Delay in Motor Development of Twins in Africa: A Prospective Cohort Study

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Twins are prone to developmental delay due to prematurity and low birthweight. However it is unknown if twinning is an independent risk factor for developmental delay. The objective of this study was to compare the attainment of a set of gross motor milestones in a cohort of twins and singletons in The Gambia. Eighty-four pairs of twins and 72 singletons were enrolled at birth and followed up until 18 months of age. The mean age at achieving milestones was higher in twins for each development outcome and the difference between twins and singletons was significant after adjustment for confounders for maintaining head, sitting without support and walking. In twins, we found a highly significant correlation within pairs for most milestones. When monozygotic and dizygotic twins were compared, a significant heritability was observed for crawling, sitting, standing and walking, with over 90% of population variance observed due to genetic factors rather than environmental factors. There was little evidence for a genetic contribution towards very early milestones. In conclusion, our data suggest that twinning is an independent risk factor for developmental delay in early life in The Gambia, and that genetic factors contribute strongly to certain motor development outcomes.

The attainment of gross motor milestones is an important indicator of motor development in early life. Motor development is likely to play a role in long-term neurodevelopmental status (Peter et al., 1999). This development can be impaired by a number of conditions. Prenatal events play a major role, since intra-uterine growth retardation (IUGR) is associated with developmental delay in early life (Hediger et al., 2002; Williams & Davies, 1974). Perinatal events such as prematurity, birth asphyxia, or intracranial haemorrage may also adversely affect development. In the postnatal period, factors like nutrition and psycho-social environment influence development. Malnutrition in mothers and in infants has been recognised as a common cause of developmental delay in the developing world (Bhargava, 2000; Gross, 1991). More specifically, iron deficiency anemia in infants is associated with delayed motor development up to 18 months of age (Sherriff et al., 2001). Among protective effects, several studies showed that breast-feeding benefits neurodevelopment (Angelsen et al., 2001; Vestergaard et al., 1999). Among psycho-social factors, maternal behavior and stimulation were shown as important predictors of cognitive development in early life (Bhargava, 2000; Ostfeld et al., 2000). Moreover, there are indications that genetic factors probably contribute to variation in motor development (Chrzanowska & Zdanska-Brincken, 1974; Koeppen-Schomerus et al., 2000; Peter et al., 1999).

It has been suggested that twins are prone to developmental delay secondary to pre and perinatal causes (Myianthopoulos et al., 1976). Twins have a greater incidence of antenatal complications, preterm delivery, low birthweight, and more malformations compared to singletons (Chrzanowska & Zdanska-Brincken, 1974; Morley et al., 1989; Okogbo & Familusi, 1997; St Lis & Janus-Kukulska, 1974). We hypothesized that African twins could be at risk for development delay independently of pre and perinatal common causes. Indeed the intrauterine environment differs, the mother being less active and fetal movement being limited, at the end of twin pregnancies. Maternal nutritional status, and micronutrients intake, might be different between twin and singleton pregnancies and influence early motor development. Psychosocial environment can also differ between families with twins and those with singletons. In Western populations, maternal depression has been found more frequently in mothers of twins than in mothers of singletons (Thorpe et al., 1991). Postnatal depression is a cause of disturbance in early mother–infant interaction and is associated with poorer infant cognitive outcome (Murray & Cooper, 1997). Moreover, twin births represent a greater child care burden to the parents, which might result in less stimulation of the infants, and therefore less opportunity for gross and fine motor experiences in early life.

The incidence of twin births is high in sub-Saharan Africa where the average twinning rate is 20 per 1000 deliveries compared to 10 per 1000 in Europe (Jaffar et al., 1998; Murphy et al., 1997; Pison, 1992). Morbidity associated with twinning is therefore an important public health problem. The objective of this study was to evaluate if motor development in early life is different in between the two groups. Our secondary objective was to assess the contribution of genetic factors on early

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motor development, by comparing monozygotic and dizygotic twins. We report a prospective cohort study assessing sequential attainment of motor milestones in twins and singletons during the first 18 months of life.

Materials and Methods

Study Population

This study was nested in a twin study aiming to evaluate the genetic control of immune responses to vaccines. Singletons were selected from a concomitant study on characterization of immune response to vaccines in infants. Twin and singleton births were recorded at the Royal Victoria Hospital (the referral hospital in the capital city) and Serrekunda Health Center (an urban Health Center with a high rate of delivery) between March 1998 and May 2000. All consecutive deliveries were recorded and all children with parental consent were enrolled in these studies. In order to better compare both groups, and exclude developmental delay due to low birth weight (LBW), only twins and singletons with a birth weight > 2.5 kg were included in this study. Informed consent was obtained from the parents soon after birth. Information recorded on enrolment included birth order, number of siblings, gender, birth weight (BW) and length, and gestational age (GA), estimated within the first 24 hours of life by the method of Dubowitz (Dubowitz et al., 1970) by one of the doctors (TG, MO, DJS, JV, MN). The babies were visited and weighed at home monthly for 5 months, and then subsequently seen at 9, 12 and 18 months of age. The age of attainment of a set of gross-motor milestones was determined on parents' reporting and checked by neurological examination. The milestones considered for this study are defined in Table 1, and were adapted from the Denver Development Screening Test (DDST; Frankenburg & Dodds, 1967). At each visit the parents were asked if their babies were developing more slowly than their other children. The parents were not aware of the hypothesis being tested.

Eighty-four twin pairs and 72 singletons were enrolled in this study. All singletons were followed up for 18 months. In contrast, among twins, 84 pairs were followed up for 4 months, 76 for 5 months, 69 for 6 months, 65 for 9 months and 44 for 18 months. The reasons for dropping out were: migration in 22%, consent withdrawn in 44% and death of one of the twins in 33%. One pair of twins was excluded due to hydrocephalus in one twin. The follow-up rate of singletons was 100%, due to the lower infant mortality rate of singletons, and to lower mobility of the mothers.

The zygosity of same-sex twins was determined genetically by typing a panel of 10 highly polymorphic micro satellite markers in both twins. The markers, located on 8 different chromosomes, were amplified using the polymerase chain reaction and fluorescently labeled primers. PCR fragment length was analysed using the ABI 377 DNA sequencer and Genescan/Genotyper software programmes (Applied Biosystems). Twin pairs with identical genotypes for all markers were classified as monozygous (Becker et al., 1997).

Statistical Analysis

Statistical analysis was performed using Stata 7 (Stata Corporation, Texas, USA). Age at developmental outcome was compared for twins and singletons using multiple linear regression, adjusting for birth weight, number of siblings as categorical variables and for non-independence within twin pairs. Differences in binary variables (prematurity, gender, development slower than siblings) were compared using multiple logistic regression, again adjusting for the same variables.

The relative contribution of genetic and environmental factors on development was estimated by comparing monozygotic (MZ) and dizygotic (DZ) twin pairs. The total phenotypic variation in age at achieving development milestones was partitioned into genetic and environmental components using the software package Mx (Neale, 1997). The heritability (i.e., the proportion of variance due to genetics) was estimated from a model allowing for both additive genetic and environmental (common to both twins, and unique to each individual) effects.

This study had the approval of the Gambia Government/ Medical Research Council Ethical Committee.

Results

The follow-up rate was 100% for singletons, 77% for twins at the age of 9 months (when 5 out of 7 of the milestones studied have been attained), and 52% at 18 months. There were no differences in baseline characteristics (sex, GA, BW) between the 44 pairs of twins followed until 18 months and the 40 followed up for a shorter time. As shown in Table 2, birth weight was significantly lower among twins (mean = 2.79 kg) compared with singletons (mean = 3.24 kg). Twins also had a greater proportion of premature births (9.6% vs. 1.5%, $p = .07$), but gestational

Table 1

Motor Milestones and Their Definitions

Maintain head	Assessed by pulling the baby's arms.
Roll over	Asked the mother if the child was able to roll over completely from prone to supine or supine to prone.
Sit without support	Defined as sitting up and maintaining the head without rear support.
Crawl	Asked the mother if the child was able to move forwards or backwards either on stomach or on hands and knees.
Sit up	Asked the mother if the baby was able to move from a lying position to a sitting position by himself.
Stand holding on	Defined as maintaining a standing position by holding on to ones hand.
Walk holding on	Defined as walking a few steps by holding on to ones hand.
Two steps	Asked the mother if the child was able to take two steps independently.

Table 2

Birth Characteristics and Age of Milestone Achievement in Twins and Singletons

	Twins $N = 168$ Mean (95% CI)	Singletons $N = 72$ Mean (95% CI)	p-value	Adjusted p-value∞
Birth weight (Kg) ($n = 240$)	2.79 (2.7–2.8)	3.24 (3.1–3.3)	< 0.001	<0.001
Gestational age (weeks) ($n = 234$)	38.9 (38.7–39.2)	38.3 (38.1–38.6)	0.006	0.02
% Premature (< 37 wks)	9.6%	1.5%	0.07	0.20
% Male	53%	53%	0.98	0.33
Birth length (cm) ($n = 229$)	49.4 (48.8–49.9)	49.9 (49.4–50.5)	0.19	0.25
Mean number siblings ($n = 236$)	3.7 (3.4–4.1)	2.1 (1.5–2.7)	< 0.001	0.002
Is development of the baby slower than of other siblings?* ($n = 204$)	33%	10%	0.005	0.11
Maintain head ($n = 236$)	3.09 (3.0–3.2)	2.53 (2.4–2.7)	< 0.001	0.003
Sit without support ($n = 224$)	4.79 (4.6–5.0)	4.34 (4.2–4.5)	0.001	0.03
Roll over ($n = 222$)	4.98 (4.8–5.2)	4.61 (4.4–4.8)	0.04	0.71
Crawl ($n = 187$)	7.20 (6.9–7.5)	6.86 (6.6–7.1)	0.10	0.89
Sit ($n = 182$)	7.37 (7.1–7.7)	7.27 (7.1–7.5)	0.65	0.56
Stand holding on ($n = 185$)	8.91 (8.6–9.2)	8.18 (8.0–8.3)	< 0.001	0.10
Walk holding on ($n = 171$)	9.81 (9.5–10.1)	8.78 (8.6–9.0)	< 0.001	0.03
Take two steps ($n = 127$)	11.2 (10.7–11.7)	10.78 (10.5–11.1)	0.15	0.52

Note: ∞ Adjustment was made for birth weight and number of siblings (as categorical variables).
* In siblings > 0

age was slightly higher in twins than in singletons. The gestational age was estimated by Dubowitz score, which has not been validated in this population where the precise GA is rarely known. Also the small difference in GA might be due to the criteria of enrolment of birthweight > 2.5kg, which excluded pairs with small GA and one LBW twin. There was little difference in gender or birth length between twins and singletons. Twins tended to have a greater number of siblings than singletons.

The age of milestone achievement was higher in twins for each outcome, and the difference was statistically significant for maintaining head ($p = .003$), sitting without support ($p = .03$), and walking (holding on) ($p = .03$), after adjustment for birth weight and number of siblings. No significant difference was observed for crawling, rolling over, sitting alone and taking two steps. In families with other children, the proportion of mothers who judged that development of the index case was slower than of other siblings was greater for twins than for singletons (33% vs. 10%; adjusted OR = 2.9 95% CI 0.78-10.9). Development was not related to the order of delivery within twin pairs. Twins had a significantly lower weight at 1 year of age than singletons (mean ± SD: 8.5 ± 0.13 and 9.8 ± 0.14, respectively). After adjustment for birth weight and length, gender, number of siblings and twin status weight at 1 year was significantly associated with development slower than siblings ($p = .05$) and maintaining head ($p = .05$).

Among the 84 twin pairs, 22 were monozygotic (MZ), and 62 were dizygotic (DZ). Age of milestones attainment was highly concordant within both MZ and DZ pairs. As shown in Table 3, the concordance was significantly higher in MZ twins than in DZ twins for crawling, sitting, standing holding on to something and taking two steps, but not for the early milestones. For crawling, sitting and walking, more than 90% of the population variation observed is estimated to be due to genetic factors rather than shared environmental factors.

Discussion

Our data suggest that twinning is a risk factor for delay of gross motor milestones in early life. The association was confounded by birth weight and number of siblings, but a significant difference between twins and singletons persisted in many milestones after adjustment. Birthweight, length

Table 3

Comparison Between Correlation Coefficient in MZ and DZ Twins Pairs for Age on Achievement of Milestone.

	MZ *n* = 22	DZ *n* = 62	Heritability (95% CI)
Spearman coefficient			
Birthweight	0.13	0.26*	0% (0–55%)
Birth Length	0.82*	0.62*	—
Weight at 1 year	0.68*	0.68*	0% (0–46%)
Maintain head	1*	0.62*	—
Sitting without support	0.40*	0.45*	0% (0–51%)
Roll over	0.71*	0.84*	0% (0–13%)
Crawl	0.92*	0.42*	93% (62–96%)
Sitting	0.87*	0.40*	94% (65–97%)
Stand holding on something	0.98*	0.60*	72% (42–99%)
Walk holding on something	0.92*	0.37*	90% (60–96%)
Two steps	0.89*	0.08	—

Note: * Significant correlation $p < .05$

and prematurity are recognised risk factors for development delay (Morris et al., 1998; St Lis & Janus-Kukulska, 1974; Tomasi, 1998). Breast-feeding has been shown to be associated with better development (Angelsen et al., 2001; Vestergaard et al., 1999), but all the infants in our study were breastfed for more than 6 months. Socioeconomic factors are likely to be important in global child development, although studies from developed countries reported a negligible influence of social class on the attainment of motor milestones (Capute et al., 1985b; Peter et al., 1999). However, in The Gambia there is no validated measure of socioeconomic status. Twins and singletons were enrolled at the same hospital/health center, and living in the same study area, where type of housing income and size of household are fairly homogeneous, suggesting there were no major differences in the social status of their families. In Papua New Guinea chronic malnutrition was associated with developmental delay (Gross, 1991). Malnutrition is common in The Gambia and is associated with a 3.8 times increased risk of death for twins compared to singletons (Jaffar et al., 1998). Although the weight at 1 year was significantly lower in twins than in singletons, it was only associated with slower development than siblings and delay in maintaining head.

Reporting bias is possible as the examiner was not blind to the status of the infant, but there were several different examiners sharing the follow up of each child, and previous questionnaires of the child were not available to the examiner. As significant sibling resemblance in age of attainment of milestones has been described (Peter et al., 1999), we asked the parents to evaluate if the development of the index was slower than that of the siblings. Twins were more frequently reported as delayed than singletons. The parents were not aware of the study hypothesis, making recall bias less likely as the explanation for the difference between the two groups. The follow up was not completed for all twins, due to the high mobility of the urban population in The Gambia, the increased infant mortality rate in twins, and withdrawal of consent. Of these reasons, only death could be linked with the outcome (children with slow development being more likely to die), but the drop out due to deaths would then lead to underestimation of the difference for the last milestones.

These findings contrast with those reported for British twins under 34 weeks of gestation in whom there were no significant differences in development compared to singletons (Morley et al., 1989). We studied African infants born after 32 weeks of gestation, who were theoretically at low risk of developmental delay. Moreover the British study was a cross-sectional observation at 18 months of life, while ours is a prospective follow up study which is less subject to recall bias. In line with our findings, a British cohort study showed mild language delay in twins as compared with singletons, which was not associated with perinatal causes (Rutter et al., 2003).

The delay observed in twins could be due to antenatal factors that do not affect birth weight and length, such as under nutrition of the mothers, reduced space in utero, or lower mobility of the mother during pregnancy. The difference in development between twins and singletons could also be due to postnatal environment. Maternal verbal stimulation has been shown to be a significant predictor of Bayley motor score in infants in Kenya (Bhargava, 2000). Thorpe et al. (1991) reported that mothers of twins suffer more from depression due to increased stress during pregnancy, extra financial, care and health burdens of bearing twins than mother of singletons. In the majority of cases, the mother represents the infant's primary environment during the first months of life. Responsiveness of depressed mother is generally poorer. It has been shown that maternal depression is significantly associated with poorer infant mental and motor development at one year of age in developed countries (Murray & Cooper, 1997). This adverse effect could also involve parenting difficulties associated with maternal depression. Another study from industrialized countries, demonstrated that mothers of premature twins exhibited fewer initiatives and responses towards offspring than mothers of singletons (Ostfeld et al., 2000). Although it is not known whether a similar phenomenon occurs in the psychosocial setting of West Africa, the role of maternal depression and/or poorer stimulation may have participated in the delayed motor development observed in our study population. In addition, the presence of a co-twin doubles the childcare burden placed on the mother compared to a singleton infant. Such a burden might lead to less stimulation from the mother, and adoption of child care practices that could reduce the mobility of the infant in order to allow the mother to cope with other tasks. For instance, practices like carrying the child on the mother's back might delay motor development. Family size is also important to consider. We found a trend (although not significant) towards slower development in families with more than one other sibling (data not shown) suggesting that development could be related to the availability of the mother. Whilst twinning rates are high all over Sub-Saharan Africa, twins are viewed differently by different cultures: either as a sign of good fortune or misfortune (Pison, 1992). The care given to twins may vary accordingly, and have an impact on development. Twins are generally well accepted in The Gambia.

Differences have been found in attainment of milestones in different cultural, racial and geographical settings (Iloeje et al., 1991). We observed that most gross-motor milestones were attained at earlier ages by Gambian singletons than the ages reported in traditional scales or in other studies (Capute & Shapiro, 1985; Frankenburg & Dodds, 1967; Gross, 1991; Iloeje et al., 1991; Largo et al., 1985; Peter et al., 1999).
The ages at which the various milestones are achieved vary considerably in the literature. This variation is probably as much due to difference in definition of the stages of development and in the method of collection of data, as differences in population environment and genetics. However, our observations are consistent with findings from Nigeria and Kenya where children attained most milestones earlier than described in developed countries (Bhargava, 2000; Iloeje et al., 1991). Surprisingly in Nigeria and in The Gambia "roll over" and "stand holding on to something" were attained later in African children. In both studies the ability to roll from prone to supine and from supine to prone were not differentiated but it is known that they may differ by a month (Capute et al., 1985b; Largo et al., 1985). The differences between development profiles in African and Western population could be attributed to cultural differences in childrearing practices, and different levels of importance attributed to some specific milestones, a different pattern of milestone progression, or could also be genetic. These observations also suggest that specific scales need to be developed for assessment of African children.

The observed concordance of age of milestones achievement within pairs of twins emphasizes the role of the familial environment in the development pattern. We found that the profile of development was significantly more concordant in MZ than in DZ pairs for the latter five milestones, but the sample size is relatively small and heritability results should be interpreted with caution. These observations suggest, like other studies, that part of the development pattern is genetically determined (Chrzanowska & Zdanska-Brincken, 1974; Koeppen-Schomerus et al., 2000; Peter et al., 1999). In line with studies showing an important contribution of genetic factors in motor skill acquisition after practice, we observed that the heritability was greater for the latter milestones (Fox et al., 1996).

Conclusion

Our study reports that motor development during the first 18 months of life was delayed in Gambian twins compared to singletons, and that this delay was independent of prematurity and lower birthweight. We also showed that genetic and familial environment are involved in early motor development. Further studies should also evaluate whether this phenomenon is specific for African children or is also present in other populations. It is not clear whether motor development during the first year of life has an effect on later performance; the intelligence quotient and motor quotient should be compared in older twins and singletons.

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Table 4

Comparison of Mean Age (Months) of Motor Milestone Attainment Between Different Studies

Milestones	DDST (Frankenburg, 1967)	Baltimore (Capute, 1985)	Zurich (Largo, 1985)	Israel (Peter, 1999)	PNG (Gross, 1991)	Nigeria (Iloeje, 1991)	The Gambia 2002
Maintain head	4.2	—	—	—	—	3.3	2.5
Roll prone to supine	2.8	4	5	—	—	—	
Roll supine to prone	—	5	6	—	—	—	
Roll over	—	—	—	4.3	—	5.6	4.6
Sit (alone)	5.5	6	—	7.2	6.9	5.4	4.3
Crawl	—	7	8	—	10.8	6.6	6.9
Come to sit	7.6	8	9	—	—	7.3	7.2
Stand holding on	5.8	8	9	8.4	—	8.2	8.1
Walk (holding on)	9.2	11	12	—	—	8.8	8.8
Walk independently	12.1	12	13	12.7	15.8	11.0	10.8

Note: The values for The Gambia are the mean of singletons' values.

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