# Technetium-99m-ECD Brain SPECT in Cerebral Palsy: Comparison with MRI

Jong Doo Lee, Dong Ik Kim, Young Hoon Ryu, Geum Ju Whang, Chang Il Park and Dong Goo Kim

*Division of Nuclear Medicine, Departments of Diagnostic Radiology, Rehabilitation Medicine and Pharmacology, Yonsei University Medical College, Seoul, Korea*

Hypoxic brain injury is one of the major causes of cerebral palsy. Therefore, this study was performed to evaluate cerebral perfusion impairments in these patients using $^{99m}$Tc-ECD brain SPECT. **Methods:** Fifty-one patients (31 boys, 20 girls; age range 6 mo to 6 yr, 11 mo) with clinical manifestations of cerebral palsy underwent brain SPECT after intravenous injection of $^{99m}$Tc-ECD. The clinical subtypes of cerebral palsy were spastic diplegia (n = 35), spastic quadriplegia (n = 11), spastic hemiparesis (n = 2), choreoathetoid (n = 2) and mixed (n = 1). Transaxial, coronal and sagittal images obtained with a brain-dedicated annular crystal gamma camera were qualitatively analyzed and compared with the findings of magnetic resonance imaging (MRI). **Results:** In SPECT, thalamic hypoperfusion was seen in all patients except one (98%), followed by hypoperfusion in the temporal lobe (52.9%, n = 27), basal ganglia (41.2%, n = 21), cerebellum (39.2%, n = 20) and extratemporal cortices (21.6%, n = 11). However, MR imaging demonstrated thalamic abnormality in seven (13.7%), basal ganglia in two (3.9%), extratemporal cortical defect in five (9.8%) and cerebellar atrophy in one (1.9%). Instead, white matter changes such as periventricular leukomalacia or ischemia (56.9%, n = 25) and thinning of corpus callosum (49%, n = 25) were the major findings. **Conclusion:** Brain SPECT is useful in the diagnosis of cerebral palsy and is more sensitive in the detection of cortical, subcortical nuclei and cerebellar abnormalities. MRI is superior in the detection of white matter changes.

**Key Words:** cerebral palsy; hypoxic brain injury; perfusion impairment; SPECT; magnetic resonance imaging

Cerebral palsy is a nonprogressive disorder that manifest as abnormalities of motion and posture due to a defect or a lesion of the developing brain. Etiologic factors contributing development of cerebral palsy are diverse. Among them, hypoxic ischemic encephalopathy (HIE) is one of the major causes. As cerebral palsy is the most life-limiting childhood disability, early detection is important to initiate therapy. The diagnosis of cerebral palsy is made in approximately 43% of cases by 6 mo, and in 70% of cases by 1 yr *(1–3)*. However, there is no specific test but careful physical examinations for the diagnosis. Anatomic imaging modality is useful; 82% of patients who had been born prematurely and 55% of patients born at term show structural abnormality on magnetic resonance imaging (MRI) *(4)*. Recently, PET using $^{18}$F-fluorodeoxyglucose (FDG) disclosed metabolic defect extended beyond the margin of focal pathology defined by structural imaging. In addition, PET revealed focal areas of cortical hypometabolism in the absence of apparent structural abnormality *(5)*. Similarly, brain SPECT may give valuable information in the diagnosis of cerebral palsy. The aim of this study was to evaluate the perfusion impairments in patients with cerebral palsy using a high-resolution, brain-dedicated annular crystal gamma camera and compare them with the findings of structural imaging.

## MATERIALS AND METHODS

### Subjects

The study population consisted of 51 patients (31 boys, 20 girls; age range 6 mo to 6 yr, 11 mo; mean age 26.1 mo) with cerebral palsy diagnosed by physical examinations and laboratory tests including electroencephalography, electromyography, visual evoked potential, auditory evoked potential and Denver developmental screening test. Patients were grouped to one of the following major clinical subtypes based on the predominant features of their motor impairments: spastic diplegia (n = 35), spastic quadriplegia (n = 11), spastic hemiparesis (n = 2), choreoathetoid (n = 2) and mixed (n = 1). Twenty patients were born with low birth weight (< 2500 g), 16 patients were born prematurely and 21 patients had a history of neonatal asphyxia.
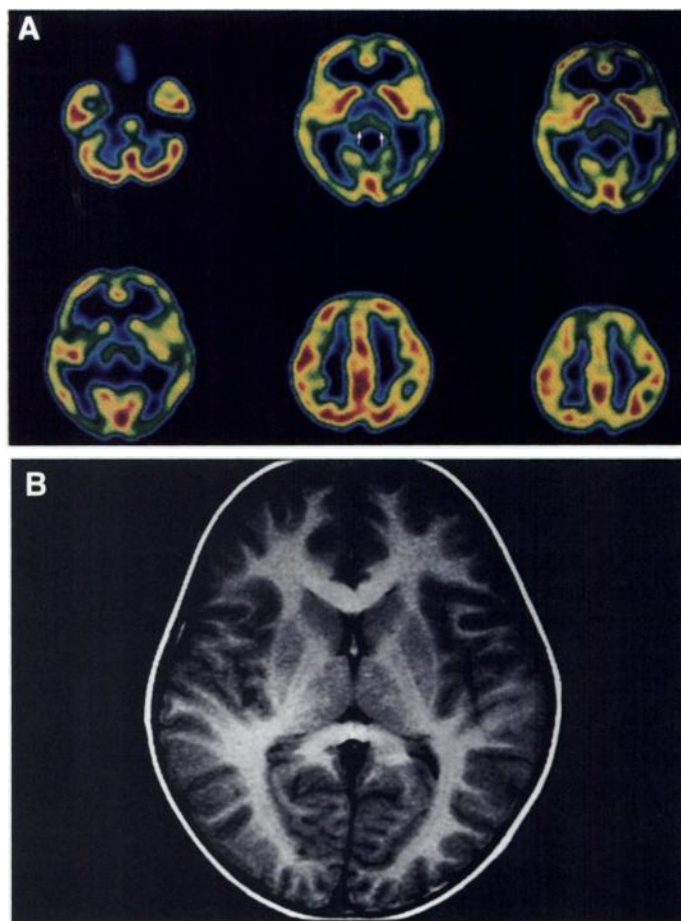


**FIGURE 1.** A 4 yr-and-2-mo-old girl with spastic diplegia born at 34 wk of gestational age. Birth weight was 2750 g. SPECT images (A) show markedly decreased perfusion within bilateral thalami (arrows); however, T1-weighted MRI appears normal (B). Periventricular white matter and thalami are intact.
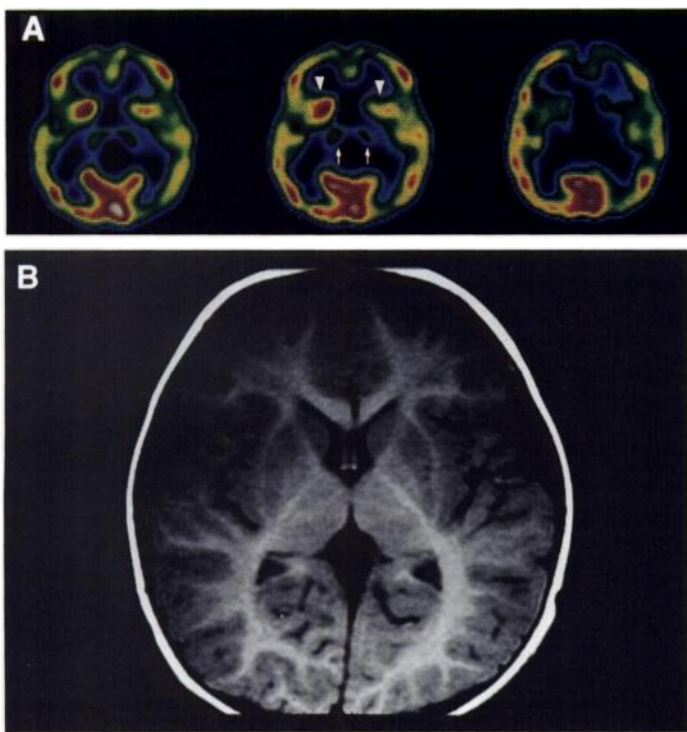
**FIGURE 2.** A 16-mo-old boy with choreoathetoid type of cerebral palsy. He was born at full term (40 wk) and birth weight was 3 kg. SPECT images (A) show severely diminished perfusion within bilateral thalami (arrows), and basal ganglia (arrow heads). MRI fails to demonstrate structural abnormality in these regions (B).

## Imaging Procedures

After sedation by intramuscular injection of 1.6 mg/kg of chlorpromazine, 185–370 MBq (5–10 mCi) $^{99m}$Tc-ECD were given intravenously, and SPECT images were obtained with a brain-dedicated annular crystal gamma camera equipped with low-energy, high-resolution, parallel-hole collimators (Digital Scintigraphics, Inc., Waltham, MA). One-hundred twenty projections were acquired using a 128 × 128 matrices for 20 min. Scatter correction and backprojection with a Butterworth filter (cutoff frequency 1.1 cycle/cm, order 0.10) were performed. Attenuation correction of the transaxial images (slice thickness = 1.67 mm) was performed by Chang's method, and coronal and sagittal slices were calculated from the original transaxial images. The SPECT images were qualitatively evaluated by two experienced nuclear medicine physicians for the evaluation of perfusion abnormality within cerebral cortices, basal ganglia, thalami and cerebellum. Semiquantitative measurement of the cortical activity was not obtained due to lack of consistent normal reference point since sensory motor cortex, basal ganglia, thalami or even cerebellum were involved in many of our patients. At the same day or within 1 mo of the SPECT study, all patients underwent MRI. T1-weighted transaxial, coronal, sagittal and T2-weighted transaxial images were evaluated for the detection of structural abnormalities within white matter, corpus callosum, basal ganglia, thalami, cerebral cortices and cerebellum.

## RESULTS

On SPECT study, all patients except one with spastic diplegia showed perfusion impairments. The most common site of hypoperfusion was thalamus (98%, n = 50), and followed by temporal lobe (52.9%, n = 27), cerebellum (39.2%, n = 20), basal ganglia (41.2%, n = 21) and extratemporal cortices (21.6%, n = 11).

Thalamic hypoperfusion (Fig. 1) was seen in all types of cerebral palsy. Hypoperfusion within basal ganglia was seen not
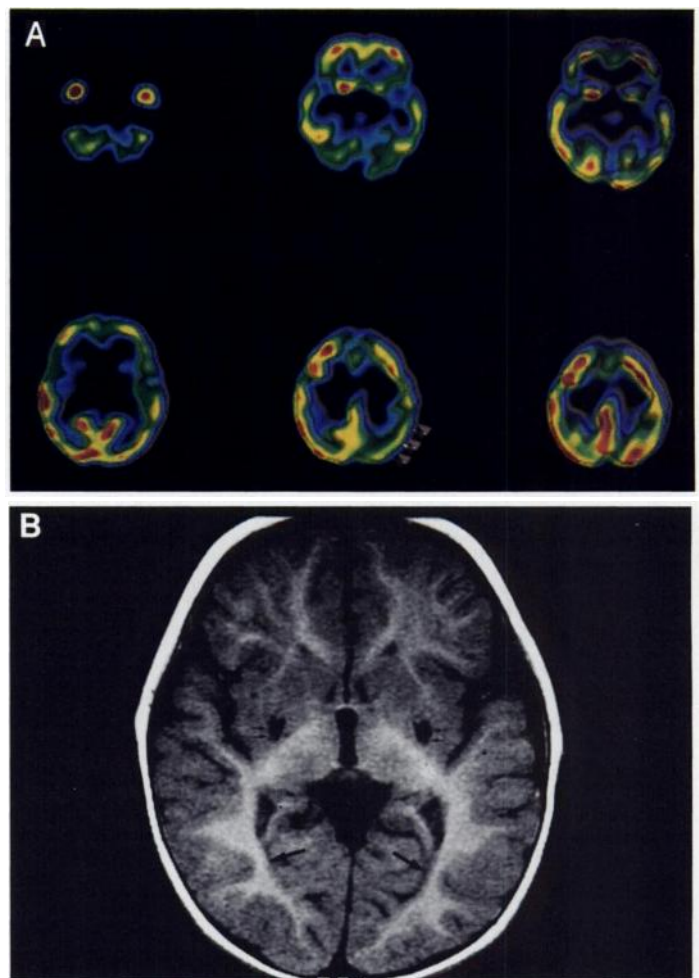




**FIGURE 3.** A 13-mo-old girl with spastic quadriplegia born at full term. Birth weight was 2.9 kg. SPECT images (A) show markedly decreased perfusion within cerebellum, basal ganglia and thalami. Hypoperfusion is also seen in left parietal lobe (arrow heads). T1-weighted MRI demonstrates focal ischemic necrosis within bilateral basal ganglia (small arrows), and thinning of periventricular white matter (arrows) and anterior limb of bilateral internal capsules (B).

only in patients with choreoathetoid (Fig. 2) and mixed types but in 31.4% of patients with spastic diplegia, 54.5% with spastic quadriplegia (Fig. 3) and 50% with spastic hemiparesis. Temporal hypoperfusion was seen in 54.3% of patients with spastic diplegia (Fig. 4), 44.4% with spastic quadriplegia, 100% with spastic hemiparesis and 50% with choreoathetoid and mixed types, respectively. Cerebellar hypoperfusion was observed in 40% of patients with spastic diplegia (Fig. 4A) and in 45.5% with spastic quadriplegia (Fig. 5A). Perfusion defect in extratemporal cerebral cortices (Fig. 5) was observed in 54.3% of patients with spastic quadriplegia and in 100% with mixed types; however, three patients with spastic diplegia also showed cortical perfusion defect. In addition to perfusion defects, areas of hypoperfusion were randomly present in all patients (Fig. 6). The SPECT data were summarized in Table 1.

On MRI study, eight patients with spastic diplegia and two with choreoathetoid were normal, but the remaining 41 patients (80.4%) had structural abnormalities. MRI demonstrated abnormality in gray matter such as extratemporal cortical defect in five cases (9.8%) (Fig. 5B), thalamic abnormality in seven (13.7%) (Fig. 3B), basal ganglia in two (3.9%) and cerebellar atrophy in one. However, ischemic change or leukomalacia in white matter (56.9%, n = 29) and thinning of corpus callosum (49%, n = 25) were the major findings. Migration anomaly
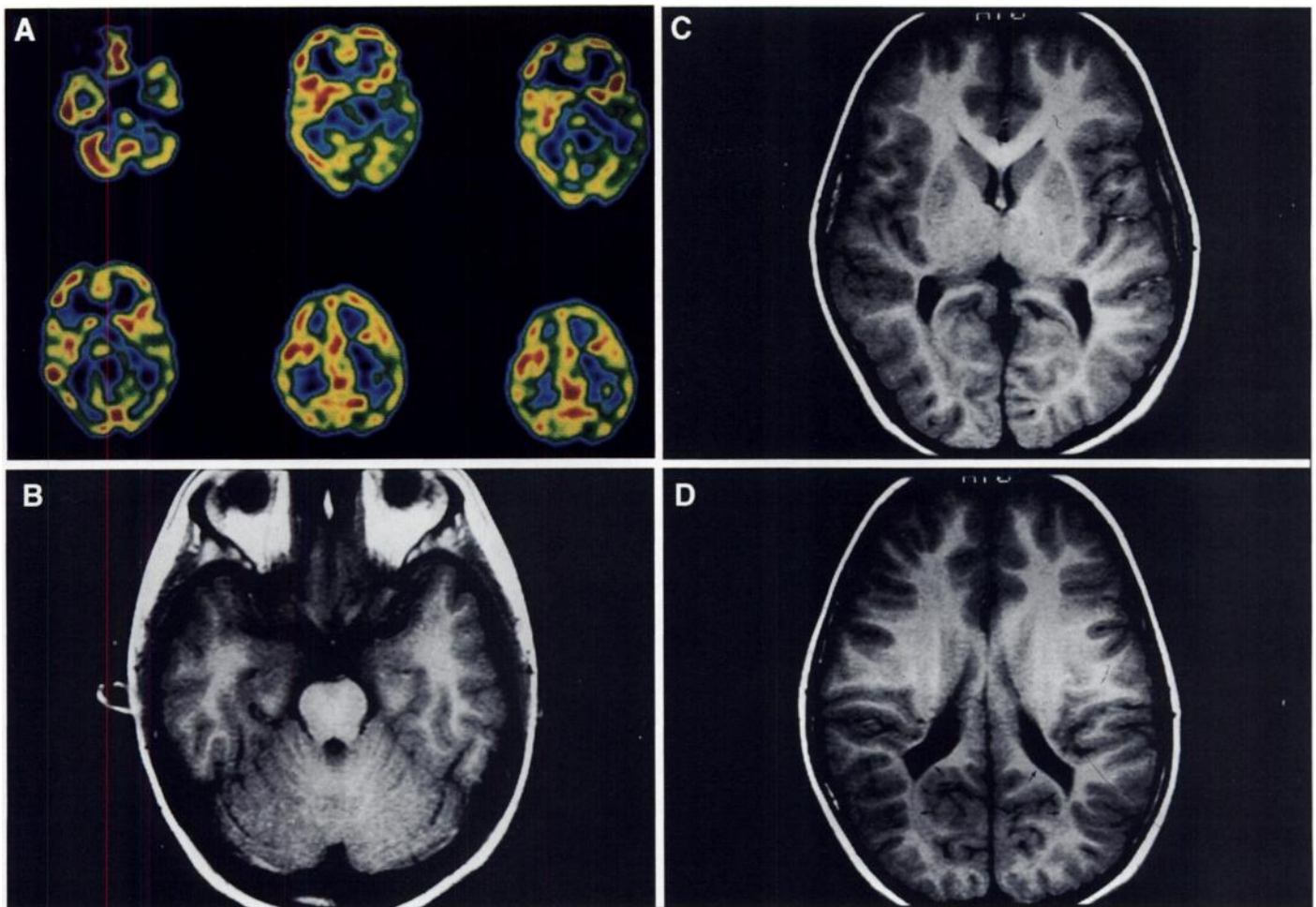
**FIGURE 4.** A 6-yr-and-11-mo-old boy with spastic diplegia born at 34 wk of gestational age. Birth weight was 2150 g. SPECT images (A) show hypoperfusion within left temporal lobe, cerebellum, parieto-occipital region, basal ganglia and bilateral thalami. Cerebellum, cerebral cortex and subcortical nuclei appear normal on MRI (B-D). However, loss of periventricular white matter and approximation of lateral ventricle to the cerebral cortex with passive dilatation of ventricle (arrows) can be seen.

such as polymicrogyria (n = 6) and lissencephaly (n = 1) was also observed. These MRI findings are summarized in Table 2.

## DISCUSSION

Cerebral palsy represents a syndrome of nonprogressive motor impairments rather than a specific etiologic diagnosis. There has been a strong historical tendency to associate this syndrome with hypoxic ischemic brain damage (6) especially in premature babies. The main features of brain injury are five basic neuropathologic states: selective neuronal necrosis, status marmoratus of basal ganglia and thalami, parasagittal cerebral injury, periventricular leukomalacia and focal or multifocal ischemic brain necrosis (7).

It is known that the response of the brain to injury changes as it matures in utero. For example, ischemic damage to the first-trimester brain results in maldevelopment ranging from anencephaly to polymicrogyria whereas a similar insult to the early third-trimester brain results in periventricular leukomalacia (PVL) (8–11). Diminished periventricular white matter, with close approximation of the posterior temporal and occipital cortices to the ventricular wall, is the typical MR findings of PVL in HIE (Fig. 4D) (8). In addition, thinning of corpus callosum especially in posterior body and splenium is an another important MRI finding. Hypoxic insult in perinatal or neonatal period results in cortical and subcortical abnormalities; hippocampi, lateral geniculate nuclei, posterolateral aspect of the lentiform nuclei, ventral lateral thalami or dorsal mesencephalon are vulnerable sites (4,8,12,13).

The clinical pictures in children with cerebral palsy depends on the distribution of the lesion. In children with PVL, spastic diplegia is common and in cases of cortical and subcortical involvement, spastic quadriplegia occurs (8). In our study, patients with spastic quadriplegia and mixed types showed higher incidence of cortical abnormality on both SPECT and MRI.

In terms of imaging modalities, MRI is useful in the diagnosis of cerebral palsy. In our study, the major MRI finding was white matter ischemic change such as PVL or thinning of corpus callosum. Gray matter involvement was less frequently observed; there was cortical defect in five, thalamic abnormality in seven and basal ganglia infarction in two. On the other hand, SPECT demonstrated hypoperfusion in all cases except one, especially in thalami. Therefore, SPECT is more sensitive than MRI in the detection of blood flow impairments. Although interpretation of brain SPECT of infants is difficult as regional cerebral blood flow pattern changes during maturation and the adult-like pattern presents at the beginning of the second year (8,14–17), detection of perfusion abnormality of the thalami, basal ganglia and cerebellum is relatively easier than cortex since regional blood flow in these areas is predominant in newborns and infants.

In our study, thalamic hypoperfusion was a characteristic SPECT finding. Similar to our result, hypometabolism of the thalami has been observed by FDG-PET. Standard uptake value of the subcortical areas was lower in cerebral palsy group
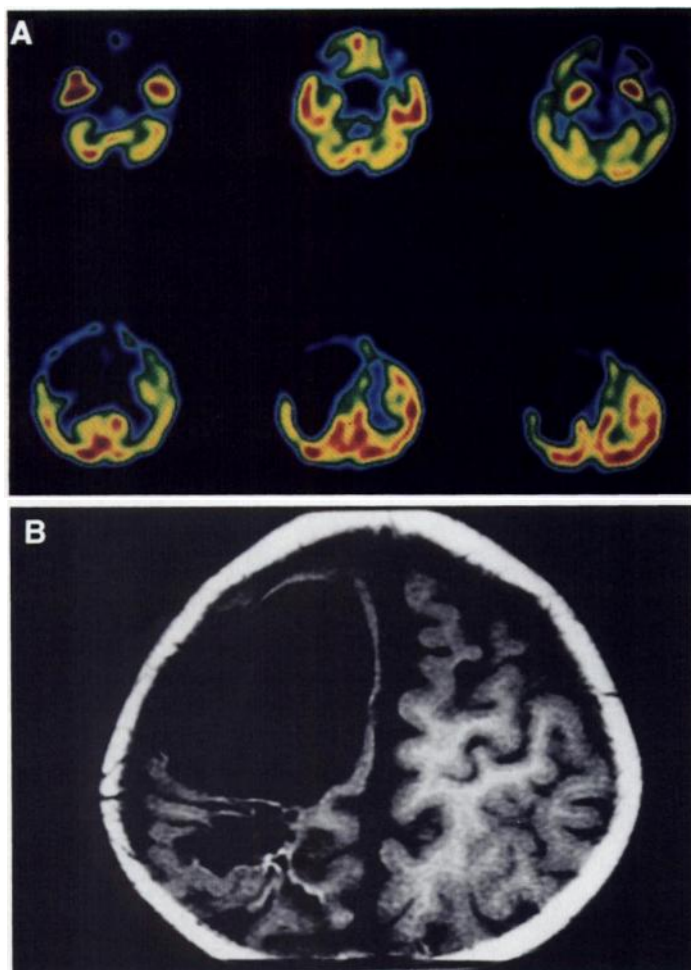
**FIGURE 5.** A 15-mo-old boy with spastic quadriplegia born at full term. Birth weight was 3 kg. SPECT images (A) show a large perfusion defect involving right fronto-parietal region with markedly reduced perfusion in left frontal lobe and bilateral thalami. MRI demonstrates cystic encephalomalacia in the same area of perfusion defect and cortical atrophy in left frontal lobe (B).
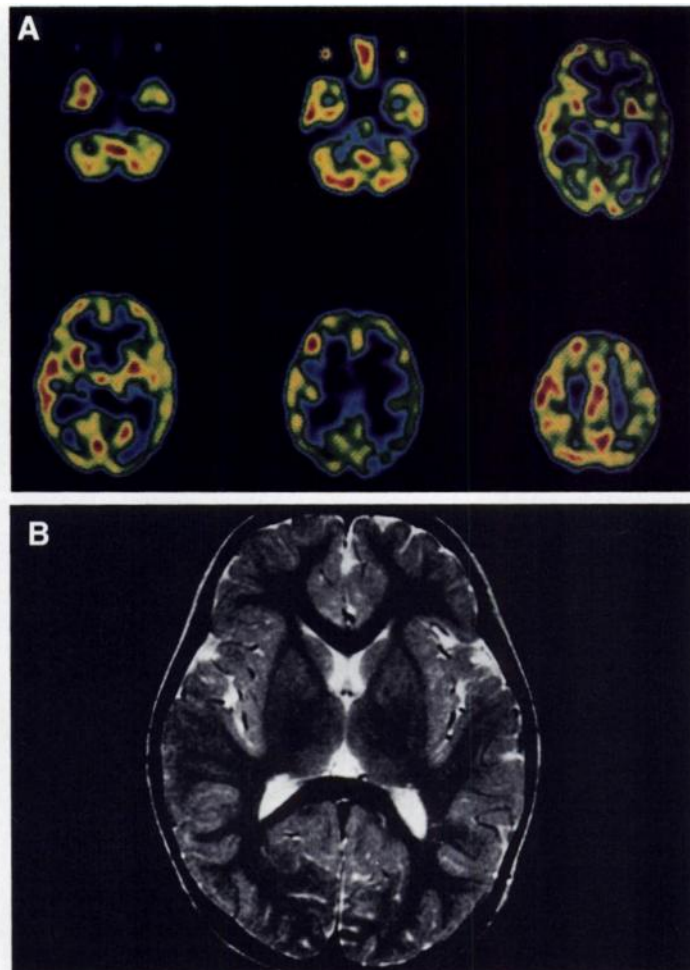
**FIGURE 6.** A 21-mo-old boy with spastic diplegia born at full term. Birth weight was 2970 g. SPECT images (A) show small size of basal ganglia and thalami. Cerebral cortical activity appear diminished randomly, especially within left temporal, parietal and bilateral occipital areas. T2-weighted MRI fails to demonstrate structural abnormality (B).

(0.86 ± 0.25) compared with that of normal control (1.73 ± 0.43) (*18*). Ferrigan et al. (*5*) observed thalamic hypometabolism in 2 of 4 patients with spastic diplegia, 6 of 7 with infantile hemiparesis, and 5 of 5 with choreoathetoid types. Therefore, thalamic hypoperfusion and hypometabolism can be considered to be important manifestations in cerebral palsy.

The exact mechanism or etiology of thalamic hypoperfusion remains to be elucidated, but there are possible explanations: Since brain SPECT is a functional imaging modality, it is able to detect areas of hypoperfusion secondary to neuronal loss whereas MRI detects only irreversible damage that can be occurred when cerebral blood flow is reduced below about 10 ml/100 g of tissue/1 min (*19*). In fact, Eken et al. (*20*) demonstrated thalamic neuronal loss by autopsy in 13 of 18 patients with a gestational age between 38–43 wk who died of HIE. Thalamocortical diaschisis may be taken into consideration as an another possible explanation. The classical thalamocortical diaschisis is a depression of metabolism or perfusion of corresponding cerebral cortex after unilateral thalamic lesion, and retrograde thalamocortical diaschisis is a reduction of metabolism or blood flow in the ipsilateral thalamus associated with the infarcted cerebral cortex (*21–23*). Therefore, white matter lesion such as PVL in patients with cerebral palsy could interrupt the important cortico-subcortical pathways that result in thalamic hypoperfusion by diachisis. In addition, ischemic injury of the thalamocortical pathway causes retrograde degen-

eration and progressive shrinkage or atrophy of the ipsilateral thalamus (*23–27*) as our case showed (Fig. 7).

Basal ganglia are known to be vulnerable sites especially in extrapyramidal cerebral palsy (*28*). In our study, SPECT demonstrated hypoperfusion within basal ganglia in 21 patients (not only in choreoathetoid type but in 31.4% of patients with spastic diplegia), while MRI detected in each one in spastic quadriplegia and mixed type. Clinically, some patients with spastic diplegia who showed hypoperfusion within basal ganglia had a mild degree of extrapyramidal symptoms, although their main clinical feature was spasticity of affected limbs. Thus, SPECT

**TABLE 1**
Perfusion Abnormalities on SPECT

| Hypoperfusion types (no.) | Thalamus | Basal ganglia | Temporal lobe | Cerebellum | Extratemporal cortex |
|---|---|---|---|---|---|
| SD (35) | 34 | 11 | 19 | 14 | 3 |
| SQ (11) | 11 | 6 | 4 | 5 | 7 |
| SH (2) | 2 | 1 | 2 | 0 | 0 |
| CA (2) | 2 | 2 | 1 | 0 | 0 |
| Mixed (1) | 1 | 1 | 1 | 1 | 1 |
| Total (51) | 50 | 21 | 27 | 20 | 11 |

SD = spastic diplegia; SQ = spastic quadriplegia; SH = spastic hemiparesis; CA = choreoathetoid.

## TABLE 2
### Structural Abnormalities on MRI

| Lesion types (no.) | White matter | Corpus callosum | Thalamus | Basal ganglia | Extratemporal cortex | Cerebellum |
|---|---|---|---|---|---|---|
| SD (35) | 21 | 15 | 2 | 0 | 0 | 1 |
| SQ (11) | 6 | 8 | 3 | 1 | 4 | 0 |
| SH (2) | 2 | 1 | 1 | 0 | 0 | 0 |
| CA (2) | 0 | 0 | 0 | 0 | 0 | 0 |
| Mixed (1) | 0 | 1 | 1 | 1 | 1 | 0 |
| Total (51) | 29 | 25 | 7 | 2 | 5 | 1 |

SD = spastic diplegia; SQ = spastic quadriplegia; SH = spastic hemiparesis; CA = choreoathetoid.

may give additional information in classifying subtypes of cerebral palsy.

In brain cortex, certain neuronal subpopulations such as hippocampal field CA1 and neocortical layers three, five and six are characteristically destroyed after hypoxic ischemic exposure. This special vulnerability may be accounted for by the central neurotoxicity of the endogenous excitatory amino-acid neurotransmitter, glutamate, released into the extracellular space (8,19). This supports the fact that more cortical abnormality could be detected by SPECT than MRI in our study (Figs. 4 and 6).

Cerebellar hypoperfusion is another important finding of SPECT. As the cerebellar granular cell continues to proliferate after birth, total asphyxia in the neonatal or prenatal periods can result in significant granular cell deficit. In fact, Yoshida et al. (29) demonstrated a 7% reduction of Purkinje cells and 13% of
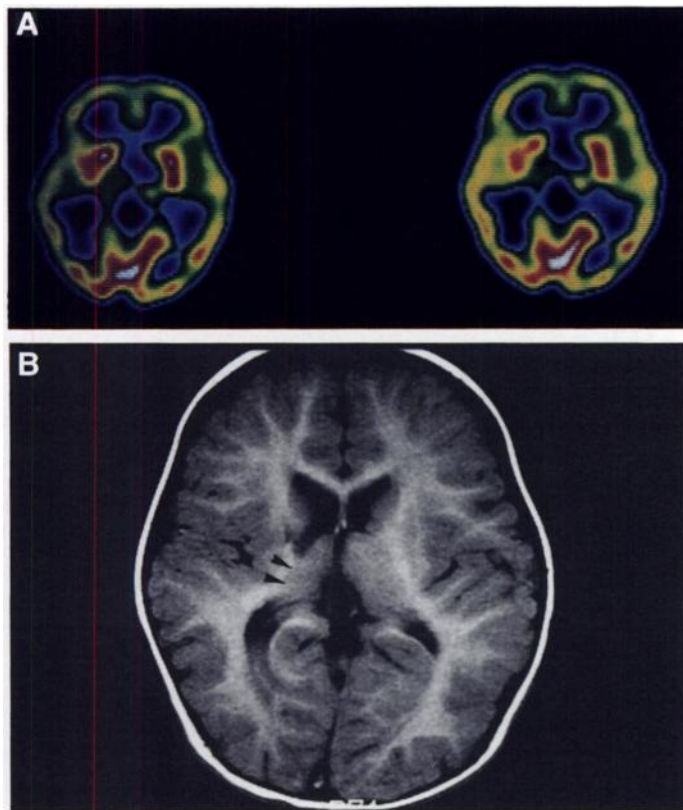


FIGURE 7. A 14-mo-old boy with spastic diplegia born at full term. Birth weight was 3230 g. SPECT images at the level of deep cortical nuclei (A) show severe hypoperfusion within right thalamus. Left thalamic activity appears decreased. T1-weighted MRI at the same level shows atrophic change of right thalamus (arrow heads) and thinning of periventricular white matter (B).

granular cells in asphyxiated animal model. As a result of the deficit of these cells, hypoperfusion may occur and cerebellar size may be smaller than normal subjects (30). In our study, SPECT demonstrated cerebellar hypoperfusion in 20 of 51 whereas MRI demonstrated cerebellar atrophy in only one.

## CONCLUSION

Brain SPECT has a role in the detection of perfusion impairments in patients with cerebral palsy, especially within cortices and subcortical nuclei, whereas MRI is valuable in the detection of the structural abnormalities of the white matter such as PVL and corpus callosal thinning.

## ACKNOWLEDGMENTS

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