Revised: 27 March 2020



ORIGINAL RESEARCH ARTICLE

The mediating role of visceral adiposity in the relationship among schooling, physical inactivity, and unhealthy metabolic phenotype

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Funding information

BioClin; Council for Scientific and Technological Development, Grant/Award Number: 481418 / 2011-3; Foundation of the State of Minas Gerais, Grant/Award Number: APQ- 00296-12

Abstract

Objective: To explore the mediating role of visceral adiposity, as assessed by the visceral adiposity index (VAI), in the relationship among schooling, physical inactivity, and unhealthy metabolic phenotype (UMP).

Methods: A cross-sectional population-based study was conducted with 854 adult individuals of both sexes from a Brazilian city. Data were collected through interviews, anthropometric evaluation, and clinical and laboratorial tests. We used multivariate path analysis, which simultaneously analyzes multiple relationships between variables. The analyses were adjusted by sex and age and stratified according to nutritional status.

Results: A positive direct effect of visceral adiposity on the UMP was observed for normal weight, standardized estimate (SE) = 0.632; confidence interval (CI 95%) = 0.547, 0.707) and overweight individuals (SE = 0.732; CI 95% = 0.647, 0.808), and negative direct effect of schooling on physical inactivity (normal weight: SE = -0.408; CI 95% = -0.550, -0.265) and overweight (SE = -0.304; CI 95% = -0.479, -0.129). Among normal-weight individuals, there was a positive direct effect (SE = 0.193; CI 95% = 0.059, 0.328) of physical inactivity on VAI. In relation to indirect effects, there was a mediating role of visceral adiposity in the association of schooling level and physical inactivity with the UMP only among normal-weight individuals.

Conclusions: Visceral adiposity has a direct effect on the UMP regardless of nutritional status, and there is a mediating effect of VAI on the relationship among schooling, physical inactivity, and UMP in normal-weight individuals.

1 | INTRODUCTION

Obesity is currently a major public health problem and a strong contributor to the global burden of diseases, especially cardiometabolic diseases (de Oliveira, Valente, & Leite, 2010). Because of the costs of treating the associated diseases, obesity implies considerable financial expenses for the health system (Gakidou et al., 2017). Given the heterogeneous nature of this disorder, the identification of its subtypes can help in decision making for the best therapeutic strategy. Studies have identified different subtypes of obesity (Andres, 1980; Ruderman, Berchtold, & Schneider, 1982; Ruderman, Schneider, & Berchtold, 1981) and described phenotypes that combine body mass index (BMI) and metabolic profile. One of the criteria proposed for the classification of the individual as

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metabolically unhealthy is the presence of at least two of the following alterations: high blood pressure, hypertriglyceridemia, low high-density lipoprotein cholesterol (HDL-c), hyperglycemia, insulin resistance, and inflammation (Wildman et al., 2008). Therefore, four phenotypes can be identified in individuals with or without overweight: metabolically healthy normal weight; metabolically unhealthy normal weight (MUNW); metabolically healthy overweight (MHO); and metabolically unhealthy overweight (MUO). Each of these phenotypes has a potential risk for developing cardiometabolic disease. MUNW individuals, who are still classified by tables as normal weight, show metabolic abnormalities typical of obesity, and the occurrence of MHO is not a benign condition (Aung, Lorenzo, Hinojosa, & Haffner, 2014). For example, there is variation in the risk of type 2 diabetes mellitus and cardiovascular disease among these phenotypes, with MUNW and MHO being considered as intermediate risk and MUO as the highest risk phenotype (Aung et al., 2014; Caleyachetty et al., 2017; Lassale et al., 2018).

Visceral adiposity plays a key role in the metabolic deterioration of an individual, contributing to the etiology of these phenotypes (Hwang et al., 2015; Samocha-Bonet et al., 2014). The possible causes are the deregulation of adipokines, leading to more production of pro-inflammatory adipokines and less of anti-inflammatory adipokines (Hamdy, Porramatikul, & Al-Ozairi, 2006; Maury & Brichard, 2010) and the greater lipolysis of this tissue. This dysregulation increases the concentration of free fatty acids (Després et al., 2008; Hermsdorff & Monteiro, 2004; Ribeiro Filho, Mariosa, Ferreira, & Zanella, 2006), which in turn interferes in the action of insulin, causing insulin resistance.

Measuring visceral adiposity directly requires expensive imaging techniques that are often unfeasible in the context of public health; hence, alternative measures have been proposed. The visceral adiposity index (VAI) is a recently developed gender-specific mathematical model that uses both biochemical and anthropometric indicators to estimate adiposity dysfunction related to cardiometabolic risk (Ahmad & Haddad, 2015; Amato et al., 2010) and has been validated as a simple surrogate marker of visceral adiposity and adipose dysfunction (Amato et al., 2010).

The influence of behavioral habits on the differentiation of metabolic phenotypes, particularly the effect of physical activity, is worthy of investigation, since it is a modifiable factor that can be used as a preventive and therapeutic strategy (Jae et al., 2017). Scientific evidence shows that physical activity is significantly associated with decreased levels of visceral fat (Kotani et al., 1994; Pitanga, Pitanga, Gabriel, & Moreira, 2014; Sasai et al., 2010). One of the probable mechanisms responsible for this relationship is the greater lipolytic response resulting from the effects of the catecholamines released during the physical activity, resulting in marked lipolysis in the abdominal tissue (Després et al., 1991).

Finally, the education level is an important marker of socioeconomic status related to several health outcomes and is another factor that must be considered when assessing different metabolic phenotypes (Ferreira, de Moura, Malta, & Sarno, 2009; Martin, Godoy, Franco, Martin, & Martins, 2014). Level of education can influence food choices and the opportunities provided for physical activity (Wagner, Navarro, Gonzalez-Chica, & Boing, 2018). In this sense, there is evidence of a direct association between low schooling level and abdominal adiposity (Nienaber-Rousseau et al., 2017; Oliveira, Velásquez-Meléndez, & Kac, 2007; Vernay et al., 2009; Wardle, Waller, & Jarvis, 2002), as well as higher level of education and more leisure-time physical activity (Knuth et al., 2011).

Although previous studies have examined separately the associations described above (Nienaber-Rousseau et al., 2017; Oliveira et al., 2007; Vernay et al., 2009; Ward et al., 2015; Wardle et al., 2002), evidence on the interrelationship among schooling level, physical activity, and visceral adiposity in the determination of metabolic phenotypes has not been explored. Thus, we hypothesize that visceral adiposity may partially explain why schooling and physical inactivity affect the metabolic profile. The objective of this study was to explore the mediating role of visceral adiposity in the relationship between schooling, physical inactivity, and unhealthy metabolic phenotype (UMP) according to nutritional status.

2 | METHODS

2.1 | Study sample

The data were obtained from a research that aimed to evaluate the health conditions of the adult population of a city of Minas Gerais, Brazil (2012-2014). It is a crosssectional, population-based study with adult individuals aged 20 to 59 years, of both sexes, and living in the urban area of the municipality. The sample was calculated using the public domain program Open Epi, online version 3.03a, considering the following parameters: estimated population of 43.431 individuals (Instituto Brasileiro de Geografia e Estatística—IBGE, 2011), 95% confidence level, expected prevalence of 50% (considering multiple outcomes, because this study is part of a survey that aims to evaluate different outcomes) (Barbosa, Pereira, da Cruz, & Leita, 2018; Ferreira et al., 2018a),

predicted sample error of 4.5%, and design effect of 1.6. The sample calculated was added with 10% to cover for losses and refusals and 10% more to control confounding factors. The required sample size was estimated to be 901 individuals. The sampling process was probabilistic, without replacement, and used a two-stage conglomerate sampling (census and domicile), in which 1229 household interviews were carried out. Of the total number of interviewees, 331 individuals did not complete the laboratory tests. A final sample of 854 individuals was investigated, since 44 individuals were excluded from the study for presenting serum triglycerides (TGs) \geq 279 mg/dL and/or BMI \geq 40 kg/m². These values may affect VAI validity according to the investigators who developed the index formula, and the exclusions aim to avoid that the predictive power assigned to VAI was ascribed to the individual variables in the model (Amato & Giordano, 2013).

The study was approved by the Research Ethics Committee of the Federal University of Viçosa (Official Letter Regulation 02/2013). All participants signed the informed consent form. More detailed information on the methodological aspects of the study is described in Segheto et al. (2015).

2.2 | Measurements

2.2.1 | Biochemical Parameters

Blood samples were collected by venipuncture using the Vacutainer system (Becton Dickinson, Plymouth, UK) after a 12-hour fast. Fasting glucose was determined by the enzymatic glucose-oxidase method. TGs and HDL-c concentration were measured by the enzymatic colorimetric method. Plasma insulin was determined by ELISA, using the Human Insulin ELISA Kit (Linco Research, St. Charles, Missouri). Insulin resistance was estimated by the homeostasis HOMA-IR model: HOMA-IR = fasting insulin (μ U/mL) × fasting glucose (mmol/L)/22.5 (Matthews et al., 1985). Ultrasensitive C-reactive protein (hs-CRP) was determined by the immunoturbidimetric assay (Bioclin, Quimbasa Quimica Básica, Belo Horizonte, Brazil).

2.2.2 | Anthropometric parameters

Body mass was measured in an electronic digital scale (TANITA model Ironman BC-554, Tokyo Japan) certified by the Inmetro, with capacity of 150 kg and precision of 100 g, with participants using as little clothing as possible and barefoot (Lohman, Roche, & Martorell, 1988). Height

was measured with a wall-mounted stadiometer, without footboard, 2.5 m of height and 0.1 cm of resolution (WELMY, Santa Bárbara D'Oeste, Brazil). Participants stood barefoot touching the measurement bar, heels together, feet forming a 45° angle, arms hanging along the body, and looking straight ahead with the head in the "Frankfort horizontal" plane (Lohman et al., 1988). BMI was calculated as the ratio of body mass (kg) to height squared (m²) (World Health Organization, 2000), considering individuals with BMI ≥ 25 kg/m² as overweight and the others as normal weight (BMI 18.5-24.9 kg/m²).

Waist circumference (WC) was measured in centimeters with an inelastic measuring tape (Sanny, São Paulo, Brazil) at the mid-point between the last rib and the iliac crest, at the end of a normal exhalation. All anthropometric measurements were performed in triplicate by one experienced examiner, considering the average values. VAI was calculated using the sex-specific formulas described below (Amato et al., 2010), with TGs and HDLc levels expressed as mmol/L. VAI was used as a continuous variable in all analyses.

Men: VAI =
$$\left(\frac{WC}{39.68 + (1.88^{*}BMI)}\right) * \left(\frac{TG}{1.03}\right) * \left(\frac{1.31}{HDL}\right).$$

Women: VAI = $\left(\frac{WC}{36.58 + (1.89^{*}BMI)}\right) * \left(\frac{TG}{0.81}\right) * \left(\frac{1.52}{HDL}\right).$

2.2.3 | Clinical parameter

Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured in duplicate using an automatic blood pressure monitor (OMRON model HEM-741 CINT, Tokyo, Japan) calibrated and certified by the Inmetro. The first measurement was taken after 5 minutes rest and the second 15 minutes after the first measurement. The mean of the two measurements was considered for analysis.

2.2.4 | Metabolic phenotypes

The criteria of Wildman et al. (Wildman et al., 2008) described in Table 1 were used for the definition of the metabolic phenotypes.

2.2.5 | Physical activity

The leisure-time physical activity level was evaluated by the International Physical Activity Questionnaire, long form, using the fourth domain, which considers the physical activities performed in the last 7 days solely for

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TABLE 1 Definition of metabolic phenotypes

Cardiometabolic abnormalities

- High blood pressure: Systolic/diastolic blood pressure ≥130/85 mmHg or use of antihypertensive medication.
- 2. High triglyceride level: Fasting triglyceride level ≥150 mg/ dL.
- 3. Decreased high-density lipoprotein cholesterol (HDL-c) level: HDL-c <40 mg/dL in men or <50 mg/dL in women or use of lipid-lowering medication.
- 4. High glucose level: Fasting glucose level ≥100 mg/dL or use of hypoglycaemic medication.
- 5. Insulin resistance: HOMA-IR >90th percentile.

6. Systemic inflammation: Level of CRP-us >90th percentile.

Criteria for definition of the unhealthy metabolic phenotype

Presence of ≥ 2 cardiometabolic abnormalities.

recreation, sport, exercise, or leisure for at least 10 continuous minutes. We decided to evaluate separately only the leisure physical activity because the different dimensions are differently related to the study variables (Costa, Salvador, Guimarães, & Florindo, 2010; De Souza, Franscisco, Lima, & Barros, 2014) and the leisure dimension is the one that most relates to cardiometabolic risk and with the greatest potential to be modified.

The level of physical activity was calculated by adding the time spent with walking and moderate physical activity plus twice the time spent with vigorous activities. Participants were classified as physically inactive (<150 min/ week) or physically active (\geq 150 min/week) (Haskell et al., 2007).

2.2.6 | Sociodemographic data

A structured questionnaire was applied to collect information on the following variables: sex (female and male), age (continuous, in years), and schooling level (0-4 years, 5-8 years, 9-11 years, and \geq 12 years of study). The schooling level was the only predictor of socioeconomic status used in this study.

2.3 | Theoretical model

Figure 1 illustrates the theoretical model used in the analysis of the present study, which was built from evidence described in the literature on the relationship between the studied variables (Du, Yu, Zhang, & Sun, 2015; Oliveira et al., 2007; Rodrigues, Melo, Assis, & Oliveira, 2017; Wardle et al., 2002) and from previous



FIGURE 1 Theoretical model

results of the same study population (Ferreira, Juvanhol, et al., 2018; Ferreira, Segheto, da Silva, Pereira, & Longo, 2018). The analyses were also stratified according to nutritional status, since previous results from the same study population (Ferreira et al., 2018a) indicated that the association between VAI and UMP varies according to the nutritional status.

2.4 | Statistical analysis

Data of categorical variables are presented as percentages and data of continuous variables are presented as means and SD. Differences between groups of phenotypes were assessed by chi-square or chi-square test for trend for the categorical variables and t test for the continuous variables. The descriptive analysis was performed using the program Stata 13.0 (StataCorp LP, College Station, Texas).

Path analysis was used to test VAI as a possible mediator in the relationship between schooling, physical inactivity, and UMP. It is a multivariate statistical technique that simultaneously performs a series of multiple regression equations. This technique allows the analysis of multiple relationships among variables, and it is possible to unfold and compare the magnitude of the effects among these variables and to test mediation effects (Gamborg et al., 2009; Hair, Anderson, Tatham, & Black, 2009).

The direct effect of each variable on the UMP was estimated from the path analysis, in which there is no mediation by any other variable included in the model. In addition, the indirect effect was estimated, that is, the one in which there is a sequence of paths with one or more mediating variables. Therefore, the total effect is obtained by the sum of the direct and indirect effects. Notably, in this study, the term "effect" is used in the sense of association, not causality.

We used for the estimation the weighted least squares method adjusted for the mean and variance (WLSMV), which is suitable for models with categorical variables regardless of whether they are predictors or outcome variables. Theta parameterization was used to control differences in residual variances (Muthén & Muthén, 2010). Non-standardized and standardized coefficients were estimated with their respective 95% confidence intervals (95% CI). Standardized estimates (SEs) are expressed as units of SD and are useful in the comparison of effects, since each variable is measured on a different scale.

The path analysis was performed using the software Mplus, version 7.4 (Muthén & Muthén, Los Angeles, California), with all associations adjusted for sex and age. The quality of the fit of the model was evaluated by the index root mean square error of approximation (RMSEA), in which a good fit is represented by an upper limit of the 90% of confidence intervals (CI 90%) of less than 0.08.Values greater than 0.95 for the comparative fit index (CFI) and for the Tucker's incremental index (Tucker Lewis index [TLI]), and a weighted root mean square residual (WRMR) of less than 1 were also considered as indicative of a good fit (Kline, 2011; Wang & Wang, 2012).

3 | RESULTS

The characteristics of the participants stratified by metabolic phenotype are presented in Table 2. There was no difference in the sex distribution among the metabolic phenotypes. Individuals with the MHO phenotype were significantly more educated than their unhealthy counterparts. In addition, metabolically unhealthy individuals were older, had higher VAI, higher Homa-IR, TGs, and glucose, and lower levels of high-density lipoprotein cholesterol than their healthy counterparts, regardless of nutritional status. There was no difference in the leisure-time physical activity level between groups of phenotypes.

The visceral adiposity in normal-weight individuals had a direct positive effect on the UMP (SE = 0.632; CI 95%: 0.547, 0.707; P < .001), showing that higher VAI is associated with the higher occurrence of this phenotype. Physical inactivity, in turn, had a positive direct effect on visceral adiposity (SE = 0.193; CI 95%: 0.059, 0.328; P = .005). On the other hand, schooling had a negative direct effect on physical inactivity (SE = -0.408; CI 95%: -0.550, -0.265; P < .001), showing that individuals with lower education levels are more physically inactive than those with higher education levels. Positive indirect effect of physical inactivity on the UMP, mediated by visceral adiposity (SE = 0.122; CI 95%: 0.035, 0.209; P = .006), was also observed. In addition, a negative indirect effect of schooling was found on the UMP, which was mediated by physical inactivity and visceral adiposity simultaneously (SE = -0.050; CI 95%: -0.092, -0.007; P = .022) (Table 3).

For the overweight individuals, a positive direct effect of visceral adiposity on the UMP (SE = 0.732; CI 95%: 0.647, 0.808; P < .001) was also observed. Schooling also had a negative direct effect on physical inactivity,

MUNW (n = 86) Pa P^a Variable MHNW (n = 436)MHO (n = 186)MUO (n = 146)Sex: female (%) 57.34 56.98 .950 46.24 52.74 .240 Schooling (years) (%) 0-4 5.05 6.98 .080 8.60 13.01 .009 5-8 8.26 15.12 13.44 25.34 9-11 21.33 19.77 23.12 16.44 65.37 54.84 45.21 ≥ 12 58.14 Physical inactivity (%) 68.81 74.42 .301 68.28 67.81 .927 <.001 Age (years)—Mean \pm SD 30.03 ± 10.08 35.35 ± 13.21 <.001 33.96 ± 10.84 40.91 ± 12.01 VAI-Mean ± SD 1.12 ± 0.58 2.44 ± 1.30 <.001 1.28 ± 0.60 2.90 ± 1.43 <.001 HOMA-IR 1.36 ± 0.66 1.76 ± 0.99 <.001 1.62 ± 0.78 2.96 ± 2.09 <.001 HDL-c (mmol/L)—Mean ± SD 14.53 ± 4.3 11.22 ± 3.44 <.001 13.53 ± 3.35 10.64 ± 3.1 <.001 TGs (mmol/L)-Mean ± SD 1.01 ± 0.42 1.62 ± 0.63 <.001 1.10 ± 0.44 1.79 ± 0.69 <.001 Gluc (mmol/L)—Mean \pm SD 4.52 ± 0.45 4.65 ± 0.69 .017 4.60 ± 0.48 5.13 ± 0.97 <.001

 TABLE 2
 Characterization of the study sample according to the metabolic phenotypes. Viçosa, Minas Gerais, Brazil, 2012-2014

Abbreviations: Gluc, glucose; HDL-c, high-density lipoprotein cholesterol; MHNW, metabolically healthy normal weight; MHO, metabolically unhealthy overweight; TGs, triglycerides; VAI, visceral adiposity index.

^aStudent *t* test or Pearson's chi-squared test of or chi-square for trend.

	Non-standardized estimate (CI 95	i%)	Standardized estimate (CI 95%)		
Paths	Direct effect	Р	Direct effect	Р	
$VAI \to MUNW$	0.944 (0.751; 1.138)	<.001	0.632 (0.547; 0.707)	<.001	
$\text{PI} \rightarrow \text{MUNW}$	-0.024 (-0.251; 0.204)	.837	-0.019 (-0.204; 0.165)	.837	
$\text{School} \rightarrow \text{MUNW}$	-0.001 (-0.230; 0.227)	.990	-0.001 (-0.195; 0.192)	.990	
$PI \to VAI$	0.159 (0.050; 0.269)	.004	0.193 (0.059; 0.328)	.005	
$School \rightarrow VAI$	0.100 (-0.015; 0.0216)	.088	0.127 (-0.019; 0.272)	.088	
$\text{School} \to \text{PI}$	-0.391 (-0.548; -0.233)	<.001	-0.408 (-0.550; -0.265)	<.001	
	Indirect effect	Р	Indirect effect	Р	
$PI \rightarrow VAI \rightarrow MUNW$	0.151 (0.042; 0.260)	.007	0.122 (0.035; 0.209)	.006	
$School \rightarrow VAI \rightarrow MUNW$	0.095 (-0.016; 0.205)	.094	0.080 (-0.013; 0.173)	.091	
$School \rightarrow PI {\rightarrow} MUNW$	0.009 (-0.079; 0.098)	.837	0.008 (-0.067; 0.083)	.837	
$School{\rightarrow} PI \rightarrow VAI \rightarrow MUNW$	-0.059 (-0.110; -0.007)	.025	-0.050 (-0.092; -0.007)	.022	
	Total effect (direct + indirect)	Р	Total effect (direct + indirect)	Р	
$\text{PI} \rightarrow \text{MUNW}$	0.127 (-0.121; 0.375)	.316	0.103 (-0.099; 0.304)	.317	
$\text{School} \rightarrow \text{MUNW}$	0.044 (-0.161; 0.248)	.675	0.037 (-0.136; 0.210)	.674	

TABLE 3Estimates and 95% confidence intervals (95% CI) for direct, indirect, and total effects among normal weight subjects. Viçosa,Minas Gerais, Brazil, 2012-2014

Note: Model adjusted for age and sex.

Abbreviations: MUNW, metabolically unhealthy normal weight; PI, physical inactivity; School, years of schooling; VAI, visceral adiposity index. Values in bold have a significant difference.

TABLE 4	Estimates and 95%	confidence intervals	(CI 95%) for direct	, indirect,	and total e	effects among o	overweight individu	ıals Viçosa,
Minas Gerais, I	Brazil, 2012-2014							

	Non-standardized estimate (CI 959	%)	Standardized estimate (CI 95%)		
Paths	Direct effect	Р	Direct effect	Р	
$VAI \to MUO$	0.884 (0.727; 1.040)	<.001	0.732 (0.647; 0.808)	<.001	
$\text{PI} \rightarrow \text{MUO}$	-0.074 (-0.305; 0.156)	.527	-0.049 (-0.200; 0.102)	.526	
$School \to MUO$	-0.041(-0.240; 0.159)	.689	-0.030 (-0.175; 0.115)	.689	
$PI \to VAI$	0.004 (-0.173; 0.182)	.961	0.004 (-0.137; 0.144)	.961	
$School \rightarrow VAI$	0.039 (-0.124; 0.202)	.637	0.035 (-0.109; 0.178)	.637	
$School \to PI$	-0.274 (-0.443; -0.105)	.002	-0.304 (-0.479; -0.129)	.001	
	Indirect effect	Р	Indirect effect	Р	
$PI \rightarrow VAI \rightarrow MUO$	0.004 (-0.153; 0.161)	.961	0.003 (-0.101; 0.106)	.961	
$School \rightarrow VAI \rightarrow MUO$	0.035 (-0.110; 0.179)	.637	0.025 (-0.080; 0.130)	.637	
$School \rightarrow PI \rightarrow MUO$	0.020 (-0.044; 0.085)	.535	0.015 (-0.032; 0.061)	.533	
$School \rightarrow PI \rightarrow VAI \rightarrow MUO$	-0.001 (-0.044; 0.042)	.961	-0.001 (-0.032; 0.031)	.961	
	Total effect (direct + indirect)	Р	Total effect (direct + indirect)	Р	
$\text{PI} \rightarrow \text{MUO}$	-0.070 (-0.350; 0.209)	.621	-0.046 (-0.229; 0.137)	.620	
$School \to MUO$	0.013 (-0.222; 0.249)	.912	0.010 (-0.162; 0.181)	.912	

Note: Model adjusted for age and sex.

Abbreviations: MUO, metabolically unhealthy overweight; PI, physical inactivity; School, years of schooling; VAI, visceral adiposity index.

(SE = -0.304; CI 95%: -0.479, -0.129; P < .001), but significant indirect effect was not observed in this group (Table 4).

The path model presented a good fit: RMSEA = 0.000 (90% CI: 0.000-0.000) and P < .05; CFI and TLI = 1 and WRMR = 0.002.

A Supplementary Material was included in order to clarify the possible doubts flawed related to the inclusion of TGs and HDL cholesterol in both VAI and UMP, we tested if WC (instead of VAI) mediates the relationship between schooling, physical inactivity, and UMPs. Found similar results, we evaluated that the significant direct effect of VAI on the UMPs is not simply due to the fact that the same variables appear in both the mediating variable and the outcome variable.

4 | DISCUSSION

To our knowledge, this is the first study to investigate the interrelationships between visceral adiposity, physical inactivity, and schooling level in the determination of the UMP according to nutritional status. The relationships studied separately are well described in the literature (Du et al., 2015; Knuth et al., 2011; Oliveira et al., 2007; Rodrigues et al., 2017; Ruderman et al., 2019; Vernay et al., 2009; Wardle et al., 2002), but our study provides an innovative solution to these interrelationships using the path analysis. Our main finding was that visceral adiposity plays a key role, mediating the association of schooling and physical inactivity with the UMP, both directly, regardless of nutritional status, and indirectly in normal-weight individuals.

As the unhealthy phenotype is characterized by a deterioration of the metabolic profile, a possible explanation for the relationship of visceral adiposity with this deteriorated profile is the differentiated metabolic behavior of the visceral adipose tissue. This tissue is more sensitive to lipolysis than the subcutaneous adipose tissue, which leads to increased levels of free fatty acids in the liver and resistance to insulin (Després et al., 2008; Hermsdorff & Monteiro, 2004; Ribeiro Filho et al., 2006). Furthermore, the release of higher concentrations of adipokines linked to pro-inflammatory processes seems to modulate the deterioration of metabolic profile (Després et al., 2008; Hamdy et al., 2006; Hermsdorff & Monteiro, 2004; Maury & Brichard, 2010).

Therefore, in agreement with reports showing that a greater accumulation of visceral adiposity is one of the central factors contributing to metabolic deterioration (Hamdy et al., 2006; Hermsdorff & Monteiro, 2004; Maury & Brichard, 2010), our results showed that higher VAI is associated with the UMP, regardless of nutritional status. Du et al. (2015) have shown that individuals with higher VAI showed the worst metabolic profile. Ding et al. (2015) showed that higher VAI was positively associated with prehypertension and hypertension in both sexes. Al-Daghri et al. (2015) verified the accuracy of the VAI index in the prediction of cardiovascular and

metabolic risk. A study conducted with Brazilian adults also showed that high VAI is associated with the components of the metabolic syndrome in healthy young adults (Schuster, Vogel, Eckhardt, Dal, & Morelo, 2014). These findings demonstrate the applicability of VAI as an early marker of cardiometabolic risk, and it has been demonstrated that VAI has a better predictive capacity of this risk than other conventional anthropometric parameters (Ahmad & Haddad, 2015).

This study identified a direct association between physical inactivity and increased visceral adiposity in normal-weight individuals. In addition, an indirect association of physical inactivity with the UMP mediated by visceral adiposity was demonstrated. These findings support the role of physical exercise in the reduction of visceral obesity, and the contributions of inactivity to increased visceral fat deposition and unfavorable metabolic phenotypes. In line with our results, Molenaar et al. (2009) showed that higher levels of physical activity are inversely associated with the volume of visceral adipose tissue. These authors state that physical activity can positively affect both subcutaneous and visceral adipose tissue. Similarly, Pitanga et al. (2014) found an inverse association between walking and moderate physical activities and visceral adiposity.

Evidence from the literature indicates that a less active lifestyle promotes greater susceptibility to positive energy balances, favoring fat accumulation. However, it is not yet clear whether the lack of physical activity selectively increases visceral fat deposition (Tchernof & Després, 2013). On the other hand, exercise is known to increase catecholamine levels, which have effects on adipocyte lipolysis through beta-adrenergic receptors (stimulation) and alpha-adrenergic receptors (inhibition) (Martin, 1996). In addition, catecholamines have more active lipolytic activity in visceral adipose tissue than in subcutaneous tissue, which may justify a possible preferential loss of visceral fat induced by exercise (Martin, 1996; Richelsen, 1986). Balducci et al. (2015) studied the effect of supervised training on liver enzymes, VAI, and liver fat index in diabetic individuals and showed that the last two were significantly lower among individuals with higher training volume.

In this study, no association was detected between physical inactivity and increased visceral adiposity among overweight individuals; consequently, the mediating effect of visceral adiposity was not statistically significant. This result does not agree with the report of McGrath et al. (2017), who found a significant association between moderate or vigorous physical activity and measures of abdominal adiposity among middle-aged African American obese individuals. It is possible that the lack of relationship between physical inactivity and abdominal \perp_{WILEY} 🍈 American Journal of Human Biology_

adiposity among obese individuals in the present study can be explained, at least partially, by the presence of reverse causality. Data on physical activity referred to the week prior to the interview, disregarding the participants' physical activity history. It is believed that overweight individuals tend to change their behaviors with the goal of reducing body adiposity, even increasing physical activity, but this trend is less likely among normal-weight individuals (Souza et al., 2010). Another possibility is that the information reported by the obese individuals underestimate their physical inactivity, as this is not a desirable behavior (World Health Organization, 2009), and the same occurring with energy intake, which is often underreported by these individuals (Avelino, Previdelli, de Castro, Marchioni, & Fisberg, 2014; Pomerleau, Østbye, & Bright-See, 1999).

Regarding the relationship between schooling level and leisure-time physical inactivity, there is evidence that higher levels of education are positively associated with the performance of leisure-time physical activity, both in high-income countries (Camões & Lopes, 2008; Federico, Falese, Marandola, & Capelli, 2013) and in middle-income countries (Costa et al., 2010; Gomez, Duperly, Lucumi, Gamez, & Venegas, 2005; Jurakic, Pedisic, & Andrijasevic, 2009). These findings allow us to infer that, as individuals with higher education usually have a higher income and better jobs, they would also have more access to physical activity facilities, as well as more opportunities for it. Thus, education is an important marker of socioeconomic status and plays an important role in the health conditions of the population, since it can influence people's lifestyle (Braveman & Gottlieb, 2014; Liberatos, Link, & Kelsey, 1988).

However, the association between schooling and obesity was shown to vary between different populations and according to gender, with an inverse relationship observed only in women (Dinsa, Goryakin, Fumagalli, & Suhrcke, 2012; Ruderman et al., 2019). However, other studies have demonstrated the positive association between low schooling level and abdominal adiposity in both sexes (Nienaber-Rousseau et al., 2017; Oliveira et al., 2007; Vernay et al., 2009).

In this study, we found an important indirect effect of schooling on the UMP among individuals with normal weight, which was mediated by physical inactivity and visceral adiposity. Thus, the influence of schooling must be evaluated considering the other factors studied together. As discussed earlier, it is known that schooling has a direct influence on health-related behaviors and may indirectly influence the occurrence of the UMP (Knuth et al., 2011; Moura & Masquio, 2014). However, it would be overly simplistic to attribute the influence on the metabolic profile of an individual solely to schooling, because the relationships between the conditions that may promote changes in this profile, such as socioeconomic status, lifestyle, and adiposity are complex and interchangeable.

In addition to the indirect effects observed in this study, research conducted with a non-institutionalized American civilian population found that abdominal obesity played a mediating role in the relationship among physical activity, inappropriate diet, hypertension, and the prediabetic state, having still a strong direct effect on prediabetes. The indirect effect of socioeconomic status was also detected on the variable hypertension mediated by physical activity (Bardenheier et al., 2013). Similarly, a study developed with a South African population using structural equation analysis found that each year of schooling was associated with declines of 0.29 mm Hg in SBP and 0.12 mm Hg in DBP. In addition, physical exercise, alcohol use, smoking, resting heart rate, and BMI in men played a mediating role in the relationship between socioeconomic status and blood pressure (Cois & Ehrlich, 2014). BMI was a strong mediator of an indirect adverse effect of socioeconomic status on blood pressure in both sexes as well (Cois & Ehrlich, 2014). In addition, these authors found a direct association with aerobic fitness and an indirect association with physical activity via aerobic fitness in the metabolic syndrome and inflammation as early as in adolescence, thus showing the importance of regular physical activity from the early stages of life (Countryman et al., 2013). Although these studies have not stratified the sample according to nutritional status, they showed a mediator effect as our study does.

As highlighted previously, in this study the mediating role of visceral adiposity on UMP was significant only among normal-weight individuals and not among overweight individuals, which is explained by the fact that physical inactivity and VAI were not significantly associated in these subjects.

In addition to the possible explanations presented for the absence of this association, another factor to be considered is the possibility of insufficient statistical power among overweight individuals, because the number of overweight individuals surveyed was smaller (n = 332) than the number of normal-weight individuals (n = 522). Since the stratified analyses were not considered for the sample size calculation, we recognize that the power of the study may not have been sufficient to identify any association.

Finally, our work has several limitations that need to be considered. First, because it is a cross-sectional study, the temporality of the associations cannot be assured and the presence of reverse causality cannot be ruled out and, second, the lack of information on the individuals' physical activity levels, as discussed previously. A direct evaluation of the participants' physical activity level would provide a more accurate and valid measure of this variable. Despite this, the use of an internationally validated questionnaire has minimized these weak points. Finally, while VAI is a good indicator of visceral adiposity, collecting biochemical data along with anthropometric data can be difficult and more expensive for largescale studies, but less expensive than studies that use magnetic resonance imaging, the gold standard for this purpose. The strengths of our work lie in the methodological rigor in the data collection, the fact that it is a population-based study, and the analytical strategy that allowed the simultaneously evaluation of multiple relationships between the variables studied.

5 | CONCLUSIONS

Our results provide evidence that visceral adiposity, being identified by the VAI index, has a direct effect on the UMP, regardless of nutritional status. In addition, a mediating effect of VAI was observed on the relationship between schooling level, physical inactivity, and UMP in normal-weight individuals.

Understanding the mechanisms that modulate the metabolic deterioration in humans will help improve the effectiveness of policies and programs to control diseases and improve the metabolic profile of adults. Our findings reinforce the applicability of VAI as a measure of visceral adiposity and cardiometabolic risk, which can be used in epidemiological studies and clinical practice. They also reaffirm the importance of assessing visceral adiposity in the identification of individuals at cardiometabolic risk.

The implications of the results of this study to public health point to the need to implement programs and policies to encourage physical activity that consider the socioeconomic differences of the population. Interventions in public environments that allow the provision of easily accessible sports facilities and proper guidance, especially among those with low educational level, can lead to a decrease in the population's physical inactivity rates and, consequently, the cardiometabolic risk.

ACKNOWLEDGMENTS

The authors thank all the participants who contributed to the study, the National Council for Scientific and Technological Development (CNPq process no. 481418/2011-3), the Research Support Foundation of the State of Minas Gerais (FAPEMIG Process No. APQ-00296-12), and BIO-CLIN for the financial support to the project.

AUTHOR CONTRIBUTIONS

Fabrícia Geralda Ferreira contributed to the data collection and analyses, wrote the initial draft of the manuscript, and assembled the final version. Leidjaira Lopes Juvanhol and Giana Zarbato Longo contributed to the study design, and data analyses, and participated in the approval of the final version of the manuscript. Aline Silva-Costa contributed to data analyses and important review of the final version to be submitted.

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REFERENCES

- Ahmad, M. N., & Haddad, F. H. (2015). Suitability of visceral adiposity index as a marker for cardiometabolic risks in Jordanian adults. *Nutrición Hospitalaria*, 32(6), 2701–2709. https://doi. org/10.3305/nh.2015.32.6.9543
- Al-Daghri, N. M., Al-Attas, O. S., Wani, K., Alnaami, A. M., Sabico, S., Al-Ajlan, A., ... Alokail, M. S. (2015). Sensitivity of various adiposity indices in identifying cardiometabolic diseases in Arab adults. *Cardiovascular Diabetology*, 14(1), 101. https://doi.org/10.1186/s12933-015-0265-5
- Amato, M. C., & Giordano, C. (2013). Clinical indications and proper use of visceral adiposity index. *Nutrition, Metabolism* and Cardiovascular Diseases, 23(8), e31–e32. https://doi.org/10. 1016/j.numecd.2013.04.006
- Amato, M. C., Giordano, C., Galia, M., Criscimanna, A., Vitttabile, S., Midiri, M., & Aldo, G. (2010). Visceral adiposity index: A reliable indicator of visceral fat function associated with cardiometabolic risk. *Diabetes Care*, 33(4), 920–922. https://doi.org/10.2337/dc09-1825
- Andres, R. (1980). Effect of obesity on total mortality. *International Journal of Obesity*, 4(4), 381–386.
- Aung, K., Lorenzo, C., Hinojosa, M., & Haffner, S. (2014). Risk of developing diabetes and cardiovascular disease in metabolically unhealthy normal-weight and metabolically healthy obese individuals. *The Journal of Clinical Endocrinology and Metabolismo*, 99(2), 462–468. https://doi.org/10.1210/jc.2013-2832
- Avelino, G. F., Previdelli, Á. N., de Castro, M. A., Marchioni, D. M. L., & Fisberg, R. M. (2014). Underreporting of energy intake and associated factors in a population-based study. *Cadernos de Saúde Pública*, 30(3), 663–668. https://doi. org/10.1590/0102-311X00073713
- Balducci, S., Cardelli, P., Pugliese, L., D'Errico, V., Haxhi, J., Alessi, E., ... Pugliese, G. (2015). Volume-dependent effect of supervised exercise training on fatty liver and visceral adiposity index in subjects with type 2 diabetes the Italian diabetes exercise study (IDES). *Diabetes Research and Clinical Practice*, 109(2), 355–363. https://doi.org/10.1016/j.diabres. 2015.05.033
- Barbosa, M., Pereira, C., da Cruz, D., & Leita, I. (2018). Prevalence and factors associated with alcohol and tobacco use among non-institutionalized elderly persons. *Revista Brasileira de Geriatria e Gerontologia*, 21(2), 125–135. https://doi.org/10. 1590/1981-22562018021.170185
- Bardenheier, B. H., Bullard, K. M., Caspersen, C. J., Cheng, Y. J., Gregg, E. W., & Geiss, L. S. (2013). A novel use of structural equation models to examine factors associated with prediabetes among adults aged 50 years and older. *Diabetes Care*, 36(9), 2655–2662. https://doi.org/10.2337/dc12-2608

- Braveman, P., & Gottlieb, L. (2014). The social determinants of health: it's time to consider the causes of the causes. Public Health Reports, 129(Suppl 2), 19-31. https://doi.org/10.1177/ 00333549141291S206
- Caleyachetty, R., Thomas, G. N., Toulis, K. A., Mohammed, N., Gokhale, K. M., Balachandran, K., & Nirantharakumar, K. (2017). Metabolically healthy obese and incident cardiovascular disease events among 3.5 million men and women. Journal of the American College of Cardiology, 70(12), 1429-1437. https:// doi.org/10.1016/j.jacc.2017.07.763
- Camões, M., & Lopes, C. (2008). Factors associated with physical activity in the Portuguese population. Revista de Saúde Pública, 42(2), 208-216. https://doi.org/10.1590/S0034-89102008000200004
- Cois, A., & Ehrlich, R. (2014). Analysing the socioeconomic determinants of hypertension in South Africa: A structural equation modelling approach. BMC Public Health, 14(1), 414. https://doi. org/10.1186/1471-2458-14-414
- Costa, E., Salvador, E., Guimarães, W., & Florindo, A. (2010). Association between different domains of physical activity and schooling in adults of Ermelino Matarazzo district in the eastern of the são Paulo, SP evelyn. Revista Brasileira de Atividade Física & Saúde, 15(3), 151-156. https://doi.org/10.1590/1678-9865201932e180276
- Countryman, A. J., Saab, P. G., Llabre, M. M., Penedo, F. J., McCalla, J. R., & Schneiderman, N. (2013). Cardiometabolic risk in adolescents: Associations with physical activity, fitness, and sleep. Annals of Behavioral Medicine, 45(1), 121-131. https://doi.org/10.1007/s12160-012-9428-8
- de Oliveira, A. F., Valente, J. G., & Leite, I. d. C. (2010). Fraction of the global burden of diabetes mellitus attributable to overweight and obesity in Brazil. Revista Panamericana de Salud Pública, 338-344. https://doi.org/10.1590/S1020-27(5), 49892010000500003
- De Souza, I., Franscisco, P., Lima, M., & Barros, M. (2014). Level of physical inactivity in different domains and associated factors in adults: Health survey in Campinas city (ISACamp 2008/2009), São Paulo state, Brazil. Epidemiologia e serviços de saúde, 23(4), 623-634. https://doi.org/10.5123/S1679-49742014000400004
- Després, J., Lemieux, I., Bergeron, J., Pibarot, P., Mathieu, P., Larose, E., ... Poirier, P. (2008). Abdominal obesity and the metabolic syndrome: Contribution to global Cardiometabolic risk. Arteriosclerosis, Thrombosis, and Vascular Biology, 28(6), 1039-1049. https://doi.org/10.1161/ATVBAHA.107.159228
- Després, J. P., Pouliot, M. C., Moorjani, S., Nadeau, A., Tremblay, A., Lupien, P. J., ... Bouchard, C. (1991). Loss of abdominal fat and metabolic response to exercise training in obese women. The American Journal of Physiology, 261(2 Pt 1), E159-E167. https://doi.org/10.1152/ajpendo.1991.261.2.E159
- Ding, Y., Gu, D., Zhang, Y., Han, W., Liu, H., & Qu, Q. (2015). Significantly increased visceral adiposity index in prehypertension. PLoS One, 10(4), e0123414. https://doi.org/10.1371/journal. pone.0123414
- Dinsa, G. D., Goryakin, Y., Fumagalli, E., & Suhrcke, M. (2012). Obesity and visceral socioeconomic status in developing countries: A systematic review. Obesity Reviews, 13(11), 1067-1079. https://doi.org/10.1111/j.1467-789X.2012.01017.x
- Du, T., Yu, X., Zhang, J., & Sun, X. (2015). Lipid accumulation product and visceral adiposity index are effective markers for identifying the metabolically obese normal-weight phenotype.

Acta Diabetologica, 52(5), 855-863. https://doi.org/10.1007/ s00592-015-0715-2

- Federico, B., Falese, L., Marandola, D., & Capelli, G. (2013). Socioeconomic differences in sport and physical activity among Italian adults. Journal of Sports Sciences, 31(4), 451-458. https:// doi.org/10.1080/02640414.2012.736630
- Ferreira, F. G., Juvanhol, L. L., da Silva, D. C. G., & Longo, G. Z. (2018). Visceral adiposity index is a better predictor of unhealthy metabolic phenotype than traditional adiposity measures: Results from a population-based study. Public Health Nutrition, 22(9) 1545-1554. https://doi.org/10.1017/S136898001800335X
- Ferreira, F. G., Segheto, W., da Silva, D. C. G., Pereira, P. F., & Longo, G. Z. (2018). Visceral adiposity index associated with behavioral and inflammatory parameters in adults: A population based study. Nutricion Hospitalaria, 35(2), 326-331. https://doi.org/10.20960/nh.1325
- Ferreira, S. R. G., de Moura, E. C., Malta, D. C., & Sarno, F. (2009). Frequency of arterial hypertension and associated factors: Brazil, 2006. Revista de Saúde Pública, 43(suppl 2), 98-106. https:// doi.org/10.1590/S0034-89102009000900013
- Gakidou, E., Afshin, A., Abajobir, A. A., Abate, K. H., Abbafati, C., Abbas, K. M., ... Murray, C. J. L. (2017). Global, regional, and national comparative risk assessment of 84 behavioural, environmental and occupational, and metabolic risks or clusters of risks, 1990-2016: A systematic analysis for the global burden of disease study 2016. The Lancet, 390(10100), 1345-1422. https:// doi.org/10.1016/S0140
- Gamborg, M., Andersen, P. K., Baker, J. L., Budtz-Jorgensen, E., Jorgensen, T., Jensen, G., & Sorensen, T. I. A. (2009). Life course path analysis of birth weight, childhood growth, and adult systolic blood pressure. American Journal of Epidemiology, 169(10), 1167-1178. https://doi.org/10.1093/aje/kwp047
- Gomez, L. F., Duperly, J., Lucumi, D. I., Gamez, R., & Venegas, A. S. (2005). Physical activity levels in adults living in Bogotá [Colombia]: Prevalence and factors associated. Gaceta Sanitaria, 19(3), 206-213. https://doi.org/10.1157/13075953
- Hair, J., Anderson, R., Tatham, R., & Black, W. (2009). Análise multivariada de dados (6th ed.). Porto Alegre, Brazil: Bookman.
- Hamdy, O., Porramatikul, S., & Al-Ozairi, E. (2006). Metabolic obesity: The paradox between visceral and subcutaneous fat. Current Diabetes Reviews, 2(4), 367-373. https://doi.org/10.2174/ 1573399810602040367
- Haskell, W. L., Lee, I.-M., Pate, R. R., Powell, K. E., Blair, S. N., Franklin, B. A., ... American Heart Association, A. (2007). Physical activity and public health updated recommendation for adults from the American College of Sports Medicine and the American Heart Association. Medicine & Science in Sports & 1423-1434. https://doi.org/10.1161/ Exercise. 39(8). CIRCULATIONAHA.107.185649
- Hermsdorff, H. H. M., & Monteiro, J. B. R. (2004). Visceral, subcutaneous or intramuscular fat: Where is the problem? Arquivos Brasileiros de Endocrinologia & Metabologia, 48(6), 803-811. https://doi.org/10.1590/S0004-27302004000600005
- Hwang, Y.-C., Hayashi, T., Fujimoto, W. Y., Kahn, S. E., Leonetti, D. L., McNeely, M. J., & Boyko, E. J. (2015). Visceral abdominal fat accumulation predicts the conversion of metabolically healthy obese subjects to an unhealthy phenotype. International Journal of Obesity, 39(9), 1365-1370. https://doi. org/10.1038/ijo.2015.75

- Instituto brasileiro de Geografia e Estatística—IBGE. (2011). *Censo demográfico 2010: caracteristica da população e do domícílio. Resultados do universo*. Rio de Janeiro, Brazil: IBGE.
- Jae, S. Y., Babu, A. S., Yoon, E. S., Kurl, S., Laukkanen, J. A., Choi, Y.-H., & Franklin, B. A. (2017). Impact of cardiorespiratory fitness and risk of systemic hypertension in nonobese versus obese men who are metabolically healthy or unhealthy. *The American Journal of Cardiology*, 120(5), 765–768. https://doi. org/10.1016/j.amjcard.2017.05.054
- Jurakic, D., Pedisic, Z., & Andrijasevic, M. (2009). Physical activity of Croatian population: Cross-sectional study using international physical activity questionnaire. *Croatian Medical Journal*, 50(2), 165–173. https://doi.org/10.3325/cmj.2009.50.165
- Kline, R. (2011). Principles and practice of structural equation modeling. New York, NY: The Guilford Press.
- Knuth, A. G., Malta, D. C., Dumith, S. C., Pereira, C. A., Morais Neto, O. L., Temporão, J. G., ... Hallal, P. C. (2011). Practice of physical activity and sedentarism among Brazilians: Results of the National Household Sample Survey-2008. *Ciência & Saúde Coletiva*, 16(9), 3697–3705. https://doi.org/10.1590/S1413-81232011001000007
- Kotani, K., Tokunaga, K., Fujioka, S., Kobatake, T., Keno, Y., Yoshida, S., ... Matsuzawa, Y. (1994). Sexual dimorphism of age-related changes in whole-body fat distribution in the obese. *International Journal of Obesity and Related Metabolic Disorders: Journal of the International Association for the Study of Obesity*, 18(4), 202–207.
- Lassale, C., Tzoulaki, I., Moons, K. G. M., Sweeting, M., Boer, J., Johnson, L., ... Butterworth, A. S. (2018). Separate and combined associations of obesity and metabolic health with coronary heart disease: A pan-European case-cohort analysis. *European Heart Journal*, 39(5), 397–406. https://doi.org/10. 1093/eurheartj/ehx448
- Liberatos, P., Link, B. G., & Kelsey, J. L. (1988). The measurement of social class in epidemiology. *Epidemiologic Reviews*, 10, 87–121.
- Lohman, T. G., Roche, A. F., & Martorell, R. (1988). Anthropometric standardization reference manual. Champaign, IL: Human Kinetics Books.
- Martin, R. d. S. e. S., Godoy, I. d., Franco, R. J. d. S., Martin, L. C., & Martins, A. S. (2014). Influence of socioeconomic status on cardiovascular risk factors. *Jornal Brasileiro de Medicina*, 102(2), 24–37.
- Martin, W. H. (1996). Effects of acute and chronic exercise on fat metabolism. *Exercise and Sport Sciences Reviews*, 24, 203–231.
- Matthews, D. R., Hosker, J. P., Rudenski, A. S., Naylor, B. A., Treacher, D. F., & Turner, R. C. (1985). Homeostasis model assessment: Insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. *Diabetologia*, 28(7), 412–419.
- Maury, E., & Brichard, S. M. (2010). Adipokine dysregulation, adipose tissue inflammation and metabolic syndrome. *Molecular* and Cellular Endocrinology, 314(1), 1–16. https://doi.org/10. 1016/j.mce.2009.07.031
- McGrath, S., Brazel, D., Dugas, L., Cao, G., Durazo-Arvizu, R., & Luke, A. (2017). Physical activity and central adiposity in a cohort of African-American adults. *BMC Obesity*, 4(1), 34. https://doi.org/10.1186/s40608-017-0170-4

- Molenaar, E. A., Massaro, J. M., Jacques, P. F., Pou, K. M., Ellison, R. C., Hoffmann, U., ... Fox, C. S. (2009). Association of Lifestyle Factors with Abdominal Subcutaneous and Visceral Adiposity: The Framingham heart study. *Diabetes Care*, 32(3), 505–510. https://doi.org/10.2337/dc08-1382
- Moura, A., & Masquio, D. (2014). The influence of education on people's view about healthy food. *Revista de Educação Popular*, 13(1), 82–94. https://doi.org/10.14393/REP-v13n12014-art07
- Muthén, L., & Muthén, B. (2010). Mplus: Statistical analysis with latent variables. User's guide (1998–2010) (6th ed.). Los Angeles, CA: Muthén & Muthén.
- Nienaber-Rousseau, C., Sotunde, O. F., Ukegbu, P. O., Myburgh, P. H., Wright, H. H., Havemann-Nrl, L., ... Kruger, H. S. (2017). Sociodemographic and lifestyle factors predict 5-year changes in adiposity among a Group of Black South African Adults. *International Journal of Environmental Research and Public Health*, 14(9), E1089. https://doi.org/10.3390/ijerph14091089
- Oliveira, E. O., Velásquez-Meléndez, G., & Kac, G. (2007). Demographic and behavioral factors associated with abdominal obesity in women attending a health care unit in Belo Horizonte, Minas Gerais, Brazil. *Revista de Nutrição*, 20(4), 361–369. https://doi.org/10.1590/S1415-52732007000400003
- Pitanga, C. P. S., Pitanga, F. J. G., Gabriel, R. E. C. D., & Moreira, M. H. R. (2014). Association between the level of physical activity and area of visceral fat in postmenopausal women. *Revista Brasileira de Medicina Do Esporte*, 20(4), 252–254. https://doi.org/10.1590/1517-86922014200402039
- Pomerleau, J., Østbye, T., & Bright-See, E. (1999). Potential underreporting of energy intake in the Ontario health survey and its relationship with nutrient and food intakes. *European Journal of Epidemiology*, 15(6), 553–557.
- Ribeiro Filho, F. F., Mariosa, L. S., Ferreira, S. R. G., & Zanella, M. T. (2006). Visceral fat and metabolic syndrome: More than a simple association. *Arquivos Brasileiros de Endocrinologia & Metabologia*, 50(2), 230–238. https://doi.org/ 10.1590/s0004-27302006000200009
- Richelsen, B. (1986). Increased alpha 2- but similar beta-adrenergic receptor activities in subcutaneous gluteal adipocytes from females compared with males. *European Journal of Clinical Investigation*, 16(4), 302–309.
- Rodrigues, P. F., Melo, M., Assis, M., & Oliveira, A. (2017). Socioeconomic conditions and practice of physical activity in adults and elderly: Systematic review. *Revista Brasileira de Atividade Física & Saúde*, 22(3), 217–232. https://doi.org/10.12820/rbafs. v.22n3p217-232
- Ruderman, A., Pérez, L. O., Adhikari, K., Navarro, P., Ramallo, V., Gallo, C., ... Goonzáles- José, R. (2019). Obesity, genomic ancestry, and socioeconomic variables in Latin American mestizos. *American Journal of Human Biology*, 31(5), e23278. https://doi. org/10.1002/ajhb.23278
- Ruderman, N. B., Berchtold, P., & Schneider, S. (1982). Obesityassociated disorders in normal-weight individuals: Some speculations. *International Journal of Obesity*, 6(Suppl 1), 151–157.
- Ruderman, N. B., Schneider, S. H., & Berchtold, P. (1981). The "metabolically-obese," normal-weight individual. *The American Journal of Clinical Nutrition*, 34(8), 1617–1621.
- Samocha-Bonet, D., Dixit, V. D., Kahn, C. R., Leibel, R. L., Lin, X., Nieuwdorp, M., ... Ravussin, E. (2014). Metabolically healthy

and unhealthy obese—The 2013 stock conference report. *Obesity Reviews*, *15*(9), 697–708. https://doi.org/10.1111/obr.12199

- Sasai, H., Katayama, Y., Nakata, Y., Eto, M., Tsujimoto, T., Ohkubo, H., & Tanaka, K. (2010). The effects of vigorous physical activity on intra-abdominal fat levels: A preliminary study of middle-aged Japanese men. *Diabetes Research and Clinical Practice*, 88(1), 34–41. https://doi.org/10.1016/j.diabres.2009.12.018
- Schuster, J., Vogel, P., Eckhardt, C., Dal, S., & Morelo, S. D. B. (2014). Applicability of the visceral adiposity index (VAI) in predicting components of metabolic syndrome in young adults. *Nutrición Hospitalaria*, 30(4), 806–812. https://doi.org/10.3305/ nh.2014.30.4.7644
- Segheto, W., Silva, D. C. G., Coelho, F. A., Reis, V. G., Morais, S. H. O., Marins, J. C. B., ... Longo, G. Z. (2015). Body adiposity index and associated factors in adults: Method and logistics of a population-based study. *Nutricion Hospitalaria*, *32* (1), 101–109. https://doi.org/10.3305/nh.2015.32.1.8391
- Souza, C., Silva, R., Assis, A., Fiacconell, R., Pinto, E., & Moraesll, L. (2010). Association between physical inactivity and overweight among adolescents in Salvador, Bahia—Brazil. *Revista Brasileira de Epidemiologia*, 13(3), 468–475. https://doi. org/10.1590/S1415-790X2010000300010
- Tchernof, A., & Després, J.-P. (2013). Pathophysiology of human visceral obesity: An update. *Physiological Reviews*, 93(1), 359–404. https://doi.org/10.1152/physrev.00033.2011
- Vernay, M., Malon, A., Oleko, A., Salanave, B., Roudier, C., Szego, E., ... Castebon, K. (2009). Association of socioeconomic status with overall overweight and central obesity in men and women: The French nutrition and health survey 2006. *BMC Public Health*, 9(215), 1–8. https://doi.org/10.1186/1471-2458-9-215
- Wagner, K. J. P., Bastos, J. L. D., Navarro, A., Gonzalez-Chica, D. A., & Boing, A. F. (2018). Posição socioeconômica na infância e obesidade em adultos: estudo de base populacional. *Revista de Saúde Pública*, 52(15), 1–10. https://doi.org/10. 11606/S1518-8787.2018052000123
- Wang, J., & Wang, X. (2012). Structural equation modeling: Applications using Mplus. Chichester, England: John Wiley & Sons.
- Ward, J. F., Friche, A. A. L., Caiaffa, W. T., Proietti, F. A., Xavier, C. C., & Roux, A. V. D. (2015). Association of socioeconomic factors with body mass index, obesity, physical activity,

and dietary factors in Belo Horizonte, Minas Gerais state, Brazil: The BH health study. *Cadernos de Saúde Pública*, *31*(Suppl. 1), 182–194. https://doi.org/10.1590/0102-311X00126914

- Wardle, J., Waller, J., & Jarvis, M. J. (2002). Sex differences in the association of socioeconomic status with obesity. *American Journal of Public Health*, 92(8), 1299–1304. https://doi.org/10. 1002/jbm.820261111
- Wildman, R., Muntner, P., Reynolds, K., McGinn, A., Rajpathak, S., Wylie-Rosett, J., & Sowers, M. (2008). The obese without cardiometabolic risk factor clustering and the normal weight with cardiometabolic risk factor clustering: Prevalence and correlates of 2 phenotypes among the US population (NHANES 1999-2004). Archives of Internal Medicine, 168(15), 1617–1624. https://doi.org/10.1001/archinte.168.15.1617
- World Health Organization. (2000). Obesity: Preventing and managing the global epidemic. Report of a WHO consultation. (WHO Tech. Rep. series 894). World Health Organization, Geneva, Switzerland. https://doi.org/10.1016/S0140-6736(57)91352-1
- World Health Organization. (2009). 2008–2013 action plan for the global strategy for the prevention and control of noncommunicable diseases. World Health Organization. Geneva, Switzerland. Available from http://whqlibdoc.who.int/publications/2009/ 9789241597418_eng.pdf

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

How to cite this article: Ferreira FG, Juvanhol LL, Silva-Costa A, Longo GZ. The mediating role of visceral adiposity in the relationship among schooling, physical inactivity, and unhealthy metabolic phenotype. *Am J Hum Biol.* 2020;e23425. <u>https://doi.org/10.1002/ajhb.</u> 23425