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The association between seven-day objectively measured habitual physical activity and 24 hr ambulatory blood pressure: the SABPA study

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ABSTRACT

Few studies have examined objective physical activity in relation to 24 hour ambulatory blood pressure (BP). We aimed to assess the association of seven-day objectively measured habitual physical activity with ambulatory BP in a sample of African and Caucasian school teachers (n=216, age 49.7 yrs) from the Sympathetic Activity and Blood Pressure in Africans prospective cohort study. Hypertension (ambulatory systolic BP≥130 and / or Diastolic BP≥80 mmHg) was prevalent in 53.2% of the sample, particularly in black Africans. The hypertensive group spent significantly more awake time in sedentary activity (51.5 vs. 40.8 % of waking hours, p=0.001), as well as doing less light (34.1 vs. 38.9%, p=0.043) and moderate- (14.0 vs. 19.7%, p=0.032) intensity activities compared with normotensives, respectively. In covariate adjusted models, light intensity activity time was associated with lower 24-hr and day-time ambulatory systolic BP (β=-0.15 ,95% CI: -0.26, -0.05, p=0.004; β=-0.14, -0.24, -0.03, p=0.011) and diastolic BP (β=-0.14, -0.25, -0.03, p=0.015; β=-0.13 ,-0.24, -0.01, p=0.030), as well as resting Systolic BP (β=-0.13 ,-0.24, -0.01, p=0.028). Sedentary time was associated only with 24 hr Systolic BP (β=0.12; 0.01, 0.22), which was largely driven by night time recordings. Participants in the upper sedentary tertile were more likely to be “non-dippers” (odds ratio=2.11, 95% CI, 0.99, 4.46, p=0.052) compared with the lowest sedentary tertile. There were no associations between moderate to vigorous activity and BP. In conclusion, objectively assessed daily light physical activity was associated with ambulatory BP in a mixed ethnic sample.

Key words: *physical activity, accelerometry measures, Actiheart, blood pressure, hypertension, ethnic differences*

INTRODUCTION

Hypertension was shown to be the most frequent risk factor for cardiovascular disease (CVD) in both rural and urban communities in sub-Saharan Africa with alarmingly low levels of awareness, treatment and control.[1] Projections in terms of the leading causes of death by 2030 for middle-income countries indicate that ischemic heart disease and contributors to non-communicable diseases (NCDs) will become greater mortality risks than HIV and AIDS.[2] Raised blood pressure (BP) was the greatest contributor to the global mortality rate, followed by tobacco use, raised blood glucose, physical inactivity, overweight and obesity.[3] In South Africa, 39.9% of men and 34.9% of women aged 25 years and older suffer from high BP.[4] An alarmingly high hypertension prevalence rate of 78% exists in South Africa for people aged 50 years and above. Only half of them are aware of their condition and a mere 14% receive treatment.[5] South Africans also demonstrate high prevalence of physical inactivity, with 46.4% and 55.7% of men and women, respectively not meeting the recommended physical activity (PA) guidelines.[2] Previous data have shown that physical inactivity predicts the likelihood of CVD beyond that of commonly measured cardiometabolic risk factors (cholesterol, glucose, BP and adiposity).[6]

The dose-response relationship between PA, risk of developing CVD and premature mortality are well documented, indicating a linear relationship of lower levels of risk with higher amounts of PA.[7,8,9] However, available data on the PA dose-response relation have primarily focused on the moderate – vigorous part of the PA spectrum using self-report questionnaires.[10] Contemporary studies that employ objective assessment of habitual PA are able to better examine other important aspects of the PA spectrum including light-intensity PA and sedentary during waking hours,[11,12,13] which are often challenging to measure with self-report. A recent review of the literature demonstrated that self-reported but not accelerometer-assessed time spent in sedentary behaviours was associated with BP,

suggesting that context may be important.[14] Nevertheless, these studies were based on single clinic BP measures. In addition, most research to date has been based on populations from North America, Australasia, and Europe,[10] leaving a paucity of data from Africa.

The aim of the current study was to assess the association of habitual PA (expressed as time spent in different metabolic equivalent of task [MET] categories), objectively measured over a period of seven days, with ambulatory BP in African and Caucasian teachers living in the North West Province of South Africa. All other lifestyle behaviours (smoking and alcohol consumption) were objectively measured and hypertension status was derived from the gold standard 24-h ambulatory BP-measurement.

METHODS

Design and subjects

This study formed part of the Sympathetic activity and Ambulatory Blood Pressure in Africans (SABPA) prospective cohort study with a target population of urban African and Caucasian school teachers from the Dr Kenneth Kaunda Education District in the North West Province of South Africa. The North West Department of Education, as well as the South African Democratic Teachers' Union, granted permission for the study and ethical approval was obtained from the North-West University (NWU), South Africa (0003607S6). The SABPA study conforms to the principles outlined in the Declaration of Helsinki (revised 2004) and all participants signed informed consent prior to the start of data collection. The cohort profile of the SABPA study is published elsewhere.[15]

Data collection commenced during February to May in 2011 (African teachers, n=173) and again during the same time frame in 2012 (Caucasian teachers, n=186), avoiding seasonal

influences. Pregnant or lactating women, individuals who donated blood or had been vaccinated in the three-months prior the commencement of testing, as well as those with a tympanum temperature greater than 37.5°C were excluded from the SABPA study. Participants (n=143) that did not comply with wearing the Actiheart-device for the full seven days or indicated more than 40 minutes of daily non-contact time during awake hours were removed from the present analysis. Thus the final analytic sample for this study comprised 216 participants (60% of original sample).

Data-collection procedure

Data were collected in four participants per weekday (February to May), with the clinical assessments performed over a two-day period during the school quarter. On day 1, at 07h00, a Cardiotens apparatus (24-h ambulatory BP measurement) was fitted to all participants at their schools. Participants then resumed their normal daily activities and were transported to the university at approximately 15h00 for the clinical assessments. They were introduced to the experimental set-up to lessen anticipation stress.[16] Participants stayed overnight in a well-controlled environment at the Metabolic Unit Research Facility of the NWU where they had a standardized dinner and were asked to refrain from taking any beverages after 22h00.

Participants were woken at 07h00 on day 2, the Cardiotens apparatus was disconnected and the anthropometric measurements commenced. Hereafter, participants rested in a semi-recumbent position for the resting 12-lead electrocardiography (ECG) and sphygmomanometer blood pressure readings, followed by blood sampling one hour later. A resting blood sample of 65 ml was obtained by a registered nurse from the brachial vein branches of the dominant arm using a winged infusion set and immediately sent to the laboratory for storage. The participants then showered and the Actiheart device for the seven-day PA measurement was fitted. Each participant received four extra electrodes to ensure

that the Actiheart was immediately refitted if it should become disconnected during the course of the seven days. Participants were instructed to carry on with their habitual daily activities wearing the monitor at all times whilst awake and asleep. The Actiheart was collected from each participant at the various schools on the eighth day and the data downloaded onto the computer for storage, viewing and analysis.

Measurements and equipment

Anthropometric measurements

Participants' height, weight and waist circumference were measured using the standardized methods of the International Society for Advancement of Kinanthropometry (ISAK).[17] These measurements were used to calculate the body mass index (BMI, $kg.m^{-2}$)[18], the body surface area (BSA, m^2)[19] and the waist-to-height-ratio (WHtR).[20] Intra- and inter-observer variability was less than 10%.

Blood pressure and biochemical measurements

The Cardiotens apparatus (Meditech CE0120®, Meditend, Hungary), a British Hypertension Society validated device, was used to obtain a 24-hour ambulatory BP-measurement (systolic blood pressure (SBP) and diastolic blood pressure (DBP)). Suitable cuff sizes were applied to the non-dominant arms and BP was measured at 30-min intervals during the day and 60-min intervals at night. Successful mean inflation rates for the ABPM period were 85% (±9.2%) in Africans and 94% (±6.0%) in Caucasians. Participants were asked to record any abnormalities such as visual disturbances, headache, nausea, fainting, palpitations, PA and emotional stress on their ambulatory diary cards. The data were analysed using the CardioVisions 1.15.2 Personal Edition software (Meditech®). Hypertension status was

95 defined as 24 hr ambulatory BP: SBP≥130 and / or DBP≥80.[21] The day time ambulatory BP
96 measurement was derived from the readings between 06h00 AM to 10h00 PM.

97 Two mercury sphygmomanometer BP readings (*Riester CE 0124® & 1.3M ™ Littman® II*
98 *S.E. Stethoscope 2205)* were obtained by a medical doctor and registered nurse using
99 Korotkoff IV or V for DBP, with a three-minute rest between measurements on the morning
100 of the second day after participants rested in the semi-recumbent position for 30 minutes.
101 The second measurement was used for statistical analyses.

102 A sterile winged infusion set was used to obtain blood samples from the antebrachial vein
103 branches by a registered nurse and handled according to standardized procedures and stored
104 at -80°C until analysis. Fasting serum samples were analysed for using the sequential
105 multiple analyser computer (Konelab 20i; Thermo Scientific, Vantaa, Finland). Serum
106 cotinine levels (objective indicator of smoking) were determined with a homogeneous
107 immunoassay (Automated Modular, Roche, Basel, Switzerland). HIV-status was measured
108 using the First Response kit (Premier Medical Corporation, India) as well as the confirmatory
109 Pareekshak test (Bhat Biotech, India).

110 *Physical activity measurement*

111 The weekly habitual PA of participants was measured over a period of seven consecutive
112 days with an Actiheart (GB0/67703®, CamNtech Ltd., Cambridge, UK) – a chest worn
113 combined heart rate and accelerometer device. The Actiheart® has been established as a valid
114 and reliable device to correctly estimate energy expenditure for humans at rest, as well as at
115 low, moderate and vigorous intensity activities which vary in studies from house hold tasks to
116 running.[22,23] Individual calibrations (step testing) prior to fitting the Actiheart devices were
117 not performed in this study due to the high clinical CVD risk of many participants.[24] Self-

reported PA was used instead to enter the current PA status for each participant on the Actiheart programme. The 12-lead ECG resting heart rate was used to calculate the sleep heart rate, required by the Actiheart programme when the device was fitted to each participant.

The seven-day recordings were visually inspected for each individual to distinguish between time awake (including sedentary hours), and time asleep for each 24-h (hour) cycle. The heart rate (HR) was considered along with the Metabolic Equivalent of Task (MET, 1 MET regarded as being asleep) and activity level to distinguish sleeping time from being awake. Where the HR in the evenings gradually dropped and the activity level was equal to zero, the participant was considered to be sleeping. The end of sleeping could clearly be seen by an immediate increase in the HR of more than 10 to 20 beats per minute relative to preceding sleeping HR, as well as an increased MET and activity level. The Actiheart software was used to derive daily time spent in various MET-categories that were then grouped according to daily awake sedentary time (≤1.5 METs), daily awake light activity time (>1.5 to 2.99 METs), daily awake moderate activity time (≥3 to 5.99 METs) and daily awake vigorous activity time (≥6METs).[25]

Statistical analyses

Statistical analyses were performed with SPSS (version 22). Departure from normality was evaluated using the Shapiro-Wilk test along with Quantile-Quantile plots. The serum γ-GT was log-transformed. Serum cotinine, as well as moderate and vigorous activity time were not log-transformed as all residual plots of the multivariate regression analyses that included these measures, indicated normal distribution. 2-tailed tests were used for analyses and statistical significance was set at $p \leq 0.05$. One-way analyses of covariance (ANCOVA) were used to determine differences between the lifestyle behaviours (habitual PA, smoking and

alcohol use) and anthropometric characteristics of hypertensive and normotensive participants adjusting for age. Forward stepwise regression analyses were performed to examine associations between PA and ambulatory SBP and DBP, adjusting for age, sex, waist circumference, lifestyle behaviours (serum cotinine and log-transformed serum γ-GT), ethnicity, anti-hypertensive and/or anti-diabetic drug use and HIV^+-status. The times spent in the different MET-categories were each separately entered into the models. Sensitivity analyses using day time SBP and DBP, as well as sphygmomanometer measured resting SBP and DBP as dependents were performed adjusting for the same covariates as above. Analyses were run using waist circumference as a continuous measure and also a binary variable with ethnic and sex-specific cut points (African men ≥ 94 cm; African women ≥ 98 cm; Caucasian men ≥ 90 cm and Caucasian women ≥ 80 cm).[26]

RESULTS

The basic characteristics of participants included in the present analysis did not differ from those excluded. For example, the proportion of men (48.1% vs 52.4%, p=0.44), black Africans (50.5% vs. 44.8%, p=0.29), and hypertensives (53.2% vs 46.2%, p=0.16) did not differ between included and excluded participants, respectively. Table 1 displays the basic lifestyle, anthropometric and ambulatory BP characteristics of the study population. The Africans comprised 52 men and 57 women, and the Caucasians 52 men and 55 women. Of the 17 hours daily awake time the group on average spent 8.0 hours sedentary. The ethnic and sex distribution of hypertensive participants (n=115) was as follows: African men = 39% (n=45), African women = 28% (n=32), Caucasian men = 23% (n=26) and Caucasian women = 10% (n=12). 31% (n=67) of the participants used anti-hypertensive drugs and 10% (n=22)

anti-diabetic drugs. Various ethnic differences were observed (Table S1), in particular black Africans recorded greater sedentary and less moderate intensity activity, and higher BP.

A race x 24-h ambulatory hypertension interaction was observed for SBP ($F(1,198) = 5.9$; $p=0.015$), therefore the sample was divided into hypertension groups with ethnicity added as covariate in all regression models. No sex x ethnicity interactions was observed for 24-h SBP or DBP.

Hypertension was prevalent in 53.2% of the sample. Hypertensives displayed greater risk factors including higher adiposity, cotinine, γ-GT (Table 2). Age adjusted ANCOVAs indicated that the hypertensive group spent significantly more waking hours in sedentary activity (51.5 vs. 40.8 % of waking hours, $p=0.001$), as well as recording less light (34.1 vs. 38.9%, $p=0.043$) and moderate- (14.0 vs. 19.7%, $p=0.032$) intensity PA compared with normotensives, respectively. The vigorous intensity activities of both groups were, however, below 10 minutes per day and not significantly different. We further examined associations between anti-hypertensive drug use and physical activity (Table S2); lower levels of light PA were observed in medicated compared with non-medicated participants (32.5 vs 38.0% of waking hours, $p=0.025$) although no other differences were noted. In addition we used a combined definition of hypertension taking into account 24hr BP readings and use of anti-hypertensive medication although results remained similar (Table S2).

Time spent in light PA was inversely associated with both ambulatory SBP and DBP after adjustment for covariates, and sedentary time was associated with SBP only (Table 3). Waist circumference, cotinine, and γ-GT were also associated with BP. As only the awake time Actiheart recordings were used in this study, a second analysis was performed using the day time (06h00 to 22h00) ambulatory SBP and DBP as dependent variables instead of the 24-h ambulatory BP – the same covariates were entered as in Table 3. Daily light activity time

was the only MET-category significantly (inversely) associated with both day time ambulatory SBP and DBP, respectively [β=-0.14 (-0.25, -0.03), p=0.011; β=-0.13 (-0.24, -0.01), p=0.030] (Table S3). There was no association between sedentary time and day time ambulatory BP. Day time ambulatory SBP was also associated with waist circumference [β=0.45 (0.35, 0.56), p≤0.001] and serum cotinine [β=0.16 (0.05, 0.26), p=0.004], while day time ambulatory DBP was positively associated with waist circumference [β=0.33 (0.22, 0.46), p≤0.001] and log γ-GT [β=0.22 (0.09, 0.34), p≤0.001). Given the link between hypertension, obesity and insulin resistance we added HbA1C as a further covariate to the models although this did not influence any of our results. For example, the association between light PA and 24hr SBP remained unchanged (β= -0.14, 95% CI, -0.25, -0.03, p=0.015). In addition associations were not altered by inclusion of other activities (ie, MVPA) in the models. We also re-analysed the data in the non-medicated sample (n=146) although results were unchanged.

A third set of analyses was performed investigating the associations with resting sphygmomanometer readings (Table S4). Light intensity activity time was inversely associated with resting SBP [β=-0.13 (-0.24, -0.01), p=0.028], however, it did not enter the model with resting DBP. Again none of the other MET-categories of PA displayed any associations with resting BP. Consistent with the ambulatory associations, greater waist circumference was associated with an increase in both resting SBP and DBP [β=0.23 (0.10, 0.35), p≤0.001] and β=0.22 (0.09, 0.35), p=0.001], respectively, and γ-GT was again positively associated with only resting DBP [β=0.18 (0.05, 0.31), p=0.007].

Given that sedentary time was associated with 24-h BP, but not with day time BP or resting sphygmomanometer readings we further explored if this relationship was being driven by night time BP and dipping status. These analyses showed that participants in the upper

sedentary tertile were more likely to be "non-dippers" (odds ratio=2.11, 95% CI, 0.99, 4.46, p=0.052) compared with the lowest sedentary tertile (Table S5).

Pearson correlation coefficients are presented for physical activity and all blood pressure measures in order to indicate the potential magnitude of relationships (see Table S6).

DISCUSSION

Few studies have investigated associations between objective PA and BP in a population at high risk of hypertension. The African and Caucasian teachers in this study who spent less daily time in light intensity PA had significantly higher 24-h ambulatory and day time SBP and DBP, as well as higher resting SBP. This is partly consistent with previous research that found arterial stiffness was inversely associated with time spent in light PA in unfit older adults[27] and other data showing associations between objectively assessed light PA and cardiometabolic health.[12,13] Experimental work has also recently shown that interrupting prolonged sitting with brief bouts of light-intensity activity reduced BP.[28]

In the current study, sedentary time was also associated with 24-h ambulatory SBP. Compared to normotensive participants, the hypertensive group on average spent 11% more of their daily awake time sedentary. Bauman and colleagues called for sedentary behaviours (watching television and working on a computer) and incidental energy expenditure (using the stairs instead of elevator) to be considered in the description of PA recommendations.[29] In the 1900s, the research of Morris and Crawford already reported that men doing sedentary jobs had more severe coronary artery disease (CAD) during middle-age than those with physically active jobs.[30] Since then, contemporary studies have indicated associations between sedentary time and cardiometabolic disease.[31-34] Prolonged inactivity has been

shown to experimentally impair microvascular function,[35] thus it is plausible that this could influence BP regulation. Data from observational studies has, however, produced inconsistent results regarding associations between sedentary behaviors and BP/ hypertension.[36-40] Indeed, a recent review[14] demonstrated that self-reported but not accelerometer-assessed time spent in sedentary behaviours was associated with BP, suggesting that context may be important. In the present study, associations between sedentary and BP were being driven by night time readings and in particular higher sedentary time was associated with non-dipping status. Since non-dipping is generally a hallmark of continued sympathetic activation this may point towards specific mechanisms that merit further investigation.

The anti-hypertensive effects of aerobic exercise training are well documented, and data suggest optimal BP lowering effects for moderate intensity exercise.[41] However, the effects of habitual physical activity remain unclear. Although the normotensive group recorded significantly more daily moderate activity minutes, the covariate adjusted regression analyses did not indicate any associations with blood pressure. The relationship between self reported MVPA and major CVD events has been described as L-shaped.[42] A meta-analysis of prospective cohort studies suggested an inverse dose-response association between recreational PA and risk of hypertension, whereas no such association was observed for occupational PA.[43]

Apart from the PA measures, waist circumference was the only variable that consistently remained associated with all the BP measures, while cotinine was more consistently linked with the SBP, and log γ-GT with the DBP measures. Schutte and colleagues found that elevated γ-GT levels and abdominal obesity were the strongest contributors in the development of hypertension among a black African sample.[44] Measures of abdominal obesity (WHtR and waist circumference) were previously found to correlate better with

arterial stiffness and subclinical atherosclerosis than measures of general obesity (BMI and body fat percentage).[45]

Although this study provides valuable information, it is not without limitations. The study is cross-sectional, thus we cannot infer causal links from the data. The sample size was relatively small and unrepresentative, which may have restricted variability in moderate and vigorous PA; indeed participants engaged in vigorous activity for only a very small proportion of the day (<1% waking hours). Given that the motion sensor was only worn for a period of 7 days it may not be a true reflection of habitual activity patterns. However, using the Actiheart (a combined heart rate and accelerometer device) to measure habitual PA ensured energy expenditure of all intensities were included for examining associations with ambulatory BP. Also, we captured habitual PA from the whole day (just over 17-hours), which is preferable to previous studies using ~10 hr wear protocols that must make various assumptions about non-wear periods.[46,47] Nevertheless, the Actiheart has been shown to under estimate sedentary time when compared to gold standard postural allocation devices,[48] and using cut points may introduce further mis-classification. The 24 hour ambulatory BP assessment incorporated measures taken whilst participants slept in our overnight clinical facility, thus unfamiliar surroundings may have influenced the readings. High correlations were observed between 24 hr ambulatory and resting sphygmomanometer BP readings (SBP, r=0.80; DBP, 0.76).

Conclusions

In conclusion, the results of the present study showed that daily light intensity activity time was inversely associated with 24-h ambulatory blood pressure. Public health interventions aimed at increasing incidental movement may be more beneficial in participants that cannot adhere to structured exercise training regimes.

Summary table

What is known about topic

- The anti-hypertensive effects of aerobic exercise training are well documented.
- The effects of daily habitual physical activity remain unclear.
- Few studies have examined objective daily physical activity in relation to 24-h ambulatory blood pressure.

What this study adds

- Hypertensive participants recorded a greater proportion of waking hours as sedentary.
- Daily light intensity activity was inversely associated with 24-h ambulatory blood pressure.
- Encouraging daily movement may be a promising alternative therapy for patients unable to adhere to structured exercise training.

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Hamer had full access to the data and takes responsibility for the integrity of the data and accuracy of the data analyses. All authors contributed to the concept and design of the study, the drafting and the critical revision of the manuscript.

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