

# Neonatal Brain MRI and Motor Outcome at School Age in Children with Neonatal Encephalopathy: A Review of Personal Experience

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## ABSTRACT

**The aim of this paper is to review (i) the spectrum of neuromotor function at school age in children who had been born full-term and presented with neonatal encephalopathy (NE) and low Apgar scores and (ii) the relation between the presence/absence of such difficulties and neonatal brain MRI. Motor outcome appears to be mainly related to the severity of basal ganglia and internal capsule involvement. Severe basal ganglia lesions were always associated with the most severe outcome, microcephaly, tetraplegia, and severe global delay, whereas more discrete basal ganglia lesions were associated with athetoid cerebral palsy, with normal cognitive development, or minor neuro-motor abnormalities. White matter lesions were associated with abnormal motor outcome only if the internal capsule was involved. Children with moderate white matter changes but normal internal capsule had normal motor outcome at school age.**

## KEYWORDS

neonatal encephalopathy, MRI, Apgar score, cognitive, motor, perceptual-motor

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## INTRODUCTION

Neonatal encephalopathy is characterized by an abnormal neurological state, with or without seizures, and affects from 2 to 8 per 1000 term infants (Nelson & Leviton, 1991; Badawi et al., 1998). Most studies have focused on infants who had neonatal encephalopathy following perinatal asphyxia, generally associated with low Apgar scores. Several studies have reported that motor outcome in children with neonatal encephalopathy can be variable, ranging from normal to severe cerebral palsy, and that the severity of outcome mainly reflects the involvement of the basal ganglia on neonatal MRI (Sarnat & Sarnat, 1976; Levene et al., 1985; Viot & Lemberg, 1987; Robertson et al., 1989; Gaffney et al., 1994; Kuenzle et al., 1994; Rosenbloom, 1994; Rutherford et al., 1994; 1996; Eken et al., 1995; Mercuri et al., 1999; 2000; 2002; Barkovich et al., 1998). Most of these studies, however, have reported only relatively short-term motor outcome, generally between 18 and 36 months. We recently reported that a proportion of infants who were regarded as normal on short term follow up have minor motor abnormalities when examined at school age (Barnett et al., 2002).

In the present paper, we review our experience of follow up in children who suffered neonatal encephalopathy, trying to establish the spectrum of motor outcome and its correlation with the patterns of lesions observed on neonatal brain MRI.

## SUBJECTS AND METHODS

The children described in this study are part of a large prospective study of a cohort of term infants born at or referred to the Hammersmith Hospital, London, UK for magnetic resonance imaging (MRI) between May 1991 and January 1996. All had neonatal encephalopathy (NE) and Apgar scores of 5 or below at 1 minute. The diagnosis of NE was made in infants who had convulsions during the first 48 hours and/or showed other signs of neurological abnormalities during the first 48 hours after delivery. Neurological abnormalities included abnormal tone, poor feeding, and altered level of consciousness. The degree of encephalopathy was classified during the first week of life as mild, moderate or severe (stages I, II or III according to Sarnat & Sarnat, 1976). Infants who subsequently had been diagnosed as suffering from genetic or metabolic syndromes or who presented with other neonatal complications, such as septicemia or neonatal meningitis, were excluded from the study. Infants with dysmorphic features or other clinical or brain MRI findings suggesting major congenital malformation were also excluded.

As part of this study all term infants with neonatal encephalopathy had a detailed neuro-developmental follow up at 3, 6, 12, and 24 months and then yearly, using a structured neurological examination (Dubowitz et al., 1999) and the Griffiths developmental scales (Griffiths, 1976). When seen between the age of 5.5 and 6.5 years, their neurological status and motor competence were assessed using a modified form of Touwen's (1979) Examination of the Child with Minor Neurological Dysfunction (Kakebeeke et al., 1993) and the Movement Assessment Battery for Children (Movement ABC, Henderson & Sugden, 1992). Cerebral palsy, when present, was graded according to the criteria described by Hagberg et al (1975). Cognitive ability was assessed using the

Wechsler Pre-School and Primary Scale of Intelligence (WPPSI, Wechsler, 1990).

## RESULTS

### Brain Magnetic Resonance Imaging

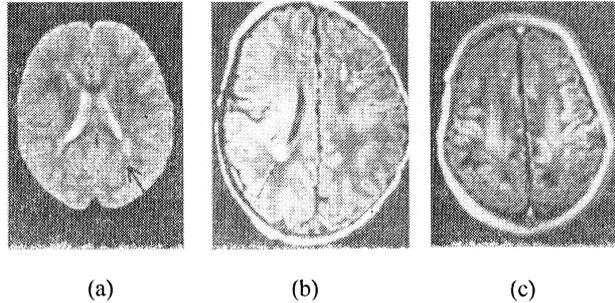
The cohort was subdivided according to MRI findings, and more specifically, according to the presence and severity of white matter and basal ganglia lesions. Examples of these lesions are shown in Figs. 1 and 2. All the infants in this group had shown brain swelling on the early brain MRI scans performed in the first days of life but by the end of the first week the scans had normalized or only showed *mild* long T1 and long T2 in the periventricular white matter only with no loss of grey white matter differentiation.

These children generally have somewhat diminished axial tone with relatively poor head control in the first months after birth but when examined at 2 years are described as normal. When assessed at school age they have normal results on all the tests assessing neuromotor, perceptual and cognitive function.

### Normal MRI and minimal white matter changes

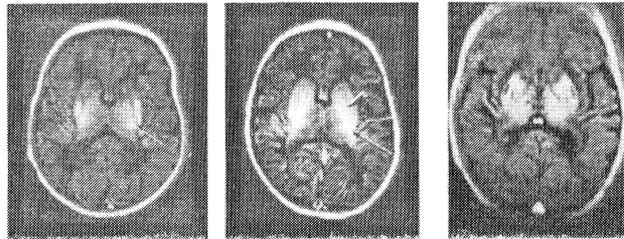
All the infants in this group had shown brain swelling on the early brain MRI scans performed in the first days of life but by the end of the first week the scans had normalized or only showed *mild* long T1 and long T2 in the periventricular white matter only with no loss of grey white matter differentiation. These children generally have somewhat diminished axial tone with relatively poor head control in the first months after birth but when examined at 2 years are described as normal. When assessed at school age they have normal results on all the tests assessing neuromotor, perceptual, and cognitive function.

## White matter lesions



**Fig. 1:** Axial IR image. Note the discrete changes in the periventricular white matter in children with mild white matter changes (a) and the more marked focal changes (moderate white matter changes) in (b). The child with severe white matter changes had diffuse abnormalities throughout the white matter (c).

## Basal ganglia lesions



**Fig.2:** Axial IR image at basal ganglia lesions. Note the discrete changes in the lentiform in (a) and the more marked lesions in lentiform and thalamus in (b). Basal ganglia and thalami have marked and diffuse abnormalities in (c).

**Moderate white matter changes**

Children in this group have a similar history and presentation as those in the previous group. Their scans showed focal abnormalities in the white matter with or without cortical involvement but with normal basal ganglia, thalami and posterior limb of internal capsule (PLIC). In the neonatal period these infants are often hypotonic and have transient feeding difficulties, and some trunkal hypotonia may persist for a few months. At school age they have normal motor function or only minor

motor abnormalities, such as poor hand function and balance on the Movement ABC.

**Severe white matter changes**

These infants generally present with more severe antenatal problems, such as reduced fetal growth associated with reduced fetal movement and superadded perinatal problems such as fetal distress.

Brain MRI reveals extensive signal changes in the white matter with associated cortical high-

lighting. Some basal ganglia changes may be noted but these are often unilateral or relatively transient. The signal in the internal capsule is always abnormal although in certain cases may normalize relatively rapidly within a few weeks or months.

Such children are initially markedly hypotonic, have poor visual alertness, and feed slowly (Dubowitz et al., 1999). These infants may show good recovery in the first months but by the end of the first year, all develop microcephaly and cerebral palsy. They generally acquire the ability to walk even though grossly delayed and in some cases only with some support. When examined at school age all have evidence of cerebral palsy (diplegia or mild quadriplegia) a moderate global delay and poor scores on the tests assessing perceptual motor abilities.

#### **Minimal and moderate basal ganglia lesions**

Children with basal ganglia and thalami (BGT) lesions often have a normal antenatal history, but sustain an acute event around the time of delivery, such as prolonged difficult delivery with fetal distress. Their MRI scans show focal abnormalities in the basal ganglia and thalami, equivocal or abnormal PLIC, with or without cortical highlighting. Clinically, they may have neonatal hypotonia and early visual and feeding difficulties, but these are transient and often not severe. When examined at school age, such children will have athetoid or dystonic cerebral palsy, but normal cognitive development.

#### **Severe basal ganglia lesions**

Children with severe basal ganglia lesions often have a severe sudden acute event around the time of delivery, such as a placental abruption, ruptured uterus, cord prolapse or had a severe fetal distress. On *brain MRI* the most striking changes

are in the basal ganglia and thalami with completely absent signal from myelin in the internal capsule. The white matter is often streaky. Some cortical highlighting may be present, but is less marked than those seen in the previous group with antenatal onset.

*Clinically*, such children initially present with marked hypotonia, fisting, and curling toes. They are unable to suck and have very poor visual and auditory alertness. They soon develop typical patterns of differential tone with increased extensor tone in the neck and extension in the legs associated to marked flexion in the arms. Dystonic posturing is frequent and movements in general are stereotyped and cramped. When such a child is seen at 6 to 8 weeks, many of the abnormal tone patterns, movements, and visual attention are even more prominent. These children all develop spastic or dystonic tetraplegia, microcephaly, a severe global delay, which makes them untestable, and severe abnormalities of visual function (Mercuri et al., 1997a; 1997b). Table 1 shows details of our recently published results in a population of children with neonatal encephalopathy.

### **DISCUSSION**

The children described in this study have been prospectively followed since birth because of neonatal encephalopathy. Using a detailed assessment of neuromotor function, we have been able to obtain more detailed information on the type of sequelae that these children are likely to develop and on their correlation with neonatal MRI.

As previously reported, the severity of the outcome seems to depend to a large degree on the extent of the basal ganglia involvement (Sarnat & Sarnat, 1976; Barkovich et al., 1998). Severe basal ganglia lesions were always associated with the most severe outcome, microcephaly, dystonic or

**TABLE 1**

Recently published results in a population of children with neonatal encephalopathy (modified, with permission from: Barnett et al, *Neuropediatrics*, 2002;33: 242-248.)

	Mov ABC	Touwen
normal MRI (n=11)	○○○○○○○○○○○○○○	○○○○○○○○○○○○○○
MCA infarct (n=3)	▶ ●○	▶ ○○
minimal WM (n=15)	○○○○○○○○○○○○○○○○	○○○○○○○○○○○○○○○○
moderate WM (n=3)	○○●	○○●
severe WM (n=4)	◆☆☆☆	◆☆☆☆
minimal BG (n=4)	○○△△	○○△△
moderate BG± WM changes (n=4)	◆◆◆◆	◆◆◆◆
severe BG± WM changes (n=23)	☆☆☆☆☆☆☆☆☆☆☆☆ ✚✚✚✚✚✚✚✚✚✚	☆☆☆☆☆☆☆☆☆☆☆☆ ✚✚✚✚✚✚✚✚✚✚

○= normal; ●= abnormal results on the test, ◆= quadriplegia, testable but abnormal results on the test; ☆ = severe quadriplegia and mental retardation, untestable, ✚= died; ▶ = hemiplegia; ☆ = diplegia; △= dystonia.

spastic quadriplegia and severe global delay, often showing no discernible development. Whereas in previous studies assessing motor outcome at one year, we reported that more discrete basal ganglia lesions were in 57% of cases associated with normal motor outcome (Mercuri et al., 2000), we found using a more detailed assessment of motor function at school age that only one of 7 children with such lesions had a completely normal motor outcome (Barnett et al., 2002). All the others either developed athetoid CP (with normal head

circumference and normal cognitive development) or had minor neuromotor abnormalities.

When basal ganglia were normal, the only other children with an abnormal motor outcome were those with severe white matter changes in whom the PLIC was affected. These findings agree with ours and with other prior findings reporting that an abnormal signal in the PLIC has an unfavorable prognostic significance (Rutherford et al., 1998). In contrast, with one exception, all the children with normal PLIC and basal ganglia

consistently showed normal motor outcome at school age, even if they had mild or moderate white matter changes.

Our findings suggest that neonatal brain MRI can predict not only the presence but often also the type of motor sequelae. The results also suggest that when discrete lesions involving the basal ganglia or the PLIC are detected, these children must be followed even if they appear to be normal on short-term follow up. The overall proportion of children who had more minor motor impairment at school age was relatively low (15% of the whole cohort). This result is very interesting as most of these children will have minimal or moderate white matter lesions. These findings are at variance with what is observed in prematurely born children in whom we and others (Jongmans et al., 1997) have reported a clear association between white matter changes and clumsiness. The difference can be only partly explained by the type and the timing of the lesions.

In conclusion, even if children with neonatal encephalopathy appear to be at low risk of developing clumsiness, they still constitute the 23.5% of those without cerebral palsy and have difficulties with everyday life tasks. The early identification of any difficulties should then lead to a meaningful program of intervention, which might help these children to cope better at home and at school.

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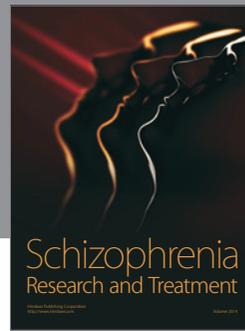
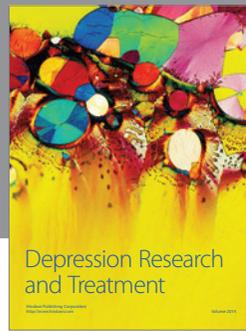
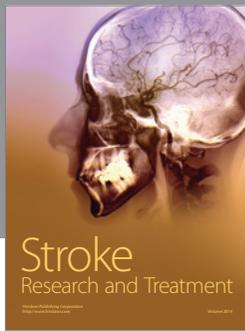
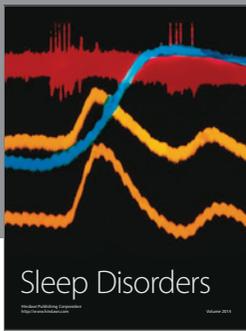
Frances Cowan, and Mary Rutherford whose work forms the basis for this paper.

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