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Magnetic resonance imaging findings in cerebral palsy

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Objective: To review all cases of cerebral palsy (CP) that had magnetic resonance imaging (MRI) over a defined period of time.
Methodology: The MRI brain scans of 42 children (12 premature, 30 full-term) with CP were studied. The scans were performed at the Royal Children's Hospital, Melbourne, between January 1995 and June 1996.
Results: Abnormalities were found in 39 of the 42 scans. Five children had cortical malformations and three children had white matter hypoplasia, indicating insults during the second trimester of pregnancy. Twenty-one children had hypoxic–ischaemic lesions (eight premature, 13 full-term) with patterns of periventricular leucomalacia, subcortical lesions or cortical infarction indicating insults perinatally or in the third trimester. Only 10 children had scans that could not be categorized into these groups.
Conclusions: In this study sample of children with CP, MRI was useful in revealing underlying brain abnormalities, most of which were due to events in the third trimester or the perinatal period.

Key words: cerebral palsy; magnetic resonance imaging brain scan.

There have been radical changes in our understanding of the aetiology of cerebral palsy (CP) over the past decade. In 1863, Little reported that spastic CP was caused by abnormal circumstances at birth.[1] From that time it was widely accepted that most cases of CP were due to birth asphyxia. This assumption was called into question by recent epidemiological research. Nelson reported that CP attributable to birth asphyxia was in the range of 3 to 13% and did not exceed 21%.[2] Blair and Stanley in a matched control study estimated that in only 15 of 183 children with spastic CP (8%) was intrapartum asphyxia the possible cause of their brain damage.[3]

In their series of term singleton births, Yudkin *et al*. reported that 10% of all cases of CP were associated with birth asphyxia.[4] Other studies of term infants suggested that prenatal factors may be the cause of 20–25% of cases, with perinatal and neonatal factors responsible for 21 to 34% of cases.[5,6] Despite advances both in the care of mothers and babies and the development of new methods of investigation, the cause of CP is unclassifiable or unknown in 41–58% of full-term children.[5,6] In premature infants, the contribution of perinatal and neonatal factors is likely to be higher than in full-term infants but the causes of prematurity are still generally elusive.

Magnetic resonance imgaing (MRI) is a relatively new technology which can provide information about the nature and timing of brain lesions. It is increasingly used in the investigation of CP but it is important to determine how much it can assist in understanding the aetiology of this condition because it is still an expensive procedure and a general anaesthetic may be required in young children.

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There have been a number of reports of MRI studies in patients with CP. Truwit *et al*. studied 40 cases and found that CP in 29 term infants was often the result of prenatal factors, and less commonly related to the perinatal period.[7] Steinlin *et al*. analysed the MRI findings of 33 children with congenital hemiplegia and their data suggested a prenatal origin in 20 to 40% of cases.[8] Krageloh-Mann *et al*. studied a series of 56 cases with bilateral spastic CP, and found a predominantly prenatal aetiology in term children. Periventricular leucomalacia (PVL) was found in 53% of term children without clinical evidence of a perinatal or neonatal aetiology and it was thus deduced to be prenatal in origin.[8]

Many questions remain regarding the aetiology of CP. The objective of this study was to review all cases of CP that had MRI over a defined period at the Royal Children's Hospital, Melbourne, to determine the spectrum of MRI abnormalities, the timing of the insults, and whether this investigation had furthered our knowledge of this important condition.

METHODS

A consecutive group of 42 children with the clinical diagnosis of CP (24 boys and 18 girls), aged 3 months to 18 years (mean age 5.4 years) were gathered from the MRI Register at the Royal Children's Hospital, Melbourne. Their scans had been performed between January 1995 and June 1996. Information concerning their birth details was obtained from the Victorian Cerebral Palsy Register. Patients with postnatally acquired CP were excluded from the study.

The MRI scans were performed on a GE Sigma 1.5 Scanner (GE Medical Systems, Milwaukee, WI, USA). Routinely, the scans obtained were transverse and coronal fast spin echo (TR 4400, TE 102, echotrain 14), axial fast spin echo FLAIR (TR 10 000, TE 220, inversion 2200), 3D fast spoiled GRASS IR prep. FSPGR (TR 22 TE 3.2 Flip 25).

Magnetic resonance imaging scans were reviewed by one paediatric radiologist who was aware of the diagnosis of CP

but blinded to clinical details such as the timing of the potential insults. In each case, the images were assessed for abnormal volume and signal within the white and cortical gray matter, the basal ganglia, thalami and cerebellum. The degree of myelination and ventricular size were routinely assessed. Any other abnormalities such as cysts or migrational abnormalities were documented.

Periventricular leucomalacia was diagnosed when the periventricular white matter demonstrated increased signal intensity on FLAIR or T2 weighted sequences in conjunction with reduced white matter volume and associated lateral ventricular enlargement (Fig. 1).

The 42 cases were separated into two groups according to their gestation. Group 1 was a group of children who were born prematurely at less than 37 weeks and consisted of 12 cases. Group 2 was a group of children who were born at term (37–42 weeks) and consisted of 30 cases.

RESULTS

Details of all cases are summarized in Table 1.

Group 1

Group 1 consisted of 12 cases who were born at less than 37 weeks gestation. Periventricular leucomalacia was found in eight of 12 cases (cases 1–8). White matter hyperintensity was seen in T2 weighted images. The three cases born between 30 and 33 weeks gestation had PVL only but the other five children had additional lesions. Three children born at 36 weeks had subcortical lesions (SCL) (Fig. 2) in addition to PVL (cases 6–8). In addition to the changes of SCL and PVL, one child with a clinical diagnosis of neurofibromatosis had MRI lesions consistent with neurofibromatosis type I (increased signal within the left globus pallidus and within the cerebellar peduncles bilaterally) and the other child had a large left temporo-occipital porencephalic cyst.

Four children did not demonstrate PVL or SCL. Case 9 had hydranencephaly due to extensive infarction of the left cerebral hemisphere and infarction of a portion of the right frontal lobe, with consequent porencephaly. Case 10 had bilateral temporal arachnoid cysts with a left temporal and a left ventricular cyst. Case 11 with a clinical diagnosis of neurofibromatosis had multiple MRI lesions typical of neurofibromatosis. The final child in the group (case 41) had a normal MRI.

Group 2

Group 2 included 30 children who were born between 37 and 42 weeks gestation. The MRI findings demonstrated three main patterns, hypoxic-ischaemic lesions (13), cortical migrational malformations (five), and disorders of white matter development (three). Seven children had miscellaneous lesions which did not fit specifically into any group and two children had normal MRI scans.

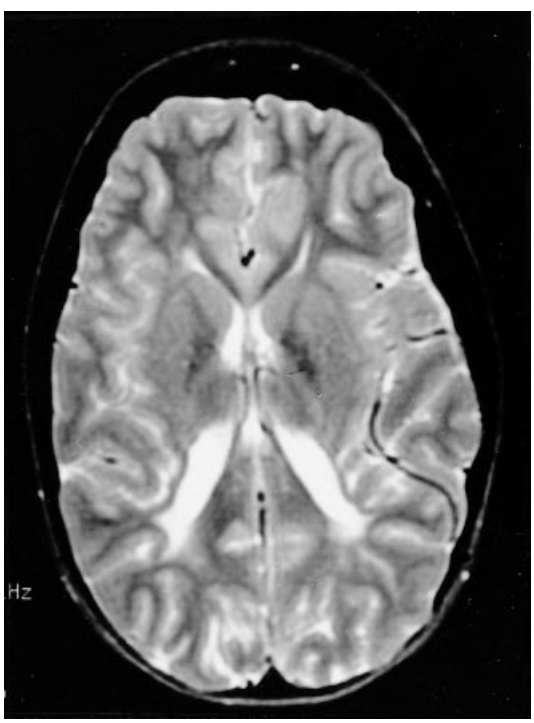

Fig. 1 Periventricular leukomalacia. The periventricular white matter is thin and shows increased signal in association with lateral ventricular enlargement. This most markedly affects the parietal and occipital white matter.

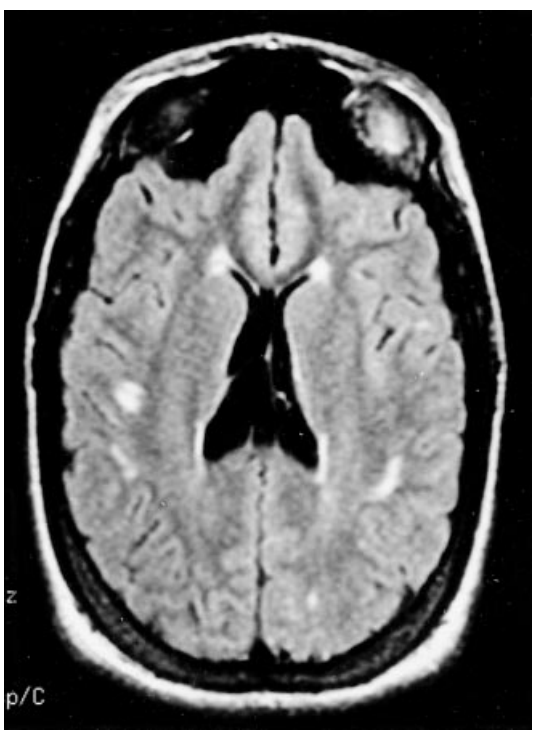

Fig. 2 Subcortical lesions. An axial FLAIR sequence demonstrates increased signal within the periventricular white matter, which are predominantly subcortical.

1. Hypoxic–ischaemic lesions

Hypoxic–ischaemic lesions were found in 13 cases. The group included PVL and SCL in nine cases and cerebral artery infarcts in four cases.

(i) PVL and SCL – nine cases (12, 14, 19–25): Seven children had SCL in addition to PVL (cases 19–25). Perinatal risk factors included fetal distress, breech presentation, hypothermia, twin pregnancy and two children had evidence of birth asphyxia. It is not possible to be certain of the role of these factors in the resulting lesions. One child had an uncomplicated perinatal history. The two cases with only PVL (cases 12, 14) were born at 40 and 42 weeks gestation, respectively. There were problems immediately before birth (persistent occipito–posterior position and deep transverse arrest in one case, obstructed labour in the other).

(ii) Main artery infarct – four cases (15–18): A pattern of cerebral artery infarction was demonstrated in four children (cases 15–18), of which three had hemiplegia and one had asymmetric quadriplegia. The middle cerebral artery was involved in three cases; the posterior cerebral artery was involved in one case. All of these cases demonstrated T2 intensity signal (well seen in FLAIR sequences) which was present bilaterally as well as an abnormal MR angiogram (MRA) in the involved arteries (attenuated or hypoplastic) which supplied the infarcted area.

2. Cortical malformations

Neuronal migration anomalies were present in five cases. Clinically, all children had spastic quadriplegia with severe intellectual disability. Three cases had lissencephaly (cases 30–32)

Table 1 Details of 42 children, including magnetic resonance imaging findings

Case	Sex	Birth-weight (g)	Gestation	Age at MRI	CP type	Severity	MRI findings
1	F	1370	30	11 y	Diplegia	Mild	PVL
2	M	2150	33	20 m	Diplegia	Mild	PVL
3	M	1620	33	9 y	Quadriplegia	Severe	PVL
4	M	2220	35	8 y	Diplegia	Mild	PVL, porencephalic cyst
5	M	1950	35	14 y	Diplegia	Moderate	PVL, neurofibromatosis
6	F	1655	36	17 y	Hemiplegia	Mild	SCL, PVL
7	F	2472	36	18 y	Quadriplegia	Mild	SCL, PVL
8	F	2350	36	16 y	Diplegia	Mild	SCL, PVL
9	F	NA	36	9 y	Hemiplegia	Mild	Infarction, porencephaly
10	M	3040	36	5 y	Quadriplegia	Moderate	Arachnoid cysts
11	M	3476	36	8 y	Diplegia	Mild	Neurofibromatosis
12	F	3346	42	17 m	Hemiplegia	Mild	PVL
13	M	3049	40	5 y	Hemiplegia	Mild	Miscellaneous
14	M	4800	40	16 y	Diplegia	Mild	PVL
15	F	2960	37	10 m	Hemiplegia	Mild	Infarction
16	M	2890	40	1 y	Hemiplegia	Mild	Infarction
17	M	NA	40	13 m	Hemiplegia	Mild	Infarction
18	M	3744	40	33 m	Quadriplegia	Mild	Infarction
19	M	3490	39	3 y	Quadriplegia	Severe	PVL, SCL
20	M	3065	40	5 m	Quadriplegia	Severe	PVL, SCL
21	M	2195	38	13 m	Hemiplegia	Mild	PVL, SCL
22	M	2225	38	1 y	Quadriplegia	NA	PVL, SCL
23	F	2230	38	26 m	Hemiplegia	Mild	PVL, SCL
24	F	2350	38	4 y	Quadriplegia	Moderate	PVL, SCL
25	F	2560	38	1 y	Quadriplegia	NA	PVL, SCL
26	M	NA	40	4 y	Diplegia	Severe	Miscellaneous
27	F	3051	40	20 m	Hemiplegia	Mild	Miscellaneous
28	M	2930	38	28 m	Quadriplegia	Severe	Miscellaneous
29	F	2780	37	11 y	Ataxia	Mild	Miscellaneous
30	F	3500	40	4 y	Quadriplegia	Severe	Lissencephaly
31	F	3345	40	6 y	Quadriplegia	Severe	Lissencephaly
32	F	3400	40	11 y	Quadriplegia	Severe	Lissencephaly
33	M	3940	41	4 y	Quadriplegia	Severe	Polymicrogyria
34	M	4190	40	3 m	Quadriplegia	Severe	Polymicrogyria
35	F	2650	41	5 y	Quadriplegia	Severe	Dis. white matter dev.
36	M	3300	40	14 m	Quadriplegia	Severe	Dis. white matter dev.
37	M	2925	41	8 m	Quadriplegia	Mild	Dis. white matter dev.
38	M	3856	41	3 y	Quadriplegia	Mild	Miscellaneous
39	F	2710	41	4 y	Quadriplegia	Severe	Miscellaneous
40	M	2900	40	3 y	Quadriplegia	Severe	Normal
41	M	2450	35	7 y	Ataxia	Mild	Normal
42	F	3660	40	3 y	Ataxia	Mild	Normal

M, male; F, female; m, month; y, year; NA, not available; PVL, periventricular leucomalacia; SCL, subcortical lesions; dis. white matter dev., disorder of white matter development; MRI, magnetic reonance imaging; CP, cerebral palsy.

(Fig. 3) and two of these children also had dysgenesis of the corpus callosum and abnormal signal in the white matter (cases 30, 31). Polymicrogyria was present in two cases (cases 33, 34). Both mothers had sustained trauma during the fifth month of gestation although the role of this injury remains uncertain. There were no known perinatal insults clinically and no evidence of underlying tissue loss or gliosis to suggest ulegyria. Case 33, with congenital microcephaly, had a neuronal migration disorder associated with pachygyria or polymicrogyria. The white matter was grossly thinned corresponding to gross thinning of the body of the corpus callosum and the ventricles were moderately dilated and irregular in shape with minimal gliosis above the bodies of the lateral ventricles. Case 34 had diffuse polymicrogyria confirmed at autopsy.

3. Disorders of white matter development

Disorders of white matter development were found in three cases. Spastic quadriplegia with athetosis and severe intellectual disability with vision and speech impairment was present in two of these cases (cases 35, 36). Case 35 demonstrated a decrease in the amount of myelinated white matter in the centrum semiovale bilaterally and diminished arborization of white matter in the subcortical regions with marked thinning of corpus callosum. There was a history of bleeding during the pregnancy. The MRI in case 36 was diffusely abnormal with marked delay in myelination and vermian hypoplasia. Diffuse white matter change was found in a case with quadriplegia (case 37). A karyotype demonstrated extra material on the long arm of chromosome 11. This MRI showed diffuse symmetrical supratentorial white matter signal abnormality with mild lateral ventricular dilatation.

4. Miscellaneous lesions

Seven children had miscellaneous lesions. *(i) Unilateral lesions – three cases (13,26,27):* Hemiplegia was present in two cases (13,27) and diplegia in the case 26. Case 13 had congenital cataracts, and the MRI showed heterotopic grey matter in the right parietal region with loss of the right sided basal ganglia and white matter suggesting previous infarction, as well as a right cerebellar abnormality suggesting infarction in the right posterior and inferior cerebral artery territories. There was abnormal high signal in the adjacent white matter. The findings were suggestive of multiple ischaemic episodes. Case 26 had severe spastic diplegia with global developmental delay and microcephaly. The MRI showed a diffusely small right cerebral hemisphere with reduced myelination. The right hippocampus was small with increased signal compatible with mesial temporal sclerosis. Case 27 had hemiplegia and an isolated cyst in the anterior tip of the right frontal horn of the lateral ventricle. Cytomegalovirus infection early in pregnancy was suggested.

(ii) Lesions not involving cerebral hemisphere white matter – four cases (28–39): Such lesions were present in three cases. Gross cerebellar cortical and vermian atrophy was present in case 28, small focal infarcts in the right thalamus were found in case 29, and case 38 showed symmetrical bilateral signal abnormality in close association with or in both claustra. Case 39 had marked and generalized dilatation of the third and lateral ventricles of uncertain significance.

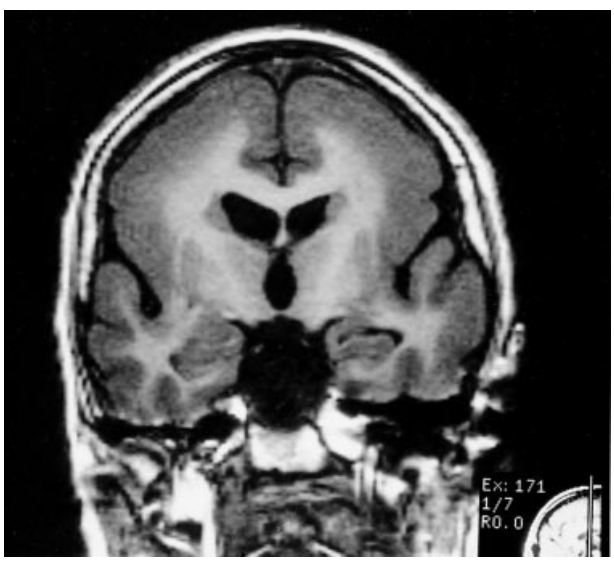

Fig. 3 Lissencephaly. A coronal T1W sequence demonstrating a diffuse smooth thickened cortex with a few broad flat gyri indicating pachygyria (incomplete lissencephaly). There is a shallow sylvian fissure.

DISCUSSION

In this series of 42 patients, there was a high rate of positive findings (39 out of 42 patients studied). This is similar to the yield of positive MRI scans in other series.[8–11] For parents seeking a cause for their child's disability, a radiological diagnosis is now possible in the majority of cases. However, this radiological diagnosis may not necessarily provide information as to why the brain lesion occurred. Important evidence for the timing of the brain lesion may be provided which can be useful not only for individuals but for directing research efforts in the future.

The pattern of brain injury of patients with CP is closely related to the gestational age of occurrence. Typical preterm brain injuries include PVL and post-haemorrhagic porencephaly. Periventricular leucomalacia usually occurs between 28 and 34 weeks of gestation[8] and is caused by an ischaemic process in the watershed zone that exists in the periventricular white matter of the immature brain.[12] The MRI features of PVL include a reduction in the quantity of periventricular white matter (late infancy and childhood), periventricular gliosis and ventriculomegaly with irregular outline of the lateral ventricles.[12,13]

After about 34 weeks of gestation, subcortical and cortical areas are the most vulnerable regions of the brain for hypoxic-ischaemic insult[8,9] and the resulting lesions include subcortical leucomalacia, multicystic encephalamalacia and gliosis.[14,15] In our study, the patients with CP who were born between 30 and 33 weeks gestation (there were no children born earlier than 30 weeks gestation) had typical PVL with obvious gliosis, while the cortex and subcortical white matter remained spared. Subcortical lesions and cortical atrophy, with or without thalamic, brain stem and cerebellar lesions, were seen in infants who were born at or after 35–36 weeks gestation. Thus we can conclude that for eight out of the 12 premature children in our series, the lesion occurred either in the third trimester or in the perinatal period.

These patterns were similar to those reported by Bardovich and Truwit[15] who reviewed the MRI scans of 25 patients with asphyxia documented at various gestational ages. They found that infants of 24 and 26 weeks gestation had irregularly enlarged ventricular trigones with minimal periventricular gliosis, patients at 28–34 weeks had variably dilated ventricles and periventricular gliosis, the 36 week infant had mild cortical and subcortical gliosis superimposed on deep white matter and periventricular gliosis and term infants had significant cortical and subcortical gliosis and atrophy in the parasagittal watershed areas.

For infants born at term, we found a similar predominance of third trimester lesions. Thirteen of the 30 cases had hypoxic–ischaemic lesions, presumed to have occurred in the third trimester or perinatal period. All of the 13 cases with hypoxic–ischaemic lesions also had PVL. It has been suggested that PVL found in infants born at term may indicate that the lesion occurred early in the third trimester[14] but that the pregnancy progressed. In a group of 152 cases with spastic CP, one-third of full-term infants demonstrated preterm patterns of brain injury and PVL was present in 10% of term cases.[14] The MRI findings of PVL in term infants was milder than those in patients born around 30 weeks gestation, indicating that the brain insult responsible for PVL in term infants was less severe, and therefore did not result in preterm birth.[15]

Four children had evidence of cortical infarction which is less common in the premature than the term infant.[16] The lesion is typically found in term babies born after an uneventful pregnancy and routine delivery.[17] Most commonly, the infarct is in the distribution of the middle cerebral artery. It has been suggested that such cerebral infarcts may occur prior to delivery[17] or within the early days of life.[16]

The four cases of cerebral infarction in our study all demonstrated abnormal intensity T2 signal on the contralateral side. This may indicate that the pathology of these full term infarcts was based on diffuse hypoxic–ischaemic brain lesions, similar to PVL and SCL. When the ischaemic lesion is more severe, it is partially due to local artery damage. There is lack of direct evidence that the attenuated cerebral artery in the involved area shown on MRA is the cause or the result of infarction.

Five out of 42 cases had cortical malformations indicating insults during the second trimester of pregnancy. The neuronal migration anomalies demonstrated in our study were lissencephaly (three cases) and polymicrogyria (two cases). Lissencephaly or complete agyria, signifies complete absence of sulci. It has been suggested that the insult occurs before the end of the third month of gestation or between the 12th and 15th week of gestation.[18,19] The corpus callosum forms during the same period[20] and it was of note that two of our cases had dysgenesis of the corpus callosum.

The two basic varieties of polymicrogyria, layered and non-layered, appear to have differing times of onset. The non-layered type represents a disorder of neuronal migration and the time of onset of this variety of polymicrogyria appears to be generally no later than the fourth to fifth month of gestation. The layered variety of polymicrogyria includes those cases with evidence of laminar neuronal necrosis in the cortex after the end of neuronal migration, that is, between 20 and 30 weeks of gestation.[21,22] In our study, there were two cases of polymicrogyria (cases 33, 34).

Three cases demonstrated varieties of cerebral white matter hypoplasia, suggesting insults during the second trimester of pregnancy. In case 35, the myelinated white matter was sparse in comparison with the gray matter structures, suggesting that the brain injury occurring early *in utero* before the glial cells had developed sufficiently to produce gliosis. Brain injury occurring during the second trimester of pregnancy, prior to the time of astrocyte generation, results in liquefaction necrosis without any glial response.[18] There is an association between maternal bleeding during pregnancy and congenital anomalies of the central nervous system. Perfusion failure of the fetal brain or fetal malnutrition may be the outcome.[23] These factors may have been responsible for the pathology in case 35. Whilst the cause of the diffusely abnormal scan with marked delay in myelination and vermian hypoplasia in case 36 is uncertain, familial white matter hypoplasia has been reported, in some cases associated with agenesis of the corpus callosum and growth deficiency.[24,25]

Partial distal deletion of chromosome 11 is associated with psychomotor delay.[26,27] Since the first case was described by Jacobsen *et al*.,[28] over 40 patients with terminal deletion of 11 long arm (Jacobsen syndrome) have been reported. Variations in the deleted parts of 11q result in different clinical features. Our patient (case 37) had similar MRI findings to those reported by Ono *et al*. with evidence of delayed myelination rather than demyelination.[27]

One child (case 27) had evidence of possible congenital cytomegalovirus infection. Congenital cytomegalovirus infection can cause a variety of lesions including neuronal migration disorders.[29] The contribution of congenital infection to the total number of children with CP remains uncertain. In a series of 489 cases with spastic CP, in only 3.3% was congenital infection considered to be the major aetiological factor.[5]

In conclusion, we have described the findings in a consecutive series of MRI scans performed to determine the cause of CP. Brain lesions occurring in the third trimester or perinatal period accounted for 50% of children with CP and 43% of full-term children. It was possible to provide an indication of the timing of events in 29 of the 42 cases. Twenty-one cases were third trimester or perinatal, three were second trimester, and five were the result of events around the end of the first trimester or early second trimester. Hence in only 10 cases was the timing uncertain.

Our findings are consistent with other studies in suggesting that insults occurring during the third trimester or the perinatal period account for a large proportion of cases of CP.[9] There was a wide age range in our series, including several older children. While it seems likely that there would be similar findings in a younger, more recent cohort of children, further studies would be useful to confirm this. Since there is evidence that perinatal insults are implicated in only a small proportion of children with CP, we believe that events in the third trimester should be closely examined to further identify the causes of CP.

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