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Physical Activity and Chronic Stress in Early Life: Findings From the 2015 Pelotas (Brazil) Birth Cohort

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Background: The association of physical activity through early childhood on children's chronic stress still is unclear. Therefore, the aim of the present study is to test the association of physical activity through early childhood (1–4 y) with chronic stress, measured by hair cortisol at age 4. ***Methods:*** Longitudinal study including children from the 2015 Pelotas (Brazil) Birth Cohort. Cortisol at age 4 was measured using a hair sample, which provided cortisol concentration from the past months. Physical activity was measured using accelerometers at 1, 2, and 4 years. Linear regression models were used to assess the association between physical activity and chronic stress. Trajectory models were also applied to examine chronic stress in relation to physical activity patterns throughout early childhood. ***Results:*** Children with valid physical activity and hair cortisol data were included in the analyses (N = 1475). Three groups of physical activity trajectories between 1 and 4 years were identified: low, medium, and high. No association between physical activity at 1, 2, and 4 years and chronic stress at age 4 was observed. However, children in the "high" physical activity trajectory presented low cortisol concentration; the magnitude of the regression coefficient was slightly larger in girls ($\beta = -0.125$; 95% confidence interval, −0.326 to 0.074) than boys ($\beta = -0.051$; 95% confidence interval, −0.196 to 0.09). ***Conclusion:*** There was no clear association between physical activity and chronic stress in early childhood. Trajectories models suggest that higher activity throughout early childhood may positively impact chronic stress; however, more studies are needed to confirm that hypothesis.

Keywords: epidemiology, mental health, pediatrics, accelerometry

Infancy and early childhood (birth to 5 y) are the most important stages of growth and development in which the brain is highly plastic, with particular potential to adapt and develop in relation to environmental stimulation.[1,2] On the one hand, positive stimulus, provided by nurturing care, physical activity, or interpersonal interaction, can benefit child health; however, negative experiences, such as poverty, exposure to violence, or food deprivation, may delay growth and development.[1–3]

One important factor that affects children's health is stress, which can be measured through cortisol released by the hypothalamic–pituitary–adrenal (HPA) axis.[3] In early childhood, stress can be triggered by diverse traumatic experiences and can also lead to poor development and difficulties in interaction with other children as well as being associated with obesity.[3–5] Stress response can be acute, which is an immediate response of the organism to perceived threats to homeostasis or well-being, and can be associated with increased muscle mass and decreased fat mass among children,[6] or it can be chronic, which represents a repeated or prolonged body response to stress,[7] which is potentially more toxic for health.

Hair cortisol represents a biomarker of chronic stress, providing an indicator of stress response over several months.[5,8,9] Considering that hair grows about 1 cm/mo, the 1 cm of hair closest to the scalp reflects the cortisol production in the last month, and so on.[8] Higher concentrations of cortisol may result from stressor chronicity, intensity, frequency, and modality.[7] In children, hair cortisol has been demonstrated to be a reliable measure for chronic and persistent stress, potentially indicating a disruption in the HPA axis regulation.[3,10] Other methods of cortisol analysis provide measures of acute cortisol concentration in saliva, blood, or urine—indicating cortisol concentration currently circulating in the body. As well as measuring chronic cortisol concentration, hair cortisol measures have the advantage of being less invasive than blood or urine cortisol collection, for example.[3]

Physical activity positively impacts physical, psychological, and health development of children.[11–14] Despite those benefits, the evidence regarding the association between physical activity and chronic stress in children is inconsistent. In 8-year-old children, those with the lowest levels of physical activity seemed to be more responsive to psychosocial stress based on saliva samples.[15] Another study that included 2- and 6-year-old children did not find associations between physical activity and hair cortisol.[16]

Considering these inconsistencies and the relevance of physical activity to children's health and development, it is important to

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evaluate the association between physical activity and chronic stress during the preschool age. Due to the characteristics of cortisol onset,[17] a more robust approach might be to evaluate physical activity through early childhood using longitudinal approaches, such as group-based trajectory models.[16] Therefore, the aim of the present study was to test the association of physical activity through early childhood (1–4 y) and chronic stress at age 4. It was hypothesized that children with higher physical activity through early childhood would present lower concentrations of hair cortisol at 4 years of age.

Methods

Participants of the Study

We used data from the 2015 Pelotas (Brazil) Birth Cohort study. This longitudinal study recruited all live births between January 1 and December 31, 2015 from mothers who lived in the urban area of the city of Pelotas, Brazil. This methodology was used to ensure the comparability with previous Pelotas Birth Cohorts—1982, 1993, and 2004.[18,19]

In the perinatal study, carried out while the mothers were still at the hospital, mothers answered a questionnaire about prenatal care, socioeconomic and demographic characteristics, and home and newborn variables. Follow-ups of the sample were conducted at 3 months and 1, 2, and 4 years of age. This article used data from all these follow-ups except for the 3 months of age. The 1-year follow-up was performed at the participants' households, and at ages 2 and 4, the follow-ups were done at the university research clinic.

This study was approved by the School of Physical Education Ethics Committee at the Federal University of Pelotas (Certificate of Presentation for Ethical Consideration registration no.: 26746414.5.0000.5313). Written informed consent was obtained from children's parents or legal guardians.

Chronic Stress

At age 4, hair samples were collected to provide an estimate of cortisol from children and mothers of the cohort. This measure is capable of assessing cortisol levels from the past months as it is able to estimate a chronic and prolonged state of stress.[3,8] Hair cortisol has been a reliable measure to assess children's chronic stress.[3,10,20]

Trained interviewers followed a protocol for the collection of hair samples. They (1) explained the procedure to the mother and the child; (2) sanitized the scissors; (3) dried the hair in cases of wet or damp hair; (4) identified the posterior vertex of the head and tied approximately 100 hair strands (half of a pencil diameter); and (5) while the participant was seated, the interviewer placed the scissors as near as possible to the scalp and cut the hair. When the hair was too short at the vertex, the instruction was to collect the same amount of hair from the tuft. If the hair from the tuft was also too short, then the instruction was to collect from several parts of the head to obtain the amount of hair necessary for the analysis. After the cut, the hair sample was stored inside a Bristol board appropriately placed and identified, sealing these materials inside a Ziploc bag (Talge).

A standardized protocol was used for hair washing, grinding, hormone extraction, and cortisol quantification by the laboratory of the Postgraduate Program in Epidemiology at the Federal University of Pelotas. The protocol was based on the following steps: (1) the 3 cm of the hair closest to the scalp was cut, placed into a Falcon 50-mL Conical Centrifuge Tube (CRALPLAST), washed with 12 mL of isopropanol and shaken by hand for 2 minutes, discarding the isopropanol at the end (this procedure was performed twice); (2) when completely dry, hair samples were ground using the mill (Retsch NM 400, RETSCH Technology); (3) cortisol extraction was made using around 35 mg of ground hair powder and 1 mL of ethanol absolute, shaken for 48 hours, and then vortexed; (4) the sample was rotated at 12,000 rpm in the centrifuge (Sigma), and the supernatant was extracted and kept in a separate tube; (5) another 1 mL of ethanol absolute was filled in the original tube, and after 48 hours more of shaking, it was centrifuged and vortexed, and the supernatant was transferred to the tube containing the first round supernatant; (6) those tubes were kept drying for 5 days until completely dry; (7) samples were suspended in 150 µL of assay diluent for 24 hours and then assayed in duplicate by ELISA using the High Sensitivity Salivary Cortisol Immunoassay Kit (Cat# 1-3002, Salimetrics), as per the manufacturer's instructions; and (8) an ELISA plate reader (Spectramax 190, Molecular Devices) was used to measure the cortisol levels, expressed in picograms per milligram. Intraassay and interassay coefficients of variance were below 10% in the present study.

Physical Activity

Physical activity was measured at ages 1, 2, and 4 using triaxial ActiGraph accelerometers (model wGT3X-BT, ActiGraph) within a ±6*g* dynamic range. The devices were set with a sampling frequency of 60 Hz. The accelerometer was placed on the nondominant wrist with a disposable bracelet. Considering the age of the sample and a previous calibration study, wrist placement was chosen due to children's better comfort and compliance.[21]

Children wore the accelerometers on the left wrist with a 24-hour per day protocol. A minimum of 16 hours of use per day was considered a valid day.[21] The number of days of use varied according to age and number of devices available for each follow-up visit and was established at 4, 3, and 7 days in the 1-, 2-, and 4-year follow-up visit, respectively. Despite these differences, the number of days was chosen according to the literature, which indicated at least 2 or 3 days of use for children at this age.[21] Raw data were downloaded in epochs of 5 seconds using the ActiLife software (version 6.1, ActiGraph Corp). Data were analyzed with the GGIR package (version 2.2-0) in the R software (http://cran.r-project.org). Raw acceleration was expressed in Euclidean Norm Minus One, which summarized data from the 3 axes ($\sum|\sqrt{x^2+y^2+z^2}-1g|$) in milli-*g* (gravitational equivalent: $1000\text{m}g = 1g = 9.81\ \text{m/s}^2$). No intensity cutoff point was used, considering the lack of validated cutoff points at this age (1, 2, and 4 y), placement site, and accelerometer brand.[22,23]

Nonwear time was calculated based on each of the 3 axes (*x*, *y*, and *z*) over periods of 15 minutes within a 60-minute window, evaluating their raw data SD and value range. Nonwear periods were considered if the SD of the window was less than 13m*g*, and the value range of the window was less than 50m*g*.[24] Finally, nonwear time was imputed, considering the average values of the same period of the day of the other days of measurement.[23]

Covariates

Several covariates were used in the study, considering that they may have been potential confounders based on the literature,[20,25,26] and a direct acyclic graph was built to understand the relation between physical activity and cortisol. From the perinatal study, the variables included were sex (male, female); maternal marital status (single, living with partner); maternal education in years (<4, 5–8, 9–11, and ≥12); maternal skin color (White, Brown, Black); and family income in Brazilian monthly minimum wages (≤1, >1–3, >3–6, >6–10, and >10). From the 1-year assessment, the following information was used: child sleep problems—whether the mother considered the child's sleep a problem (no, yes); medication use in the 15 days before the interview (no, yes); any stressful events—like getting hurt, falling, or experiencing a cut, burn, or other type of accident (no, yes); and body mass index for age (in SD units).

Analyses

Children with accelerometer data at 1, 2, and 4 years and with cortisol data at age 4 were considered as the analytical sample (Figure 1). Cortisol and physical activity outliers were excluded from the analytical sample when values were ≤4 or ≥4 SDs from the mean. Children's characteristics were described using absolute values and proportions for categorical variables and means and 95% confidence intervals for numeric variables. To check whether there were any differences between the analytical sample and the full cohort, 95% confidence intervals were compared.

For the purposes of analyses, physical activity was presented as Euclidean Norm Minus One in milli-*g* units. This measure represents overall acceleration, and 1m*g* unit can be compared with approximately 500 steps a day or a 5-minute brisk walk in inactive adults.[27] Considering the consistent differences between physical activity in boys and girls,[28,29] and that sex can be an important confounder in cortisol analyses,[20] all associations in the present paper were stratified by sex. Mean and median cortisol and physical activity values were described according to sex. Differences of median values were calculated using the nonparametric equality-of-medians test. The distribution of cortisol was nonnormal at 4 years and was, therefore, log-transformed to be included in the regression models.

The association of physical activity and chronic stress was tested using linear regression models. At first, nonadjusted models assessed the association between physical activity at all follow-ups and chronic stress at 4 years of age. Then, a model was adjusted for all covariates (sex, sleep problems, medication use, stressful events, maternal marital status, maternal skin color, maternal education, family income, and body mass index for age), and beta coefficients with their 95% confidence intervals were calculated. Nonlinearity of the associations was tested using a locally weighted regression and fractional polynomials, but linear models remained the most suitable. All assumptions of linear regression were checked. To improve comparability and temporal causality on the models, all variables considered for the adjusted regressions were collected at birth or at the 1-year follow-up.

Trajectories of physical activity from age 1 to 4 were estimated using group-based trajectories models. These models identified groups of individuals following similar trajectories based on a finite mixtures approach, providing clusters of individual trajectories. The number and format of trajectories were based on the best fit model considering Bayesian information criteria, the number of participants in each group, and the interpretability of the trajectories (Supplementary Table S1 [available online]). Trajectories were also tested according to sex but presented a similar number and shape to the whole sample. The probability of an individual belonging to each trajectory group was tested (it was considered appropriate if it was superior to 70%).[30] The trajectory model was based on the analytical sample, not including children with missing data for physical activity. Three quadratic trajectory groups were found and interpreted considering the shape of the groups (Supplementary Figure S1 [available online]).[12]

Results

Out of the 4275 children included in the original cohort, 1475 had valid data for physical activity from 1 to 4 years and cortisol at age 4 and were included in the analytical sample of the present study (Figure 1). When comparing the characteristics of the original cohort and the analytical sample, there were no differences in any of the variables evaluated (Table 1). At birth, about 85% of mothers lived with a partner, 71% were White, 33% had 12 years of education or more, and most families had an income between 1 and 6 monthly minimum wages (73.5%).

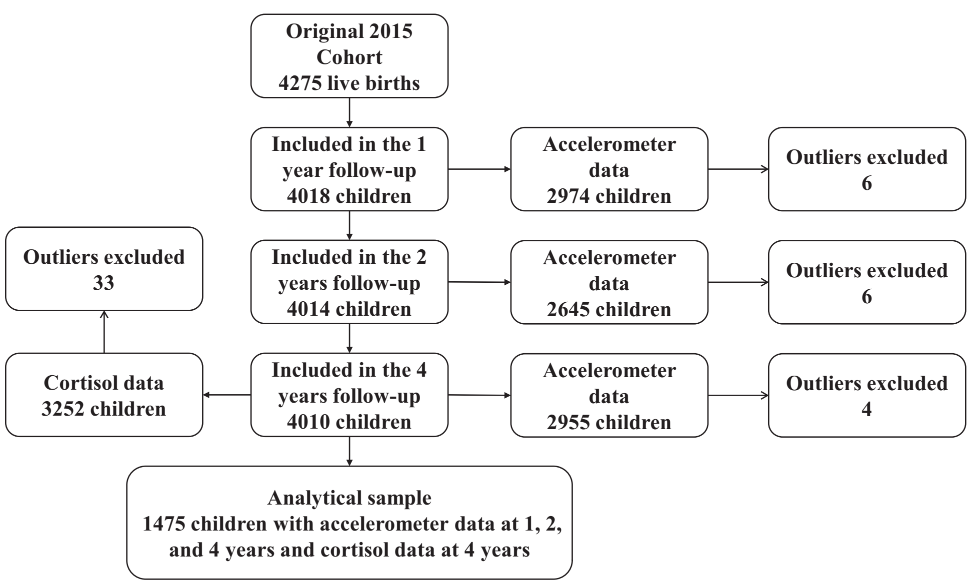

Figure 1 — Flowchart of children from the 2015 Pelotas Birth Cohort and the children included in the study.

Table 1 Descriptive Characteristics of the 2015 Pelotas (Brazil) Cohort Sample and the Analytical Sample (Sample Characteristics)

	Cohort sample (N = 4275)		Analytical sample (N = 1475)	
	n (%)	95% CI	n (%)	95% CI
Sex				
Female	2111 (49.4)	47.9 to 50.9	708 (48.0)	45.4 to 50.5
Male	2164 (50.6)	49.1 to 52.1	767 (52.0)	49.4 to 54.5
Maternal marital status				
Single	607 (14.2)	13.2 to 15.3	178 (12.1)	10.5 to 13.8
With partner	3667 (85.8)	84.7 to 86.8	1296 (87.9)	86.1 to 89.5
Maternal skin color				
White	3024 (71.3)	69.9 to 72.6	1044 (71.2)	68.8 to 73.4
Brown	551 (13.0)	12.0 to 14.0	175 (11.9)	10.4 to 13.7
Black	667 (15.7)	14.6 to 16.8	248 (16.9)	15.1 to 18.9
Maternal education, y				
<4	391 (9.2)	8.3 to 10.0	99 (6.7)	5.5 to 8.1
5–8	1095 (25.6)	24.3 to 26.9	323 (21.9)	19.9 to 24.1
9–11	1458 (34.1)	32.7 to 35.5	560 (38.0)	35.5 to 40.5
≥12	1330 (31.1)	29.7 to 32.5	492 (33.4)	31.0 to 35.8
Family income (monthly minimum wages)				
≤1	538 (12.6)	11.6 to 13.6	146 (9.9)	8.5 to 11.5
>1–3	2014 (47.1)	45.6 to 48.6	702 (47.7)	45.1 to 50.2
>3–6	1127 (26.4)	25.1 to 27.7	442 (30.0)	27.7 to 32.4
>6–10	324 (7.6)	6.8 to 8.4	91 (6.2)	5.0 to 7.5
>10	270 (6.3)	5.6 to 7.1	92 (6.2)	5.1 to 7.6
Sleep problems (age 1)				
No	3650 (90.8)	89.9 to 91.7	1348 (91.4)	89.8 to 92.7
Yes	368 (9.2)	8.3 to 10.1	127 (8.6)	7.3 to 10.1
Medication use (age 1)				
No	1278 (31.8)	30.4 to 33.3	444 (30.1)	27.8 to 32.5
Yes	2740 (68.2)	66.7 to 69.6	1031 (69.9)	67.5 to 72.2
Stressful events (age 1)				
No	1946 (48.5)	46.9 to 50.0	722 (49.0)	46.5 to 51.6
Yes	2067 (51.5)	49.9 to 53.0	751 (51.0)	48.4 to 53.5
	Mean (SD)	**95% CI**	**Mean (SD)**	**95% CI**
BMI for age (age 1)	17.7 (2.0)	17.6 to 17.7	17.7 (1.9)	17.6 to 17.8

Abbreviations: BMI, body mass index; CI, confidence interval.

Mean physical activity was about 26.2m*g* at age 1 and increased to 36.8m*g* and 48.3m*g* at 2 and 4 years, respectively (Table 2). In all follow-ups, the mean physical activity was higher in boys than in girls. Group-based trajectories (Supplementary Figure S1 [available online]) revealed 3 groups of physical activity patterns between 1 and 4 years: (1) low (37.5%), (2) medium (51.9%), and (3) high (10.6%). All groups increased physical activity from 1 to 4 years of age.

The distribution of cortisol values according to physical activity can be observed in Figure 2. No clear pattern was observed. The association of physical activity and chronic stress is presented in Table 3. No significant and consistent associations were found. Despite that, when we consider the direction of association, children in the "high" physical activity trajectory group showed lower concentration of hair cortisol compared with children in the "low" physical activity group. When considering the magnitude, we observed that the magnitude of association was higher for girls in the "high" group than for boys for the same group (Table 3).

Discussion

In summary, the results did not show a clear association between physical activity at 1, 2, and 4 years of age and chronic stress at 4 years of age. The direction of association based on the physical activity trajectories shows that children in the "high" physical activity trajectory presented lower cortisol concentrations, with the magnitude of association being higher in girls than boys, but no association was statically significant. Such results advance the knowledge on the association between physical activity and chronic stress in children, showing that these possible benefits may be related to a consistent active behavior.

Table 2 Summary of Cortisol and Physical Activity Variables of the Analytical Sample (N = 1475)

	Total		Boys		Girls		
	Mean (95% CI)	Median (IQR)	Mean (95% CI)	Median (IQR)	Mean (95% CI)	Median (IQR)	P^b
Cortisol at age 4, pg/mg	9.4 (9.1 to 9.7)	8.2 (5.7–11.4)	9.2 (8.8 to 9.7)	7.9 (5.4–11.2)	9.6 (9.2 to 10.1)	8.5 (6.0–11.7)	.06
Log[a] cortisol at age 4, pg/mg	2.1 (2.0 to 2.1)	2.1 (1.7–2.4)	2.0 (2.0 to 2.1)	2.1 (1.7–2.4)	2.1 (2.1 to 2.2)	2.1 (1.8–2.5)	.03
Physical activity, m*g*/d							
Age 1	26.2 (25.9 to 26.5)	25.8 (21.8–30.0)	26.8 (26.3 to 27.2)	26.2 (22.1–30.5)	25.6 (25.1 to 26.0)	25.2 (21.4–29.2)	<.001
Age 2	36.8 (36.3 to 37.3)	35.3 (30.2–41.7)	38.0 (37.2 to 38.7)	36.3 (31.1–42.8)	35.5 (34.9 to 36.2)	34.4 (29.5–40.6)	<.001
Age 4	48.3 (47.7 to 48.9)	47.7 (40.6–55.2)	50.5 (49.7 to 51.3)	50.1 (42.4–58.0)	45.9 (45.2 to 46.7)	45.4 (39.1–52.1)	<.001

Abbreviations: CI, confidence interval; IQR, interquartile range; m*g*, milli-*g*.
[a]Log natural. [b]Nonparametric equality-of-medians test between boys and girls.

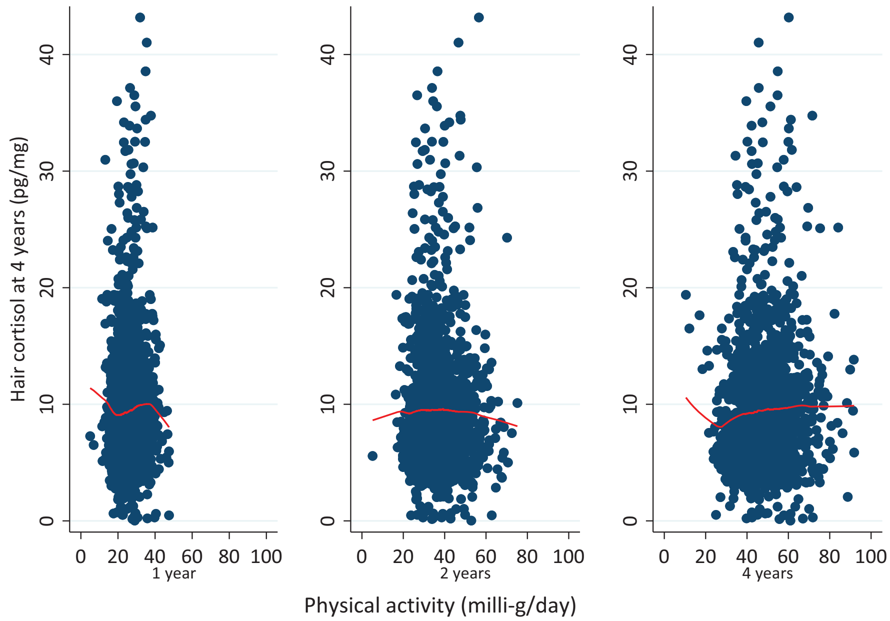

Figure 2 — Regressed values of hair cortisol levels according to physical activity levels.

Table 3 Linear Regression Models of the Associations Between Physical Activity and Chronic Stress

	All		Boys		Girls	
	β	95% CI	*β*	95% CI	*β*	95% CI
Physical activity, mg/d						
1 y	0.002	−0.003 to 0.007	0.002	−0.005 to 0.010	0.002	−0.005 to 0.010
2 y	−0.002	−0.005 to 0.001	−0.001	−0.005 to 0.004	−0.003	−0.009 to 0.002
4 y	0.001	−0.001 to 0.004	0.002	−0.002 to 0.005	0.002	−0.002 to 0.006
Trajectories from 1 to 4 y						
Low	Ref.		Ref.		Ref.	
Medium	0.012	−0.055 to 0.080	0.001	−0.098 to 0.101	0.037	−0.056 to 0.130
High	−0.067	−0.180 to 0.045	−0.030	−0.174 to 0.113	−0.115	−0.313 to 0.084
Adjusted[a]						
Physical activity, mg/d						
Age 1	0.003	−0.003 to 0.008	0.001	−0.006 to 0.009	0.003	−0.004 to 0.011
Age 2	−0.002	−0.005 to 0.001	−0.001	−0.006 to 0.003	−0.003	−0.010 to 0.001
Age 4	0.002	−0.001 to 0.005	0.001	−0.003 to 0.005	0.002	−0.002 to 0.006
Trajectories from age 1 to 4						
Low	Ref.		Ref.		Ref.	
Medium	0.013	−0.056 to 0.082	−0.012	−0.113 to 0.088	0.03	−0.062 to 0.127
High	−0.055	−0.171 to 0.060	−0.051	−0.196 to 0.09	−0.125	−0.326 to 0.074

Abbreviations: BMI, body mass index; CI, confidence interval; Ref., reference.
[a]Adjusted for sleep problems, medication use, stressful events, maternal marital status, maternal skin color, maternal education, family income, and BMI for age. For the whole sample, sex was also included in the model.

The lack of a clear association between physical activity and hair cortisol is consistent with other studies. In a Danish study that included children aged 2–6 years old, the authors did not find an association between physical activity and hair cortisol.[16] One important limitation of this Danish study is its cross-sectional design, which limits the interpretation of this association. In our study, we used physical activity data at 1, 2, and 4 years of age and modeled them into different trajectories over those years. This approach suggests that higher physical activity at each time point does not associate with cortisol at 4 years, but trajectories that represent a "consistent" exposure to physical activity may be related to lower levels of hair cortisol.

The magnitude of the association between trajectories of physical activity and chronic stress was small. This may be due to the physical activity variable that was used, which represents overall movement, not indicating intensity or type of activities.[31] It may be possible that more specific activities, which involve interaction and a social component, may be more important to stress than overall movement.[32] In addition, it is important to emphasize that physical activity has a positive effect on psychosocial stress reactivity, which may improve how children cope with stressful day-to-day experiences.[15]

Despite evidence that boys are more active than girls throughout life,[28,29] the results of the present study suggest that the association between physical activity through early childhood (1–4 y) with chronic stress at 4 years of age seems to be stronger among girls. This means that girls should be encouraged to engage in more physical activity at this age, which will not only benefit their growth and development[12] but also lower this gender gap, which may improve stress levels in preschool children.

The differences between sexes can be attributed to various mechanisms, like interactions between the HPA and hypothalamus–pituitary–gonadal axis.[33] Some studies have observed a higher concentration of the hormone cortisol among boys when compared with girls[20,25,34]; however, the literature indicates that, as children grow older, HPA increases synthesis, secretion, and the triggered responses that are higher among women.[35] In addition, this is in line with physical activity research that usually observes a higher magnitude of association for health outcomes in less active groups, considering that, in general, more activity benefits inactive people more than already active individuals.

One of the main strengths of the present study is the use of 3 device-measured physical activity assessments over early childhood (1, 2, and 4 y). In addition, this study used a unique approach to fit trajectory models and enhance the investigation of longitudinal associations between device-measured physical activity and chronic stress. The use of accelerometers also provides a robust estimate of physical activity as it is capable of detecting the whole spectrum of children's movements.[31] Another strength of the study is the use of hair cortisol, which provides an estimate of chronic stress.[3,8,10] To build the regression models, direct acyclic graphs were used to appropriately test the association between physical activity and chronic stress. Finally, the use of data from a low- and middle-income country allows a better understanding of this association in a setting of a variety of socioeconomic contexts and disparities.

Some limitations of the study must be recognized. First, despite the high attrition rates for each follow-up (over 90%), the number of children included in the analyses was lower than the children from the original sample; however, there were no differences in their characteristics (Table 1). The second is that, despite the estimate of chronic stress, the outcome was measured only at one point, which can limit the interpretation of the findings considering that in early childhood, the HPA axis is still developing.[7] Third, the accelerometer measure cannot distinguish between the types of activity children are performing, making it impossible to understand how each specific activity impacts on chronic stress. Finally, the raw accelerometer estimates (in milli-*g*) are difficult to interpret; however, the literature indicates that 1m*g* may have a minimum clinical importance, which improves the interpretation of the findings.[27] Considering that there are no standardized cut-off points for this age (1, 2, and 4y), device placement, and brand, raw estimates are indicated not only because they can provide an overall picture of child acceleration, but they are much more comparable with other studies.[22,36]

Conclusion

Physical activity at 1, 2, and 4 years of age was not associated with chronic stress at 4 years of age. However, when trajectory models were applied, children with higher physical activity levels through early childhood presented an association in the expected direction, showing lower cortisol concentration than less active children during early childhood. Considering the small magnitude of this association, more studies are necessary to improve the interpretation of the longitudinal influence of physical activity on cortisol in children.

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