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

Kevin M. Barrett, BA; Robert H. Ackerman, MD, MPH; Georg Gahn, MD; Javier M. Romero, MD; Morelia Candia, MD

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 change⁴ 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.⁵ 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
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 pulse-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

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-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 pulse-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

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 pulse-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

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 pulse-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

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
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 \(V_2\) - \(V_1\)/\(V_1\) \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 as the MCA value in the analyses comparing BA CVR and MCA CVR. The Shapiro-Wilkes test for normality showed the slope and percent per second parameters 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 (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 PaCO\(_2\) or administration of acetazolamide. However, no prior similar studies of basilar CVR 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 PaCO\(_2\) 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

### TABLE 1. CVR in Control and Patient Groups

<table>
<thead>
<tr>
<th>Parameter</th>
<th>BA (n=11)</th>
<th>MCA (n=12)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Controls</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>11</td>
<td>11</td>
<td></td>
</tr>
<tr>
<td>Slope ± SD</td>
<td>1.86 ± 1.28</td>
<td>1.68 ± 0.70</td>
<td>0.5426</td>
</tr>
<tr>
<td>Percent per second ± SEM*</td>
<td>1.87 ± 0.24</td>
<td>1.80 ± 0.18</td>
<td>0.6255</td>
</tr>
</tbody>
</table>

*See text for definitions.

### TABLE 2. Direct Comparison of CVR in MCA and BA

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Controls (n=11)</th>
<th>Patients (n=12)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean MCA-BA %</td>
<td>−4.49 ± 6.92*</td>
<td>4.65 ± 4.69</td>
<td>0.2300†</td>
</tr>
</tbody>
</table>

*Negative value indicates mean % change in BA is greater than in MCA.
†Nonsignificant (Mann-Whitney U test).

### TABLE 3. CVR According to Presence/Absence of Noninvasive Atheromatous Disease of the VB System

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Normal (n=16)</th>
<th>Stenotic (n=7)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean % per second MCA</td>
<td>1.77 ± 0.12</td>
<td>1.69 ± 0.19</td>
<td>0.7167*</td>
</tr>
<tr>
<td>Mean % per second BA</td>
<td>1.79 ± 0.18</td>
<td>2.15 ± 0.40</td>
<td>0.4830†</td>
</tr>
<tr>
<td>Mean slope MCA</td>
<td>1.73 ± 0.69</td>
<td>1.41 ± 0.64</td>
<td>0.3142*</td>
</tr>
<tr>
<td>Mean slope BA</td>
<td>1.81 ± 1.08</td>
<td>1.98 ± 1.05</td>
<td>0.6641†</td>
</tr>
<tr>
<td>Mean MCA-BA % Δ difference</td>
<td>−2.09 ± 5.68‡</td>
<td>5.68 ± 3.82</td>
<td>0.5255‡</td>
</tr>
</tbody>
</table>

*Negative value indicates mean % change in BA is greater than in MCA.
†Nonsignificant (Mann-Whitney U test).
‡Negative value indicates mean % change in BA is greater than in MCA.
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 ^133^Xe) does not alter with age.6 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.7 Such correlations suggest that our present 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.

**Acknowledgments**

The authors acknowledge the cooperation of DWL of Sipplingen, Germany, in providing hardware and software modifications to the Multi-Dop X4 TCD to accommodate the needs of this study. This research was supported by the generous contributions of patients and their families, particularly Richard and Winnie Bell, John and Geneva DeJesus, Arthur and Ann Flaherty, Maurice and Nell Lazarus, Morton and Helen Oppenheim, and the late (Dr) Jan and Ann Taams.

**References**

Basilar and Middle Cerebral Artery Reserve: A Comparative Study Using Transcranial Doppler and Breath-Holding Techniques
Kevin M. Barrett, Robert H. Ackerman, Georg Gahn, Javier M. Romero and Morelia Candia

Stroke. 2001;32:2793-2796
doi: 10.1161/hs1201.098640

Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2001 American Heart Association, Inc. All rights reserved.
Print ISSN: 0039-2499. Online ISSN: 1524-4628

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://stroke.ahajournals.org/content/32/12/2793