Research Paper

Attenuated cerebral vasodilatory capacity in response to hypercapnia in college-aged African Americans

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New Findings

- **What is the central question of this study?**
  The main purpose of this investigation is to determine whether there is a difference in cerebral vasodilatory capacity in response to rebreathing-induced hypercapnia between African Americans and Caucasian Americans.
- **What is the main finding and its importance?**
  College-aged African Americans have reduced cerebral vasodilatory capacity during hypercapnia when compared with Caucasian counterparts, a finding that suggests cerebral vascular dysfunction in this population. These findings may contribute to the understanding of the greater prevalence of cerebral vascular disease in this population.

African Americans (AAs) have increased risk for cardiovascular, cerebral vascular and metabolic disease, including hypertension, stroke, coronary artery disease, metabolic syndrome and type II diabetes, relative to Caucasian Americans (CAs). While it is accepted that endothelial function is impaired in AAs, less is known regarding their cerebral vasodilatory capacity in response to hypercapnia. We hypothesized that AAs have a reduction in the total range of change in cerebral blood flow velocity (CBFV) measured in the middle cerebral artery and an index of cerebral vascular conductance (CVCI) in response to changes in the partial pressure of end-tidal carbon dioxide (P_{ET,CO_2}) during rebreathing-induced hypercapnia when compared with CAs. Twenty-one healthy, college-aged AA (10 male) and 21 age- and sex-matched CA (10 male) subjects participated in this study. A four-parameter logistic regression was used for curve fitting the responses of CBFV and CVCI relative to changes in P_{ET,CO_2}. The total ranges of change in CBFV (101 ± 18 *versus* 69 ± 23%; $P < 0.001$) and CVCI (83 ± 21 *versus* 58 ± 21%; $P < 0.001$) as well as the maximal increase in CBFV (205 ± 24 *versus* 169 ± 24%; $P < 0.001$) and CVCI (188 ± 30 *versus* 154 ± 19%; $P < 0.001$) were reduced during hypercapnia in AAs relative to CAs despite a similar increase in P_{ET,CO_2} (change, 15 ± 3 *versus* 15 ± 3 mmHg; $P = 0.65$). In conclusion, these data indicate that AAs have attenuated cerebral vascular capacity to respond to hypercapnia when compared with CAs.

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Introduction

African Americans (AAs) are at an increased risk for cardiovascular and metabolic disease, including hypertension, stroke, coronary artery disease, metabolic syndrome and type II diabetes, relative to Caucasian Americans (CAs). The underlying mechanisms for this increased risk remain unresolved; however, blunted

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endothelial function is a major contributing factor (Perregaux *et al.* 2000). Endothelial dysfunction results in impaired vasodilatation in the cerebral vasculature, and thus, leads to a dysfunction in cerebral blood flow (CBF) regulation (Zimmermann & Haberl, 2003; Lavi *et al.* 2006; Vicenzini *et al.* 2007). In this regard, AAs suffer from a greater prevalence of cerebral vascular disease, including stroke, relative to CAs (Roger *et al.* 2011).

The cerebral circulation is tightly regulated by arterial carbon dioxide tension (P_{aCO_2}), with hypercapnia increasing and hypocapnia decreasing CBF (Ide *et al.* 2003; Willie *et al.* 2014). The relationship between changes in CBF and P_{aCO_2} is often assessed to evaluate cerebral vascular function (Ringelstein *et al.* 1988; Kleiser & Widder, 1992). The cerebrovascular response to changes in CO_2 is diminished in some clinical conditions, including diabetes (Kadoi *et al.* 2003), hypertension (Lavi *et al.* 2006) and carotid artery disease (Ringelstein *et al.* 1988), and is believed to be not only a predictor but also a contributor to stroke (Gur *et al.* 1996; Nur *et al.* 2009). The increase in CBF and/or cerebral vascular conductance during hypercapnia occurs primarily through modulation of the cerebral microcirculation, and thus, is a powerful tool that provides a non-invasive index of cerebral vascular health (Ringelstein *et al.* 1988; Lavi *et al.* 2003, 2006).

We hypothesized that the cerebral vasodilatory capacity, indexed by the range of change in cerebral blood flow velocity (CBFV) and an index of cerebral vascular conductance (CVCI), as well as the maximal value of CBFV and CVCI achieved during rebreathing-induced hypercapnia, are reduced in healthy college-aged AAs relative to CAs.

Methods

Ethical approval

The Institutional Review Board at The University of Texas at Austin approved all study procedures and the consent process used in the present study. Subjects were given a verbal description of all procedures and informed of the purpose and risks involved in the study before providing their informed, written consent. The study conformed to the provisions of the Declaration of Helsinki.

Subjects

Twenty-one Caucasian Americans (CAs; 10 males) and 21 African Americans (AAs; 10 males) participated in this study (Table 1). A subject's ethnicity was defined as AA or CA and was only accepted if both parents were AA or CA, respectively. Subjects were non-smokers, were not taking medications and were free from cardiovascular, neurological, metabolic or cognitive diseases. All studies were conducted in the morning following an overnight fast (>12 h). Subjects refrained from strenuous exercise and alcoholic beverages for 24 h prior to and refrained from consuming caffeine and food for 12 h prior to the experimental trial, which was conducted in a temperature-controlled laboratory (~24°C and 40% relative humidity).

Instrumentation and measurements

All data were collected in the supine position. Each subject was instrumented for continuous measurement of heart rate (HR) and cardiac rhythms from an electrocardiogram (HP Patient Monitor; Agilent, Santa Clara, CA, USA) interfaced with a cardiotachometer (CWE, Ardmore, PA, USA). Continuous mean arterial pressure (MAP) was recorded and monitored from a finger using the Penaz method (CNAP, Biopac Monitor 500, Bruck an der Mur, Austria). The CBFV was measured continuously using transcranial Doppler ultrasonography. The right middle cerebral artery was imaged through a 2 MHz Doppler probe (Multi-flow; DWL Elektronische Systeme, Singen, Germany) adjusted over the temporal window until a signal was identified. The probe was fixed securely in place using a head strap to prevent any slight movement of the Doppler probe. The CVCI was calculated from the ratio of CBFV to MAP. End-tidal carbon dioxide tension (P_{ET,CO_2}) was measured continuously using a capnograph, through a mouthpiece, during all data collection periods and was used as an index of P_{aCO_2} (VitalCap Capnograph Monitor; Oridion, Needham, MA, USA).

Experimental protocol

Following instrumentation, subjects rested quietly in the supine position for 20 min. Following the resting period, subjects were fitted with a nose-clip and breathed through a mouthpiece attached to a Y-valve. One end of the Y-valve was connected to a 5 litre bag and the other end was open to room air. Subjects breathed room air for a 6 min period of baseline data collection while CBFV, MAP, HR and P_{ET,CO_2} data were collected. Subjects were then exposed to a rebreathing protocol. Subjects first performed a deep inspiration and exhaled into an empty rebreathing bag via the Y-valve. The subjects continued to rebreathe for ~3 min before switching the valve for a recovery period. During the rebreathing period, arterial oxygen saturation was held constant (between 97 and 98%) by bleeding a small amount of oxygen into the rebreathing bag (Claassen *et al.* 2007).

Data analysis

Data for MAP, HR, CBFV and P_{ET,CO_2} were collected at 125 Hz via a data-acquisition system (Biopac System,

Santa Barbara, CA, USA) during baseline conditions. Average cerebrovascular responses (CBFV and CVCI) during baseline and rebreathing conditions were assessed on a breath-by-breath basis. The percentage change in CBFV and CVCI was determined, while the absolute change in P_{ET,CO_2} was determined. A four-parameter logistic regression was employed for sigmoidal curve fitting (Kent *et al.* 1972; Claassen *et al.* 2007, 2009), as follows:

$$f(x) = y_0 - \left(\frac{a}{1 + e^{b(x-x_0)}}\right)$$

where a represents the range of change in the percentage of CBFV or CVCI, b is a constant that determines the overall sigmoidal property of the curve, x_0 is the level of P_{ET,CO_2} where cerebral vasomotor reactivity for CBFV or CVCI is maximal, and y_0 represents the maximal value of CBFV and CVCI during hypercapnia (Fig. 1). Maximal cerebral vasomotor reactivity [CVMR ($CVMR_{max}$ − CBFV and $CVMR_{max}$ − CVCI)], which was obtained at $x = x_0$, was calculated from the first-order derivative of the following logistic function:

$$f'(x) = \frac{ab \times e^{[b(x-x_0)]}}{\left\{1 + e^{[b(x-x_0)]}\right\}^2}$$

In order to compare with a four-parameter logistic curve model, CVMR using linear regression of changes in CBFV and CVCI (expressed as percentages) in response to a change (Δ) of 9 mmHg from its baseline P_{ET,CO_2} value was assessed. The Δ9 mmHg was chosen because it was the highest common change in P_{ET,CO_2} that all subjects achieved during hypercapnia.

In order to assess cerebral vascular function further, indices of cerebral autoregulation were assessed by transfer function analysis over a specified frequency range (very low, 0.02–0.07 Hz; low, 0.07–0.20 Hz; and high, 0.20–0.35 Hz; Zhang *et al.* 1998). Transfer phase, gain and coherence functions were calculated using commercially available software (DADiSP; DSP Development, Cambridge, MA, USA).

Statistical analysis

Statistical analyses were performed using a statistical software package (SigmaPlot 12.5; Systat Software, Inc., San Jose, CA, USA). Subject characteristics, baseline haemodynamic data, transfer function analysis data, and all parameters and estimates of CVMR from a four-parameter logistic function and linear regression were compared using Student's two-tailed unpaired *t* tests. A χ^2 test was used for difference in sex ratio between the two groups. All significance was set at $P \leq 0.05$, and data are presented as means ± SD.

Table 1. Subject characteristics

Variable	Caucasian Americans ($n = 21$)	African Americans ($n = 21$)	*P* Value
Age (years)	23 ± 3	23 ± 4	0.97
Sex (male/female)	10/11	10/11	1.00
Body mass index (kg m^{-2})	23 ± 3	24 ± 4	0.07
Height (cm)	174 ± 8	173 ± 9	0.85
Weight (kg)	68 ± 12	73 ± 14	0.24

Values are means ± SD.

Results

Subject characteristics and haemodynamic values during baseline period

There were no differences between groups for age, sex, body mass index, height or weight (Table 1; $P > 0.05$ for all comparisons). During the eucapnic baseline period, there were no differences between groups for HR, MAP, CBFV, P_{ET,CO_2} and CVCI (Table 2; $P > 0.05$ for all comparisons).

Cerebrovascular responses during hypercapnia

Representative examples of the relationship between CBFV *versus* P_{ET,CO_2} and CVCI *versus* P_{ET,CO_2} are illustrated in Fig. 2*A* and *B*, respectively. Table 3 shows the group-averaged parameters and estimates of CVMR from the logistic and the linear regressions. Maximal CBF (CBFV, as a percentage of baseline) during hypercapnia was lower in AA relative to CA subjects (CA, 195 ± 17% *versus* AA, 170 ± 20%; $P < 0.001$). Likewise, maximal conductance was reduced in AAs (CA, 178 ± 17% *versus* AA, 153 ± 16%; $P < 0.001$). The magnitude of hypercapnia ($\Delta P_{ET,CO_2}$) induced by rebreathing was similar between groups (CA, 15 ± 3 mmHg *versus* AA, 15 ± 3 mmHg; $P = 0.65$).

Curve fitting and model parameters

The correlation coefficients (r^2) for logistic regression were 0.95 and 0.94 for CBFV *versus* P_{ET,CO_2} and CVCI *versus* P_{ET,CO_2}, respectively. From Table 3, the total range of changes in CBFV (a; as a percentage) was attenuated in AAs (CA, 101 ± 18% *versus* AA, 69 ± 23%; $P < 0.001$). Likewise, the total range of changes in CVCI (a; as a percentage) was reduced in AAs (CA, 83 ± 21% *versus* AA, 58 ± 21%; $P < 0.001$). The maximal increase in CBFV (y_0; as a percentage) was lower in AAs (CA, 205 ± 24% *versus* AA, 169 ± 24%; $P < 0.001$). Likewise, the maximal increase in CVCI (y_0; as a percentage) was lower in AAs (CA, 188 ± 28% *versus* AA, 154 ± 19%; $P < 0.001$). The levels of P_{ET,CO_2} that exhibited the highest CO_2 sensitivity (x_0; in millimetres of mercury) were not different between

the two groups. Group differences for a and y_0 are shown graphically in Fig. 3*A* and *B*, respectively.

Estimates of CVMR

No difference in maximal CVMR for CBFV and CVCI was observed between the two groups. In linear regression, there was no significant difference in the CVMR between the two groups ($P = 0.35$ and $P = 0.82$ for group differences of CBFV *versus* P_{ET,CO_2} and CVCI *versus* P_{ET,CO_2}, respectively).

Transfer function analysis

The estimates of transfer phase, gain and coherence functions are shown in Table 4. In the very low-frequency range, there was no difference in phase between CAs and AAs (CA, 0.038 ± 0.026 radians *versus* AA, 0.024 ± 0.030 radians; $P = 0.18$). In contrast, in the low-frequency and high-frequency ranges, the transfer phase function was lower in AAs relative to CAs ($P = 0.04$ and $P = 0.02$, respectively). Transfer gain and coherence functions in all frequency ranges were not significantly different between CAs and AAs ($P > 0.05$ for all comparisons).

Table 2. Haemodynamic values during baseline period prior to rebreathing protocol

Variable	Caucasian Americans ($n = 21$)	African Americans ($n = 21$)	*P* Value
HR (beats min^{-1})	57 ± 10	61 ± 9	0.15
MAP (mmHg)	98 ± 15	99 ± 13	0.91
CBFV (cm s^{-1})	63 ± 13	65 ± 16	0.71
P_{ET,CO_2} (mmHg)	38 ± 4	40 ± 5	0.29
CVCI (cm s^{-1} mmHg^{-1})	0.66 ± 0.2	0.67 ± 0.2	0.89

Values are means ± SD. Abbreviations: CBFV, velocity of blood in the middle cerebral artery; CVCI, index of cerebral vascular conductance; HR, heart rate; MAP, mean arterial pressure; and P_{ET,CO_2}, partial pressure of end-tidal carbon dioxide.

Discussion

The present study demonstrates that cerebral vasodilatation in response to rebreathing-induced hypercapnia is attenuated in young and healthy AAs compared with CAs. The lower cerebral vasodilatory response in AAs is a novel finding and may help to explain the greater prevalence of cerebral vascular disease in this population, although the underlying mechanisms need to be investigated further.

Carbon dioxide is a potent stimulus for changes in cerebral perfusion, and the sensitivity of this unique feature of the cerebral circulation is needed to ensure an adequate nutrient and oxygen supply as well as removal of metabolic waste products from brain tissue (Ringelstein *et al.* 1988; Kleiser & Widder, 1992). The ability of the brain to regulate its perfusion in response to changes in P_{aCO_2} is an indicator of cerebral vascular health (Ringelstein *et al.* 1988; Kleiser & Widder, 1992). A reduction in cerebral vasodilatation impairs the ability to provide adequate nutrient and oxygen supply to

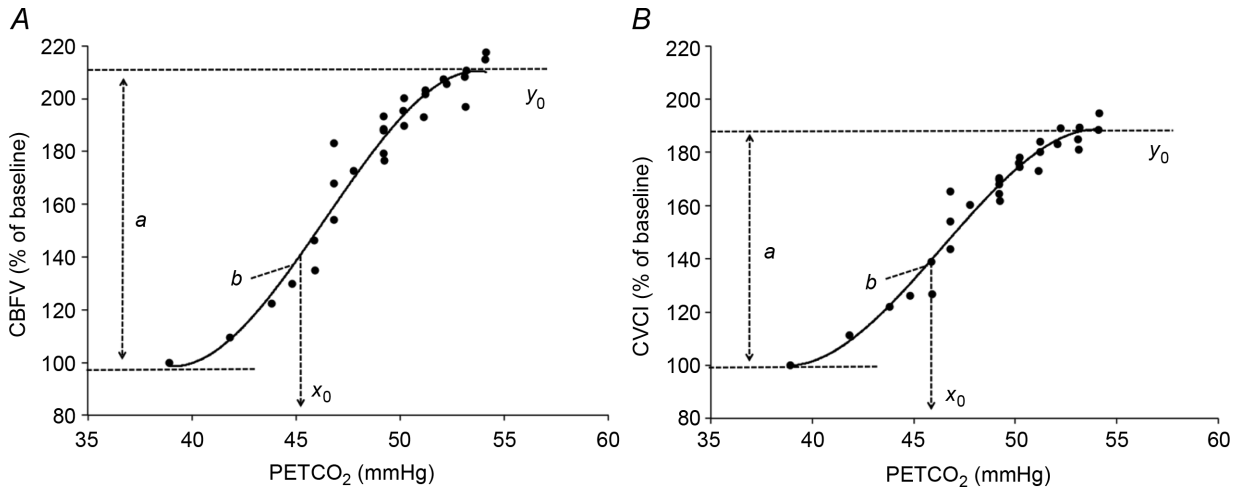

Figure 1. Schematic representations of logistic regressions
A logistic regression and four parameters of the velocity of blood in the middle cerebral artery (CBFV) and index of cerebral vascular conductance (CVCI) *versus* the partial pressure of end-tidal carbon dioxide (P_{ET,CO_2}) are displayed in *A* and *B*, respectively. The parameter a represents the range of change in the percentage of CBFV or CVCI, b is a constant that determines the overall sigmoidal property of the curve, x_0 is the level of P_{ET,CO_2} at which cerebral vasomotor reactivity for CBFV or CVCI is maximal, and y_0 represents the maximal value of CBFV and CVCI during the hypercapnic rebreathing protocol.

the cerebral microcirculation as well as to prevent fluctuations in pH status (Lavi *et al.* 2003, 2006). In this regard, the present findings are particularly important, given the high prevalence of a variety of diseases and conditions, including stroke, Alzheimer's disease and cognitive dysfunction, in the AA population (Mensah *et al.* 2005; Melikian *et al.* 2007).

From the examples depicted in Fig. 2*A* and *B*, an increase in CBFV and CVCI tends to be similar until a change of ∼10 mmHg of P_{ET,CO_2}, and this tendency is reflected in the CVMR results that were the same between the two groups (Table 3). Despite the similarity in this variable, AA subjects achieved maximal CBFV and CVCI prematurely, which resulted in a plateau as the hypercapnic period continued. In other words, the maximal increase and total range of increase in CBFV and CVCI were blunted in the AA subjects. In comparison, CAs exhibited a relatively stable elevation in CBFV and CVCI. Seven AA subjects showed a complete plateau similar to Fig. 2*A* and *B*, whereas no CA subjects showed this plateau. This trend for a plateau in AAs was reflected in a higher value of *b*, which is the curvilinear property of the regression curve. Taken together, these findings further support the hypothesis of reduced cerebral vascular function in AAs. The underlying mechanisms for the attenuated cerebral vasodilatory response in AAs are multifactorial; however, several possibilities can be proposed, as outlined below.

Cerebral autoregulation

Damage to the cerebral microcirculation as a result of impaired cerebral autoregulation may explain why the capacity of the brain vasculature to dilate in response to changes in CO_2 was reduced in AAs. Cerebral autoregulation is a mechanism to protect the cerebral vasculature against changes in blood pressure and to stabilize CBF (Meel-van den Abeelen *et al.* 2014; Willie *et al.* 2014). Impaired cerebral autoregulation is associated with increased morbidity and mortality (Hu *et al.* 2008) and is present in patients with hypertension, ischaemic stroke, severe head injury, Parkinson's disease and carotid artery disease (Czosnyka *et al.* 1996; Eames *et al.* 2002, 2003; Vokatch *et al.* 2007; Reinhard *et al.* 2008). Long-term dysfunction of cerebral autoregulation induces physiological alterations, including cerebral microvascular remodelling and rarefaction (Levy *et al.* 2008; Reinhard *et al.* 2008), which limits maximal cerebral vasodilatory capacity, and if present in AAs, could partly explain the present findings. The transfer estimates of phase (a reflection of the temporal shift required to align the MAP signal with the CBFV signal) were lower in AAs in the low- and high-frequency ranges (Table 4). These findings suggest impaired cerebral autoregulation (Blaber *et al.* 1997; Zhang *et al.* 1998). However, transfer estimates of gain (the relative amplitude between changes in MAP and CBFV) and coherence (the linear relationship between MAP and CBFV) were similar between AAs and CAs in all frequency ranges (Table 4). These findings suggest similar autoregulation between groups. Based on these findings, differences in cerebral autoregulation between AAs and CAs are inconclusive and warrant further investigation.

Endothelial dysfunction and CO_2-mediated pathway in the brain

Cerebral blood flow is controlled by a CO_2-mediated pathway and endothelial signals in response to sheer stress as well as changes in blood pressure. Thus, endothelial

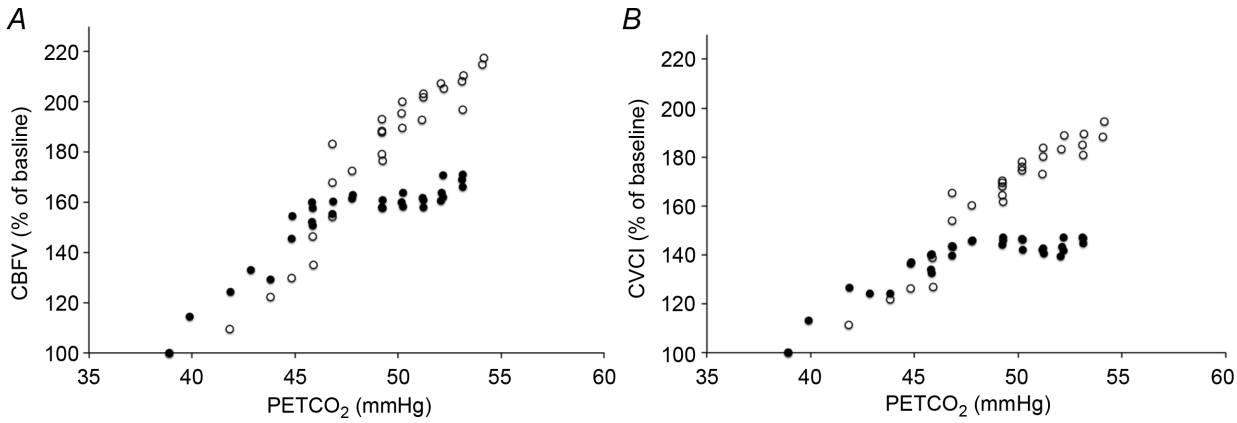

Figure 2. Representative examples of cerebral vasodilatory response in African Americans (AAs) and Caucasian Americans (CAs)
Two examples of the changes in middle cerebral artery blood velocity (CBFV; *A*) and cerebral vascular conductance index (CVCI; *B*) with increase in P_{ET,CO_2} for an AA (filled circle) and a CA subject (open circle) are illustrated. The magnitude of increase in CBFV and CVCI was blunted in the AA relative to the CA.

Table 3. Cerebrovascular response to hypercapnia and parameters from logistic model

Variable		Caucasian Americans	African Americans	*P* Value
Hypercapnia				
Maximal flow (CBFV; % of baseline)		195 (17)	170 (20)	<0.001
Maximal conductance (CVCI; % of baseline)		178 (17)	153 (16)	<0.001
Magnitude of hypercapnia achieved ($\Delta P_{ET,CO_2}$; mmHg)		15 (3)	15 (3)	0.65
Parameters from logistic model				
Flow	*a* (%)	101 (18)	69 (23)	<0.001
	b	0.34 (0.2)	0.50 (0.3)	0.06
	x_0 (mmHg)	45 (5)	44 (4)	0.47
	y_0 (%)	205 (24)	169 (24)	<0.001
Conductance	*a* (%)	83 (21)	58 (21)	<0.001
	b	0.34 (0.2)	0.58 (0.4)	0.018
	x_0 (mmHg)	44 (6)	43 (4)	0.43
	y_0 (%)	188 (28)	154 (19)	<0.001
Estimates of CVMR				
Logistic regression				
$CVMR_{max}$ – CBFV (% $mmHg^{-1}$)		8.3 (3.8)	7.3 (2.8)	0.35
$CVMR_{max}$ – CVCI (% $mmHg^{-1}$)		6.8 (3.7)	7.1 (2.9)	0.82
Linear regression (Δ9 mmHg)				
$CVMR_{max}$ – CBFV (% $mmHg^{-1}$)		6.6 (2)	6.1 (2)	0.40
$CVMR_{max}$ – CVCI (% $mmHg^{-1}$)		5.6 (2)	5.1 (2)	0.39

Values are means ± SD. Abbreviations: *a*, the range of change in percentage of CBFV or CVCI; *b*, a constant that determines the overall sigmoidal property of the curve; x_0, the level of P_{ET,CO_2} at which cerebral vasomotor reactivity for CBFV or CVCI is maximal; and y_0, the maximal value of CBFV and CVCI during the hypercapnic rebreathing protocol; CVMRmax, the maximal cerebral vasomotor reactivity using logistic regression analysis and linear regression analysis. Other abbreviations are as for Table 2.

dysfunction or an impaired CO_2-mediated pathway in the brain would restrict cerebral vasodilatory capacity. Nitric oxide synthase inhibition reduces basal CBF (Joshi *et al.* 2000) and blunts CBF in response to hypercapnia in rats (Buchanan & Phillis, 1993), primates (Thompson *et al.* 1996) and humans (Schmetterer *et al.* 1997), indicating that basal cerebral perfusion as well as the response to hypercapnia is regulated, in part, by NO. This response is reversed by internal carotid artery infusion of L-arginine, a precursor for NO synthesis, in primates (Thompson *et al.* 1996) and in individuals with elevated cerebral vascular risk (Zimmermann & Haberl, 2003). The effect of NO synthase inhibition is greater as P_{aCO_2} increases during hypercapnia (Buchanan & Phillis, 1993), suggesting a positive correlation. Furthermore, hypertensive and diabetic patients with impaired peripheral endothelial

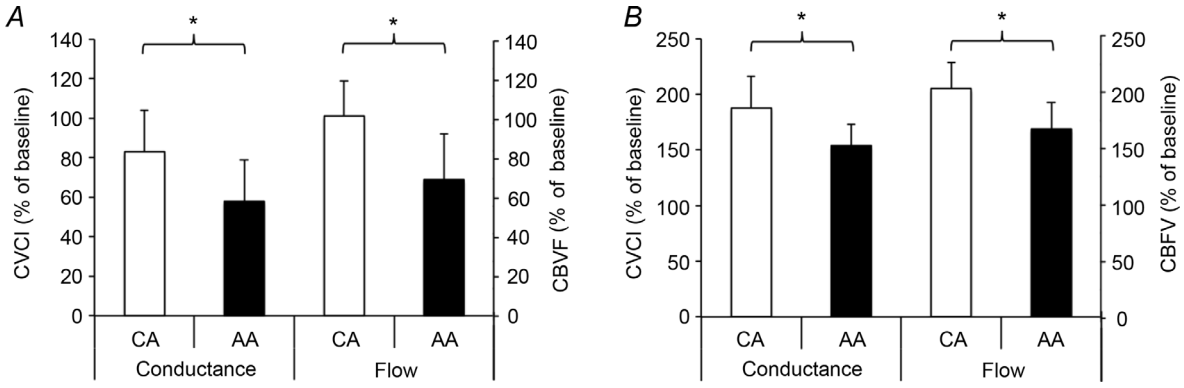

Figure 3. Group differences for *a* and y_0
Total range of change in CVCI and CBFV (parameter *a*; *A*) as well as the maximal increase in CVCI and CBFV (parameter y_0; *B*) during hypercapnic period were attenuated in AA relative to CA. The left Y axis in each figure represents the CVCI values while the right Y axis in each figure represents the CBFV values. Values are shown as means + SD. $^*P < 0.001$.

Table 4. Transfer function analysis

Parameter		Caucasian Americans	African Americans	*P* Value
Phase (radians)	Very low	0.038 (0.026)	0.024 (0.030)	0.18
	Low	0.056 (0.042)	0.021 (0.071)	0.04
	High	0.028 (0.099)	−0.045 (0.109)	0.02
Gain (cm s^{-1} $mmHg^{-1}$)	Very low	0.83 (0.47)	1.16 (0.76)	0.17
	Low	0.79 (0.34)	0.86 (0.21)	0.71
	High	0.61 (0.34)	0.51 (0.15)	0.20
Coherence	Very low	0.37 (0.16)	0.43 (0.19)	0.39
	Low	0.54 (0.15)	0.47 (0.16)	0.13
	High	0.42 (0.12)	0.40 (0.11)	0.51

Values are means ± SD. The following three different frequency ranges were used for the transfer function analysis: very low, 0.02–0.07 Hz; low, 0.07–0.20 Hz; and high, 0.20–0.35 Hz.

function have impaired cerebral vascular responses to hypercapnia, and this impairment was abolished following administration of the exogenous NO donor sodium nitroprusside (Lavi *et al.* 2006). African Americans have impaired endothelial function (Perregaux *et al.* 2000), reduced NO bioavailability (Melikian *et al.* 2007) and impaired NO-dependent vasodilatation (Perregaux *et al.* 2000). These impairments could contribute to the reduced cerebral vasodilatory capacity in this population.

Limitations

The CBFV reflects CBF only if the diameter of the middle cerebral artery is constant. Previous studies (Huber & Handa, 1967; Bradac *et al.* 1976; Serrador *et al.* 2000) demonstrated that the diameter of the middle cerebral artery does not change significantly during moderate changes in arterial blood pressure and carbon dioxide tension in plasma (within the range in the present study); thus, changes in CBFV reflect changes in CBF and can be used as an index of cerebral perfusion.

We did not measure P_{aCO_2}. Instead, P_{ET,CO_2} was used as an index of P_{aCO_2}. However, Phan *et al.* (1987) and others (Whitesell *et al.* 1981; Yosefy *et al.* 2004) have demonstrated that P_{ET,CO_2} is correlated well with P_{aCO_2} at rest. Moreover, Xie *et al.* (2006) reported that there were no differences in CVMR values between P_{ET,CO_2} and P_{aCO_2} during hypercapnia. Thus, we believe that P_{ET,CO_2} is a valid index for representing P_{aCO_2} during both rest and hypercapnia.

Conclusions

In conclusion, we observed that young, otherwise healthy African Americans had reduced cerebral vasodilatory capacity in response to the same degree of elevation in P_{ET,CO_2} induced by hypercapnic rebreathing when compared with their Caucasian counterparts. This finding supports the hypothesis that the cerebral vascular response is reduced in relatively young, healthy African Americans. Given that African Americans are at higher risk of cardiovascular and cerebral vascular disease, the findings indicate that reduced cardiovascular and cerebrovascular function is present at an early age in African Americans, leaving a long period of time to become progressively worse and develop into overt cardiovascular and cerebral vascular diseases and their complications with advancing age.

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Additional information

Competing interests

None declared.

Author contributions

C.H. contributed to the study design, data analysis and data interpretation, and drafted this manuscript. K.K., M.L.H. and R.M.B. contributed to the study design, data collection, data analysis, data interpretation and editorial process of the manuscript. All authors approved the final version of this manuscript. All experiments of the present study were conducted in the Environmental and Autonomic Physiology Laboratory at The University of Texas at Austin.

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