ORIGINAL ARTICLE

Baroreceptor sensitivity, cardiovascular responses and ECG left ventricular hypertrophy in men: The SABPA study

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Abstract

Aim. Research has shown a significant relationship between hypertension and attenuated baroreceptor sensitivity (BRS), which in turn reflects alterations of autonomic control of the cardiovascular system. The objective of this study was to compare the BRS of African and Caucasian men and determine possible associations with blood pressure and left ventricular hypertrophy. Materials and methods. Participants included African (n = 82) and Caucasian (n = 100) male teachers, aged between 20 and 65 years, recruited in the North-West Province, South Africa. Ambulatory blood pressure monitoring was conducted for a 22–23-h period and, thereafter, cardiovascular parameters were recorded with a Finometer and 12-lead ECG during rest and while challenging the cardiovascular system with the cold pressor and Stroop color–word conflict tests. Spontaneous BRS was calculated as well as the Cornell product [marker of left ventricular hypertrophy (LVH)]. Results. The African men had significantly lower BRS stress responses. Attenuated BRS coupled to an α-adrenergic response pattern predicted elevation of blood pressure in the African men. BRS reduction did not prove to be a significant predictor of LVH. Conclusion. Lower BRS, especially during stress, may pose a significant health threat for African men regarding earlier development or promotion of α-adrenergic-driven hypertension and greater risk for cardiovascular disease.

Key Words: African, baroreceptor sensitivity, cardiovascular responses, Caucasian, left ventricular hypertrophy

Introduction

The evaluation of baroreceptor sensitivity (BRS) has proven to be of great value in the assessment of autonomic control of the cardiovascular system (1) and changes of the sensitivity may indicate autonomic imbalance (2–4). This imbalance may be characterized by an increase of sympathetic activity, a decrease of parasympathetic activity or possibly a combination of both (1,5). Various researchers have found a significant relationship between BRS attenuation and chronic blood pressure elevation in hypertensive (6), borderline hypertensive (7,8) as well as normotensive subjects (2). Furthermore, high blood pressure, prolonged sympathetic hyperactivity and blunted BRS poses a significant threat to much faster development of target organ damage including left ventricular hypertrophy (LVH) (1,9).

It is established that hypertension is one of the most pertinent health problems for urban black African men (10–13) and sympathetic hyperactivity has been implicated as a possible significant contributor (14). Whether a decrease of BRS contributes to hypertension in black African men is unknown. Furthermore, other research indicated a lack of any significant differences in BRS where black participants (African American as well as West Africans) were compared with Caucasians (15–17). Whether this is also the case in this population group is uncertain.

The aim of this study is, therefore, to determine if BRS is significantly lower in African men in comparison to their Caucasian counterparts and whether attenuation of BRS predicts an elevation of ambulatory blood pressure as well as LVH in these population groups.

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Materials and methods

Study design and population

The SABPA (Sympathetic Activity and Ambulatory Blood Pressure in Africans) study was conducted in the North-West Province, South African during the same timeframe in 2008 and 2009 (to avoid seasonal changes). This target population comparative study included 82 black African (hereafter referred to as African) and 100 Caucasian male teachers. All participants worked as teachers for the Department of Education in the Dr Kenneth Kaunda Education District of the North-West Province. The reason for this selection was to obtain a homogenous sample from a similar socio-economic class. Participants were aged between 20 and 65 years and exclusion from the study was based on the following criteria: ear temperature >37.5°C, use of alpha- and beta-blockers, vaccinated or blood donors in the previous 3 months, as well as diabetic medication users (one Caucasian and six African men) and clinically confirmed HIV positive status (13 African men).

All participants signed an informed consent form. The study complied with all applicable regulations, in particular, the Helsinki Declaration of 1975 (as revised in 2004) for investigation of human participants (18). The Ethics Review Board of the North-West University approved the study (project number: NWU-00036-07-S6).

Procedure

Ambulatory blood pressure measurements (ABPM) were conducted during working days. Between 07:00 and 08:00, participants were fitted with a British Hypertension Society-validated apparatus (Meditech CE120° Cardiotens, Budapest, Hungary). Blood pressure cuffs of appropriate size were attached to the non-dominant arm. The ABPM apparatuses were programmed to measure blood pressure (oscillographically) in 30-min intervals during the day (08:00–22:00) and 60-min intervals during the night (22:00–06:00) according to a preset program (19). The successful mean inflation rate for the 22–23-h ABPM period was 82.7% (±3.8%) in African and 94.6% (±3.7%) in Caucasian men, respectively. The office blood pressure of each participant was also obtained. Actical® accelerometers (Montréal, Québec) were also applied to measure physical activity (in kilocalories) over the ABPM recording period, taking resting metabolic rate into account (20). Participants were asked to continue with their usual daily activities and complete ambulatory diary cards, reporting any abnormalities associated with cardiovascular disease such as headache, visual disturbances, nausea and fatigue (21). Participants spent the night at the Metabolic Unit Research Facility of the North-West University (consisting of 10 bedrooms, two bathrooms, one kitchen, one dining room and one television room). Upon arriving, participants were introduced to the experimental setup to lessen anticipation stress (22). Each participant received HIV/AIDS pre-counseling from a registered nurse.

The following morning after the last ABPM at 06:00, the ABPM and Actical® apparatuses were removed. Following anthropometric measurements, participants were in a semi-recumbent position for 2 h. A resting 12-lead electrocardiograph activity of six cardiac cycles (Norav NHH1200° Kiryat Bialik, Israel) as well as 5-min continuous measurement of cardiovascular variables was recorded (Finometer, Finapres Medical Systems, Amsterdam, The Netherlands). Hereafter, blood samples were collected from the participant’s right arm brachial vein branches with a sterile winged infusion set. A rest period of 5–10 min was allowed before participants were exposed to two stressors in counterbalanced design. The duration of each stressor was 1 min with a recovery period of 30 min between stressor applications. The stressors were the Stroop color–word conflict test, which elicits a dominant β-adrenergic responsiveness and the cold pressor test (foot immersed in icy water at ±4°C up to the ankle), which induces dominant α-adrenergic responsiveness (23). An increase of total peripheral resistance (TPR) and diastolic blood pressure (DBP) as well as a decrease of arterial compliance is indicative of a dominant α-adrenergic response pattern (24). A β-adrenergic response pattern is characterized by an increase of heart rate, systolic blood pressure (SBP) and cardiac output (CO) (24). ECG and cardiovascular measurements were obtained during mental stress testing.

After completion of all procedures, participants were thanked for their participation, received a monetary incentive for the Color–word conflict stressor according to their performance, enjoyed a breakfast and received post-counseling for HIV/AIDS. After freshening up, participants were transported back to their workplace and received feedback on their health profile within 1 week.

Anthropometric measurements

The stretched stature of each participant was measured to the nearest 0.1 cm using a stadiometer. A KRUPS scale was used to determine the mass of each participant to the nearest 0.1 kg. The listed measurements were done in triplicate and body mass index (BMI; body mass/height²) calculated (25). Waist circumference was measured to the nearest 0.1 cm.

Questionnaires

Participants completed a general health questionnaire (indicating blood pressure, diabetic and statin-containing medication use) as well as a physical
activity questionnaire. The Berlin questionnaire for risk assessment for sleep apnea (26) was also completed where categorization into low or high risk was based on various criteria including snoring, sleepiness during the day, BMI and blood pressure status.

**Cardiovascular measurements**

ABPM data was downloaded into a database using the CardioVisions 1.9 Personal Edition. Stressor responses across tasks were aggregated (27) and used to calculate reactivity using the formula: \( \% = \left( \frac{X_{\text{stressor}} - X_{\text{resting}}}{X_{\text{resting}}} \right) \times 100 \). Finometer measurements were processed with BeatScope 1.1 software (FMS, Finapres Medical Systems, Amsterdam, The Netherlands) to obtain SBP, DBP, CO, TPR and Windkessel arterial compliance \( (C_w) \) (28). Using software also developed by FMS, spontaneous BRS was calculated with the validated cross-correlation BRS method (29). This method computes BRS through time-domain analysis of spontaneous blood pressure and heart interval variability (29).

**Biochemical measurements**

Fasting blood samples were handled and prepared according to standardized procedures. HIV status was determined with an antibody test First Response Kit (Premier Medical Corporation LTD, Daman, India) and Confirmatory Pareeksh test (Bhat BioTech India (P) LTD, Bangalore, India). In serum, gamma-glutamyl transferase (\( \gamma-GT \)) (indicative of alcohol consumption) levels were determined, by making use of the Konelab TM 20i Sequential Multiple Analyzer Computer (SMAC) (Thermo Scientific, Vantaa, Finland). Through homogeneous immunoassay of the serum samples, cotinine levels (indicative of smoking) and electrochemiluminescence immunoassay (ECLA), estrogen, were measured with the Roche Modular system (Roche, Basel, Switzerland).

**ECG LVH**

Data from the 12-lead ECG was used to determine the gender specific Cornell product as a marker of LVH. The Cornell product is calculated with the formula: \((\text{RaVL} + \text{SV3} > 2.8 \text{ mV in men}) \times \text{QRS} > 244 \text{ mV.ms} \) (30).

**Statistical analysis**

Statistica Version 9.0 (Statsoft Inc., Tulsa, OK, USA, 2009) was used for database management and statistical analysis. All variables used for analysis were normally distributed, determined by the Shapiro–Wilkes analysis. Means and proportions were compared by a standard \( t \)-test and the chi-square test, respectively. A one-way analysis of covariance (ANCOVA) using least-square means was performed on cardiovascular and LVH variables to show significant differences between groups. Covariates included age, \( \gamma-GT \), cotinine, physical activity, estrogen, body surface area (for TPR indicated as TPR index and CO indicated as CO index) (31) and for cardiovascular responses, resting values were added as covariates. Because of the sensitivity of BRS for age as well as \( C_w \) it was additionally included as covariate for BRS (6,29,32). Linear regression analysis, using the forward stepwise method determined associations between ambulatory BP (models 1 and 2) and the Cornell product (models 3 and 4) (dependent variables) and cardiovascular variables as well as apnea risk (independent variables). Results were regarded as statistically significant when \( p < 0.05 \).

**Results**

The characteristics of each group are described in Table I. The mean BMI of both African and Caucasian men fell within the overweight category (BMI 25–30 kg/m\(^2\)) (33). The African men had higher estrogen levels which were still within normal ranges (<184 pmol/l) (34), whereas their \( \gamma-GT \) levels were also higher compared with Caucasian men and exceeded the normal bounds of 0–45 u/l (35). In comparison to the Caucasian men, the R wave voltage in lead aVL of the African men was significantly higher.

In Figure 1, the African men demonstrated statistically significant higher ambulatory BP, which was also within hypertensive ranges according to ESH guidelines (ambulatory SBP >125 mmHg and ambulatory DBP >80 mmHg) (21). They also had higher CO, heart rate and Cornell product in comparison to their Caucasian counterparts. The Cornell product values of both groups were still below the cutoff for LVH of 244 mV.ms (30). The African men also showed increased 24-hDBP and \( \alpha \)-adrenergic responses (decreased \( C_w \) and CO) during stressor exposure coupled to greater decrease of BRS in comparison to the Caucasian men (Figure 2).

**Predictors of BP and ECG LVH**

In Table II, model 1 (resting BP) attenuated resting BRS predicted ambulatory SBP whilst resting \( \alpha \)-adrenergic responses, i.e. \( C_w \) predicted ambulatory SBP and DBP, respectively in Africans. In Caucasians, the Berlin sleep apnea risk, resting \( \beta \)-adrenergic responses (decreased TPR index and increased CO) predicted ambulatory DBP and SBP, respectively. In Table II, model 2 (BP \( \% \Delta \) \( \alpha \)-adrenergic responses (decreased \( C_w \) predicted ambulatory BP in both ethnic groups. Additionally an \( \alpha \)-adrenergic response, TPR index, was also associated with ambulatory DBP in African men. In Table III, model 3, only
resting α-adrenergic responses, $C_w$ predicted ECG LVH in African men.

**Sensitivity analyses**

Sensitivity analysis performed for usage of hypertension medication did not affect the outcome of our results. Additional analysis adjusting for height and weight was similar when adjusting for BSA.

**Discussion**

The aim of the study was to determine whether BRS is significantly lower in African men when compared with their Caucasian counterparts and whether attenuation of BRS predicts an elevation of ambulatory BP as well as LVH in these population groups. Our main findings revealed that resting attenuated BRS and decreased arterial compliance predicted the elevation of ambulatory blood pressure, although only decreased arterial compliance predicted LVH in African men. The BP profile of the Caucasian men was stronger associated with increased obesity, sleep apnea and related decrease in arterial compliance.

Despite different algorithms of BRS determination, the lack of ethnic differences in resting BRS in our study is in agreement with previous findings in African-Americans (15,16) and West Africans (17).

![Figure 1](https://example.com/figure1.png)

**Figure 1.** A comparison of resting cardiovascular and left ventricular hypertrophy variables between African and Caucasian men (adjusted for age, body surface area, physical activity, cotinine, gamma-glutamyl transferase, arterial compliance additional for baroreceptor sensitivity); *significant differences (p < 0.05).
Figure 2. A comparison of the aggregated cardiovascular stress responses between African and Caucasian men (adjusted for age, BSA, physical activity, cotinine, gamma-glutamyl transferase, arterial compliance additional for BRS and resting cardiovascular variables); * significant differences (p < 0.05).

However, further results in our participant group showed greater decreases in BRS responses to mental stress in the African men.

The findings of this study also support the notion that reduced BRS contributes to chronic blood pressure elevation (3). This significant association was only present in African men who showed a dominant α-adrenergic sympathetic response pattern (24) and a reduced BRS during stressor application in contrast to the Caucasian men. These findings are contradictory to those of Parmer and co-workers (15), where similar abnormalities in autonomic control of the cardiovascular system, including attenuated BRS and α-adrenergic driven blood pressure elevation, were found for black (African-American) and Caucasian participants. The notion that an imbalance of sympathetic and parasympathetic activity is accompanied by blunted BRS and specifically may contribute to blood pressure elevation was nonetheless supported (4,5).

Table II. Independent associations of cardiovascular variables with ambulatory blood pressure in African and Caucasian men.

<table>
<thead>
<tr>
<th></th>
<th>African men (n = 82)</th>
<th>Caucasian men (n = 100)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Ambulatory SBP (mmHg)</td>
<td>Ambulatory DBP (mmHg)</td>
</tr>
<tr>
<td>Model 1 (Resting values)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adjusted $R^2$</td>
<td>0.59</td>
<td>0.58</td>
</tr>
<tr>
<td>Berlin Sleep apnea</td>
<td>$\beta \pm 95%$ CI</td>
<td>$p$</td>
</tr>
<tr>
<td>high risk</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Arterial compliance</td>
<td>$-0.84 \pm 0.25$</td>
<td>$&lt;0.001$</td>
</tr>
<tr>
<td>(ml/mmHg)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiac output (l/min)</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Total peripheral resistance (mmHg/ml/s)</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Baroreceptor sensitivity (ms/mmHg)</td>
<td>$-0.24 \pm 0.18$</td>
<td>0.011</td>
</tr>
<tr>
<td>Model 2 (Stressor application)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adjusted $R^2$</td>
<td>0.68</td>
<td>0.70</td>
</tr>
<tr>
<td>$\Delta$ Arterial compliance (%)</td>
<td>$-0.31 \pm 0.14$</td>
<td>$&lt;0.001$</td>
</tr>
<tr>
<td>$\Delta$ Total peripheral resistance (%)</td>
<td>–</td>
<td>–</td>
</tr>
</tbody>
</table>

F to enter 2.5. Model 1: Ambulatory SBP and ambulatory DBP resting: adjusted for age, TPR and CO indexes, physical activity, gamma-glutamyl transferase, cotinine, estrogen and arterial compliance (for baroreceptor sensitivity); Model 2: Ambulatory SBP and ambulatory DBP responses: adjusted for age, TPR and CO indexes, physical activity, gamma-glutamyl transferase, cotinine, estrogen, arterial compliance (for baroreceptor sensitivity) and for all resting cardiovascular values.
In contrast to other studies (1,9), our findings did not indicate lower BRS as a possible predictor for LVH, although the Cornell product of the African men was significantly higher. It can be speculated that this result may be because a large part of the participant group was still in their forties and represent a normal population. The LVH index average was still well under the cutoff point, which could mask a possible trend. However, significant associations between blunted BRS and increased risk for cardiovascular disease were demonstrated in other studies, especially in the presence of elevated blood pressure (36–38). Our data could also support findings by Verdeccia et al. (39), who determined that the risk for cardiovascular disease increases by 9% for each 0.1 mV higher value of the R wave voltage in lead aVL. Accordingly, the risk for cardiovascular disease in African men would be 10.8% greater in comparison to the Caucasian men and the risk could be even potentiated by a reduced BRS (40,41).

Although BRS did not predict LVH, results of this study may still have further clinical implications. It has been indicated that before morphological changes of the left ventricle can be detected, functional changes may already be present (42). Several studies have found significantly lower BRS in patients with diastolic dysfunction (9,42,43). This is further aggravated by chronically elevated sympathetic activity (43,44), especially elevated heart rate (45). If we consider these results, it is imperative to explore further both functional and structural changes, e.g. catecholamine, nitric oxide as well as echocardiography profiles in the African men.

A limitation of our study is that no direct marker of sympathetic nervous system activity was used. An advantage, however, is the use of the gold standard blood pressure measurements ensuring high reliability results. As it was a cross-sectional study, we could not test or deduce causal factors or the causal reverse of reduced BRS driving chronic elevated blood pressure.

In conclusion, lower BRS, especially during stress, as demonstrated in our male African group may contribute to the development or promotion of α-adrenergic response driven hypertension. If this is coupled to higher RaVL and Cornell product values, it may increase the risk for future cardiovascular events (46).

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Declaration of interest: The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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