PAPER

Dynamic cerebral autoregulation and beat to beat blood pressure control are impaired in acute ischaemic stroke

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Objectives: Hypertension and chronic cerebrovascular disease are known to alter static cerebral autoregulation (CA) but the effects of acute stroke on dynamic CA (dCA) have not been studied in detail. Those studies to date measuring dCA have used sympathetically induced blood pressure (BP) changes, which may themselves directly affect dCA. This study assessed whether dCA is compromised after acute stroke using spontaneous blood pressure (BP) changes as the stimulus for the dCA response.
Methods: 56 patients with ischaemic stroke (aged 70 (SD 9) years), studied within 72 hours of ictus were compared with 56 age, sex, and BP matched normal controls. Cerebral blood flow velocity was measured using transcranial Doppler ultrasound (TCD) with non-invasive beat to beat arterial BP levels, surface ECG, and transcutaneous CO_2 levels and a dynamic autoregulatory index (dARI) calculated.
Results: Beat to beat BP, but not pulse interval variability was significantly increased and cardiac baroreceptor sensitivity (BRS) decreased in the patients with stroke. Dynamic CA was significantly reduced in patients with stroke compared with controls (strokes: ARI 3.8 (SD 2.2) and 3.2 (SD 2.0) for pressor and depressor stimuli respectively *v* controls: ARI 4.7 (SD 2.2) and 4.5 (SD 2.0) respectively ($p<0.05$ in all cases)). There was no difference between stroke and non-stroke hemispheres in ARI, which was also independent of severity of stroke, BP, BP variability, BRS, sex, and age.
Conclusion: Dynamic cerebral autoregulation, as assessed using spontaneous transient pressor and depressor BP stimuli, is globally impaired after acute ischaemic stroke and may prove to be an important factor in predicting outcome.

Cerebral autoregulation (CA) is the ability of the brain to maintain relatively constant cerebral blood flow (CBF) despite changes in perfusion pressure. Before the development of transcranial Doppler ultrasound, static CA was assessed using steady state blood pressure (BP) changes and assessing the alteration in CBF without taking into account the speed at which the CBF recovers following a change in BP. Transcranial Doppler ultrasound (TCD) and non-invasive beat to beat BP monitors have allowed the dynamic relation between cerebral blood flow velocity (CBFV) and mean arterial pressure (MAP) to be quantified (changes in BP taking place over 5 to 10 seconds) giving a measure of dynamic CA (dCA). Dynamic CA may have different underlying pathophysiological control mechanisms to static CA.[1] Dynamic CA has been shown to be influenced differently from static CA in disease states such as stroke.[2]

Non-pharmacological manoeuvres to induce rapid perturbations in BP—for example, the sudden release of thigh cuffs or the Valsalva manoeuvre—have been used to assess dCA but are problematic.[3] They may be unacceptable or impractical for some patients and can induce changes in sympathetic nervous system activity, respiration, cardiac output, and carbon dioxide concentration, all of which may affect dCA directly or indirectly. These potential problems could be avoided by using spontaneous BP fluctuations in recordings made at rest.

A widely applicable method of measuring dCA in patients with acute stroke is needed to allow detailed investigation of the relation between altered cardiovascular homeostasis and outcome, and may ultimately be relevant in the treatment of BP in the acute stroke period.

After acute stroke normal cardiovascular homeostatic mechanisms are impaired and in the immediate postictal phase BP levels are often increased, tending to fall spontaneously over the subsequent 10–14 days.[4–6] Although hypertension is a major risk factor for primary stroke, its prognostic relevance in the acute poststroke period is uncertain. If CA is impaired after acute ischaemic stroke, then CBF flow becomes dependent on systemic BP and increasing BP may result in cerebral oedema or haemorrhagic transformation of the infarct, whereas reducing systemic BP could reduce flow to the ischaemic penumbra and increase infarct size.

Clinical studies reporting BP and outcome after acute stroke are at variance[7–9] and have not clarified these diametrically opposed theoretical views as to the benefits of BP reduction after acute stroke and the role of CA has not been investigated. Beat to beat BP variability hyperperfusion is known to be increased in acute stroke[10] and associated with a worse prognosis in terms of death and disability, independently of MAP levels and stroke severity.[11] This adverse outcome associated with increased BP variability could be mediated by impairment in dCA, which could result in hyperperfusion and/or hypoperfusion of the ischaemic penumbra with spontaneous pressor and depressor BP changes. Cardiac baroreceptor sensitivity (BRS) is also reduced after stroke[12] and may account for the increased BP variability seen. It is therefore important to assess the relation between dCA, BP, and cardiac BRS, to understand how these parameters influence one another and their clinical significance.

The aims of this study were to assess if dCA is impaired after acute cerebral infarction, using spontaneous, rather than induced, transient changes in BP as the BP stimulus, and to

Abbreviations: CA, cerebral autoregulation; CBF, constant cerebral blood flow; BP, blood pressure; TCD, transcranial Doppler ultrasound; CBFV, cerebral blood flow velocity; MAP, mean arterial pressure; dCA, dynamic CA; BPV, BP variability; BRS, baroreceptor sensitivity; OCSP, Oxford Community Stroke Project; MCA, middle cerebral artery; dARI, dynamic autoregulatory index; PI, pulse interval; TACI, total anterior circulation infarct; PACI, partial anterior circulation infarct; LACI, lacunar infarct; POCI, posterior circulation infarct;

Table 1 Baseline demographic data for stroke and control groups

	Control n=56	Stroke n=56
Age (y)	69 (7) (51 to 81)	70 (9) (45 to 87)*
Sex (M:F)	43:13	43:13
BMI (kg/m^2)	28 (4) (20 to 35)	25 (4) (17 to 35)*
Systolic BP (mm Hg)	150 (22) (103 to 208)	156 (29) (104 to 215)
Diastolic BP (mm Hg)	76 (13) (53 to 112)	80 (17) (47 to 129)*
Mean BP (mm Hg)	101 (15) (68 to 146)	106 (18) (71 to 146)
Mean pulse interval (ms)	960 (154) (652 to 1325)	866 (114) (584 to 1195)*
CBFV (cm/s)	44 (9)	41 (11)
Barthel index	N/A	60 (35, 89)

BMI,body mass index; *p=0.05 for differences between stroke and control groups; blood pressure taken as mean of two 10 minute Finapres recordings; Data are presented as mean (SD) (range). Barthel index is presented as median and IQR.

study the relation between the changes in dCA after stroke with cardiac BRS and beat to beat BPV.

SUBJECTS AND METHODS

Methods

Fifty six patients with ischaemic stroke diagnosed by CT or MRI were recruited within 72 hours of ictus from the acute stroke units at Glenfield Hospital NHS Trust and Leicester General Hospital. Stroke types were classified using the Oxford Community Stroke Project (OCSP) classification[13] and functional severity was graded using the Barthel index.[14] Patients were excluded if they had a history of previous stroke. They were pair matched with 56 controls for age (to within 10 years), sex, and MAP (to within 10 mm Hg), who were recruited from a volunteer register and from departmental staff. Some controls were hypertensive (BP≥160/90 mm Hg) but were otherwise free from cardiovascular or cerebrovascular disease based on history, clinical examination, and baseline investigations including a 12 lead ECG. None of the patients or controls was in atrial fibrillation or was diabetic, had autonomic disturbance, or were taking any medication known to affect the cardiovascular or autonomic nervous system at the time of the study. No other criteria were set for inclusion or exclusion of patients or controls.

Protocol

Subjects avoided caffeine, nicotine, and alcohol for 12 hours before the recordings, which were made in a dedicated research room kept at a constant temperature (20°C–24°C) with external stimuli minimised. Subjects lay supine with the head supported on two pillows and after resting for 10 minutes supine baseline BP was recorded at the brachial artery using an automatic BP monitor (Omron 711).

The middle cerebral arteries (MCAs) were insonated bilaterally as described by Aaslid *et al*,[15] and CBFV was measured indirectly using TCD (SciMed QVL 120X, Bristol, UK). Once the MCAs had been identified through the temporal windows (the thinnest part of the temporal bone) the probes were held in place with a custom made head frame. A three lead surface ECG was fitted and beat to beat arterial BP was measured using a servo-controlled plethysmograph (Finapres 2300, Ohmeda, USA) on the middle finger of the non-paretic hand, supported at atrial level. Carbon dioxide (pCO_2) concentrations were measured using a previously validated transcutaneous gas monitor (TINA, Radiometer, Copenhagen). Once a stable baseline had been achieved (<10% variation in BP and CBFV) two recordings of 5 minutes duration, taken 5 minutes apart, were then made with the patient remaining supine and awake and the mean values from these two recordings were used for statistical analysis. A fast Fourier transform was applied to convert the Doppler signals into maximum frequency envelopes with a window of 6.25 ms. The Finapres, TINA, and ECG output signals were directly converted at 200 Hz and all data were recorded synchronously in real time onto digital tape (DAT, Sony PC-108M). The data were then read onto a dedicated microcomputer for editing and analysis where they were first individually inspected and artefactual data spikes removed by linear interpolation. Using spline interpolation and resampling the data at 0.2 seconds a uniform time base for all the data was achieved and an estimate of mean CBFV, systolic BP (SBP), diastolic BP (DBP), and MAP levels were calculated for each cardiac cycle.

Dynamic cerebral autoregulation

The MAP trace was inspected and spontaneous transient pressor and depressor changes were manually selected. Using the method of Tiecks *et al*,[1] the calculated dynamic autoregulatory index (dARI) was derived from the response of the CBFV to spontaneous transient pressor and depressor changes in MAP (transient BP changes defined as≥5 mm Hg). 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. The dARI was graded to one decimal place according to where it most closely fitted in the family of curves with a dARI of 0 indicating absent dCA and 9 perfect dCA.

Cardiac baroreceptor sensitivity (BRS) and SBP and PI variability

Using inhouse software, power spectral analysis estimates of pulse interval (PI) variability and SBP variability were obtained by calculation of the square root of the powers of PI and SBP respectively for the very low frequency (VLF) band (0.02 to 0.05 Hz), the low frequency (LF) band (0.05 to 0.15Hz), and the high frequency (HF) band (0.15 to 0.4Hz). Power spectral estimates of the cardiac BRS were obtained by calculation of the α index (square root of the ratio of the powers of PI to SBP) for the low frequency band.[12] Systolic blood pressure, MAP, and DBP beat to beat variability were separately calculated as the SD of the beat to beat changes derived from the 10 minute baseline recordings.

Statistical methods

Student's paired *t* tests were used for comparison between the individual pairs for patients with stroke and controls and to test for differences within non-stroke and stroke hemispheres in the same patient. These data are presented as mean (SD) along with 95% confidence intervals (95% CIs). Data not normally distributed were compared with the Mann-Whitney test, which was used for comparison of variables between right hemispheric and left hemispheric strokes and these data are presented as median and interquartile range (IQR).To compare variables between three categories of stroke types a Kruskal-Wallis test was used. Linear regression was used to assess the relation between ARI and age, sex, MAP, stroke severity, BRS, and BP variability. Two way analysis of variance (ANOVA) was used to compare the differences between very

Table 2 Dynamic cerebral autoregulation index (dARI), along with magnitude and rate of blood pressure change for spontaneous transient pressor and depressor stimuli in the stroke and control groups

	Stroke	Control	Difference (95% CI)	p Value
Pressor stimulus (n=48):				
BP rise (mm Hg)	9.2 (2.8)	8.7 (2.8)	0.5 (4.8) (0.9 to 1.9)	0.47
Rate of BP change (mm Hg/s)	3.4 (1.9)	3.1 (1.1)	0.3 (2.3) (0.4 to 0.9)	0.42
DARI	3.2 (2.0)	4.5 (2.0)	1.3 (2.9) (0.5 to 2.1)	0.003
Depressor stimulus (n=47):				
BP fall (mm Hg)	10.3 (4.2)	9.5 (3.2)	0.8 (3.2) (0.9 to 2.5)	0.33
Rate of BP change (mm Hg/s)	2.9 (1.7)	2.7 (1.2)	0.2 (2.2) (0.4 to 0.9)	0.46
DARI	3.8 (2.2)	4.7 (2.2)	1.0 (2.9) (0.1 to 1.8)	0.03

Mean of data for right and left hemispheres used in each case. Data are presented as mean (SD); n, number of stroke and control matched pairs used for comparison; Not all subjects had a pressor or depressor stimulus=5 mm Hg during the two 5 minute recordings (see results section); p value for differences between stroke and control groups.

Table 3 Differences in dARI in patients with stroke between stroke hemispheres and with pressor and depressor stimuli

	Pressor stimulus		Depressor stimulus		
	n	dARI (IQR)	n	dARI (IQR)	Difference in dARI between pressor and depressor stimuli† (95% CI)
Right hemispheric stroke:					
Affected side	20	3.2 (1.4 to 5.0)	22	3.7 (1.7 to 6.6)	0.4±2.4 (1.6 to 0.7) p=0.42
Non-affected side	19	3.0 (1.8 to 4.8)	20	4.0 (2.2 to 5.3)	0.3±1.4 (1.0 to 0.4) p=0.35
Left hemispheric stroke:					
Affected side	28	3.0 (2.1 to 4.5)	29	2.8 (1.8 to 4.8)	0.4 (2.7) (0.7 to 1.5) p=0.47
Non-affected side	30	3.3 (0.6 to 4.8)	29	3.3 (1.0 to 5.6)	0.0 (3.0) (1.2 to 1.1) p=0.94
Difference between right and left hemispheric stroke* (95% CI)		0.1 (1.5 to 1.1) p=0.93		0.7 (0.8 to 2.1) p=0.37	

Data are presented as medians and interquartile range; *Comparison between right and left hemisphere strokes (using Mann-Whitney test); †Comparison of dARI derived from pressor and depressor stimuli (Student's paired *t* test); A spontaneous transient blood pressure rise or fall≥5 mm Hg could not be found in four and three patients with stroke respectively.

low frequency, low frequency, and high frequency variability in pulse interval and SBP in each group. Statistical significance was taken at the 5% level using the statistical package Minitab for Windows, release 12.21, Minitab Inc. All participants gave written informed consent and the Leicestershire ethics committee approved the study.

RESULTS

Fifty six patients with stroke individually pair matched for age, sex, and MAP with controls were studied; baseline demographic details are given in table 1. Using the OCSP classification the stroke group comprised 25 total and partial anterior circulation infarcts (TACI and PACI), 21 lacunar infarcts (LACI), and 10 posterior circulation infarcts (POCI).

Despite pair matching, the stroke group as a whole was 2 (SD 5) years older than the control group ($p<0.05$) and their DBP was also slightly higher (4 (SD 15) mm Hg, 95% CI 0–8; $p<0.05$), although there was no significant difference in MAP or SBP (table 1). Pulse interval was lower in the stroke group than in the control group by 94 (SD 177) ms (95% CI 44–144, $p<0.001$). Transcutaneous CO_2 concentrations remained constant in all subjects throughout the study and there was no difference between patients with stroke and controls.

Of the 56 patients with stroke, a spontaneous transient BP rise or fall equal to or greater than 5 mm Hg could not be found in four and three patients respectively, and for the 56 controls, a spontaneous transient BP rise or fall equal to or greater than 5 mm Hg could not be found in four and seven subjects respectively.

Mean CBFV was similar for both hemispheres in the stroke and control groups and also between controls and the non-affected side in patients with stroke (43.5 (SD 8.7) cm/s and 42.1 (SD 10.6) cm/s respectively). No difference was found in the magnitude or rate of change of spontaneous pressor and depressor BP transients between patients with stroke and controls (table 2).

There was no significant difference in dARI between the affected and unaffected hemispheres in the stroke group (table 3) or between the right and left hemispheres in the controls so the mean value for the two hemispheres was used in further comparisons. Dynamic CA, whether assessed using pressor or depressor BP transients, was significantly reduced in patients with stroke compared with controls (table 2). Linear regression showed that the dARI in both patients with stroke and controls was independent of baseline BP, age, and sex. Stroke type, defined using the OCSP classification, did not significantly influence dARI (table 4). No significant correlation was found between stroke severity, as reflected by the Barthel index, and dARI derived using pressor BP stimuli ($p=0.09$) or depressor stimuli ($p=0.052$) when tested using Spearman's rank correlation test.

Two way ANOVA showed that very low frequency, low frequency, and high frequency variability in pulse interval and SBP were significantly different from one another within each study group, strokes and controls ($p<0.005$) (table 5).

Variability in SBP was significantly greater in the stroke group than in the controls in the very low frequency band ($p=0.008$) but not in the low frequency or high frequency bands as assessed using power spectral analysis but was similar in the low frequency and high frequency bands (table 5). The SBP, DBP, and MAP variabilities were also all significantly higher in the stroke group than the controls when taken as the SD of all measurements during the recording period, being 8.2 (SD 3.1) mm Hg, 3.9 (SD 1.5) mm Hg, and 5.2 (SD 1.8) mm Hg respectively in the patient group, and 6.7 (SD 2.1 mm Hg, 3.2 (SD 1.3 mm Hg, and 4.3 (SD 1.5) mm Hg respectively in the control group ($p<0.05$ for all BP groups). Variability in PI was similar in the patients with stroke and controls, and between patients with right and left hemispheric stroke

Table 4 dARI, pulse interval, and SBP variability and cardiac baroreceptor sensitivity for patients with stroke in different OCSP classification groups

	PACI /TACI (n=25)	LACI (n=21	POCI (n=10)
dARI pressor:			
Affected hemisphere	3.0 (2.0 to 4.0)	3.4 (1.4 to 5.0)	4.3 (2.9 to 5.2)
Unaffected hemisphere	2.3 (0.4 to 5.4)	3.5 (1.9 to 4.1)	3.0 (1.8 to 4.5)
dARI depressor:			
Affected hemisphere	2.9 (2.0 to 5.7)	3.4 (1.7 to 6.0)	2.8 (1.4 to 4.2)
Unaffected hemisphere	4.8 (1.0 to 6.0)	3.2 (1.5 to 4.9)	4.3 (1.5 to 5.2)
Pulse interval variability (ms)	25 (20 to 35)	20 (18 to 27)	22 (15 to 30)
SBP variability (mm Hg)	6.0 (4.9 to 8.0)	7.3 (5.5 to 9.3)	4.7 (4.1 to 8.4)
BRS (ms/mm Hg)	4.3 (3.5 to 6.7)	4.2 (2.5 to 5.9)	5.2 (2.4 to 7.8)
Barthel index	43 (20 to 65)	80 (54 to 100)	65 (44 to 93)

Data are expressed as median and interquartile range; BRS, square root of the ratio of the powers of PI to SBP from spectral analysis; SBP variability , square root of the total power of SBP from spectral analysis; PI variability, square root of the total power of PI from spectral analysis; no significant differences were seen between stroke types for the above parameters.

Table 5 Pulse Interval and SBP variability assessed by spectral analysis

		Pulse interval variability (ms)				SBP variability (mm Hg)			
Frequency ranges*	n	All Frequencies	VLF	LF	HF	All Frequencies	VLF	LF	HF
Stroke	51	28.8 (19.7)	16.4 (12.7)	13.0 (10.7)	10.4 (7.4)	6.6 (2.2)	4.2 (1.8)	2.6 (1.1)	1.9 (0.9)
Control	51	31.2 (13.4)	16.0 (7.6)	14.6 (6.9)	13.1 (7.7)	5.7 (1.7)	3.4 (1.2)	2.5 (0.8)	1.8 (0.9)
Difference		2.4 (23.9)	0.4 (14.3)	1.6 (13.4)	2.7 (11.5)	1.0 (2.9)	0.8 (2.1)	0.1 (1.4)	0.2 (1.3)
95% CI		(–4.3 to 9.1)	(–4.0 to 3.6)	(–2.1 to 5.4)	(–0.6 to 5.9)	(0.2 to 1.8)	(–0.2 to –1.4)	(–0.5 to 0.3)	(–0.5 to 0.2)
p Value		0.476	0.849	0.388	0.107	0.018	0.008	0.49	0.337

*VLF=0.02–0.05 Hz; LF=0.05–0.15 Hz; HF=0.15–0.4 Hz; Data are presented as mean (SD) with 95% CI; p values are for the differences between stroke and control groups; two patients with stroke and three controls had too many ectopic beats on their ECG to be included in spectral analysis, therefore 51 pairs used in analysis.

Table 6 Pulse interval variability and SBP variability for patients with right and left hemispheric stroke

		Pulse interval variability (ms)				SBP variability (mm Hg)			
Hemisphere affected by stroke	n	All Frequencies	VLF	LF	HF	All Frequencies	VLF	LF	HF
Right	24	24.7 (19.3 to 31.0)	13.2 (9.8 to 18.7)	9.9 (8.9 to 13.7)	8.1 (6.6 to 12.2)	6.1 (4.8 to 8.2)	3.7 (3.0 to 5.0)	2.4 (1.7 to 3.1)	1.9 (1.2 to 2.7)
Left	30	21.2 (18.0 to 30.6)	12.4 (10.1 to 15.9)	8.9 (6.3 to 13.0)	6.8 (4.7 to 12.2)	6.4 (4.5 to 8.5)	3.7 (2.8 to 5.3)	2.5 (1.6 to 3.4)	1.7 (1.2 to 2.3)
95% CI		(–2.8 to 7.7)	(–2.0 to 4.9)	(–0.4 to 4.1)	(–0.9 to 3.4)	(–1.0 to 1.6)	(–0.7 to 1.2)	(–0.4 to 0.9)	(–0.3 to 0.7)
p Value		0.38	0.40	0.11	0.21	0.83	0.86	0.46	0.4

Data are presented as median and interquartile range; two patients had too many ectopic beats on their ECG to be included in spectral analysis.

(tables 5 and 6). Multiple regression analysis showed that baseline mean BP and PI values for the study groups did not significantly influence these results.

Cardiac baroreceptor sensitivity was significantly reduced in the patients with stroke, being 4.9 (SD 2.6) ms/mm Hg compared with 6.2 (SD 3.2) ms/mm Hg in the control group (p=0.026).

Stroke type, as defined by the OCSP classification, or stroke severity (based on Barthel index) did not influence PI or SBP variability or BRS (table 4).

DISCUSSION

In the present study dCA in patients with stroke, assessed using spontaneous transient pressor and depressor changes in MAP recorded over a 10 minute period, was globally impaired, SBP variability was increased, and cardiac baroreceptor sensitivity reduced when compared with an age, sex, and MAP pair matched control group.

This is consistent with a smaller study that used only thigh cuff release to stimulate a depressor change, where a dARI value of 4.1 (SD 3.3) and 6.2 (SD 2.3) was found for the stroke and the control groups respectively.[2] As the thigh cuff technique is often painful it was unclear whether the previously reported difference was related to the possible increase in sympathetic nervous system activity provoked by the stimulus itself or was a true phenomenon related to cerebral ischaemia. That significant differences in dCA were also found using spontaneous transient pressor and depressor stimuli suggests that this is a true phenomenon but as the mechanisms underlying CA are poorly understood it cannot be assumed that pressor and depressor stimuli necessarily invoke the same pathophysiological mechanisms.

As far as we know this is the first use of spontaneous transient BP changes in the analysis of dCA in patients with stroke. The use of spontaneous transient changes in BP avoids stimulation of the sympathetic nervous system, eliminates the need for subject participation, and does not affect respiratory rate or depth and, hence, pCO2 concentrations and cardiac output, which may occur to varying degrees in interactive tests—for example, thigh cuff release or the Valsalva manoeuvre. In normal subjects dARI was found to be independent of the type of manoeuvre used to induce the BP change when

positive and negative spontaneous transients, thigh cuff release, the cold pressor test, isometric hand grip, lower body negative pressure release, and the Valsalva manoeuvre were tested despite the different magnitudes of the BP stimuli induced by the different manoeuvres.[3]

The reproducibility of the ARI derived using spontaneous transient changes in blood pressure has been reported by our group in normal volunteers, and no significant difference was found in dCA measured on two occasions 6 weeks apart, giving an SD of the difference for dynamic ARI of 2.3 and 2.6 based on pressor and depressor BP stimuli respectively.[16]

The reduction in dCA in patients with stroke compared with controls could not be accounted for by differences in systemic MAP or age as matching eliminated these as factors and, additionally, linear regression showed ARI to be independent of these variables. This is in keeping with recently published data from our group showing no effect of age[17] or BP[17 18] on dCA, and with work by Lipsitz *et al* showing that cerebral autoregulatory capacity is retained in elderly normotensive and elderly hypertensive subjects in response to orthostatic hypotension.[19] In the present study the stimuli used to test dCA were similar in the stroke and control groups in both the magnitude of the BP rise and fall and in its rate of change and so stimulus characteristics could also not account for the differences found.

The impairment in dCA was not confined to the stroke hemisphere and the lack of a significant difference in dCA between the affected and unaffected sides indicates a global impairment of dCA with stroke. It has previously been shown that CBF,[20 21] cerebral metabolism,[22 21] sCA,[23] and dCA[2] can be depressed both locally and distant from the site of infarction. The mechanism of this transhemispheric communication may be diaschisis where there is distant functional depression due to the effects of loss of axons (mainly facilitatory) arising at the site of the lesion and, in the case of the cerebral hemispheres, these may synapse with neurons in the contralateral hemisphere via the corpus callosum.

Overall BP variability was increased, mainly in the very low frequency band in patients with stroke compared with controls but no significant difference was found in pulse interval variability in any spectral band. In the BP spectra the high frequency band is largely independent of cardiac vagal tone and is mostly influenced by the mechanical effects of respiration on the heart and great vessels. The low frequency power is determined by a combination of factors including sympathetic activity and vagal tone, the cardiac baroreflex arc (which was impaired in the stroke group), and vasomotor reactivity. The very low frequency band is thought to be influenced by certain factors that contribute to vasomotor tone, such as the renin-angiotensin system, endothelial factors, and local thermoregulatory mechanisms. The increase in BP variability in the absence of a change in PI variability might be explained by changes in the baroreflex control of vasomotor tone, which has been demonstrated in acute patients with stroke[24] and by the reduction in cardiac baroreceptor sensitivity although the exact underlying mechanisms are uncertain. This study was not designed to consider the underlying mechanisms for these physiological changes.

Increased beat to beat BP variability has been shown to be associated with a worse prognosis in terms of death and disability in acute patients with stroke[25] although the exact mechanism of these findings is unknown but could be related to the impairment in dCA. The long term prognostic significance of these findings is currently undergoing assessment. No relation was seen between stroke severity, OCSP classification, or affected hemisphere and dCA, BRS, or BP variability but this may be just due to the size of the study.

A limitation of this work in common with any work using measurement of CBFV rather than CBF is that changes in CBF can only be reliably deduced from CBFV providing that changes do not occur in the diameter of the insonated vessel. It has been recently reported that changes in MCA diameter were not detected on MRI during the physiological stimuli of moderate lower body negative pressure where the BP changes were larger than seen in this study, or during changes in end tidal CO_2 concentrations.[26] The CBFV measured by transcranial Doppler ultrasound was seen to accurately reflect relative changes in internal carotid artery flow measured using electromagnetic flowmetry during open surgery when thigh cuff release was used to induce sharp decreases in blood pressure.[27] No change has been found in the diameter of large intracerebral arteries after the pressor response to an infusion of noradrenaline (norepinephrine) into the internal carotid artery.[28] At rest and with constant CO_2 concentrations there are unlikely to be any significant changes in MCA diameter.

We do not know whether the impairment of dCA is a permanent or transient change after stroke and, as yet, there are no long term follow up data available. Data obtained using thigh cuff release in the acute postictal phase and again at 20 days showed no recovery of dCA over that period.[29] We also do not know whether abnormalities in dCA occur as a consequence of the stroke, as is commonly supposed, or whether the reduction in dCA actually predates the stroke and therefore defines a population more at risk of cerebrovascular disease. More work is needed to explore the relation between impaired dCA and acute stroke.

CONCLUSION

The study has demonstrated that acute ischaemic stroke is associated with a global impairment of dynamic CA, as assessed using spontaneous pressor and depressor BP transients.

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