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Moderating effect of the neighbourhood physical activity environment on the relation between psychosocial factors and physical activity in children: a longitudinal study

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ABSTRACT

Background Few studies have examined the moderating role of neighbourhood environments on the relation between psychosocial factors and physical activity, and results of these studies are mixed. This study examined this relationship in 636 fifth to seventh graders from South Carolina, USA.

Methods From 2010 to 2013, children and their parent/guardian completed annual self-reported surveys assessing psychosocial factors, and children wore accelerometers for 1 week each year. Neighbourhood environments were classified as supportive or non-supportive for physical activity (PA) based on in-person audits of facilities near children's homes and windshield surveys of children's streets. Growth curve analyses were completed to assess the moderating effect of the neighbourhood physical activity environment (NPAE) on the relation between psychosocial factors and total physical activity (TPA) over time.

Results Significant interactions on TPA were found for (1) time, NPAE and parent-reported parent support for PA; (2) time, NPAE and child-reported equipment in the home; (3) child-reported parental support for PA and time; (4) child-reported parental support for PA and NPAE; (5) PA self-schema and time and (6) child-reported parental encouragement and time. Parental support and a supportive NPAE were important for TPA, especially as children transitioned to middle school, whereas home equipment and a supportive NPAE were important for fifth graders' TPA.

Conclusion Consistent with the socioecological model, PA behaviour was dependent on interacting effects across levels of influence. Generally, both a supportive NPAE and positive psychosocial factors were needed to support TPA. Factors influencing PA across multiple levels should be addressed in PA interventions.

INTRODUCTION

Children's physical activity (PA) promotes overall health¹ and numerous factors can support or inhibit PA.² Studies of how neighbourhood characteristics, such as park availability, conduciveness for walking (ie, walkability) and safety, affect PA have proliferated.³ While many studies link supportive neighbourhood features to more PA, others find no association.⁴ Conflicting evidence may derive from unexamined moderating (ie, interacting) factors.⁵

The socioecological model, which examines multiple levels of influence on behaviours (eg, individual, social, environmental factors), is commonly used to understand PA behaviour.⁶ Exploring the interaction of effects across levels of influence is a central tenet of the socioecological model; however, few studies have examined these relationships.⁵

Most studies exploring moderating effects have examined demographic attributes. Generally, demographic factors have been found to moderate the association between neighbourhood characteristics and PA, with some inconsistent findings. For example, youth studies have found gender differences in the association between PA and neighbourhood features⁷⁻⁹ (eg, park area) and adult studies have found variation by age,^{10 11} gender¹¹ and socioeconomic status (SES),¹² regarding PA and walkability¹⁰ and safety.^{11 12}

Fewer studies have examined neighbourhood features and PA in light of psychosocial characteristics. Parental perception of infrastructure (eg, crosswalks, street lighting) affects active commuting to school in children in smart growth communities (ie, compact, walkable communities), but not other community types.¹³ Neighbourhood walkability improved PA in adolescents who perceived many barriers to PA and few benefits of PA in low-income communities but not high-income communities.¹⁴ Both functionality of the perceived physical environment (eg, availability and quality of footpaths/cycle paths) and traffic safety moderated the relation between perceived parental responsibility for PA and amount of outside play.¹⁵ In a national study using self-reported neighbourhood features and PA, psychosocial factors of adolescents like friend support and attitudes were more strongly associated with PA in neighbourhoods with high PA resources.¹⁶ In contrast, D'Haese found no consistent evidence that psychosocial factors of children moderated the relationship between walkability and PA in a cross-sectional study.¹⁷

The current study contributes to the evolving literature by examining the moderating role of objectively measured neighbourhood features in the association between child and parental psychosocial factors and objectively measured PA in children. Using a longitudinal study design, over 600 children in South Carolina, USA, were followed as they transitioned from elementary school to middle



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school (fifth through seventh grade), a critical period during which PA levels decrease.¹⁸

METHODS

Participants and settings

The Transitions and Activity Changes in Kids study was a multi-level longitudinal study examining changes in PA as children transitioned from elementary school to middle school. In two South Carolina school districts, 21 of 24 elementary schools agreed to participate from 2010 to 2013. All ambulatory fifth graders without physical limitations that would invalidate accelerometry data were invited to participate. Recruitment activities included information flyers, consent forms sent home to all fifth grade students, assemblies at each school, posters in the gym and reminders about the study in physical education. A total of 1080 fifth graders (501 boys, 579 girls) were recruited at baseline (64% and 57% of fifth graders in each district), which was representative in terms of gender and race/ethnicity.

Children were measured in fifth, sixth and seventh grades. Child assent and parent/guardian consent were obtained prior to data collection. During each year of data collection, children and parents/guardians were asked to complete a questionnaire and children received an accelerometer to assess PA. All neighbourhood data were collected at one time point between fifth and sixth grade (windshield survey) or sixth and seventh grade (Physical Activity Resource Assessment (PARA)). For the present study, children were excluded for missing data on: fifth grade PA (N=81); neighbourhood (N=260); sixth and seventh grade PA (N=88); race (N=2); parent report (N=13). The analytic sample for this study included 636 children. There were no significant differences between the analytic sample and the excluded sample across age, gender, race/ethnicity, total physical activity (TPA) or neighbourhood SES (nSES).

Total PA

PA was measured in grades 5, 6 and 7 using accelerometry (Acti-Graph GT1M and GT3X models, Pensacola, Florida, USA). Each participant received an accelerometer to wear on the right hip during waking hours for seven consecutive days, except while bathing, swimming or sleeping. Accelerometer data were collected in 60 s epochs and periods of non-wear time (≥ 60 min of consecutive zeroes) were set to missing. Data for Sundays were excluded from analysis because of the shorter amount of wear time and lower compliance. Children had to provide at least 2 days of eight or more hours of data for each day to be included (weekend day not required). For children who met wear time requirements, multiple imputation using Proc MI in SAS (V.9.3) was employed to estimate missing values. On average, 73% of total possible records from Monday to Saturday were available over the 3 years. Using cut-points established by Freedson *et al.*,¹⁹ accelerometer activity counts were used to determine time spent in light-intensity, moderate-intensity and vigorous-intensity activities. An average cut-point was used based on the ages in the study. The outcome variable of interest was TPA, which is expressed as mean daily minutes of TPA per hour of wear time. TPA was defined as ≥ 100 activity counts per minute and includes light-activity, moderate-activity and vigorous-activity levels.^{19 20}

Demographics

Children self-reported their age, sex and race/ethnicity. Age was reported as years and expressed as a continuous variable. Sex was reported as male or female. For race, children were instructed

to select each applicable race category. For ethnicity, children indicated whether they were of Hispanic or Latino origin. Race and ethnicity variables were collapsed into one variable with the following categories: Non-Hispanic White, Non-Hispanic Black, Hispanic and other (includes multiracial).

Child-reported and parent-reported variables

Table 2 provides a list of child-reported and parent-reported constructs utilised, including a definition, number of survey items, range of response options, Cronbach's alpha and mean value. Briefly, the student questionnaire included five intrapersonal and five interpersonal psychosocial constructs and one home environmental variable. The parent questionnaire included two intrapersonal and four interpersonal psychosocial variables and two home environmental variables. Online supplementary appendix 1 lists each item included and the reference for the items/construct.

Neighbourhood/community variables

For nSES, percent of residents living in poverty in the child's census tract during the last year was obtained using data from USA Census Bureau's American Community Survey 5-year estimates for 2006–2010. Two instruments were used to assess attributes of the neighbourhood PA environment (NPAE): a windshield survey, which used direct observation to document attributes of the children's street segments,²¹ and the PARA, which used in-person audits to document features and incivilities at PA facilities (ie, churches, commercial facilities, trails, parks and schools).²²

For windshield survey data, trained research assistants drove the length of the street segment corresponding to each participant's home address multiple times to document various attributes.^{21 23} Two subscales were used: physical incivilities (eg, trash) and social spaces (eg, at least 1/3 of homes have porches). All items and their coding are described in the online supplementary appendix 1. Interobserver reliability for each subscale in the current study was over 0.80.

Potential PA facilities (ie, churches, commercial facilities, trails, parks and schools) in each county were identified using internet resources and common databases. Trained data assistants visited each potential facility and, if it had PA resources, completed a PARA. A PARA index score was calculated for each PA facility by summing the number of features (eg, baseball field) at the facility then reducing the score based on the degree of incivilities on the premises.²² This scoring was used because facilities with more features are used more often²⁴ and incivilities are associated with lower PA.³ A child-specific PARA score was created by summing the PARA index scores for all facilities within a two-mile, street network buffer around the home using GIS software (ArcGIS V.10.1).

A measure of the NPAE was created using windshield survey and PARA data. Each participant's neighbourhood was classified as having a supportive or non-supportive NPAE. Neighbourhoods were classified as non-supportive of PA when the following criteria were met: (1) physical incivilities present on street segment, (2) social spaces score below three on a scale from 0 to 9, meaning few social spaces, and (3) PARA index score below the 50th percentile for the sample, which indicates less than 20 features across all PA facilities in the neighbourhood (assuming no incivilities present). Otherwise, neighbourhoods were classified as supportive.

Statistical analyses

Means and SD were calculated for child age, TPA, nSES and psychosocial factors by supportive and non-supportive NPAE.

The t-tests were used to test for significant differences. Frequencies were calculated for sex and race/ethnicity by supportive and non-supportive NPAEs. The χ^2 analyses were used to test for significant differences.

Preliminary growth curve analyses

Four preliminary models were run using growth curve analyses with TPA as the dependent variable, adjusting for race, gender, nSES and children nested in schools. Models included time and time squared (the latter due to the non-linear nature of TPA over time). Time-varying child-reported variables (ie, values from fifth, sixth, and seventh grade) with time interactions (time, but not time-squared) were evaluated in a mixed model separately for supportive and non-supportive environments. Then time-varying parent-reported variables with time interactions were evaluated separately by environment. Backward elimination was run eliminating variables with $p > 0.20$.

A second wave of preliminary analyses was performed combining parent and child variables from the first set of analyses for each environment strata adjusting for race, gender, nSES and children nested in schools. Time-varying child and parent-reported variables with time interactions were evaluated in a mixed model separately for supportive and non-supportive environments. Models included time and time squared. Backward elimination was performed deleting variables that were $p > 0.05$.

Final growth curve

For the final model, NPAE was entered into the model as a categorical variable along with the significant variables resulting from the second wave of preliminary analyses. All two-way (variable*time; variable*environment) and three-way (variable*environment*time) interactions were included. Then a backward elimination was performed, deleting variables with $p > 0.05$.

For ease of interpretation, the continuous variables were centred by subtracting grand means of the variable at each time point, and time was coded as 0, 1 and 2. Intercept and slope (ie, time) were modelled as random effects and children were nested in schools. An unstructured covariance matrix was used for all models. To evaluate the interactions, centred variables were categorised as 0 (≤ 0) or 1 (> 0) and models were rerun with dichotomous variables to obtain adjusted least square means (LSM).

RESULTS

In fifth grade, the mean age was 10.6 (± 0.6) years. The sample was nearly equal boys (46%) and girls (54%). Twenty-six percent of children were classified as living in non-supportive NPAE. The sample was racially and ethnically diverse (35.7% black, 9.4% Hispanic, 37.7% white and 17.1% other races/multiracial). Average TPA was 28 min/hour. Few significant differences were found in the bivariate analysis between children in supportive and non-supportive NPAEs in fifth grade (see table 1). Children in non-supportive (vs supportive) NPAEs were slightly younger and had a greater percentage of persons living in poverty in their census tract.

Across the psychosocial factors, fifth graders in supportive NPAEs reported significantly lower motives to be physically active due to appearance and a significantly higher number of active friends. Parents of children in supportive NPAEs reported significantly higher enjoyment of PA and were significantly more likely to report participation in sports (see table 2).

Final growth curve

After preliminary growth curve analysis, seven unique variables remained (see table 3 for variables). These variables were entered into a final model with three-way (time*environment*variable) and two-way interactions. Significant three-way interactions were found including time and NPAE by child-reported equipment in the home and by parent-reported parent support for PA (see table 3). Four significant two-way interactions with TPA were found, including child-reported perception of parental support for PA with (1) time and (2) NPAE, as well as time by (3) PA self-schema and (4) child-reported perception of parental PA encouragement. Finally, both perception of PA skill and parental report of the child enjoying PA were predictive of TPA levels.

Adjusted LSM

LSM were used to visually represent and interpret the significant interactions. With respect to the three-way interaction between NPAE, time and parent-reported support for PA, children in supportive NPAEs with high parental support for PA generally maintained higher TPA levels compared with children with low parental support (although the difference was significant in sixth grade only in LSM analysis). In non-supportive NPAE, children whose parent reported high parental support for PA had higher

Table 1 Sample descriptives of children overall and by neighbourhood physical activity environment

Individual characteristics (at fifth grade)	Total sample (n=636)	Neighbourhood physical activity environment	
		Non-supportive (n=166)	Supportive (n=470)
Age (mean, SD)	10.6 (0.6)	10.5 (0.5)	10.6 (0.5)*
Sex (n, %)			
Male	292 (45.9%)	79 (47.6%)	213 (45.3%)
Female	344 (54.1%)	87 (52.4%)	257 (54.7%)
Race/ethnicity (n,%)			
White	240 (37.7%)	57 (34.3%)	183 (38.9%)
Black	227 (35.7%)	67 (40.4%)	160 (34.0%)
Hispanic	60 (9.4%)	17 (10.2%)	43 (9.2%)
Other	109 (17.1%)	25 (15.1%)	84 (17.9%)
Total physical activity (min/hour) (mean, SD)	28.2 (4.7)	27.8 (4.6)	28.4 (4.7)
Neighbourhood characteristics			
Neighbourhood socioeconomic status† (mean, SD)	16.2 (7.1)	17.3 (7.2)	15.9 (7.0)*

* $p < 0.05$.

†Percentage of persons below poverty in the census tract for child's home address.

Table 2 Student and parent survey variables and means (SE) for fifth grade by neighbourhood physical activity environment

Variable	Operational definition	# of items (range)	Cronbach's alpha	Non-supportive PA environment (n=166)	Supportive PA environment (n=470)
Child-reported intrapersonal variables					
Self-efficacy	Confidence to be physically active most days of the week	8 (1–5)	0.78	3.24 (0.04)	3.27 (0.02)
Barriers	Barriers to PA	5 (1–5)	0.47	1.64 (0.03)	1.63 (0.02)
Enjoyment	Motives for being physically active related to enjoyment	6 (1–4)	0.80	3.57 (0.05)	3.63 (0.02)
Appearance	Motives for being physically active related to appearance	6 (1–4)	0.87	3.14 (0.06)	2.99 (0.04)*
Fitness	Motives for being physically active related to fitness	3 (1–3)	0.67	3.72 (0.03)	3.69 (0.02)
Competence	Motives for being physically active related to competence	4 (1–4)	0.70	3.50 (0.04)	3.47 (0.03)
Social	Motives for being physically active related to social	3 (1–3)	0.66	3.11 (0.06)	3.07 (0.03)
PA self-schema	Self-identity as a physically active person	6 (1–25)	NA	24.97 (0.76)	26.10 (0.42)
Perception of skill	How do you rate your PA	1 (1–5)	NA	3.53 (0.08)	3.58 (0.05)
Child-reported interpersonal variables					
Parent support	Parent support for PA	8 (1–5)	0.88	3.31 (0.08)	3.30 (0.05)
Parent encouragement	Perceived parent encouragement for PA	2 (1–5)	0.67	3.73 (0.05)	3.73 (0.08)
Friend support	Friend support for PA	3 (1–5)	0.71	3.49 (0.08)	3.36 (0.05)
# of active friends	Number of active friends	# reported	NA	3.56 (0.11)	3.92 (0.06)*
Encourage peers	Peer encouragement to be physically active	1 (1–5)	NA	3.46 (0.10)	3.48 (0.06)
Child-reported home environmental variables					
PA equipment	Availability of PA equipment in home	1 (1–4)	NA	3.20 (0.08)	3.37 (0.04)
Parent-reported intrapersonal variables					
Child enjoy PA	Child enjoys PA	1 (1–4)	NA	2.49 (0.06)	2.61 (0.03)
Importance of child PA	How important it is for child to be physically active	1 (1–4)	NA	3.60 (0.04)	3.66 (0.03)
Parent-reported interpersonal variables					
Support for PA	Encourages child to be physically active	4 (1–5)	0.76	2.77 (0.07)	2.89 (0.04)
Parent leisure time PA	How parent spends leisure time	4 (1–5)	0.26	2.47 (0.05)	2.58 (0.03)
Parent sports	If and how often parent participates in sports	4 (4–9)	0.65	1.91 (0.05)	2.13 (0.04)*
Parent enjoys PA	Parent's enjoyment of PA	1 (1–4)	NA	3.07 (0.07)	3.27 (0.04)*
Parent-reported home environmental variables					
PA equipment at home	Number of PA resources child has access to at home	# of checked equipment	NA	3.20 (0.08)	3.38 (0.04)
Parental rules for PA/ sedentary behaviour	Parental rules for PA/sedentary behaviour	3 (1–4)	0.31	2.37 (0.05)	2.43 (0.02)

*p<0.05; **p<0.01; ***p<0.001.

NA, Not applicable; PA, physical activity.

levels of TPA compared with children with low parental support in fifth grade, but parental support for PA in a non-supportive NPAE was not sufficient to maintain higher PA relative to those with low parental support (figure 1).

For the three-way interaction between NPAE, time and home equipment, fifth graders in supportive NPAE with high home equipment had higher levels of TPA than those with low home equipment (see figure 2). This difference in TPA disappeared over time. In non-supportive NPAE, there was no difference in TPA between high and low home equipment across each grade level.

A significant interaction between child-reported self-schema for PA and time showed sixth and seventh graders (but not fifth graders) with high PA self-schema had significantly higher levels of TPA.

A similar pattern was found for child-reported perception of parental encouragement for PA. After fifth grade, children who reported high parental encouragement were more physically active (though this difference was not significant in the LSM).

Similar to parent-reported parental support, for children in supportive NPAEs, those reporting high parental support for PA were significantly more physically active than those reporting

Research report

Table 3 Formal interaction test† of the moderating role of neighbourhood physical activity (PA) environment on total physical activity in children (N=636)

Fixed effects	Main effects B (SE)	Time×variable interaction B (SE)	PA environment×variable interaction B (SE)	PA environment×time ×variable interaction B (SE)
Child-reported				
PA self-schema	-0.0001 (0.02)	0.03 (0.01)*		
Parental encouragement	-0.22 (0.19)	0.32 (0.16)*		
Perception of skill	0.30 (0.12)*			
Parent support	-0.14 (0.30)	-0.35 (0.18)*	0.73 (0.28)**	
PA equipment at home	-0.17 (0.33)	0.22 (0.25)	0.64 (0.37)	-0.68 (0.29)*
Parent-reported				
Child enjoys PA	0.68 (0.18)***			
Support for PA	1.21 (0.39)***	-0.62 (0.30)*	-0.94 (0.46)*	0.73 (0.35)*
PA environment (ref=supportive)	0.34 (0.41)	-0.16 (0.28)		

*p<0.05; **p<0.01; ***p<0.001.

†Adjusted for time, time*time, gender, race and neighbourhood socioeconomic status.

low child-reported parental support (significantly different in fifth and sixth grades in the LSM). TPA did not differ in any year in non-supportive NPAEs by child-reported parental support.

Finally, children who reported higher perceptions of skill in PA accrued more TPA and children whose parents reported higher levels of child's enjoyment of PA had higher levels of TPA.

DISCUSSION

During the transition from elementary to middle school, neighbourhood features modified the effect of the relation between TPA and two psychosocial factors: parental support and equipment in the home. Children with parental support while living in a supportive NPAE had higher TPA levels. In earlier grades, parental support was also directly associated with TPA, regardless of the neighbourhood environment. Further, children with equipment in the home and a supportive NPAE had higher TPA in fifth grade. In a non-supportive NPAE, equipment in the home was not associated with TPA in any grade.

Parental support has been consistently associated with PA in children,²⁵⁻²⁷ particularly younger children.²⁷ We found

parental support associated with TPA regardless of NPAE at younger ages, but as children transitioned to middle school this association remained only for those in supportive NPAEs. This suggests neighbourhood PA features and parental support together minimise the decrease in TPA over time. This may help explain the lack of association and mixed results for parental support and PA at older ages in previous studies that did not consider neighbourhood. Fewer studies have looked at parental support and TPA (vs moderate-to-vigorous PA). A recent review of parental support by type of PA (including TPA) found mostly null associations between parental support and TPA with the exception of parental involvement and father's PA.²⁸ The vast majority of TPA studies in this review utilised self-reported measures and were cross-sectional, which might explain the different findings.

A few studies have examined moderating effects on the relationship between parental support and PA. In a meta-analysis examining the association between parental support and PA, only measurement type (but not age, geographical location, or study design) moderated the association: self-reported PA

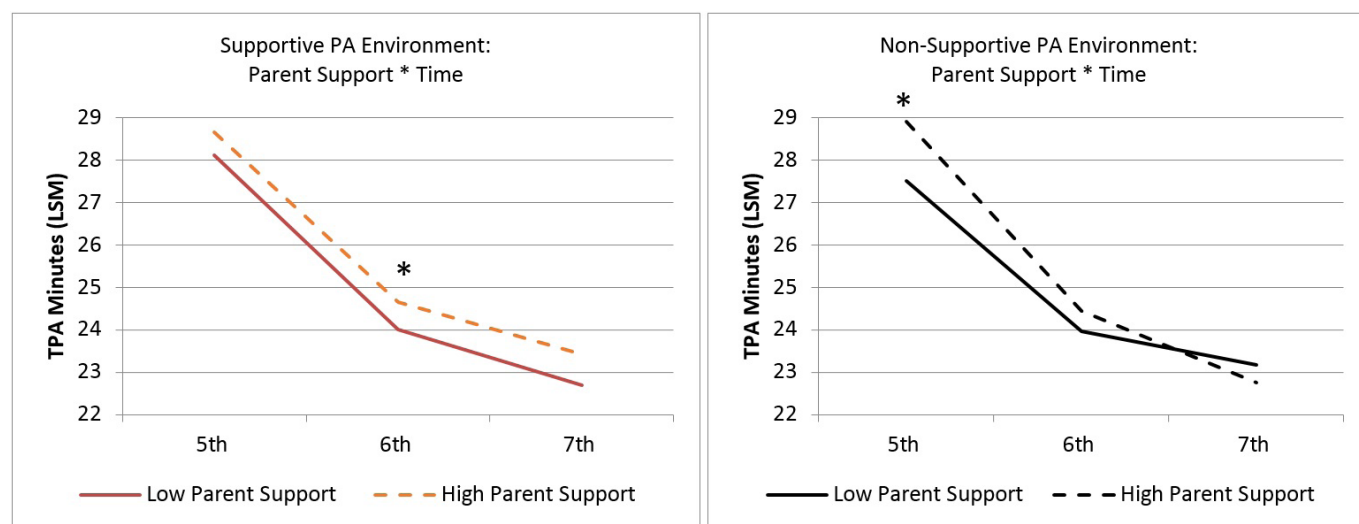


Figure 1 Adjusted least square means (LSM): total physical activity (TPA) across time by neighbourhood physical activity (PA) environment and parent support. (*p<0.05)

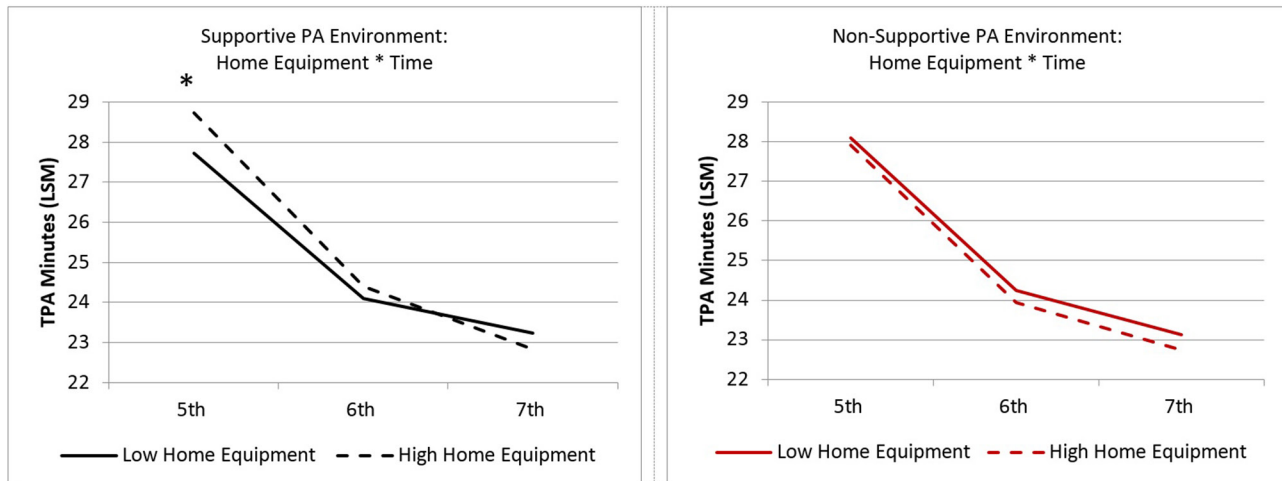


Figure 2 Adjusted least square means (LSM): total physical activity (TPA) across time by neighbourhood physical activity (PA) environment and home equipment. (* $p < 0.05$)

What is already known on this subject

- ▶ Numerous studies have examined the association between the neighbourhood physical activity environment and child physical activity but the results of these studies are mixed and most of the studies are cross-sectional.
- ▶ Few studies have examined whether the neighbourhood physical activity environment moderates the association between individual-level characteristics (eg, demographics, psychosocial factors) and physical activity.
- ▶ Identifying moderating effects (ie, for whom the environment matters) may help to explain the mixed findings in the literature.

What this study adds

- ▶ This study found the association between both parental support and having equipment in the home on total physical activity was dependent on whether the child lived in a supportive neighbourhood physical activity environment.
- ▶ Parent support was associated with total physical activity in fifth grade regardless of the child's neighbourhood physical activity environment, but as children transitioned from elementary school to middle school both parental support and a supportive neighbourhood physical activity environment were needed to limit the decrease in total physical activity.
- ▶ Having equipment in the home along with a supportive neighbourhood physical activity environment was associated with greater total physical activity in fifth grade only. Equipment in the home was not associated with total physical activity for children in non-supportive neighbourhood physical activity environments at any age in the study.
- ▶ Generally both supportive neighbourhood physical activity environments and positive psychosocial factors were needed to support total physical activity.
- ▶ Interventions that target multiple levels of influence and recognise the interacting effects across levels of influence are needed to support total physical activity.

had moderate effect sizes whereas objective PA measures had small effect sizes.²⁹ Similarly, D'Haese found no consistent interactions between psychosocial factors (including parental support) and neighbourhood walkability and PA.¹⁷ Our study utilised a comprehensive definition of supportive environments, including availability of PA facilities, presence of social spaces, and lack of incivilities, which may explain the significant results.

Reviews of the effect of home equipment have found limited evidence of an association with PA^{30,31} and moderate evidence for an inverse association with sedentary behaviour.³¹ We found no association between TPA and home equipment for children who lived in non-supportive NPAEs and an association at fifth grade for children in supportive NPAEs. Again, these findings suggest a combination of supportive resources is needed to support PA, although this combination of influence was not sufficient to support TPA as children transitioned to middle school.

Our moderation analyses found both supportive NPAEs and supportive psychosocial factors were needed to support TPA in children—consistent with other findings of psychosocial factors, PA and neighbourhood environment.¹⁶ In adults, the direction of association between neighbourhood environments, psychosocial factors and PA is less consistent.^{32,33}

This study had important strengths, including a diverse sample of children followed during a critical period when PA levels decline.¹⁸ Objective measures were utilised for TPA and the environment and detailed environmental data at multiple scales were used. Study limitations include potential findings due to multiple comparisons; inability to make comparisons to studies examining moderate-to-vigorous activity; limited number of exposures related to screen time and not requiring a weekend day of TPA or analysing weekdays separate from weekends, though the influence of parental support may depend on such classifications.^{34,35} It will be important for future studies to include children who live in different types of environments.

In this study, the association of parental support and home equipment to TPA depended on living in a supportive NPAE. While parental support alone may be enough to support TPA in fifth grade, both parental support and supportive NPAE are needed during the transition from elementary to middle school. These findings suggest that considering the interacting

effects of multiple levels of influence, a central tenet of the socioecological model, is critical for understanding PA behaviour. Future studies should examine factors at multiple levels so effective interventions to maintain PA over time can be developed.

Contributors NC, MD, RKD, DEP and RRP contributed to the study conception. NC and MNC made substantial contributions to the drafting the manuscript. NC, MNC and MD made substantial contributions to data analysis. KLM and RRP made substantial contributions to acquisition of the data. All authors contributed to the interpretation of the data, critically revised drafts of the work for intellectual content, read and approved the final manuscript to be published and agree to be accountable for all aspects of the work.

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Competing interests None declared.

Patient consent for publication. Not required.

Ethics approval All protocols were approved by the Institutional Review Board at the University of South Carolina.

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