

Physical inactivity and headache disorders: Cross-sectional analysis in the Brazilian Longitudinal Study of Adult Health (ELSA-Brasil)

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Abstract

Background: Physical inactivity has been linked to headache disorders but estimates based on the current World Health Organization physical activity guidelines are unknown.

Objective: To test the associations between headache disorders and physical inactivity in the ELSA-Brasil cohort.

Methods: In a cross-sectional analysis, linear (continuous variables) and logistic regression models (categorical variables) tested the associations of physical activity levels in the leisure time, commuting time, and combined leisure time physical activity + commuting time physical activity domains with headache disorders, adjusted for the effects of socio-demographic data, cardiovascular risk variables, psychiatric disorders, and migraine prophylaxis medication.

Results: Of 15,105 participants, 14,847 (54.4% women) provided data on physical activity levels and headache. Higher physical activity levels (continuous values) in the leisure time physical activity domain associated with lower migraine and tension-type headache occurrence and lower headache attack frequency, while in the commuting time physical activity domain it associated with more frequent headache attacks. Compared to people who met World Health Organization physical activity levels in the leisure time physical activity or combining leisure time physical activity + commuting time physical activity domains (i.e. ≥ 150 min.wk⁻¹ of moderate and/or ≥ 75 min.wk⁻¹ of vigorous physical activity), physical inactivity associated with higher migraine occurrence, while somewhat active (i.e. not meeting World Health Organization recommendations) associated with higher migraine and tension-type headache occurrence. Physical inactivity in the commuting time physical activity domain associated with higher tension-type headache in men and lower migraine in women. Physical inactivity within vigorous leisure time physical activity intensity, but not moderate leisure time physical activity, associated with higher migraine, mostly in women. Finally, physical inactivity associated with higher headache attack frequency regardless headache subtype.

Conclusion: Physical inactivity and unmet World Health Organization physical activity levels associate with primary headaches, with heterogeneous associations regarding headache subtype, sex, physical activity domain/intensity, and headache frequency in the ELSA-Brasil study.

Keywords

Physical activity, migraine, tension-type headache, active commuting, healthy lifestyle

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Introduction

Physical inactivity has been associated with headache disorders (1–3), whereas regular physical activity (PA) is associated with lower migraine and non-migraine headaches prevalence (4–6). The available data have shown that leisure-time PA (LTPA) levels is differently associated with headache disorders depending on sex, headache subtype, and PA intensity (2–5,7), without a dose-response effect (3,4,6). LTPA is more consistently associated with migraine (3–5,7) than tension-type headache (TTH) (2). Likewise, LTPA has been associated with reduced prevalence of migraine but not TTH in Brazil (6,8).

Less is known regarding commuting PA (CPA) and headache disorders. CPA is also a PA domain associated with mortality and major health outcomes (9). In fact, to our knowledge, there is no study investigating the association between headache disorders and physical inactivity specifically within the CPA domain.

Furthermore, the epidemiological studies investigating headache disorders and PA did not properly address these associations considering the LTPA levels definitions based on the World Health Organization (WHO) recommendations for adults' health (10). A quantitative interpretation of current data is limited by the lack of studies using validated PA questionnaires, or no standardized parameter of PA intensity (1,6,8,11,12). The current WHO PA guidelines for health promotion in adults establishes a weekly amount of 150–300 min of moderate-intensity aerobic PA, or at least 75–150 min of vigorous-intensity aerobic PA, or an equivalent combination of both (13). This PA amount should be complemented by reduced sedentary time (13). Nevertheless, the current WHO PA guidelines are more inclusive and recognize any PA amount as better than none, which is embodied in its awareness campaign's slogan "every move counts". It is also unknown whether PA below the weekly 150-min threshold is also associated with headache disorders. From the perspective of public health, assessing physical inactivity in people with headache disorders under the parameters of the WHO PA guidelines would provide standardized estimates with clinical implications on PA recommendations for this population.

Therefore, the purpose of this study is to conduct a cross-sectional analysis of the associations between physical inactivity and headache disorders in the ELSA-Brasil study, exploring the differences between headache subtypes, sex, PA domains and intensity, and headache attack frequency. Because both LTPA and CPA are associated with cardiovascular outcomes (9,14), while PA behaviour is associated with psychiatric disorders (15), we also considered the influence of

cohort's cardiovascular risk profile and psychiatric comorbidities in our analyses.

Methods

Study design and population

This is a cross-sectional analysis of the baseline data from the Brazilian Longitudinal Study of Adult Health (ELSA-Brasil). The ELSA-Brasil is a prospective multicenter cohort study, which recruited 15,105 civil servants from six capitals from three regions of Brazil (São Paulo, Rio de Janeiro, Belo Horizonte, Salvador, Porto Alegre, and Vitória). Baseline data were retrieved from workplace-based interviews and clinic visits for biochemical sampling and assessments, conducted between August 2008 and December 2010.

Inclusion criteria were active or retired employees from six public institutions, aged between 35 and 74 years. Exclusion criteria were current or recent pregnancy (<4 months before the interview), intention to quit working at the institution, severe cognitive or communication impairment, and living outside of a study center's corresponding metropolitan area (for retired participants). The ELSA-Brasil cohort population's sociodemographic characteristics showed higher monthly income, higher educational levels, and more access to health care than the Brazilian Census' population (16). Nevertheless, ELSA-Brasil's population included participants within a range of occupations classified as unskilled, technical/clerical and faculty and professional staff, which allowed us to stratify socioeconomic levels across the sample.

Approvals from all institutional review boards of the institutions involved in the ELSA-Brasil study and signed informed consent was provided. Further information regarding ELSA-Brasil study's design is detailed elsewhere (16,17).

Outcomes

The primary outcome was the association between headache disorders and physical inactivity in the LTPA and CPA domains separately and combined. The association between physical inactivity and headache attack frequency was set as a secondary outcome.

Headache disorders diagnosis

All participants in the study ($n = 15,105$) who answered "yes" to the question "In the last 12 months, did you have a headache?" at the ELSA-Brasil baseline evaluation were invited to answer a detailed headache questionnaire based on the International Classification of Headache Disorders (ICHD 2nd edition (18)), which has been validated and previously used in Brazil (19).

Briefly, it investigates pain frequency, duration, quality, location, intensity, triggering factors and accompanying symptoms, such as nausea or vomiting. We classified individuals who answered “yes” to the question about headache and fulfilled all criteria for migraine as “definite migraine”. We classified individuals who answered “yes” to the question about headache and fulfilled all criteria for migraine but one as “probable migraine”. We classified individuals who answered “yes” to the question about headache and fulfilled all criteria for TTH as “definite TTH”. We classified individuals who answered “yes” to the question about headache and fulfilled all criteria but one for TTH as “probable TTH”. Other headaches were defined as headaches that did not fulfil criteria for primary headaches. Participants experiencing no headache in the past 12 months were classified as the “no headache” group.

Since the diagnoses of headaches were not mutually exclusive, when we had the possibility of two types of main primary headaches (TTH or migraine), we always chose that classified as definite. In cases in which both probable TTH and migraine occurred, we always considered migraine as the main type due its relevance to PA (20).

The data on headache attack frequency was collected through a closed-ended question with the following response options: “once in a while”, “1 to 2 per month”, “once a week”, “more than once a week”, and “daily”.

Physical activity levels

In the baseline wave of the ELSA-Brasil study, only PA levels in the LTPA and CPA domains were collected. The PA data were retrieved using the international Physical Activity Questionnaire (IPAQ) long-form, which has been translated and validated for the Brazilian population (21). In the IPAQ, LTPA refers to PA of moderate and vigorous intensity related to recreation, sport, exercise, or leisure. CPA only considers moderate bicycling and walking related to travel to and from work, to do errands, or to go from place to place (21). Physical activity levels in the LTPA and CPA domains were analysed pooled together (combined LTPA + CPA) and separately to provide specific information on each PA domain. PA levels were computed by multiplying the weekly frequency (number of days) by the duration (minutes per day) of PA performed. Only physical activities performed for at least 10 min per week (min.wk^{-1}) were computed. PA level definitions within the LTPA, CPA, and combined (LTPA + CPA) domains, were set based on the WHO's PA guidelines for adult's health. That is, to be considered physically active, one should accumulate

the minimum amount of 150 min.wk^{-1} of moderate or 75 min.wk^{-1} of vigorous PA (10). Because the current WHO PA guidelines are more inclusive and recognize that PA levels under 150 min.wk^{-1} are still better than none (10), we set as “somewhat active” those who did not meet this minimum recommended amount. Thus, PA levels in every PA domain were categorized into three levels: “inactive”, for those not performing the minimum accountable amount of weekly PA (i.e. $<10 \text{ min.wk}^{-1}$); “somewhat active”, for participants reporting $10\text{--}149 \text{ min.wk}^{-1}$ of moderate or $10\text{--}74 \text{ min.wk}^{-1}$ of vigorous PA; and “active”, for participants engaging in $\geq 150 \text{ min.wk}^{-1}$ of moderate and/or $\geq 75 \text{ min.wk}^{-1}$ of vigorous PA.

For the LTPA domain, the frequency and duration of both moderate and vigorous PA intensities were computed and categorized separately. Regarding LTPA intensity, the same PA levels categories were set for moderate (active: $\geq 150 \text{ min.wk}^{-1}$; somewhat active: $10\text{--}149 \text{ min.wk}^{-1}$; inactive: $<10 \text{ min.wk}^{-1}$) and vigorous PA intensities (active: $\geq 75 \text{ min.wk}^{-1}$; somewhat active: $10\text{--}74 \text{ min.wk}^{-1}$; inactive: $<10 \text{ min.wk}^{-1}$).

Confounder variables

Our adjusted analyses included sociodemographic variables (age, sex, household income, educational level, ethnicity, and marital status); cardiovascular risk variables (hypertension, diabetes, metabolic syndrome (MS), obesity, and smoking); psychiatric variables (depression and generalized anxiety disorder (GAD)); and medications for migraine prophylaxis. The cardiovascular risk profile of our sample was obtained through standardized anthropometric and laboratory procedures and testing. We used data on blood pressure, fasting glycemia, total cholesterol and fractions (i.e. LDL, HDL), triglycerides, glycosylated haemoglobin, insulin, HOMA-IR index, and smoking status. Hypertension diagnosis was based on previous clinical history and/or systolic blood pressure $\geq 140 \text{ mmHg}$ and/or diastolic blood pressure $\geq 90 \text{ mmHg}$ and/or use of medication to treat hypertension. Diabetes was diagnosed based on previous medical history of diabetes and/or use of medication to treat diabetes, and/or a fasting plasma glucose $\geq 126 \text{ mg/dl}$, and/or a 2-h plasma glucose $\geq 200 \text{ mg/dl}$, and/or a haemoglobin A1C (HbA1C) $\geq 6.5\%$. The homeostasis model assessment for insulin (HOMA-IR) was estimated for insulin resistance based on the formula: $\text{Fasting glucose (mg/dl)} \times \text{insulin (mIU/ml)} / 405$ HOMA-IR values. Dyslipidaemia and metabolic syndrome diagnoses were defined according to National Cholesterol Program-Adult Treatment Panel III (NCEP ATP III) criteria (22); that is, LDL cholesterol $\geq 130 \text{ mg/dl}$ and/or lipid-lowering drugs, and three criteria: Waist

measurement >88 cm for women or >102 cm for men, HDL cholesterol <50 mg/dl for women or <40 mg/dl for men, an SBP ≥ 130 mmHg or ≥ 85 mmHg, serum triglyceride levels ≥ 150 mg/dl, and fasting plasma glucose ≥ 110 mg/dl. Obesity was defined according to WHO criteria based on body mass index (BMI): >30 kg/m² (23).

Psychiatric comorbidity diagnoses were determined by an adapted Brazilian-Portuguese version of the Clinical Interview Schedule – Revised (CIS-R), applied by trained interviewers (24). The CIS-R is a structured interview for measurement and diagnosis of non-psychotic psychiatric morbidity in the community and a suitable instrument to be adopted in epidemiological studies (16,17).

Regarding migraine prophylactic medications, we included medications with evidence level A and B classed by the American Academy of Neurology's guidelines (25). Level A: Antiepileptic drugs (divalproex sodium, sodium valproate, topiramate), beta-blockers (propranolol, metoprolol, timolol); Level B: Antidepressants (amitriptyline, venlafaxine) and beta-blockers (atenolol, nadolol).

Statistical analysis

Descriptive statistics of socioeconomic, cardiovascular risk profile, and physical activity data are reported as mean with standard deviation (SD) or 95% confidence interval, median with interquartile range (IQR), or proportion, according to variable features. The Clopper–Pearson method was adopted for calculating the 1-year prevalence estimates of any headache disorder and each type of headache in the overall sample.

Comparisons between headache disorder subtypes and no headache groups for variables of interest were performed by χ^2 test (categorical variables), one-way ANOVA, or Kruskal Wallis (continuous variables), depending on sample distribution characteristics.

Univariate general linear models (GLM) and multinomial logistic regressions analyses were conducted to explore the associations between PA levels and headache disorders. These analyses included crude and multivariable-adjusted models, which controlled for the effects of confounder variables: Sociodemographic variables (age, sex, household income, educational level, and ethnicity); cardiovascular risk variables (hypertension, diabetes, MS, obesity, and smoking); psychiatric comorbidities (depression and GAD), and use of migraine prophylactic medication.

A series of GLMs for each PA domain (i.e. LTPA, CPA, and combined LTPA + CPA) were performed for testing the associations between PA levels in minutes per week (continuous dependent variable) and headache disorders (independent variable), controlled for

the effects of confounder variables. Separated GLM analyses tested the sex interaction effects in the associations between PA levels and headache disorders, adjusted for confounder variables. One-way ANOVA contrasts were computed to test for a linear trend in PA levels (in all domains) across the headache attack frequency groups (“once in a while”, “1 to 2 per month”, “once a week”, “more than once a week”, and “daily”).

Multinomial logistic regression models computed the odds ratio for associations between headache diagnosis groups (“no headache” set as the reference group) and categorical PA levels “inactive”, “somewhat active”, and “active” (“active” group set as the reference group) for each PA domain (LTPA, CPA, and combined LTPA + CPA). In the LTPA domain, separate logistic regression models computed the odds for headache disorders according with moderate and vigorous PA intensities (“active” as reference group). For the associations between categorical PA levels and headache attack frequency, “once in a while” was set as the reference group.

Logistic regression models stratified by sex were performed to evaluate sex patterns for the associations between PA levels and headache disorders. In these later analyses, the same confounders variables, except sex, were also included in the adjusted models.

Finally, to investigate the effect of retirees' data in the context of the association between headaches and CPA, we performed a sensitivity analysis excluding retired participants ($n=1426$) to check whether the associations between headache disorders and PA levels in the CPA alone and combined CPA + LTPA domains would change.

Missing data for the primary outcome variables represented $<2.8\%$ of the sample at most, thus was within acceptable limits ($<5\%$). For all tests, a p -value <0.05 was considered statistically significant. Statistics were computed by SPSS software (IBM SPSS Statistics for Windows, Version 20.0.; Armonk, NY).

Results

From the 15,105 participants, 14,874 participants provided full information on headaches and physical activity levels. Most participants were women (56.4%) and aged 52 ± 9 (mean \pm SD) years old. The 1-year prevalence of any headache disorder was 70.4% (95% CI: 69.7–71.2%). For each headache subtype the 1-year prevalences were as follows: Definite migraine 8.4% (95% CI: 7.9–8.8%), probable migraine 20.8% (95% CI: 20.1–21.4%), TTH 33.0% (95% CI: 32.2–33.7%), probable TTH 7.2% (95% CI: 6.8–7.6%), and other headaches 0.92% (95% CI: 0.77–1.08%). Overall, participants with headache disorders were predominantly female, younger, had higher education and household

income, higher psychiatric comorbidities, and lower cardiovascular risk factor profile. Definite and probable migraine presented the higher proportion of frequent headache attacks (i.e. a higher proportion in the “more than once” and “daily” categories) compared to those in the “once in a while” category. Table 1 summarizes the data regarding sociodemographic characteristics, clinical and cardiovascular risk variables, psychiatric comorbidities, and physical activity levels between groups.

There were significant associations between headache disorders and LTPA ($\chi^2=88,537$, $df=10$, $p<0.001$), CPA ($\chi^2=30,444$, $df=10$, $p=0.001$), and combined LTPA+CPA ($\chi^2=76,424$, $df=10$, $p<0.001$). Regarding LTPA, there was a higher proportion of “inactive” and lower proportion of “active” among participants with definite migraine and probable migraine (Table 1). Regarding CPA, there was a lower proportion of active participants with probable migraine and TTH. For the combined LTPA + CPA domain, there was a higher proportion of “inactive” and “somewhat active”, and a lower proportion of “active” among participants with definite migraine and probable migraine (Table 1). There were significant between-group differences for PA levels when analysed as continuous variables in the LTPA ($F[5, 14,854]=26,150$, $p<0.001$), CPA ($F[5, 14,843]=7766$, $p<0.001$), and combined LTPA + CPA ($F[5, 14,829]=23,112$, $p<0.001$) domains. All headache disorders but “other headaches” showed lower PA levels than the “no headache” group in all PA domains after post hoc Bonferroni-adjusted analyses (Table 1).

Table 2 shows the results of the crude and adjusted GLM analyses, as well as the interaction effects of sex, for PA levels as continuous values in the LTPA, CPA, and LTPA+ CPA domains. Lower PA levels in the LTPA domain (negative coefficient values) associated with all headache disorders but other headaches compared to the no headache group. PA levels in the CPA domain were not associated with any headache disorder. Definite migraine showed no interaction effect of sex in any PA domain, while definite TTH showed interaction effects of sex in all PA domains, with men showing higher PA levels than women (positive coefficient values) in all PA domains. In the combined PA levels, lower PA levels were associated with migraine, probable migraine and probable TTH compared to the no headache group (Table 2).

After the categorization of PA levels according to WHO PA guidelines, the adjusted logistic regression models for the LTPA domain in the whole cohort showed increased odds ratio (95% CI) for definite migraine (OR: 1.37 [1.16–1.61], $p<0.001$) and probable migraine (OR: 1.18 [1.05–1.33], $p<0.01$) in the “inactive” level (Table 3). Both migraine subtypes

also associated with “somewhat active” (definite migraine = OR: 1.27 [1.02–1.56], $p<0.05$; probable migraine = OR: 1.27 [1.04–1.55], $p<0.001$). There was no association between PA levels in the CPA domain and headache disorders (Table 3). “Somewhat active” in the combined LTPA + CPA domain showed increased odds for definite migraine (OR: 1.27 [1.08–1.49], $p<0.01$), probable migraine (OR: 1.22 [1.08–1.38], $p<0.01$), and probable TTH (OR: 1.12 [1.01–1.24], $p<0.05$) (Table 3).

In the analysis stratified by sex, among women, “inactive” in the LTPA domain showed increased odds for all headache disorders but “other headaches”, while “somewhat active” was associated with probable migraine (OR: 1.26 [1.04–1.52], $p<0.05$) (Table 3). In the CPA domain, “inactive” showed reduced odds for definite migraine (0.76 [0.61–0.95], $p<0.05$) and probable migraine (OR: 0.77 [0.64–0.92], $p<0.01$). For the combined LTPA + CPA domain, “somewhat active” showed higher odds for definite migraine (OR: 1.31 [1.08–1.59] $p<0.01$), probable migraine (OR: 1.23 [1.05–1.45] $p<0.01$), and definite TTH (OR: 1.21 [1.03–1.41] $p<0.05$) (Table 3). In men, “somewhat active” showed higher odds for probable migraine in the LTPA (OR: 1.42 [1.15–1.75] $p<0.01$) and LTPA + CPA (OR: 1.26 [1.04–1.53] $p<0.05$) domains, and probable TTH in the CPA domain (OR: 1.35 [1.06–1.72] $p<0.05$).

Regarding PA intensity in the LTPA domain, compared to “active” within moderate PA intensity, there were no associations between PA levels and headache disorder in the whole cohort, either in women or in men (Table 4). However, compared to “active” within vigorous PA intensity, either “inactive” or “somewhat active” presented with higher odds for definite migraine and probable migraine in the whole cohort (Table 4). “Inactive” within vigorous PA intensity showed increased odds for definite migraine in women (OR: 1.37 [1.08–1.71] $p<0.05$), and probable migraine in both men (OR: 1.47 [1.15–1.88] $p<0.01$) and women (OR: 1.45 [1.07–1.96] $p<0.05$) (Table 4).

Regarding headache attack frequency, there was a strong linear trend for the association of lower PA levels (continuous values) with higher headache attack frequency in the LTPA (p -trend <0.001) and combined LTPA + CPA (p -trend <0.05) domains; however, there was a linear trend for higher PA levels and higher headache attack frequency in the CPA domain (p -trend <0.05) (Figure 1). For the categorical PA levels, there was a progressive increase in the odds for higher frequency of headache attacks in “inactive” in the LTPA domain, even after controlling for confounder variables and headache subtype (Table 5). In the CPA domain, only “somewhat active” showed increased odds for daily headache attacks (OR: 1.39

Table 1. Sociodemographic, clinical, cardiovascular risk profile, and physical activity levels of the ELSA-Brasil study at baseline.

Groups						
	Definite migraine (n = 1244)	Probable migraine (n = 3095)	Definite TTH (n = 4911)	Probable TTH (n = 1074)	Other headaches (n = 137)	No headaches (n = 4413)
Age, years (mean SD)	49.0 (7.6) ^b	50.1 (8.1) ^b	51.2 (9.9) ^b	51.1 (9.6) ^b	52.2 (9.1) ^b	55.6 (9.2)
Age Range, n (%)						
≤44	357 (28.7) ^c	817 (26.4) ^c	1242 (25.3) ^c	247 (23.0) ^c	35 (25.5) ^c	556 (12.6)
45–54	605 (48.7) ^c	1369 (44.2) ^c	1964 (40.0) ^c	455 (42.4) ^c	43 (31.4)	1418 (32.2)
55–64	238 (19.1) ^c	760 (24.6) ^c	1270 (25.9) ^c	294 (27.4) ^c	47 (34.3)	1573 (35.6)
≥65	44 (3.5) ^c	149 (4.8) ^c	435 (8.9) ^c	78 (7.3) ^c	12 (8.8) ^c	866 (19.6)
Gender, n (%)						
Female	1086 (87.3) ^c	2223 (71.8) ^c	2398 (48.8) ^c	622 (57.9) ^c	84 (61.3) ^c	1681 (38.1)
Ethnicity – self-reported, n (%)						
White	240 (19.4)	503 (16.4)	714 (14.7) ^c	157 (14.8)	13 (9.8)	750 (17.2)
Brown	347 (28.1)	893 (29.2)	1311 (26.9)	305 (28.9)	34 (25.8)	1254 (28.9)
Black	605 (49.1)	1568 (51.2)	2681 (55.1) ^c	557 (52.7)	81 (60.4)	2161 (49.8)
Other (yellow, indigenous, or native)	42 (3.4)	99 (3.2)	161 (3.3)	38 (3.6)	6 (4.5)	177 (4.1)
Education						
Up to incomplete high school	122 (9.8) ^c	346 (11.2) ^c	518 (10.5) ^c	140 (13.0) ^c	7 (4.1) ^c	770 (17.4)
High school, incomplete graduation	528 (42.4) ^c	1185 (38.3) ^c	1547 (31.5)	375 (35.0)	31 (23.6)	1473 (33.4)
Complete graduation	594 (47.8)	1564 (50.5)	2846 (58.0) ^c	558 (52.0)	99 (72.3) ^c	2170 (49.2)
Household income						
<US\$1245	391 (31.5)	861 (27.9)	1121 (22.9) ^c	280 (26.2)	27 (19.4)	1246 (28.4)
US\$1245–3319	584 (47.1) ^c	1463 (47.5) ^c	2113 (43.2)	599 (46.8) ^c	52 (38.8)	1806 (41.1)
>US\$3319	265 (21.4) ^c	760 (24.6) ^c	1658 (33.9) ^c	288 (27.0)	57 (41.8)	1341 (30.5)
Clinical data						
Median (IQR) BMI (kg/cm ²)	26.0 (25.7–26.4)	26.4 (26.1–26.6)	26.2 (26.1–26.4)	26.4 (26.4–26.8)	26.2 (25.5–27.2)	26.7 (26.5–26.9)
Obesity, n (%)	282 (23.0)	758 (24.9)	1054 (21.8)	240 (22.6)	29 (21.5)	1049 (24.2)
Median (IQR) SBP (mmHg)	114 (113–115) ^b	117 (116–118) ^b	120 (119–121) ^b	118 (117–120) ^b	114 (112–119) ^b	123 (122–124)
Hypertension, n (%) [†]	330 (26.5) ^c	996 (32.2) ^c	1659 (33.8) ^c	371 (34.6) ^c	46 (34.1)	1935 (43.9)
Antihypertensive medication, n (%)	307 (24.7) ^c	852 (27.6) ^c	1302 (26.5) ^c	292 (27.2) ^c	40 (29.6)	1569 (35.6)
Diabetes, n (%) ^{††}	179 (14.4) ^c	511 (16.5) ^c	870 (17.7) ^c	192 (17.9) ^c	20 (14.6) ^c	1166 (26.4)
Dyslipidaemia (%) ^{†††}	765 (61.6) ^c	1955 (63.2) ^c	3103 (63.2) ^c	651 (60.7) ^c	87 (63.5)	2962 (67.2)
Metabolic Syndrome, n (%)	155 (12.5)	370 (12.0)	505 (10.3) ^c	123 (11.5)	16 (11.9)	573 (13.0)
Migraine preventive medication use, n (%)	141 (11.3) ^c	280 (9.1) ^c	305 (6.2)	68 (6.3)	6 (4.4)	223 (5.1)
Headache attacks' frequency, n (%)						
Once in a while	284 (22.9)	1356 (43.9)	3296 (67.2)	657 (61.3)	83 (61.5)	..
1–2 times/month	417 (33.6)	805 (26.1)	910 (18.5)	199 (18.6)	26 (19.3)	..
Once a week	147 (11.9)	319 (10.3)	306 (6.2)	95 (8.9)	8 (5.9)	..
More than once a week	296 (23.9)	475 (15.4)	318 (6.5)	92 (8.6)	17 (12.7)	..
Daily	96 (7.7)	135 (4.4)	78 (1.6)	28 (2.6)	1 (0.7)	..
Biomarkers, median (IQR)						
Total cholesterol (mg/dl)	213 (210–216)	212 (211–214)	211 (210–213)	208 (206–212)	205 (199–220)	213 (212–215)
LDL cholesterol (mg/dl)	129 (128–132)	129 (128–131)	129 (128–131)	127 (125–129)	125 (120–133)	128 (127–130)

(continued)

Table 1. Continued.

Groups						
	Definite migraine (n = 1244)	Probable migraine (n = 3095)	Definite TTH (n = 4911)	Probable TTH (n = 1074)	Other headaches (n = 137)	No headaches (n = 4413)
HDL cholesterol (mg/dl)	58 (56–58) ^b	56 (56–57) ^b	54 (54–55)	54 (53–56)	52 (49–56)	53 (53–54)
Triglycerides (mg/dl)	105 (103–109) ^b	110 (107–113) ^b	114 (112–117) ^b	113 (110–119) ^a	110 (104–126)	122 (120–125)
Fasting glucose (mg/dl)	97 (96–98) ^b	98 (98–99) ^b	100 (100–101) ^b	100 (99–101) ^b	100 (98–104) ^b	103 (103–104)
Glycated haemoglobin (HbA1c %)	5.2 (5.2–5.3) ^b	5.3 (5.3–5.4) ^b	5.3 (5.3–5.4) ^b	5.3 (5.3–5.4) ^b	5.2 (5.2–5.4) ^b	5.4 (5.4–5.5)
HOMA-IR	1.52 (1.46–1.60) ^b	1.64 (1.58–1.71) ^b	1.67 (1.63–1.73) ^b	1.68 (1.58–1.78) ^a	1.69 (1.61–2.0)	1.78 (1.72–1.85)
hs-CRP (mg/dl)	1.51 (1.43–1.64)	1.58 (1.50–1.68)	1.40 (1.35–1.46)	1.48 (1.40–1.65)	1.39 (1.16–1.62)	1.47 (1.42–1.54)
Current smoking, n (%)	169 (13.6)	405 (13.1)	592 (12.1) ^c	141 (13.1)	18 (13.1)	625 (14.2)
Depression, n (%) [‡]	126 (10.1) ^c	239 (7.7) ^c	112 (2.3)	43 (4.0) ^c	7 (5.1)	99 (2.2)
Generalized anxiety disorder, n (%) [‡]	327 (26.6) ^c	632 (20.7) ^c	484 (10) ^c	162 (15.2) ^c	17 (12.5) ^c	308 (7)
Physical activity levels, mean (95% CI)						
LTPA (min.wk ⁻¹)	101.3 (91.6–110.9) ^b	113.8 (108.0–119.6) ^b	140.3 (134.9–145.8) ^a	127.4 (117.0–137.7) ^b	141.6 (9108.4–174.8)	154.7 (148.6–160.9)
CPA (min.wk ⁻¹)	147.9 (136.2–159.7) ^a	153.4 (144.9–162.0) ^b	155.5 (148.0–163.0) ^b	154.6 (138.0–171.1) ^a	114.8 (82.9–146.7)	181.8 (173.1–190.5)
LTPA + CPA (min.wk ⁻¹)	248.4 (232.4–264.5) ^b	267.3 (256.8–277.9) ^b	295.9 (286.4–305.4) ^b	282.3 (262.7–301.9) ^b	255.3 (205.7–304.8)	336.8 (325.8–347.7)
Physical activity levels, n (%)						
LTPA						
Inactive	887 (71.3) ^c	2090 (67.5) ^c	2968 (60.4)	678 (63.2)	83 (60.6)	2712 (61.5)
Somewhat active	115 (9.2) ^c	377 (12.2)	653 (13.3)	138 (12.8)	16 (11.7)	570 (12.9)
Active	242 (19.5) ^c	628 (20.3) ^c	1290 (26.3)	258 (24.0)	38 (27.1)	1131 (25.6)
CPA						
Inactive	331 (26.6)	823 (26.6)	1359 (27.7)	298 (27.8)	49 (36.3) ^c	1103 (25.1)
Somewhat active	481 (38.7)	1221 (39.5)	1926 (39.3)	419 (39.1)	51 (37.8)	1658 (37.6)
Active	431 (34.7)	1047 (33.9) ^c	1619 (33.0) ^c	355 (33.1)	35 (25.9)	1641 (37.3)
LTPA + CPA						
Inactive	185 (14.9) ^c	419 (13.6) ^c	625 (12.8)	137 (12.8)	21 (15.6)	495 (11.3)
Somewhat active	361 (29.1) ^c	853 (27.6) ^c	1196 (24.4)	278 (26)	37 (27.4)	970 (22.1)
Active	696 (56) ^c	1818 (58.8) ^c	3078 (62.8) ^c	655 (61.2) ^c	77 (57)	2934 (66.7)

^ap-value < 0.01 compared to “no headache”, Bonferroni-adjusted, one-way ANOVA.^bp-value < 0.001 compared to “no headache”, Bonferroni-adjusted, one-way ANOVA.^cp-value < 0.05 compared to “no headache”, Bonferroni-corrected χ^2 test.[†]Hypertension was defined by systolic blood pressure > 140 mmHg or diastolic blood pressure > 90 mmHg, history of hypertension diagnosed by physician, or current treatment.^{††}Diabetes was defined as previous medical history of diabetes, use of medication to treat diabetes, a fasting plasma glucose > 126 mg/dl, a 2-h plasma glucose > 200 mg/dl, or an HbA1C > 6.5%.^{†††}Dyslipidemia was assessed according to the National Cholesterol Program-Adult Treatment Panel III (NCP-ATPIII) guidelines (21) as follows: LDL cholesterol > 130 mg/dl or use of lipid-lowering drug.

ELSA-Brasil: Brazilian Longitudinal Study of Adult Health; BMI: body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure; HDL: high-density lipoprotein; hs-CRP: high-sensitivity C-reactive protein.

[‡]psychiatric diagnoses were based on the Clinical Interview Schedule – Revised (CIS-R) (24).

Table 2. GLM Coefficient values of the associations between headache disorders and PA levels, with sex interactions effects, in the LTPA, CPA, and combined LTPA + CPA domains in the ELSA-Brasil study at baseline.

	Crude				Adjusted				Sex interactions - adjusted			
	B		p		B		p		B		p	
	B	S.E.	t		B	S.E.	t		B	S.E.	t	p
LTPA												
Definite migraine (n = 1244)	-53.4	6.1	-8.7	<0.001	-26.7	7.5	-3.5	<0.001	29.9	16.2	1.8	0.065
Probable migraine (n = 3095)	-40.8	4.4	-9.1	<0.001	-22.8	6.2	-3.6	<0.001	35.5	7.5	4.6	<0.001
Definite TTH (n = 4911)	-14.3	3.9	-3.6	<0.001	-16.1	6.0	-2.6	<0.01	40.5	5.5	7.3	<0.001
Probable TTH (n = 1074)	-27.3	6.4	-4.2	<0.001	-22.6	8.9	-2.5	<0.05	46.2	11.7	3.9	<0.001
Other headaches (n = 137)	-13.1	16.5	-0.7	0.428	-15.9	21.1	-0.7	0.451	34.7	33.4	1.0	0.299
CPA												
Definite migraine (n = 1244)	-33.8	8.5	-3.9	<0.001	-13.3	9.1	-1.4	0.143	-2.4	23.0	-0.1	0.915
Probable migraine (n = 3095)	-28.3	6.2	-4.5	<0.001	-8.4	6.6	-1.2	0.205	17.6	10.7	1.6	0.102
Definite TTH (n = 4911)	-26.2	5.5	-4.7	<0.001	-7.8	5.6	-1.3	0.169	39.1	7.7	5.0	<0.001
Probable TTH (n = 1074)	-27.3	9.0	-3.0	<0.001	-12.3	9.2	-1.3	0.182	22.0	16.5	1.3	0.184
Other headaches (n = 137)	-66.9	23.3	-2.8	<0.01	-33.9	23.4	-1.4	0.147	38.7	8.5	4.5	<0.001
LTPA+CPA												
Definite migraine (n = 1244)	-88.3	10.8	-8.1	<0.001	-32.5	13.4	-2.4	<0.05	28.5	29.1	0.9	0.327
Probable migraine (n = 3095)	-69.4	7.8	-8.7	<0.001	-22.9	11.2	-2.0	<0.05	53.1	13.6	3.9	<0.001
Definite TTH (n = 4911)	-40.8	6.9	-5.8	<0.001	-23.4	10.9	-2.1	<0.05	79.7	9.8	8.0	<0.001
Probable TTH (n = 1074)	-54.4	11.4	-4.7	<0.001	-26.2	15.9	-1.6	0.101	68.0	21.0	3.2	<0.01
Other headaches (n = 137)	-81.4	29.3	-2.7	<0.01	-49.5	37.8	-1.3	0.191	74.5	10.8	6.8	<0.001

LTPA: leisure-time physical activity; CPA: commuting physical activity; TTH: tension-type headache; Reference group: no headaches (n = 4413 among all participants; n = 1675 among women; n = 2727 among men); reference group for interactions effects of sex: women.

Note: The adjusted models were controlled for socioeconomic data, cardiovascular risk variables, psychiatric comorbidities, and medications for migraine prophylaxis.

Table 3. Odds ratio (OR) for headache according to PA levels categories in the LTPA, CPA, and combined LTPA + CPA domains in the ELSA-Brasil study at baseline.

	Definite migraine	Probable migraine	Definite TTH	Probable TTH	Other headaches
All participants (n = 14,874)	(n = 1244)	(n = 3095)	(n = 4911)	(n = 1074)	(n = 137)
LTPA – crude					
Active	Ref. (1.0)	Ref. (1.0)	Ref. (1.0)	Ref. (1.0)	Ref. (1.0)
Somewhat Active	0.94 (0.73–1.20)	1.19 (1.01–1.40) ^c	1.00 (0.87–1.15)	1.06 (0.84–1.33)	0.83 (0.46–1.51)
Inactive	1.52 (1.3–1.79) ^b	1.38 (1.24–1.55) ^a	0.96 (0.87–1.05)	1.09 (0.93–1.28)	0.91 (0.61–1.34)
CPA – crude					
Active	Ref. (1.0)	Ref. (1.0)	Ref. (1.0)	Ref. (1.0)	Ref. (1.0)
Somewhat Active	1.10 (0.95–1.27)	1.15 (1.03–1.28) ^b	1.17 (1.07–1.29) ^b	1.17 (1.00–1.36) ^a	1.44 (0.93–2.22)
Inactive	1.14 (0.97–1.34)	1.16 (1.03–1.31) ^b	1.24 (1.12–1.38) ^c	1.24 (1.05–1.48) ^a	2.08 (1.34–3.23) ^b
LTPA + CPA – crude					
Active	Ref. (1.0)	Ref. (1.0)	Ref. (1.0)	Ref. (1.0)	Ref. (1.0)
Somewhat Active	1.56 (1.35–1.81) ^c	1.41 (1.27–1.58) ^c	1.17 (1.06–1.29) ^b	1.28 (1.09–1.50) ^b	1.45 (0.97–2.16)
Inactive	1.57 (1.30–1.90) ^c	1.36 (1.18–1.57) ^c	1.20 (1.05–1.36) ^b	1.24 (1.01–1.52) ^a	1.61 (0.989–2.64)
LTPA – adjusted					
Active	Ref. (1.0)	Ref. (1.0)	Ref. (1.0)	Ref. (1.0)	Ref. (1.0)
Somewhat Active	1.27 (1.02–1.56) ^a	1.27 (1.04–1.55) ^c	1.11 (0.99–1.24)	1.18 (0.98–1.43)	1.10 (0.68–1.77)
Inactive	1.37 (1.16–1.61) ^c	1.18 (1.05–1.33) ^b	1.10 (0.99–1.21)	1.08 (0.91–1.27)	1.16 (0.77–1.76)
CPA – adjusted					
Active	Ref. (1.0)	Ref. (1.0)	Ref. (1.0)	Ref. (1.0)	Ref. (1.0)
Somewhat Active	1.05 (0.89–1.23)	1.07 (0.95–1.20)	1.08 (0.97–1.19)	1.10 (0.93–1.29)	1.25 (0.80–1.96)
Inactive	0.87 (0.73–1.05)	0.90 (0.79–1.03)	0.99 (0.88–1.11)	1.04 (0.87–1.25)	1.46 (0.91–2.33)
LTPA + CPA – adjusted					
Active	Ref. (1.0)	Ref. (1.0)	Ref. (1.0)	Ref. (1.0)	Ref. (1.0)
Somewhat Active	1.27 (1.08–1.49) ^b	1.22 (1.08–1.38) ^b	1.12 (1.01–1.24) ^a	1.17 (1.01–1.38)	1.42 (0.94–2.13)
Inactive	1.05 (0.85–1.29)	0.98 (0.84–1.15)	1.03 (0.90–1.18)	0.99 (0.80–1.24)	1.27 (0.75–2.15)
Women (n = 8076)	(n = 1085)	(n = 2220)	(n = 2393)	(n = 620)	(n = 83)
LTPA – crude					
Active	Ref. (1.0)	Ref. (1.0)	Ref. (1.0)	Ref. (1.0)	Ref. (1.0)
Somewhat active	1.33 (1.06–1.66) ^a	1.32 (1.11–1.58) ^b	1.08 (0.91–1.29)	1.24 (0.95–1.61)	0.80 (0.42–1.53)
Inactive	1.75 (1.46–2.09) ^c	1.46 (1.26–1.68) ^c	1.13 (0.98–1.30)	1.35 (1.09–1.67) ^b	1.01 (0.62–1.65)
CPA – crude					
Active	Ref. (1.0)	Ref. (1.0)	Ref. (1.0)	Ref. (1.0)	Ref. (1.0)
Somewhat active	1.07 (0.90–1.28)	1.08 (0.93–1.25)	1.23 (1.06–1.43) ^b	1.01 (0.81–1.25)	1.14 (0.65–2.00)
Inactive	0.93 (0.76–1.13)	0.95 (0.81–1.12)	1.14 (0.97–1.34)	1.00 (0.79–1.27)	1.63 (0.94–2.84)
LTPA + CPA – crude					
Active	Ref. (1.0)	Ref. (1.0)	Ref. (1.0)	Ref. (1.0)	Ref. (1.0)
Somewhat active	1.48 (1.23–1.77) ^c	1.36 (1.17–1.58) ^c	1.25 (1.08–1.45) ^b	1.28 (1.03–1.59) ^a	1.45 (0.87–2.41)

(continued)

Table 3. Continued.

	Definite migraine	Probable migraine	Definite TTH	Probable TTH	Other headaches
Inactive	1.32 (1.05–1.65) ^a	1.15 (0.95–1.39)	1.18 (0.98–1.42)	1.13 (0.86–1.49)	1.46 (0.79–2.71)
LTPA – adjusted					
Active	Ref. (1.0)	Ref. (1.0)	Ref. (1.0)	Ref. (1.0)	Ref. (1.0)
Somewhat active	1.25 (0.99–1.59)	1.26 (1.04–1.52) ^a	1.10 (0.91–1.32)	1.27 (0.97–1.66)	0.88 (0.46–1.71)
Inactive	1.42 (1.16–1.73) ^c	1.24 (1.05–1.46) ^b	1.19 (1.02–1.39) ^b	1.29 (1.03–1.63) ^a	1.24 (0.73–2.09)
CPA – adjusted					
Active	Ref. (1.0)	Ref. (1.0)	Ref. (1.0)	Ref. (1.0)	Ref. (1.0)
Somewhat active	1.03 (0.85–1.25)	1.02 (0.87–1.19)	1.12 (0.96–1.31)	0.92 (0.73–1.16)	1.10 (0.62–1.96)
Inactive	0.76 (0.61–0.95) ^a	0.77 (0.64–0.92) ^b	0.87 (0.73–1.04)	0.82 (0.64–1.06)	1.30 (0.72–2.33)
LTPA + CPA – adjusted					
Active	Ref. (1.0)	Ref. (1.0)	Ref. (1.0)	Ref. (1.0)	Ref. (1.0)
Somewhat active	1.31 (1.08–1.59) ^b	1.23 (1.05–1.45) ^b	1.21 (1.03–1.41) ^a	1.21 (0.96–1.51)	1.54 (0.91–2.59)
Inactive	0.98 (0.77–1.25)	0.87 (0.71–1.07)	0.98 (0.80–1.19)	0.93 (0.70–1.24)	1.43 (0.76–2.69)
Men (n = 6771)	(n = 158)	(n = 871)	(n = 2511)	(n = 452)	(n = 52)
LTPA – crude					
Active	Ref. (1.0)	Ref. (1.0)	Ref. (1.0)	Ref. (1.0)	Ref. (1.0)
Somewhat active	1.23 (0.79–1.92)	1.41 (1.16–1.79) ^a	1.12 (0.97–1.29)	1.12 (0.87–1.45)	1.35 (0.67–2.69)
Inactive	1.47 (1.02–2.12)	1.18 (0.99–1.41) ^b	0.98 (0.87–1.11)	0.91 (0.72–1.15)	1.04 (0.55–1.96)
CPA – crude					
Active	Ref. (1.0)	Ref. (1.0)	Ref. (1.0)	Ref. (1.0)	Ref. (1.0)
Somewhat active	0.90 (0.62–1.30)	1.19 (0.99–1.42)	1.11 (0.98–1.26)	1.35 (1.07–1.70) ^a	1.86 (0.91–3.78)
Inactive	1.08 (0.71–1.63)	1.26 (1.03–1.54) ^a	1.24 (1.08–1.43) ^b	1.42 (1.09–1.85) ^b	2.62 (1.25–5.48) ^b
LTPA + CPA – crude					
Active	Ref. (1.0)	Ref. (1.0)	Ref. (1.0)	Ref. (1.0)	Ref. (1.0)
Somewhat active	1.20 (0.81–1.76)	1.28 (1.06–1.54) ^a	1.05 (0.92–1.21)	1.18 (0.93–1.50)	1.31 (0.68–2.51)
Inactive	1.22 (0.73–2.05)	1.37 (1.07–1.75) ^b	1.13 (0.94–1.36)	1.18 (0.85–1.63)	1.51 (0.66–3.47)
LTPA – adjusted					
Active	Ref. (1.0)	Ref. (1.0)	Ref. (1.0)	Ref. (1.0)	Ref. (1.0)
Somewhat active	1.21 (0.75–1.93)	1.42 (1.15–1.75) ^b	1.12 (0.96–1.30)	1.12 (0.86–1.47)	1.43 (0.70–2.90)
Inactive	1.33 (0.90–1.97)	1.11 (0.92–1.34)	1.03 (0.90–1.18)	0.88 (0.69–1.12)	1.11 (0.56–2.21)
CPA – adjusted					
Active	Ref. (1.0)	Ref. (1.0)	Ref. (1.0)	Ref. (1.0)	Ref. (1.0)
Somewhat active	0.96 (0.65–1.41)	1.15 (0.95–1.38)	1.02 (0.89–1.16)	1.35 (1.06–1.72) ^a	1.52 (0.74–3.14)
Inactive	1.05 (0.68–1.63)	1.09 (0.88–1.35)	1.08 (0.92–1.25)	1.31 (0.99–1.73)	1.58 (0.72–3.49)
LTPA + CPA – adjusted					
Active	Ref. (1.0)	Ref. (1.0)	Ref. (1.0)	Ref. (1.0)	Ref. (1.0)
Somewhat active	1.15 (0.77–1.73)	1.26 (1.04–1.53) ^a	1.05 (0.91–1.21)	1.17 (0.91–1.50)	1.29 (0.66–2.51)
Inactive	1.10 (0.64–1.89)	1.18 (0.91–1.53)	1.07 (0.88–1.29)	1.03 (0.73–1.45)	0.94 (0.36–2.50)

^a $p < 0.05$; ^b $p < 0.01$; ^c $p < 0.001$.

LTPA: leisure-time physical activity; CPA: commuting physical activity; TTH: tension-type headache; Reference group: “no headaches” (n = 4413 among all participants; n = 1675 among women; n = 2727 among men).

Note: The adjusted models were controlled for socioeconomic data, cardiovascular risk variables, psychiatric comorbidities, and, and medications for migraine prophylaxis.

Table 4. Odds ratio (OR) for headache disorders according to LTPA intensity (moderate or vigorous) performed in the ELSA-Brasil study at baseline.

	Definite migraine	Probable migraine	Definite TTH	Probable TTH	Other headaches
All participants (n = 14,874)	(n = 1244)	(n = 3095)	(n = 4911)	(n = 1074)	(n = 137)
Moderate LTPA – crude					
Active	Ref. (1.0)	Ref. (1.0)	Ref. (1.0)	Ref. (1.0)	Ref. (1.0)
Somewhat active	0.88 (0.65–1.19)	1.10 (0.89–1.36)	1.11 (0.93–1.33)	1.14 (0.84–1.54)	0.96 (0.45–2.04)
Inactive	1.37 (1.07–1.76) ^a	1.30 (1.09–1.55) ^b	1.07 (0.92–1.24)	1.21 (0.93–1.56)	1.08 (0.57–2.02)
Moderate LTPA – adjusted					
Active	Ref. (1.0)	Ref. (1.0)	Ref. (1.0)	Ref. (1.0)	Ref. (1.0)
Somewhat active	0.91 (0.65–1.26)	1.08 (0.86–1.36)	1.07 (0.89–1.28)	1.19 (0.86–1.62)	0.92 (0.42–1.98)
Inactive	1.12 (0.86–1.47)	1.13 (0.93–1.36)	1.05 (0.90–1.24)	1.18 (0.90–1.55)	1.16 (0.61–2.21)
Vigorous LTPA – crude					
Active	Ref. (1.0)	Ref. (1.0)	Ref. (1.0)	Ref. (1.0)	Ref. (1.0)
Somewhat active	1.21 (0.90–1.63)	1.15 (0.94–1.42)	0.92 (0.78–1.09)	1.12 (0.85–1.48)	0.95 (0.47–1.91)
Inactive	1.71 (1.37–2.14) ^c	1.50 (1.28–1.74) ^c	0.90 (0.79–1.01)	1.09 (0.88–1.34)	0.95 (0.57–1.58)
Vigorous LTPA – adjusted					
Active	Ref. (1.0)	Ref. (1.0)	Ref. (1.0)	Ref. (1.0)	Ref. (1.0)
Somewhat active	1.40 (1.01–1.93) ^a	1.27 (1.02–1.58) ^a	1.03 (0.86–1.22)	1.20 (0.90–1.60)	1.08 (0.53–2.18)
Inactive	1.48 (1.16–1.89) ^b	1.44 (1.22–1.70) ^c	1.08 (0.95–1.24)	1.14 (0.91–1.42)	1.10 (0.65–1.86)
Women (n = 8076)	(n = 1085)	(n = 2220)	(n = 2393)	(n = 620)	(n = 83)
Moderate LTPA – crude					
Active	Ref. (1.0)	Ref. (1.0)	Ref. (1.0)	Ref. (1.0)	Ref. (1.0)
Somewhat active	1.10 (0.77–1.57)	1.20 (0.91–1.59)	1.31 (1.0–1.72) ^a	1.14 (0.74–1.75)	1.23 (0.48–3.16)
Inactive	1.56 (1.16–2.10) ^b	1.40 (1.11–1.77) ^b	1.23 (0.98–1.54)	1.43 (1.01–2.03) ^a	1.11 (0.50–2.47)
Moderate LTPA – adjusted					
Active	Ref. (1.0)	Ref. (1.0)	Ref. (1.0)	Ref. (1.0)	Ref. (1.0)
Somewhat active	1.00 (0.68–1.46)	1.11 (0.82–1.49)	1.20 (0.91–1.59)	1.14 (0.73–1.78)	1.11 (0.42–2.92)
Inactive	1.15 (0.84–1.57)	1.10 (0.86–1.42)	1.14 (0.90–1.45)	1.31 (0.90–1.90)	1.22 (0.54–2.76)
Vigorous LTPA – crude					
Active	Ref. (1.0)	Ref. (1.0)	Ref. (1.0)	Ref. (1.0)	Ref. (1.0)
Somewhat active	1.29 (0.88–1.89)	1.19 (0.87–1.63)	0.83 (0.61–1.11)	1.19 (0.77–1.84)	1.06 (0.37–3.02)
Inactive	1.33 (1.01–1.76) ^a	1.27 (1.01–1.59) ^a	0.82 (0.67–1.01)	1.01 (0.73–1.39)	1.00 (0.47–2.11)
Vigorous LTPA – adjusted					
Active	Ref. (1.0)	Ref. (1.0)	Ref. (1.0)	Ref. (1.0)	Ref. (1.0)
Somewhat active	1.39 (0.93–2.08)	1.22 (0.88–1.70)	0.90 (0.66–1.23)	1.22 (0.78–1.91)	1.10 (0.38–3.15)
Inactive	1.45 (1.07–1.96) ^a	1.37 (1.08–1.71) ^a	1.06 (0.85–1.32)	1.15 (0.83–1.61)	1.32 (0.61–2.86)
Men (n = 6771)	(n = 158)	(n = 871)	(n = 2511)	(n = 452)	(n = 52)
Moderate LTPA – crude					
Active	Ref. (1.0)	Ref. (1.0)	Ref. (1.0)	Ref. (1.0)	Ref. (1.0)
Somewhat active	0.61 (0.28–1.29)	1.24 (0.87–1.76)	1.01 (0.80–1.27)	1.23 (0.80–1.89)	0.74 (0.20–2.67)
Inactive	1.03 (0.57–1.86)	1.29 (0.94–1.75)	0.96 (0.78–1.17)	1.02 (0.70–1.50)	1.12 (0.39–3.15)

(continued)

Table 4. Continued.

	Definite migraine	Probable migraine	Definite TTH	Probable TTH	Other headaches
Moderate LTPA – adjusted					
Active	Ref. (1.0)	Ref. (1.0)	Ref. (1.0)	Ref. (1.0)	Ref. (1.0)
Somewhat active	0.64 (0.29–1.44)	1.13 (0.79–1.63)	0.96 (0.75–1.23)	1.24 (0.79–1.96)	0.67 (0.18–2.44)
Inactive	1.06 (0.56–2.02)	1.17 (0.85–1.61)	0.97 (0.79–1.20)	1.03 (0.69–1.54)	1.05 (0.37–3.01)
Vigorous LTPA – crude					
Active	Ref. (1.0)	Ref. (1.0)	Ref. (1.0)	Ref. (1.0)	Ref. (1.0)
Somewhat active	1.17 (0.62–2.20)	1.19 (0.88–1.60)	0.99 (0.81–1.22)	1.10 (0.76–1.59)	0.89 (0.34–2.29)
Inactive	1.16 (0.71–1.90)	1.21 (0.96–1.53)	0.86 (0.74–1.00)	0.95 (0.71–1.26)	0.69 (0.34–1.42)
Vigorous LTPA – adjusted					
Active	Ref. (1.0)	Ref. (1.0)	Ref. (1.0)	Ref. (1.0)	Ref. (1.0)
Somewhat active	1.19 (0.61–2.33)	1.29 (0.95–1.77)	1.09 (0.88–1.35)	1.19 (0.81–1.74)	1.03 (0.40–2.68)
Inactive	1.43 (0.86–2.40)	1.47 (1.15–1.88) ^b	1.07 (0.91–1.26)	1.11 (0.82–1.49)	0.85 (0.40–1.79)

^a $p < 0.05$; ^b $p < 0.01$; ^c $p < 0.001$.

LTPA: leisure-time physical activity; CPA: commuting physical activity; TTH: tension-type headache; reference group: “no headaches” ($n = 4413$ among all participants; $n = 1675$ among women; $n = 2727$ among men).

Note: The adjusted models were controlled for socioeconomic data, cardiovascular risk variables, psychiatric comorbidities, and medications for migraine prophylaxis.

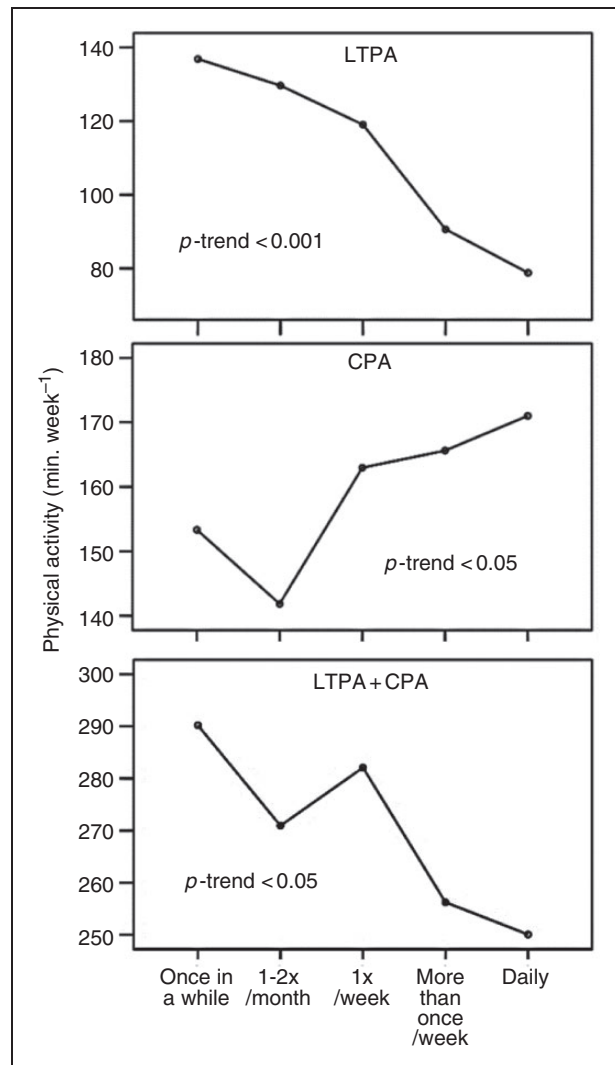


Figure 1. Means plot of the linear trend analysis for the associations between PA levels (dependent continuous variable) and headache attack frequency categories in the LTPA, CPA, and combined LTPA + CPA domains in 10,444 participants of the ELSA-Brasil cohort at baseline.

LTPA: Leisure-time physical activity; CPA: Commuting physical activity.

[1.06–1.83]). For combined LTPA + CPA, there were increased odds for headache attacks once a week (OR: 1.28 [1.07–1.52]) and more than once a week (OR: 1.58 [1.34–1.86]) in the inactive level (Table 5).

In the sensitivity analysis, excluding retirees from the analyses of CPA and LTPA + CPA, there were no changes in the pattern of associations between headache disorders and CPA alone or combined domains, neither for PA levels analyzed as continuous values or categorical variables, except for the “other headaches” group, which showed significant associations with “inactive” in the CPA domain (OR: 1.68 [1.01–2.79], $p = 0.044$) in the adjusted model. There were also no

Table 5. Odds ratio (OR) for headache attacks frequency according to PA levels categories in the LTPA, CPA, and combined LTPA + CPA domains in 10,444 people in the ELSA-Brasil study at baseline.

	1–2×/month (n = 2357) OR (95 % CI)	1×/week (n = 875) OR (95 % CI)	More than once/week (n = 1198) OR (95 % CI)	Daily (n = 338) OR (95 % CI)
LTPA – crude model				
Active	Reference (1.0)	Reference (1.0)	Reference (1.0)	Reference (1.0)
Somewhat active	0.98 (0.83–1.1)	1.07 (0.83–1.3)	1.62 (1.2–2.0)	1.70 (1.0–2.7)
Inactive	0.94 (0.84–1.0)	1.17 (0.98–1.3)	1.95 (1.6–2.3)	2.51 (1.7–3.5)
LTPA – adjusted model				
Active	Reference (1.0)	Reference (1.0)	Reference (1.0)	Reference (1.0)
Somewhat active	1.04 (0.87–1.23)	1.10 (0.84–1.42)	1.57 (1.22–2.02) ^c	1.69 (1.03–2.75) ^a
Inactive	1.04 (0.93–1.18)	1.26 (1.05–1.52) ^a	1.70 (1.41–2.04) ^c	1.74 (1.21–2.50) ^b
CPA – crude model				
Active	Reference (1.0)	Reference (1.0)	Reference (1.0)	Reference (1.0)
Somewhat active	1.12 (1.0–1.2)	1.02 (0.86–1.2)	0.97 (0.84–1.1)	1.23 (0.95–1.5)
Inactive	1.18 (1.0–1.3)	1.04 (0.86–1.2)	0.92 (0.78–1.0)	1.01 (0.75–1.3)
CPA – adjusted model				
Active	Reference (1.0)	Reference (1.0)	Reference (1.0)	Reference (1.0)
Somewhat active	1.07 (0.95–1.21)	1.00 (0.84–1.19)	1.00 (0.86–1.17)	1.39 (1.06–1.83) ^a
Inactive	1.07 (0.94–1.23)	0.96 (0.79–1.16)	0.93 (0.78–1.10)	1.20 (0.88–1.65)
LTPA+CPA – crude model				
Active	Reference (1.0)	Reference (1.0)	Reference (1.0)	Reference (1.0)
Somewhat active	1.09 (0.96–1.24)	1.32 (1.12–1.56) ^b	1.52 (1.27–1.83) ^c	1.16 (0.82–1.64)
Inactive	1.05 (0.94–1.17)	1.18 (0.97–1.44)	2.12 (1.82–2.47) ^c	2.20 (1.69–2.87) ^c
LTPA+CPA – adjusted model				
Active	Reference (1.0)	Reference (1.0)	Reference (1.0)	Reference (1.0)
Somewhat active	1.06 (0.93–1.22)	1.17 (0.95–1.43)	1.40 (1.15–1.70) ^b	0.94 (0.65–1.36)
Inactive	0.99 (0.88–1.12)	1.28 (1.07–1.52) ^b	1.58 (1.34–1.86) ^c	1.29 (0.97–1.72)

^a $p < 0.05$; ^b $p < 0.01$; ^c $p < 0.001$.

LTPA: leisure-time physical activity; CPA: commuting physical activity; reference group: “once in a while” ($n = 5676$).

Note: The adjusted models were controlled for socioeconomic data, cardiovascular risk variables, psychiatric disorders, medications for migraine prophylaxis, and headache subtypes.

changes in the pattern of the associations between frequency of headache attacks and CPA levels. We observed similar findings in the analyses stratified by sex.

Discussion

As for the recent release of the WHO guidelines on PA and sedentary behaviour, which establishes the amount of PA recommended for promoting health and to reduce the risks of major chronic non-communicable diseases, this study intended to evaluate the associations of physical inactivity and headache disorders under the tenets of these recommendations (10). Our analyses revealed that, overall, physical inactivity and even PA levels below the current WHO PA guidelines associate with major primary headache disorders, especially migraine, but with distinct associations regarding PA domain and intensity, sex, headache subtype, and headache frequency.

In general, our findings corroborate another population-based cross-sectional study showing a

positive association between migraine and physical inactivity (3), and that physical inactivity is associated with increased headache attack frequency regardless of the headache subtype (3). Also, we confirmed a more consistent association of PA with migraine rather than non-migraine headaches (1,3–8).

Many studies have investigated the associations between headache disorders and PA levels (1,3–8). These studies have shown heterogeneous associations regarding PA intensity, gender, and headache subtype. These discrepant data are partly explained by factors such as different population characteristics, the lack of standardized PA levels or the use of non-validated questionnaires, the headache diagnosis data (self-reported vs. IHS criteria-based), separate analysis by headache subtype, and statistical methods (e.g. variables controlled in the models) (1,3–8).

Most studies have assessed PA levels in the LTPA domain, while no study has assessed CPA or combined PA levels so far. Because of the cross-sectional nature of our data, one should interpret the findings on PA domains in their respective context and following two

lines of evidence, either assuming physical inactivity/“somewhat active” as the cause or a consequence of headache disorders.

LTPA and primary headache disorders

The data on PA levels in the LTPA domain suggest that physical inactivity could be a risk factor for major primary headache disorders such as migraine and TTH. The strong trend for the association between PA levels and headache attack frequency regardless of headache subtype suggests that physical inactivity could also participate in the chronification processes of headache disorders. Alternatively, recurrent pain itself may rather constitute a barrier to PA in leisure time, a plausible hypothesis supported by evidence from another population-based study (3), as well as smaller observational studies in patients with migraine (26), TTH (27), and with both conditions (28).

Regarding migraine, on the one hand the more consistent associations between migraine/probable migraine and LTPA may suggest that people with migraine may avoid PA, especially of vigorous intensity. Vigorous exercise is a common migraine attack trigger (29–31) and headache aggravated or provoked by routine physical effort is a “canonical” characteristic of migraine (20). The recent body of evidence suggests the involvement of physiological (32,33) and psychological (34–36) mechanisms underlying exercise-triggered migraine attacks and exercise avoidance in this population. Because we controlled for the effects of depression and anxiety, our data suggest that a more specific psychological construct could influence LTPA levels in people with migraine, such as intentional avoidance (34), *kinesiophobia* (36), or *cephalalgiphobia* (37), which in this context are grounded on the fear of an impending migraine attack triggered by physical exercise.

On the other hand, it could imply that physical inactivity in this population could lead to higher migraine susceptibility and more frequent headache attacks owing to the dysregulation of mechanisms modulating pain processing and perception that are activated by regular PA. In agreement, small clinical studies have suggested significant effects of moderate aerobic exercise training on putative molecules involved in pain modulation and migraine pathophysiology (38–42), with evidence for superior therapeutic effects of vigorous over moderate aerobic exercise in people with migraine (43).

Regarding TTH, our data diverge from other population studies (2,4), including in Brazil (8), which showed no significant associations between LTPA levels and TTH, or rather showed physical inactivity in the leisure time associated with TTH in men (2) but

not women. This discrepant data may be due to the more robust control of confounder variables strongly associated with headache disorders in our analysis (e.g. obesity and psychiatric comorbidities). Higher LTPA levels in men than women with TTH and the association of physical inactivity only with women with TTH in our study suggest that sex factors such as hormones and premenstrual syndrome may impact LTPA in these group. Other putative factors reported in smaller observational studies and not assessed in our analysis are the co-existence of TTH with migraine and neck pain. Køll et al. (2017) (28) assessed LTPA levels in patients from a tertiary clinic ($n = 148$). They found a high prevalence (67%) of patients with co-existing migraine, TTH, and neck pain. The patients with co-existing conditions significantly associated with low PA levels assessed by IPAQ, higher stress levels, and lower psychological wellbeing scores. They also reported migraine as the most burdensome condition that hampered LTPA participation, followed by TTH and neck pain (28). Interestingly, this same research group showed that after an intervention program with aerobic exercise, patients with co-existing migraine, TTH, and neck pain reported higher ability to engage in PA due to reduced burden of TTH and neck pain (44). Physical inactivity may associate with TTH through a combination of higher stress-mediated tenderness of pericranial muscles involving myofascial mechanisms and/or impaired function of descending pain modulation mechanisms at central level (28,44–46).

CPA and primary headache disorders

A novelty in this study, physical inactivity in the CPA domain associated with lower migraine and probable migraine in women, while “somewhat active” associated with increased probable TTH in men. Also, higher PA levels in the CPA domain associated with more frequent headache attacks, and men showed higher PA levels than women with TTH. These findings may indicate a detrimental effect of CPA on major primary headache disorders, possibly due to the influence of other factors not accounted for in our models, as well as owing to sex- and aetiologic-specific characteristics of migraine and TTH. For example, the ELSA-Brasil cohort represents a population living in large metropolitan areas, therefore exposed to the interference of environmental factors such as air pollution. Air pollution exposure has been associated with migraine attack frequency (47) and prevalence (48). Although pollution and odours have been reported as perceived triggers of headache attacks by both migraine and TTH patients (49), migraine patients rather than TTH patients often report osmophobia as a symptom (50). As such, we speculate that in migraine patients this

could result in reverse association due to avoidance of potential perceived environmental triggers, whereas the lack of avoidance in men with TTH would allow them to perform higher PA levels but render them more exposed to the trigger effects of air pollution. In agreement, CPA levels also associated with higher odds for hypertension in women in another study with the ELSA-Brasil cohort (51).

Possible negative effects of CPA on headache disorders would cast doubt on the therapeutic effects of recommending CPA as adopted by current WHO PA guidelines embodied in its “*every move counts*” awareness campaign (52), at least for populations with these specific headache disorders living in large metropolitan areas.

Conversely, the linear trend of higher PA levels in the CPA domain with higher headache attacks could mean that people with increasing headache attack frequency may associate it with a poorer health status and try to comply with a healthier lifestyle by including CPA more often in their daily routine. In fact, the ELSA-Brasil cohort represents a population with more access to programs aiming at health promotion, and more awareness of healthier behaviours, including CPA. These hypotheses need to be tested in further investigations.

Combined PA levels and primary headache disorders

Even combining the LTPA and CPA domains, reduced PA levels were positively associated with definite migraine, probable migraine, TTH, as well as with headache attack frequency. Men showed higher PA levels than women in all headache disorders but migraine. In the analysis of PA levels according to WHO recommendation categories, physical inactivity showed no association with headache disorders. However, not meeting WHO PA recommendations was still associated with higher migraine, probable migraine, and TTH. Similar findings were observed among women, but not in men. Physical inactivity or PA below WHO recommendations was associated with frequent headache attacks.

These findings may reflect the balance between inverse and positive associations depending on the PA domain, and partly explain the lack of association of physical inactivity in the combined PA domain with any headache disorder and headache attack frequency. Nevertheless, these data strengthen the notion that people with major headache disorders such as migraine and TTH, could only comply with PA levels below current WHO PA recommendations on a multidimensional domain. The more consistent associations of lower PA levels (regardless of sex) and unmet levels of recommended PA with migraine are akin to

behavioural aspects involving exercise avoidance in this headache entity, which may impact PA behaviour in general (20,26,34,36,37). Accordingly, Bond et al. (2015) (53) assessed PA through accelerometers and reported lower daily PA levels in women with comorbid migraine and obesity ($n = 25$) compared to women with obesity without migraine ($n = 25$) during a 7-day period. Nevertheless, TTH may also impact PA levels. Kikuchi et al. (2007) (54) measured daily PA levels by actigraphy and computerized ecological momentary assessment in 34 patients with TTH for 7 days. The authors found that higher headache attack intensity caused less daily PA. However, this latter study did not include a control group to compare daily PA levels with people without headache disorders 54.

The data on combined PA underscores the necessity of assessing PA domains separately in people with headache disorders to establish specific associations and their clinical implications. Unlike many associations between PA and health outcomes for other major chronic non-communicable diseases (i.e. cardiovascular diseases, diabetes, cancer, etc.) (10), PA and headache disorders show no linear dose-response effects, in particular in the LTPA domain. For example, heavy PA at work was associated with higher migraine prevalence in women in the Danish population (5).

Further studies should evaluate the impact of other PA domains (e.g. occupational and housework) and sedentary behaviour (e.g. sitting time), in order to fully understand the associations of specific and multidimensional PA domains with headache disorder subtypes. Moreover, studies should also explore the associations of headache disorders with other PA modalities and intensities, as patients may feel safer and may be more adherent to light/mild PA modalities. Such studies should adopt prospective designs and collect PA data through objective measures (e.g. actigraphy, accelerometers) to avoid recall bias and provide accurate estimates on specific and multidimensional PA domains. These data could help to identify optimal dose-response effects and PA intensity for each headache subtype and contribute to the development of headache-tailored PA guidelines to help reduce the headache burden.

The impact of physical inactivity on major primary headaches is relevant in terms of public health, as their prevalence and disability peak at the population's most productive age, contributing to lower quality of life and poorer lifestyle behaviours in young adults and the middle aged, with consequential personal and socioeconomic burden (55).

In practical terms, this study provides a ready interpretation with immediate clinical application in terms of PA recommendations. That is, based on our results,

recommending a weekly amount of 150 minutes of moderate PA in leisure time for people with migraine and TTH should be encouraged by health care professionals and clinicians managing this clinical population, with caution on recommending PA in commuting time in large metropolitan areas for people with migraine. For women with migraine, accumulating 75 min of vigorous LTPA per week should be rather encouraged. This opens an avenue to implement more feasible PA modalities of shorter duration (e.g. 15 min/day, 5 days/week), such as high intensity interval training (HIIT). Importantly, interventions with PA activity should also address patient psychoeducation approaches to highlight the benefits of complying with PA guidelines and manage negative beliefs about exercise to reduce avoidance (35,36).

Limitations and strengths

Our study carries limitations and strengths worth mentioning. As a cross-sectional data, it is not possible to establish causality between variables. This is not a population-based study, thus the generalizability of our findings is limited. However, the ELSA-Brasil study is a large cohort composed of a population of middle-aged civil servants from large metropolitan areas with LTPA data in accordance with previous findings from the Risk and Protective Factors Surveillance System for Chronic Non-communicable Diseases (VIGITEL) study, a large system of surveillance of risk factors by telephone for variables measured using a similar strategy in both studies (56,57). The data on PA levels, albeit retrieved by validated questionnaire, is not based upon objective measures and therefore is susceptible to recall bias. Although the IPAQ contains five PA domains, in the baseline wave of the ELSA-Brasil study only LTPA and CPA

were collected. Sitting time was not collected either. Thus, data on a broader, multidimensional PA dimension is still lacking. Caution while interpreting the data on headache attack frequency is advised and chronic migraine/TTH diagnosis were not possible, as responses were based on categorical options rather than number of days, and specific diagnosis criteria for the chronic form of these headache types were not evaluated. Additionally, although we controlled for the effects of cardiovascular and psychiatric comorbidities in the analyses, we did not include nutritional factors, which were found to be associated with PA behaviour in the ELSA-Brasil study (58). Finally, as the ELSA-Brasil study is focused on cardiovascular diseases and diabetes, only participants 35 to 74 years of age at baseline were included. Therefore, individuals younger than 35 years, in which headache disorders are highly prevalent (6,8), were not considered in this study.

On the other hand, the strengths of this study are as the robust headache diagnosis data retrieved by validated questionnaire adopting IHS criteria, the use of a validated questionnaire to allow comparison with international PA parameters, and the control of confounding variables that could influence the relationship between PA and headaches, such as cardiovascular risk variables, common psychiatric comorbidities and migraine preventive medication.

In summary, physical inactivity is associated with the occurrence of higher major primary headache disorders in the ELSA-Brasil cohort. The distinct associations regarding headache subtype, sex, PA domain and intensity, and headache frequency call for additional studies aiming at identifying specific associations and their implications for headache-tailored physical activity recommendations.

Public health relevance

- Higher PA levels in leisure time associate with lower occurrence of migraine and tension-type headache and headache attack frequency, while in commuting time it associates with more frequent headache attacks.
- Physical inactivity in leisure time associates with higher headache disorders, mostly migraine, while in commuting time it is associated with higher probable tension-type headache in men and lower migraine in women.
- Not meeting WHO's guidelines for vigorous PA associates with higher migraine.
- Not meeting WHO's guidelines for combined leisure-time and commuting PA associates with higher migraine and tension-type headache.
- Not meeting WHO's PA guidelines associates with more frequent headache attack, regardless of headache subtype.

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