obtained simultaneously. All subjects were scanned at the axial tomographylevel at least from the midbrain to the upper ventricular level. The PET images were reconstructed using attenuation correction. Venous and arterial catheters were inserted in the dorsal venous network of the hand and radial artery, respectively, under local anesthesia. Thiopental sodium was administered (3 mg/kg, intravenous) just prior to the transmission scan to immobilize the patient during the examination. If this did not bring about sufficient sedation, an additional dose (2 mg/kg) was given. All visual, auditory, and other sensory stimuli were
minimized. Measurements of rCBF, and rCMRO₂, and OEF were carried out using the steady state inhalation method with C15O₂ and 15O₂, respectively. Arterial blood was drawn for the analysis of blood gases and radioactivity. Head counts in each emission scan were corrected for tissue attenuation using previously performed transmission scan. Oval regions of interest were defined in the primary cerebral cortex, basal ganglia, and association cortex, and verified by magnetic resonance imaging. The absolute values for the children were compared to adult values.

Results

1. rCBF: Infants rCBF values were lower than adults values. rCBF values in the primary cerebral cortex and basal ganglia were higher than those in the cerebral association cortex. rCBF reached the adult level at approximately age 6 months in the primary cortex and basal ganglia, and at age 1 year in the association cortex. Subsequently, gradual increases of rCBF values in all cerebral regions were observed, peaking around age 7 years. Thereafter, the rCBF values fell to the adult level during adolescence (Figure 1 a,b).

2. rCMRO₂: Infant rCMRO₂ values followed the same trends as rCBF, but the values were somewhat lower than adult values. rCMRO₂ gradually increased in all cerebral regions during childhood, reaching the adult level in the primary cerebral cortex and basal ganglia during early childhood, and in the cerebral association cortex after adolescence (Figure 2 a,b).

3. rOEF: rOEF was uniform in all brain regions and showed no remarkable changes during development, but stayed within the adult level. Somewhat lower values were observed in school age subjects (Figure 3 a,b).

Discussion

During development, the brain undergoes the sequential anatomical, functional, and organizational changes necessary to support the complex adaptive behavior of a fully mature normal individual and has good plasticity. One approach to the study of these phenomena has been to measure regional substrate utilization at different stages of cerebral maturation. Since the development of the N₂O method for measuring cerebral blood flow⁶, due to progress the non-invasive method for measuring cerebral blood flow and metabolism such as single photon emission computed tomography and positron emission tomography, the measurements of cerebral blood flow and metabolism are useful for not only adults but also children⁷,⁸,⁹, both in normal and pathological individuals⁸,¹⁰. But in children, it is difficult to judge the value because of no normal control value including changes during development⁹.

The reports for developmental changes of regional cerebral blood flow and metabolism from infant to adult were rare, Chugani et al studied regional cerebral metabolic rates for glucose (rCMRglc) using 2-deoxy-2[¹⁸F]fluoro-D-glucose³,⁴. In these studies, the distribution of high values for rCMRGlce corresponded to the well developed cerebral regions
for every childhood. Therefore the changes of the distribution for rCMRGlc were considered to be the change of the brain during development. In our study, in the distribution for rCBF and rCMRO₂ the same trend were observed. But the period and course of the changes for rCBF and rCMRO₂ were different, furthermore rOEF was uniform during childhood. These results were very interesting to consider the developing brain.

This study will contribute to clarifying not only functional development but also much pathophysiology in child’s brain. For example in the report of CBF and oxygen metabolism in infants with hydrocephalus⁹, lower rCBF and higher rOEF values were observed, and the regional differences in rCMRO₂ were not as evident as those observed in rCBF. Higher rOEF was obviously abnormal, this indicated metabolic deterioration produced by ventriculomegaly. On the other hand, maturational raise in rCMRO₂ is somewhat later than in rCBF. Just because this phenomenon would be obtained, metabolic deterioration do not always occur. The value should be investigated detailed in accordance with the results of this study.

Conclusion

1. A notable increase in rCBF and rCMRO₂ occurred during early childhood. rCBF values were higher than those of adults, peaking around age 7 years, while rCMRO₂ showed a gradual increase.

2. rCBF and rCMRO₂ values reached the adult level during adolescence.

3. Dynamic changes were observed in rCBF and rCMRO₂ in infants and young children, while rOEF was stable during childhood.

References

Fig. 1. Sequential changes of rCBF at visual and visual association cortices (a; ■ visual, ◻ visual association), and at sensorimotor and frontal association cortices (b; ■ sensorimotor, ◻ frontal association). Adult's values are indicated with lines at visual (a), and sensorimotor cortices (b), and with dotted lines at visual association (a), and frontal association (b) cortices.
Fig. 2. Sequential changes of rCMRO₂ at visual and visual association cortices (a; ■: visual, □: visual association), and at sensorimotor and frontal association cortices (b; ■: sensorimotor, □: frontal association). Adult's values are indicated with lines at visual (a), and sensorimotor cortices (b), and with dotted lines at visual association (a), and frontal association (b) cortices.
Fig. 3. Sequential changes of rOEF at visual and visual association cortices (a; ■ : visual, □ : visual association), and at sensorimotor and frontal association cortices (b; ■ : sensorimotor, □ : frontal association). Adult's values are indicated with lines at visual (a), and sensorimotor cortices (b), and with dotted lines at visual association (a), and frontal association (b) cortices.