Gross Motor Milestones and Subsequent Development

Akhgar Ghassabian, MD, PhD,[a] Rajeshwari Sundaram, PhD,[b] Erin Bell, PhD,[c,d] Scott C. Bello, MD, MPH,[e] Christopher Kus, MD, MPH,[f] Edwina Yeung, PhD[a]

abstract

OBJECTIVE: We examined the longitudinal associations of age at achieving gross motor milestones and children's development in a US cohort of singletons and twins.

METHODS: In the Upstate KIDS study, a population-based study of children born between 2008 and 2010, information on age at achievement of motor milestones and developmental skills was available in 599 children (314 singletons, 259 twins, and 26 triplets). Mothers reported their children's major motor milestones at ~4, 8, 12, 18, and 24 months. At age 4 years, children's development was clinically assessed by using the Battelle Developmental Inventory, Second Edition (BDI-2). Primary analyses by using multivariate linear regressions were conducted in singletons. We also examined the associations in twins.

RESULTS: Later achievement of standing with assistance predicted lower BDI-2 scores in singletons in adjusted models (B per SD of age at achievement, –21.9 [95% confidence interval (CI), –41.5 to –2.2]). Post hoc analysis on age of standing with assistance showed that associations were driven by differences in adaptive skills (B = –5.3 [95% CI, –9.0 to –1.6]) and cognitive skills (B = –5.9 [95% CI, –11.5 to –0.4]). Analyses restricted to twins suggested no association between the age at achievement of milestones and total BDI-2 score after adjustment for gestational age and birth weight.

CONCLUSIONS: This study provides evidence that the age of achieving motor milestones may be an important basis for various aspects of later child development. In twins, key predictors of later development (eg, perinatal factors) overshadow the predictive role of milestones in infancy.

[a]*Epidemiology Branch and* [b]*Biostatistics and Bioinformatics Branch, Division of Intramural Population Health Research,* Eunice Kennedy Shriver *National Institute of Child Health and Human Development, National Institutes of Health, Bethesda, Maryland; Departments of* [c]*Environmental Health Sciences and* [d]*Epidemiology and Biostatistics, University at Albany School of Public Health, Albany, New York;* [e]*CapitalCare Pediatrics–Troy, Troy, New York; and* [f]*Division of Family Health, New York State Department of Health, Albany, New York*

Dr Yeung conceptualized and designed the study, conducted the initial analyses, and reviewed and revised the manuscript; Dr Ghassabian conducted the initial analyses, drafted the initial manuscript, and reviewed and revised the manuscript; Dr Sundaram conducted the initial analyses and reviewed and revised the manuscript; Drs Bell and Kus conceptualized and designed the study and reviewed and revised the manuscript; Dr Bello reviewed and revised the manuscript; and all authors approved the final manuscript as submitted.

DOI: 10.1542/peds.2015-4372

Accepted for publication Apr 28, 2016

Address correspondence to Edwina Yeung, PhD, 6100 Executive Blvd, 7B03, Bethesda, MD 20892. E-mail: yeungedw@mail.nih.gov

PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

WHAT'S KNOWN ON THIS SUBJECT: Significant delays in achieving milestones during infancy are important prodromal symptoms of developmental disabilities. Less clear is whether later achievement of gross motor milestones is associated with less favorable outcomes in children across the normal range of developmental skills.

WHAT THIS STUDY ADDS: We showed that the importance of infant motor development may not be limited to children with disabilities. Within the normal range, achieving a gross motor milestone earlier than peers may have favorable effects on adaptive and cognitive skills in childhood.

To cite: Ghassabian A, Sundaram R, Bell E, et al. Gross Motor Milestones and Subsequent Development. *Pediatrics.* 2016;138(1):e20154372

Significant delays in achievement of motor milestones in infancy are important prodromal symptoms of severe impairments such as intellectual disabilities.[1] Furthermore, minor deviances from normal motor development during infancy (eg, low-tone symptoms) predict cognition and language in toddlers and school-aged children.[2–4] However, follow-up studies exploring the relationship between age of achieving motor milestones in infancy and cognitive abilities at a later age are sparse and inconsistent.[5–7] Using retrospective reports of mothers on their children's milestones at age 2 years in the 1946 British Birth Cohort, Murray et al[5] reported that the age of standing alone is associated with intelligence as measured repeatedly until age 53 years. Similarly, in the Northern Finland 1966 Birth Cohort study, standing early was associated with better higher order cognitive processes, known as executive function, in adulthood.[6] In typically developing children born at term, Jenni et al[7] found that the age at achieving walking only weakly predicted a child's later cognition or motor performance; no association was reported between the time to sit without support and intelligence in children up to age 18 years. Factors such as reliability of retrospective assessment of time to achieve milestones, different sample characteristics (term versus preterm), and evaluation methods partly explain these inconsistent findings.[8,9]

Whether a better performance in infancy predicts a child's development at an older age is an important question for parents and health care professionals. Preterm children or children with very low birth weight have better motor performance and cognition if they achieve age-appropriate gross motor skills in infancy.[10,11] However, less clear is whether later achievement of gross motor milestones is associated with less favorable cognitive outcomes in children, independent of gestational age or birth weight. Twins also remain understudied and were frequently excluded in previous research.[5] To address the gap in knowledge, we examined the longitudinal association of time to achieve gross motor milestones in the first 2 years of life, as reported by mothers, and clinically measured children's developmental skills. We used data from a US birth cohort, which followed up singletons and twins from birth to age 4 years. Previous reports confirm the validity of maternal reports on child development and support the accuracy of maternal rating on infant's motor milestone achievement.[12,13] In particular, questionnaires administered repeatedly and with short intervals minimize recall bias and make it less likely that mothers err in their reporting of milestone ages. We hypothesized that delayed motor development is adversely associated with a child's adaptive, social, communication, motor, and cognitive skills in both singletons and twins.

METHODS

Participants

This analysis was conducted in the Upstate KIDS study, a population-based birth cohort focused on examining the association between infertility treatment and child development.[14] Briefly, from 2008 to 2010, the study used birth certificate information to sample infertility treatment exposure. For every singleton who was conceived by treatment, 3 singletons not conceived by treatment were enrolled, frequency matched on perinatal region of birth. Because of the high rate of multiples in pregnancies after infertility treatment, the study included all twins and other higher order births, irrespective of the mode of conception.

The New York State Department of Health and the University of Albany Institutional Review Board (IRB) approved the study (NYSDOH IRB #07-097; UAlbany #08-179) and served as the IRB designated by the National Institutes of Health for this study under a reliance agreement. Parents provided written informed consent on behalf of their children.

Of the 6171 children originally enrolled in the Upstate KIDS study, a subgroup was invited to participate in an in-depth assessment at age 4 years. These were: (1) children who failed a developmental screening questionnaire (Ages and Stages Questionnaire[15] at age 36 or 30 months or the Modified Checklist for Autism in Toddlers[16] at age 18 or 24 months); (2) children referred to the New York State Early Intervention Program for clinical evaluation; (3) higher order multiples and twins (irrespective of their screening fail/pass status); and (4) a random selection of the children who passed the Ages and Stages Questionnaire or Modified Checklist for Autism in Toddlers. Due to the geographical distribution of participants, a subgroup of subjects was invited to participate in clinical evaluations in 2 centers for Leadership in Education and Neurodevelopmental Related Disorders, located in Westchester and Rochester, New York, along with CapitalCare Developmental-Behavioral Pediatrics in Latham, New York. All the invitees were residents of New York State, English-speaking, and consented to assessments.

Of the 2154 children invited to participate in the clinic visit, 601 (27.9%) children completed a visit (mean age, 4 years and 4 months; range, 3 years and 1 month–5 years and 8 months). Among these children, information on age at achievement of motor milestones in infancy was available from 599 children (314 singletons, 259 twins, and 26 triplets). Triplets were excluded from the present analysis because of the small number.

Measurements

Mothers reported their children's gross motor development at ~4, 8, 12, 18, and 24 months. Mothers were provided with health journals to track children's milestone achievement in the form of a diary and were encouraged to use it to complete the questionnaires. Maternal report of gross motor encompasses 6 major milestones: sitting without support, standing with assistance, crawling on hands and knees, walking with assistance, standing alone, and walking alone. A description of each milestone was given to the mothers (Supplemental Table 5). The mothers were asked to indicate achievement of each milestone and recall the date of achievement. We calculated the time to achieve gross motor milestones by subtracting the date of birth from each date of achievement provided. The age at achievement of milestones in this study was comparable to the normative sample of the World Health Organization's Multicentre Growth Reference Study.[17]

During the clinic visit at age 4 years, the children were assessed by trained personnel using the Battelle Developmental Inventory, Second Edition (BDI-2). The BDI-2 is an individually administered and standardized assessment that is used to measure developmental skills in children up to age 7 years, 11 months.[18] The 450 items of the BDI-2 assess 5 domains of development: personal/social, adaptive, motor, communication, and cognitive on a 3-point scale. The BDI-2 provides a total score for the battery as well as scores for each of the 5 domains. The BDI-2 has acceptable reliability and excellent internal consistency, as well as acceptable content and criterion validity.

Based on the clinical evaluations, the developmental pediatricians provided up to 4 diagnoses for each child. Developmental disability was defined as having ≥1 of the following diagnoses: autism spectrum disorder; attention-deficit/hyperactivity disorder; language, learning, and speech disorders; cognitive deficits; cerebral palsy; and/or sensory impairments.

Information on all the covariates (including maternal age, sociodemographic characteristics [eg, highest acquired education level and race/ethnicity], history of smoking and pregnancy alcohol consumption, prepregnancy weight and height, as well as gestational age, birth size, having a sibling, and infant day care attendance) was obtained from self-administered maternal questionnaires or vital records.

Statistical Analyses

We used χ^2 tests and independent sample t tests to compare maternal and child characteristics between children included in the analyses (n = 599) and eligible children excluded due to nonparticipation for the clinic visit or missing milestone information (n = 1555). Number of valid observations for age of achievement of motor milestones ranged between 382 for walking with assistance and 479 for sitting without supports. The percentage of missing for covariates was <5%.

Because of possible differences in neurodevelopment of singletons and twins, analyses were stratified according to plurality. The associations between age at achievement of motor milestones and children's developmental skills were analyzed by using multivariable linear regression in singletons. Associations were examined in twins by using generalized estimating equations to account for the correlation between sibships. To limit multiple comparisons, we first tested the association of age at achievement of milestones with the total BDI-2 score. Consequently, we explored whether any observed associations were accounted for by specific domains of BDI-2. We additionally accounted for oversampling of children conceived by infertility treatment or children at risk for developmental delay by adjusting all analyses for fertility treatment and fail/pass status on developmental screening. The ages at achieving 6 motor milestones were divided by their SD so that their associations with BDI-2 developmental scores could be interpreted per SD increase in age (month). All analyses were rerun in the subsample with no diagnosis of developmental disabilities to explore if the results were driven by children with a developmental delay (57 singletons and 38 twins).

Covariates in the model were selected a priori on the basis of background knowledge about the study question.[5–7,19] Model 1 was adjusted for maternal age, education, race, prepregnancy BMI, smoking, drinking, being married, having private insurance, and a child's sex, age, having older siblings, and day care attendance before 12 months. Model 2 additionally adjusted for gestational age and birth weight; and model 3 was additionally adjusted for developmental screening status and exposure to infertility treatment.

Statistical analysis was conducted by using SAS version 9.4 (SAS Institute, Inc, Cary, NC).

RESULTS

The mothers of the 599 children included in the analyses were older (mean difference, 1.3 years; P < .001) and had higher socioeconomic status, including having higher education (38.1% vs 33.1%; P < .001), conceiving with infertility treatment (44.6% vs 36.0%; P = .001), and having private insurance (86.8% vs 79.5%; P < .001) compared

TABLE 1 Characteristics of Study Participants, the Eligible Cohort, and the Full Cohort

Characteristic	Study Population (*n* = 599)	Invited for the Clinic Visit (*n* = 2154)	Full Cohort (*N* = 6171)
Child characteristics			
Male sex	50.1	51.6	51.4
Age at developmental assessment, mo	52.0 ± 5.5	—	—
Plurality			
Singletons	52.4	55.0	63.3
Twins	43.2	41.5	34.5
Triplets	4.3	3.3	2.0
Quadruplets	0	0.2	0.2
Gestational age, wk	38 (36–39)	38 (36–39)	38 (36–39)
Birth weight, g	2926 ± 769	2932 ± 799	3023 ± 752
Having an older sibling	52.2	51.7	54.4
Day care attendance <12 mo	59.6	55.0	53.6
Age at achievement of motor milestones, mo			
Sitting without support	6.8 ± 1.6	6.8 ± 1.8	6.7 ± 1.7
Standing with assistance	8.9 ± 2.1	8.7 ± 2.1	8.5 ± 2.0
Hands-and-knees crawling	8.9 ± 2.0	8.8 ± 2.1	8.5 ± 2.0
Standing alone	11.3 ± 2.2	11.3 ± 2.4	11.0 ± 2.3
Walking with assistance	10.2 ± 2.2	10.2 ± 2.4	9.9 ± 2.3
Walking alone	13.0 ± .7	12.9 ± 5.5	12.7 ± 4.7
Developmental scale scores			
Adaptive domain	22.7 ± 7.2	—	—
Personal/social domain	41.0 ± 11.2	—	—
Communication	25.2 ± 8.3	—	—
Motor	34.1 ± 10.0	—	—
Cognitive	35.0 ± 10.6	—	—
Total	158.3 ± 39.8	—	—
Maternal characteristics			
Age, y	32.4 ± 5.5	31.4 ± 6.0	30.7 ± 6.0
Parity, primipara	47.4	48.1	45.4
Race/ethnicity			
Non-Hispanic white	85.8	82.9	80.4
Not white or other	14.2	17.1	19.6
Educational level			
Less than high school	2.3	4.3	6.0
High school equivalent	6.7	10.1	12.5
Some college	25.5	26.9	29.9
College graduate	27.4	24.2	22.5
Graduate/professional school	38.1	34.5	29.1
Private health insurance	86.8	81.5	75.8
Married	93.4	90.9	88.4
History of smoking in pregnancy	8.2	9.8	13.6
Alcohol consumption during pregnancy	10.9	11.1	11.6
Prepregnancy BMI	26.2 (23.0–31.1)	25.5 (22.3–30.5)	25.5 (22.2–30.6)
Infertility treatment	44.6	38.4	32.4

Data are presented as mean ± SD for continuous normally distributed variables, median (90% range) for continuous variables with skewed distribution, and percentages for categorical variables. Developmental scale scores were derived by using the BDI-2.

with mothers of the 1555 children excluded from analyses because they did not participate in the clinic visit (*n* = 1553) or had no milestone data (*n* = 2). There was no difference between the 2 groups in sex, birth weight, or age at achievement of motor milestones.

Baseline characteristics of the study population (*n* = 599), those invited to participate in the clinic visit (*n* = 2154), and the full cohort (*N* = 6171) are presented in Table 1. Among the participants, 50% of children were boys, 52.4% were singletons, and 59.6% attended day care in the first year of life. In total, 44.6% of women received infertility treatment of the index pregnancy, and 85.8% of them were non-Hispanic white. The comparison of the study participants with the full cohort indicates the representativeness of this sample, even though twins and children conceived with infertility treatment were overrepresented.

We found that an older age of achieving motor milestones was associated with lower total developmental skills in singletons, independent of gestational age or birth weight (model 2) (Table 2). When models were additionally adjusted for factors related to the sampling framework (model 3), we observed that if children

TABLE 2 Age at Achievement of Gross Motor Milestones in Infancy and Total Developmental Scale Score at Age 4 Years: Upstate KIDS Study

Milestone	Model 1	Model 2	Model 3
	B (95% CI), *P*	B (95% CI), *P*	B (95% CI), *P*
Singletons (*n* = 314)			
Sitting without support	−34.0 (−57.9 to −10.1), .01	−36.0 (−62.3 to −9.6), .01	−17.6 (−40.7 to 5.4), .14
Hands-and-knees crawling	−29.6 (−52.6 to −6.6), .01	−29.2 (−54.0 to −4.5), .02	−12.5 (−34.9 to 9.9), .28
Standing with assistance	−42.1 (−63.2 to −21.0), <.001	−42.6 (−64.5 to −20.7), <.001	−21.9 (−41.5 to −2.2), .03
Standing alone	−23.2 (−52.0 to 5.7), .12	−28.5 (−59.7 to 2.7), .08	−6.2 (−35.2 to 22.9), .68
Walking with assistance	−35.5 (−58.7 to −12.4), .003	−42.7 (−67.6 to −17.8), <.001	−19.6 (−42.7 to 3.5), .10
Walking alone	−25.9 (−52.8 to 0.9), .06	−28.4 (−31.5 to −0.1), .05	−5.4 (−31.5 to 20.7), .69
Twins (*n* = 259)			
Sitting without support	−2.6 (−28.3 to 23.1), .84	8.4 (−18.7 to 35.4), .55	7.8 (−19.0 to 34.6), .57
Hands-and-knees crawling	2.5 (−18.5 to 23.4), .82	9.9 (−13.8 to 33.6), .41	11.7 (−10.6 to 34.0), .30
Standing with assistance	−3.9 (−29.5 to 21.6), .76	5.0 (−23.4 to 33.4), .73	6.1 (−20.0 to 32.1), .65
Standing alone	−29.2 (−54.0 to −4.4), .02	−23.6 (−53.2 to 5.9), .12	−21.4 (−47.1 to 4.3), .10
Walking with assistance	−27.7 (−47.7 to−7.8), .01	−18.3 (−40.0 to 3.4), .10	−10.9 (−34.7 to 13.0), .37
Walking alone	−15.5 (−40.5 to 9.6), .23	−11.3 (−37.2 to 14.6), .39	−8.1 (−28.9 to12.7), .44

Developmental skills were assessed by using the BDI-2. Model 1: adjusted for maternal age, education, race, prepregnancy BMI, smoking, drinking, being married, having private insurance, having older sibling for the child, and a child's sex, age, and day care attendance before 12 months. Model 2: additionally adjusted for gestational age and birth weight. Model 3: additionally adjusted for developmental screening status and exposure to infertility treatment. Descriptions of each milestone are given in Supplemental Table 5.

TABLE 3 Age at Standing With Assistance in Infancy and Developmental Scale Scores at Age 4 Years: Upstate KIDS Study (Singletons, *n* = 314)

Developmental Skill	Model 1	Model 2	Model 3
	B (95% CI), *P*	B (95% CI), *P*	B (95% CI), *P*
Adaptive	−8.8 (−12.6 to −5.1), <.001	−8.7 (−12.6 to −4.7), <.001	−5.3 (−9.0 to −1.6), .01
Personal/social	−6.8 (−13.1 to −0.6), .03	−5.9 (−12.4 to 0.6), .08	−0.2 (−6.3 to 5.9), .95
Communication	−7.9 (−12.2 to −3.6), <.001	−7.9 (12.5 to −3.3), .001	−3.5 (−7.7 to 0.7), .11
Motor	−9.6 (−14.8 to −4.5), <.001	−8.9 (−14.3 to −3.5), .001	−4.9 (−10.0 to 0.2), .06
Cognitive	−11.2 (−15.8 to −6.6), <.001	−10.6 (−16.4 to −4.8), <.001	−5.9 (−11.5 to −0.4), .04

Developmental skills were assessed by using the BDI-2. Model 1: adjusted for maternal age, education, race, prepregnancy BMI, smoking, drinking, being married, having private insurance, having older sibling for the child, and a child's sex, age, and day care attendance before 12 months. Model 2: additionally adjusted for gestational age and birth weight. Model 3: additionally adjusted for developmental screening status and exposure to infertility treatment.

achieved milestones of standing with assistance by 2.1 months later (SD for age of achievement of standing with assistance in this sample), their BDI-2 developmental scores decreased by 21.9 scores (95% confidence interval [CI], −41.5 to −2.2). When analyses were restricted to twins, the associations between the ages of achieving milestones of standing alone and walking with assistance and total BDI-2 scores attenuated and became not significant when models were adjusted for gestational age, birth weight, and factors related to the sampling framework.

Post hoc analysis on age of standing with assistance in singletons showed that associations were primarily driven by differences in adaptive skills (B per SD of age, −5.3 [95% CI, −9.0 to −1.6]) and cognitive skills (B per SD of age, −5.9 [95% CI, −11.5 to −0.4]) at age 4 years (Table 3). The association between time to achieve standing with assistance with motor skills was borderline significant in model 3 (B per SD of age, −4.9 [95% CI, −10.0 to 0.2]).

When the children with a developmental disability were excluded, longitudinal associations were observed between ages at achievement of crawling and standing with assistance and developmental skills at 4 years. These associations slightly attenuated after adjustment for infertility treatment (B per SD of age at crawling, −23.4 [95% CI, −42.9 to −3.9]; B per SD of age at standing with assistance, −18.4 [95% CI, −37.1 to 0.4]) (Table 4).

DISCUSSION

These longitudinal analyses in a US contemporary cohort of singletons and twins suggest that an earlier achievement of standing with assistance predicts better developmental skills in singletons independent of gestational age or birth weight. The associations existed across the normal range of development and were in particular observed for adaptive skills and cognitive abilities. In contrast to our hypothesis, there was no association between age at achievement of milestones in infancy and later development in twins, when accounting for perinatal factors.

In preterm infants and infants with developmental disabilities, early motor development has been used for a long time as a prognostic factor for later age neurologic development.[20] Studies have shown that optimal motor development in healthy infants is related to later cognition or language skills.[3,4]

TABLE 4 Age at Achievement of Gross Motor Milestones in Infancy and Total Developmental Scale Score at Age 4 Years in Singletons With No Developmental Disabilities (n = 257): Upstate KIDS Study

Gross Motor Milestones	Total Developmental Scale Score at Age 4 y		
	Model 1	Model 2	Model 3
	B (95% CI), *P*	B (95% CI), *P*	B (95% CI), *P*
Sitting without support	−16.4 (−37.1 to 4.3), .12	−9.4 (−30.8 to 12.0), .39	−10.1 (−31.4 to 11.2), .35
Hands-and-knees crawling	−22.1 (−40.8 to −3.5), .02	−23.0 (−42.5 to −3.5), .02	−23.4 (−42.9 to −3.9), .02
Standing with assistance	−21.4 (−39.6 to −3.1), .02	−18.7 (−37.5 to 0.01), .05	−18.4 (−37.1 to 0.4), .06
Standing alone	6.4 (−18.3 to 31.1), .61	0.4 (−25.5 to 29.7), .98	0.3 (−25.6 to 26.3), .99
Walking with assistance	−7.7 (−27.5 to 12.1), .45	−13.5 (−34.7 to 7.7), .21	−13.8 (−35.1 to 7.6), .21
Walking alone	−7.0 (−29.0 to 15.1), .54	−7.2 (−29.7 to 15.2), .53	−8.0 (−30.6 to 14.7), .49

Developmental skills were assessed by using the BDI-2. Model 1: adjusted for maternal age, education, race, prepregnancy BMI, smoking, drinking, being married, having private insurance, having older sibling for the child, and a child's sex, age, and day care attendance before 12 months. Model 2: additionally adjusted for gestational age and birth weight. Model 3: additionally adjusted for exposure to infertility treatment.

A common neural substrate is postulated to underlie the association between motor development in infancy and cognition at an older age. The basal ganglia, as part of the complex neural system of cerebral cortex–cerebellum–basal ganglia, have been traditionally known for motor control. Recent evidence confirms that the basal ganglia, specifically the caudate nucleus, interact closely with the executive parts of the frontal lobes to regulate cognitive function.[21] In addition, basal ganglia are essential elements of linguistic learning in humans.

In the Upstate KIDS study, the age a child first stood was a significant predictor of later cognition. This finding is consistent with previous investigations in older cohorts that highlight the influence of the speed of development during infancy on later cognition.[5,6] In these studies, there was a linear relation between the age at achievement of standing and IQ in adolescents and neuropsychological performance in adults. One speculative explanation for this finding is that early establishment of connection loops between cortical and subcortical circuits in the brain may have a favorable influence on the early development of motor function as well as cognitive abilities in an older age. In line with this hypothesis, a longitudinal neuroimaging study in the general population showed positive associations of an earlier age at achievement of motor milestones with greater gray matter density in the premotor cortex and caudate nucleus and with white matter volume in the frontal and parietal lobes in adulthood.[22] We observed that the age a child first stood predicted his or her adaptive skills (self-care in young children [eg, a child's ability of feeding with a utensil]) at age 4 years. A child's surrounding is a critical component in formation of adaptive skills. Nevertheless, the observed associations are not surprising because for many of these activities, an optimal motor development is needed. Our finding of a relation between age of achieving motor milestones in infancy and motor skills observed at age 4 years by a specialist and reports of others[7] supports this explanation. We found no association between infants' age of milestone achievement and children's personal/social or communication skills. Although some studies have shown a moderate association between infant suboptimal neuromotor development and language delays,[4,23] others failed to show similar associations.[24,25] Further investigation is needed to explore whether the continuity between infant motor milestone and development is restricted to adaptive or cognitive domain only or it also exists in other domains of development.

Other studies have shown that the milestone of walking weakly predicts cognition at an older age.[26] We found that walking was not a significant predictor of a child's development at age 4 years, particularly so after adjustment for perinatal factors and excluding children with developmental disabilities. Capute et al also found that the relation between the age of walking and intelligence was mainly driven by the children with extreme cognitive abilities.[27] Moreover, we found no relation between time to achieve motor milestones and social skills in singletons or twins. Retrospective observation of children with autism spectrum disorder showed that these children had minor deviances in motor development in infancy.[28] Nevertheless, whether this association exists within the normal range of gross motor milestones is less clear. Furthermore, prospective studies in children at risk for autism spectrum disorder reported that gross motor abnormalities in these children did not emerge before the age of 2 years.[29]

To the best of our knowledge, this study is the first to examine the longitudinal association of time to achieve milestones and later development in twins. Compared with singletons, otherwise healthy twins are usually born at earlier weeks of gestation, have slightly lower Apgar scores at birth, and are born to older mothers.[30] Therefore, multiple competing risk factors of delayed development exist in twins that could potentially overshadow the predictive role of milestones in infancy for later development. Future studies are needed to confirm our findings.

Despite its strengths, including prospective assessment of motor milestones, inclusion of a wide range of covariates, and direct observation of cognitive, social, and personal skills in children, this study faced limitations. First, because of the limited geographical distribution of the clinics available for participants to attend, there was a large nonresponse. The participants who failed to attend the clinic visit were younger mothers, with lower education, and no private insurance; this scenario indicates that mothers who may have had lower socioeconomic status may not have been represented in the study. Nevertheless, we observed no differences in infants' characteristics or age at achievement of milestones between the study sample and nonparticipants. In addition, the age of achievement of milestones in this sample was similar to the full cohort. Second, we had to rely on maternal report of age at achievement of milestones. However, standardized tests assessing children's milestones also have limitations in capturing the exact age of achieving milestones.

CONCLUSIONS

These results imply that the importance of normal progression of infant motor development to subsequent developmental status may not be limited to children with developmental disabilities. Rather, within the normal range, achieving a gross motor milestone earlier than peers may have favorable effects on adaptive skills and cognitive performance in childhood. Clinically, our findings suggest age of achieving motor milestones in infancy may be an important basis for various aspects of later child development. Furthermore, the predictive value of an easy-administered simple assessment, such as age at achievement of standing, for later adaptive and cognitive skills in children has a public health impact. Further studies are needed to explore the underlying mechanisms that explain the significance of achieving the milestone of standing for later development.

ACKNOWLEDGMENTS

The authors thank all the Upstate KIDS families and staff for their important contributions.

ABBREVIATIONS

BDI-2: Battelle Developmental Inventory, Second Edition
CI: confidence interval
IRB: institutional review board

FINANCIAL DISCLOSURE: The authors have indicated they have no financial relationships relevant to this article to disclose.

FUNDING: Supported by the Intramural Research Program of the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (HHSN275201200005C and HHSN267200700019C). Funded by the National Institutes of Health (NIH).

POTENTIAL CONFLICT OF INTEREST: The authors have indicated they have no potential conflicts of interest to disclose.

REFERENCES

1. von Wendt L, Mäkinen H, Rantakallio P. Psychomotor development in the first year and mental retardation—a prospective study. *J Ment Defic Res*. 1984;28(pt 3):219–225
2. Piek JP, Dawson L, Smith LM, Gasson N. The role of early fine and gross motor development on later motor and cognitive ability. *Hum Mov Sci*. 2008;27(5):668–681
3. Hitzert MM, Roze E, Van Braeckel KN, Bos AF. Motor development in 3-month-old healthy term-born infants is associated with cognitive and behavioural outcomes at early school age. *Dev Med Child Neurol*. 2014;56(9):869–876
4. van Batenburg-Eddes T, Henrichs J, Schenk JJ, et al. Early infant neuromotor assessment is associated with language and nonverbal cognitive function in toddlers: the Generation R Study. *J Dev Behav Pediatr*. 2013;34(5):326–334
5. Murray GK, Jones PB, Kuh D, Richards M. Infant developmental milestones and subsequent cognitive function. *Ann Neurol*. 2007;62(2):128–136
6. Murray GK, Veijola J, Moilanen K, et al. Infant motor development is associated with adult cognitive categorisation in a longitudinal birth cohort study. *J Child Psychol Psychiatry*. 2006;47(1): 25–29
7. Jenni OG, Chaouch A, Caflisch J, Rousson V. Infant motor milestones: poor predictive value for outcome of healthy children. *Acta Paediatr*. 2013;102(4):e181–e184
8. Shaywitz BA, Ferrer E, Shaywitz SE. A case of less than meets the eye. *Ann Neurol*. 2007;62(2):109–111
9. Largo RH. Early motor development in preterm children. In: Savelsbergh GJP, ed. *Advances in Psychology*. Vol 97. Amsterdam, Netherlands: Elsevier; 1993:425–444
10. Butcher PR, van Braeckel K, Bouma A, Einspieler C, Stremmelaar EF, Bos AF. The quality of preterm infants' spontaneous movements: an early indicator of intelligence and behaviour at school age. *J Child Psychol Psychiatry*. 2009;50(8): 920–930
11. Burns Y, O'Callaghan M, McDonell B, Rogers Y. Movement and motor development in ELBW infants at 1 year is related to cognitive and motor

abilities at 4 years. *Early Hum Dev*. 2004;80(1):19–29

12. Bodnarchuk JL, Eaton WO. Can parent reports be trusted?: Validity of daily checklists of gross motor milestone attainment. *J Appl Dev Psychol*. 2004;25(4):481–490
13. Langendonk JM, van Beijsterveldt CE, Brouwer SI, Stroet T, Hudziak JJ, Boomsma DI. Assessment of motor milestones in twins. *Twin Res Hum Genet*. 2007;10(6):835–839
14. Buck Louis GM, Hediger ML, Bell EM, et al. Methodology for establishing a population-based birth cohort focusing on couple fertility and children's development, the Upstate KIDS study. *Paediatr Perinat Epidemiol*. 2014;28(3):191–202
15. Bricker DD, Squires J, Mounts L. *Ages & Stages Questionnaires: A Parent-Completed, Child-Monitoring System*. Baltimore, MD: Paul H. Brookes Publishing; 1999
16. Robins DL, Fein D, Barton ML, Green JA. The Modified Checklist for Autism in Toddlers: an initial study investigating the early detection of autism and pervasive developmental disorders. *J Autism Dev Disord*. 2001;31(2):131–144
17. WHO Multicentre Growth Reference Study Group. WHO Motor Development Study: windows of achievement for six gross motor development milestones. *Acta Paediatr Suppl*. 2006;450:86–95
18. Newborg J. *Battelle Developmental Inventory*. 2nd ed. Itasca, IL: Riverside; 2005
19. van Batenburg-Eddes T, de Groot L, Steegers EA, et al. Fetal programming of infant neuromotor development: the generation R study. *Pediatr Res*. 2010;67(2):132–137
20. Rosenbaum PL, Walter SD, Hanna SE, et al. Prognosis for gross motor function in cerebral palsy: creation of motor development curves. *JAMA*. 2002;288(11):1357–1363
21. Leisman G, Braun-Benjamin O, Melillo R. Cognitive-motor interactions of the basal ganglia in development. *Front Syst Neurosci*. 2014;8:16
22. Ridler K, Veijola JM, Tanskanen P, et al. Fronto-cerebellar systems are associated with infant motor and adult executive functions in healthy adults but not in schizophrenia. *Proc Natl Acad Sci USA*. 2006;103(42):15651–15656
23. Iverson JM. Developing language in a developing body: the relationship between motor development and language development. *J Child Lang*. 2010;37(2):229–261
24. Serdarevic F, van Batenburg-Eddes T, Mous SE, et al. Relation of infant motor development with nonverbal intelligence, language comprehension and neuropsychological functioning in childhood: a population-based study [published online ahead of print November 8, 2015]. *Dev Sci*. doi: 10.1111/desc.12326
25. Darrah J, Hodge M, Magill-Evans J, Kembhavi G. Stability of serial assessments of motor and communication abilities in typically developing infants—implications for screening. *Early Hum Dev*. 2003;72(2):97–110
26. Hamadani JD, Tofail F, Cole T, Grantham-McGregor S. The relation between age of attainment of motor milestones and future cognitive and motor development in Bangladeshi children. *Matern Child Nutr*. 2013;9(suppl 1):89–104
27. Capute AJ, Shapiro BK, Palmer FB, Ross A, Wachtel RC. Cognitive-motor interactions. The relationship of infant gross motor attainment to IQ at 3 years. *Clin Pediatr (Phila)*. 1985;24(12):671–675
28. Ming X, Brimacombe M, Wagner GC. Prevalence of motor impairment in autism spectrum disorders. *Brain Dev*. 2007;29(9):565–570
29. Landa R, Garrett-Mayer E. Development in infants with autism spectrum disorders: a prospective study. *J Child Psychol Psychiatry*. 2006;47(6):629–638
30. Sutcliffe AG, Derom C. Follow-up of twins: health, behaviour, speech, language outcomes and implications for parents. *Early Hum Dev*. 2006;82(6):379–386

PEDIATRICS
OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

Gross Motor Milestones and Subsequent Development

Akhgar Ghassabian, Rajeshwari Sundaram, Erin Bell, Scott C. Bello, Christopher Kus and Edwina Yeung

Pediatrics 2016;138;
DOI: 10.1542/peds.2015-4372 originally published online June 27, 2016;