Basilar and Middle Cerebral Artery Reserve
A Comparative Study Using Transcranial Doppler and Breath-Holding Techniques

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Background and Purpose—A 1997 report suggests that the posterior circulation of the normal brain has diminished vasoreactivity compared with the anterior circulation. To further study this, we quantified and compared the vasodilatory capacities of the middle cerebral (MCA) and basilar artery (BA) territories in response to changes in PaCO₂, as indices of respective cerebrovascular reserve (CVR). If posterior circulation CVR is indeed physiologically lower than that of the MCA, it might indicate a greater risk of low-flow ischemia distal to basilar obstructive cerebrovascular lesions and provide a rationale for earlier treatment of such lesions with interventional techniques. We also wished to establish normal baseline CVR values for the posterior circulation.

Methods—Twelve patients with signs and/or symptoms suggestive of posterior circulation disease but without flow-limiting obstructive changes and 11 normal controls were entered into the study. With the use of transcranial Doppler techniques, alterations in blood flow velocity in response to sequential breath-holding trials of varying duration were simultaneously monitored in both MCAs and the BA. CVR was measured as the percent velocity increase (during breath-holding) from resting baseline values.

Results—No significant differences were found in CVR between the MCA and BA territories in or between patients and controls.

Conclusions—Our study suggests that the anterior and posterior circulations have similar reserve capacities in individuals without flow-limiting cerebrovascular obstructive lesions and that the BA territory, relative to the MCA territory, is not at increased risk for low-flow stroke on the basis of limited reserve potential. (Stroke. 2001;32:2793-2796.)

Key Words: basilar artery ■ cerebrovascular circulation ■ middle cerebral artery ■ stroke, ischemic ■ ultrasonography, Doppler, transcranial

In patients with obstructive cerebrovascular disease, a number of methods have been used to determine the reserve capacity (cerebrovascular reserve [CVR]) of the cerebral vessels as an index of the integrity of intracranial hemodynamics. These have included raising PaCO₂ (with the use of exogenous CO₂ or through simple breath-holding) and administration of acetazolamide. Studies that have compared these stimuli in patients at risk for low-flow ischemic change¹,² report good correlation between their findings. Most recent investigations of CVR have focused on the vasoreactivity of the cerebral circulation supplied by the middle cerebral arteries (MCAs), as transcranial Doppler (TCD) techniques have provided easy, real-time sampling of flow velocities in the MCA.³ We find no prior study that has investigated basilar reserve in response to changes in PaCO₂, nor are normal values available. However, a 1997 study using TCD techniques to test vasoreactivity in response to step hypoxia found, in normal individuals, that reactivity in the basilar artery (BA) system is diminished compared with that in the MCA territory.⁴ If this were true as well for vasoreactivity in response to changes in PaCO₂, it would effectively limit reserve potential in the BA system.

We used TCD to simultaneously compare BA and MCA reserve in response to elevations in PaCO₂ produced by simple breath-holding.

Subjects and Methods

Subjects
Twelve patients (6 men, 6 women; mean age, 59.0±14.5 years; range, 24 to 79 years) with suspected vertebrobasilar system disease and 11 normal controls (9 men, 2 women; mean age, 49.4±23.5 years; range, 22 to 76 years) were entered into the study. Accrual began with the patient population; the normal subjects were studied to confirm whether the observations in patients with symptoms and/or early atheromatous change could be generalized to the normal

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population. All patients were referred to our Neurovascular Laboratory for signs and/or symptoms of possible posterior circulation ischemia. The 11 normal controls were volunteers recruited from among individuals who were normotensive, on no medications, and without neurological/vascular problems or predisposing conditions such as diabetes. One 74-year-old normal control, included in the study, was subsequently found to be on a mild antihypertensive medication. Blood pressure at the time of the study was 140/60 mm Hg. All of the patients and controls had normal carotids or no more than mild carotid atheromatous changes by carotid duplex examination. Five additional patients and 1 potential control subject failed to meet entry criteria because of inadequate bony windows or concomitant hemodynamically significant carotid disease. No patient was entered who had >50% stenosis in the BA or in both vertebral arteries. Four of the patient subjects had TCD evidence of vertebral (n=2) or basilar (n=2) stenosis. In each of the respective cases with vertebral stenosis, 1 vertebral artery was severely stenosed or occluded by TCD evidence, but the other was widely patent. Conventional angiography was done in the occlusion case, confirming the TCD findings. Neither of the basilar cases had more than moderate (approximately 50%) stenosis by TCD examination. Conventional angiography in one case confirmed the finding; in the other the peak systolic velocity in the BA was 150 cm/s. Three patients with no vertebral artery or BA disease, who had sustained robust BA waveforms, had subclavian stenoses that caused hemodynamic vertebral artery changes (unilaterally in 2 cases and bilaterally in the third). The unilateral vertebral artery changes were characterized by biphasic waveforms (with negative subclavian steal testing) in one case and positive subclavian steal testing in the second. The bilateral changes, in the third patient, were characterized by biphasic waveforms (with negative subclavian steal testing). Five patients had no TCD evidence of vertebrobasilar (VB) or subclavian artery disease. The absence of VB disease was radiologically confirmed in 3 patients, in 1 with conventional angiography and in 2 with MR angiography.

Presenting symptoms in the patients were lightheadedness, vertigo, unsteadiness, diplopia, and/or bilateral visual obstructions. Of the latter, one was a patient who had a fixed scintillating right homonymous scotoma and left occipital infarction but no evidence of VB disease. This was the only patient with a known stroke, presumably embolic. The other patient with a visual obscurcation initially was studied for VB symptoms but later insisted he had experienced only a transient monocular visual disturbance.

Cerebrovascular Reserve Measurements

Cerebrovascular reserve measurements were done with the use of a breath-holding method developed in the Massachusetts General Hospital Neurovascular Laboratory. Our standard CVR protocol for the MCA territory typically consists of 6 sequential, randomized breath-holding periods of varying duration, performed with the subject in both the supine and standing positions. The sequential breath-holds are for randomized intervals of 10, 15, 20, 25, and 30 seconds and 1 maximum breath-hold. For VB and combined MCA/VB CVR studies, such as those performed in this investigation, the patients are examined in the sitting position with the neck flexed. Some of our older patients in this study found it uncomfortable to breath-hold for prolonged periods with the neck flexed and were given 4 challenges. Careful instructions were provided to each patient to avoid or minimize a Valsalva maneuver during the breath-hold. That simple breath-holding maneuvers produce physiologically relevant changes in arterial carbon dioxide tension that are associated with correlative, reproducible, TCD-detectable alterations in MCA flow velocities has been documented previously.

TCD Studies

Both MCAs and the BA were insonated simultaneously in all normal controls and 9 of 12 patients. In 3 patient cases only 1 MCA (because of limited transtemporal windows) and the BA were simultaneously monitored. The studies were performed with a DWL Multi-Dop X4 TCD instrument. A 2-MHz pulsed-wave Doppler probe was fixed over each transtemporal window with a rubber headband. A third hand-held 2-MHz probe was positioned on the back of the neck and directed toward the foramen magnum throughout the study. The optimal signal for the MCA was obtained at a depth of 50 to 60 mm and for the BA at a depth of 85 to 95 mm. Software included on the DWL instrument allowed continuous recording of mean velocities in
all 3 arteries during baseline and breath-holding challenges. Baseline was defined as a stable velocity for 30 seconds near or at that found during an initial 5-minute resting trial. The baseline measurement for each breath-holding trial was taken as the average mean velocity over these 30 seconds. Peak velocity was measured at the highest mean velocity reached, which usually occurred several seconds after release of breath-hold and often persisted for several cardiac cycles (Figure 1).

Parameters Used
For each vessel insonated, the percent change in blood flow velocity (from baseline to peak mean velocity) was calculated for each of the 4 to 6 breath-holds obtained in each subject. This was determined by the formula \( V_2 / V_1 \times 100 \), where \( V_1 \) is the baseline and \( V_2 \) the peak mean velocity, in centimeters per second. Dividing each percent change value by its respective length of breath-hold gave the percent per second change, which is analogous to the breath-holding index of some other authors. For each vessel in each subject the cumulative values acquired during sequential breath-hold trials were used to calculate (1) the slope (best-fit line) described by each percent change in blood flow velocity plotted as a function of the respective length of breath-hold (Figure 2) and (2) the mean of the percent per second changes in velocity generated for all 4 to 6 breath-hold periods. The other main parameter determined was the mean MCA-BA percent change difference, which was derived by calculating an MCA-BA difference in percent change for each of the 4 to 6 breath-holds and taking their mean. This parameter gives the most direct estimate of the difference in response between MCA and BA systems.

Results
No significant differences (paired t test) were found between the right and left MCAs in each subject studied (controls and patients) for the slope and percent per second parameters. Therefore, the mean of the right and left MCAs (in the 20 cases in whom bilateral monitoring was performed) was used as the MCA value in the analyses comparing BA CVR and MCA CVR. The Shapiro-Wilkes test for normality showed the slope MCA and mean percent per second MCA values to be normally distributed. The slope BA, mean percent per second BA, and mean MCA-BA percent change difference were not normally distributed, and therefore nonparametric statistics were used during analysis of these indices.

The mean slopes and mean percent per second changes for the MCAs and BAs (Table 1) and the mean MCA-BA percent change difference (Table 2) were not significantly different in or between controls or patients.

All subjects were stratified according to presence or absence of intrusive atheromatous disease in the immediate cerebrovascular supply, which, for the purposes of this study, was defined as up to 50% stenosis of the BA or mild to severe atheromatous change in 1 vertebral artery or in both subclavian arteries. (Patients with BA or bilateral vertebral artery stenosis >50% were excluded from the study; see Subjects and Methods.) The group with intrusive atheromatous disease included 2 patients with moderate basilar stenosis, 2 with severe unilateral vertebral artery disease (with a widely patent contralateral vessel), and 3 with severe subclavian artery disease (2 unilateral, 1 bilateral) but widely patent vertebral arteries and robust BA waveforms. This group with intrusive disease showed no significant difference in CVR from those with absence of posterior circulation atheromatous changes (Table 3).

Discussion
The purpose of studying CVR is to help identify patients at risk for low-flow ischemic change who may require pharmacological or surgical therapy to increase regional cerebral perfusion pressure. CVR studies also can help clinicians to resolve the often vexing problem of differentiating low-flow from embolic ischemic events.

A reasonably large experience has been accumulated with CVR studies that use TCD to monitor velocity changes in the MCA in response to an increase in PaCO₂ or administration of acetazolamide. However, no prior similar studies of basilar reserve have been reported. Garbin and colleagues,4 using TCD in normal subjects to assess relative increases in MCA mean flow velocities in response to step hypoxia, have reported significantly diminished BA compared with MCA territory vascular reactivity. They propose that developmental differences between the 2 vascular systems result in less efficient adaptation of the basilar system to vasoregulatory stimuli, which would include altered PaCO₂ challenges.

We find that the physiological vasodilatory capacity (vasoreactivity, reserve) of the BA system during breath-holding is comparable to that in the MCA system. Moreover, this
finding is true in the presence or absence of VB atheromatous disease that is intrusive (≤50%) as well as with more marked unilateral vertebral or bilateral subclavian artery changes that produce no distal flow-limiting effects. In some patients such segmental disease might serve as an index of more subtle widespread pathology affecting VB vasoreactivity by altering compliance, distensibility, resistance, or vessel thickness.

In our patient group, the mean slope and mean percent per second values tend to be higher for the BA than for the MCA territories. The mean of the MCA CVR slope values in these normal subjects (1.68±0.70) is not significantly different from that found for 35 different middle-aged normal subjects (1.36±0.62; P=0.1545) examined previously, but in the supine position, in our Neurovascular Laboratory (23 men: mean age, 56.5±18.6 years; 12 women: mean age, 51.4±20.5 years; G. Gahn, MD, and R.H. Ackerman, MD, unpublished data, 1997). In neither normal group was a significant change in CVR found as a function of age for the MCA territory. This is consistent with our previous reported findings that cerebrovascular CO₂ reactivity (measured in response to hyperventilation with ¹³³Xe) does not alter with age. Moreover, the percent per second findings in all our subjects are well above the analogous breath-holding index threshold for abnormality (<0.69) validated prospectively by Vernieri et al. Such correlations suggest that our present observations may be generalizable to normal and similar patient subjects outside this investigation.

The discrepancy between the findings of Garbin et al. and ourselves is not readily apparent and is not obviously explained by the main differences between our investigations: Garbin et al examined only young normal subjects (mean age, 30.5 years), they studied the response to hypoxia rather than hypercarbia, they examined the anterior circulation with handheld probes, and they did not simultaneously monitor TCD velocities in the anterior and posterior circulations. Studying CVR with the use of hypoxic challenges is a methodology for which the stability and reproducibility of the results in the same or different populations are not well established, but the technique represents a physiologically reasonable approach. The lack of fixed MCA probes and of simultaneous measurements in the anterior and posterior circulations could introduce greater potential for testing variability, but not on a systematic basis.

Our finding of similar vasoreactivity in the territories of supply of the MCA and BA may well be due to the typically dominant supply of the BA to the posterior cerebral arteries. Our data do not allow us to comment on the expected magnitude of basilar reserve in subjects whose basilar arteries end, as a normal variation, with their bifurcation into the superior cerebellar arteries. None of our patients had known fetal posterior cerebral arteries. Even if basilar reserve findings are strongly influenced by reactivity in the posterior cerebral artery territory, the fact remains that an impaired response due to BA or to bilateral vertebral artery lesions indicates severely compromised flow to all tissues at and beyond the obstructive process, whether in the posterior fossa or in more distal cerebral tissues.

We conclude that BA reserve, as tested by TCD methodology and breath-holding techniques, is comparable to MCA reserve in normal subjects and in those with clinically insignificant posterior circulation disease.

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