

# Minor congenital anomalies and ataxic cerebral palsy

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**SUMMARY** The incidence of minor congenital anomalies was examined in 36 patients with ataxic cerebral palsy, in unaffected family members, and in 100 unrelated control subjects. None of the control subjects or family members had more than four anomalies, and 25 of 36 (69%) of the patients had more than four. The distribution of anomalies differed considerably, with 60% of the index cases having seven or more, and 94% of the controls having three or less. The number occurring in the patients was significantly more than in their relatives. Of the 25 patients with more than four anomalies, 16 (64%) had undergone potentially adverse perinatal or early postnatal events. Thus minor congenital anomalies were considerably more frequent in those with ataxic cerebral palsy than in related or unrelated control subjects. These anomalies may be markers of early prenatal factors that contributed to the adverse outcome either directly or by predisposing to perinatal difficulties.

Retrospective allocation of a cause of cerebral palsy is strongly influenced by observer bias. It has often been guessed at after reading inadequately recorded histories, and coloured by known associations such as preterm birth and diplegia.<sup>1</sup> It would therefore be of value to devise some marker that might indicate an association with a prenatal event, such as minor congenital anomalies. These are relatively infrequent physical features that in themselves have neither medical nor cosmetic importance.<sup>2</sup> They are harmless phenomena that may occur in completely healthy individuals. The recognition of these indicators of altered morphogenesis does, however, alert the clinician to the possibility of a more serious defect, and it has been argued that in excess they correlate with disturbances of neurological development occurring during embryogenesis.<sup>3–6</sup> In ataxic cerebral palsy these early prenatal disturbances are probably of the utmost importance.<sup>7</sup> Patients with this syndrome were therefore examined to find out whether they had significantly more minor congenital anomalies than a normal population and their own families. The prenatal, perinatal, and postnatal histories were also analysed.

The purpose of this study was to see if patients with ataxic cerebral palsy had more minor congenital anomalies, and if so to see if this finding correlated with the history.

## Patients and methods

### DIAGNOSIS

Cerebral palsy is defined as a group of disorders of

movement and posture due to a non-progressive defect or lesion of the developing brain.<sup>8</sup> When this disorder is an ataxia that is not primarily due to muscle weakness, spasticity, choreoathetosis, or dystonia, it is called ataxic cerebral palsy. Thirty six cases, all over 5 years of age, were found, and personally examined to ensure that they fulfilled the criteria for diagnosis.

### HISTORY

A full history was taken. Further information and as many aspects as possible were checked against the records of various institutions, hospitals, medical practitioners, and a comprehensive cerebral palsy register.<sup>9</sup> Particular emphasis was placed on certain aspects.

#### *Prenatal history*

This included items such as drugs, maternal illnesses and accidents, surgical operations, threatened abortions and antepartum haemorrhage, toxæmia, length of gestation, and birth weight. Events that occurred after 4 months' gestation and before the onset of labour were termed late prenatal. Where there was an uneventful history, evidence of Mendelian inheritance, or the presence of overt congenital abnormalities, then an association with the period of embryogenesis was implied. These findings were termed early prenatal.

#### *Perinatal history*

This covered the time from the onset of labour up until day 7 of life. It included quality and quantity

of labour, presentation, obstetric intervention, measures of fetal distress, resuscitation, time to spontaneous respiration, Apgar scores, and condition during the first week of life—for example, tube feeding, assisted ventilation, seizures, intracranial haemorrhage, and infection of the central nervous system.

#### Postnatal history

This covered the time from day 7 to 2 years of age. Events sought included severe illnesses (particularly if they concerned the central nervous system) and serious surgical operations.

#### MINOR CONGENITAL ANOMALIES

The index cases, their parents and siblings, any children of the siblings, and a control group were examined for the presence of minor congenital anomalies. The control subjects (100) consisted of adults and children over 5 years of age in whom there was no history of neurodevelopmental disability. They were chosen at random from those attending a busy primary care clinic. All the subjects were caucasian.

The minor congenital anomalies studied were selected if they were either indisputably recognisable or easily measured. They were all characteristics determined by about the 16th week of gestation. The methods for identification, measurement and normal values have been well described previously.<sup>10-13</sup> Forty four anomalies were sought (table 1). The aim was to see if the index cases had more anomalies than their families or a control population. If there was a significant difference this was taken to indicate an association with an event during embryogenesis (that is, early prenatal) and compared with the patient's history.

#### Results

Thirty six patients (two of whom were sisters) were diagnosed as having ataxic cerebral palsy; their mean age was 14 years (range 5-34).

Table 2 shows the incidence of minor congenital anomalies in the control population; none had more than four. Thus if more than four were found in any of the cerebral palsy patients, this was considered significant. The probability of misclassifying a control as a patient using this discriminant is statistically highly unlikely (binomial distribution,  $p < 0.0005$ ).

Table 3 shows the number of minor congenital anomalies in the index cases and the family members. For the analysis, the sign test was carried out by examining the difference between the number of anomalies in the patient and the number in the

relative with the maximum number of minor congenital anomalies; the patients had significantly more ( $p < 0.01$ ). Apart from the family with two affected sisters, no family member had more than four minor congenital anomalies.

The relevant parts of the histories (some of which contained events that might retrospectively have been thought to contribute towards the neurological deficit) and the number of minor congenital anomalies found are given in tables 4 and 5. Table 4 shows those cases in which an early prenatal event might be associated with the development of cerebral palsy as judged from their histories, and table 5, those

Table 1 *Minor congenital anomalies*

<b>Mouth:</b>	<b>Eyes:</b>
High arched palate	Epicanthic folds
Furrowed tongue	Upslanting of palpebral fissures
Bifid uvula	Downslanting of palpebral fissures
<b>Hair:</b>	Hypertelorism
Two or more parietal whorls	Hypotelorism
Abnormal posterior whorl	
Cowlick	<b>Ears and neck:</b>
Widow's peak	Malformed ears
<b>Hands:</b>	Asymmetric ears
Clinodactyly	Preauricular tags
Partial cutaneous syndactyly	Preauricular pits
Simian crease	Protruding ears
Sydney crease	Adherent ear lobes
Middle finger/hand size	Lack of lobulus
Hypoplastic nails	Incomplete scapha helix
<b>Trunk:</b>	Neck webbing
Accessory nipples	Small ears
	Low set ears
	Abnormally slanted ears
<b>Feet:</b>	Ear lobe creases
Broad hallux	<b>Face and nose:</b>
Hypoplastic hallux	Synophrys
Wide distance between first and second toes	(under 10 years)
Third toe longer than second	Coarse prominent supraorbital ridges
Deep crease between first and second toes	Prominent metopic suture
Syndactyly	Anteverted nostrils
Overriding or curly toes	Bifid tip of nose

Table 2 *Incidence of minor congenital anomalies in control population (n=100)*

<i>No of anomalies/person</i>	<i>Percentage of control population</i>
0	17
1	34
2	28
3	15
4	6

Table 3 Minor congenital anomalies in patients and family members

Case No	No of anomalies/patient	No of anomalies among family members*
1	7	2, 1, 1, 1
2	4	3, 2, 2, 2
3	6	3, 2, 2, 1
4	2	1, 0, 1, 2
5	7	2, 2, 0, 1
6	4	2, 4, 1, 2
7	7	1, 3, 1, 2
8	6	0, 0, 1, 1
9	9	1, 2, 2, 1, 2
10	9	2, 2, 0, 1
11	8	1, 2, 1, 2
12	1	1, 0, 2, 2, 2
13	2	1, 2, 1, 0
14	3	4, 1, 1, 1
15	8	3, 3, 3, 1
16	9	2, 2, 0, 4, 3
17	1	1, 0, 3, 1, 4
18	7	1, 1, 2, 1
19	5	1, 1, 1, 0
20	6	1, 1, 2, 1
21	2	3, 3, 2, 0
22	3	2, 3, 0, 2
23	7	3, 2, 1, 3
24	4	1, 1, 1, 0
25	6	0, 1, 1, 2, 1
26	8	0, 0, 1, 1
27	6	1, 0, 1, 1
28	6	0, 2, 2, 1
29	10	1, 0, 1, 0
30	9	2, 2, 0, 1, 3
31	6	1, 0, 2, 2, 2
32	6	1, 0, 2, 2, 2
33	6	0, 1, 1, 1
34	8	0, 3, 3, 1
35	0	2, 1, 1, 0
36	7	1, 3, 3, 2

\*The family member with the greatest number of anomalies was used for comparison.

with a possible late prenatal, perinatal, or postnatal association. Unless otherwise stated, all were of normal birth weight and gestation.

When using the presence of more than four minor congenital anomalies to imply an early prenatal origin, 25 of 36 (69%) cases were found. Most of these obviously differed from the controls, 15 of them (60%) having seven or more anomalies.

Of the 15 cases (table 4) with a history suggesting an early prenatal cause, 11 (73%) had more than four minor congenital anomalies. When the numbers of patients with histories suggesting an association with early prenatal events are combined with those with more than four minor congenital anomalies, the total becomes 29 of 36 (81%). There are four cases (4, 22, 24, 35) shown in table 4 who did not

Table 4 Patients in whom early prenatal events were thought to have been associated with cerebral palsy

Case No	No of minor congenital anomalies	History
1	7	Uneventful
15	8	Uneventful
16	9	Uneventful
18	9	Threatened abortion
20	6	Uneventful
29	10	Uneventful
30	9	Uneventful
31	6	Sister with similar condition, possible Joubert's syndrome
32	6	As case 31
33	6	Encephalocele
36	7	Uneventful
4	2	Mother has similar non-progressive condition
22	3	Congenital hydrocephalus, frequent blocked shunts
24	4	Uneventful
35	0	Suprasellar cyst. Several episodes of decompensated hydrocephalus

have more than four minor congenital anomalies but whose histories suggested an early prenatal origin. Case 4 had a mother with a similar non-progressive condition, cases 22 and 35 had congenital hydrocephalus with histories of frequent episodes of raised intracranial pressure (which could be responsible for the ataxic syndrome), and case 24 had four minor congenital anomalies and none of his family had more than one.

There are three cases (3, 12, 13) which, from their histories, seem to be of postnatal origin; two of these did not have more than four minor congenital anomalies. The third case was a 'near miss SIDS' and one might speculate that the infant was abnormal before the event.

Of the 25 cases with more than four minor congenital anomalies, 16 (64%) had serious obstetric complications. Eight had abnormal presentations, five of whom had failed attempted versions, several required resuscitation at birth, were slow to establish spontaneous respirations, or were documented as having fetal distress.

## Discussion

Since the description by Little in 1862 of the influence of prematurity and abnormal birth on the development of child handicap,<sup>14</sup> many clinicians and non-medical personnel have easily attributed the cause of cerebral palsy to these events. This is despite the statement by Freud as long ago as 1897 that it is impossible to identify the timing or nature

Table 5 Patients in whom events occurring after four months' gestation were thought to be associated with cerebral palsy

Case No	No of minor congenital anomalies	Suggested pathogenetic period from history	History
5	7	Perinatal	Thirty five weeks preterm, instrumental breech delivery, resuscitation required at birth
7	7	Perinatal	Delay in second stage, fetal distress, delivery by forceps under general anaesthesia
8	6	Late prenatal	Severe pre-eclamptic toxæmia
9	9	Perinatal	Occipitoposterior presentation, delay in second stage, fetal distress with meconium stained liquor
10	9	Perinatal	Prolonged second stage, more than three minutes to establish spontaneous respiration, resuscitation after birth
11	8	Perinatal	Occipitoposterior presentation, vacuum extraction, resuscitation after birth
19	5	Perinatal	Threatened abortion, failed external version twice at seven months, followed by version under general anaesthesia, placental separation and large antepartum haemorrhage
23	7	Perinatal	Apgar score of 5 at five minutes, more than three minutes to establish spontaneous respirations
25	6	Late prenatal and perinatal	Threatened abortion, antepartum haemorrhage at five months, eclamptic seizures, 33 weeks preterm, high forceps delivery, resuscitation after birth
26	8	Late prenatal and perinatal	Threatened abortion twice, failed external version, deep transverse arrest, rotation with Kielland's forceps under caudal block
27	6	Late prenatal and perinatal	External version three times, second stage less than five minutes, more than three minutes to establish spontaneous respirations
28	6	Late prenatal and perinatal	External version twice, fetal distress, delay in establishing spontaneous respirations, resuscitation required after birth
34	8	Perinatal	Preterm twin
2	4	Late prenatal	Severe pre-eclamptic toxæmia, SGA
6	4	Perinatal	Vacuum extraction for fetal distress
14	3	Perinatal	Twenty eight weeks preterm, resuscitation required at birth, necrotising enterocolitis requiring operation at 6 days
17	1	Perinatal	Twin, transverse lie, breech delivery, neonatal brain abscess, hydrocephalus, frequent blocked shunts
21	2	Perinatal	Fetal distress, emergency caesarean section, over two minutes to establish spontaneous respirations
3	6	Postnatal	'Near miss SIDS'
12	1	Postnatal	Encephalitis at 2 years of age
13	2	Postnatal	Severe shock and 'collapse' after operation for reimplantation of ureters at 3 months

of the event that caused the brain damage, and that there may be many factors operating in the prenatal, perinatal, and postnatal periods.<sup>15</sup> He proposed that some cases were caused by both predisposing and immediate events, and later authors have given this some support.<sup>16-18</sup> Paneth wrote that the hypothesis of a direct association between parturitional difficulties and cerebral palsy influences the practices of many obstetricians and paediatricians, and accounts in part for high rates of malpractice.<sup>18</sup> Epidemiological studies, however, have not supported this hypothesis.<sup>17</sup> It seems that most cerebral palsy is of early prenatal origin, or has a prenatal event that makes an important contribution to its aetiology. Severe asphyxial intrapartum and perinatal events may, however, be associated with later neurological deficit if the baby survives,<sup>19 20</sup> even though many of these survivors may be intact. This has led to

increasing obstetric awareness, monitoring, and intervention, even though little correlation has been found between markers of fetal distress and later disability (MJ Painter, M Scott, R Depp. Neurological and developmental follow up of children at 6 to 9 years relative to intrapartum fetal heart rate patterns. Presented at the Society of Perinatal Obstetricians annual meeting, Las Vegas, 1985),<sup>21</sup> and the incidence of cerebral palsy is not falling.<sup>22</sup> Despite these statements it is difficult for those concerned in the care of handicapped children not to attribute a primarily causative role to serious obstetric complications.

This study evaluated these factors by finding out that in a select cerebral palsy population, a high proportion of which were expected to be of early prenatal origin, most had more than four minor congenital anomalies. These characteristics would

have been determined by about 16 weeks' gestation, or earlier. The distribution of anomalies in the controls and the index cases differed considerably, with 60% of the index cases having seven or more minor congenital anomalies, and 94% of the controls three or less. The method would have benefited from an interobserver control. The minor congenital anomalies chosen were, however, indisputably present, or easily measured and compared with established normal values. The incidence of minor congenital anomalies, and what constitutes a significantly increased number, vary among studies, probably because different methods have been used and different features have been sought, the incidence increasing with the number.<sup>23</sup> The results of many studies have suggested that excessive numbers of minor congenital anomalies correlate with disturbances of neurological and mental development,<sup>3-6 24</sup> and this study supports this view. Although the association is difficult to prove,<sup>25</sup> a significantly increased number of minor congenital anomalies in a patient with a static encephalopathy provides strong circumstantial evidence of an early prenatal contribution to the disorder. This study is not claiming a definite causal relationship, however, but is reporting an association.

It would seem then that a controlled search for a significantly increased number of minor congenital anomalies in a cerebral palsy population might supply circumstantial evidence for a pathogenetic period. Using this method, this study shows the importance of an association between early prenatal and later events. Of those with an increased number of minor congenital anomalies, 64% had later adverse events, many of which might have been thought to be primarily causal. A recent study of congenital anomalies in high risk children also reported this association,<sup>26</sup> although they excluded the most severely handicapped children, and their obstetric complications were not as serious as those presented here. The National Collaborative Perinatal Project has reported the poor correlation between 'obstetric risk factors' and cerebral palsy, and has shown an association between markers of asphyxia and major congenital malformations or other intrinsic defects that might have contributed to an unfavourable outcome.<sup>17</sup> One of the predictors of cerebral palsy was breech presentation and in this present study eight had abnormal presentations, five of which had failed attempts at external version and fetal distress.

The historical data given are retrospective, and at times their recording was somewhat variable, although obtained from multiple sources. They are presented to show that even the most unfavourable recorded perinatal events, that are followed by

cerebral palsy, may be associated with evidence of an earlier prenatal insult. The results suggest that if further prospective studies were carried out on larger populations using the methods described here, added support would be given to the concept that although adverse perinatal events have the potential to cause brain injury, and interfere with subsequent development, their role in producing later neurological impairment should not be over-estimated.

I am indebted to Dr Fiona Stanley and Ms Linda Watson for access to the cerebral palsy register of Western Australia, to Dr Valerie Gracey for statistical advice, and to those with cerebral palsy and their families who participated in the study.

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Accepted 1 December 1988