Longitudinal Associations Between Device-Measured Physical Activity and Early Childhood Neurodevelopment

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Background: The aim of this study was to investigate longitudinal associations between physical activity and early childhood neurodevelopment. **Methods:** Data from 1673 children from the 2015 Pelotas (Brazil) birth cohort study were analyzed. Physical activity was measured using accelerometers on the wrist at ages 1, 2, and 4 years. Neurodevelopment was measured using the Battelle Development Inventory at age 4 years. Linear regression models were used to test trajectories and cumulative associations of physical activity with child neurodevelopment. **Results:** Of the 3 physical activity trajectories observed, children in the medium ($\beta = 1.17$; 95% confidence interval, 0.25 to 2.10) and high ($\beta = 2.22$; 95% confidence interval, 0.61 to 3.82) trajectories showed higher neurodevelopment scores than children in the lower activity trajectory. Cumulative analyses showed that children in the highest tertile of physical activity in all follow-ups presented a mean neurodevelopment score 4.57 (95% confidence interval, 2.63 to 6.51) higher than children in the lowest tertile in all follow-ups. All analyses showed a dose–response characteristic of association, with higher physical activity indicating higher neurodevelopment scores. **Conclusions:** Physical activity may be an important predictor of neurodevelopment through early childhood.

Keywords: pediatrics, accelerometry, movement, growth, development

In recent years, there has been a growth in the evidence about the positive effects of physical activity on child health, including benefits to bone and cardiovascular health, cognition, motor skills, and psychological and social well-being.^{1–6} Moreover, studies have shown that physical activity during childhood is an important predictor of physical activity levels during adolescence and adulthood, making early childhood an optimal developmental window for interventions.^{7–9}

To date, systematic reviews of observational studies have shown that physical activity and participation in sports in early childhood (<5 y) are associated with improved cognitive and language development during childhood.^{10–12} Furthermore, meta-analyses of intervention studies that investigated the effects of physical activity on neurodevelopment found that physical activity is likely to improve cognition and metacognition in youth¹³ and motor skills and cognitive development in preschool children.¹⁴ The potential relationship between physical activity and childhood neurodevelopment has also been supported by clinical experimental studies that measured brain function and microstructures, such as white matter.^{15,16}

Despite the potential benefits of physical activity for child neurodevelopment, a major limitation is that most studies assessed physical activity using questionnaires or reports from parents/ caregivers/teachers.^{1,11} This is a limitation because self-report measurement of physical activity in this age group may be inappropriate given the intermittent and unstructured characteristics^{17–20} of physical activity; thus, the true influence of physical activity on neurodevelopment remains unclear.

Device-based measurement of physical activity is particularly suitable and feasible for young children^{20–22} because it can capture high resolution and nonpurposeful physical activity.^{20–24} However, only a few studies investigated the association between device-measured physical activity and cognitive development in early childhood,¹² and none of these studies were conducted in low- and middle-income countries.¹² Moreover, most of these studies were conducted in small samples, were cross-sectional, and used a variety of methods to process and analyze device-measured physical activity.

The use of different cutoff points to classify physical activity intensity, the lack of accelerometer raw estimates to enhance comparability between studies, and the lack of longitudinal studies with large samples limit the understanding of the association between physical activity and child neurodevelopment.^{3,10–12,14–16} Therefore, the overall aim of this study was to investigate the longitudinal association of device-measured physical activity and early childhood neurodevelopment in the participants of the 2015 Pelotas (Brazil) Birth Cohort Study. The specific aims of this study were to investigate: (1) the individual associations of device-measured physical activity at ages 1, 2, and 4 years with child neurodevelopment at 4 years; (2) the association between trajectories of physical activity from ages 1 to 4 years and neurodevelopment at 4 years; and (3) the potential effect of total device-measured physical activity accumulated from ages 1 to 4 years on childhood neurodevelopment at 4 years.

Methods

Population

The present study used data of children from the 2015 Pelotas (Brazil) Birth Cohort Study. This cohort included 99% of all

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hospital-delivered newborn children between January 1 and December 31 in 2015 in Pelotas, Brazil (N = 4275). Participants were invited for further follow-up assessments when the infants were aged 1, 2, and 4 years. Of the 4275 children in the original cohort, 95.4% were assessed at ages 1, 2, and 4 years. In all interviews, caregivers provided written informed consent. The 2015 Pelotas (Brazil) Birth Cohort Study was approved by the School of Physical Education Ethics Committee from the Federal University of Pelotas (CAAE registration number: 26746414.5. 0000.5313). Detailed information on recruitment and the logistics of the 2015 Pelotas (Brazil) Birth Cohort Study has been published elsewhere.^{25,26} For the present study, the analytic sample was composed of children with accelerometer data at 1, 2, and 4 years and neurodevelopment data at 4 years (n = 1673) (Supplementary Figure S1 [available online]).

Neurodevelopment Measure

Child's neurodevelopment was assessed at 4 years using an adapted version of the Battelle Development Inventory (BDI). The instrument included 66 items, which were used to assess 5 domains of neurodevelopment (personal-social, adaptive, fine and gross motor, communication, and cognitive).²⁷ Trained interviewers, under the supervision of psychologists specialized in child development, administrated the instrument.27,28 Based on direct observation of children and structured interviews with caregivers, a total development score ranging from 0 to 132 was generated, with higher values indicating better development. In addition, developmental scores for each subdomain were also calculated. This instrument was found to have good and stable correlations with the Woodcook-Johnson Test of Achievement-Revised,²⁹ a norm-referenced tool of academic achievement indicating broad knowledge and skills like letter-word identification (mean of correlations = .74; ranging from .40 to $.94^{29}$). In the current follow-up, intraclass correlation coefficient was calculated to evaluate the consistency between the interviewers' and quality evaluators' scores. The personal-social (r = .62), adaptive (r = .58), and motor (r=.59) domains showed moderate correlation (r=.50-.70). For the communication (r=.82) and cognitive (r=.71) domains, a strong intraclass correlation (r=.71-1.00)was observed. For Battelle's final score, intraclass correlation coefficient was .70, showing moderate correlation.

Physical Activity Measure

At 1, 2, and 4 years, children wore an ActiGraph (model wGT3X-BT; ActiGraph, Pensacola, FL), a waterproof device that measured acceleration in 3 axis (*x*, forward/backward; *y*, right/left; and *z*, up/ down) within a $\pm 6g$ dynamic range. Accelerometers were set with a sampling frequency at 60 Hz and 5-second epoch. The device was placed on the left wrist using a disposable bracelet. Wrist placement was chosen based on a previous calibration study in the same sample and the literature, which has shown better compliance and comfort comparing with ankle.^{19,30}

In all follow-up assessments, children were instructed to wear the accelerometers during 24 hours with a minimum of 16 hours of use to be considered a valid day.³⁰ At 1 and 2 years, children wore the device for 4 and 3 days, respectively. The number of days was chosen based on protocol studies on young children, which indicated at least 2 days of use to represent a week of data.^{30,31} At 4 years, given the availability of accelerometers, children wore the device for 7 days, including at least 3 valid days. Accelerometer data were downloaded and raw data files were extracted using the ActiLife software (version 6.1, ActiGraph Corp, Pensacola, FL). Raw data were analyzed with R package GGIR (http://cran.r-project.org). Raw acceleration was expressed based on the Euclidian norm minus one measure, which summarized 3-dimensional raw data activity acceleration (from *x*, *y*, and *z* axis) (Euclidian norm minus one $= \Sigma |\sqrt{(x^2 + y^2 + z^2)} - 1g|$). Data were expressed in milligravitational units (gravitational equivalent: 1000mg = 1g = 9.81 m/s²).

Nonwear time detection was estimated based on the SD and value range of each accelerometer axis. Classification of nonwear time was estimated in 15-minute blocks based on the characteristics of the 60-minute window centered in this block. Finally, a block was considered nonwear time if the SD of the 60-minute window was <13.0mg and the value range <50mg for at least 2 of the 3 accelerometer axis.³² Nonwear time was imputed with the average values for the same time of day of all different days of measure, as in previous studies.³³

For the purposes of analyses, average acceleration over 24 hours was summarized on 5-second epochs (expressed in milligravitational units).³² To allow comparability within and between participants, and given the lack of specific threshold to define physical activity in different intensities, in each follow-up, the mean acceleration per valid day of use was calculated.

Trajectories of Physical Activity

To explore the associations between different trajectories of physical activity and neurodevelopment, a range of physical activity variables were computed. Initially, average acceleration was categorized in tertiles in each follow-up measure. Based on tertiles of acceleration for each follow-up assessment, a cumulative physical activity score was created. For this, tertiles of physical activity were scored from 1 (lowest tertile) to 3 (highest tertile), and the cumulative score was created by summing scores (1-3) at ages 1, 2, and 4 years. Therefore, in the cumulative score, which ranges from 3 to 9, "3" represented children in the lowest tertile of acceleration in all 3 follow-ups.

To identify different patterns of physical activity through early childhood, a group-based trajectory modeling was used with data from 1, 2, and 4 years. This approach identified groups of individuals following similar trajectories based on finite mixtures approach, providing practical and flexible clusters of individual trajectories. The number and shape of trajectories were based on the best fit of the Bayesian information criteria and the interpretability of trajectories obtained. Selection of the models was confirmed using the posterior probability of subject's probability of belonging in each trajectory group, for which values of average posterior probabilities in each group were superior to 70%, as recommended.³⁴

Covariates

Child and maternal characteristics were used as covariates in the study, considering their potential influence on both physical activity and neurodevelopment.^{27,35} From the perinatal assessment, the following variables were used: sex (male and female); maternal education (0–4, 5–8, 9–11, and 12+ y of schooling); maternal age (<20, 20–34, and \geq 35 y); low birthweight (yes, no; based on weight <2500 g); and preterm birth (yes, no; based on <37 wk of gestational age). Maternal physical activity at 1 year was measured

using a questionnaire, and women were classified as active if they reported participation in any kind of physical activity in the past 7 days.³⁶ Also at 1 year, mothers reported whether their child played with someone (yes and no) and on who looked after their children, identifying those children who attended center-based childcare (yes and no). Maternal depression at 1 year was measured using the Edinburgh Postnatal Depression Scale.³⁷ For the purpose of analysis, a cutoff point of \geq 13 points was used to indicate the presence of at least moderate depression, based on previous validation studies.³⁸ Child neurodevelopment at 1 year was assessed using the Oxford Neurodevelopmental Assessment Tool, measuring the domains of language, cognitive, executive, attention, socioemotional reactivity, and positive affection.³⁹

Statistical Analysis

Description of sample characteristics was performed using proportions and confidence intervals (CIs) to compare the analytical sample and children from the whole 2015 cohort. Mean and SDs were used to describe the development and physical activity variables according to the covariates. Statistical differences were assessed using t tests or analysis of variance.

Linear regression models were used to test the association of physical activity with BDI scores. First, the association of physical activity from each follow-up (1, 2, and 4 y) and BDI score was tested. Second, the association of trajectories of physical activity from 1 to 4 years was tested. Third, the association of cumulative effects, based on the sum of follow-up tertiles, was tested. For these linear regression models, a 3-step approach was used: crude, model I (adjusted for sex, family income, maternal education, maternal age, low birthweight, preterm birth, maternal depression, maternal physical activity, playing with someone, and center-based childcare) and model II (adjusted for all variables included in model I plus Oxford Neurodevelopmental Assessment Tool). Model II was used to account for the potential reverse causality in the association between physical activity and neurodevelopment and, therefore, reinforce the longitudinal associations between these variables. Beta coefficients and CIs were calculated. Sensitivity analyses using the Battelle domains separately were performed and are presented in Supplementary Tables S4 (available online). All assumptions of linear regression models were checked. All statistical analyses were performed using Stata (version 16.0; StataCorp, College Station, TX).

Results

Of the 4275 children in the original cohort, 1673 (39.1%) had full valid accelerometer data at 1, 2, and 4 years and neurodevelopment data at 4 years and composed the analytic sample. In the analytic sample, 52% of children were boys, 67% had mothers with more than 9 years of formal education, and 70% had mothers aged 20–34 years. Nearly 10% of children were born preterm and with low birthweight. In the 1-year follow-up, 15.9% of mothers had high depression scores, and 7.2% reported participation in physical activity in the last week. At the same follow-up, only 7.5% of children had no one to play with, and only 13.6% attended centerbased childcare (Table 1). Overall, the distribution of sociodemographic variables of children and mothers in the analytical sample was similar to the distribution of these variables in the original cohort (Table 1).

The mean number of days with valid accelerometer data was 2, 2, and 7 at ages 1, 2, and 4 years, respectively. Average daily acceleration was 26.2mg (SD=6.2), 37.0mg (SD=9.4), and

48.2mg (SD = 11.3) at ages 1, 2, and 4 years, respectively. Average acceleration at ages 1, 2, and 4 years according to sociodemographic variables is presented in Table 2. Overall, average acceleration was higher for boys than girls at all 3 follow-up periods. At 2 and 4 years, children from mothers in the lowest categories of formal education had higher average accelerations. No other marked differences in the distribution of acceleration were observed. The acceleration tertiles of each follow-up had the following milligravitational averages: 1 year (low = 19.9, medium = 25.9, and high = 33.0); 2 years (low = 27.6, medium = 36.1, and high = 48.0); and 4 years (low = 36.3, medium = 47.4, and high = 60.5) (data not shown in table).

Although the average acceleration in the sample increased from 1 to 4 years, the magnitude of this increase varied. Based on the best-fitted model (Supplementary Table S2 [available online]), 3 trajectories of increasing average acceleration were identified (see Figure 1). The first trajectory included children with low average acceleration across all time points, comprising 35.8% (n = 582) of children in the sample. For these children, the average acceleration increased from 22mg at age 1 year to 37mg at age 4 years. The second trajectory group included more than half of the sample (52.9%) with a mean acceleration of 27mg in the first year and 51mg at 4 years. The third trajectory group (11.3% of the sample; n = 179) included children with a mean acceleration that increased from nearly 31 to 65mg between the first and the last assessment. Overall, girls were more likely than boys to be in the lowest categories of acceleration in the cumulative and trajectory analyses (Supplementary Table S5 [available online]). In addition, children from mothers with higher educational levels were in the lower categories of the cumulative and trajectory variables (Supplementary Table S5 [available online]).

Mean score of BDI at 4 years of age was 113.7 (SD = 8.6) for the analytical sample, similar to the whole cohort sample followed at 4 years (113.4, SD = 9.0) (Supplementary Table S1 [available online]). Overall, the highest scores of BDI were for girls, children from the highest quintile of family income, and children from mothers with 12 or more years of formal education and younger than 35 years old. The BDI scores were slightly lower among children who were born preterm, children born with low birthweight, children from mothers who did not report physical activity, and children who did not attend center-based childcare (Supplementary Table S1 [available online]).

The crude and adjusted associations of physical activity at ages 1, 2, and 4 years and trajectories of physical activity with BDI scores are presented in Table 3. In the crude models, children in the highest tertiles of physical activity at ages 1 and 4 years had higher BDI scores than those in the lowest tertiles. The magnitude of these associations increased when the analyses were adjusted for confounding variables and development at age 1 year. In the fully adjusted model, BDI scores at 4 years of age were, on average, 1.67 (95% CI, 0.62 to 2.71), 0.75 (95% CI, -0.31 to 1.82), and 2.09 (95% CI, 1.01 to 3.17) points higher for those who were in the highest tertiles of physical activity than those in the lowest tertiles of physical activity at ages 1, 2, and 4 years, respectively. At all ages, a dose–response association between tertiles of physical activity and BDI was observed.

A dose–response association between trajectories of physical activity and BDI scores was observed. Children in the "medium, increasing" and "high, increasing" categories had, on average, 1.17 (95% CI, 0.25 to 2.10) and 2.22 (95% CI, 0.61 to 3.82) points higher BDI scores than children in the "low, increasing" category (Table 3). Children who were in the highest tertiles of physical

	Analytical sample [#]		2015 cohort		
	N (%)	95% confidence interval	N (%)	95% confidence interval	
Total	1673 (100.0)		4275 (100.0)		
Sex					
Female	790 (47.2)	44.8 to 49.6	2111 (49.4)	47.9 to 50.9	
Male	883 (52.8)	50.4 to 55.2	2164 (50.6)	49.1 to 52.1	
Maternal education, y					
0-4	141 (8.4)	7.2 to 9.9	391 (9.2)	8.3 to 10.0	
5–8	417 (25.0)	22.9 to 27.1	1095 (25.6)	24.3 to 26.9	
9–11	612 (36.6)	34.3 to 38.9	1458 (34.1)	32.7 to 35.5	
12+	502 (30.0)	27.9 to 32.3	1330 (31.1)	29.7 to 32.5	
Maternal age, y					
<20	237 (14.2)	12.6 to 15.9	623 (14.6)	13.5 to 15.7	
20–34	1196 (71.5)	69.3 to 73.6	3018 (70.6)	69.2 to 72.0	
≥35	240 (14.3)	12.7 to 16.1	633 (14.8)	13.8 to 15.9	
Low birthweight					
No	1538 (91.9)	90.5 to 93.1	3830 (89.9)	89.0 to 90.8	
Yes	135 (8.1)	6.8 to 9.5	428 (10.1)	9.2 to 11.0	
Preterm birth					
No	1446 (86.4)	84.7 to 88.0	3612 (84.5)	83.4 to 85.5	
Yes	227 (13.6)	12.0 to 15.3	663 (15.5)	14.4 to 16.6	
Maternal depression (1y)					
No	1392 (84.1)	82.3 to 85.8	3333 (83.9)	82.7 to 85.0	
Yes	263 (15.9)	14.2 to 17.7	639 (16.1)	15.0 to 17.3	
Maternal physical activity (1y)					
No	1540 (92.8)	91.5 to 94.0	3666 (92.0)	91.1 to 92.8	
Yes	119 (7.2)	6.0 to 8.5	317 (8.0)	7.1 to 8.8	
Play with someone (1y)					
No	126 (7.5)	6.3 to 8.9	333 (8.3)	7.5 to 9.2	
Yes	1547 (92.5)	91.1 to 93.6	3685 (91.7)	90.8 to 92.5	
Center-based childcare (1y)					
No	1445 (86.4)	84.6 to 87.9	3546 (88.3)	87.2 to 89.2	
Yes	228 (13.6)	12.1 to 15.3	472 (11.7)	10.8 to 12.8	

Table 1 Maternal and Child Characteristics According to the Study Sample (2015) Pelotas Birth Cohort

activity in the 3 follow-ups had higher scores of BDI ($\beta = 4.57$; 95% CI, 2.63 to 6.51) than children in the lowest category in all follow-ups (Figure 2). Overall, the strongest magnitude of associations was observed in the analyses adjusted for variables in model I. Compared with estimates from model I, the magnitude of associations was slightly attenuated when the analyses were adjusted for development at 1 year of age (model II). Crude and model I models of adjusted cumulative effect analyses are displayed in Supplementary Table S3 (available online).

Sensitivity analyses were performed for each of the 5 subdomains of BDI (Supplementary Table S4 [available online]). Overall, the pattern and direction of association remained similar to the total score for all domains. At 1 year, children in the highest tertile of acceleration had higher values for all domains than children from the lowest tertile, with the cognitive, communication, and personal–social domains presenting overall higher benefits. At 2 years, the overall pattern of association was positive; however, those associations were mostly null. At 4 years, the pattern of association was similar to 1 year; however, stronger associations were observed in the motor domain, for which children in the top tertile had, on average, 0.71 (95% CI, 0.41 to 1.00) points higher scores than those in the lowest tertile. Cumulative effect analyses showed that children in the top tertiles of physical activity presented higher development scores for every domain, with a greater magnitude for cognitive and motor domains. Trajectory analyses presented a positive pattern across all domains; however, the only significant benefits were observed in higher trajectory of motor (β =0.78; 95% CI, 0.36 to 1.21) and personal–social (β =0.59; 95% CI, 0.17 to 1.01) domains compared with the lowest trajectory.

Discussion

This study provides evidence on the positive longitudinal associations between device-measured physical activity and childhood neurodevelopment. A positive dose–response association of total physical activity at different ages, trajectories of increasing physical activity, and cumulative physical activity with child neurodevelopment was consistent across different domains. Findings of this unique population-based cohort study from Brazil are

	1 y		2 у		4 y	
	ENMO,	mg/d	ng/d ENMO, mg/d		ENMO,	mg/d
	Mean (SD)	P value	Mean (SD)	P value	Mean (SD)	P value
Total	26.2 (6.2)		37.0 (9.4)		48.2 (11.3)	
Sex		<.001		<.001		<.001
Female	25.7 (6.2)		35.7 (8.7)		46.0 (10.2)	
Male	26.7 (6.2)		38.1 (9.9)		50.2 (11.9)	
Family income, quintiles ^a		.43		.44		.02
1 (lowest)	26.0 (6.1)		37.1 (9.6)		48.1 (11.5)	
2	26.7 (6.3)		37.7 (9.8)		49.7 (11.5)	
3	26.0 (6.9)		36.7 (9.9)		48.0 (11.1)	
4	26.5 (5.9)		36.8 (9.5)		47.0 (11.8)	
5 (highest)	25.9 (6.0)		36.4 (8.1)		48.4 (10.4)	
Maternal education, y		.43		.001		<.004
0–4	26.7 (6.3)		39.2 (10.0)		49.9 (11.3)	
5–8	26.5 (6.9)		37.7 (9.6)		48.4 (12.3)	
9–11	26.3 (6.0)		36.8 (9.4)		48.0 (11.5)	
12+	25.9 (5.9)		35.9 (9.0)		47.0 (10.0)	
Maternal age, y		.14		.99		.82
<20	27.0 (7.2)		37.0 (9.6)		48.6 (11.6)	
20–34	26.1 (6.1)		37.0 (9.4)		48.1 (11.2)	
≥35	26.3 (6.3)		37.2 (9.4)		48.4 (11.8)	
Low birthweight		.54		.26		.99
No	26.3 (6.3)		37.1 (9.5)		48.2 (11.4)	
Yes	25.9 (6.0)		36.1 (8.4)		48.2 (10.5)	
Preterm birth		.69		.15		.90
No	26.2 (6.3)		37.1 (9.5)		48.2 (11.3)	
Yes	26.4 (5.7)		36.1 (9.0)		48.3 (11.3)	
Maternal depression (1y)		.87		.76		.37
No	26.3 (6.3)		36.9 (9.5)		48.3 (11.5)	
Yes	26.2 (6.2)		37.1 (8.8)		47.7 (10.5)	
Maternal physical activity (1y)		.27		.03		.20
No	26.3 (6.3)		36.8 (9.4)		48.1 (11.3)	
Yes	25.6 (5.1)		38.8 (9.9)		49.5 (11.7)	
Play with someone (1y)		.42		.95		.77
No	25.8 (6.2)		36.9 (9.7)		47.9 (10.8)	
Yes	26.3 (6.2)		37.0 (9.4)		48.2 (11.4)	
Center-based childcare (1y)	× /	.12	· · ·	.97	× /	.17
No	26.3 (6.3)		37.0 (9.5)		48.4 (11.5)	
Yes	25.6 (5.5)		37.0 (9.2)		47.3 (10.0)	

 Table 2 Physical Activity Based on ENMO Means According to Population Characteristics, 2015, Pelotas Birth

 Cohort (N = 1673)

Abbreviation: ENMO, Euclidian Norm Minus One.

important because this is the largest study to explore the potential benefits of total physical activity, using device-measured technology to estimate movement, for child development. This is also the first study to describe trajectories of device-measured physical activity from age 1 to 4 years.

Total physical activity, based on average acceleration, increased around 20mg from age 1 to 4 years. In addition, boys were more active than girls at all ages. This sex difference is commonly reported in the literature,^{40,41} including in the same city

with different ages from the Pelotas birth cohorts.^{42,43} Despite this expected result, this study shows that this difference does not seem to be influenced by other factors, like parents' physical activity and behavior,⁴⁰ considering that the observed difference starts at a very young age and persists throughout early childhood.

Overall, previous studies with device measures found positive associations between physical activity and motor skills,^{44–47} whereas null or inconclusive associations were observed for cognitive^{46,48–50} and psychosocial development.^{46,48,49} Those studies that found null associations were based on cross-sectional or longitudinal designs with short follow-up (1 y) and with small samples sizes,^{46,48–50} which may not be sufficient to detect meaningful associations with these domains of neurodevelopment. In the present study, those factors were attenuated with an analytical sample size of 1600 children and with different measures through an interval of 3 years, higher than observed in the literature, improving the current evidence regarding the association of physical activity in children under 5 years of age.

Sensitivity analyses revealed no important differences in the association of physical activity with total neurodevelopment score and cognitive, motor, communication, adaptive, and personal– social subdomains. The overall pattern of association remained



Figure 1 — Physical activity trajectories from 1 to 4 years (N = 1673) based on ENMO. ENMO indicates Euclidian Norm Minus One.

a positive dose–response relationship but with varying magnitude, with higher benefits being observed for motor and cognitive subdomains. These minimal differences according to domains may be explained by the use of raw data to explore physical activity, which represents general movement based on body acceleration rather than a specific intensity or type of physical activity.^{18,21,51} In addition, it may be expected that the association with motor domain was stronger, considering the high correlation between physical activity and motor competence in the early years and their reciprocal relationship across childhood.^{52,53}

Other studies using accelerometers, which found null or inconclusive associations with neurodevelopment, used different cutoff points to calculate physical activity intensities,^{46,48–50} representing more specific and structured activities, which may influence this association. Considering the characteristics of young children's physical activity, which is sporadic, intermittent, and most of the time unstructured, the use of accelerometer raw data enhances the capability to understand the true effects of general movement on neurodevelopment outcomes at this age.^{17–20} In addition, the use of raw data enhances the comparison across studies at this age and with older populations.^{19,51}

Longitudinal analyses based on cumulative effects and different trajectories revealed a positive dose–response pattern in which children who moved more throughout early childhood presented higher neurodevelopment scores at 4 years. Such results provide advances in the potential dose–response relation-ship with neurodevelopment,¹¹ which seems to have benefits for other health indicators in young children.¹ Even though the present results cannot be compared with the present physical activity guidelines for early years, the dose–response pattern observed agrees with the World Health Organization statement regarding physical activity behavior seems to track over time,^{7–9} it is important to stimulate such healthy behavior starting at birth.

	Crude	Model I	<u>Model II</u> β (95% Cl)	
ENMO	β (95% Cl)	β (95% Cl)		
1 y (tertile)				
1 (lowest)	0	0	0	
2	0.43 (-0.58 to 1.45)	0.82 (-0.16 to 1.81)	0.51 (-0.53 to 1.56)	
3 (highest)	1.31 (0.30 to 2.32)	1.86 (0.87 to 2.84)	1.67 (0.62 to 2.71)	
2 y (tertile)				
1 (lowest)	0	0	0	
2	0.38 (-0.62 to 1.39)	0.44 (-0.53 to 1.42)	0.53 (-0.51 to 1.58)	
3 (highest)	0.54 (-0.48 to 1.56)	1.09 (0.08 to 2.09)	0.75 (-0.31 to 1.82)	
4 y (tertile)				
1 (lowest)	0	0	0	
2	0.40 (-0.62 to 1.42)	0.67 (-0.32 to 1.66)	0.43 (-0.62 to 1.48)	
3 (highest)	1.17 (0.16 to 2.19)	1.96 (0.95 to 2.96)	2.09 (1.01 to 3.17)	
Trajectories				
Low, increasing	0	0	0	
Medium, increasing	0.71 (-0.17 to 1.60)	1.15 (0.29 to 2.02)	1.17 (0.25 to 2.10)	
High, increasing	0.73 (-0.81 to 2.27)	2.09 (0.56 to 3.62)	2.22 (0.61 to 3.82)	

Table 3Crude and Adjusted Linear Models of the Association Between Physical Activity (ENMO) and EarlyChildhood Neurodevelopment (N = 1673)

Abbreviations: CI, confidence interval; ENMO, Euclidian Norm Minus One.



Figure 2 — Fully adjusted cumulative effect of physical activity from 1, 2, and 4 years on child neurodevelopment at 4 years (N = 1673). CI indicates confidence interval; ENMO, Euclidian Norm Minus One.

Considering the mechanisms through which physical activity may impact neurodevelopment, it is expected that more physical activity, or acceleration, can improve learning opportunities at early ages, providing different stimuli to learn. Beyond those learning opportunities, physical activity can increase cerebral blood flow and produce positive adaptations in the central nervous system, enhancing a child's neurodevelopment capacity through early childhood.^{5,55} Those biological mechanisms for neurodevelopment only reinforce the importance of physical activity in the early years.

Some of the strengths of this study include the use of accelerometers to estimate physical activity in this population, providing a valid and reliable measure of children's behavior. In addition, the use of raw accelerometer data allows an analysis regardless of cutoff points and specific metrics, improving the capability to measure general movement and enhancing comparability with other studies. Second, the availability of data in 3 follow-ups with more than 1500 children from a well-established birth cohort provides strong evidence on the temporal association between physical activity and child neurodevelopment.

One of the study's limitations is the small number of children in longitudinal analyses when compared with the sample from individual follow-ups. However, the analytical sample size did not differ much from the original cohort and seemed sufficient to test the associations. Despite the benefits of raw accelerometer data, like the ability to assess children's intermittent activity and enhance comparison across studies, the unit of measure (in milligravitational units) is difficult to interpret and cannot provide practical considerations in terms of duration, frequency, or intensities of activities. In addition, even though the use of an accelerometer placed on the wrist is recommended for children, the output represents the movement from that body site and cannot represent whole-body activity. Finally, the use of 2 adjusted models was performed to clarify the association of physical activity and neurodevelopment; however, as in most observational studies, reverse causality cannot be ruled out.

This study provides important insights into the relationships between device-measured physical activity and domains of early neurodevelopment. This study mainly adds to our understanding of the potential clinical meaning of using raw acceleration to describe associations between device-measured physical activity and early neurodevelopment. This is important because, despite the advantages and growing use of raw acceleration data in the scientific literature, little is known about the quantifiable health effects associated with physical activity measured in units of acceleration. The findings of our study pragmatically suggest that the total accumulation of body movement/physical activity, regardless of the context and how it is accumulated, may be linked to improved early childhood neurodevelopment. However, specific and structured activities, such as active play, are likely to explain this association. Furthermore, the findings of our study only explored the relationships between device-measured physical activity and domains of neurodevelopment in children 1-4 years old. Thus, future studies should investigate this association at different ages, including late childhood and early adolescence.

The present study indicates that a child's physical activity from 1–4 years of age has a positive and consistent association with neurodevelopment at 4 years. In addition, cumulative and trajectory models confirm this pattern, indicating a dose–response relationship in which more movement throughout early childhood associates with higher neurodevelopment scores. These results provide further evidence demonstrating that stimulating activities based on movement could contribute to healthy child development across multiple domains.

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