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Early Developmental Progress of Preterm Twins Discordant for Birthweight and Risk

A. Stauffer, W.J. Burns, K.A. Burns, J. Melamed, C.E. Herman

Department of Pediatrics, Northwestern University Medical School and Northwestern Memorial Hospital, Chicago, Illinois, USA

Abstract. Studies of developmental progress in high-risk twins have disparate findings. In this study, we report the outcome of 45 twin pairs born between 26 and 37 weeks gestation, and whose birthweights ranged from 840 to 2000 g. No significant differences were found for weight, risk and birth order. However, earlier preterm infants were found to have significantly lower mental scores on the Bayley Scales of Infant Development at 24 months, and lower IQ scores on the Stanford Binet Intelligence Scale at 36 months. These findings imply that gestational age is a powerful variable in determining developmental outcome.

Key words: Prematurity, Infant development, Follow-up

INTRODUCTION

Studies of developmental progress in twin pairs have examined the variables of both birthweight [12] and birth order [9]. How these results apply to preterm twins whose progress differs depending on the extent of prematurity and number of postnatal complications is unclear.

When twins differ in birthweight, one finding is that the larger twin is more behaviorally competent than the smaller one [12]. Other research suggests that the lower birthweight twin of a pair has a slower rate of physical and cognitive development [2,3,15]. A possibility is that the lower birthweight twin may have developmental lags due to a smaller portion of oxygen and nutrients of the intrauterine environment [12]. Other studies report no differences among discordant twin pairs [6,16]. Field et al [5] argued that the earlier conflicting results were the results of design problems. They explained that the studies had different criteria for discordance, and hypothesized that the lower birthweight twin might in fact be expected to show a developmental advantage by one year due to more affiliation with the mothers. Their hypothesis was confirmed. They found that the lower birthweight twin of discordant pairs actually performed better on the Bayley Scales at one year, perhaps because of compensatory treatment from the caregiver who perceived this smaller twin to be more vulnerable.

A second factor that may count for differences in developmental outcome in twin pairs is birth order. Ellis et al [4] found that the second infant born of 100-500 g pair was at very high risk for complications and mortality. Other studies of term infant suggest similar results [9].

Although the studies noted above suggest differences in developmental outcome in twin pairs depending on birth order and weight order, results are difficult to generalize in speculating about outcome in the high-risk preterm twin population followed at the Prentice Hospital Developmental Evaluation Clinic. Recent well-designed perspective, and longitudinal studies have followed the outcome of full-term children with no medical complications [8,11,13]. Field et al [5], who looked at the effects of weight discordance, followed preterm infant twins who where 33-36 weeks gestational age at birth, and had fewer postnatal complications than many of the twins we followed. In addition, the number of follow-up appointments were not frequent enough or continued far enough beyond early infancy to determine if cognitive differences between these twin pairs existed or not.

At present, most information about the course of high-risk premature infants exists in developmental outcome studies of singletons, not twin pairs. The body of knowledge about developmental outcome in high-risk prematures has expanded in the past decade. Design characteristics of these studies vary. Many studies lump high-risk premature infants together with little regard for type of medical complications, or extent of prematurity [7,14]. Consequently, although we now know that a significantly larger proportion of premature infants have developmental problems that require early intervention, we do not yet have clear information that helps us know what the mediating variables of recovery are. It is difficult to know which parents to strongly encourage to bring their children for follow-up, and to judge how long infants should be followed before discharge from follow-up programs if their appointments are favorable.

Evaluation of the literature led to the following questions that might be answered by evaluating our sample of high-risk twin infants. First, could high-risk premature twins be distinguished later in development by the variables of weight order and/or birth order? If so, would we see the same compensation effect Field et al [5] reported with the weaker twin scoring better developmentally by the age of 12 months? If high-risk premature infants are separated into subgroups of prematurity by gestational age and risk by perinatal complications, are there differences within the premature population according to these variables?

MATERIALS AND METHODS

Subjects

The 45 twin pairs of the sample were seen for developmental follow-up at birth, 3, 6, 9, 12, 24, and 36 months at the Northwestern Memorial Hospital Developmental Evaluation Clinic between 1979 and 1983. All babies met the criteria for developmental follow-up delineated in Table 1. Because of failure to attend clinic appointments by one or both twins at various points in time, the size of the sample varied at each age level (see Table 2). Babies were of 27-46 weeks gestational age at birth with a mean age of 31.5 weeks. They weighed 840-2000 g at birth. Since one group of analyses was proposed to determine how developmental outcome varied depending on weight order, weight discordance was established in the same manner as Field et al [5] with the heavier twin 15% heavier.

Table 1 - Criteria for follow-up: At least one of these had to be met for enrollment

1. Birthweight less than or equal to 1500 g
2. Respiratory distress requiring more than 5 days of assisted ventilation
3. Documented intracranial hemorrhage
4. Evidence of hypoxic-ischemic encephalopathy
5. Documented TORCH infection
6. Documented bacterial meningitis
7. Maternal chemical dependency
8. Maternal diabetes mellitus
9. Conditions known to be associated with developmental disorders such as chromosomal anomalies, idiopathic seizure disorder, genetic syndromes, aminoacid/metabolic disorders

Table 2 - Mean Bayley MDI and Binet IQ scores x risk category

Age (months)	High				Moderate			
	N	Early	N	Late	N	Early	N	Late
3	17	98	8	96	9	100	15	101
6	9	93	11	100	8	97	12	106
9	11	96	10	100	7	94	10	89
12	12	97	7	96	10	99	15	93
18	11	90	10	102	6	94	11	95
24*	10	89	4	105	4	87	9	108
36**	9	82	3	98	6	86	9	111

*$P < 0.05$
**$P < 0.001$

There are several reasons for the large variance at different age intervals. First of all, the number of babies seen for developmental follow-up at the clinic increased steadily since its beginning in 1977. Consequently, many of these infants have not yet reached the age of 36 months. Secondly, a number of parents elected to discontinue follow-up because of the expense of visits or because, of their own or their pediatrician's judgment, the

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infant seemed to be progressing adequately. Table 2 depicts the size of the sample of twins at the large levels evaluated.

Twin pairs came from families evenly distributed between the upper, middle, and lower classes as measured by the Hollingshead norms. In families where there was no active father, the education and occupation of the head of the household was used to compute the scores. Adjustment for prematurity was made in the infant's ages before scores were computed.

Procedure

Infants were seen for developmental follow-up at term, and 3, 6, 9, 12, 24, and 36 months. Brazelton exams and Bayley exams were given by psychologists who had been assessed for scoring reliability. Bayley exams were given by the staff psychologist and the clinic postdoctoral psychology fellow, with a small percentage done by graduate students under the close supervision of staff psychologists. All infants also had medical exams and were given home programs by the clinic educators if they did not attend a regular infant program. Evaluations by physical or occupational therapists and a speech and language pathologists were provided as needed.

Extent of risk for each infant was measured by the Postnatal Complications Scale [10]. Medical charts from the special care nursery stay of each infant were used to compute scores. Babies in the present sample were separated into two groups according to risk: moderate risk, high risk. Although Parmalee scores can range from 50 (highest risk) to 160, infants in the present study had scores ranging from 55 to 104 (Table 3). These scores suggest that all infants in the present study were very-high-risk infants with many medical complications. Gestational age at birth was assessed by the attending neonatalogist, who assigned an age in weeks by Dubowitz exam at the delivery. Table 3 depicts the population when separated into two groups of gestational age and two risk categories. Because zygosity was not a significant variable in a recent study of cognitive development

Table 3 - Number of newborns entering study at each gestational age and risk category: Risk on the postnatal complications scale

Gestational age	High (55-67)	Moderate (72-104)	
27	4	0	
28	2	2	
29	2	4	
30	10	6	
31	8	2	
Total early preterms	26	14	40
32	11	11	
33	2	10	
34	3	5	
35	0	2	
36	2	2	
37	0	2	
Total late preterms	18	32	50
Grand total	44	46	90

in discordant twin pairs [5] and because of the expense involved in laboratory testing, the variable of zygosity was not included.

RESULTS

The data were analyzed using 2-way analyses of covariance. Because socioeconomic status has been a potent variable in multiple studies examining cognitive functioning, the Hollingshead score was included as a covariate in all analyses. Given the intermittent return of many twins to follow-up visits, it was not possible to use a repeated measure design to evaluate most of our data; the size of our group was reduced too far for statistical tests to be powerful when a longitudinal design was attempted. Therefore, the data were evaluated cross-sectionally except for designated analyses. Neonatal assessments were scored using the Als [1] cluster which load scores from the 57 item exam into the following four categories: interactive process, motoring functioning, state control, and physiologic response to stress (Table 4).

Table 4 - Means for neonatal measures of newborns categorized by gestational age and degree of risk

	Early preterm		Late preterm	
	High risk (N = 26)	Moderate risk (N = 14)	High risk (N = 18)	Moderate risk (N = 32)
Gestational age	30	30	33	35
Birthweight	1315	1108	1415	1746
Mean weight discordance	262 g		239 g	
Brazelton interaction	2.30	2.94	2.82	3.02
Motor	2.33	2.48	2.39	2.51
State	2.33	1.95	2.04	2.41
Response to stress	1.15	1.26	1.99	1.28
Postnatal complications	63	82	67	79

The first question of interest was whether twins would differ in developmental outcome depending on weight order. ANCOVA' scores were computed for each age grouping with the independent variables of weight order and dependent variable of Bayley Mental and Motor Scores. Covariates were risk and SES. No significant differences at any age level were observed across discordant twin pairs whether the dependent variable was the Bayley MDI or PDI.

A second group of analyses was performed to examine differences in twin development that might be accounted for by birth order. A 2-way ANCOVA compared twin groups by birth order at 3, 6, and 12 months. Risk and SES were covariates in both cases. No significant findings were obtained from these analyses.

A third group of analyses examined whether extent of risk and extent of prematurity determined developmental outcome. Parmalee scores separated the infants into two groups: high risk and moderate risk. Babies were also separated into two groups by gestational age: 32-37 weeks, and 26-31 weeks. In these analyses, the babies were grouped together as a singular group of high-risk prematures, differing by gestational age and extent of medical complications.

Significant results at 24 and 36 months ($P < 0.05$) suggested that infants born between 26 and 31 weeks had significantly lower Bayley mental scores at 24 months and Binet intelligence scores at 36 months than infants born between 32 and 37 weeks gestation. This finding held whether risk based on medical complications was moderate or high. Analyses for data collected for these same babies at 3, 6, 9, 12, and 18 months were not significant. Analyses of Brazelton cluster scores also yielded significant finding for the factors of interactive process and state organization.

DISCUSSION

In the present study, differences in developmental outcome in discordant twin pairs were not found. Neither the benefit of a higher birth weight and possible better intrauterine nourishment, nor the possible benefit of receiving compensatory treatment from a caregiver as the lower birthweight more vulnerable twin was observed. Studies of high-risk twin pairs discussed earlier most often indicate postnatal illness as a potent variable in outcome. Since our sample was at very high risk, it could be that the similarity of postnatal medical complications was very powerful and erased differences that might have been based on differences in the intrauterine environment.

Differences in developmental outcome based on birth order were also not observed in the present study. Again, it is possible that postnatal complications and prematurity were so powerful that the benefit of being first born and having better continuous oxygen supply during the birth process was erased. It is also possible that the number of cesarean section deliveries in our population of high-risk twin pairs moderated a possible significant finding.

Most interesting was the finding that high-risk infants born between 26 and 31 weeks and those born between 32 and 37 weeks had similar developmental courses until 24 months. At 24 months, the younger infants could be distinguished from the older ones, not by the risk factor, but by gestational age at birth. This finding persisted in the group at 36 months. Since some parents opted to discontinue clinic visits at 24 months, it could be argued that the population that remained was indeed one with more apparent developmental lags. Regardless, in the group that was seen, it is notable that the children could be separated by gestational age and that postnatal illness was no longer a significant factor. Socioeconomic status was not significant in accounting for this finding. The implication is that gestational age at birth is a powerful mediating variable across social classes in predicting outcome for high-risk premature infants. It seems that recovery from the complications of prematurity is more complete if the infants is 32-37 weeks at birth.

A question in the minds of pediatricians, neonatologists, family practitioners, and others who are asked to judge whether infants must continue to be followed in special programs, is how long they should be observed if they seem to fall within normal limits in early infancy. The results of the present study suggest that infants born before 32 weeks should be followed continuously through the preschool years so that these children might benefit from the advantage of early intervention services as necessary.

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Correspondence: Dr. W.J. Burns, Prentice Women's Hospital, Suite 462, 333 E. Superior Street, Chicago, IL 60611, USA.