Genetic and Environmental Influences on Developmental Milestones and Movement: Results from the Gemini Cohort study

Running Head: Developmental Milestones and Movement

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Abstract

Purpose: Variability in the timing of infant developmental milestones is poorly understood. We used a twin analysis to estimate genetic and environmental influences on motor development and activity levels in infancy. **Method:** Data were from the Gemini study, a twin birth cohort of 2402 families with twins born in the UK in 2007. Parents reported motor activity level for each of the twins at age 3 months using the Revised Infant Behavior Rating Scale (IBQ-R), and also reported the age at which they first sat unsupported, crawled, and walked unaided. **Results:** Activity level at 3 months, and age of first sitting and crawling were about equally influenced by the shared family environment (45%-54%) and genes (45%-48%). Genetic influences dominated for the age of taking first independent steps (84%). **Conclusion:** Aspects of the shared family environment appear to be important influences on motor activity levels and early milestones, although the timing of walking may have a stronger genetic influence. Further research to identify the specific environmental and genetic factors that promote early activity may be important for longer-term health outcomes.

Keywords: twin; activity; child; motor

The foundations of an active lifestyle are laid in early infancy, with evidence that the age of achieving developmental milestones in infancy is related to future sports participation (Ridgeway et al., 2009). Motor milestones have also been associated with critical transitions such as school readiness (Cowen et al., 1994), and with educational outcomes throughout life (Taanila et al., 2005). Age of attainment of early developmental milestones is important evidence for parents and paediatricians that infants are developing normally.

Conventional cohort studies are not designed to distinguish environmental from genetic effects, but studies of twins make it possible to obtain quantitative estimates of genetic and environmental influences (Plomin et al., 2008). Several smaller twin studies have examined infant activity level (e.g. movement of arms and legs, squirming). In a sample of 302 pairs of twins aged 3-16 months, genetic factors explained 55% of the variance in infant activity level and the unique environment (which includes measurement error) explained the remainder (Goldsmith & Campos, 1999). In 60 pairs of twins, monozygotic (MZ) correlations were higher than dizygotic (DZ) correlations for both parent-rated, and objectively measured, infant activity level, suggesting genetic influence (Saudino & Eaton, 1991). However, larger samples are needed to distinguish shared and non-shared environment effects.

Few twin studies have examined the age of attaining milestones such as sitting unsupported, crawling, or walking unaided, and results have been inconsistent. One study involving 626 siblings and 98 pairs of twins found that shared environmental influences explained more than half the variance in age of sitting without support, turning over and walking five steps unaided (Peter et al., 1999). In contrast, in a sample of 84 pairs of twins, genetic factors explained the majority of the variation in age of sitting, crawling and standing (Goetghebuer et al., 2003). This variability is likely to be a consequence of limited sample sizes.

The present study used data from a large, population-based twin cohort (n=4804 children) to assess genetic and environmental influences on movement activity level and three important developmental milestones in infancy: first sitting unsupported, first crawling, and first steps.

Method

Gemini Study and Participants

Gemini is a cohort of twins born in the UK in 2007, designed to assess genetic and environmental influences on growth and development (van Jaarsveld et al., 2010). Half of all families with twins born in England and Wales during the recruitment period (Mar-Dec, 2007) agreed to be contacted about the study (n=3435). Families where there had been a death were not contacted. Just under 40% (n=2402) returned the baseline questionnaire when twins were around 8.2 months old (SD=2.2, range 4.0-20.3 months). The first follow-up questionnaire was completed by 1931 families (80.4% of the baseline sample), when twins were 15.8 months old (SD 1.1, range 14.0-27.4 months). Participants classified their own ethnicity. Opposite-sex twins were classified as dizygotic (DZ). Parents of same-sex twins were asked to complete a set of 20 questions validated against polymorphic DNA markers

(Price et al., 2000) to determine whether the twins were monozygotic (MZ) or dizygotic (DZ). Zygosity was uncertain in 68 pairs and they were excluded from these analyses. Each pair of twins were raised in the same environment.

Comparisons with national twin statistics (ONS, 2006) indicate that the Gemini cohort is representative of UK twins on sex, zygosity distribution, gestational age at birth, and birth weight (van Jaarsvled et al., 2010). Gemini parents tend to be slightly healthier than the general population in terms of fruit and vegetable intake, smoking rates and BMI, and the majority are White-British and married (van Jaarsvled et al., 2010). Parents who did not complete the follow-up questionnaire were slightly younger (mean 32 SD 5 years vs 34 SD 5 years; $p<0.001$), had slightly lower educational qualifications (2.9 SD 1.9 vs 3.6 SD 1.9; $p<0.001$) and were more likely to be from a non-white ethnic group ($p<0.001$). Informed consent was provided by all parents. Ethical approval was granted by the University College London Committee of non-National Health Service Human Research.

Infant Movement Activity Level

Infant movement activity level was assessed in the baseline questionnaire using a subscale from the Revised Infant Behavior Questionnaire (IBQ-R; Gartstein and Rothbart, 2003). The IBQ-R is widely used in developmental research and the activity subscale demonstrates good reliability and validity (Gartstein & Rothbart, 2003). Parents were asked to think about each child's behavior in the first 3 months of life and report on several aspects (e.g., 'during feeding how often did your babies squirm or kick; 'during sleep how often did your babies toss about in the crib'; when placed in a seat did your babies wave or kick their arms') using a 5 point Likert scale (very rarely; less than half the time; about half the time; more than half the time; almost always). An overall infant movement activity level score was calculated for each child, higher scores indicated higher levels. Where $\geq$5 values were missing, data were excluded from analyses (n=120 children) leaving a total of 2274 pairs of twins. The IBQ-R in Gemini demonstrated good internal consistency (Cronbach's alpha = 0.85).

Early Motor Milestones

Parents were asked a series of questions, in each case responding separately for the first-born and second-born twin: 'How old were your twins when they could sit up without being supported'; 'How old were your twins when they could first crawl on hands and knees'; 'How old were your twins when they could take a few steps without any support'. Parents also had the option to select 'not yet'. First sit and first crawl were asked in both the baseline and 15 month questionnaires; first steps were only asked in the 15 month questionnaire. If parents responded to the sit and crawl questions on both occasions and there was a discrepancy of >2 months between values, data were counted as missing. Where responses were $\leq$2 months different, values from the baseline questionnaire were used, but results were checked using the 15 month data and there were no differences. A few children had not yet reached each milestone by the time the 15 month questionnaire was returned (first sit 0.6% and first steps 23%) and 2% of children were 'non-crawlers'. Exact numbers of infants included are provided in the results section.

Statistical Analyses

Associations between infant movement activity level and developmental milestones were assessed using partial correlations adjusting for gestational age. For twin analyses, data were regressed on age (gestational age and age of twins at questionnaire completion) and sex. Residuals from regressions were used for all analyses. Within-pair intraclass correlations were computed to provide preliminary evidence of genetic influence, based on the assumption that MZ (identical) twins share all of their genes and DZ (fraternal) twins share on average half their segregating genes. If a trait is purely genetic, MZ twins would be perfectly correlated (1.0) and the DZ correlation would be 0.5. Intraclass correlations were computed using SPSS software.

Structural equation modelling was used to generate quantitative estimates of additive genetic effects (A), shared environment effects (C), and unshared environment effects plus measurement error (E) using MX Maximum likelihood Structural Equation Modelling Software (version 32; Virginia Commonwealth University, Richmond VA). Parsimony of sub-models (CE, AE and E) was tested with two goodness-of fit-statistics: change in X^2 and Akaike’s Information Criteria (AIC). Post-hoc power calculations were conducted in MX. To test for contrast effects, MZ and DZ correlations were examined and equal variance by zygosity was tested (Levine’s test). Significance was set at alpha<0.05.

Results

Participant characteristics are presented in **Table 1**. There were no significant differences between MZ and DZ twins in age at time of questionnaire completion, infant movement activity level, or age of first steps (p’s all >0.05). First sit was slightly later in

MZ than DZ twins: mean difference 0.34 months (95% confidence interval (CI) 0.12, 0.39; $d=0.216$), as was first crawl: mean difference 0.25 months (CI 0.12, 0.39; $p<0.001$; $d=0.133$).

Correlations between infant movement activity level and developmental milestones are presented in **Table 2**. There was a low correlation ($r=-0.212$; $p<0.001$) between higher infant movement activity level and first crawl at a younger age, although there was no correlation between higher infant movement activity level and first sit (-0.168; $p<0.001$) and first steps (-0.135; $p<0.001$) at younger age. There was moderate correlations between first sit and first crawl ($r=0.468$; $p<0.001$) and between first crawl and first steps ($r=0.476$; $p<0.001$). In addition, a low correlation was found between first sit and first steps ($r=0.296$; $p<0.001$).

Sex Differences in Infant Movement Activity Level and Developmental Milestones

Infant movement activity level was higher in boys (mean 2.38, SD 0.72) than girls (mean 2.31, SD 0.72; p for difference <0.001), although the effect size was small ($d=0.097$). Age of first sit was slightly earlier in boys (7.36 months, SD 1.51) than girls (7.54 months, SD 1.61; $p<0.001$), also with a small effect size ($d=0.115$). Age of first crawl and first steps were not significantly different between the sexes. Genetic and environmental estimates were broadly similar for boys and girls (data available from the corresponding author) therefore analyses are presented using whole group data.

Analyses of Genetic and Environmental Influences

Within-pair intraclass correlations (ICC) for infant movement activity level and developmental milestones are presented in **Figure 1**. MZ correlations were higher than DZ correlations for all outcomes, indicating genetic influence. DZ correlations were more than half that of the MZ correlations for infant movement activity level, first sit, and first crawl, indicating a shared environment effect. The DZ correlation was around half that of the MZ correlation for first steps, indicating strong genetic influence.

Quantitative estimates (full models presented in **Table 3**) confirmed the indications from the intraclass correlations. The best fitting model for infant movement activity level was the full ACE model; with genes explaining 48% of the variance and the shared environment explaining 45%. A small percentage (7%) of variance was explained by the unique environment plus measurement error. Similarly, the age that children could sit unsupported was significantly influenced by genes (48%) and the shared environment (42%), with a small contribution (10%) from the unique environment. The heritability estimate for the age that children first crawled was similar (54%), with contributions from shared (33%) and unique (13%) environments. The more parsimonious AE model was the best fit for first steps; indicating that 84% of the variance was explained by genes with no detectable effect of the shared environment.

Based on these parameters, power to detect a shared environment effect at alpha 0.05 for movement activity, first crawl and first sit was 100%. For first steps, power to detect a significant shared environment effect was slightly lower because the sample size was smaller but, the power to detect a significant shared environmental effect of 17% (the upper bound of the confidence interval observed in the quantitative analyses) was 100%. There was no evidence of contrast effects in our data.

Discussion

The results of this study indicate the environment has an important role in infant movement activity level and motor development, although genetic factors dominate the emergence of walking (first steps). The magnitude of the genetic effect on movement activity level in our study (around 48%) was very similar to that observed in smaller twin studies using the IBQ activity subscale [15] or objective measures (Saudino & Eaton, 1991; Saudino & Eaton, 1995). It is unclear whether infant movement activity (movement of arms and legs) maps on to 'fidgeting' which also demonstrates high heritability (Fisher et al., 2010), or is more related to play behavior (Saudino & Zapfe, 2008). Relationships between these childhood activity behaviors merit future research.

Finding a significant shared environment effect raises the interesting question of which specific environmental factors are responsible. Parental intervention may play an important role at this stage of life – for example coaxing babies to wave their arms in response to a toy, or encouraging them to practice sitting. Aspects of the psychosocial environment (e.g. parental encouragement and modelling) are known to affect childhood activity levels (Hinkley et al., 2008), and they may also be important in infancy. Preschool children with more siblings tend to be more active (Hesketh et al., 2006), perhaps because infants try to copy the movements of their older siblings. Similarly, older siblings can influence motor development by providing more interaction (Berger & Nuzzo, 2008). Availability of age-appropriate toys or parental knowledge of expected developmental milestones may also affect motor development. However, parents also encourage walking and we found no evidence for any shared environmental influence, suggesting that family effects for the other milestones are likely to be more than mere encouragement.

One possibility is that the key parental influences are not related to advancing motor milestones but retarding them. The available literature indicates that children need to be as active and free as possible for adequate motor development. For example, they must develop the strength required to push against gravity required in development of sitting (Tecklin, 2008). Use of devices such as infant walkers, swings, bouncers and car seats may have a negative impact on early motor development (Tecklin, 2008) and reaching developmental milestones is universally later now than in previous years (Piek, 2006). This could be a product of an increasingly sedentary population with more access to such devices. At present we do not know whether this influences development of physical activity behavior and preferences, but this is a possibility.

A survey of 400 paediatric occupational therapists expressed the view that modern infants spend too long on their backs (for example, in car seats that can be removed and attached directly to strollers or swings; www.pathwaysawareness.org/research-at-pathways). While parents are generally aware of the American Academy of Paediatrics' (1992) recommendation to place infants on their backs when sleeping, fewer caregivers are aware of the 'Prone to Play' message, which encourages parents to place infants on their fronts during waking time for optimal early motor development (Zachry et al., 2011). There is evidence that some parents purposely place infants on their backs even when awake due to a misconception that this will reduce the incidence of Sudden Infant Death Syndrome (SIDS; Zachry et al., 2011). Parents may need to be more clearly informed that the 'Back to Sleep' and 'Prone to Play' messages advocated by AAP are complimentary rather than contradictory. Interestingly, a longitudinal cohort study found that prone time only influenced early motor milestones (including crawling and sitting) and did not influence first steps (Kuo et al., 2008). This is consistent with our finding that the shared environment was significant for earlier milestones, but not for walking.

In further support of a shared environment effect, a number of modifiable factors that influence achievement of developmental milestones have already been identified, for example maternal smoking during pregnancy and in the first year predict developmental delay (Slykerman et al., 2007). Breast feeding is highly beneficial for motor development and may influence infant activity (Worobey, 1998). Children from lower socioeconomic groups are more likely to be more developmentally delayed (Bradley and Corwyn, 2002) and the childcare setting can also influence age of achievement of milestones (Mulligan et al., 1998).

One study found no genetic influence on sitting without support, but did show significant genetic influence on crawling and first steps (>90%). However, the small sample size meant that confidence intervals included zero, so it is difficult to draw conclusions (Goetghebuer et al., 2003). In their sample of twins and siblings, Peter et al. (1999) found that the shared environment explained more than 50% of the variance in sitting unsupported and walking. Our results support these estimates for sitting, but we found that genetic factors explained most of the variance in first walking unaided. Different measures could contribute to the differences, Peter et al. asked when infants could walk at least five steps unsupported, whereas we asked about first walking unaided, but more likely it is a sample size effect.

In support of our findings of genetic influences, motor development and skill level are likely to be influenced by factors such as muscle-fibre type and mitochondrial activity, which, although trainable, are partly genetically determined (Mulligan et al., 1998). There have been few studies of specific genes that influence motor activity level, although the dopamine system is implicated in motor activity. For example, infants with the long allele of the dopamine receptor DRD4 showed higher motor activity (Auerbach et al., 2001).

Our study is the largest to date to examine genetic and environmental influences on infant motor development, and has the statistical power to generate good estimates of both environmental and genetic parameters. The large sample size meant that we were reliant on parental reports rather than objective measures, but the error term was not strikingly high and there was little evidence in our data of contrast bias (parents overestimating differences between DZ twins and underestimating MZ differences; Saudino et al., 2000). While our genetic estimates for infant activity level are similar to previous studies, finding a strong shared (as opposed to unique) environment effect is novel (Goldsmith & Campos, 1999; Saudino & Eaton, 1991; Saudino, 2005). It is possible that use of parental retrospective recall of infant activity inflated the shared environment estimate. However, it is also possible that the environment has changed since these earlier studies and that parental and societal patterns are exerting stronger effects. Twins attain their developmental milestones slightly later than singletons, although a study comparing 2151 twin pairs and 2151 singletons found no significant differences in age of reaching five developmental milestones (turn, sit, crawl, stand and walk) within the normal range (Brouwer et al., 2006). There is no reason to suppose that the magnitude of genetic and environmental influences would differ between twins and singletons. In our sample a proportion of infants had not begun walking by the time the 15 month questionnaire was returned therefore, our results may not be fully generalizable to late developing infants.

Conclusions

Genes are significant determinants of early life motor activity and developmental motor milestones, but the environment also plays an important role. These results support the need for research to identify the specific genes and specific environmental factors that influence motor development.

What Does this Study Add?

Variability in the timing of infant developmental milestones is poorly understood. This paper estimates genetic and environmental influences on motor development and infant movement activity level. The shared family environment appears to influence infants motor activity levels. The timing of independent first steps may have a stronger genetic influence.

Conflicts of Interest

The authors declare no conflicts of interest.

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