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Original article

Quantitative evaluation of regional cerebral blood flow changes during childhood using ^{123}I-N-isopropyl-iodoamphetamine single-photon emission computed tomography

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Abstract

Objective: To quantitatively evaluate regional cerebral blood flow (rCBF) and regional developmental changes during childhood using ^{123}I-N-isopropyl-iodoamphetamine single-photon emission computed tomography (SPECT) and autoradiography.

Methods: We retrospectively analyzed quantitative values of rCBF in 75 children (29 girls) aged between 16 days and 178 months (median: 12 months), whose brain images, including magnetic resonance imaging and SPECT data, were normal under visual inspection at Saitama Children's Medical Center between 2005 and 2015. The subjects had normal psychomotor development, no focal neurological abnormalities, and neither respiratory nor cardiac disease at the time of examination. Regions of interest were placed automatically using a three-dimensional stereotactic template.

Results: rCBF was lowest in neonates, who had greater rCBF in the lenticular nucleus, thalamus, and cerebellum than the cerebral cortices. rCBF increased rapidly during the first year of life, reaching approximately twice the adult levels at 8 years, and then fell to approximately adult levels in the late teenage years. Cerebral cortex rCBF sequentially increased in the posterior, central, parietal, temporal, and callosomarginal regions during infancy and childhood.

Conclusions: rCBF changed dramatically throughout childhood and ranged from lower than adult values to approximately two times higher than adult values. It had different trajectories in each region during brain development. Understanding this dynamic developmental change is necessary for SPECT image evaluation in children.
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Keywords: Cerebral blood flow; Quantitative evaluation; Developmental change; Regional difference; Single-photon emission computed topography

1. Introduction

Human brain development involves various changes including sequential anatomical and histological alteration. Various developmental changes occur dynamically during childhood and especially in infancy. Brain development is related to the emergence of corresponding functions. Cerebral blood flow (CBF) and cerebral metabolism changes correspond to cerebral activity. Brain functional images of CBF and cerebral metabolism are used to evaluate cerebral activity in many brain diseases including infarction, dementia,

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epilepsy, tumor, and encephalitis. However it is difficult to interpret these findings in children because their brains undergo various changes and have normal deviations associated with brain development.

Assessment of CBF and its age-related changes during childhood has been addressed by several nuclear medicine approaches: single-photon emission computed tomography (SPECT) using ^{133}Xe, ^{99m}Tc-ethylcysteinate dimer, ^{123}I-N-isopropyl-iodoamphetamine (^{123}I-IMP), and $C^{15}O_2$ positron emission tomography (PET) [1–5]. These previous studies have reported that regional CBF (rCBF) increases in early childhood, peaks between 4 and 7 years of age, and then declines to reach the adult levels. Several studies have also found that infants have higher rCBF in the basal ganglia and visual and sensorimotor cortices than in other regions. These studies have also reported that rCBF in the frontal region increases slowly. Similar age-related patterns have been reported for brain metabolism, as measured using fluorodeoxyglucose (FDG) PET [6–8]. However, regional differences in CBF changes during development are unclear because there have only been a few quantitative analytical studies of nuclear medicines. These studies have been performed in small numbers of subjects, and several studies have included subjects with abnormal brain images and cerebrovascular diseases. Arterial spin-labeling perfusion magnetic resonance imaging (MRI) has adapted for evaluation of rCBF developmental changes in recent studies [9–11]. These studies have shown that rCBF is decreased beginning before 10 years of age, similar to the results using nuclear medicines. However, there have been few studies in infants and toddlers using arterial spin-labeling perfusion MRI, and rCBF changes in early childhood have not been revealed. Therefor, we have not enough knowledge of developmental changes in rCBF, especially regarding regional differences.

Quantitative evaluation of childhood rCBF is necessary to understand brain development, plasticity, and the clinical and pathological conditions of central nervous system diseases. Quantitative analysis of rCBF during developmental period using SPECT requires an appropriate tracer, objective and reproducible region of interest (ROI) settings, and large number of subjects. ^{123}I-IMP SPECT can be used to measure rCBF. ^{123}I-IMP has a relatively high first-pass extraction among rCBF SPECT tracers and can be quantitatively evaluated. Three-dimensional stereotactic ROI template (3DSRT) is a program that anatomically standardizes brain SPECT images and quantitatively analyzes them using a three-dimensional stereotactic ROI template. Using 3DSRT enable the creation of objective and universal ROI settings. There has been no report regarding developmental changes in rCBF measured using ^{123}I-IMP SPECT data analyzed with 3DSRT. We aimed to quantitatively analyze rCBF developmental changes and to investigate characteristic regional patterns throughout childhood using ^{123}I-IMP SPECT and 3DSRT.

2. Subjects and methods

This retrospective reviews was approved by the Saitama Children's Medical Center Institutional Review Board. Informed consent for ^{123}I-IMP SPECT was obtained from the children's parent and assent was obtained from the children. Medical histories were established for each child and the child's family prior to the scan.

2.1. Participants

We searched a database of children who received ^{123}I-IMP SPECT and underwent autoradiography (ARG) between January 2005 and December 2015 at Saitama Children's Medical Center. The children had transient neurological events and suspected intracranial disease. We selected children according to the following 6 criteria at the time of examination to analyze approximate normal rCBF values: 1) normal brain images on computed tomography or MRI; 2) no respiratory or cardiac disease; 3) normal psychomotor development at the time of examination or normal psychomotor development one year after SPECT for infants younger than 18 months; 4) no focal abnormalities in neurological examinations; 5) normal SPECT findings detected in visual inspections by more than 2 physicians, including a radiologist specializing in SPECT; and 6) SPECT performed with appropriate timing of arterial blood sampling and under a resting or sleeping state.

2.2. SPECT image acquisition

Quantitative rCBF measurements were conducted using the ARG method developed by Iida et al [12]. A triple-head gamma camera (Siemens Multispect3; Siemens Medical Systems Inc.; Hoffman Estates, IL) equipped with a fan beam collimator was used. Data were acquired using a 128×128 matrix for 120 degrees and 24 min with 5-degree steps of 60 s per frame. Siemens Icon-P (Siemens Medical Systems Inc.) was used to reconstruct SPECT image and a Butterworth filter and attenuation correction (Chang, $\mu = 0.1\ cm^{-1}$) were used to produce scanning images with an orbitomeatal line and 256×256 matrix (1.2 mm/pixel). We intravenously injected ^{123}I-IMP up to a dose of 83 MBq in children younger than 1 year of age, up to 111 MBq in children between 1 and 7 years old, and up to 167 MBq in children older than 8 years. Ten minutes after the ^{123}I-IMP injection, arterial blood was collected from

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