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Triplets Across the First 5 Years: The Discordant Infant at Birth Remains at Developmental Risk



WHAT'S KNOWN ON THIS SUBJECT: There has been no study of the development of triplets across the first years of life in a well-matched longitudinal design.



WHAT THIS STUDY ADDS: This study shows the development of triplets in the cognitive, neuropsychological, social, and emotional domains from birth to 5 years. We show that although most triplets display developmental catch-up in all domains, discordant triplets remain at a developmental risk.

abstract

OBJECTIVES: To examine whether the risk posed to infant development by triplet birth persists into childhood and whether growth-discordant triplets are at a particularly high developmental risk.

METHODS: Twenty-one sets of triplets were matched with 21 sets of twins and 21 singletons ($N = 126$) for medical and demographic conditions and were followed from birth to 5 years. At 6, 12, and 24 months, cognitive development was assessed and mother-infant interactions were coded for maternal sensitivity and child social engagement. At 5 years, the children's cognitive development and neuropsychological skills were tested, social engagement was coded from mother-child interactions, and behavior problems were examined. Maternal adjustment was assessed during interviews at 1 and 5 years.

RESULTS: Although triplets showed lower cognitive performance at 6, 12, and 24 months as compared with singletons and twins, differences were attenuated by 5 years in both global IQ and executive functions. Similarly, the lower social engagement observed across infancy and the higher internalizing symptoms reported at 2 years for those in the triplet group were no longer found at 5 years. Difficulties in maternal adjustment among mothers of triplets decreased from 1 to 5 years. However, in 65.2% of the initial sample there was a weight discordance of $>15\%$ at birth, and the discordant triplets showed poorer cognitive and social development as compared with their siblings across infancy. At 5 years, the discordant children demonstrated lower cognitive and executive functions performance, decreased social engagement, and higher internalizing symptoms as compared with both siblings and peers.

CONCLUSIONS: Whereas most triplets catch up after an early developmental delay, the risk for discordant triplets seems to persist into childhood. Such infants, who are at both biological and environmental risk, should receive special and consistent professional care. *Pediatrics* 2009; 124:316–323

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KEY WORDS

triplets, twins, multiple birth, cognitive development, executive functions, social engagement, parent-child relationship, longitudinal studies

ABBREVIATIONS

AGA—appropriate for gestational age
CIB—Coding Interactive Behavior
CRIB—Clinical Risk Index for Babies
MANCOVA—multivariate analysis of covariance
ANCOVA—analysis of covariance
ES—effect size

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Although triplets are the fastest growing birth populations in the Western world^{1–6} and medical outcome of triplet pregnancies has improved markedly in recent years,^{7–16} little is known about the long-term development of children born as part of a triplet set. To date, no well-designed longitudinal study has followed the development of triplets across the first years of life, leaving a gap in current knowledge as to the cognitive, social, emotional, and neuropsychological development of this population. In previous publications,^{17–19} we reported on the development of triplets across the first 2 years as compared with twins and singletons matched for demographic and medical conditions. We found that triplets as a group showed slower cognitive and social-emotional growth across infancy. Parents reported high parenting stress, the parent-infant relationship was less optimal, and triplets displayed more internalizing symptoms at 2 years. Consistent with research linking these early markers with later psychopathology and compromised functioning,^{20–23} the findings show that triplets are at a higher risk for later cognitive deficits, academic underachievement, poor social adaptation, and lower self-regulation and underscore the need to assess whether this risk attenuates or increases with time.

The risk imposed by triplet birth to infant development was further intensified for a specific subgroup of triplets who suffered growth retardation. Growth retardation is considered a special risk condition for infant development that is associated with cognitive delays, intrusive parenting, emotion dysregulation, and neurodevelopmental immaturity.^{24–28} For 65.2% of the triplet sets in our sample, birth weight discordance occurred. These discordant triplets displayed poorer cognitive development and social-

emotional functioning in comparison to their normally grown siblings and received the lowest amounts of sensitive parenting.^{17–19} Thus, in addition to being born at a greater risk as a result of the cumulative effects of multiple birth, growth retardation, and, often, prematurity, the discordant infant was raised in an environment marked by minimal opportunities for attuned parenting. Such conditions create a paradoxical situation in which growth-retarded infants, who require higher levels of sensitive parenting to reach normative milestones,²⁹ receive the least amount of parental sensitivity, which places them at a higher developmental risk compared with singletons, twins, and nondiscordant appropriate-for-gestational-age (AGA) triplets.

The period between 2 and 5 years marks a stage of significant growth in children's cognitive and social-emotional skills.^{30,31} Global cognitive development is complemented by the development of neuropsychological skills, particularly executive functions that enable goal-directed planning, inhibition, and hierarchical ordering of information. The development of executive functions is particularly important before school entry and reflects the maturation of the prefrontal cortex during the preschool years.^{32,33} Children's social engagement during interactions with their parents increases, and preschool-aged children show a growing adaptation to society's codes of behavior.^{34–36} The preschool years also signify an important time in the development of premature infants, who often show significant catch-up of physical and mental growth by school age.^{37,38} In light of these developments, is it important to assess whether the abnormalities noted in triplets across infancy persist into later childhood or whether they attenuate as children mature, gain independence,

and acquire new cognitive and social competencies.

Cumulative risk models of infant development are guided by 2 central propositions. First, early risk inherent in the infant's biology or environment carries a lasting impact on developmental outcome.^{39,40} For instance, a compromised neurologic profile or stable environmental adversity, such as poverty or domestic violence, bear long-term negative consequence on children's growth. Second, risk conditions exert both cumulative and interactive effects on development, and the impact of intertwined risk is greater than the sum of each risk experienced independently. The triplet situation represents a unique condition, because the environment is typically not marked by persistent adversity only but by transitional stress related to the parenting of 3 infants simultaneously. Because the triplets in our sample did not show greater neurologic impairments as compared with the matched singletons and twins, it was postulated that a developmental catch-up would occur for the triplet group as a whole between 2 and 5 years. However, given that the discordant triplets suffered from several independent risk conditions related to multiple birth, growth retardation, and especially low parental investment, it was hypothesized that the interactions of these risks may lead to a persistent developmental delay in this subgroup.

In light of the factors described above, with this study we examined the development of triplets from birth to 5 years. The initial sample of carefully matched triplets, twins, and singletons was tested at 5 years for cognitive development and neuropsychological skills, with a focus on executive functions, social engagement, and behavior adaptation. Trajectories of cognitive and social development across the first 5 years were examined in 4

groups of children: singletons, twins, triplets, and discordant triplets. We hypothesized that the stress experienced by parents would decrease at 5 years and triplets would show catch-up after early developmental delay; however, among the discordant triplets, the catch-up would be less successful and low cognitive, neuropsychological, social, and emotional abilities would still be observed at 5 years.

METHODS

Participants

The initial cohort included 23 consecutive sets of triplets born at a tertiary medical hospital in Israel. Each set of triplets was matched with a set of twins and a singleton child born during the same period. Infants were matched for birth weight, gestational age, medical risk, and family demographics (maternal and paternal age and education). Birth weight was matched to the average of the triplet set while maintaining a comparable ratio of small for gestational age (birth weight <10th percentile)/AGA (birth weight between the 10th and 90th percentiles) and male/female infants in the 3 groups. Discordance, defined as birth weight >15% between the triplet with the highest birth weight and the triplet with the lowest birth weight, was found in 15 (65.2%) of the sets.

Only 1 infant per set met criteria of discordance. Among twins, discordance was noted in 5 (21%) sets. All children came from 2-parent families in which at least 1 parent was employed, mothers were older than 20 years, and families were middle class. Exclusion criteria were intraventricular hemorrhage grades III or IV, periventricular leukomalacia, perinatal asphyxia (defined as a 5-minute Apgar score of <7), and the absence of signs of clinical encephalopathy, metabolic or genetic disease, and central nervous system infection or abnormal neurologic examination results at discharge. At 5 years, 2 families with triplets missed appointments (1 because of scheduling difficulties and the other because of an inability to locate the family), and the matching twins and singletons were taken out of the final analysis, resulting in 21 sets of triplets, 21 sets of twins, and 21 singletons ($N = 126$). Of the initial 15 sets with a discordant triplet, 14 returned at 5 years. Demographic and medical information for the 126 participants appear in Table 1 and show no group differences. The study was approved by the institutional review board, and all families signed an informed-consent form.

Procedure and Measures

Cognitive development was assessed by trained psychologists at 6, 12, and

24 months (corrected age) with the Bayley Scales of Infant Development, 2nd Edition⁴¹ and at 5 years (mean: 5.32 years [SD: 0.60]) with the Wechsler Preschool and Primary Scale of Intelligence⁴². Executive functions were tested at 5 years with the Developmental Neuropsychological Assessment.⁴³ Child social engagement was coded from 10 minutes of free mother-child interactions (with each child separately for twins and triplets) at 6, 12, and 24 months and 5 years by using the Coding Interactive Behavior (CIB) manual.⁴⁴ Mothers reported children's behavior problems at 2 and 5 years on the Child Behavior Checklist,⁴⁵ and maternal adjustment was assessed at 1 and 5 years during the Parenting Triplets Interview.¹⁹

Infant medical risk was measured by the Clinical Risk Index for Babies (CRIB).⁴⁶

Cognitive Testing

The Mental Development Index (MDI) of the Bayley Scales of Infant Development, 2nd Edition⁴¹ was used at 6, 12, and 24 months, and the verbal IQ score of the Wechsler Preschool and Primary Scale of Intelligence⁴² was used at 5 years. Tests are normed to a mean of 100 (SD: 15). The MDI was selected on the basis of our previous findings that mental, but not psychomotor, abilities are lower in triplets across infancy. Verbal IQ is considered to be continuous with early mental abilities.

Executive Functions

The executive functions score from the Developmental Neuropsychological Assessment,⁴³ a standardized instrument for assessing neuropsychological skills in preschool- and school-aged children, was used, normed to a mean of 100 (SD: 15).

Mother-Child Interaction

Interactions were coded by trained observers blind to birth status by using

TABLE 1 Infant Medical and Family Demographic Factors

	Singletons ($N = 21$)		Twins ($N = 21$ Sets, 42 Infants)		Triplets ($N = 21$ Sets, 63 Infants)	
	Mean	SD	Mean	SD	Mean	SD
Birth weight, g	1674.11	422.17	1646.38	475.28	1651.45	465.38
Gestational age, wk	32.24	2.71	32.52	2.76	32.38	2.74
Medical risk, CRIB score	1.63	2.45	1.30	1.90	1.43	2.19
Mother's age, y	27.84	5.46	28.55	6.03	29.25	4.68
Mother's education, y	14.56	2.42	14.21	1.47	14.01	2.33
Father's age, y	30.08	5.95	31.93	7.59	32.06	5.01
Father's education, y	13.50	3.01	13.93	2.56	14.15	2.95
Gender, % male	52.3		54.7		58.7	
No. of siblings	1.50	1.13	1.32	1.21	1.0	.77
SGA percent	8.7		9.0		8.6	

There were no significant differences between groups for any factor. SGA indicates small for gestational age.

the CIB manual.⁴⁴ The CIB is a global rating system of parent-infant interaction including 42 codes rated from 1 (low) to 5 (high) with good psychometric properties.^{17,18,27,34,47–50} The child social engagement composite was used, which includes child alertness, social initiation, vocalizations/verbal output, gaze, positive affect, joint attention, competent use of environment, and symbolic-creative play (Cronbach's $\alpha = .83-.91$). Two coders were trained to 90% agreement. Reliability, measured on 15 sessions at each stage, averaged 95% ($\kappa = 0.83$). Mean social engagement scores in healthy term infants are 3.10 (SD: 0.64) at 6 months, 3.45 (SD: 0.68) at 12 months, 3.76 (SD: 0.67) at 24 months, and 4.00 (SD: 0.59) at 5 years.

Behavior Problems

The internalizing score of the widely used parent-report Child Behavior Checklist⁴⁵ was used on the basis of our previous findings that internalizing, but not externalizing, problems were especially high in triplets at 2 years.¹⁹ Internalizing scores of >60 indicate mild risk, and scores of >64 indicate severe psychopathology.

Maternal Adjustment

Maternal adjustment scores averaged 4 questions from the hour-long interview considering maternal adaptation to parenting ($\alpha = .78$ and $.72$ at 1 and 5 years, respectively).

Statistical Analysis

Trajectories of cognitive development and social engagement at 6, 12, and 24 months and 5 years were examined with multivariate analysis of covariance (MANCOVA) with repeated measure, with group (singletons, twins, triplets, discordant triplets) and child gender as the between-subject factors and children's birth weight and CRIB scores as covariates. The repeated polynomial was used to assess

changes between each time point and the next. Following main effects for group, univariate analysis of variance with posthoc Scheffé tests was conducted. Internalizing symptoms at 2 and 5 years were examined with repeated-measure MANCOVA with group and child gender as the between-subject factors and birth weight and CRIB scores as covariates. Group differences in executive functions were examined with analysis of covariance (ANCOVA), controlling for birth weight and CRIB scores and with posthoc Scheffé tests. Using Pearson's correlation we examined associations between outcome measures at 5 years. The sample size provided sufficient power ($d = 0.85$) to detect a medium effect size (ES) of 0.5.⁵¹

RESULTS

Cognitive Abilities

Repeated-measure MANCOVA controlling for birth weight and CRIB score yielded a significant overall main effect for time, indicating that intelligence changed with age for all infants (sphericity assumed $F_3 = 10.64$; $P < .001$; ES = 0.14). IQ decreased from 6 to 12 months ($F_{1,118} = 21.22$; $P < .001$; ES = 0.27), increased from 12 to 24 months ($F_{1,118} = 8.44$; $P < .001$; ES = 0.12), and further increased from 2 to 5 years ($F_{1,118} = 12.03$; $P < .001$; ES = 0.14). A main effect was found for group ($F_{3,120} = 7.36$; $P < .01$; ES = 0.11). ANCOVA with posthoc Scheffé tests showed that at 6 months singletons and twins scored higher than triplets and discordant triplets and that at 12 and 24 months singletons and twins scored higher than triplets, who scored higher than discordant triplets. However, at 5 years, differences were only found between singletons, twins, and triplets on the one hand and discordant triplets on the other. The findings are presented in Fig 1, and data for 5 years appear in Table 2.

Social Engagement

Repeated-measure MANCOVA showed a main effect for time, indicating that social engagement changed with age (sphericity assumed $F_3 = 24.87$; $P < .001$; ES = 0.43). Social engagement increased from 6 to 12 months ($F_{1,118} = 7.96$; $P < .001$; ES = 0.08), increased from 12 to 24 months ($F_{1,118} = 5.12$; $P < .01$; ES = 0.06), and further increased from 2 to 5 years ($F_{1,118} = 4.99$; $P < .05$; ES = 0.06). Posthoc tests showed that at 6 months singletons and twins scored higher than triplets and discordant triplets; at 12 and 24 months, singletons and twins scored higher than triplets, and triplets scored higher than discordant triplets; and at 5 years, singletons, twins, and triplets scored higher than discordant triplets (Fig 2; Table 2).

Internalizing Symptoms

Repeated-measure MANCOVA showed no overall change from 2 to 5 years. However, the interaction of time and group was significant ($F_{3,120} = 3.74$; $P < .01$; ES = 0.07). Whereas at 2 years singletons and twins scored lower than triplets who scored lower than discordant triplets, at 5 years the discordant triplets scored above all other groups (Fig 3; Table 2).

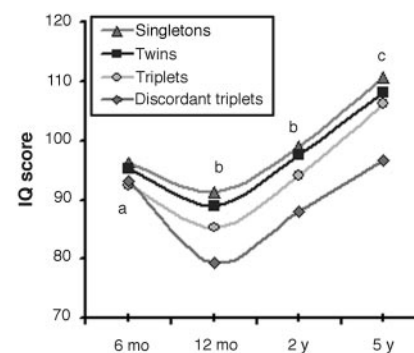


FIGURE 1

Cognitive development from 6 months to 5 years in singletons (S), twins (T), triplets (Tr), and discordant triplets (DTr). ^a S, T > Tr, DTr, ^b S, T > Tr > DTr, and ^c S, T, Tr > DTr ($P < .05$).

TABLE 2 Developmental Outcomes at 5 Years in Singletons, Twins, Triplets, and Discordant Triplets

	Singletons (N = 21)		Twins (N = 42)		Triplets (N = 49)		Discordant Triplets (N = 14)		Univariate F; 2	P
	Mean	SD	Mean	SD	Mean	SD	Mean	SD		
Verbal IQ	110.72	14.66	108.31	17.51	106.27	16.42	95.63	15.31	4.03 ^a ; S, T, Tr > DTr	.034
Social engagement	3.71	0.94	3.58	.87	3.43	0.75	2.92	0.69	4.21 ^a ; S, T, Tr > DTr	.028
Internalizing symptoms	47.89	10.38	48.03	11.69	48.71	10.87	53.26	10.26	3.84 ^a ; S, T, Tr < DTr	.047
Executive functions	102.68	12.61	98.86	13.38	97.73	13.45	91.62	11.34	3.81 ^a ; S, T, Tr > DTr	.049

S indicates singleton; T, twins; DTr, discordant triplets.

Executive Functions

ANCOVA with posthoc Scheffé tests showed a significant effect for group ($F_{3,120} = 3.96$; $P < .05$; $ES = 0.05$), and differences were found between the first 3 groups and the discordant triplets (Table 2). Discordant triplets scored especially poorly on the visual attention and “tower” (planning) subsets.

Maternal Adjustment

Repeated-measure MANCOVA showed an overall change in maternal adjustment from 1 to 5 years ($F_{1,56} = 3.32$; $P < .01$; $ES = 0.05$), indicating better adjustment to parenting for all mothers. A group-by-time interaction was found ($F_{1,56} = 3.77$; $P < .01$; $ES = 0.07$), indicating greater change in adjustment among mothers of triplets.

Correlations Between Outcome Measures at 5 Years

Cognitive development correlated with executive functions ($r = 0.36$; $P < .001$), and IQ correlated with child social engagement ($r = 0.25$; $P < .05$). Social engagement, in turn, was related to lower internalizing symptoms ($r = -0.30$; $P < .01$). Higher maternal adjustment correlated with child social engagement ($r = 0.29$; $P < .01$), executive functions ($r = 0.19$; $P < .05$), and lower internalizing symptoms ($r = -0.33$; $P < .01$).

Discordant twins ($n = 5$) did not show poorer performance than their sibling on any test at 5 years, indicating that the combination of discordance and triplet birth predisposes children to higher risk.

DISCUSSION

To our knowledge, this was the first study to follow the development of triplets across the first 5 years of life in the cognitive, neuropsychological, social, and emotional domains. Results indicate that after an initial delay in infancy, triplets showed a developmental catch-up, and differences between singletons, twins, and triplets as a group were no longer observed at 5 years. However, a subgroup of triplet children, who were born with discordant low birth weights compared with their siblings and had an especially poor performance across infancy, continued to demonstrate lower cognitive performance, executive functions, and

social engagement as compared with singletons, twins, and normally grown triplets at 5 years. We postulate that the critical factor contributing to this persistent lower performance was the comparative low birth weight of the discordant infant, reflecting a poor intrauterine environment for this fetus compared with the siblings, and not any absolute weight percentile.⁵² These findings have practical implications for the care of triplets and their parents in general and the need for special attention to discordant triplets in particular.

The triplet situation marks a unique developmental risk that likely stems from a combination of biological factors (including triplet pregnancy and, often, prematurity) and environmental factors, particularly high parenting stress. Yet, triplets are often raised in environments with only transient risk.

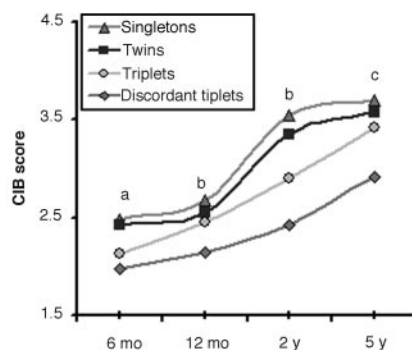


FIGURE 2 Social engagement from 6 months to 5 years in singletons (S), twins (T), triplets (Tr), and discordant triplets (DTr). ^a S, T > Tr, DTr, ^b S, T > Tr > DTr, and ^c S, T, Tr > DTr ($P < .05$).

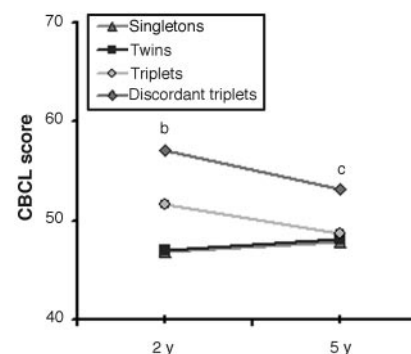


FIGURE 3 Internalizing Symptoms at 2 and 5 Years in singletons (S), twins (T), triplets (Tr), and discordant triplets (DTr). ^a S, T > Tr > DTr and ^b S, T, Tr > DTr ($P < .05$). CBCL indicates Child Behavior Checklist.

During the preschool years, children enter out-of-home care, form friendships, and engage in meaningful interactions within the sibling group; thus, nonkin providers, friends, and siblings become important contributors to growth and skill acquisition. At that stage, parenting stress decreases, and the effects of early biological risk are reduced among children with no neurologic impairments. The catch-up documented here between 2 and 5 years is unique in the developmental literature, particularly as it demonstrates such across-the-board improvement in multiple developmental domains. These findings highlight the plasticity of development and send an optimistic message to parents and triplets as well as to researchers and clinicians who focus on the effects of early intervention.

In contrast, consistent with models on cumulative risk,^{21,22,27,39,40} the discordant growth-retarded triplets remained at high risk. It is important to note, however, that the persistent delay for the discordant group occurred in the context of much developmental growth, and the children's intelligence and social engagement increased dra-

matically from 1 to 5 years. Yet, the gains shown by these growth-retarded triplets were less than those observed in their siblings and significantly smaller than the substantial gains required to catch up with their normally developing peers. This inability to close the developmental gap placed the discordant triplets at a higher risk during the entire dynamic preschool period.

The findings have clear implications for intervention and social policy. The data emphasize the need to find medical methods to decrease the rates of growth retardation in multiple-gestation pregnancies and to guide parents on the potential pitfalls in raising the discordant child. Parents should be aware of the need of growth-retarded children for maximal sensitivity during the first years to compensate for their low inborn regulatory abilities. The findings also highlight the importance of allocating funds to help parents of triplets during the stressful period of infancy. Parents typically report the centrality of instrumental help during the first months,⁵³⁻⁵⁶ and such assistance may reduce the developmental delay observed during infancy.

Finally, the delay in executive functions found among the growth-retarded triplets, particularly in planning and visual attention skills, may be especially harmful on school entry. Early awareness of these difficulties may lead to special interventions for fostering these skills before school failure.

Limitations of the study relate to the fact that the sample was of middle-to-high socioeconomic status and all infants were of low medical risk; thus, the generalizability of the findings may be limited, especially because our growth-retarded children probably presented optimal functioning for this group. Future research is required to follow both AGA and growth-retarded triplets into later childhood and adolescence to ascertain if the neurodevelopmental abnormalities demonstrated here persist into later childhood and adolescence.

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