Original Contributions

Regional Cerebral Blood Flow in Essential Hypertension: Data Evaluation by a Mapping System

G. Rodriguez, F. Arvigo, S. Marenco, F. Nobili, P. Romano, G. Sandini, and G. Rosadini

Regional cerebral blood flow was studied by means of the ^{133}Xe inhalation method in 26 untreated and 10 treated patients with essential hypertension. The untreated subjects were divided into newly and previously diagnosed groups to assess the relation between regional cerebral blood flow and the duration of hypertension. The overall flow reduction was more marked in the frontal and temporal regions in the previously diagnosed group, and this was attributed to pathological changes in the district served by the middle cerebral artery. Regional temporal lobe impairment was also noted in the newly diagnosed and treated subjects. A significant correlation was found between regional cerebral blood flow and mean arterial blood pressure. (*Stroke* 1987;18:13–20)

HYPERTENSION is the primary prelude to stroke and other cerebrovascular diseases. Its status as a risk factor is apparent in several randomized and controlled epidemiological studies indicating a high correlation between blood pressure and the incidence of stroke. There is evidence, too, that proper drug management is effective in reducing the risk of cerebrovascular accidents, even in mild hypertensives.[1–4] Furthermore, though clear proof is not yet available, there is reason to suppose that the declining incidence of stroke in recent years is ascribable to extensive educational programs and the precise detection and therapy of hypertension.[5–7] Given this close relation between hypertension and cerebrovascular disease, the cerebral blood flow (CBF) is naturally a key parameter. While CBF changes have been demonstrated in chronic hypertension,[8–12] no specific data are available for mild or moderate forms or for during the initial stages of the disease. This study reports a ^{133}Xe inhalation assessment[13,14] of regional cerebral blood flow (rCBF) in patients with treated and untreated mild or moderate hypertension. The untreated subjects were divided into "newly" and "previously" diagnosed groups to look for a relation between CBF and the duration of hypertension. An age-matched population served as the control. A computer system providing a two-dimensional color mapping display devised in our laboratory[15] was used in the statistical processing to provide a visual indication of the rCBF.

From the Institute of Neurophysiopathology (G.R., F.A., S.M., F.N., G.R.), and the Department of Informatic and Computer Science, University Center of Cerebral Neurophysiology (P.R., G.S.), Genova, Italy.

Address for reprints: G. Rodriguez, MD, Institute of Neurophysiopathology, Ospedale San Martino, 16132 Genova, Italy.

Received December 6, 1985; accepted August 21, 1986.

Subjects and Methods

Patients with hypertension were selected from 162 subjects to form untreated (26 patients) and treated (10 patients) groups.

UNTREATED GROUP. 1) Mild (diastolic pressure 90–104 mm Hg) or moderate (diastolic pressure 105–114 mm Hg) hypertension according to Freis[16] as shown by conventional diagnostic assessment[17]; 2) no history of significant disorders, asymptomatic and normal neurological and general pictures, obese patients (more than 120% of ideal body weight) excluded; 3) normal serum cholesterol, triglycerides, glucose, and total proteins, normal hematocrit and platelet count; 4) no current treatment of any kind and no history of antihypertensive management.

A further distinction was drawn between patients diagnosed for the first time by us (newly diagnosed; Group 1: 6 men and 7 women aged 50–74 years, mean = 62.84 ± 6.78; mean arterial blood pressure [MABP] = 121.0 ± 5.19 mm Hg; Table 1) and those diagnosed at least 6 months previously (previously diagnosed; Group 2: 8 men and 5 women aged 50–72 years, mean = 61.30 ± 6.63; MABP = 122.90 ± 6.70 mm Hg; duration of hypertension 0.5–4 years, mean = 1.34 ± 1.10; Table 2).

TREATED GROUP. Group 3: 5 men and 5 women aged 50–72 years, mean = 63.10 ± 7.03, meeting criteria 1–3 of the untreated group; MABP = 112.30 ± 6.17; known duration of hypertension 0.5–20 years, mean = 8.15 ± 7.62; Table 3). These patients had been treated with various drugs since their hypertension was discovered.

The fundus oculi was examined in all patients in Groups 1, 2, and 3 (Tables 1–3). The Keith-Wagener classification was used in the assessment of retinopathy.

Table 1. Clinical Summary of the Newly Diagnosed Hypertensives (Group 1)

Case	Age (yr)	Sex	BP (mm Hg)	MABP (mm Hg)	MGV's (ISI)	Fundus (K-W)
1	61	F	165/95	118	40	0
2	68	M	170/95	120	44	I
3	50	F	190/100	130	47	0
4	69	F	175/95	122	40	II
5	60	F	170/110	130	41	0
6	68	F	160/100	120	45	I
7	74	M	165/100	122	42	I
8	62	M	160/100	120	36	0
9	57	F	140/100	113	48	0
10	53	M	150/100	117	45	0
11	68	M	150/100	117	46	II
12	64	M	180/100	127	50	I
13	63	F	150/100	117	43	0

M = male; F = female; BP = blood pressure; MABP = mean arterial blood pressure; MGV's = mean global ISI values; K-W = Keith-Wagener classification of hypertensive retinopathy.

The controls were healthy volunteers: 11 men and 15 women aged 48–80 years, mean = 62.05 ± 9.10; MABP = 97.65 ± 5.64.

Informed consent was received from all subjects.

All rCBF examinations were performed under the same laboratory conditions. rCBF at rest was measured by the ^{133}Xe inhalation method, using a Harshaw TASC 5 system with 32 detectors (16 on each hemisphere). Expired end-tidal P_{CO_2} was monitored using a Goddard Mark II capnograph.

The air–^{133}Xe mixture was administered through a facemask at 6–7 mCi/l in the first minute. The patient then received room air for 10 minutes. The washout curves were subjected to a two-compartment analysis[14] using a Digital PDP 11/04 computer. For the purpose of this report only the initial slope index (ISI) was considered, since it is regarded as the most indicative of cerebral pathology.[18] ISI values were not corrected for individual P_{CO_2} levels.[19] All subjects were normocapnic: Mean end-tidal P_{CO_2} values in Group 1 were 39.9 ± 3.2; in Group 2, 38.7 ± 3.9; in Group 3, 39.2 ± 4.2; in controls, 38.6 ± 3.3.

For statistical purposes, the mean ISI value of each probe (mean single probe values = MSPV's), of all probes in both hemispheres (mean global values = MGV's), and in each hemisphere (mean hemispheric values = MHV's) were calculated. Using the unpaired *t* test, MSPV's, MHV's, and MGV's were compared between each patient group and the controls, and among the groups of patients.

In untreated patients (Group 1 + Group 2), the MGV's were regressed against the duration of hypertension and age respectively; in the controls, MGV's were regressed against age. MABP's were correlated with MGV's in all subjects regarded as a single population. Analysis of variance (ANOVA) was used to evaluate interhemispherical differences in each group.

An additional statistical evaluation of rCBF was obtained with an original computer-assisted system developed in our laboratory.[15] Briefly, a) the skull locations of and relative distances between the 32 probes were shown on a 64 × 64 matrix. The matrix within each hemisphere was formed into triangular patches by lines joining triplets of nearby probes (Figure 1); b) the flow value for each probe was ascribed to the corresponding vertex of each triangle. The numerical values of the pixels inside each triangle were interpolated from the values at the vertices; c) a relation was established between a 12-grade green-to-red color scale and raw numerical data; d) simultaneous presentation of the interpolated colored triangular patches on a monitor gave a bidimensional map of flow values over the whole brain surface; e) the mean flow value maps of two different populations were automatically compared using the unpaired *t* test. The graphic output of the comparison was a topographic distribution of the statistical probability of the differences displayed as a 6-level pseudocolor scale. Data processing to obtain the color maps was performed on a Digital PDP 11/23 Plus connected to an image processing system (VDS 701).

Results

Mean Global Values (MGV's)

1. ISI values: The MGV of each subject and the group means ± SD are presented in Figure 2. In Table 4, the results of the comparisons are reported. MGV's were significantly reduced ($p < 0.01$) in Group 2 and in all untreated cases compared with the controls. No other significant differences were found.

2. Correlations between MGV's and age: No significant correlation was found between MGV's and age in all untreated patients ($r = -0.29$), nor in the controls ($r = -0.09$).

3. Correlations between MGV's and duration of

Table 2. Clinical Summary of the Previously Diagnosed Hypertensives (Group 2)

Case	Age (yr)	Sex	BP (mm Hg)	MABP (mm Hg)	HT duration (yr)	MGV's (ISI)	Fundus (K-W)
14	66	M	160/100	120	2	32	II
15	59	M	180/100	127	0.5	43	I
16	63	M	190/114	139	4	37	II
17	69	F	155/100	118	0.5	44	0
18	55	M	160/95	117	3	34	I
19	72	M	170/100	123	1	31	II
20	58	F	160/100	120	1	47	0
21	69	F	165/105	125	2	44	0
22	50	M	160/95	117	0.5	53	0
23	54	F	180/105	130	0.5	45	0
24	63	M	170/100	123	1	38	0
25	56	F	150/100	117	1	35	II
26	63	M	150/100	117	0.5	41	0

Abbreviations as in Table 1; HT = hypertension.

Table 3. Clinical Summary of the Treated Hypertensives (Group 3)

Case	Age (yr)	Sex	BP (mm Hg)	MABP (mm Hg)	HT duration (yr)	MGV's (ISI)	Fundus (K-W)	Therapy
1	50	F	150/80	103	4	50	0	Atenolol, chlorthalidone, captopril
2	72	M	145/90	108	20	51	I	Chlorthalidone, methyldopa
3	72	F	160/85	110	20	40	II	Hydrochlorothiazide, methyldopa
4	71	F	150/90	110	10	45	II	Hydrochlorothiazide
5	61	M	140/80	100	0.5	57	0	Hydrochlorothiazide
6	62	M	170/100	123	5	35	III	Hydrochlorothiazide, spironolactone
7	59	F	155/90	112	2	43	I	Furosemide
8	65	M	150/100	117	4	33	0	Nifedipine
9	60	M	160/100	120	15	41	II	Hydrochlorothiazide, spironolactone
10	59	M	160/100	120	1	38	I	Chlorthalidone, atenolol

Abbreviations as in Table 2.

hypertension: A significant correlation was found in all untreated patients ($r = -0.48$; $p < 0.02$).

4. Correlations between MABP's and MGV's: MABP's and MGV's in the whole group (patients + controls) were significantly correlated ($r = -0.43$; $p < 0.01$) (Figure 3).

Mean Hemispheric Values (MHV's)

The comparisons between each group of patients and the controls are reported in Table 4. Group 1 showed only a slightly significant reduction in the left ($p < 0.02$) and right ($p < 0.05$) hemispheres; Group 2 showed the greatest reduction in both hemispheres ($p < 0.001$). No other comparison was significant.

Mean Single Probe Values (MSPV's)

The MSPV's and significant differences are reported in Table 5. Group 1 presented significantly reduced ISI only in probes 13, 14, and 16 in the right and probes 27, 29–32 in the left hemisphere. Group 2 had reduced ISI values in all probes. Group 3 showed a

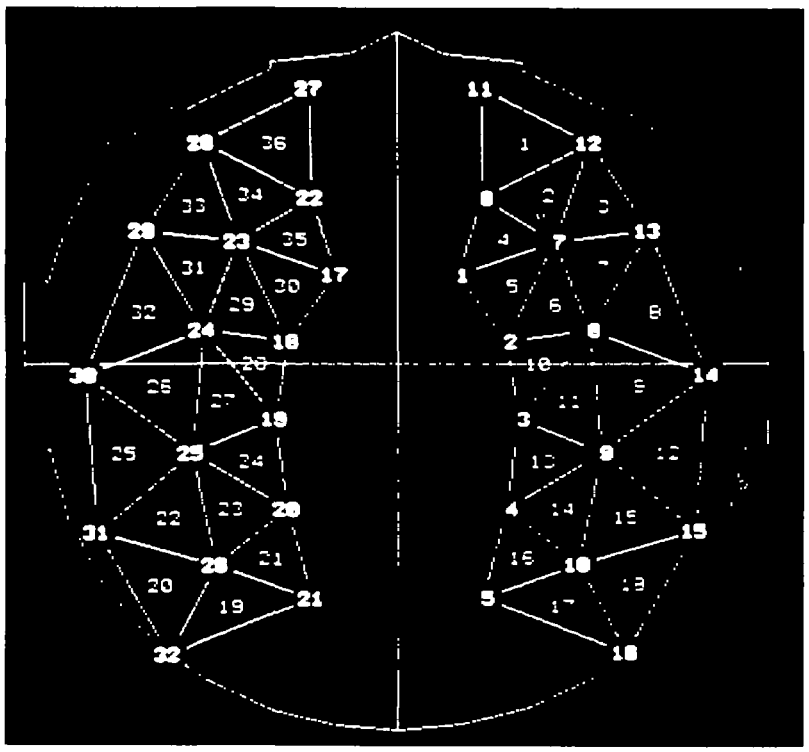

FIGURE 1. *Layout of the 32 probes on the matrix and triangles chosen for interpolation.*

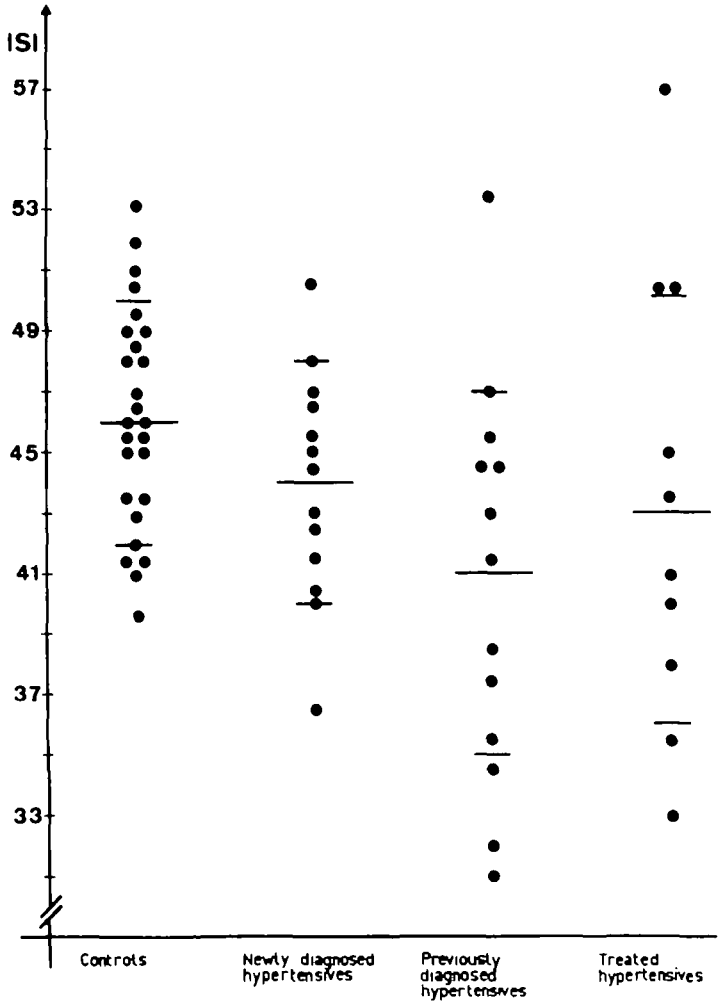

FIGURE 2. *Mean global ISI values (MGV's) and means ± SD: Controls (n = 26); newly diagnosed hypertensives (Group 1, n = 13); previously diagnosed hypertensives (Group 2, n = 13); and treated hypertensives (Group 3, n = 10).*

significant reduction of ISI values only in probes 27, 29–31 in the left hemisphere.

ANOVA failed to show significant interhemispheric differences.

Bidimensional Maps

The map of the statistical comparison between controls (CNTRLS) and Group 1 (NDHT) demonstrated a flow decrease in the temporal regions only (Figure 4). This decrease was more marked in the left hemisphere ($p < 0.01$) than in the right ($p < 0.02$). The controls (CNTRLS) and Group 2 (PDHT) are compared in Figure 5. (The slight difference between the significance of MSPV's in Tables and Figures is solely due to the different computerized approximation procedures adopted for raw data processing and statistical mapping.) There was widespread ISI reduction ($p < 0.01$) in almost all regions. Comparison between the controls (CNTRLS) and Group 3 (TRHT) showed an ISI reduction ($p < 0.02$) in the left frontal and temporal regions only (Figure 6).

Discussion

Mean Global Values and Mean Hemispheric Values

There was a significant reduction in overall CBF, particularly in the previously diagnosed group, Group 2. This may be ascribable to vascular hypertrophy,[20,21] which is the main anatomical change observed in cere-

Table 4. Mean Hemispheric ISI Values (MHV's), Mean Global ISI Values (MGV's), and Statistical Significance of Comparisons between Each Group of Patients and Controls

Group	*n*	R MHV's	L MHV's	MGV's
Controls	26	46 ± 4	46 ± 3	46 ± 4
Untreated patients (Group 1 + Group 2)	26	43 ± 5‡	42 ± 5§	42 ± 5‡
Newly diagnosed hypertensives (Group 1)	13	44 ± 4*	44 ± 4†	44 ± 4
Previously diagnosed hypertensives (Group 2)	13	41 ± 6§	40 ± 6§	41 ± 6‡
Treated hypertensives (Group 3)	10	44 ± 7	43 ± 7	48 ± 7

R = right; L = left.
* = $p < 0.05$; † = $p < 0.02$; ‡ = $p < 0.01$; § = $p < 0.001$ (unpaired *t* test).

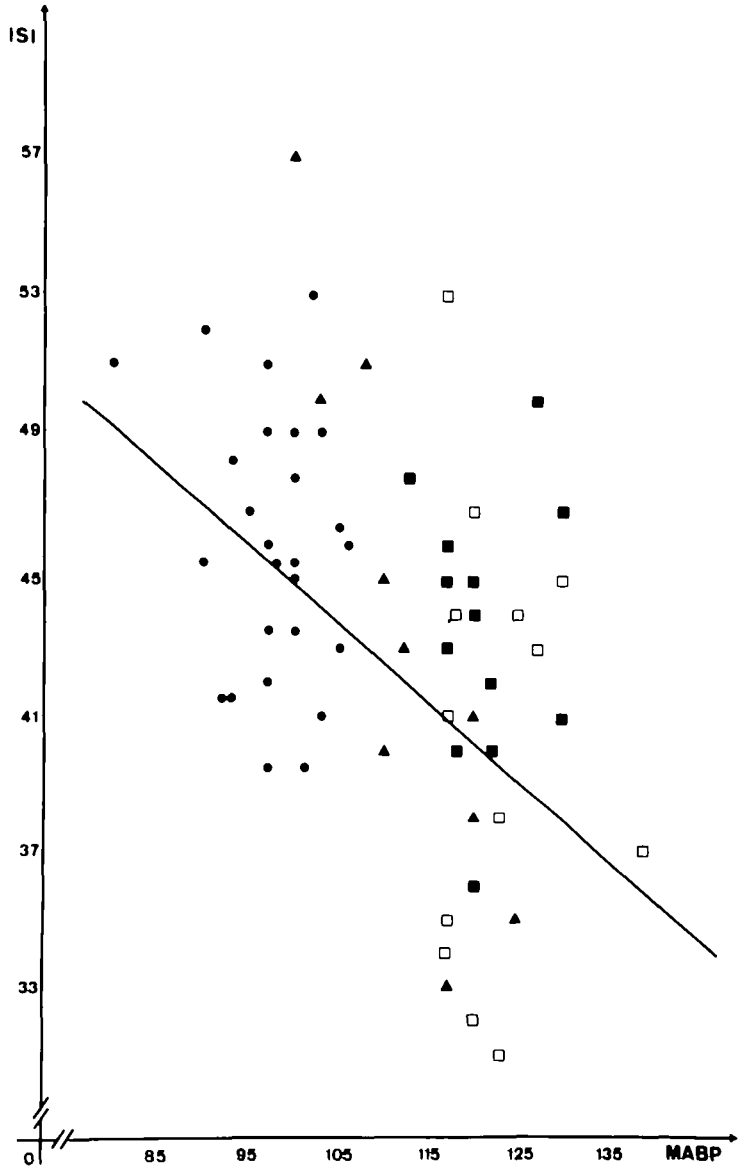

FIGURE 3. *Correlation between ISI and MABP values in controls (●), newly diagnosed (■), previously diagnosed (□), and treated patients (▲). Linear regression analysis:* $r = -0.43$, $(p < 0.01)$.

bral vessels in hypertension and which increases the wall:lumen ratio. Hypertrophy was primarily found in medium-sized and small vessels in an autopsy study of 100 chronic hypertensive patients, with only minor involvement of the larger arteries.[22] Other workers have found that even the capillaries may be affected.[23]

It may be presumed that these arteriosclerotic changes protect both the vessels and the brain from the effects of hypertension. On the other hand, arteriosclerosis alters the supply of oxygen and other nutrients to the neurons. Since CBF is linked to the brain metabolic rate,[24] it may thus be assumed that hypertrophy results in an overall fall in CBF, as was apparent in our untreated subjects. There is other evidence along these lines. Terashi has shown that hypertension plus arteriosclerosis decreases both CBF and brain metabolism.[12] Thickening of the arterial wall in the terminal stage of severe hypertension was responsible for a severe and irreversible decrease in rCBF in Yamori and Horie's stroke-prone spontaneously hypertensive rats.[8] Moreover, hypertension, along with hyperlipemia, smoking, and diabetes, is a well-known risk factor for atherosclerosis. Our study did not take smoking habits into account. The other risk factors, however, were excluded. Atherosclerosis was not clinically evident and other examinations (e.g., angiography) to detect it were not undertaken. If present, it could have contributed to reduced CBF in the untreated group. The conclusion to be drawn is that these findings, which are partly coincident with those of Naritomi et al[25] and Shaw et al,[11] could reflect a combination of hypertension and atherosclerosis.

The treated group was comparable with the controls. Antihypertensive management increased CBF in direct proportion to the reduction of blood pressure in Yamori and Horie's rats.[8] No inference can be drawn with regard to management's efficacy from our small series of poorly homogeneous patients in Group 3 (different drugs and blood pressure, blood pressure at time of diagnosis unknown, different hypertension duration

Table 5. Mean Single Probe ISI Values (MSPV's): Average Across Subjects Relative to Single Probes in Newly Diagnosed Hypertensives (Group 1, n = 13), Previously Diagnosed Hypertensives (Group 2, n = 13), Treated Hypertensives (Group 3, n = 10), and in Controls (n = 26) and Statistical Comparisons between the Two Groups

Right hemisphere					Left hemisphere				
Probe	Group 1	Group 2	Group 3	Controls	Probe	Group 1	Group 2	Group 3	Controls
1	44±5	40±6‡	44±8	46±5	17	44±4	41±7‡	43±6	46±4
2	43±4	40±7‡	43±7	45±4	18	44±5	38±7‡	42±5	43±5
3	43±4	39±7†	42±7	44±5	19	43±5	38±6‡	43±2	44±5
4	43±4	39±7†	43±8	44±5	20	43±5	38±9†	42±7	44±4
5	44±4	41±7†	43±6	44±4	21	43±4	40±7‡	43±8	45±4
6	44±4	39±7‡	43±9	44±4	22	43±4	39±8‡	42±7	45±4
7	44±4	40±7†	44±9	44±5	23	43±4	39±8‡	42±7	45±4
8	44±4	40±6‡	43±8	45±4	24	43±4	39±8‡	41±7	45±4
9	44±4	39±7‡	43±9	45±4	25	42±4	39±7‡	41±8	44±4
10	45±5	41±8*	42±7	45±4	26	44±5	40±7†	43±8	44±5
11	45±3	41±7‡	45±3	47±4	27	45±4*	41±8‡	43±7†	48±4
12	46±4	42±6‡	45±8	47±5	28	46±4	42±7‡	45±9	48±4
13	47±4†	44±6§	47±8	51±5	29	45±3‡	43±7‡	45±8*	49±5
14	46±4*	44±6‡	47±9	50±6	30	43±4‡	43±5‡	43±6†	48±5
15	46±6	43±7‡	46±8	49±5	31	43±4‡	42±5‡	43±8*	48±5
16	45±6*	44±7†	46±8	49±5	32	43±5*	43±6*	43±7	47±5

* = $p < 0.05$; † = $p < 0.02$; ‡ = $p < 0.01$; § = $p < 0.001$ (unpaired t test).

and length of treatment). Even so, it would seem that antihypertensive therapy may alter the natural course of the disease as far as CBF is concerned. Meyer et al, for example, observed a significant increase in CBF in treated as opposed to untreated patients one month after a stroke.[26] That reduction of CBF is the result of hypertension as opposed to normal aging is made strikingly clear by the significant negative linear correlation between MABP and ISI, whereas no correlation could be found between ISI and age.

The relation between MGV's and duration of hypertension is not clear. One study shows that hypertension causes a temporary decrease in CBF, whereas longstanding hypertension results in arteriosclerosis followed by a depressed CBF.[9] Tazaki found high and low CBF in hypertensives under 50 and over 50 re-

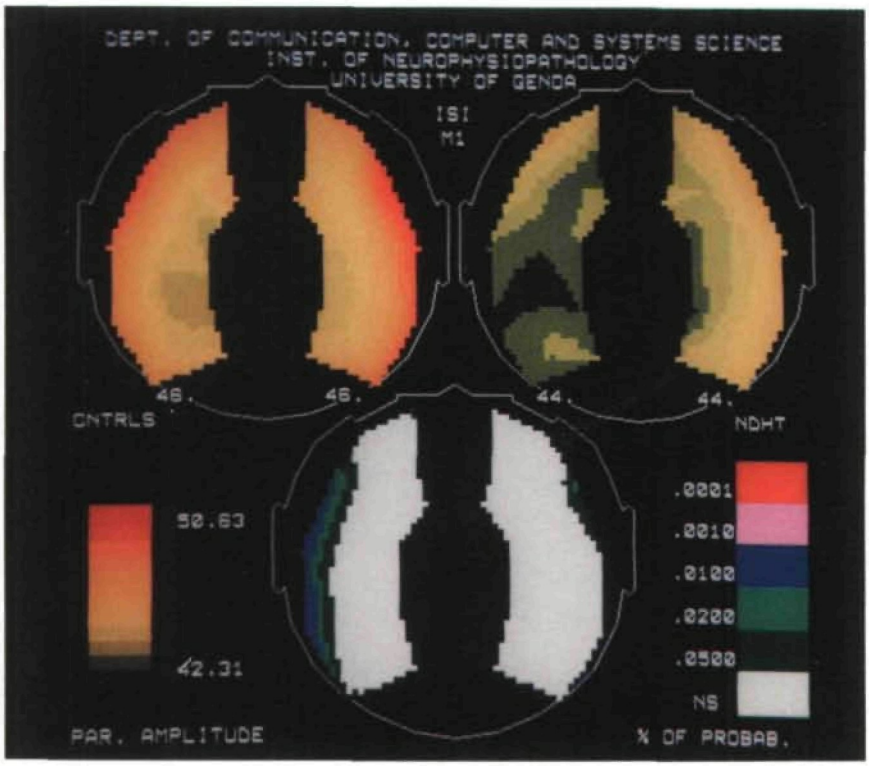

FIGURE 4. *Bidimensional mapping (see text) of the statistical comparison. The two upper maps show the mean ISI values of controls (CNTRLS) and newly diagnosed hypertensives (Group 1, NDHT). The hemispheric mean values are written below the corresponding hemispheres. The scale in the bottom left corner gives the correspondence between the colors and the computed ISI values. The scale is the same for both maps and ranges from the minimum to the maximum computed ISI values, reported on the right side of the scale. The lower map refers to the results of the statistical comparison (unpaired t test) between the flow values of the two upper maps. The 6-level pseudocolor scale in the bottom right corner is graded according to the significance level of the differences.*

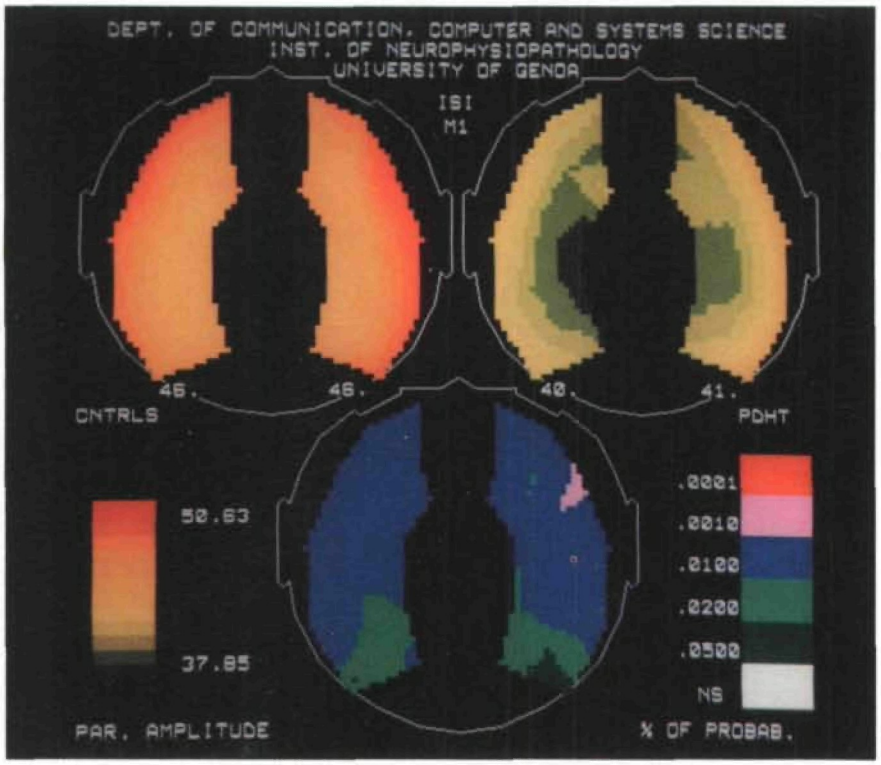

FIGURE 5. *Bidimensional mapping of the comparison between controls (CNTRLS) and previously diagnosed hypertensives (Group 3, PDHT). All details as in Figure 4.*

spectively, suggesting that aging plus chronic hypertension results in cerebrovascular changes leading to a reduction in CBF.[10] The slightly significant correlation between MGV's and the duration of hypertension in our untreated subjects can be seen as an expression of gradual CBF impairment over time. The stages of this process, of course, cannot be deduced from our data.

Mean Single Probe Values

Regional CBF decreases in the untreated group were indicative of a pathological process spreading from the temporal areas to the whole brain, especially to the districts served by the middle cerebral artery. Our results are in line with those of Naritomi et al[25] and Shaw et al[11] and the picture observed at necropsy.[27,28] Newly

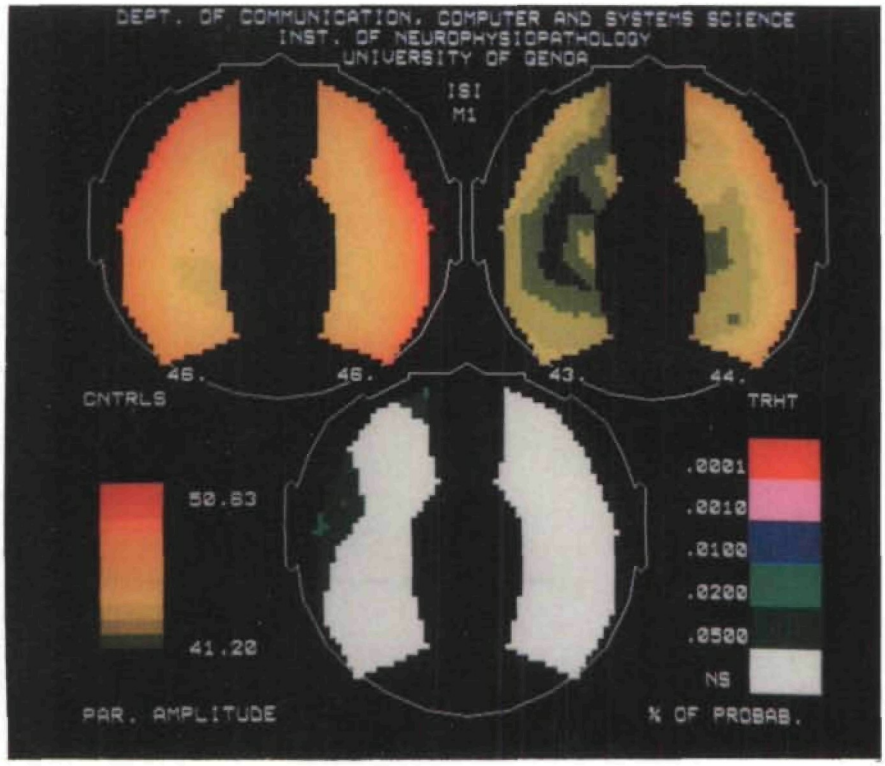

FIGURE 6. *Bidimensional mapping of the comparison between controls (CNTRLS) and treated hypertensives (Group 3, TRHT). All details as in Figure 4.*

diagnosed patients displayed a marked reduction in the left temporal area. This was also true, though to a lesser degree, in the treated group. It may be that this area is especially prone to vascular damage, even though no significant difference between the hemispheres was detected.

Summing up: A reduction in ISI values was observed in mild–moderate untreated hypertensives, whereas patients whose blood pressure had been lowered by therapy displayed only slight left temporal rCBF impairment.

Acknowledgments

We thank Alessandra Ponta for typing the manuscript and Roberta and Daniela Sabatini for the technical help.

References

1. Hypertension Detection and Follow-up Program Cooperative Group: Five-year findings of the hypertension detection and follow-up programs. 1. Reduction in mortality of persons with high blood pressure, including mild hypertension. *JAMA* 1979;242:2562–2571
2. Australian National Blood Pressure Study Management Committee: The Australian therapeutic trial in mild hypertension. *Lancet* 1980;1:1261–1267
3. Taguchi J, Freis ED: Partial reduction of blood pressure and prevention of complications in hypertension. *N Engl J Med* 1974;291:329–331
4. Beevers DG, Johnston J, Devine BL, Dunn FG, Larkin H, Titterington DM: Relation between prognosis and the blood pressures before and during treatment of hypertensive patients. *Clin Sci Mol Med* 1978;55(suppl): 333–336
5. Metropolitan Life Insurance Company: Recent trends in mortality from cerebrovascular disease. *Stat Bull Metrop Life Found* 1975;56:2–4
6. Harborman S, Capildeo R, Rosa FC: The changing mortality of cerebrovascular disease. *Q J Med* 1978;47:71–88
7. Levy RI: Stroke decline: Implications and prospects. *N Engl J Med* 1979;300:490–491
8. Yamori Y, Horie R: Developmental course of hypertension and regional cerebral blood flow in stroke-prone spontaneously hypertensive rats. *Stroke* 1977;8:456–461
9. Gotoh F: Effect of blood pressure on cerebral circulation. *Keio J Med* 1959;8:13–29
10. Tazaki Y: Cerebral circulation and metabolism in hypertension (in Japanese). *J Jpn Soc Intern Med* 1956;45:731–740
11. Shaw TG, Mortel KF, Meyer JS, Rogers RL, Handenberg J, Cutaia MM: Cerebral blood flow changes in benign aging and cerebrovascular disease. *Neurology* 1984;34:855–862
12. Terashi A, Atarashi J: Cerebral circulation in cerebral stroke (in Japanese). *Cerebral Stroke* 1976;3:69–82
13. Obrist WD, Thompson HK Jr, King CH, Wang HS: Determination of regional cerebral blood flow by inhalation of 133-Xenon. *Circ Res* 1967;20:124–135
14. Obrist WD, Thompson HK, Wang HS, Wilkinson WE: Regional cerebral blood flow estimated by 133-Xenon inhalation. *Stroke* 1975;6:245–256
15. Sandini G, Rodriguez G, Romano P, Rosadini G: Topographic mapping of rCBF data, in Battistin L (ed): *PET and NMR: New Perspectives in Neuroimaging and Clinical Neurochemistry.* New York, Alan R Liss Inc (in press)
16. Freis ED: The clinical spectrum of essential hypertension. *Arch Intern Med* 1974;133:982–987
17. *Arterial hypertension, report of a WHO expert committee*, technical report series 628. Geneve, World Health Organization, 1978
18. Risberg J, Ali Z, Wilson EM, Wills EL, Halsey JH: Regional cerebral blood flow by 133-Xenon inhalation. Preliminary evaluation of an initial slope index in patients with unstable flow compartments. *Stroke* 1975;6:142–148
19. Meric P, Luft A, Seylaz J, Mamo H: Analysis of reproducibility and sensitivity of atraumatic measurements of rCBF in cerebrovascular diseases. *Stroke* 1983;14:82–87
20. Folkow B, Hallback M, Lundgren Y, Weiss L: Structurally based increase of flow resistance in spontaneously hypertensive rats. *Acta Physiol Scand* 1970;79:373–391
21. Hart M, Heistad DD, Brody MJ: Effect of chronic hypertension and sympathetic denervation on wall–lumen ratio of cerebral vessels. *Hypertension* 1980;2:419–423
22. Cole FM, Yates PO: Comparative incidence of cerebrovascular lesions in normotensive and hypertensive patients. *Neurology* 1968;18:255–259
23. Garcia JH, Ben-David E, Conger KA, Geer JC, Hollander W: Arterial hypertension injures brain capillaries. Definition of the lesions. Possible pathogenesis. *Stroke* 1981;12:410–413
24. Raichle MA, Grubb RL, Gado MH, Eichling JO, Ter-Pogossian MM: Correlation between regional cerebral blood flow and oxidative metabolism. *Arch Neurol* 1976;33:523–526
25. Naritomi H, Meyer JS, Sakai F, Yamaguchi F, Shaw T: Effects of advancing age on regional cerebral blood flow. *Arch Neurol* 1979;36:410–416
26. Meyer JS, Sawada T, Kitamura A, Toyda M: Cerebral blood flow after control of hypertension in stroke. *Neurology* 1968; 18:772–781
27. Wilkins RH, Roberts JC Jr, Moses C: Autopsy studies in atherosclerosis. III. Distribution and severity of atherosclerosis in the presence of obesity, hypertension, nephrosclerosis and rheumatic heart disease. *Circulation* 1959;20:511–519
28. Blumenthal HT, Handler FP, Blake JO: The histogenesis of arteriosclerosis of the larger cerebral arteries with an analysis of the importance of mechanical factors. *Am J Med* 1954;17: 337–347

KEY WORDS • rCBF • hypertension • mapping system