ORIGINAL ARTICLE

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Objective measured physical activity and metabolic syndrome score in children and adolescents: The UP&DOWN longitudinal study

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Funding information

National Plan for Scientific and Technical Research and Innovation 2017-2020, Grant/Award Number: FPU20/02938

Abstract

Introduction: We aimed to analyze the cross-sectional and longitudinal association of physical activity (PA) levels and PA patterns with metabolic syndrome score (MetS) in children and adolescents.

Methods: A total of 175 children (82 females) and 188 adolescents (95 females) were included. Objective PA levels and patterns were determined by accelerometry. MetS was computed from waist circumference, systolic blood pressure, triglycerides, high-density lipoprotein cholesterol, and glucose levels. Different linear regression models were implemented to examine the associations of PA with MetS.

Results: Vigorous PA, moderate-vigorous PA, number of bouts per day in 10min (N10), and total time in bouts per day in 10min (T10) were negatively associated with MetS in male children and adolescents at cross-sectional level (*β* ranging from −0.005 to −0.164, all *p*<0.05). Total time in bouts per day in 20min in male children, and vigorous PA and N10 in female children were longitudinally and negatively associated with MetS (*β* ranging from −0.011 to −0.247, all *p*<0.05).

Conclusions: Associations of PA and MetS were observed at cross-sectional level in males and longitudinally in female children. The associations in PA patterns were found when patterns were grouped into bouts of 10min. Therefore, for future studies of PA with health markers in the pediatric population, it would be advisable to choose bouts of shorter duration.

KEYWORDS

accelerometry, cardiovascular diseases, child, metabolic diseases, physical activity patterns, youth

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1 | **INTRODUCTION**

Cardiovascular diseases (CVD) are the leading cause of death from noncommunicable diseases in developed countries.^{[1](#page-12-0)} It is estimated that in 2016 there were 17.9 million deaths caused by $CVD¹$ $CVD¹$ $CVD¹$ Although CVD occur mainly after the fifth decade of life, $\frac{2}{3}$ $\frac{2}{3}$ $\frac{2}{3}$ its precursors are already present at early ages. 3 Interestingly, the cluster of CVD risk factors in childhood and adolescence track into adulthood.^{[4](#page-12-3)} The well-known metabolic syndrome score (MetS), which is the clustering of abdominal obesity, elevated systolic blood pressure (SBP), elevated triglycerides, decreased high-density lipoprotein cholesterol (HDL-c), and elevated fasting plasma glucose, remains a major public health burden with the prevalence of the syndrome increasing in concert with obesity and sedentary lifestyles.^{[5](#page-12-4)} MetS affects both youths and adults and has been linked with clinical manifestations in CVD and type 2 diabetes. $6,7$

Physical inactivity, defined as not meeting physical activity (PA) recommendations, $\frac{8}{3}$ $\frac{8}{3}$ $\frac{8}{3}$ is a key contributor to poor health status. $9,10$ Low levels of PA (i.e., any bodily movement produced by skeletal muscles that results in energy expenditure 11) are detrimentally associated with MetS risk factors in school-aged children and adolescents.^{[12,13](#page-12-9)} Furthermore, not only being inactive at a certain time is associated with poor health status, but also maintaining a persistent physically inactive lifestyle over the years is associated with impaired cardiometabolic risk profile in adulthood.^{[14](#page-12-10)} In this sense, children are more active than adolescents, and PA consistently declines with age. 15 These reductions in PA with age has also been linked to an increased risk for MetS.^{[16](#page-12-12)}

A recent systematic review and meta-analysis concluded that moderate-vigorous PA (MVPA) is beneficially associated with cardiometabolic health in youth.¹⁷ From the studies that analyzed objectively measured PA with accelerometry, we found that most of them were cross-sectional^{[12,13,18–22](#page-12-9)} and only a few studies were longitudinal.^{23,24} In addition, to our knowledge, when analyzing patterns of PA (i.e., different ways of accumulating PA throughout the day), only cross-sectional studies have been performed.^{[19,20,22](#page-12-15)}

In this sense, the association of PA patterns and MetS risk factors in children and adolescents is still unclear and there is a lack of consensus in the literature when it comes to defining patterns of PA and cardio metabolic risk in youth. 25 This lack of consensus is due to the fact that some authors express the results of PA patterns in different ways, for example in patterns of $1-4$ min, $19,20$ >5 min,^{[19,20,22](#page-12-15)} and >10 min.^{19,20,26} In addition, only one study analyzes the association between patterns of PA and the Met $S₁₉$ $S₁₉$ $S₁₉$ ¹⁹ while the other studies analyze the patterns of

PA with individual factors of the MetS (i.e., waist circum-ference and HDL-c).^{[20,22,26](#page-12-16)}

Given the lack of longitudinal studies, the heterogeneity in the definition of PA patterns and the limited evidence to date, no solid conclusions can be drawn. Thus, the aim of the current study was to analyze the cross-sectional and longitudinal associations of PA levels and patterns with MetS risk in children and adolescents.

2 | **MATERIALS AND METHODS**

2.1 | **Study design and population**

Participants took part of the UP&DOWN study.^{[27](#page-13-1)} In brief, this 2-year longitudinal study aimed to assess the impact on health indicators of PA, sedentary behaviors, and health-related physical fitness in apparently healthy primary and secondary schoolchildren from Spain. The total UP&DOWN study sample consisted of 2264 healthy children (6–11.9 years) and adolescents (12–17.9 years) enrolled from schools in Cádiz and Madrid, respectively, of whom 1226 were children (580 females) and 1038 adolescents (502 females). According to the Spanish Institute of National Statistics, the UP&DOWN sample size represents the 50% and 5% of the total population of school children and adolescents, respectively. After selecting a random one-fourth for blood sampling, the resulting sample with complete data of PA, body composition, SBP, and blood sampling at baseline was 458 children and adolescents, being 229 children (106 females) and 229 adolescents (110 females). In the follow-up, some participants dropped out of the study (23.6% children and 17.9% adolescent) and the final sample with complete data was 363 participants, of which 175 were children (82 females) and 188 adolescents (95 females). We collected baseline data from September 2011 to June 2012, and the follow-up was performed from September 2013 to June 2014. Participants' parents were informed about the purposes of the study, and written informed consents were provided. The study protocol was accepted by The Ethics Committee of the Hospital Puerta del Hierro (Madrid, Spain), the Bioethics Committee of the National Research Council (Madrid, Spain), and the Committee for Research Involving Human Subjects of the University of Cádiz (Cádiz, Spain).

2.2 | **Blood pressure**

SBP was measured with a validated digital automatic blood pressure monitor (OMRON M6; OMRON HEALTH CARE Co., Ltd.) according to the standardized and valid International Protocol of the European Society of Hypertension.^{[28](#page-13-2)} Two measurements were taken 1 to 2 min apart. If the first two readings differed in >5mmHg, an additional measurement was taken, and the farthest value was removed. The average value of the two measurements was selected.

2.3 | **Blood sampling**

In the morning, after an overnight fast, 13.5 mL of blood was extracted from the cubital vein of each participant. Once the blood was collected, it was immediately transported to standard laboratories in each city. About 3.5 mL of the blood sample was collected in ethylenediaminetetraacetic acid and analyzed to acquire hemogram data. The remaining blood was collected in dried gel and sodium citrate and centrifuged to remove serum and plasma. Finally, serum and plasma were frozen at −80°C for future analyses. In the current study, enzymatic colorimetric methods (Olympus AU2700 Analyzer; Olympus UK Ltd) were used to analyze serum lipid triglycerides, HDL-c and glucose.

2.4 | **Body composition**

Weight and height were measured with an electronic scale (Type SECA 861; range, 0.05–130 kg; precision, 0.05kg; Hamburg, Germany) and a telescopic staturemeasuring instrument (type SECA 225; range, 60–200 cm; precision, 1mm; Hamburg, Germany) respectively. These measurements were conducted with participants dressed in lightweight clothing and without shoes. Body mass index was calculated as weight/height squared (kg/m²). Waist circumference (WC) was measured at the level of the narrowest part of the torso, using a non-elastic tape (SECA 200; range, 0–150 cm; precision, 1mm; Hamburg, Germany).

2.5 | **Physical activity**

PA was measured by ActiGraph accelerometer models GT1M, GT3X, and GT3X+ (Actigraph TM, LLC). Previous studies have demonstrated that there is strong agreement among outputs from the three Actigraph models.^{[29,30](#page-13-3)} The participants wore the accelerometer on the lower back, fitted with an elastic belt during waking hours for 7 consecutive days and were instructed to remove them for bed times and water-based activities. Data were reintegrated into 10-s epochs before analysis.³¹ Non-wearing time was defined as period of 60min of zero counts and an allowance for up to two consecutives minutes of <100 counts

per minute (CPM) with the up/downstream of 30min, consecutive of zero counts for period for detection of arti-fact movements.^{[31,32](#page-13-4)} Data were downloaded and analyzed by using the ACTILIFE software (v.6.11.7 Actigraph TM). Inclusion criteria for the analyses were (1) at least 3days of valid data and (2) a minimum of 8h of registration per day ³¹ Evenson cut points³³ were used to define light-(101–2295 CPM), moderate- $(\geq 2296$ CPM), and vigorousintensity (≥4012CPM) PA. These cut points show the best overall performance across all intensity levels 34 and sug-gested as the most appropriate cut points for youth.^{[35](#page-13-7)}

Epoch values that were equivalent to 2296CPM were considered to be minutes of MVPA.³³ Because there is no accepted consensus on the minimal or optimal bout length, we defined bouts MVPA using two different thresholds for the minimal bout length: 10 and 20min. We also considered a 30min threshold; however, preliminary analyses revealed that 40% of the study sample did not have any 30min MVPA bout over the 7days measurement period. Variables included in the present analyses were light PA (LPA), moderate PA (MPA), vigorous PA (VPA), and MVPA expressed in minutes per day, number of bouts per day in 10min (N10) or 20min (N20) periods, expressed as number of 10- or 20-min blocks of MVPA accumulation, total time in bouts per day in 10min (T10) or 20min (T20) periods, defined astotal time of MVPA accumulated in periods ≥10 or ≥20min, and average time per day in bouts of 10min (A10) or 20min (A20) periods, calculated as total time of MVPA accumulated in those periods divided by the number of bouts in this period.

2.6 | **Metabolic syndrome score**

MetS was created from the mean of the standardized values of each individual CVD risk factor (i.e., WC, SBP, triglycerides, HDL-c, and glucose) by age groups (children and adolescents) and sex (males and females). This index has been previously used by the International Diabetes Federation to assess cardiovascular health in children and adolescents.³⁶ The standardized value for HDL-c was multiplied by (−1) since higher HDL-c levels represent lower CVD risk.

2.7 | **Data analyses**

Significant interactions by sex (males and females) and age groups (children and adolescents) in the studied associations were observed. Consequently, all analyses were performed differentiating by sex and age groups. All variables were checked for normality. Descriptive statistics were presented as mean \pm standard deviation. T tests were **2302 WII FY WII FY**

used to analyze the differences in the variables of interest between sex for both age groups at both time points.

To examine the cross-sectional association of PA with MetS, linear regression models were used, where PA variables (i.e., LPA, MPA, VPA, MVPA, N10, N20, T10, T20, A10, and A20), at baseline were individually introduced as independent variables, and MetS at baseline was individually introduced as a dependent variable. In Model 1, all analyses were controlled for age, educational center, and mother's education level at baseline. Model 2 was Model 1+sedentary time at baseline.

To study the longitudinal association of PA variables and MetS, linear regression models were used, where PA variables at baseline were individually introduced as independent variables, and MetS at 2-years follow-up as a dependent variable.In Model 1, we adjusted by age, educational center, mother's education level, and MetS at baseline. Model 2 was Model 1+sedentary time at baseline.

To analyze whether changes in PA variables were associated with future MetS risk, linear regression models were used, where the change (follow-up value – baseline value) of LPA, MPA, VPA, MVPA, N10, N20, T10, T20, A10, and A20 was individually introduced as independent variables, and MetS at 2-year follow-up were individually introduced as a dependent variable. In Model 1, we adjusted by age, educational center, mother's education level and MetS at baseline, Model 2 was Model 1+sedentary time at baseline and Model 3 was Model 1+changes in sedentary time. Analyses were performed using the environment for statistical computing R, version 4.0.3 (R Foundation for Statistical Computing). The significance was set at $p < 0.05$.

3 | **RESULTS**

Participant characteristics are shown in Table [1](#page-4-0). Overall, at baseline, female children and adolescents showed lower levels of MPA, VPA, and MVPA (all *p*<0.05) compared to male children and adolescents, respectively. At follow-up, female children and adolescents had lower levels of VPA and MVPA (all $p < 0.05$) than male children and adolescents. In adolescents, females presented lower SBP, higher HDL-c, and lower levels of VPA and MVPA compared to male adolescents (all $p < 0.05$).

Cross-sectional associations of PA and MetS at baseline are depicted in Table [2.](#page-7-0) VPA, MVPA, N10, and T10 were negatively associated with MetS in male children and male adolescents in both models (β ranging from -0.005) to −0.164, all *p* < 0.05).

Table [3](#page-8-0) shows the longitudinal associations of PA variables at baseline and MetS at 2-years follow-up. T20 was negatively associated with MetS in male children in Model

 $1(\beta = -0.059, p = 0.048)$. While in female children VPA and N10 were negatively associated with MetS in Model 1 and Model 2 (*β* ranging from −0.011 to −0.247, all *p*<0.05) and T10 was negatively associated with MetS only in Model 1 (*β*=−0.016, *p*=0.046). Finally, A20 was negatively associated with MetS in male adolescent $(\beta = -0.007, p = 0.043)$. Similar results were observed when sedentary time at baseline was included in the model (Model 2) $(\beta = -0.007,$ $p=0.047$). No associations were found between PA variables and follow-up MetS in female adolescents.

Table [4](#page-9-0) shows the association of changes in PA variables and MetS at follow-up. Changes in N20 and T20 were positively associated with MetS in male children in all models (β ranging from 0.034 to 0.834, all $p < 0.05$). In contrast, A10 was negatively associated with MetS in female adolescents in all models (β =−0.012, all *p* <0.05).

4 | **DISCUSSION**

The aim of the current study was to analyze the crosssectional and longitudinal associations of PA levels and patterns with MetS risk in children and adolescents. Overall, PA levels (i.e., VPA and MVPA), and PA accumulated in shorter patterns (i.e., N10 and T10) were negatively associated with MetS in males at cross-sectional level, while in female children VPA and N10 were negatively and longitudinally associated with MetS. Contrary, PA of lighter intensities and PA accumulated in longer patterns were generally not associated with MetS in male and female children and adolescents.

Our cross-sectional results showed a negative association of PA and MetS in males, especially when PA was moderate or of higher intensities. This is consistent with other research where metabolically healthy children and adolescents had higher MVPA levels than their metabolically unhealthy counterparts. 37 The negative cross-sectional association of PA and MetS has only been shown in males and not in females. This outcome may be due to the fact that males perform higher levels of PA than females at these ages.^{[38](#page-13-10)} However, at the longitudinal analysis, we did not find such effects. Overall, PA seemed to have a greater impactin future MetS in female children compared to male children. However, other authors have shown that MPA at baseline predicts metabolic health (i.e., lower triglyceride concentration and lower HOMA-IR) at follow-up, regardless of sex. 39 In our study, this may be since that females present a lower reduction of MVPA over the 2-year follow-up compared to male children and adolescents. In this sense, previous studies showed how the progression of PA levels, and not only PA levels at a specific point, can play a crucial role in future health status. 14 In terms of changes of PA levels, previous evidence have observed

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TABLE 2 Cross-sectional association between PA and MetS in children and adolescents. and adalasassets. سميان $\frac{1}{2}$ Mater in \overline{D} d ariti , Ŕ Ċ ϵ

Note: β, standardized coefficient. Model 1: analyses were controlled by age, educational center and mother's education level. Model 2: Model 1 plus sedentary time at baseline. Statistically significant values are
highlig Note: A, standardized coefficient. Model 1: analyses were controlled by age, educational center and mother's education level. Model 2: Model 1 plus sedentary time at baseline. Statistically significant values are highlighted in bold.

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Statistically significant values are highlighted in bold.

Statistically significant values are highlighted in bold.

TABLE 4 Association between changes in PA and MetS at 2 years follow-up. **TABLE 4** Association between changes in PA and MetS at 2 years follow-up.

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TABLE 4 (Continued)

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Model 3: Model 1 plus changes in sedentary time. Statistically significant values are highlighted in bold.

Model 3: Model 1 plus changes in sedentary time. Statistically significant values are highlighted in bold.

how reductions in MVPA and LPA negatively affect different cardiometabolic risks. 23 23 23 From a physiological point of view, maintaining high levels of PA or increasing these levels over time can influence cardiometabolic health in different ways.^{[40](#page-13-12)} One is through improved metabolic flexibility, which involves better use of carbohydrates and fats, which is a determinant of health at later ages.^{[41](#page-13-13)} On the contrary, high levels of PA are associated with a reduction in adiposity, 42 which also reverberates to a favorable hormonal environment. Furthermore, increased levels of PA have been associated with a decreased insulin resistance and a lower triglyceride concentration.^{[43](#page-13-15)} Contrary, in our study, no associations were observed between changes in PA levels and MetS. This result could be due to the rela tively low level of changes (homogenous data from base line to follow-up) in our study sample compared to the PA changes observed in other studies. 23 23 23

Regarding PA patterns, the evidence is scarce since, to our knowledge, only one study analyzed the association between PA patterns and MetS,^{[44](#page-13-16)} while other studies analyzed the patterns of PA with individual factors that affect the MetS (i.e., WC and HDL-c). $20,22$ The length of the bouts used in these studies ranged from bouts lengths of \langle 1 min,^{[22,45](#page-12-17)} between 1 and 5 min,^{[19,20,45](#page-12-15)} and between 5 and $10 \text{min.}^{19,20}$ $10 \text{min.}^{19,20}$ $10 \text{min.}^{19,20}$ Indeed, our results may indicate that using bouts longer than 10min were ineffective in the pediatric population. For instance, only a 17.7% of the total study sample at baseline, and a 22.6% at follow-up attained one or more bouts of 20min of duration. This may be due to the fact that children and adolescents normally display short periods of PA of high intensity interspersed with frequent periods of resting.^{[46](#page-13-17)} In this sense, a brief interruption in the children's movement may cease the detec tion of PA bouts recorded by the accelerometer, which may result in an impediment for children to accumulate long duration bouts. Previous studies using shorter MVPA bouts have found beneficial results for some MetS indica - tors such as WC,^{[19,22](#page-12-15)} HDL-c,^{[19](#page-12-15)} or for overall MetS.¹⁹ This is in line with the latest PA recommendations by $WHO₁₀⁴⁰$ $WHO₁₀⁴⁰$ $WHO₁₀⁴⁰$ stating that every minute of PA is of value in relation to health. In this context, bouts of longer duration discard a PA of short duration that could, in fact, impact the health of children and adolescents. In agreement, Holman et al. showed associations of PA pattern with MetS in periods shorter than 10min at the cross-sectional level; therefore, these results could support ours. 19 However, since these authors used the entire population without differentiating by sex, we cannot confirm the sex differences observed in the current study.^{[19](#page-12-15)} In our case, at a cross-sectional level, we found differences in the association between males and females for PA patterns. From our point of view, derived from the current results and previous published research, PA variables and their implication for MetS seem to differ between sexes. By differentiating analyses by sex, a deeper view could be attained from future studies.

Finally, when changes in PA patterns were analyzed, significant positive associations were shown between changes in N20 and T20 with MetS in male children. Nonetheless, changes in N20 were only observed in 13 male children (5 increased and 8 decreased their N20 levels), and therefore, these associations should be considered with caution. In conclusion, some associations of PA levels and MetS were observed at the cross-sectional level in male children and adolescents. Longitudinally, VPA and N10 were negatively associated with MetS in female children. A low percentage of children and adolescents attained one or more N20. Therefore, for future studies analyzing the relationship between PA and health markers in the pediatric population, it would be advisable to choose bouts of shorter duration. In addition, more longitudinal studies are needed to analyze the sex-specific association between PA patterns and MetS in the pediatric population.

5 | **PERSPECTIVE**

In preceding studies that measured PA with accelerometry, we observed an absence of longitudinal studies and consensus in scientific literature when defining patterns of PA and cardio metabolic risk in youth.²⁵ As a result, our purposes were to assess the cross-sectional, longitudinal and change associations of PA levels and patterns with MetS risk in children and adolescents, finding that associations of PA and MetS occur mainly at the cross-sectional level in males and when PA patterns were grouped into bouts of 10min. Therefore, we would advise to choose shorter length bouts in order to enhance the quality of upcoming studies of PA with health markers in the pediatric population. We believe that our findings could encourage the practice of PA even in short periods of time to improve cardiovascular health in young people. Furthermore, they could be useful to set a length of PA patterns when assessing PA patterns in youth, as well as to improve the methodology of future research relating school-age PA patterns to short- and long-term cardiovascular health outcomes.

6 | **STRENGTHS AND LIMITATIONS**

Several limitations should be mentioned. First, since we used a descriptive cross-sectional and longitudinal design, the causation of the associations could not be properly determined. Second, the generalization of these results should be considered cautiously because we could not determine the influence of ethnicity and

country's economic development on these associations, given that only urban and Caucasian Spanish youths participated in this study. Third, the ActiGraph accelerometers cannot be worn during swimming activities, and uniaxial (vertical) accelerometers underestimate activities that do not involve vertical accelerations such as skating and cycling. Therefore, PA may have been underestimated. Fourth, although the latest consensus of practical recommendations in accelerometry advise to wear the accelerometer on the hip or wrist, 47 participants in our study wore the accelerometer on the lower back, due to our study was carried out prior to this publication.

Fifth, Evenson cutoff points were selected because they are the most widely used in the young population.^{[35](#page-13-7)} Although these cutoff points for defining LPA, MPA, VPA, and MVPA were validated with an epoch length of $15 s₁⁴⁷$ $15 s₁⁴⁷$ $15 s₁⁴⁷$ the present project stored the accelerometry data with an epoch length of 10s to increase sensitivity to sporadic movement behaviors typical of children and adolescents. Finally, as there are not many children and adolescents who reach 20-min bouts, we have had difficulty analyzing the MetS with PA patterns in periods of 20 min. Otherwise, the current research presents some strengths. The longitudinal design and the relatively large sample, which allows us to conduct the analyses differentiating by sex and age groups, are major strengths of the present study. Moreover, the use of clustered MetS risk factors has been suggested as a good indicator of cardiovascular health, compared with in-dividual MetS risk factors.^{[4](#page-12-3)} Finally, although our study ended in 2014, the current landscape of PA in pediatric population has not improved, 48 so the results obtained are still applicable in current practice.

ACKNOWLEDGMENTS

We thank the participation of children and adolescents in this study, as well as parents and headmasters and teachers of the participating schools.

FUNDING INFORMATION

This work was supported by the National Plan for Research, Development and Innovation (RDi) from the Spanish Ministry of Science and Innovation (DEP 2010-21 662-C04-00 [DEP 2010-21 662-C04-01: DEP 2010-21 662-C04-02: DEP 2010-21 662-C04-03: DEP 2010-21 662-C04-04]). The funding organizations had no role in data collection, analyses, interpretation, or final report of the study.

CONFLICT OF INTEREST STATEMENT

No potential conflicts of interest relevant to this article were reported.

DATA AVAILABILITY STATEMENT

Raw data were generated at University of Cadiz, Autonomous University of Madrid and Institute of Food Science, Technology and Nutrition. Derived data supporting the findings of this study are available from the corresponding author SSP on request.

CONSENT

Participants' parents were informed about the purposes of the study, and written informed consents were provided.

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How to cite this article: Sánchez-Delgado A, Sánchez-Parente S, Martínez-Gómez D, et al. Objective measured physical activity and metabolic syndrome score in children and adolescents: The UP&DOWN longitudinal study. *Scand J Med Sci Sports*. 2023;33:2299-2312. doi[:10.1111/sms.14452](https://doi.org/10.1111/sms.14452)