Comparative Development of Surviving Co-Twins of Vanishing Twin Conceptions, Twins and Singletons

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Early loss of one fetus in a multiple gestation as a 'vanishing' twin is a well recognized phenomenon. It is uncertain whether this has an impact on the development of the surviving co-twin. The aim of this study is to compare the development of singletons, twins and the surviving co-twins of a vanishing twin. The 324 children born to 229 women who were recruited into the study between 1999 and 2001 formed the study population. Children were assessed at 1 year of age with Griffiths Mental and Developmental Scales. A neurological examination was performed using an optimality score to exclude those with severe neurodisability. Three hundred and five children (92 singletons, 180 twins and 33 survivors with a vanishing twin) were included. The sub- and general quotient scores in singletons and surviving co-twins of a vanishing twin did not differ significantly. Twins had significantly lower scores than singletons in all areas of development and were more likely to be born early with lower birthweights. Following adjustment for gestation and birthweight, the difference between the two groups was nullified suggesting that the slower development of twins is related to their prematurity and lower birthweight.

Several reports have noted that twins are less cognitively able than singletons (Clark & Dickman, 1984; Deary et al., 2005; Ronalds et al., 2005). In some multiple gestations there may be the loss of one or more fetuses early in gestation, the 'vanishing' twin (VT; Landy et al., 1986). It is not clear whether the development of the surviving co-twin of a VT is comparable to that of twins or singletons.

Most early studies comparing the development of twins and singletons were done when standards of obstetric and neonatal intensive care differed from that currently available. Women who go into early labour now receive antenatal steroids. Postnatally, many preterm infants receive prophylactic surfactant therapy. In addition, there has been a significant improvement in ventilation strategies used. These have contributed to the reduction in mortality and morbidity among premature infants. In addition, there has been a rise in the frequency of multiple births attributable to the increasing use of assisted reproductive techniques. These innovations have resulted in significant changes in the population characteristics of both singletons and twins. It is pertinent, therefore, to determine whether there are differences in the development of twins and singletons in this altered population.

The aim of this study is to compare the development of co-twin survivors of an early fetal loss, singletons and twins.

Materials and Methods

This prospective study is a component of a larger study aimed at exploring the consequences for the survivor in a twin gestation with a VT. The development of singleton survivors of a VT, twins and singletons is compared. The study population recruitment of surviving co-twins of a VT and control twin and singleton groups has been previously described (Anand et al., 2007).

Follow-Up

Children from 229 pregnancies (95 singleton, 95 twin and 39 VT) underwent developmental assessment and neurological examination at 1 year of age using Griffiths Mental and Developmental scales (Griffiths, 1996) and an Optimality score (Haataja et al., 1999). Among the 39 VT, there was a pair of twins from triplet conception with a vanishing embryo. To maintain the uniformity of the group these twins were excluded. In one twin pair there was a late fetal death and the co-twin was a livebirth. There remained a total of 322 children from 228 pregnancies that were assessed (95 singletons, 189 twins and 38 children from VT gestations). In three singletons, six twins and five children from VT pregnancies the assessment was incomplete as the children did not cooperate in the assessment. One child was not assessed

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Table 1
General Characteristics of Participants

	Singletons	Vanishing	Twins
	92	33	180
Male:Female	50:42	20:13	100:80
Mean gestational age (weeks)	39.5	39.8	35.3
Mean birthweight (grams)	3479	3430	2408
Mean head circumference (cm) at birth	34.8	34.7	32.4
Mean head circumference (cm) at 1 year	47.0	47.1	46.8

because of incapacity from a fractured arm. In one twin pair, the assessment could not be performed until the twins were 2 years old. This pair was excluded from the analysis. Following these exclusions, data from 305 children were used in the final analysis.

Statistical Analysis

The data were analyzed using SPSS v12. Differences between the groups for subquotient and general quotient scores were tested using the Student's t test. Analysis of co-variance was used when adjusting for confounding variables. In an analysis of co-variance, it is assumed that the observations in the groups being compared are independent. However, both members of a twin pair are not statistically independent. Therefore, comparisons between singletons and twins were made using either Twin 1 or Twin 2 or the twin with the lowest birthweight in an analysis of covariance. Within twin pair comparisons were made using the matched pair t test. Differences in birthweight and developmental scores within twin pair were correlated using Pearson's product moment correlation coefficient.

Results

Developmental assessment was performed at a mean age of 13 (range 12–16) months. The general characteristics of the different groups are presented in Table 1.

Comparison of Index Singletons and Control Singletons

The gestational age and birthweight in these two groups are similar. In 21 cases the diagnosis of VT was 'definite' and in 12 it was 'probable'. The subquotient scores were similar in both these groups (data not shown) and both groups were combined for comparison with control singletons.

When compared with control singletons the subquotient scores of survivors of the VT index group were

Table 2
Comparison of Singletons and Children From Vanishing Twin Pregnancies

Scale	Mean quotients		Difference in means (confidence intervals); *p* value
	Singletons $N = 92$	Vanishing $N = 33$	
Locomotor	99.6	97.0	2.6 (–4.0 to +9.2.5); *ns*
Personal–social	104.6	102.5	2.1 (–2.9 to +7.2); *ns*
Hearing and language	107.8	103.7	4.1 (–1.0 to + 9.2); *ns*
Eye and hand coordination	110.5	110.6	–0.1 (–5.3 to +4.9); *ns*
Performance	103.2	101.9	1.3 (–3.9 to +6.5); *ns*
General quotient	105.3	102.5	2.8 (–1.7 to +7.1); *ns*

Note: *ns* = not significant

Table 3
Comparison of Singletons and Twins

Scale	Mean quotients		Difference in means before adjustment (confidence intervals); *p* value	Difference in means after adjustment for gestational age and birthweight (confidence intervals); *p* value
	Singletons $N = 92$	Twins $N = 180$		
Locomotor	99.6	87.3	12.3 (8.0–16.5); < .001	0.7 (–4.7 to +6.2); *ns*
Personal–social	104.4	94.1	10.3 (7.3–13.2); < .001	1.6 (–2.1 to +5.4); *ns*
Hearing and language	107.5	100.2	7.3 (4.0– 0.4); < .001	0.5 (–4.6 to +3.6); *ns*
Eye and hand coordination	110.3	99.6	10.7 (7.6–13.8); < .001	1.9 (–1.9 to +5.9); *ns*
Performance	103.1	91.7	11.4 (8.0–14.7); < .001	2.4 (–1.7 to +6.8); *ns*
General quotient	105.1	94.3	10.8 (8.1–13.6); < .001	1.9 (–2.1 to +4.5); *ns*

Note: *ns* = not significant

Table 4

Comparison of Lower Birthweight (LoBW) and Higher Birthweight (HiBW) Twins

Scale	Mean quotients		Difference in means (confidence intervals); *p* value
	LoBW twin *N* = 88	HiBW twin *N* = 88	
Locomotor	87.8	87.1	0.7 (–2.1 to +3.5); *ns*
Personal–social	94.6	93.5	1.1 (–0.6 to +2.7); *ns*
Hearing and language	99.4	99.8	–0.4 (–1.9 to +1.1); *ns*
Eye and hand coordination	99.6	99.5	0.1 (–2.1 to +2.3); *ns*
Performance	92.3	90.8	1.5 (–1.1 to +4.0); *ns*
General quotient	94.4	93.8	0.6 (–0.8 to +2.1); *ns*

Note: *ns* = not significant

Table 5

Comparison of Monochorionic and Dichorionic Twins

Scale	Mean quotients		Difference in means (confidence intervals); *p* value
	Monochorionic *N* = 32	Dichorionic *N* = 140	
Locomotor	86.5	87.1	–0.6 (–7.1 to +6.0); *ns*
Personal–social	92.8	94.2	–1.4 (–6.0 to +3.3); *ns*
Hearing and language	104.4	98.6	5.8 (0.8 to 10.7); .02
Eye and hand coordination	98.7	99.6	–0.9 (–5.5 to +3.7); *ns*
Performance	91.0	91.8	–0.8 (–5.9 to +4.4); *ns*
General quotient	94.7	93.8	0.8 (–3.3 to +5.0); *ns*

Note: *ns* = not significant

similar in all areas of development (Table 2). At the age of 1 year, the development of children from VT conceptions is similar to that of singleton control pregnancies.

Twins and Singletons

There was a 4-week difference in mean gestational age of twins and singletons (35.3 weeks vs. 39.5 weeks). The mean birthweight also differed significantly (2408 g vs. 3479 g).

In all areas of development, twins were noted to be significantly slower than singletons. However, twins were born earlier and had a lower birthweight. Following adjustment for gestational age and birthweight, no significant differences in developmental scores between the twins and singletons were found (Table 3). Using only Twin 1 or Twin 2 or the twin with the lowest birthweight for comparison did not alter the findings significantly.

Twins

A within-pair development comparison of twins was made. Matched data were available for 88 pairs. There were no significant differences in development scores within twin pairs (Table 4). Furthermore, there was no association within twin pairs between birthweight difference and developmental score difference (Figure 1).

Monochorionic (MC) twins are at greater risk than dichorionic (DC) twins for several neurodevelopmental and other problems. Therefore, comparisons were made between the development of MC and DC twins. No significant differences in the developmental

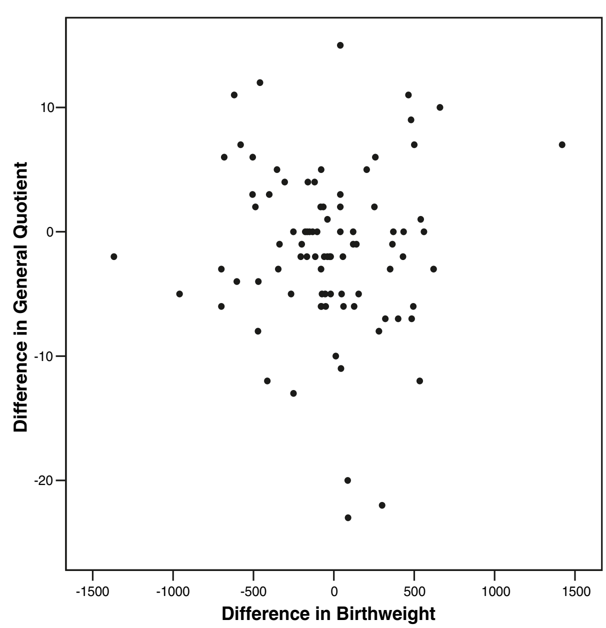

Figure 1

Correlation between difference in birthweight and general quotient within twin pair.

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abilities were found except for hearing and language skills where MC twins did better than DC twins (Table 5).

Gender Comparison

When comparison was made between singletons and twins based on gender, twin girls and boys had significantly lower scores than their singleton controls. However, when adjusted for gestation and birthweight their development was comparable. Among the singletons there was no difference in developmental scores of boys and girls (Table 6), but in twins hearing and language skills were better in girls than boys (Table 7). No differences were found for other developmental indices.

Discussion

At 1 year of age, the development of singletons from VT conceptions is comparable to that of control singletons. Twins lag behind singletons in their developmental milestones. As expected, twins had a lower gestational age and birthweight than the singleton controls. When adjusted for these factors, the difference in developmental milestones did not persist, suggesting that delay in attaining the milestones among twins was attributable to their prematurity. The strength of this study lay in all the children being followed prospectively from early gestation, and all were examined by a single investigator, thereby nullifying interobserver bias.

The development of co-twin survivors of a VT was found to be similar to that of singletons. Although the VT is from an initial multiple gestation, reduction to a singleton in early gestation means that there is no later competition for intrauterine space or nutrition. Co-twin survivors of a VT were born at term with normal birthweight and their development was comparable to that of singletons. This suggests that, in a multiple pregnancy, the sharing of intrauterine space and nutrition predisposes to preterm delivery and low birthweight that compromises subsequent development.

The slower development of twins compared to singletons is attributable to their lower gestational age and birthweight. Similar findings have been noted when differences in IQ between twins and singletons were assessed (Ronalds et al., 2005). A difference of 5.3 and 6.0 IQ points at ages 7 and 9 years, respectively, was observed, but adjustment for gestational age and birthweight attenuated the difference to 2.6 points and was no longer statistically significant. Earlier studies that found differences in mental development between twins and singletons did not adjust for the variation in gestational age and birthweight (Myrianthopoulos et al., 1976; Wilson, 1974). In the present study, twins were born about 4 weeks earlier than singletons and had a correspondingly lower birthweight. Both factors have long-term implications. As the incidence of preterm delivery is greater among twin pregnancies, some may have received antenatal

Table 6

Comparison of Singleton Boys and Girls

Scale	Mean quotients		Difference in means (confidence intervals); *p* value
	Boys *N* = 50	Girls *N* = 42	
Locomotor	98.6	100.7	–1.9 (–8.9 to +5.1); *ns*
Personal–social	103.7	105.6	–1.9 (–6.8 to +2.8); *ns*
Hearing and language	107.2	108.7	–1.5 (–6.5 to +3.5); *ns*
Eye and hand coordination	109.2	111.8	–2.6 (–8.1 to +2.7); *ns*
Performance	102.9	103.6	–0.7 (–6.2 to +4.9); *ns*
General quotient	104.5	106.3	–1.8 (–6.3 to +2.8); *ns*

Note: *ns* = not significant

Table 7

Comparison of Twin Boys and Girls

Scale	Mean quotients		Difference in means (confidence intervals); *p* value
	Boys *N* = 100	Girls *N* = 80	
Locomotor	88.8	85.3	3.5 (–1.4 to +8.5); *ns*
Personal–social	92.9	95.4	–2.5 (–6.0 to +0.9); *ns*
Hearing and language	97.9	102.7	–4.9 (–8.6 to –1.1); .01
Eye and Hand coordination	99.5	99.6	–0.1 (–3.6 to +3.4); *ns*
Performance	91.7	91.6	0.1 (–3.8 to +3.9); *ns*
General quotient	93.8	94.6	–0.9 (–4.1 to +2.3); *ns*

Note: *ns* = not significant

steroids which are thought to affect cerebral development (French et al., 1999; Uno et al., 1990). Prematurity predisposes twins to feeding problems thereby influencing nutrition, growth and development (Dobbing, 1981), and premature twins are more prone to have suboptimal thyroid hormone levels which may have consequences for brain development (Van Wassenaer et al., 1999). Any combination of these factors may play a role in the slower development of twins compared to singletons.

Environmental factors such as parent–infant interaction and socioeconomic factors may play a role in the slower development of twins compared to singletons, but these factors were not within the scope of the original study. Recently, two large population-based studies (Deary et al., 2005; Ronalds et al., 2005) did not find any significant differences in environmental factors between twins and singletons.

Within-twin pair comparison of the development of the lighter and heavier twin revealed no differences. There was also no correlation, within twin pair, between the difference in birthweights and developmental scores. These findings suggest that gestational immaturity is the main contributor to the delay in attaining milestones among twins. Differences in cognitive ability have been found when twins of low birthweight were compared with those of normal birthweight (Drillien et al., 1980; Wilson, 1983, 1984). However, the role of gestational age was not investigated. When twins and singletons born at term were compared at age 4 years, no differences were found in language or locomotor development, nor was there a significant difference in the total development score (Akerman & Thomassen, 1991).

Gender Comparison

Twin girls and boys both had lower scores in comparison to singletons in all areas of development but this was also attributable to the lower gestational age and birthweight of twins. The differences were lost after adjustment for these factors. Among the singletons there were no gender differences in any of the scales, but in twins females were significantly better than males in hearing and language skills. This gender difference in language skills has been found in other studies (Neils & Aram, 1986; Robinson, 1991). At 30 months of age, twin boys were 8 months behind in expressive language and 6 months behind in verbal comprehension (Hay et al., 1987) compared to girls. Similarly, when male twin pairs were compared with female or different-sex pair twins using a language test, it was noted that female and opposite-sex twin pairs performed better than male twin pairs (Garitte et al., 2002). The reason for this gender difference is unclear.

Comparison Based on Chorionicity

Previous studies have reported comparative development of monozygotic (MZ) and dizygotic (DZ) twins. The findings were contradictory. One report found that MZ twins tend to obtain lower average scores on all the ability tests compared to DZ twins (Akerman & Fischbein, 1991), whereas another study noted poor performance by DZ twins (Nathan & Guttman, 1984). It is now well recognized that, within the MZ twins, the MC twins are more prone to cerebral impairment and other problems. There are no studies comparing the development of MC and DC twins. In this study, no significant differences were noted in the development of MC and DC twins other than the unexpected observation that MC twins had better hearing and language skills than DC twins.

Conclusions

At 1 year of age twins lag behind singletons in their development. This delay is attributable to lower gestational age. The development of children from index VT pregnancies was comparable to that of control singletons. Among the twins there was no difference in the development of lower versus higher birthweight twins. There was no effect of chorionicity on the development except on hearing and language skills.

Among the twins, the hearing and language skills were better in girls than boys but there was no difference in other skills. No gender differences were found among singletons.

The differences between singletons and twins noted in the study as a result of immaturity may resolve later in childhood. A further follow-up will determine whether twins catch up with singletons.

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