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# Genetic analysis of motor milestones attainment in early childhood

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**The age of attainment for four motor developmental traits, such as turning over, sitting up without support, pulling up to a standing position and walking without support, was examined in 822 children, including 626 siblings from families with 2 to 6 children, 68 pairs of dizygotic twins and 30 pairs of monozygotic twins. Correlation analysis, carried out separately for each type of sibship, showed the highest pairwise correlations in monozygotic twins and the lowest correlation in non-twin siblings for all motor milestones. Variance component analysis was used to decompose the different independent components forming the variation of the studied trait, such as genetic effect, common twin environment, common sib environment and residual factors. The results revealed that the major proportion of the total variance after adjustment for gestation age for the attainment of each motor skill, except pulling up to standing position, is explained by the common twin environment (50.5 to 66.6%), whilst a moderate proportion is explained by additive genetic factors (22.2 to 33.5%). Gestational age was found to be an important predictor of appearance of all motor milestones, affecting delay of 4.5 to 8.6 days for the attainment of the motor abilities for each week of earlier gestation. The age of attainment of the standing position was affected only by shared sibs environment (33.3% of the total variance) and showed no influence of either genetic or common twin environment. Phenotypic between trait correlations were high and significant for all studied traits (range between 0.40 and 0.67, $P < 0.01$ in all instances). Genetic cross correlations, however, were not easily interpreted and did not show clear variance trends among the different groups of children.**

**Keywords:** early child motor development, variance decomposition analysis, genetic and environmental factors

## Introduction

Motor development is defined as the changes in motor skills over the life span and the processes that underlie these changes.[1] Sequential attainment of specific motor development milestones, in turn, has been found to be one of the major patterns of early child development.[2] Although the appearance of these developmental landmarks has been extensively documented since the 1930s,[3,4] no agreement has been reached as to which factors affect this process: genetic or environmental, or the degree of their interrelation.

In the past ten years advances in the research of human movement have enabled scientists to discover unique patterns of infant motor behaviour and development. Ultrasound registration, for example, has shown that the first spontaneous motor movement can be seen in the seventh to eighth gestational week. Movement patterns develop fast, and during mid-pregnancy all patterns are observed that can be found in the newborn baby.[5] During infancy normal development is characterised by variability of performances and developmental sequences, and these are not easy to evaluate. In order to assess the motor developmental status among the very young, the attainment of gross motor milestones (eg turning over, sitting up for a few seconds without support, pulling up to a standing position, walking without support) is usually mentioned. This status is very important in the prediction of future child development.[6–8] Moreover, monitoring of motor milestone attainment has advantages compared with other methods (eg assessment of general movements[9]), including ease of administration, low cost, no need for highly trained personnel, not dependent on one or two skills, but on their sequential nature, usefulness in early diagnosis of pathological disorders.

Paediatricians often apply the motor landmarks to screen infant motor development during sequential visits as a multistep screening process. It has been found that there is a high degree of correlation between the developmental sequence by which

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certain mental abilities form and the ages at which the basic motor abilities appear. For example, motor milestones have been found to be very sensitive indicators in serial screening tests to identify developmental disorders, such as spinal muscular atrophies[10] or cerebral palsy.[11] However, this method has its disadvantages, being predictive only for some neurological disorders, as well as in its dependence on subjective opinions as a result of interview data collection.

Despite the usefulness of motor milestones for the monitoring of early child development and a long history of their use, involvement of familial factors and, in particular, the genetic contribution to inter-individual variation of these characteristics remains largely unknown. Livshits and collaborators in a series of papers have examined family resemblance for four major motor milestones.[12–14] These studies used various samples of siblings and showed that regardless of sibship, sex, and time difference in date of birth of sibs, sibling correlations for all milestones adjusted for gestational age were positive and statistically significant. The correlation coefficients between sibs were substantial, ranging between about 0.3 and 0.4, depending on the motor milestone. However, further breakdown of these relations into, for example, common environmental and genetic components was impossible with this kind of data. For the past few years our team has collected the follow-up data on early physical growth and motor development of a sample of twins (monozygotic and dizygotic). Accordingly, the main purpose of the present study was to estimate the relative contribution of genetic, prenatal environmental, and postnatal environmental effects on the appearance of four gross motor milestones: turning over, sitting up, pulling to stand, and walking.

## Materials and methods

### *Population sample*

This work is a part of the multipurpose longitudinal study on early child development. The infants, whose mothers participated in the survey, have been measured for body weight, body length and head circumference from birth for several years (1982–1997) at Child Care Centres in the Tel Aviv area, Israel. At the first visit to the centre (during the first month of life), the parents were asked to record the age at which the motor developmental traits, such as fully turning over (TURN), sitting up for a few seconds without support (SIT), pulling up to a standing position (STAND) and walking five steps without support (WALK), made their first appearance. Since the visits to the Child Care Centres were frequent (mean number of visits for body weight measurements, for example, was 12.5 ranging between 7 and 21 during the first year of life), chances that the parents could have made gross errors in remembering the appearance of motor milestones were negligible. Moreover, experienced nurses have evaluated the parents' reports during each visit to the Centre. Questionable or problematic data were excluded from the study. Therefore some children had missing values for a few characteristics, and the total sample represented in Table 1 was slightly larger than the subsamples for each studied trait. To evaluate roughly the reliability of the collected data, educational status of the interviewed parents was evaluated: mean number of years of education for mothers was 13.1 ± 2.2, and for fathers, 13.6 ± 3.0.

The design of the genetic analysis performed in this work (see following Statistical Analysis section) required at least one individual sibling within the family with no missing data for all the studied variables, otherwise the complete family data were excluded from the study. This fact reduced the initial total sample of 942 families to 361 families with two to six siblings born at different gestational ages (26–42 weeks), including 70 dizygotic and 30 monozygotic twins, out of a total of 822 children. Zygosity of most of twin pairs was assessed by the test for

**Table 1** Sample size and descriptive statistics for motor milestones and birth characteristics

| *Sample and traits* | *Sibship type* | | |
|---|---|---|---|
| | *Non-twin SIB* | *DZ twins* | *MZ twins* |
| Sample size | 622 | 140 | 60 |
| No. of families with | | | |
| 2 children | 200 | 70 | 30 |
| 3 children | 43 | – | – |
| 4 children | 11 | – | – |
| 5 children | 5 | – | – |
| 6 children | 4 | – | – |
| Descriptive statistics | | | |
| TURN, months | 4.28±1.25 | 6.13±0.82 | 5.71±0.65 |
| SIT, months | 7.24±1.62 | 9.56±1.39 | 9.12±1.33 |
| STAND, months | 8.42±1.81 | 9.63±1.30 | 9.36±1.61 |
| WALK, months | 12.70±2.28 | 15.19±3.07 | 14.84±2.91 |
| GA, weeks | 39.31±2.23 | 36.66±2.63 | 36.37±2.22 |
| WT at birth, gr | 3164.99±539.62 | 2442.02±537.91 | 2259.40±320.56 |

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blood subgroups. A small sample of twins (less than 4%) was estimated for zygosity by interviewing their parents about the number of placentas *and* the childrens' physical resemblance after 2 years of life.

### *Statistical analysis*

Pearson's pairwise correlations were computed for each of the motor development traits for each group of sibships: non-twin siblings (SIB), dizygotic (DZ) and monozygotic twins (MZ). Non-twin sibling correlations were estimated for all possible combinations of sibling pairs. Correlations estimated between each motor milestone and gestational age (GA) were computed for one child from each family in order to form a sample of unrelated individuals, and to evaluate the effect of gestational age on the age of attainment of the first motor milestones.

To examine genetic and environmental influences on early child motor development a variance component analysis was undertaken, as an implement to the FISHER statistical package[15] with minor modifications. This method allowed one to distinguish between the different independent components forming the variation of the studied trait ($V_T$), such as additive genetic effect ($V_{ADD}$), intrauterine environment shared by twins during prenatal development (common twin environment, $V_{CTE}$), common environment shared by siblings during postnatal development (common sib environment, or household, $V_{CSE}$), and environmental effect specific for each child (residual effect, $V_{RES}$). The variance components of trait variation in different types of sibs were considered in the present study as follows: $V_{SIB} = 1/2V_{ADD} + V_{CSE} + V_{RES}$; $V_{DZ} = 1/2V_{ADD} + V_{CTE} + V_{CSE} + V_{RES}$; $V_{MZ} = V_{ADD} + V_{CTE} + V_{CSE} + V_{RES}$. This system of equations allows a total trait variation to be presented as a sum of four variance components:

$$V_T = V_{ADD} + V_{CTE} + V_{CSE} + V_{RES}$$

Influences of gestational age and gender were estimated simultaneously along with the variance components by using a linear function of GA:

$$\mu_b = \alpha_b + \beta_b (GA_b - GA_{b(min)}), \text{ and } \mu_g = \alpha_g + \beta_g (GA_g - GA_{g(min)})$$

where $\mu_b$ and $\mu_g$ are trait values for boys and girls, respectively; $\alpha_b$ and $\alpha_g$ their intercepts, $\beta_b$ and $\beta_g$ slope components, $GA_b$ and $GA_g$ individual gestational age, $GA_{b(min)}$ and $GA_{g(min)}$ minimal gestational age in the sample of boys and girls, respectively.

The general model of this study included eight parameters: the four variance components ($V_{ADD}$, $V_{CTE}$, $V_{CSE}$ and $V_{RES}$) and linear regression parameters estimating the sex specific effect of GA ($\alpha_b$, $\alpha_g$, $\beta_b$ and $\beta_g$). To remove parameters which are statistically not significant in explanation of the studied trait, each of the studied parameters was sequentially constrained to zero or constrained to be equal to the other parameter (eg $\alpha_b = \alpha_g$). The acceptance of a more parsimonious model was each time tested by log likelihood ratio test between the general model ($logLH_{GM}$) and the restricted one ($logLH_{PM}$), which is equivalent to: $\chi^2 = -2(logLH_{PM} - logLH_{GM})$ with degrees of freedom equal to the number of parameters reduced. In case the logLH of the more parsimonious model came out significantly worse than that of the general one, the effect of the restricted parameter on the total variance of the trait was considered to be significant. The model with the minimum number of estimated parameters, which did not differ significantly from the general one according to the $\chi^2$ test, was chosen as the most parsimonious model.

In this study there was no model which could distinguish between the $V_{CSE}$ and $V_{ADD}$ components due to the absence of other types of relatives in pedigrees, except for siblings, for all variables. Both components could not be constrained to zero simultaneously in any trait's parsimonious model of inheritance, showing much worse likelihood value *vs* general model ($P < 0.001$). When, however, only one of these variance components, either additive genetic or common household, was restricted to zero, the likelihood ratio reached the *same* for both acceptable value for any of TURN, SIT, STAND or WALK. Yet, in three instances (TURN, SIT and WALK) the percentage of explained variance was higher, whilst $V_{RES}$ value was lower when $V_{ADD}$ was estimated, indicating preference of the $V_{ADD}$ effect. In the case of STAND, $V_{CSE}$ was preferred on $V_{ADD}$ not only because of lower $V_{RES}$ but because the correlations between DZ and MZ twins for this trait were virtually equal (0.55 *vs* 0.56). This fact suggested no genetic influence for STAND as determined for the present sample.

At the next stage of the genetic analysis, it was assumed that the age of appearance of different motor milestones might be genetically correlated one with another, since substantial and significant phenotypic correlations between some of these milestones were found in our previous study.[2] To test this hypothesis, cross correlations between the phenotypic values of traits X and Y were determined according to Falconer and Mackay[16] as $COV_{X,Y}/(V_X V_Y)^{1/2}$, where $COV_{X,Y} = 1/2(r_{S1XS2Y} + r_{S1YS2X})$ and $V_X V_Y = r_{S1XS2X} \times r_{S1YS2Y}$. Here, $r_{S1XS2Y}$ is a phenotypic correlation between the trait X of the first sib and the trait Y of the second one, $r_{S1YS2X}$ between Y of the first sib and X of the second one, and $r_{S1XS2X}$ and $r_{S1YS2Y}$ between two sibs in the pedigree for X and Y, respectively. The cross correlations were assumed to be attributable to pleiotropic interactions of a number of loci, as well as to linkage disequilibrium,[16,17] but they can also be the result of environmental factors which simultaneously affect both traits. Significance level of each cross correlation was deemed to be the same as for $COV_{X,Y}$.

To determine the possible extent of genetic and environmental covariation between the studied traits, covariance decomposition analysis (bivariate analysis) was undertaken employing the same FISHER package. This time both genetic and environmental correlations between all possible pairs of traits were estimated in a pairwise manner. Finally, the between-trait covariance matrices $\Omega_{XX}$ and $\Omega_{YY}$ for traits X and Y were computed as follows:[18]

$$\Omega_{XX} = \Omega_{YY} = \sigma_{ADDXY} 2\Phi + \sigma_{CTEXY} CTE + \sigma_{RESXY} RES$$

where $\sigma_{XY}$ is the unknown covariance component (ADD: additive, CTE: common twin environment, and RES: residual) and $2\Phi$ the covariance matrix for additive genetic variance. The choice of $\Omega_{XX} = \Omega_{YY}$ is based on the assumption that the expected covariance between value $X_i$ of individual *i* for one trait and value $Y_j$ of individual *j* for another trait should equal the expected covariance between the $X_j$ and $Y_i$.[18]

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## Results

### *Statistical analysis*

Table 1 provides the basic descriptive statistics for each of the studied motor milestones according to sibship, as well as the sample size description. Since the sample was not random due to the interfamily relationship between the siblings, especially in the twin families, descriptive statistics are provided to give a general idea of the range of variation for the motor characteristics of this sample.

Correlation between the attainment of motor milestones and GA, as well as corresponding intra-pair sibling correlations are given in Table 2. It will be seen that GA negatively correlated with the age of attainment for all of the motor milestones with lowest estimates for STAND (r = –0.29) and highest for TURN (r = –0.45). The age of milestone achievements was adjusted for GA and then sibling correlations were computed. The results showed that all correlations were highly significant. The highest similarity among the children within the family was found for MZ twins for each of the studied motor traits (from 0.56 for STAND to 0.89 for WALK). On the other hand, non-twin siblings demonstrated the lowest correlations, namely, 0.34 for WALK *vs* 0.47 for SIT. Moreover, it is of interest to note the relatively narrow range of correlations between studied motor traits within each type of sibship *vs* substantial differences between correlations for the same trait, according to type of sibship. The only exception is STAND between MZ twins (Table 2).

### *Genetic analysis*

*Univariate analysis* Tables 3 and 4 present the results of the genetic analysis. Parameter estimates for a general model and the most parsimonious model are given with their asymptotic standard errors for each motor milestone, as well as with the proportion of variance attributable to the respective factor. In addition, maximum log-likelihood value for each model is also shown in both Tables 3 and 4.

**Table 2** Sibling correlations for parameters of motor development

| *Variables* | *SIBS* | *DZ twins* | *MZ twins* | *GA*[a] |
|---|---|---|---|---|
| TURN | 0.3968 | 0.6655 | 0.7433 | –0.4467 |
| SIT | 0.4683 | 0.5227 | 0.7720 | –0.4090 |
| STAND | 0.4262 | 0.5536 | 0.5609 | –0.2871 |
| WALK | 0.3355 | 0.5836 | 0.8940 | –0.3587 |
| Sample size | 480 | 64 | 29 | 317 |

$P<0.01$ throughout; [a]Correlation between trait value and gestational age was computed on 1 child from each sibship only, regardless of sex.

*Turning over:* Variance decomposition analysis for TURN with simultaneous parameter estimates for sex and GA effect (Table 3) demonstrated that the major part of the total variance was explained by common twin effect (50.5%) adjusted for GA. Genetic factors, in turn, contributed 33.5% to the total variance of the trait adjusted for GA. There was no significant gender effect on turning over, and there was no significant sex differences for the gestational age effect on the appearance of this motor milestone. The effect of GA on TURN was substantial, indicating on average 4.4 days delay in appearance of this skill for each week of earlier gestational age among both boys and girls. This effect could not be rejected since the model with β slopes constrained to zero for both genders was statistically unacceptable ($\chi^2 = 51.42$; d.f. = 2; $P < 0.001$). About 17.9% of inter-individual variation in TURN was attributable to GA effect.

*Sitting up without support:* Results of the genetic analysis of SIT milestone for the general and most parsimonious models, are also shown in Table 3. They were similar to those of TURN, denoting the major role of common twin environment for sitting up. Some 56% of the total inter-individual variation in SIT, adjusted for GA, was explained by common twin environment, whilst additive genetic effect surpassed 30% of the total variance. Similar to TURN there were also no gender differences in the trait intercept and no sex differences in gestational age effect on the rate of SIT attaining. However, the GA effect itself was higher and indicated, on average, an 8.6 day delay in appearance of this milestone for each week of earlier gestational age lacking, and accounted for 20.1% of the total variance.

*Pulling up to a standing position:* The results of the variance decomposition analysis of STAND (Table 4) reveal that only common sib environment effect (33.3%) was detectable in variation of this trait. As expected by no differences between MZ and DZ correlations, the additive genetic effect was negligible. However, the proportion of variance attributable to the common twin environment was also virtually zero with respect to the age of appearance of this motor ability. Considering the GA effect on starting to pull up to stand, the 6.7 days gap was found between the children with a one week difference in gestational age. No sex differences in GA effect were detected. Finally, about 12.7% of the total variance was attributable to differences in GA among infants.

*Walking without support:* Results of the genetic analysis on WALK (Table 4) show that more than 88% of the total variance of this trait was explained.

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**Table 3** Variance decomposition analysis of motor milestones: TURN and SIT

| *Parameter estimates* | *Motor milestones* | | | |
|---|---|---|---|---|
| | *TURN* | | *SIT* | |
| | *General* | *Parsimonious* | *General* | *Parsimonious* |
| GA – effect: | | | | |
| Intercept (α): boys | 6.21[b] | 6.32[b] | 11.03[b] | 10.94[b] |
| (stand. error) | (0.35) | (0.27) | (0.44) | (0.34) |
| girls | 6.41[b] | 6.32[b, c] | 10.84[b] | 10.94[b, c] |
| (stand. error) | (0.33) | (0.27) | (0.42) | (0.34) |
| regression coeff. (β): boys | –0.14[d] | –0.15[d] | –0.28[d] | –0.28[d] |
| (stand. error) | (0.03) | (0.02) | (0.03) | (0.03) |
| girls | –0.15[d] | –0.15[c, d] | –0.28[d] | –0.28[c, d] |
| (stand. error) | (0.03) | (0.02) | (0.03) | (0.03) |
| SEX – effect: | | | | |
| Boys (mean GA = 39 wks) | 4.39[b] | 4.37[b] | 7.39[b] | 7.30[b] |
| Girls (mean GA = 39 wks) | 4.46[b] | 4.37[b] | 7.20[b] | 7.30[b] |
| Genetic and environmental effects: | | | | |
| Additive variance | 0.75 | 0.75 | 1.31 | 1.32 |
| (stand. error) | (0.11) | (0.11) | (0.18) | (0.18) |
| V, %[a] | 33.48% | 33.48% | 30.82% | 31.21% |
| Common twin variance | 1.13 | 1.13 | 2.40 | 2.37 |
| (stand. error) | (0.32) | (0.32) | (0.60) | (0.60) |
| V, % | 50.45% | 50.45% | 56.47% | 56.03% |
| Common sib household variance | 0[e] | 0[e] | 0[e] | 0[e] |
| (stand. error) | – | – | – | – |
| V, % | 0% | 0% | 0% | 0% |
| Residual variance | 0.36 | 0.36 | 0.54 | 0.54 |
| (stand. error) | (0.09) | (0.09) | (0.14) | (0.14) |
| V, % | 16.07% | 16.07% | 12.71% | 12.76% |
| logLH | –523.258 | –523.584 | –763.098 | –765.350 |
| d.f. | – | 2 | – | 2 |
| $\chi^2$ | – | 0.65 | – | 4.50 |

[a]Proportion of variance attributable to the effect of the respective factor (%); [b]Milestone in months from day of birth; [c]Parameter constrained to be equal to parameter estimate above in the Table; [d]Rate of change per week; [e]Parameter bounded at zero.

As seen, the major proportion of variance for 'beginning to walk' is attributed, similar to that of TURN and SIT, to common twin environment (66.6%). Additive genetic effects contributed about 22% to the total variance. There was no significant sex effect on the regression intercept of WALK produced by GA. However, the rate of attainment of WALK as affected by GA (regression coefficient, β) showed significant sex differences. Whilst the GA effect indicated 7.3 days difference in achievement of this motor milestone in boys, it showed 8.2 days in girls per week of preterm birth. The difference between the sexes was highly significant ($\chi^2$ = 13.96, d.f. = 1; $P < 0.001$).

*Bivariate analysis* The pairwise phenotypic correlations and cross-correlations according to type of sibships are given in Table 5. The first were estimated on the total sample for all pairs of studied characteristics and were significant ($P < 0.01$), with correlations ranging from 0.40 for TURN/WALK to 0.68 for SIT/STAND. Cross correlations, in turn, were estimated for each group of sibships separately. They were mostly significant but not as easy to interpret as sibling correlations and did not show any clear tendency to vary. The lowest correlations were observed for TURN/WALK for all groups of siblings; this is not surprising since their pairwise phenotypic correlations were the lowest. Significant differences were indicated in TURN/SIT and SIT/WALK cross correlations between DZ and MZ twins, which were reflected by significant genetic correlations estimated in bivariate analysis. STAND/SIT cross correlations were extremely high, but the same for DZ and MZ twins. Those for TURN/STAND showed a clear tendency to increase with sib similarity: from 0.33 for SIB to 0.66 for MZ. It is interesting that the highest cross correlation for STAND/WALK was observed in non-twin siblings, whilst the lowest was in MZ twins. The low and non-significant values of some MZ cross correlations might possibly be also due to a relatively low number of MZ twin pairs ($n$ = 29).

Genetic and environmental correlations were found only between three pairs of studied characteristics (TURN, SIT and WALK), since there were no

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**Table 4** Variance decomposition analysis of motor milestones: STAND and WALK

| *Parameter estimates* | *Motor milestones* | | | |
|---|---|---|---|---|
| | *STAND* | | *WALK* | |
| | *General* | *Parsimonious* | *General* | *Parsimonious* |
| GA – effect: | | | | |
| Intercept (α): boys | 11.96[b] | 11.54[b] | 15.64[b] | 15.61[b] |
| (stand. error) | (0.45) | (0.34) | (0.69) | (0.53) |
| girls | 11.13[b] | 11.54[b, c] | 15.58[b] | 15.61[b, c] |
| (stand. error) | (0.44) | (0.34) | (0.65) | (0.53) |
| regression coeff. (β): boys | –0.25[d] | –0.22[d] | –0.24[d] | –0.24[d] |
| (stand. error) | (0.04) | (0.03) | (0.05) | (0.05) |
| girls | –0.19[d] | –0.22[c, d] | –0.27[d] | –0.27[d] |
| (stand. error) | (0.03) | (0.03) | (0.05) | (0.05) |
| SEX – effect: | | | | |
| Boys (mean GA = 39 wks) | 8.71[b] | 8.68[b] | 12.52[b] | 12.49[b] |
| Girls (mean GA = 39 wks) | 8.66[b] | 8.68[b] | 12.07[b] | 12.10[b] |
| Genetic and environmental effects: | | | | |
| Additive variance | 0[e] | 0[e] | 2.80 | 2.80 |
| (stand. error) | – | – | (0.42) | (0.42) |
| V, %[a] | 0% | 0% | 22.24% | 22.24% |
| Common twin variance | $1.6 \times 10^{-3}$ | 0[e] | 8.38 | 8.38 |
| (stand. error) | (0) | – | (1.76) | (1.76) |
| V, % | 0% | 0% | 66.56% | 66.56% |
| Common sib household variance | 0.87 | 0.88 | 0[e] | 0[e] |
| (stand. error) | (0.13) | (0.13) | – | – |
| V, % | 33.08% | 33.33% | 0% | 0% |
| Residual variance | 1.77 | 1.77 | 1.41 | 1.41 |
| (stand. error) | (0.12) | (0.12) | (0.34) | (0.34) |
| V, % | 66.92% | 66.67% | 11.21% | 11.21% |
| logLH | –881.549 | –882.013 | –1157.175 | –1157.178 |
| d.f. | – | 3 | – | 1 |
| $\chi^2$ | – | 0.93 | – | 0.006 |

[a]Proportion of variance attributable to the effect of the respective factor (%); [b]Milestone in months from day of birth; [c]Parameter constrained to be equal to parameter estimate above in the Table; [d]Rate of change per week; [e]Parameter bounded at zero.

**Table 5** Phenotipic, genetic and environmental and cross correlations for the pairs of motor development traits

| *Traits* | $r_{PHEN}$[a] | *Cross correlations* | | | $r_{ADD} \pm SE$ | $r_{CTE} \pm SE$ | $r_{RES} \pm SE$ | $\varkappa^2$ | d.f. |
|---|---|---|---|---|---|---|---|---|---|
| | | *SIB* | *DZ* | *MZ* | | | | | |
| TURN/SIT | 0.6177[b] | 0.4869[b] | 0.4577[b] | 0.5927[b] | 0.4169±0.0719 | 0.9990±0.0000 | 0.3673±0.4978 | 0 | – |
| TURN/WALK | 0.3973[b] | 0.2760[b] | 0.3738[b] | 0.0716[ns] | 0[d] | 0.8331±0.2197 | 0.5714±0.3133 | 1.346 | 1 |
| SIT/WALK | 0.5655[b] | 0.5628[b] | 0.3400[c] | 0.4890[c] | 0.5791±0.0782 | 0.7217±0.1491 | 0[d] | 0.382 | 1 |
| STAND/TURN | 0.4895[b] | 0.3284[b] | 0.5163[b] | 0.6569[b] | – | – | – | – | – |
| STAND/SIT | 0.6774[b] | 0.5568[b] | 0.9486[b] | 0.9597[b] | – | – | – | – | – |
| STAND/WALK | 0.5019[b] | 0.5388[b] | 0.4776[b] | 0.2205[ns] | – | – | – | – | – |

[a]Phenotypic correlations were computed on 1 child from each sibship only, regardless of sex; [b]$P<0.01$; [c]$P<0.05$; [d]Parameter bounded at zero; [ns]non significant.

common parameters estimated for STAND and the other variables. The highest correlations were attributed to common twin environment for all three pairs of characteristics (from 0.72 for SIT/WALK to almost 1.0 for TURN/SIT). The pairwise genetic correlations were relatively high and significant for TURN/SIT and SIT/WALK (0.42 and 0.58, respectively). The correlation for TURN/WALK, in turn, was constrained to zero without significant change in log likelihood. The pairwise residual correlations were not significant (for SIT/WALK it was constrained to zero) and showed very high asymptotic standard errors.

## Discussion

Motor milestones are an excellent indicator of the development of child motor competence.[19] Attainment of gross motor milestones, such as turning over, sitting up, pulling up to a standing position, walking

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without support, has clinical importance. Delay in their appearance has been described in connection with Down syndrome,[20] mitochondrial encephalomyopathy,[21] Dejerine-Sottas neuropathy,[22] congenital muscular dystrophy[23,24] and many other disorders. 75% of patients with congenital bilateral perisylvian syndrome[25] and 50% of patients with cerebellar ataxia[26] were found to have delay in the onset of these motor skills. An abnormal sequence for achieving major motor milestones has been indicated for children with osteogenesis imperfecta.[27] Moreover, loss of motor milestones is one of the most common representations of HIV disease among infants and young children.[28] Therefore the assessment of these motor abilities may be very informative for monitoring the development of high-risk infants.[29] These evaluations may also serve as a first step in a multistep diagnostic system for early manifestation of motor disorders.

Numerous aspects of early child motor development have already been investigated. A direct relationship was found between sequential motor milestones (the most important predictor variable for each consequent milestone is the milestone already attained), and an indirect one with growth rate variables and birth measurements.[2] Social and demographic factors, in turn, did not indicate any significant relation to age of milestone achievement.[30,31] Anthropometric data did not influence the level of childhood motor development either.[32,33] Ethnic differences were reported by Iloeje *et al*[34] who showed that black children attain gross motor milestones earlier than white children. With regard to the effects of environment and genotype on motor development, evidence exists only for older children. Wolanski *et al*[35] revealed that in parallel to maternal and paternal genetic factors, which explain 12% and 11% of total variance, respectively, cultural factors also determine motor development of children, contributing some 26% of the variance. However, quantitative studies on motor development in early childhood are still very limited. Furthermore, there are no studies that attempt to distinguish between genetic and environmental effects on early child motor development, and compare the time of the appearance of major motor milestones between different types of sibship. Greater similarities in MZ twin pairs compared with DZ and regular siblings might be interpreted as a reflection of genetic influences on this process.

The sample with three types of sibship in this study allowed us to compare appearance of the four gross motor milestones between non-twin siblings, MZ and DZ twins. We observed a clear tendency for motor milestones to appear more concordantly in MZ twins and less concordantly in sibs. Our correlations for non-twin siblings (Table 2) were moderately high and were similar to those reported by Otremski *et al*[31] – 0.40 *vs* 0.31 for TURN, 0.47 *vs* 0.40 for SIT, 0.43 *vs* 0.40 for STAND, and 0.34 *vs* 0.31 for WALK. However, these correlations were much lower than those for DZ and MZ twins (Table 2). The correlation estimates between twins, to our knowledge, have never been reported before.

Since sibling correlations cannot really be interpreted as coefficients of heritability, it was assumed that the ages of motor milestone appearance are more similar within families. Moreover, it was of interest to establish if this familial similarity is attributed to genetic or to common environmental factors.[13,14] Variance component analysis for three groups of children in this study enabled us to break the total variation of each milestone down to three independent components representing genetic factors, a common twin environment, and a residual component representing environmental factors specific to each individual and error variance. The results were surprising: the largest proportion of the total variance in the appearance of TURN, SIT and WALK was explained by common twin environment (from 50.5% to 66.6%) after adjustment for GA. GA was found to be an important predictor of the appearance of motor skills, affecting delays of 4.5 to 8.6 days in attainment of studied motor milestones for each week of earlier gestation.

It should be stressed that the 'twin component' may in fact represent not only maternal effect on simultaneously developing foetuses. It may well also reflect the homogeneity of other shared environmental conditions for the growth of twins up to the age of appearance of the specific motor ability. It is less obvious for a characteristic like TURN and much more probable for WALK.

Despite the fact that pairwise phenotypic correlations were computed only for one child from each sibship, the correlations were higher than those of Livshits *et al*[2] – 0.62 *vs* 0.47 for TURN/SIT, 0.49 *vs* 0.21 for TURN/STAND, 0.57 *vs* 0.23 for SIT/WALK, 0.50 *vs* 0.24 for STAND/WALK, but similar for SIT/STAND – 0.68 *vs* 0.62. Livshits[12] also estimated associations between pairs of motor milestones. In that study phenotypic correlations were even lower than in Livshits *et al*.[2] However, the common tendency of lowest correlation for TURN/WALK compared with the highest one for SIT/STAND has been replicated. Moreover, cross correlations obtained in the Livshits[12] study came out low and insignificant, in comparison with our findings that correlations ranged from 0.22 for TURN/WALK to 0.96 for SIT/STAND, with one exception (0.07 for TURN/WALK), all for MZ twins. The most remarkable cross correlations found by our study may indicate that the appearance of some motor milestones is subject to a common pleiotropic factor

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effect: genetic where intra-pair correlation estimates were higher for MZ twins compared with DZ ones (for example, TURN/SIT or SIT/WALK), or environmental where the latter estimates were the same or even lower for MZ twins *vs* DZ twins (for example, SIT/STAND).

Two findings clearly follow from the above:

1. Significant sibling resemblance in age of appearance of the basic milestones, reported by previous studies[12–14] was strongly confirmed by the present study sample of DZ and MZ twins.
2. The observed correlations cannot be attributable to genetic factors only. Substantial familial environment effect is involved into the process of early motor development.

Because of the clinical importance of motor development, additional investigations are needed to evaluate the genetic contribution to the appearance of the major motor milestones, and to identify the specific environmental factors which sustain a similarity between twins and sibs at stages of motor milestone achievements.

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