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Cerebral Autoregulation Indices Are Unimpaired by Hypertension in Middle Aged and Older People

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Background: Hypertension is known to increase the limits of static cerebral autoregulation (CA) but its effects on other aspects of CA such as efficiency and latency are unknown. In this study we test the hypothesis that dynamic cerebral autoregulation and the efficiency of static cerebral autoregulation are impaired by untreated hypertension.

Methods: Cerebral blood flow velocity was recorded using transcranial Doppler ultrasound, along with noninvasive beat-to-beat blood pressure (BP), electrocardiogram, and transcutaneous carbon dioxide levels, with subjects at rest and during isometric hand grip, thigh cuff, and the Valsalva maneuver. Static and dynamic CA indices were calculated.

Results: No significant difference was seen in static or dynamic CA indices between normotensive and hypertensive groups for any pressor or depressor stimulus. Spearman's rank correlation showed no relation between static or dynamic CA indices and systemic BP levels for all maneuvers, but a significant relationship between age and static CA index, determined using isometric handgrip ($P = .002$), was found.

Conclusions: In middle-aged and older people, sustained untreated hypertension does not alter dynamic CA or the efficiency of static CA within the BP limits studied. Am J Hypertens 2003;16:746–753 © 2003 American Journal of Hypertension, Ltd.

Key Words: Hypertension, cerebral autoregulation, transcranial Doppler ultrasound.

The process of cerebral autoregulation (CA) maintains cerebral blood flow (CBF) at a relatively constant level in humans despite large changes in perfusion pressure resulting from perturbations in systemic arterial blood pressure (BP).[1] The pathophysiology of CA is poorly understood but myogenic, neurogenic, and metabolic mechanisms are likely to be involved, the final common pathway being vasomotor adjustments in cerebrovascular resistance (CVR), mediated at arteriolar level.[1] Physiologic adjustments involved in CA occur at differing rates and are influenced by factors that can alter the degree of vasodilatation or vasoconstriction of cerebral vessels (eg, arterial carbon dioxide [CO_2] tension).[1] Under normal circumstances CA occurs between mean arterial pressure (MAP) limits around 60 to 150 mm Hg, beyond which, autoregulatory vasodilatation or vasoconstriction become inadequate and CBF is pressure passive with a risk of cerebral hypoperfusion or hyperperfusion.[1]

Static CA was initially studied in humans by measuring CBF in response to steady state changes in BP and deriving an index of the efficiency but not latency of autoregulation (ie, the change in CVR to a given BP change). With the development of transcranial Doppler ultrasound (TCD), changes in cerebral blood flow velocity (CBFV), an accurate surrogate measure for CBF,[2–4] can be followed with excellent temporal resolution, allowing both the efficiency and latency of the CBF response to rapid changes in BP to be characterized as dynamic CA.[5] Dynamic CA has been shown to be affected to a greater degree than static CA in disease states (eg, stroke)[6] and may have different control mechanisms from static CA.

Sustained hypertension causes structural and functional changes in the cerebral arteriolar walls. It alters endothelial nitric oxide (NO) synthesis, which is intimately involved in dynamic CA.[7] The upper and lower limits of static CA increase with increased systemic BP levels[1] and

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there is some evidence that dynamic CA is retained in hypertensive patients already on antihypertensive medication,[8,9] but no information to my knowledge is available on the effect of never treated hypertension on either dynamic CA or the efficiency of static CA.

Aging is known to be associated with a decrease in CBFV[10] and an increase in the lower limit of the static CA curve in animal models.[11] We have previously shown dynamic CA to be unaffected by aging,[12] but little information exists on the combined effects of aging and hypertension on either dynamic CA or the efficiency of static CA.

The hypothesis that sustained untreated hypertension will impair the efficiency of static CA or dynamic CA was tested in this study in a group of healthy middle-aged and elderly volunteers with a wide range of systemic BP levels. The secondary hypothesis that there may be differences in dynamic and static CA response to pressor and depressor stimuli and that these differences might be greater in hypertensive subjects was also tested.

Methods

Subjects

Eighty-one volunteers, aged 67 ± 6 years (range, 55 to 81 years), were recruited, 68 from the Departmental register at the Glenfield Hospital, UK, of volunteers who responded to two local newspaper articles and 13 from the Hypertension Clinic and general practitioner referrals. They were subsequently classified as normotensive (daytime ambulatory BP ≤135/85 mm Hg) and hypertensive (daytime ambulatory BP ≥140/90 mm Hg) according to British Hypertension Society guidelines,[13] although daily activities and sleep during the monitoring were not recorded.

All subjects were free of cardiovascular (apart from never treated hypertension, duration at least 6 months before the study), cerebrovascular (including severe carotid artery stenosis), and autonomic disease as determined by history, full physical examination, routine hematologic and biochemical investigations, and 12-lead electrocardiogram (ECG). None were taking any medication known to affect cardiovascular or cerebrovascular responses.

All participants gave informed consent and the study was approved by the local Leicestershire ethical committee.

Protocol

Each subject underwent home 24-h ambulatory BP monitoring (Spacelabs 90207, Redmond, WA) recording at 20-min intervals during the day (7 AM to 11 PM) and 30-min intervals at night (11:01 PM to 6:59 AM) before presenting for CA studies.

Subjects avoided caffeine, nicotine, and alcohol for 12 h before the CA recordings and were studied at least 2 h postprandial. Studies were conducted in a dedicated research room kept at a constant temperature (20° to 24°C) with external stimuli minimized.

The middle cerebral arteries (MCA) were insonated bilaterally as described by Aaslid et al,[14] and middle cerebral artery flow velocity (MCAV) measured using TCD (SciMed QVL 842X, Bristol, UK). A three-lead surface ECG was fitted and beat-to-beat arterial BP was measured noninvasively by a servocontrolled plethysmograph (Finapres 2300, Ohmeda, Englewood, CO) on the middle finger of the right hand, supported at atrial level throughout the studies. Carbon dioxide levels were measured using a previously validated transcutaneous monitor (TINA, Radiometer, Copenhagen, Denmark).

The maximum frequency velocity envelope was calculated by the FFT spectrum analyzer on the SciMed QVL 842X. The TCD, Finapres BP, ECG, and TINA output signals were directly converted at 200 Hz and recorded on digital tape (DAT, Sony PC-108M, Japan).

After 20 min of supine rest and once a stable baseline had been achieved (<10% variation in BP and MCAV) two baseline recordings of 5 min duration were made before induced pressor and depressor tests were performed. Only BP changes ≥10 mm Hg were accepted as an adequate stimulus for analysis. All tests have been described previously,[15] were randomly allocated.

Static Tests: Depressor: Lower Body Negative Pressure (LBNP) After a 1-min baseline recording, pressure was reduced in the box to cause a gradual reduction in systolic BP of between 10 and 20 mm Hg, which was maintained for 3 min.

Static Tests: Pressor: Isometric Hand Grip (HDG) After a 1-min baseline recording, subjects squeezed a rolled up, slightly inflated sphygmomanometer cuff with their left hand, at 30% maximal voluntary compression for 2 min. Ventilation was maintained during handgrip to avoid an inadvertent Valsalva-like maneuver.

Static Tests: Pressor: Thigh Cuff Inflation (THC) Wide BP cuffs (DURA-CUF thigh cuff, Johnson & Johnson) were placed around both thighs and after a 1-min baseline recording the cuffs were inflated for 90 sec.

Dynamic Tests: Depressor: Thigh Cuff Deflation The BP fall at the point of rapid deflation of the cuff was used as a dynamic depressor stimulus.

Dynamic Tests: Depressor: Isometric Hand Grip The BP fall at the point of release of grip was used as a dynamic depressor stimulus.

Dynamic Tests: Depressor: Negative Spontaneous Transients (NT) Spontaneous transient depressor changes manually selected from the 10-min baseline BP recording were used as dynamic depressor stimuli.

Dynamic Tests: Pressor: Valsalva Maneuver (VLS) Subjects blew into a syringe with an integral constant-bleed device attached to a pressure transducer and an

intrathoracic pressure of 40 mm Hg was maintained for 15 sec. The BP response during phase IV was used as the dynamic pressor stimulus.

Dynamic Tests: Pressor: Positive Spontaneous Transients (PT) Spontaneous transient pressor changes selected from the 10-min baseline BP recording were used as dynamic pressor stimuli.

Data Analysis

The digital audiotape recording was downloaded onto a microcomputer and the BP signal calibrated at the start of each recording. All signals were visually inspected for artifacts or noise. Narrow spikes on the MCAV signals were removed by linear interpolation and the four signals were low pass filtered with a zero-phase eighth-order Butterworth digital filter with a cut-off frequency of 20 Hz.

Ectopics occurring more than once in 30 sec led to rejection of the data. Spline interpolation was used to resample the data at 0.2 sec to create a uniform time base.

Determination of Static CA

Data were selected to include a baseline period and the period of static BP change, then divided into contiguous 8-sec intervals and the mean values of MCAV and BP were calculated for each interval. Cerebrovascular resistance (mm Hg/m/sec) was estimated for each segment and a static autoregulatory index (ARI) was calculated as previously described.[16] A change in CVR that would fully compensate for the MAP change gives a static ARI of 100% and no change in CVR (ie, absent autoregulation) would give a result of 0%.

Dynamic CA

Using the method of Tiecks et al,[16] with modifications previously used by our department,[6] the calculated dynamic ARI was derived from the response of the CBFV to dynamic pressor and depressor changes in MAP. The actual CBFV response was compared with a family of 10 theoretical curves, generated using the BP change and specific combinations of time constant, damping factor, and autoregulatory dynamic gain.[16] The dynamic ARI was calculated to one decimal place according to where it most closely fitted in the family of curves with a dynamic ARI of 0 indicating absent dCA and 9 best possible dCA.

Baroreceptor Sensitivity Calculation

Cardiac baroreceptor sensitivity (BRS) was estimated using standard methodology involving fast Fourier transform for pulse interval and systolic BP.[17]

Statistical Methods

Student paired *t* tests were used for comparison of normally distributed data, which are presented as mean and standard deviation (SD) with 95% confidence intervals (CI). For data not normally distributed the Mann-Whitney U test was used and data presented as median and interquartile range (IQR).

Spearman's rank correlation test was used to assess the relationship between ARI and age, sex, Finapres, and ambulatory BP data.

Linear regression was used to assess the relationship between cardiac BRS and age and ambulatory BP data.

To compare static ARIs and their respective BP changes between the different BP stimuli the data were modeled using a linear model where missing values were treated with multiple imputations.

To compare the dynamic ARIs and their respective BP changes between the different BP stimuli a group of 29 people with complete data for four dynamic stimuli, THC, VLS, PT, and NT, were selected and a two-way ANOVA applied.

The statistical packages SPSS 10.0.5 for Windows (Microsoft), MINITAB 12 for Windows (Microsoft) and Splus 6 for Windows (Insightful Corp.) were used and statistical significance taken at the 5% level.

Results

Demographic and BP data for the 81 volunteers and for the normotensive ($n = 35$) and hypertensive ($n = 46$) groups are given in Table 1. For the whole group there was no significant difference between the mean MCAV for right and left MCAs (median, 42 cm/sec [range, 26 to 65 cm/sec]; median, 43 cm/sec [range, 29 to 66 cm/sec], respectively) (Table 1). The baseline CO_2 levels were similar between the normotensive and hypertensive groups, 38.6 ± 4.8 mm Hg and 39.7 ± 4.1 mm Hg, respectively.

Not all patients underwent every test due to frailty, obesity (some were too big to get in the LBNP box or use the THC), and refusal to tolerate a test. Some test recordings could not be analyzed because the TCD or Finapres recordings were unusable for technical reasons and not all of the tests that were performed were accepted for analysis due to strict criteria set.

There was no significant difference between static ARI or dynamic ARI calculated from the right and left MCAs; therefore, the mean of the two sides for each subject was used in the analysis.

Static CA

There was no significant difference in static ARI between maneuvers (maximum difference 95% one-sided CI (0, 29) $P = .327$). Using Spearman's rank correlation there was no correlation between static ARI, calculated from THC or LBNP and age or BMI, but a significant correlation with age ($P = 0.370$, $P = .002$) for static ARI calculated from HDG was found. No relation was found between static ARI calculated from any BP stimulus and daytime ambulatory or Finapres BP. There was no significant difference in static ARI or the magnitude of BP change between the

Table 1. Baseline demographic data for all subjects and for normotensive and hypertensive groups

	All (n = 81)	Normotensive (n = 35)	Hypertensive (n = 46)
Age (y)	67 ± 6 (55–81)	68 ± 6 (55–81)	67 ± 6 (56–79)
Gender m:f	37:44	16:19	28:18
BMI (kg/m^2)	27 ± 4 (19–35)	26 ± 4 (20–35)	28 ± 4 (19–35)*
Daytime ambulatory BP			
Systolic BP (mm Hg)	140 ± 18 (102–206)	124 ± 8 (102–135)	152 ± 12 (137–206)*
Diastolic BP (mm Hg)	83 ± 10 (59–121)	76 ± 6 (59–85)	89 ± 9 (71–121)*
Mean BP (mm Hg)	103 ± 12 (76–151)	93 ± 6 (76–102)	111 ± 9 (96–151)*
Heart rate (beats/min)	74 ± 9 (56–93)	71 ± 8 (57–89)	76 ± 9 (56–93)*
Finapres BP			
Systolic BP (mm Hg)	151 ± 22 (103–208)	137 ± 17 (103–191)	162 ± 19 (126–208)*
Diastolic BP (mm Hg)	77 ± 12 (53–113)	72 ± 9 (53–89)	80 ± 13 (58–113)*
Mean BP (mm Hg)	102 ± 15 (68–147)	94 ± 11 (68–119)	108 ± 15 (79–147)*
Cardiac BRS (ms/mm Hg)	6.4 ± 2.7 (1.1–15.2)	7.2 ± 2.7 (1.1–15.2)	5.7 ± 2.5 (1.9–13.2)*
Mean MCAV (cm/sec)†	44 ± 8 (27–63)	45 ± 8 (28–61)	43 ± 8 (27–63)

* Significant difference between normotensive and hypertensive groups ($P \leq .05$).
† Mean of right and left MCAVs.
Data presented as mean ± SD (range).
BMI = body mass index; BRS = baroreceptor sensitivity; MCAV = middle cerebral artery flow velocity.

normotensive and hypertensive groups for any BP stimulus (Table 2).

Dynamic CA

The dynamic ARI and magnitude of BP change for each of the five stimuli for the whole group are shown in Table 3.

No significant correlation was found between dynamic ARI determined using HDG, THC, VLS, PT, or NT with age, BMI, or any parameter of daytime ambulatory or Finapres BP. No significant difference was seen in dynamic ARI from any BP stimulus between the normotensive and hypertensive groups (Table 3).

In a subset of 27 subjects (8 normotensive; 19 hypertensive) who had complete data for dynamic ARI from THC, VLS, PT, and NT (Table 4), there was no significant difference in dynamic ARI between maneuvers (two-way ANOVA, maximum difference 95% one-sided CI (0, 1.6), $P = .81$). Within this group no significant difference was seen in dynamic ARI or magnitude of BP stimulus between the normotensive and hypertensive groups (Table 4).

Cardiac BRS was lower in the hypertensive group ($P = .023$) (Table 1) and decreased with increasing daytime ambulatory systolic BP and MAP, respectively ($r = 0.33$, $P = .005$ and $r = 0.30$, $P = .011$) but not with age ($r = 0.16$; $P = .2$).

Discussion

There is a large body of work, including both human and animal studies, on the effects of hypertension on cerebral hemodynamics and cerebrovascular histology but very little data exist so far involving the influence of increasing systemic BP levels on dynamic CA or the efficiency of

Table 2. Static ARI and BP changes for THC, HDG, and LBNP

		All		Normotensive		Hypertensive	Difference Static ARI (95% CI)
THC							
Static ARI %	n = 68	52 (31–86)	n = 28	49 (27, 96)	n = 40	56 (35, 78)	7 (−24, 15)
BP change (mm Hg)		17 (14–23)		16 (13, 22)		18 (15, 27)	
HDG							
Static ARI %	n = 67	45 (12–68)	n = 32	40 (14, 63)	n = 35	52 (10, 73)	12 (−24, 11)
BP change (mm Hg)		17 (14–21)		17 (13, 21)		19 (14, 22)	
LBNP							
Static ARI %	n = 36	64 (16–100)	n = 18	83 (45, 100)	n = 18	52 (5, 91)	31 (−2, 45)
BP change (mm Hg)		16 (14–19)		16 (14, 19)		15 (12, 19)	

Data presented as median and IQR.
There were no significant differences between normotensive and hypertensive groups for static ARI from any maneuver ($P > .05$).
THC = thigh cuff; HDG = hand grip; LBNP = lower body negative pressure; ARI = autoregulatory index.

Table 3. Dynamic ARI and BP change for HDG, THC, VLS, PT, and NT

	All		Normotensive		Hypertensive		Difference Dynamic ARI (95% CI)
HDG							
Dynamic ARI	$n = 27$	3.9 (0.5, 7.6)	$n = 13$	4.4 (0.5, 8.4)	$n = 14$	3.0 (0.4, 6.5)	1.4 (−1.5, 4.7)
BP change (mm Hg)		−15 (−12, −21)		−13 (−11, −25)		−17 (−13, −22)	
THC							
Dynamic ARI	$n = 51$	6.6 (5.4, 7.5)	$n = 21$	6.5 (5.5, 8.1)	$n = 30$	6.7 (5.2, 7.3)	−0.2 (−0.8, 1.3)
BP change (mm Hg)		−15 (−13, −18)		−14 (−13, −19)		−15 (−14, −18)	
VLS							
Dynamic ARI	$n = 63$	5.6 (3.7, 7.3)	$n = 27$	6.6 (4.0, 8.0)	$n = 36$	5.4 (3.6, 6.9)	1.2 (−0.1, 2.4)
BP change (mm Hg)		29 (22, 37)		26 (18, 33)		31 (24, 40)	
PT							
Dynamic ARI	$n = 65$	5.9 (3.8, 7.3)	$n = 24$	6.3 (3.9, 7.9)	$n = 41$	5.5 (3.3, 7.2)	0.8 (−0.4, 1.9)
BP change (mm Hg)		12 (11, 16)		12 (11, 15)		13 (11, 18)	
NT							
Dynamic ARI	$n = 58$	5.7 (4.4, 7.4)	$n = 22$	5.5 (4.1, 7.0)	$n = 36$	6.0 (4.4, 7.5)	−0.5 (−1.8, 0.7)
BP change (mm Hg)		−14 (−12, −16)		−14 (−11, −16)		−14 (−13, −17)	

Data presented as median and IQR.

There were no significant differences between normotensive and hypertensive groups for dynamic ARI from any maneuver ($P > .05$).

VLS = valsalva; PT = positive spontaneous transient; NT = negative spontaneous transient. Other abbreviations as in Table 2.

Table 4. Dynamic ARI for THC, VLS, PT, and NT in the group with data for all stimuli

	All		Normotensive		Hypertensive		Difference Dynamic ARI (95% CI)
THC							
Dynamic ARI	$n = 27$	6.6 (4.9, 7.7)	$n = 8$	6.9 (4.9, 8.2)	$n = 19$	6.6 (4.9, 7.3)	0.7 (−1.3, 2.2)
BP change (mm Hg)		−16 (−14, −20)		−15 (−13, −18)		−17 (−15, −21)	
VLS							
Dynamic ARI	$n = 27$	5.6 (3.7, 7.0)	$n = 8$	6.7 (3.9, 7.0)	$n = 19$	5.6 (3.7, 7.4)	0.5 (−1.4, 2.7)
BP change (mm Hg)		35 (27, 41)		32 (23, 41)		35 (28, 40)	
PT							
Dynamic ARI	$n = 27$	5.6 (3.9, 7.3)	$n = 8$	5.5 (4.0, 7.6)	$n = 19$	5.9 (3.9, 7.3)	0.1 (−1.9, 1.9)
BP change (mm Hg)		14 (11, 19)		14 (11, 18)		13 (11, 21)	
NT							
Dynamic ARI	$n = 27$	5.6 (4.5, 7.5)	$n = 8$	6.3 (5.3, 7.5)	$n = 19$	5.4 (4.4, 7.5)	0.5 (−1.1, 2.8)
BP change (mm Hg)		−15 (−12, −17)		−15 (−11, −18)		−14 (−13, −17)	

Data presented as median and IQR.

There were no significant differences between normotensive and hypertensive groups for dynamic ARI from any maneuver ($P > .05$).

Abbreviations as in Tables 2 and 3.

static CA. This large study of middle-aged and older volunteers is the first to our knowledge investigating the effect of sustained but, importantly, never treated hypertension on dynamic CA and the efficiency of static CA. The range of tests included both pressor and depressor stimuli in the measurement of both static and dynamic ARI and no association was found between BP levels and static ARI or dynamic ARI for whichever type of BP stimulus used.

Using similar methodology, our group has shown reductions in dynamic CA in the range 1.3 to 2.6 after an acute ischemic stroke[6,18] and in patients with vasovagal syncope[19] in comparison to normal controls.

Our results are in keeping with the smaller study of Lipsitz et al,[9] who reported that, in all three of their study groups, young normotensive ($n = 10$; baseline BP 116 ± 4/69 ± 3 mm Hg), elderly normotensive ($n = 10$; 123 ± 5/68 ± 4 mm Hg), and elderly treated hypertensive ($n = 10$; 153 ± 6/90 ± 3 mm Hg), there was a reduction in CVR and a relative preservation of CBFV in response to an immediate postural decrease in BP, indicating that autoregulatory capacity was retained. Another small study comparing currently treated hypertensive patients ($n = 21$; baseline mean BP 92 ± 12 mm Hg) and normotensive controls ($n = 21$; baseline mean BP 67 ± 11 mm Hg) has also demonstrated no differences in the rate of change of CVR in response to the BP decrease induced by standing after squatting as a measure of dynamic CA between the two groups.[8] It is unclear what effect antihypertensive treatment may have had on autoregulatory capacity in these studies or whether any potential effects are reversed once medication has stopped.

Sustained hypertension causes degenerative changes in arteriolar walls, with narrowing of the lumen[20] and increased CVR,[21] and is also associated with reduced endothelial NO synthesis.[22] Nitric oxide is involved in the regulation of basal CBF and dynamic CA,[7] and could represent a mechanism by which hypertension might affect dynamic CA. Although some studies suggested that CBF was unaffected by sustained hypertension,[23] other studies have shown a reduction in CBF[21] and cerebral oxygen uptake.[24] Cerebrovascular reactivity to inhaled CO_2 in humans has been shown either to be reduced,[25] or to remain unchanged,[26] with sustained hypertension and it has been suggested in animal experiments that the effect may depend on the duration of the hypertension.[27] It is well established that the lower limits of static CA are increased in hypertension in human[28] and animal[29] studies and there is evidence to suggest this may be prevented, or modified, by good BP control, at least in the early stages before histologic changes become permanent.[11] However, in a group of 4 patients with severe uncontrolled hypertension, no overall improvement in the lower limit of static CA was seen after 8 to 12 months of antihypertensive treatment, although in 1 patient the autoregulatory curve appeared to have moved toward normal.[28] There is little information on the effect of sustained hypertension on the upper limit of static CA in humans, but in baboons this has been shown to be increased.[30]

The range of systemic BP levels in this study population was wide with daytime ambulatory BP ranging from 102/59 to 206/121 mm Hg, but is likely that all subjects remained on the cerebral autoregulatory plateau despite the BP stimuli.

One of the strengths of this study is the inclusion of multiple autoregulatory stimuli including both pressor and depressor BP stimuli to test both static and dynamic autoregulation. It is not known whether responses to pressor and depressor stimuli are equivalent either at so-called normal BP levels or after adaptive changes to hypertension are likely to have occurred. In this study dynamic ARI was not influenced by the nature of the physiologic maneuver in the group of patients with complete data for THC, VLS, PT, and NT tests in keeping with previous results.[15] No significant difference in dynamic ARI in the group or static ARI was seen between the group ARI means for the different pressor and depressor BP stimuli.

Other methods of assessing CA, using techniques such as frequency or time domain analysis,[31] can also be applied to our data and such analyses confirmed the lack of difference between normotensive and hypertensive subsets (data not shown).

In keeping with previous work,[12] aging did not affect dynamic ARI or static ARI determined using THC and LBNP. A decrease in cardiac BRS was seen with increasing BP levels, as shown in other studies,[32] but not with age, also consistent with other work that has shown the main age-related decrease in cardiac BRS occurs in the age range 20 to 50 years,[33] which is younger than our study population. This suggests that our subjects were representative of the general population in terms of the expected age- and BP-associated cardiovascular changes.

Limitations

The use of CBFV as a surrogate for CBF is only valid if the diameter of the insonated vessel remains constant. It was recently reported that MCA diameter changes were not detected on magnetic resonance imaging during LBNP where the BP changes were larger than seen in this study, or during changes in end-tidal CO_2 levels.[2] Measurement of MCAV using TCD was seen to accurately reflect relative changes in direct measurement of internal carotid artery flow in response to THC release.[3] Direct observation of the MCA during surgery detected only minor changes in diameter with relatively large changes in BP and arterial CO_2 tension.[4] At rest there are unlikely to be any significant changes in MCA diameter.

The volunteers did not record their activities during the 24-h BP assessment but as a distinct division in BP levels was made between those classified as normotensive and hypertensive it is unlikely that misclassification of BP status systematically affected the results. Also no correla-

tion was found between static or dynamic ARI and any parameter of BP in the whole study group.

In this age group there may be some subjects with occult cerebrovascular disease and the subjects were not neuroradiologically screened. Studies have shown altered CBF, cerebrovascular reactivity,[34] and CA,[35] in relation to cerebral deep white matter lesions that are not uncommon in hypertensive patients and older subjects. Occult cerebrovascular disease may explain some of the low dynamic ARI values seen, but similar values were seen in both normotensive and hypertensive groups. Also, although no subject had evidence of significant carotid artery disease by auscultation for carotid bruits and none of the subjects had MCA velocities that indicated evidence of carotid stenosis, we cannot exclude that some subjects may have had subclinical carotid artery disease, as carotid duplex scanning was not routinely performed. However, as no difference was found between CA in the normotensive and hypertensive groups, it is unlikely that the results were significantly affected by occult cerebrovascular or carotid disease.

Most of the BP stimuli used to test CA in this study were of relatively small magnitude (~15 mm Hg; our aim being to mimic normal physiological changes seen during daily activities), except for VLS where the mean increase in BP was almost twice that seen with other tests and, although autoregulation was seen to occur, perhaps larger BP changes would reveal differences in CA between normotensive and hypertensive subjects but would also risk crossing the limits of the autoregulatory plateau.

In conclusion, increasing systemic BP levels are not associated with a significant alteration in either static or dynamic CA, although the expected decrease in cardiac BRS with increasing BP levels was found.

If differences in such parameters are found in similar study groups then this is likely to be due to pathologic features other than increased BP levels.

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