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A seven year follow-up study of the cognitive development of children who experienced common perinatal problems

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Abstract The prevalence of perinatal problems in a sample of 1037 children was described. There was no significant association between perinatal problems and socio-economic status. The association between perinatal problems and cognitive development was examined by stepwise regression analyses of the more common perinatal problems on cognitive factor scores, using measures of language and intelligence taken when the children were aged 3, 5, and 7 years. Of 14 perinatal problems analysed in this manner, only two, being a twin or being small for gestational age, were found to be consistently associated with a significantly lower cognitive factor score.

Key words: perinatal characteristics; longitudinal studies; cognitive development; intelligence; language development.

The theory of a 'continuum of reproductive casualty' proposes that perinatal problems may result in a continuum of damage to the newborn, ranging from mental retardation or cerebral palsy to less severe problems of behaviour and adjustment.[1,2] A variety of perinatal problems have been implicated in the production of damage to the newborn including low birth weight and being preterm,[3] idiopathic respiratory distress syndrome,[4] apnoea[5] and hyperbilirubinaemia.[6] However, the literature on these problems is often conflicting in terms of results obtained. This may stem from the interrelatedness of many perinatal problems and from improvements over recent years in the medical care of the fetus and newborn infant which have significantly lowered mortality and morbidity.[7] Results from a number of studies have helped highlight those perinatal problems which are associated with later developmental problems and those which no longer have adverse sequelae.[8] However, continued research into the effects of perinatal problems is necessary to identify those still requiring preventive efforts.[9]

The Dunedin Multidisciplinary Child Development Study is a longitudinal investigation of the health, development and behaviour of a large sample of New Zealand children. One of its primary aims has been to study the association between the more prevalent perinatal problems and the course of child development. Some of the preliminary findings concerning the effects of different perinatal problems have been reported by McGee and Silva.[10] This paper presents the findings of the association between some of the more common perinatal problems and general cognitive development at 3, 5 and 7 years of age. Such a longitudinal approach allows the study of the effects of perinatal problems with age. It may be that the adverse consequences of such problems are evident early in development, but attenuate over time.[11] Conversely, such effects may be more evident as children become older and have to deal with adjustment to school life. A related issue is to determine whether particular perinatal problems have age-specific associations with cognitive development.

METHODS

Sample

The sample consisted of 1037 children who were enrolled in the Dunedin Multidisciplinary Child Development Study. These were drawn from a cohort born at Dunedin's one obstetric hospital (Queen Mary) between 1 April 1972 and 31 March 1973 whose mothers lived in the Dunedin metropolitan area. During this 12-month period, there were 1661 infants born at Queen Mary Hospital whose mothers were resident in the Dunedin metropolitan area. At the time of the first follow up at age 3, 1139 of the children were known to be still resident in Otago. Of the remaining 522 children, 12 had died before age 3 and 510 could not be traced or were known to be living beyond Otago. Of the 1139 children known to be resident in Otago, 1037 (91%) were successfully traced and assessed within about a month of their third birthdays. Those not seen were either traced too late for assessment at 3 (n=34) or their parents were unable to co-operate (n=68). A full description of the sample and its setting is provided elsewhere.[10]

When those not assessed at age 3 were compared with those who were, there were no significant differences in the prevalence of prenatal problems, mode of delivery, birth weight, gestational age, or neonatal problems. Those followed however, were under-representative of children whose mothers had been unmarried at the time of the child's birth. Only 5.4% of those who were seen had unmarried mothers and 15.5% of the sample not assessed had unmarried mothers at birth.

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A further comparison was made between the socio-economic levels of the 1037 children followed at age 3 and those of the country as a whole, using the Elley and Irving Scale[12] which provides a six point ranking according to father's occupation. The Dunedin sample was slightly socio-economically advantaged. In addition, the Dunedin sample was under-representative of the Maori and other Polynesian races; 2% were more than half Maori or Polynesian compared with about 10% for the whole of New Zealand.

The sample was assessed at age 5 (n=991) and 7 (n=954). Losses to the sample over this time were due to withdrawal of parental co-operation (n=30 by age 7) or because the families had moved beyond the province of Otago. Furthermore, there were some incomplete results for a number of the tests administered, as some children were not assessed at the Dunedin unit but in other parts of New Zealand (n=80). There were also some incomplete results at age 3 owing to a lack of co-operation on some of the tests by the children (n=57). Five children with moderate or severe mental retardation were not included in the analyses of results because of inability to do the tests. Only one of these children was known to have experienced any perinatal problems.

A final point needs to be made about the Dunedin sample. As pointed out in a recent editorial,[13] the results of studies such as the present one need to be interpreted with some caution because of possible sources of bias which might limit the generality of the findings. Such bias may arise from changes in obstetric and neonatal care over time, cultural differences between countries and local hospital practice. In this regard, while Queen Mary Hospital is an obstetric hospital for the Otago area, this sample was made up of women from the Dunedin urban area. They were not specifically referred to this hospital because of complications in the pregnancy, and consequently were not a specially selected group.

Method of data collection

The infants were examined and the perinatal data recorded from the medical records shortly after birth. This included information about prenatal problems, mode of delivery, condition at birth (Apgar Score), gestational age, birth weight, and any neonatal problems. The documentation of the sample has been described by Buckfield.[14]

The children were recalled for examination within approximately one month of their third, fifth, and seventh birthdays at which time their cognitive development was assessed by

Table 1 Prevalence of perinatal problems experienced by the 3-year-old sample (n=1037).

Perinatal problems	N	Percentage
Prenatal problems		
Diabetes	1	0.1
Pre diabetes	1	0.1
Epilepsy	4	0.4
Glycosuria	7	0.7
Hypertension Mild (Diastolic 90–99 mmHg)	60*	5.8
Hypertension Moderate (100–109 mmHg)	24*	2.3
Hypertension Severe (>109 mmHg)	11*	1.1
Ante-partum haemorrhage 1st trimester	6	0.6
Ante-partum haemorrhage 2nd or 3rd trimester	12*	1.2
Accidental haemorrhage	1	0.1
Placenta previa	3	0.3
Twins	24 (children)*	2.3
Delivery other than spontaneous		
Forceps and rotation vertex delivery	74*	7.1
Caesarean section	48*	4.6
Breech birth	28*	2.7
Low Apgar score at birth (Required resuscitation, n = 3; regular respiration not established 10 min after birth, n = 1; at 5 min heart rate less than 100 beats/min, respiration irregular or absent and signs of ventral cyanosis, n = 8)	12*	1.2
Neonatal problems		
Small for gestational age (10th percentile of birth weight for gestational age or less)	96*	9.3
Preterm (<37 weeks gestational age)	41*	4.0
Idiopathic respiratory distress syndrome (IRDS)	32*	3.1
Apnoea	8	0.8
Minor neurological signs of the neonatal period (jitteriness, tenseness, limpness, hypotonicity)	27*	2.6
Major neurological signs	2	0.2
Non-haemolytic hyperbilirubinaemia (serum bilirubinaemia levels > 15 mg/100 ml)	12*	1.2
Rh incompatibility and hyperbilirubinaemia	2	0.2
ABO incompatibility and hyperbilirubinaemia	2	0.2

*Problem selected for further analysis.

trained psychometrists who were unaware of the perinatal histories of the children or of previous test results.

Cognitive ability

Cognitive development was assessed at each age level using comprehension and expressive language tests and an intelligence test. At age 3, the Reynell Developmental Language Scales[15] were used to provide a measure of verbal comprehension and verbal expression and intelligence was assessed by the Peabody Picture Vocabulary Test.[16] At age 5, the Reynell scales were re-administered together with the Stanford Binet Intelligence Scale.[17] At age 7, verbal comprehension and expression were assessed using the Illinois Test of Psycholinguistic Abilities[18] Auditory Reception and Verbal Expression scales; intelligence was measured by the Revised Wechsler Intelligence Scale for Children.[19]

Because the three measures of cognitive development at each age level were highly correlated, a factor analysis was performed on each group of three measures using the principal factor method with iteration.[20] A one factor solution was appropriate for each analysis and factor scores were calculated to provide a general measure of cognitive ability at each of the three ages. These factor scores were used as the dependent variables in the subsequent analyses. Perinatal problems were used as the independent or predictor variables.

RESULTS

Prevalence of perinatal problems in the sample

The prevalence of individual perinatal problems are set out in Table 1. Perinatal problems were experienced by 46% of the sample of 1037 children; 26.6% had one problem, 12.5% had two problems, and 6.9% had three or more problems. More detailed descriptions of the perinatal problems and birth weight for gestational age are given elsewhere.[10] Forty children weighed < 2500 g at birth; 28 were between 2000–2500 g; nine were between 1500–2000 g; and only three weighed < 1500 g. There was no significant association between the perinatal problems and socio-economic status as measured by the Elley and Irving Index.[12]

Perinatal problems and cognitive development

The associations between the more common perinatal problems set out in Table 1 and cognitive development were analysed by carrying out three stepwise multiple regression analyses,[21] using each perinatal problem as a dichotomous (yes/no) independent variable and the cognitive factor scores at each age as the dependent variables. This method of analysis takes into account the correlations between the predictor variables (perinatal problems) and the dependent variables (the general cognitive factor scores) and also the correlations among the predictors themselves. Table 2 shows the correlation coefficients between the various perinatal problems and the cognitive factor scores at 3, 5 and 7 years of age. Only those perinatal problems which occurred in at least 1% of the sample (n=10) were included in this analysis. The remaining problems (*see* Table 1) were excluded because of their low base rate being considered insufficient for reliable analysis.

Examination of Table 2 indicates that the correlations between individual perinatal problems and cognitive factor scores at each age were very small. At age 3, being small for gestational age (SGA), a twin or preterm were weakly associated with poorer general cognitive ability. These correlations were further reduced as the children grew older. By age 7, the problems of being SGA or a twin and low Apgar score were weakly associated with poorer cognitive ability. The only individual perinatal problem to show a consistent statistically significant relationship with cognitive ability was being SGA.

The three overall regression analyses were significant ($P<0.01$) at each age level: $F(3,975)=11.67$ at 3 years; $F(2,929)=10.22$ at 5 years; and $F(2,884)=5.61$ at 7 years. Table 3 shows the summarized results of these analyses at each age for those variables with significant regression coefficients. The addition of the other perinatal variables in these analyses did not significantly increase the proportion of variance of the cognitive scores explained. For the most part, the perinatal problems making a significant contribution to the prediction of the factor scores were those identified above in Table 2. However, SGA did not enter into the regression at age 7. It should be recognized that in overall terms, the regression analyses accounted for a very small proportion of the variance of the cognitive factor scores. Furthermore, this proportion became smaller with increasing age: some 3% at age 3, 2% at age 5 and 1% at age 7.

Table 2 Correlations between each perinatal problem and the general cognitive ability factor scores at ages 3, 5 and 7.

Perinatal problem	Cognitive factor score Age 3 (n = 979)	Age 5 (n = 932)	Age 7 (n = 887)
Small for gestational age (SGA)	−0.15*	−0.12*	−0.08*
Twins	−0.11*	−0.06	−0.08*
Preterm	−0.09*	−0.03	−0.03
Idiopathic respiratory distress syndrome (IRDS)	−0.07	0.02	0.01
Breech delivery	−0.05	−0.09*	−0.04
Caesarean delivery	0.03	0.05	−0.02
Forceps delivery	−0.03	0.00	−0.02
Low Apgar score	−0.03	0.00	−0.08*
Ante partum haemorrhage (APH) — trimester 2/3	−0.03	0.02	−0.02
Mild hypertension	−0.04	−0.02	−0.02
Moderate hypertension	−0.04	−0.07	−0.02
Severe hypertension	−0.02	−0.02	0.01
Minor neurological signs	−0.03	−0.02	0.00
Hyperbilirubinaemia	−0.01	−0.02	0.02

*P < 0.01

Table 3 Summary table for the stepwise regression analyses of perinatal problems on the cognitive factor scores at each age.

Variable	Simple R	Multiple R	% Variance explained	Regression coefficient
Age 3				
SGA	−0.15	0.15	2.25	−0.42
Twins	−0.11	0.17	2.89	−0.50
Preterm	−0.09	0.18	3.24	−0.36
Age 5				
SGA	−0.12	0.12	1.44	−0.37
Breech	−0.09	0.15	2.25	−0.50
Age 7				
Twins	−0.08	0.08	0.64	−0.44
Low Apgar	−0.08	0.11	1.21	−0.62

Children small for gestational age

A separate study was made of the 96 children who were small for gestational age as this problem appeared to be associated more consistently with lower cognitive ability. Moreover, being small for gestational age as a problem is commonly associated with other perinatal problems. Forty-two of the 96 children (43.8%) who were SGA had at least one other perinatal problem. The other perinatal problems included maternal hypertension (n=20), ante partum haemorrhage (n=1), delivery involving rotation with forceps (n=10), Caesarean section, (n=4), breech births (n=5), low Apgar scores at birth (n=2), the idiopathic respiratory syndrome (n=6), apnoea (n=1), minor neurological signs (n=1), non haemolytic hyperbilirubinaemia (n=1), preterm delivery (n=6), and six were twins. These two groups, SGA with or without other perinatal problem(s), were compared with the remainder of the sample on the three cognitive measures at each age. The three groups were compared using one-way analysis of variance and the results of this analysis are shown in Table 4.

There were significant differences among the groups only at ages 3 and 5; no differences were significant at 7. All three measures showed differences among the groups at 3, but only verbal comprehension and IQ revealed differences at 5. Post-hoc comparisons among the groups with Scheffe tests[22] indicated that for those measures showing overall significant differences among the groups, the SGA groups with and without additional problem(s) did not differ ($P>0.05$). However, comparisons of the average of the two SGA groups with the sample remainder on these measures were significant ($P<0.05$). SGA was associated with poorer performance on all measures at 3 years and poorer verbal comprehension and IQ at 5 years.

DISCUSSION

The present study found that in a large sample of 1037 infants and their mothers in Dunedin, perinatal problems were relatively common: 46% had experienced at least one problem while 19% had experienced two or more problems. However, most of these perinatal difficulties were not significantly associated with later cognitive disadvantage. Furthermore, the perinatal problems accounted for only a small percentage of the variance of the cognitive ability measures; 3% at age 3, reducing to only 1% by age 7. This suggests an attenuation of some of the effects of perinatal problems over time. It should be emphasized, however, that this result does not preclude larger effects being found in the very small number of children who experience severe perinatal problems, such as very low birth weight plus neonatal complications. In addition, the effects of some perinatal problems could not be studied in this sample because of their low base rate.

The finding that the majority of perinatal problems were not associated with disadvantaged cognitive development is encouraging. In contrast to much overseas research which has linked perinatal problems with disadvantaged cognitive development, the Dunedin results suggest that children who experience these problems cannot be considered to be significantly disadvantaged in this respect. The results from the Dunedin study may reflect important differences between Dunedin and other settings where similar research has been carried out and this is supported by the lack of a significant

Table 4 Comparison of SGA groups with and without additional perinatal problems and the remainder of the sample on language and intelligence measures (values are means).

Measure	Group: SGA only	SGA plus other problem(s)	Remainder	Test-statistic
Age 3	n = 53†	n = 40	n = 935	F(2,1025)
Verbal comprehension	31.4	30.6	35.2	9.78*
Verbal expression	34.1	31.3	36.1	7.43*
Picture vocabulary	21.2	19.2	23.8	5.92*
Age 5	n = 51	n = 39	n = 896	F(2,983)
Verbal comprehension	49.1	48.6	51.1	6.57*
Verbal expression	48.8	48.6	50.4	2.34‡
IQ	100.3	100.9	106.4	5.06*
Age 7	n = 46	n = 36	n = 868	F(2,947)
Verbal comprehension	26.5	27.1	29.1	2.97‡
Verbal expression	27.8	28.4	29.7	1.24‡
IQ	103.4	103.1	107.2	2.77‡

†Values of n differed slightly for each measure owing to missing data. n Values shown are the maximum number in the groups at any one age. *$P<0.01$; ‡ n.s. not significant.

association between perinatal problems and socio-economic status in the present sample. In most overseas studies,[23] children who experience perinatal problems tend to come from significantly socio-economically disadvantaged backgrounds.

Two perinatal problems appeared to be consistently associated with some degree of alteration of cognitive development. These were being small for gestational age, particularly at age 3 and 5 years, and being a twin. The finding of an association between being SGA and later disadvantage in cognitive development is of some interest, as these children did not have significant socio-economic disadvantage. This result is similar to those of several overseas studies[3,24–29] and suggests that low birthweight for gestational age deserves further study and preventive efforts. Both early language (most noticeably verbal comprehension) and intelligence decrements were associated with SGA. This particular perinatal problem was frequently accompanied by other problems in the present sample. However, the presence of additional perinatal complications did not modify the effect of SGA on cognitive development. A promising direction for future research is given by a recent study by Parkinson *et al.*[30] who found that a group of small for gestational age children whose growth of head size began to slow before 26 weeks gestation performed less well at school than those who had no evidence of slow intrauterine head growth. The authors concluded that school achievement in children who were small for gestational age is partly related to severity of slow growth before birth. Further research might include serial measures of prenatal head growth among other perinatal factors in the search for reasons why children who were small for gestational age experience disadvantaged cognitive development during the first seven years of life.

Twins were found to be at a significant disadvantage in comparison with singletons particularly at ages 3 and 7. The absence of a significant effect at age 5 may be due to chance fluctuations in the data associated with the relatively small sample of twins. Elsewhere in a more detailed study of the development of twins as 3-year-olds,[31] it was noted that nearly three-quarters of these children experienced multiple perinatal problems. When these twins were compared with a group of children matched in terms of their perinatal histories, the differences in cognitive development disappeared. This was interpreted as suggesting that twins tend to have more developmental problems than singletons because of perinatal rather than postnatal disadvantage.

It is of note that low Apgar scores at birth while not being associated with early cognitive disadvantage did show an association with poor cognitive ability at age 7. At this age, the 12 children in this group were, on average, ten IQ points below the sample remainder.[10] Once again, this may be due to chance variation in the data, it may be related to other problems experienced by the children with low Apgar scores, or it may indicate a disadvantage which only becomes apparent with age. The follow-up of these children as they become older should indicate whether this later disadvantage represents a stable effect.

Finally, while further detailed perinatal research with other samples is desirable, it is also necessary to continue to chart the long-term development of the present sample. This will enable a study of whether the disadvantaged development during the first seven years of life associated with being a twin or small for gestational age continues until adolescence or becomes less significant with time. At the same time, it will be of interest to see whether any of the other perinatal problems turn out to be associated with cognitive disadvantage during a later stage of development.

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