

# The role of magnetic resonance imaging in early prediction of cerebral palsy

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**SUMMARY:** Hnatyszyn G, Cyrylowski L, Czeszynska MB, Walecka A, Konefal H, Szmigiel O, Gizewska M, Dawid G. The role of magnetic resonance imaging in early prediction of cerebral palsy. Turk J Pediatr 2010; 52: 278-284.

This work was undertaken to assess the usefulness of magnetic resonance imaging (MRI) of the brain for early prognosis of cerebral palsy. The study group included 47 neonates (24 term and 23 preterm) with symptoms of perinatal asphyxia. MRI examinations in term neonates were performed during the first month of life but not before the second week of life, while in preterm neonates MRI data were acquired between 38 and 40 weeks from conception. MRI of the brain demonstrated hypoxic-ischemic findings in all neonates born with perinatal asphyxia who later progressed to cerebral palsy. These results support the hypothesis that MRI performed in the neonatal period plays an essential role in predicting cerebral palsy in both term and preterm neonates, regardless of their gestational age.

**Key words:** asphyxia, magnetic resonance imaging, newborn, cerebral palsy.

A growing number of studies have provided evidences of a unique role of magnetic resonance imaging (MRI) in the detection of cerebral hypoxic-ischemic lesions in both preterm and term neonates.

Magnetic resonance imaging was first used to search for lesions accompanying perinatal asphyxia in the nineties. Initially, MRI was recommended for brain imaging in infants and children with cerebral palsy (CP)<sup>1-3</sup>. Recently, it has been used for diagnosing term and preterm neonates, as well as fetuses<sup>4-11</sup>. Combined conventional MRI and advanced techniques, such as diffusion tensor imaging, diffusion-weighted imaging, or magnetic resonance spectroscopy, provide a more complete image of structural and functional brain abnormalities<sup>12,13</sup>. Conventional MRI findings, spectroscopically measured absolute N-acetyl aspartate and choline concentrations, and apparent diffusion coefficients are complementary tools for predicting individual outcomes in severely asphyxiated term neonates<sup>14</sup>. By studying the distribution, extent and evolution of ischemic injury, MRI makes it largely possible

to establish the prognosis for the infant<sup>1,4,5,15-17</sup>. CP is the most important neurological disorder directly associated with perinatal asphyxia. Early diagnosis of CP remains a challenge in contemporary medicine.

The aim of this study was to assess the usefulness of MRI of the brain for the early prediction of CP in both term and preterm neonates with signs of perinatal asphyxia.

## Material and Methods

Forty-seven neonates with symptoms of perinatal asphyxia were included in a prospective study. The neonates were allocated to two groups as follows:

Group T (term neonates) included 24 infants born between weeks 37 and 41 of gestation. Group P (preterm neonates) included 23 infants born between weeks 27 and 36 of gestation. All preterm neonates were patients in the intensive care unit.

## Inclusion criteria

1. Term neonates:

Clinical symptoms of hypoxic-ischemic encephalopathy (HIE) according to Sarnats and risk factors of prenatal intrauterine hypoxia leading to fetal distress or symptoms of intrapartum asphyxia.

## 2. Preterm neonates:

Because there are no defined criteria of asphyxia for preterm neonates in the literature, the following inclusion criteria were used: combination of risk factors of intrauterine hypoxia, fetal distress and postnatal hypoxia.

### ***Risk factors of prenatal intrauterine hypoxia included:***

1. Coexistence of pregnancy and maternal disease: diabetes mellitus, cyanotic heart defect, chronic lung disease, systemic lupus erythematosus, nicotinism, epilepsy;
2. Complications of pregnancy: pregnancy-induced arterial hypertension, risk of eclampsia, intrauterine growth retardation, oligoamnios, severe Rh immunization, multiple pregnancy and blood exchange between fetuses, intrauterine infection, placental abruption, uterine rupture, cord compression.

Criteria of intrapartum asphyxia were as follows: pH <7.1 in umbilical artery, meconium in amniotic fluid, Apgar score at one minute < 3, Apgar score at five minutes < 5, and resuscitation after the birth.

Manifestations of fetal distress included: abnormal biophysical profile of the fetus, abnormal cardiotocography findings (delayed decelerations, low variability, bradycardia), and circulatory centralization seen with Doppler ultrasound.

Criteria of postnatal hypoxia included: respiratory distress syndrome, apnea, circulatory failure, persistent fetal circulation, and convulsions.

The following *exclusion criteria* were used: central nervous system malformation, chromosomal aberrations, congenital metabolic disease, and intracranial hemorrhage (apart from intraventricular hemorrhage degrees I and II).

In this prospective study, all infants underwent MRI in the neonatal period and neurological examination in the second year of life. For preterm neonates, the corrected age was

respected<sup>1</sup>.

Magnetic resonance imaging was done with Picker Eclipse 1.5 T scanner. Term neonates were studied between weeks 2 and 4 of life, while preterm infants were studied at term-equivalent age (between weeks 38 and 40 from conception). The brain was visualized using T1 and T2 fast spin echo (FSE) and FLAIR sequences in the axial, coronal and sagittal planes. All infants were clinically stable at the time of the MRI. The examination was done during physiological sleep, approximately 30 minutes after feeding, except in five neonates who were studied during pharmacological sleep with prior consent of the mother.

The basal ganglia, thalamus, posterior limb of the internal capsule, white matter, and cortex were carefully assessed in particular. Hypoxic-ischemic lesions were diagnosed as signal attenuation on T1-weighted scans of the posterior limb of the internal capsule, signal intensities on T2-weighted scans of the basal ganglia, thalamus, white matter, and parasagittal cortex, or as minute ischemic foci, hemorrhagic foci, stroke foci, periventricular leukomalacia, and polycystic cerebral necrosis. The location and severity of the lesions were recorded. No scale of ischemia was used.

### ***The neurological diagnosis was one of the following:***

1. Norm;
2. CP;
3. Other disorders, without CP (epilepsy, developmental delay, hyperactivity).

### ***Statistical Analysis***

Correlations between MRI findings and diagnosis of CP were studied with Spearman's rank coefficients ( $r$ ). The sensitivity and specificity of MRI as a diagnostic method for the detection of CP were calculated (sensitivity: number of neonates with CP and an abnormal MRI divided by the number of neonates with CP; specificity: number of neonates without CP and a normal MRI divided by the number of neonates without CP).

### ***Results***

Hypoxic-ischemic lesions were detected in 19

neonates, including 9 term (38% of Group T) and 10 preterm (43% of Group P). CP was diagnosed in 9 children: 4 term and 5 preterm. Diffuse, bilateral lesions in the basal ganglia and thalamus were present in two term neonates with severe perinatal asphyxia, coexisting with multicystic encephalomalacia in one of them (Figs. 1, 2). Both infants progressed to bilateral hemiplegia with epilepsy (infantile spasms). One preterm neonate with bilateral leukomalacia extending to the occipital lobes also developed tetraparesis with epilepsy (infantile spasms). One term and two preterm neonates with bilateral periventricular leukomalacia showed spastic diplegia in the second year of life. Two other newborns (one term and one preterm), who progressed to CP, had a single stroke lesion. In one case, the lesion was located in the anterior lentiform nucleus on the right side (Fig. 3), while in the other, it was found subcortically in the left parietal lobe. Both patients were later diagnosed with mild spastic hemiplegia. Another infant with ischemic foci in the occipital lobes had epilepsy but without motor disorders.

In one preterm neonate examined at term-equivalent age, MRI demonstrated diffuse excessive high signal intensity (DEHSI) on T2-weighted images (Fig. 4). Serial ultrasound examinations performed during the neonatal period failed to reveal any echo intensification from periventricular white matter, nor leukomalacia. However, lateral ventricles were moderately enlarged in the second year of life.

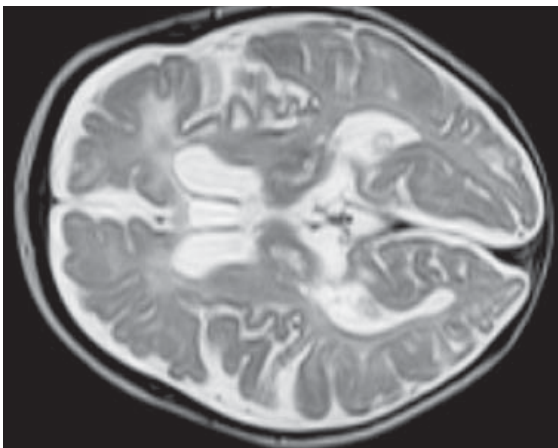


Fig. 1. Excessive hyperintensity in both thalami in a four-week-old infant (axial T2-weighted magnetic resonance image).

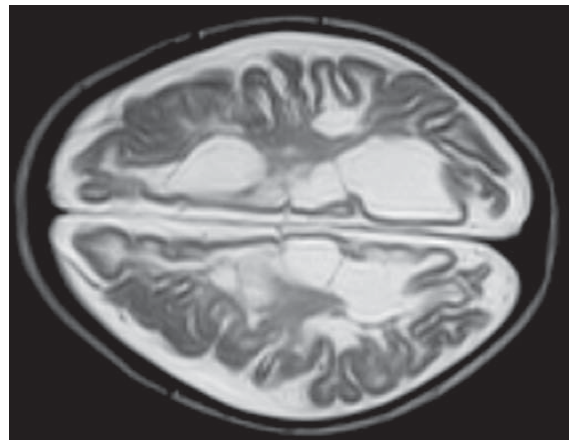


Fig. 2. Excessive multicystic necrosis in a four-week old infant (the same as in Fig. 1) (axial MRI scans). The child developed spastic quadriplegia and infantile spasm.

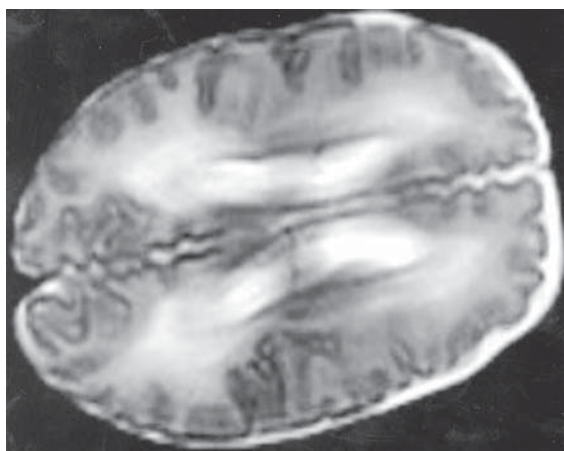
This patient had a mild form of spastic diplegia, hypoacusis and hyperactivity.

The remaining 9 neonates had insignificant abnormalities on MRI examination. There were limited ischemic lesions in the white matter without accompanying cysts and small ischemic foci in the basal ganglia. One of these patients had an isolated focus of leukomalacia. None of these children progressed to CP; 3 of them presented with hyperactivity, while 6 had normal neurological status.

In this study, the correlation between MRI findings in neonatal period and future CP in both term and preterm neonates was determined. In term neonates, this correlation was significant ( $r=0.60$ ,  $p<0.01$ ). In preterm neonates, the correlation between brain abnormalities and CP was likewise significant ( $r=0.47$ ,  $p<0.05$ ). In term and preterm neonates, the sensitivity of MRI in prognosticating CP was 100% and the specificity was high: 75% and 72%, respectively. All asphyxiated neonates who progressed to CP had brain abnormalities detected by MRI in the neonatal period, regardless of their gestational age.

## Discussion

In the presented study, the presence of abnormal MRI findings was confirmed in all term and preterm neonates with perinatal asphyxia who progressed to CP (sensitivity =



**Fig. 3.** Ischemic lesion in anterior lentiform nucleus on the right side in a four-week-old infant (axial T1 MRI scans). The child developed mild form left-sided spastic hemiplegia.

100%). The time between weeks 2 and 4 of life in term neonates and at term-equivalent age in preterm infants was right for prognostication of CP in asphyxiated newborns.

Belet et al.<sup>17</sup> examined asphyxiated term neonates with serial MRI up to four years of age. For predicting the neurologic outcome at four years of age, MRI findings in the neonatal period had the highest negative predictive value, whereas MRI findings at four months of age and four years of age had the highest positive predictive value. In the prediction of neurologic outcome, the sensitivity and specificity of MRI findings in the neonatal period were 100% and 44.4%, respectively.

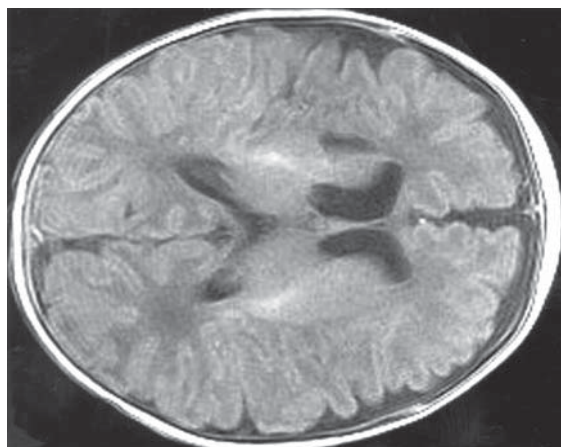
Woorward et al.<sup>11</sup> examined 167 very preterm infants to assess the associations between qualitatively defined white matter and gray matter abnormalities on MRI at term-equivalent age and the risks of severe neurological outcome. They reported that abnormal findings on MRI at term-equivalent age in very preterm infants strongly predicted adverse neurodevelopmental outcomes at two years of age.

Valkama et al.<sup>9</sup> reported that a parenchymal lesion seen on MRI in very low birth weight infants at term-equivalent age predicted neuromotor outcome. All parenchymal lesions seen on MRI predicted CP with 100% sensitivity and 79% specificity. Parenchymal lesions in MRI, excluding subependymal hemorrhage,

predicted CP with a sensitivity of 82% and a specificity of 97%.

The results presented in our study are in line with other reports on the usefulness of MRI in predicting neurological outcome in neonates with a history of perinatal asphyxia. However, in this report, we wanted to underline a significant value of neonatal MRI in early prediction of CP, in all asphyxiated infants, regardless of their gestational age.

Magnetic resonance imaging findings in asphyxiated neonates depend on the extent of hypoxia and on the time elapsed from asphyxia. Some researchers recommend performing neonatal MRI between days 7 and 30 of life, after resolution of edema but before the onset of brain atrophy<sup>1,4,18,19</sup>. Results of the above-mentioned studies may lead to the conclusion that in order to predict further development of a newborn with perinatal asphyxia, there is no need to obtain neonatal MRI scans in the first days of life, when symptoms of respiratory distress may be present. Furthermore, in a presented study, neonatal MRI scans obtained in term neonates between weeks 2 and 4 of life demonstrated hypoxic-ischemic findings in all babies born with perinatal asphyxia who later progressed to CP. In our study, some specific MRI findings were consistently associated with specific neurologic outcome, a finding compatible with the literature.



**Fig. 4.** Axial T2-weighted image, obtained in a preterm newborn, demonstrates diffuse, excessive high signal intensity corresponding to noncystic white matter injury. In the second year of age, the child had signs of a mild spastic diplegia.

Rutherford et al.<sup>1</sup> demonstrated a correlation between early and late hypoxic lesions revealed by MRI and neurological status in term neonates with HIE. They concluded that bilateral, extensive lesions in the basal ganglia and thalami coexist with severe neurological disorders. Minor lesions in the white matter were present in neonates developing normally during the first two years of life. Later, Haataja et al.<sup>20</sup>, from the same research center, studied term neonates with HIE. They found that the neurological status was normal in all infants with a normal brain scan or with moderate lesions in the white matter, as well as in 80% of infants with minimal and in 20% with moderate lesions in the basal ganglia. All neonates with severe lesions in the basal ganglia or white matter, as well as neonates with moderate lesions in both locations, demonstrated the lowest optimality score and the worst prognosis. Many researchers found that extensive damage to the subcortical gray matter coexists with severe neurological disorders corresponding clinically to the extrapyramidal form of CP or bilateral hemiplegia<sup>4,5,17,21-24</sup>. Further, in our study, two neonates with multicystic encephalomalacia with bilateral lesions in the basal ganglia progressed to bilateral hemiplegia with epilepsy (infantile spasms). Three other neonates with unilateral minor lesions in the basal ganglia and thalami did not present with CP.

In 1998, Aida et al.<sup>23</sup> studied the relationship between the location of hypoxic lesions revealed by MRI with the type of neurological outcome and noted that isolated lesions are not symptomatic of CP. Sreenan et al.<sup>25</sup> diagnosed CP in 22 of 46 term neonates with stroke foci confirmed by MRI. According to Mercuri<sup>26</sup>, approximately 20% of neonates with stroke foci progress to spastic hemiplegia. Prognosis appeared most favorable when stroke foci were not accompanied by symptoms of perinatal asphyxia<sup>27,28</sup>. In our present study, MRI disclosed a single stroke focus in two asphyxiated neonates, who later progressed to spastic hemiplegia. Another infant with stroke foci in the occipital lobes had epilepsy but no motor disorders.

Sie et al.<sup>29</sup> in 2000 confirmed the exceptional value of MRI for the assessment of periventricular leukomalacia. In a retrospective study of 104

infants with hypoxic lesions revealed on MRI, they noted that periventricular leukomalacia may also be diagnosed in term neonates. This type of hypoxic-ischemic lesion was associated with prematurity only in 71% on the infants studied<sup>30</sup>. In our study, four of five neonates with leukomalacia developed spastic diplegia; one of them was born at term.

Recent reports have disclosed that DEHSI in T2-weighted scans of the white matter is the lesion without cyst formation found at term-equivalent age in preterm infants<sup>6,31-36</sup>. Domizio et al.<sup>34</sup> were the first to report results of the two-year follow-up in 16 term children diagnosed with DEHSI: half of them had severe or mild mental impairment, 10 children had severe or mild motoric deficits, and one child presented with seizures. This type of brain damage was also observed in one of our preterm neonates. This infant progressed to CP in the mild form of spastic diplegia.

Most researchers agree that mild hypoxic lesions in term neonates involving white matter without cyst formation or lesions in subcortical gray matter have a good prognosis and carry no risk of CP<sup>5,15,19,20,22,23</sup>. Rutherford<sup>5</sup> believes that the only outcome in these infants is learning difficulties. In our study, this type of hypoxic-ischemic lesion in white matter was observed on MRI in five term neonates. Three of them were normal at the age of two years, while the remaining two demonstrated hyperactivity.

In conclusion, MRI plays an especially important role for prediction of CP due to its extremely high sensitivity resulting from correlation between MRI hypoxic-ischemic findings and further progression to CP in both term and preterm neonates with perinatal asphyxia. MRI should be recommended as a routine work-up in the first month of life in all asphyxiated term newborns and at term-equivalent age in all asphyxiated preterm infants, regardless of their gestational age.

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