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Research Paper

Racial differences in baroreflex function: Implications for the cardiovascular conundrum

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ABSTRACT

Study objective: African Americans (AAs) show early signs of vascular dysfunction paired with elevated blood pressure (BP) and total peripheral resistance (TPR), which is thought to underlie their increased rates of cardiovascular health complications relative to European Americans (EAs). AAs paradoxically have higher cardiac vagal tone, indexed by heart rate variability (HRV), which is cardio-protective. This paradox has been termed the *Cardiovascular Conundrum*. The physiological mechanism underlying this phenomenon is not well understood. We examined race differences in baroreflex function, which might be an important mechanism underlying the *Cardiovascular Conundrum*.
Design: Participants completed a 5-minute baseline period where resting cardiac metrics were assessed.
Setting: Laboratory.
Participants: 130 college-aged individuals (54 women, 57 AAs).
Main outcome measures: Baroreflex function was indexed as baroreflex sensitivity (BRS; the magnitude of changes in cardiovascular activity in accordance with BP changes) and effectiveness (BEI; the ratio of BP changes that elicit changes in cardiovascular activity) in the cardiac, vascular, and myocardial limbs.
Results and conclusions: Results showed AAs to have higher HRV and cardiac BRS in comparison to EAs, suggesting the baroreflex is more sensitive to correcting the heart period for changes in BP among AAs compared to EAs. However, AAs showed lower vascular BEI relative to EAs, suggesting less effective control of TPR. In sum, lower BEI in the vascular branch might be an important mechanism underlying the *Cardiovascular Conundrum* (i.e., higher HRV and BP) and by extension, health disparities in cardiovascular diseases between AAs and EAs.

1. Introduction

In comparison to European Americans (EAs), African Americans (AAs) are at an elevated risk for mortality and morbidity from leading causes of death, including cardiovascular diseases such as hypertension [1]. Indeed, hypertension remains relatively uncontrolled among AAs, which may serve as a catalyst for additional health disparities [1]. Meta-analyses and community samples consistently show that after adjusting for factors such as diet, exercise, and socioeconomic status, health disparities persist [2].

Thus, basic physiological differences have been examined between AAs and EAs to explain cardiovascular complications among AAs. For example, and in line with existing health disparities, a meta-analysis showed AAs to have higher total peripheral resistance (TPR) and

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blood pressure (BP) relative to EAs [3]. These physiological differences are seen in early life, such that vascular hypertrophy (i.e., vessel stiffening) occurs in young AAs compared to young EAs [4]. Indeed, higher BP via increased TPR is associated with end-organ damage and leaves the host particularly susceptible to negative cardiovascular outcomes. Yet a separate meta-analysis paradoxically showed AAs had higher cardiac vagal tone, as indexed by resting vagally-mediated heart rate variability (HRV), compared to EAs [5]. This represents a paradox as higher HRV should be cardioprotective and therefore linked with lower BP, lower TPR, and better overall health [5]. This paradox has been termed the *Cardiovascular Conundrum* [6].

The regulation of BP is important here; mean arterial pressure (MAP) equals cardiac output (CO) times total peripheral resistance (TPR) (MAP=CO X TPR). CO equals stroke volume (SV) times heart rate (HR) (CO=SV X HR). Thus, a given level of BP can be achieved by the tandem regulation of CO and TPR. When BP increases, pressure-sensitive mechanoreceptors in the aorta and carotid sinus "sense" this distension and send signals to the nucleus tractus solitarius via vagal afferent fibers. In a reflexive manner, the nucleus tractus solitarius then initiates efferent sympathoinhibition and concomitant parasympathetic activation to reduce TPR, SV, and heart rate to return BP to its previous level and the reverse occurs in response to decreases in BP. These reflexive actions are carried out via the baroreflex [7]. As such, vagal activity, as indexed by HRV, and TPR are *normally* inversely correlated. Thus, the greater HRV *and* greater TPR in AAs represent a "conundrum" [5,6].

Indeed, the baroreflex is an important mechanism allowing for the effective reflexive changes in BP in accordance with HR and thus, proper BP regulation. The most studied limb of the baroreflex is the cardiac branch that links changes in BP to changes in HR. However, there are also vascular and myocardial limbs of the baroreflex that affect the vasculature (TPR adjustment) and myocardium (SV adjustment) respectively. Our group has pioneered [8] the assessment of these three different limbs using time-domain measurements of beat-to-beat changes in systolic BP, HR, SV, and TPR to calculate both baroreflex sensitivity (BRS) and baroreflex effectiveness (BEI) for the three limbs of the baroreflex (cardiac, myocardium, and vasculature). We recently showed higher HRV predicted lower BP and TPR six years later in EAs but not in AAs [9,10]. This lends direct evidence of a breakdown in BP regulation despite higher HRV among AAs, and baroreflex dysfunction might be an important mechanism in this regard.

Given that the baroreflex has been implicated in both short- and long-term BP regulation [7] and that BP and cardiovascular complications remain elevated despite higher HRV among AAs, differences in baroreflex function might be underlying the cardiovascular conundrum and thus cardiovascular health inequities. However, studies have yet to investigate this adequately. In our novel cross-sectional investigation, we sought to examine differences between AAs and EAs in HRV and hemodynamics including BP, CO, SV, TPR, HRV, and both BRS and BEI in the three aforementioned baroreflex limbs.

1.1. Participants and procedure

In the present study, data were available for 130 individuals between the ages of 18 and 30 (54 women, mean age of 19.7 years, standard deviation of 2 years). Of the 130 subjects, there were 57 AAs (33 women, mean age of 19.7 years) and 73 EAs (21 women, mean age of 19.6 years). Subjects self-reported their racial identity, for which those who reported that they were either White/European American, or Black/African American. Subjects were not of Hispanic or Latino/a/background.

Subjects were recruited via the Research Experience Program pool at The Ohio State University, allowing students to participate in research for partial class credit in an introductory level psychology course. Participants were not eligible to complete the study if they completed any physical activity, smoking, or caffeine consumption at least two hours prior to the experimental session. The study was approved by the institutional review board, and all participants signed written informed consent.

Participants were seated in a soundproof experimental room that was equipped with a camera and a microphone. Upon completion of the consent form, height and weight were collected to assess body mass index (BMI). Then, participants were attached to a beat-to-beat blood pressure device that collected hemodynamic parameters of interest. Participants first completed a 5-min baseline-resting period, in which they sat in a resting position with the television displaying a blank, gray screen while breathing spontaneously. Participants were instructed not to move or fall asleep.

1.2. Continuous baseline measures

Hemodynamic activity was recorded continuously via the Finometer Midi® device, which is a non-invasive photoplethysmography (PPG) device that records beat-to-beat blood pressure. The device was attached to the participants' non-dominant arm and finger cuff sizes were adjusted on a participant-to-participant basis. Beat-to-beat systolic BP, TPR, SV, and inter-beat-intervals (IBIs) were collected using this device, and each was extracted into a single text file for each participant. Text files were then subjected to a custom program Beatscope Easy [11]. Utilizing Model-flow methods, derived variables included mean values of the root mean square of successive differences (RMSSD) from inter-beat-intervals (IBI; index of heart rate/period) as an index of HRV [12,13], systolic BP (mmHg), TPR (mmHg.s/ml), SV (l/min) and CO (l/min) were calculated.

Sequences of consecutive cardiac beats are sought in which an increase in SBP is accompanied by an increase in IBI (or a decrease in vascular tone or cardiac contractility) or in which a decrease in SBP is accompanied by a decrease in IBI (or an increase in vascular tone or cardiac contractility). Specifically, this custom program locates sequences of 3 to 6 consecutive cardiac cycles in which SBP increases ("up" sequences) are accompanied by increases in IBIs, and those in which SBP decreases ("down" sequences) are accompanied by IBIs decreases. The systolic BP changes (progressive decrease or increase) are taken as a probe input to the baroreceptors. In order to avoid the inclusion of possible extreme or artifact values in the computation of sequences, values greater or lower than 20 % of the averaged mean for IBI and TPR, and 10 % for SV (criteria is also lower given the reduced range of variation in these measures), were rejected in detection of reflex sequences. Two main indices are obtained with this method: sensitivity (BRS; ms) and effectiveness (BEI; percentage). The regression line between the systolic BP and IBI (or vasomotor tone or myocardial contractility) values within sequences produce an estimate of BRS from the change in IBI (or in the other measures) per unit change in systolic BP (e.g., ms/mmHg). The proportion (in percentage) in which the baroreflex is able to induce changes in response to the change in systolic BP is quantified with the baroreflex effectiveness index (BEI). BRS in the vascular and myocardial branches were reverse coded so that higher scores represent higher sensitivity. Additional details regarding this methodology has been discussed elsewhere [8]. Systolic BP variability, TPR variability, and SV variability were calculated as the standard deviation of the respective mean index.

Two beat lags were calculated for both myocardial and cardiac limbs. Four beat lags were calculated for the vascular limb. Beat lags presented in our analyses are those with the highest effectiveness for the sample as previously described [8]. For the current analysis, this included beat lag 0 for the cardiac, beat lag 6 for the vascular, and beat lag 2 for the myocardial limbs.

1.3. Statistical methods

All statistical tests were performed using IBM SPSS Statistics 22 (IBM Corp., Armonk, NY) and StatsSoft Statistica 6.0 (StatSoft, Inc., Tulsa, OK). Frequency analyses were used to determine means and standard deviations (SD) for the full sample. Independent sample *t*-tests were used

to determine differences in demographic and cardiovascular variables between AAs and EAs. Univariate ANOVA tests were used to probe these differences while adjusting for relevant covariates including body mass index (BMI), age, and physical activity, and gender. Correlation analyses were used to determine the relationships between all three limbs of the baroreflex function and the corresponding mean cardiovascular variables. Specifically, we evaluated the association between: (i) cardiac BRS and BEI, and IBI (mean heart period) and HRV (variability in the heart period); (ii) vascular BRS and BEI, and mean TPR and TPR variability; (iii) myocardial BRS and BEI, and mean SV and SV variability. Fisher's r-to-z transformation was used to examine differential correlations of interest between AAs and EAs. Missing data were excluded in case-wise fashion. All tests were two-tailed level and evaluated with an alpha of 0.05.

2. Results

See Table 1 for means and standard deviations for all variables in the full sample and stratified by AAs and EAs. Results showed significant differences in gender between AAs and EAs ($\chi^2 = 12.53$, $p = .001$). AAs also had higher BMI relative to EAs ($t_{(126)} = -2.48$, $r = 0.216$, $p = .016$). No significant differences were found in age ($t_{(126)} = 0.37$, $r = 0.032$, $p = .710$) or physical activity ($t_{(122)} = 1.74$, $r = 0.156$, $p = .086$). Baroreflex results showed AAs to have higher HRV ($t_{(126)} = -2.56$, $r = 0.222$, $p = .012$), cardiac BRS ($t_{(125)} = 3.04$, $r = 0.261$, $p = .053$), and myocardial BRS ($t_{(126)} = 2.65$, $r = 0.230$, $p = .009$) relative to EAs. AAs showed lower vascular BEI ($t_{(125)} = -2.37$, $r = 0.207$, $p = .003$). No other significant differences were observed (each $p > .05$). Adjusting for gender, age, and BMI, and physical activity, results showed AAs to only have higher HRV ($F_{(1,119)} = 4.18$, $r = 0.184$, $p = .043$) and lower vascular BEI ($F_{(1,119)} = 4.08$, $r = 0.182$, $p = .046$) in comparison to EAss. No other group comparisons were significant when including covariates; comparisons are presented in Table 1.

Correlations of interest in the full sample, and stratified between AAs and EAs, are presented in Table 2. In the full sample, correlations between each baroreflex function limb and their corresponding mean outputs showed relatively high correlations, with moderate size correlations observed within the myocardial limb ($r = 0.228$, $p = .011$). Such findings are virtually identical to that of prior work [8]. In both prior

Table 2
Correlations between baroreflex function and corresponding mean and variability variables.

Variables	Mean output	Variability output	Mean p	Variability p
All cBRS	0.515**	0.853**	–	–
AAs cBRS	**0.404****	**0.815****	0.027	–
EAs cBRS	**0.680****	**0.903****	–	0.056
All cBEI	−0.013	0.124	–	–
AAs cBEI	−0.159	**−0.044**	0.139	
EAs cBEI	0.107	**0.310****	–	0.044
All vBRS	0.459**	0.843**		–
AAs vBRS	0.431**	0.869**	0.582	–
EAs vBRS	0.511**	0.868**	–	0.984
All vBEI	−0.166	−0.328**	–	–
AA vBEI	−0.178	−0.305*	0.865	–
EAs vBEI	−0.147	−0.340**	–	0.834
All mBRS	0.228*	0.714**	–	–
AAs mBRS	0.243	0.574**	0.810	–
EAs mBRS	0.201	0.831**	–	0.089
All mBEI	−0.052	−0.001	–	–
AA mBEI	−0.119	−0.119	0.528	–
EA mBEI	0.006	0.124	–	0.177

Note. Note. Displayed correlations correspond to the mean and variability outputs of the three baroreflex limbs in the full (All) sample and stratified by African Americans (AAs) and European Americans (EAs). For baroreflex sensitivity (BRS) and effectiveness (BI; shaded gray), limbs are denoted as: c = cardiac, v = vascular, m = myocardial. Bolded values denote significant differences between ethnicities on the corresponding correlation. Mean p refers to the significance test between AAs and EAs on mean output correlations. Variability p refers to the significance test between AAs and EAs on variability output correlation *$p < .05$. **$p < .001$.

Table 1
Descriptive statistics for demographic and baseline physiological variables.

	Full sample		AAs		EAs					
	M	*SD*	*M*	*SD*	*M*	*SD*	*p*	mDiff	Lower	Upper
Gender	54 (76)		33 (21)		21 (52)		**0.01**			
Age	19.68	1.96	19.61	1.92	19.74	1.99	0.70	0.14	−0.55	0.82
BMI	25.52	4.93	**26.75**	**5.83**	**24.59**	**3.92**	**0.01**	−2.16	−3.85	−0.47
Activity	4.25	2.15	3.81	2.36	4.57	1.93	0.08	0.75	0.00	1.51
HRV	54.86	25.89	**61.41**	**28.17**	**49.90**	**23.00**	**0.01**	−11.51	−20.40	−2.63
HR	73.44	10.88	72.63	9.74	74.06	11.70	0.46	1.42	−2.40	5.24
MAP	81.99	12.87	81.71	12.47	81.58	12.82	0.96	−0.13	−4.72	4.47
SBP	119.50	16.54	118.50	15.21	120.43	16.99	0.52	1.93	−3.96	7.82
DBP	64.05	11.74	63.57	11.17	63.81	11.63	0.91	0.24	−3.91	4.39
TPR	0.83	0.28	0.85	0.29	0.83	0.28	0.74	−0.02	−0.12	0.09
CO	6.25	1.47	6.20	1.53	6.31	1.44	0.71	0.10	−0.44	0.64
SV	84.91	20.38	85.11	23.23	84.42	17.63	0.10	−0.69	−8.04	6.66
SBPv	4.22	2.09	3.88	1.27	4.49	2.53	0.10	0.61	−0.12	1.34
TPRv	59.29	38.23	62.21	36.60	57.06	39.53	0.45	−5.15	−18.61	8.31
cBRS	16.84	8.82	**18.94**	**10.58**	**15.26**	**6.88**	**0.02**	−3.68	−6.72	−0.65
cBEI	63.77	11.79	64.10	13.26	63.52	10.63	0.78	−0.58	−4.72	3.57
vBRS	16.03	12.56	17.27	15.25	15.08	10.04	0.33	2.18	−2.24	6.60
vBEI	34.12	10.33	**31.20**	**10.13**	**36.35**	**9.98**	**0.00**	5.15	1.62	8.68
mBRS	1.78	0.83	**1.98**	**0.91**	**1.62**	**0.74**	**0.01**	0.37	0.08	0.65
mBEI	36.43	15.22	35.70	16.69	36.98	14.09	0.64	1.27	−4.07	6.62

Note. This table provides means and standard deviations for all variables of interest for the full sample and stratified by African Americans (AAs) and European Americans (EAs), with associated t-test significance values and upper and lower confidence intervals (noted as upper and lower, respectively). Chi-squared tests were used to determine group differences in gender (represented in this table as count, men in brackets). Age in years; body mass index (BMI); Houston Non-Exercise Inventory (Activity); heart rate variability (HRV; ms), heart rate (HR; beats per minute); systolic blood pressure (SBP; mmHg); diastolic blood pressure (DBP; mmHg); total peripheral resistance (TPR; mmHg.s/ml); cardiac output (CO; l/min); stroke volume (SV; l/min); systolic blood pressure variability (SBPv); total peripheral resistance variability (TPRv) baroreflex sensitivity (BRS; ms) and baroreflex effectiveness (BEI; %). Limbs are denoted as: c = cardiac, v = vascular, m = myocardial. Bolded lines denote significant differences.

In the present study, data were available for 130 individuals between the ages of 18 and 30 (54 women, mean age of 19.7 years, standard deviation of 2 years). Of the 130 subjects, there were 57 AAs (33 females, mean age of 19.7 years) and 73 EAs (21 females, mean age of 19.6 years).

work [8] and the current study, BEI showed weaker and non-significant associations among mean and variability measures each ($p > .05$).

AAs showed weaker relationships between IBI and both cBRS ($z = -2.21, p = .027$) and cBEI ($z = -1.91, p = .056$) relative to EAs. AAs also showed an attenuated relationship between HRV and cBEI ($z = 2.01, p = .044$). No other significant differences were observed.

3. Discussion

The *Cardiovascular Conundrum* is a phenotype that represents a cardio-physiological paradox in which AAs show greater BP and associated negative health consequences despite greater cardiac vagal tone, as indexed by higher HRV. Our investigation lends important findings in this regard. First, HRV was higher in AAs relative to EAs, which is in line with prior work and the *Cardiovascular Conundrum*. However, vascular BEI, which should effectively adjust TPR in accordance with heart activity, was lower among AAs relative to EAs. This suggests that despite greater efforts to downregulate as indexed by higher HRV, this might not be as effective in properly regulating TPR in AAs as in EAs.

This is important to understand in the context of our sample, which were relatively young and healthy college-aged individuals. We did not see BP and TPR differences between AAs and EAs, However, differences were trending in the expected direction of AAs showing elevated BP, and the strength of this effect is likely attenuated due to young age. We propose that our findings of a less effective vascular limb of the baroreflex might lend itself to the cardiovascular complications AAs often experience as age increases. In sum, the current data suggests that the proportion of expected reflex modulation of TPR following the systolic BP inputs to the baroreceptors is lower in AAs compared to EAs. This indicates that despite higher resting HRV in AAs, BP can remain uncontrolled via this less effective baroreflex.

As early as 1948, the baroreflex was thought to play a role in both long-term and short-term BP regulation [14]. Despite some conflicting empirical studies (e.g., [15]) due to potential methodological issues [16], decades of research suggest that the baroreflex, mediated by the vagus and associated brain regions, is a major determinant of long-term BP regulation (see [7] for review). Therefore, given that AAs consistently show higher cardiac vagal tone (including in the current data), it is plausible that this can have a long-term impact on future cardiovascular complications. This idea is supported by a prior study which showed that in 385 normotensive youths, higher HRV significantly predicted both lower TPR and BP six years later among EAs, yet these associations were attenuated and not significant among AAs [10]. HRV did not significantly predict cardiac output at follow-up in EAs or AAs [10]. These findings highlighted that AAs show TPR mediated long-term increases in BP irrespective of resting HRV, providing a physiological pathway linking AAs with a greater risk for mortality and morbidity from hypertension and potentially other cardiovascular disease. This, taken with the current data, proposes that poorer vascular BEI among AAs relative to EAs is an extremely important mechanism potentially underlying long-term BP regulation differences between AAs and EAs. In sum, our data is the first to suggest the baroreflex might play an important role in the differential hemodynamics underlying long-term BP regulation and associated health outcomes between AAs and EAs.

As mentioned, the correlations between baroreflex function and corresponding mean and variability outputs were similar to prior work [8]. It is important to note that positive correlations for myocardial and vascular BRS correlations are a function of our transformation (see Methods). Interestingly, the link between mean outputs (i.e., IBI) and corresponding cardiac BRS and BE, in addition to variability outputs (i.e., HRV) and BEI only, varied by race such that AAs had weaker associations relative to EAs. In other words, AAs have higher cardiac BRS, which physiologically explains higher HRV, yet the link between BRS and the prevailing mean and variability outputs are weaker among AAs; this is accompanied by lesser BEI in the vascular limb of the baroreflex. Taken together, this supports the notion of a general disconnect between HRV and vascular control among AAs relative to EAs, thereby potentially extending to health outcomes and associated inequities.

In this regard, converging evidence supports the notion that both structural and interpersonal inequities have a profound impact on cardiovascular and overall health among marginalized individuals, including AAs [17,18]. While access to healthcare and related structural factors (e.g., health behavior, socioeconomic status, nutrition) perpetuate health disparities, epidemiological and community-based samples show that these health inequities persist when accounting for such structural factors [17]. Therefore, research continues to identify how individual-level factors such as interpersonal discrimination might perpetuate poorer physiological function and thus health among AAs. While self-reported measures of discrimination and related unfair treatment were not available in the current study, prior evidence suggests that such experiences likely impact the cardiovascular metrics presented here (for review, see [5]). Research has yet to examine experiences of discrimination and baroreflex function extensively and thus, research is warranted in this domain. Nonetheless, historical and current-day inequities remain a key driver of health disparities between AAs and EAs [19], and our study suggests that the baroreflex might be an important pathway as to how such inequities might get "under the skin", yet additional research is needed to examine this directly.

The current study is not without its limitations. The level of regular physical activity was generally low across the entire sample, however, there were no significant differences in physical activity as a function of race. Moreover, our sample was relatively young and healthy, and our relatively small sample size. Thus, these data should be interpreted with caution and future studies should consider these results in a larger sample and across varying ages ranges. Likewise, our data are cross-sectional and thus, directionality cannot be examined or determined. Given the reciprocal activity between the cardiovascular parameters examined in our investigation, bidirectional impact is physiologically plausible. Also, our data only partially support the *Cardiovascular Conundrum*, in which AAs had higher HRV however no significant differences emerged for BP or TPR. We propose that this is due to the age of our sample and with time, this less effective BEI might manifest into higher TPR, as shown by a previous meta-analysis. Nonetheless, research should reconsider the current results in a sample of AAs who show the full *Cardiovascular Conundrum*. Additionally, our study is relatively limited given that these are archival data analyses, and future study should consider how the cardiovascular metrics presented in this study are linked with discrimination and related forms of societal inequalities.

In closing, lower BEI in the vascular branch might be a particularly important mechanism underlying elevated BP and poorer health outcomes among AAs relative to EAs, and over time might manifest as the previously identified *Cardiovascular Conundrum*. We suggest that health professionals pay close attention to baroreflex function in AAs, as this might be a key target in promoting cardiovascular longevity.

CRediT authorship contribution statement

DeWayne P. Williams: Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Investigation, Formal analysis, Data curation, Conceptualization. **Cameron R. Wiley:** Writing – review & editing, Writing – original draft, Visualization, Validation, Formal analysis, Data curation, Conceptualization. **Julia Birenbaum:** Writing – review & editing. **Grace M. Fishback:** Writing – review & editing. **Lassiter F. Speller:** Writing – review & editing, Supervision, Investigation. **Julian Koenig:** Writing – review & editing, Supervision, Conceptualization. **Marc Jarczok:** Writing – review & editing, Conceptualization. **Gaston Kapuku:** Writing – review & editing, Supervision, Conceptualization. **Gustavo A. Reyes del Paso:** Writing – review & editing, Formal analysis, Conceptualization. **LaBarron K. Hill:** Writing – review & editing, Supervision, Project administration, Funding acquisition, Formal analysis, Conceptualization. **Julian F. Thayer:**

Writing – review & editing, Supervision, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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