# Effects of the Valsalva Maneuver on Cerebral Circulation in Healthy Adults

## A Transcranial Doppler Study

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***Background and Purpose*** Knowledge is limited about the effects of the Valsalva maneuver on cerebral circulation because of the poor temporal resolution of traditional cerebral blood flow measurements. The purpose of this study was to investigate changes in cerebral blood flow during the Valsalva maneuver and to explore its potential use for the evaluation of cerebral autoregulation.

***Methods*** Using transcranial Doppler ultrasonography, we simultaneously recorded systemic arterial blood pressure in the radial artery and flow velocities in both middle cerebral arteries in 10 healthy adults during the Valsalva maneuver. Gosling's pulsatility index was calculated for all phases of the Valsalva maneuver. Autoregulatory capacities were estimated from the change in cerebrovascular resistance (flow velocity in relationship to blood pressure) during phase II and changes in the velocity-pressure relationship in phase IV relative to phase I.

***Results*** The characteristic changes in blood pressure (phases I to IV) were seen in all subjects, accompanying distinct changes in cerebral blood flow velocity. The relative changes in mean velocity during phases II and IV were significantly greater than those in mean blood pressure. Compared with the baseline value, velocity decreased by 35% in phase IIa, then rose by 56.5% in phase IV (corresponding changes in blood pressure were −10.2% and +29.8%, respectively). During phase II, the pulsatility and cerebrovascular resistance decreased by 19.9%. The increase in cerebral blood flow velocity in phase IV was significantly higher than in phase I ($P<.0004$), and there was no corresponding significant difference in blood pressure.

***Conclusions*** These results demonstrated that in healthy humans the Valsalva maneuver causes characteristic changes in systemic blood pressure as well as in flow velocity in the middle cerebral artery, reflecting the sympathetic and cerebral autoregulatory responses, respectively. Analysis of these changes may provide an estimate of autoregulatory capacity. (***Stroke.* 1995;26:1386-1392.**)

***Key Words*** • autoregulation • blood flow velocity • cerebral blood flow • ultrasonics

The VM is frequently encountered in many daily activities in which straining occurs. Lifting of heavy loads, defecation, playing of wind instruments, coughing, and vomiting are all activities that simulate the VM. Its cardiovascular effects have been subject to intensive studies, and the underlying physiological mechanisms as well as the four distinct phases are well described.[1-3] With the beginning of the strain, there is a transient increase in ABP that is thought to result from transmission of the intrathoracic pressure to the arterial tree (phase I). This is followed by a fall in ABP due to impaired atrial filling of the heart (early phase II, or phase IIa). In normal subjects, however, a sympathetic response to the fall in ABP, mediated mainly by baroreceptors of the carotid sinus, leads to a rise in ABP and an increase in heart rate (late phase II, or phase IIb). When the strain is released, the sudden decrease in intrathoracic pressure is again transmitted to the arterial system and a transient decrease in ABP occurs (phase III). This is immediately followed by an overshoot in ABP above baseline, as the sympathetic tone and systemic vascular resistance remain elevated, after atrial filling has normalized (phase IV). The increase in ABP then again acts on the baroreceptors, resulting in transient bradycardia before normal conditions are restored.

Clinically the VM has been used to test the integrity of autonomic function,[4-6] in the auscultation of cardiac murmurs,[7] to relieve angina pectoris[8] or paroxysmal tachycardia,[9] and to assess the patency of the foramen ovale.[10] The VM has also been known to cause temporary cerebral ischemia and fainting,[2,11] and has been associated with aneurysm rupture and subarachnoid hemorrhage.[12] There is, however, only limited knowledge about the effects of the VM on the cerebral circulation in the normal brain, mainly because of the poor temporal resolution of conventional CBF measurements.

The VM may represent a dynamic challenge to the autoregulatory mechanisms of the cerebral circulation, which maintains a constant CBF over a wide range of changes in CPP.[13] During the VM there are simultaneous changes in ABP and CPP within a short period of time, highlighted by the decrease of CPP during early phase II, when ABP falls and ICP increases.[14] This decrease in CPP should provoke an autoregulatory response.[13] Autoregulatory changes in the human cerebral circulation have been studied continuously and noninvasively by monitoring of the MCA velocity by use

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**Selected Abbreviations and Acronyms**

ABP = arterial blood pressure
AI = autoregulatory index
CBF = cerebral blood flow
CBFV = cerebral blood flow velocity
CPP = cerebral perfusion pressure
CVR = cerebrovascular resistance
ICP = intracranial pressure
MCA = middle cerebral artery
PI = Gosling's pulsatility index
TCD = transcranial Doppler sonography
VM = Valsalva maneuver

of TCD.[15-17] We hypothesized that, by comparing the changes in CBFV to those in ABP, it would be possible to distinguish the effects of the autoregulatory mechanism from the sympathetic response.

Thus, the aims of this study were twofold: (1) to characterize the effects of the VM at two levels of intrathoracic pressure on the cerebral circulation in relation to the systemic sympathetic response, and (2) to explore the potential use of the VM in assessment of the cerebral autoregulatory capacity.

## Subjects and Methods

Ten healthy volunteers (three male, seven female, aged 30±9 years [mean±SD]) were studied in the Cerebrovascular Laboratory at Harborview Medical Center, Seattle, Wash. They performed the VM in a supine position with a 40° inclination of the upper body after stable baseline readings of ABP and CBFV on both sides had been obtained for several minutes. Both MCAs were identified in the usual manner[18] before the ultrasound probes were fixed in place with a headband. A computerized bilateral TCD recording system (DWL-Multi-Dop X) with an analog input for simultaneously recorded ABP readings was used. Continuous ABP measurements of one radial artery were carried out noninvasively by use of a tonometric blood pressure monitor (Nellcor, N-Cat N-500). Each subject was asked to maintain an intrathoracic pressure of 20 or 40 mm Hg for 15 seconds, by first taking a large tidal breath and then exhaling forcefully against a closed valve connected to an aneroid pressure gauge, while the maximum velocity outlines of the spectral wave forms together with the ABP readings were being recorded continuously. Each subject was studied twice and the sequence of the two intrathoracic pressures was randomized, with at least 5 minutes of rest between studies, when both CBFV and ABP had returned to baseline values.

The mean ABP and CBFV values were recorded and used in all subsequent mathematical calculations. We derived from the velocity and ABP data the changes in CVR for phase II using the equation (change in CVR)=(change in ABP)/(change in CBFV). This is deemed valid because CPP varies with ABP (ICP is practically constant during phase II[14,19]) and CBFV varies with CBF.

Another measurement of vascular resistance, PI,[20] was calculated from the readings of the spectral wave forms for all phases.

All velocity and pressure calculations were performed off-line, and percentage change in time, averaged mean velocity, and mean ABP in all phases are calculated from the initial stable baseline values. In all calculations the respective maximal and minimal values of CBFV and ABP are used to characterize each phase.

Data evaluation was carried out by standard statistical techniques and data are reported as mean±SD.

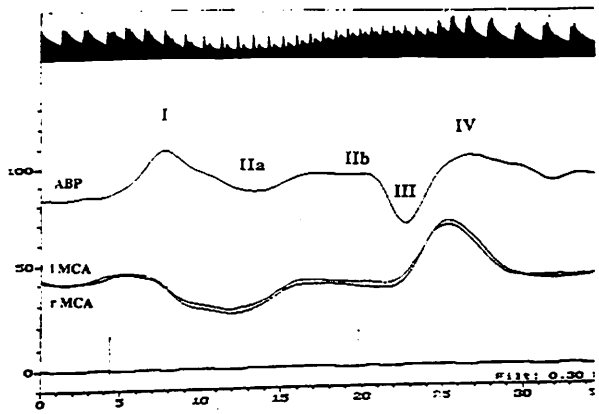


FIG 1. Illustrative recording obtained during the VM at 40 mm Hg of intrathoracic pressure shows CBFV spectrum (upper tracing), ABP (low-frequency [0.3 Hz]-filtered) (middle tracing), and mean CBFV velocity (lower tracing). Interval marked indicates duration of strain. *x*-axis shows time in seconds; *y*-axis shows mm Hg (ABP) or cm/s (CBFV). I through IV indicate phases of the VM; lMCA, flow velocity in left MCA; and rMCA, flow velocity in right MCA.

## Results

### Changes in CBFV and ABP

Fig 1 shows the typical time course of CBFV and ABP at 40 mm Hg of intrathoracic pressure. The drop of CBFV in phase IIa, its partial restoration in phase IIb, and its subsequent overshoot in phase IV were significantly greater than the corresponding changes in ABP at both intrathoracic pressures. At 40 mm Hg the mean drop in CBFV from baseline during phase II was 35% for both sides (25.3% at 20 mm Hg), whereas ABP fell by only 10.2% (10.1% at 20 mm Hg). This was followed by a mean rise in CBFV in phase IV of 56.5% above baseline (32.1% at 20 mm Hg), whereas ABP increased by only 29.8% (26.7% at 20 mm Hg). The maximum drop in CBFV in our series was 52% and the maximum increase was 95%. Baseline values for individual subjects are shown in Table 1. Absolute values for individual subjects and percentage changes relative to baseline in ABP during the VM are shown in Tables 2 and 3, and those for CBFV are shown in Fig 2. When the effects of the VM on the two intrathoracic pressures were compared, CBFV was seen to be significantly more affected in both directions at 40 mm Hg, but the ABP changes were not different between 20 and 40 mm Hg. We did not find obvious differences among our subjects in terms of sex or age, and the sequence of the trial (ie, whether 20 or 40 mm Hg of intrathoracic pressure was applied first) did not affect the results.

### Autoregulatory Response

There was a significantly greater restoration of CBFV during phase II than the corresponding increase in ABP, which is reflected by the changes in CVR during phase II (Table 4). Also, the peak increase in CBFV in phase IV was higher than in phase I in all subjects ($P<.0004$ by Student's $t$ test at both pressures), whereas there was no corresponding ABP difference.

To allow further quantitative analysis of the autoregulatory response, we introduced two AIs. Because the expected autoregulatory response to the decrease in CPP in early phase II (IIa) should lead to dilatation of

**TABLE 1. General Subject Data and Baseline Values**

| Subject | Sex | Age, y | Pulse, bpm | ABP, mm Hg | $V_{left}$, cm/s | $V_{right}$, cm/s |
|---|---|---|---|---|---|---|
| 1 | M | 30 | 60 | 78 (78) | 69 (69) | 55 (55) |
| 2 | F | 24 | 80 | 81 (66) | 71 (59) | 83 (68) |
| 3 | F | 24 | 72 | 80 (84) | 78 (79) | 81 (81) |
| 4 | F | 27 | 54 | 81 (81) | 82 (82) | 92 (92) |
| 5 | M | 18 | 80 | 88 (73) | 50 (42) | 53 (54) |
| 6 | F | 23 | 70 | 77 (76) | 71 (75) | 55 (58) |
| 7 | F | 38 | 58 | 78 (70) | 39 (37) | 58 (57) |
| 8 | M | 43 | 78 | 96 (80) | 38 (46) | 39 (45) |
| 9 | F | 42 | 52 | 77 (80) | 52 (46) | 47 (45) |
| 10 | F | 29 | 58 | 79 (86) | 83 (73) | 79 (74) |
| Mean±SD | | 30±9 | 66±11 | 82±6 | 63±17 | 64±18 |
| | | | | (78±7) | (60±18) | (62±16) |

$V_{left}$ indicates left middle cerebral artery mean flow velocity; $V_{right}$ indicates right middle cerebral artery mean flow velocity. Values are given as baseline values at 20 mm Hg of intrathoracic pressure; values for 40 mm Hg are in parentheses.

the cerebral resistance vessels, we hypothesized that the partial restoration of CBFV during phase IIb should exceed the concomitant ABP response relative to the respective minimal value in phase IIa. We therefore defined the AI for phase II as follows:

$$\text{AI-II} = \frac{\text{CBFV (phase IIb} - \text{phase IIa)/CBFV (phase IIa)}}{\text{ABP (phase IIb} - \text{phase IIa)/ABP (phase IIa)}}$$

Similarly, vasodilation of the resistance vessels should still be detectable in phase IV, because autoregulation is not instantaneous.[15,19] Therefore, the autoregulatory response would be reflected at this phase as an increase in CBFV relative to ABP. We defined the AI for phase IV as follows:

$$\text{AI-IV} = \frac{\text{CBFV (phase IV)/CBFV (phase I)}}{\text{ABP (IV)/ABP (I)}}$$

We chose the phase I value instead of the baseline for normalization because the response in phase I represents and standardizes the magnitude of each subject's response to the strain.

For both indexes, values greater than 1.00 are compatible with the presence of autoregulation and values of 1.00 or less would be indicative of absence of autoregulation. For both indexes we found values considerably higher than 1.00 in each subject (Table 5).

Changes in pulsatility were less uniform among subjects during the 20 mm Hg strain. However, the difference in PI from baseline was significant during phase II and between phases III and IV (Fig 3). With the 40 mm Hg strain, the changes were marked, as demonstrated in a typical spectrum recording showing a steep rise in diastolic velocity between phase IIa and phase IIb, which tapers off toward the end of the strain (Fig 1, upper recording).

## Discussion

Our findings demonstrate marked changes in CBFV during the VM, with characteristic phase-related changes that are significantly greater than the concomitant ABP changes. During phase IIb and phase IV, the relative increases in CBFV are significantly higher than those in ABP, resulting in AIs that are consistently greater than 1.00.

Before we interpret the systemic-cerebral hemodynamics of each phase and discuss the potential use of the VM for the evaluation of autoregulation, one methodological aspect, measurement of CBF, should be addressed.

### Measurement of Relative CBF Changes by TCD

The excellent temporal resolution of TCD allows real-time analysis of the fast changes in CBFV during

**TABLE 2. Individual Data at 20 mm Hg**

| | ABP, mm Hg | | | | | $V_{left}$, cm/s | | | | | $V_{right}$, cm/s | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Subject | I | IIa | IIb | III | IV | I | IIa | IIb | III | IV | I | IIa | IIb | III | IV |
| 1 | 88 | 77 | 82 | 77 | 84 | 82 | 64 | 80 | 78 | 91 | 75 | 57 | 69 | 66 | 79 |
| 2 | 88 | 67 | 74 | 70 | 85 | 88 | 58 | 80 | 76 | 114 | 101 | 71 | 95 | 91 | 130 |
| 3 | 103 | 65 | 78 | 73 | 102 | 85 | 48 | 66 | 61 | 110 | 92 | 53 | 70 | 63 | 103 |
| 4 | 84 | 68 | 92 | 80 | 94 | 82 | 62 | 80 | 72 | 89 | 93 | 75 | 90 | 81 | 97 |
| 5 | 92 | 70 | 87 | 84 | 94 | 51 | 29 | 49 | 47 | 56 | 62 | 31 | 56 | 54 | 69 |
| 6 | 108 | 84 | 101 | 92 | 114 | 96 | 59 | 81 | 75 | 109 | 71 | 43 | 65 | 58 | 87 |
| 7 | 91 | 72 | 76 | 72 | 84 | 37 | 30 | 39 | 35 | 45 | 54 | 44 | 57 | 53 | 68 |
| 8 | 129 | 30 | 90 | 80 | 135 | 33 | 26 | 38 | 27 | 53 | 46 | 30 | 38 | 29 | 56 |
| 9 | 100 | 69 | 75 | 68 | 99 | 47 | 29 | 39 | 36 | 59 | 47 | 29 | 38 | 36 | 61 |
| 10 | 95 | 88 | 97 | 78 | 106 | 84 | 68 | 81 | 77 | 120 | 84 | 70 | 79 | 76 | 116 |
| Mean±SD | 96±9* | 74±8* | 85±10* | 77±7* | 99±16* | 79±22 | 47±17* | 63±20* | 58±20 | 85±29* | 72±20* | 50±18* | 66±19* | 61±19 | 87±25 |

$V_{left}$ indicates left middle cerebral artery mean flow velocity; $V_{right}$, right middle cerebral artery mean flow velocity; and I through IV, phases of the Valsalva maneuver.

*$P<.05$ compared with the previous phase.

TABLE 3. Individual Data at 40 mm Hg

| | ABP, mm Hg | | | | | $V_{left}$, cm/s | | | | | $V_{right}$, cm/s | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Subject | I | IIa | IIb | III | IV | I | IIa | IIb | III | IV | I | IIa | IIb | III | IV |
| 1 | 109 | 75 | 91 | 68 | 111 | 87 | 43 | 67 | 62 | 117 | 69 | 34 | 53 | 49 | 90 |
| 2 | 63 | 43 | 63 | 61 | 77 | 84 | 48 | 84 | 81 | 105 | 96 | 55 | 92 | 90 | 120 |
| 3 | 112 | 81 | 92 | 78 | 110 | 101 | 45 | 66 | 63 | 117 | 105 | 52 | 70 | 67 | 115 |
| 4 | 106 | 63 | 106 | 88 | 110 | 80 | 43 | 91 | 89 | 107 | 93 | 53 | 100 | 98 | 115 |
| 5 | 92 | 57 | 63 | 51 | 78 | 65 | 25 | 37 | 37 | 74 | 80 | 26 | 48 | 48 | 88 |
| 6 | 104 | 66 | 77 | 71 | 87 | 82 | 45 | 68 | 71 | 134 | 62 | 32 | 51 | 53 | 113 |
| 7 | 81 | 66 | 75 | 74 | 83 | 41 | 25 | 31 | 31 | 50 | 63 | 45 | 62 | 62 | 76 |
| 8 | 110 | 60 | 60 | 48 | 116 | 40 | 20 | 28 | 24 | 60 | 40 | 23 | 28 | 26 | 61 |
| 9 | 109 | 86 | 94 | 68 | 103 | 46 | 27 | 40 | 38 | 68 | 46 | 25 | 38 | 35 | 66 |
| 10 | 97 | 90 | 96 | 86 | 111 | 80 | 68 | 78 | 78 | 118 | 83 | 70 | 80 | 80 | 116 |
| Mean±SD | 98±16* | 69±14* | 82±16* | 70±13* | 99±16* | 71±21* | 39±15*† | 59±23* | 57±23 | 95±29*† | 73±22* | 41±16*† | 62±23* | 61±23 | 96±23*† |

$V_{left}$ indicates left middle cerebral artery mean flow velocity; $V_{right}$, right middle cerebral artery mean flow velocity; and I through IV, phases of the Valsalva maneuver.

*$P<.05$ compared with the previous phase; †$P<.05$ between 20 and 40 mm Hg.

the VM, but for them to be accepted as relative changes in CBF, one important assumption has to be made: ie, that the diameter of the MCA remains constant.[21] There is considerable evidence from comparisons of CBFV recordings by TCD and CBF measurements by electromagnetic flowmetry and the $^{133}Xe$ method that these variables correlate well during tests of autoregulation.[16,17]

The possibility remains, however, that there could be some vasoconstriction of the MCA due to sympathetic action in the course of the VM. In certain animal species sympathetic stimuli have been shown to decrease the diameter of larger branches of the MCA.[22,23] There are, however, several reasons that it is unlikely that the restoration of CBFV during phase IIb is due to constriction of the MCA. First, the finding of a very strongly diminished pulsatility is more typical for a decrease in peripheral resistance than for a decrease in diameter of the insonated vessel.[24] Second, angiographic studies by Oleson[25] have demonstrated that the diameter of the large cerebral arteries is not affected by direct intra-arterial administration of sympathomimetic agents. Although this may have been due to a lack of contact of the sympathomimetic agents with the receptors in the vessel walls in the study by Oleson, the fact that direct intraoperative measurements of proximal MCA diameter demonstrated little change with potent vasoactive agents and changes in ABP suggests that the change in CBFV is unlikely to be the result of vasoconstriction.[26] Finally, an electromagnetic flow study (not dependent on vessel diameter) demonstrated that changes in CBF during the VM were similar to our CBFV findings both in terms of the pattern and the percentage changes[19]; if we calculate the change in CVR during phase II, we find a decrease in CVR during the strain of 12.7% (right) and 15% (left) at 20 mm Hg (see Table 2). This corresponds well to the findings of Greenfield et al,[19] who found a fall of 10% in CVR at phase II during 20 mm Hg strain. Thus, TCD is more than likely to accurately reflect relative changes in CBF at all phases of the VM.

### Systemic-Cerebral Interaction During the Four Phases

With the rise in intrathoracic pressure in phase I, there is a sudden increase in ABP due to transmission of this pressure to the arterial tree.[1-3] This increase in ABP theoretically should also increase cerebral perfusion because human autoregulation cannot compensate instantaneously for a sudden change in perfusion pressure.[15,19] Therefore, one might expect a corresponding increase in CBFV in phase I. It is known, however, that during the strain the venous and cerebrospinal fluid pressure (and therefore the ICP) rise approximately by the magnitude of the intrathoracic pressure.[14,19] Thus, the increase in ICP counteracts the increase in ABP, producing a relatively unchanged CPP and only a slightly increased CBFV.

However, the raised ICP magnifies the effect of decreased ABP due to impaired atrial filling in phase IIa,

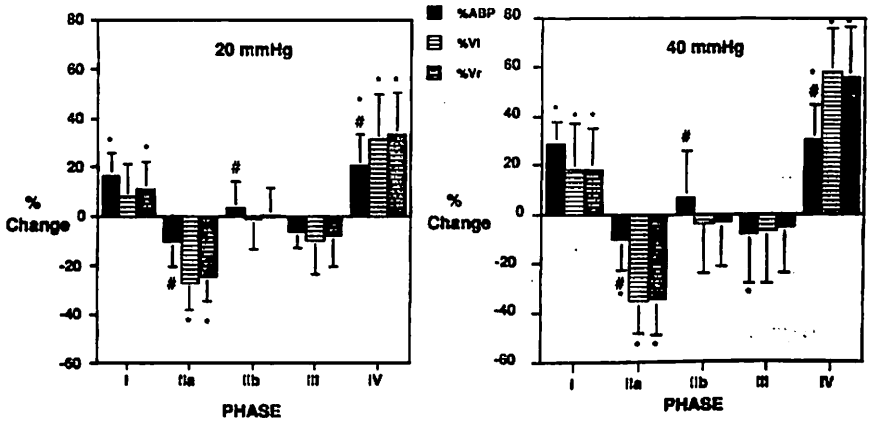


FIG 2. Bar graphs show percentage changes from baseline in ABP (solid bars) and CBFV during the VM at 20 mm Hg and 40 mm Hg. %Vl (light gray bars) indicates percentage of velocity, left side; %Vr (dark gray bars), percentage of velocity, right side; and I through IV, phases of the VM. *$P<.05$ compared with baseline; #$P<.05$ compared with CBFV. All values are mean±SD.

**TABLE 4. Percentage Change in ABP, CBFV, and CVR Between Phase IIa and Phase IIb at Intrathoracic Pressures of 20 and 40 mm Hg**

| | ABP | $V_{left}$ | $V_{right}$ | $CVR_{left}$ | $CVR_{right}$ |
|---|---|---|---|---|---|
| 20 mm Hg | 15.4±9.3 | 36.5±13.7* | 34.0±19.3* | −15.0±8.9* | −12.7±11.8* |
| 40 mm Hg | 20.9±19.8 | 52.0±26.9*† | 52.8±24.4*† | −20.0±7.3* | −19.8±9.8* |

$V_{left}$ indicates flow velocity in left middle cerebral artery: $V_{right}$, flow velocity in right middle cerebral artery; $CVR_{left}$, estimated cerebral vascular resistance calculated from $ABP/V_{left}$; and $CVR_{right}$, estimated cerebral vascular resistance calculated from $ABP/V_{right}$. Values are mean±SD.

*$P<.05$ compared with corresponding ABP changes.

†$P<.05$ between 20 and 40 mm Hg.

accounting for the significantly greater decrease in CBFV. The percentage decrease observed in our healthy volunteers was up to 52%, which illustrates why fainting may occur during the VM. Strain during coughing, for example, may produce an intrathoracic pressure of up to 300 mm Hg for several seconds.[27] The degree of the decrease in CBFV, however, may be modified with several factors that affect the CPP. These include function of the autonomic nervous system[11] and the heart,[28,29] blood-volume status,[29] body position,[30] and venous tone.[2]

After CBFV had reached its minimum in phase IIa, we found a relatively sharp velocity increase that was significantly higher than the corresponding ABP response mediated by sympathetic activation during phase IIb. This was paralleled by a disproportionate rise in diastolic CBFV relative to systolic CBFV, resulting in a gradual decrease in PI, especially during the first part of the rise. Because ICP should be constant during this phase, the disproportionate rise in CBFV and the PI changes reflect a change in CVR and not merely passive CBF in response to the ABP changes.

After release of the strain (phase III), ABP drops transiently because of passive transmission of intrathoracic pressure to the arteries. A similar change in CBFV is usually not evident. The elevated sympathetic tone leads to an immediate increase in ABP, which exceeds baseline but not the ABP peak in phase I (phase IV). In contrast, CBFV consistently overshoots this reference mark. The mean increase in CBFV at 40 mm Hg of intrathoracic pressure was more than 50% above baseline, and the maximum value reached almost 100% in one subject. This may be the stage of the VM with the highest risk for aneurysm rupture or tissue damage in susceptible patients, because of the combination of the simultaneous decrease in the "protective" extravascular cerebrospinal fluid pressure[2,14] and the rise in arterial pressure, resulting in a major increase in the transmural pressure gradient.

### Autoregulatory Response

We believe the discrepancy between ABP and CBFV in phases IIb, III, and IV is secondary to autoregulatory compensation.

As shown before, the fall in ABP and the increase in ICP in phase II lead to a decrease in CPP. This stimulus for an autoregulatory response[13] continues throughout the strain; even though ABP is usually restored in phase IIb, ICP remains elevated, resulting in reduced CPP. In addition, the rise in venous pressure may constitute a stimulus for autoregulation by itself.[31] To compensate for these challenges, the adequate autoregulatory response must lead to vasodilatation of the cerebral arterioles.

This explains the disproportionate increase in CBFV in comparison with ABP during phase IIb, which typically begins shortly before the respective ABP increase. It also accounts for the change in PI from a high-resistance profile at the beginning of phase II to low pulsatility, which typically reflects a diminishing cerebrovascular resistance.[20,24] Vasodilatation of cerebral resistance vessels could theoretically be explained by a change in $CO_2$ due to breath holding. In this instance one would, however, expect CBFV to increase gradually rather than to taper off. We plotted in seven subjects the respective values of mean and diastolic ABP and CBFV for every heartbeat after the minimum in phase IIa. The result showed a significantly smaller increase in mean and diastolic CBFV (but not in ABP) between the 6th and the 11th heartbeat compared with the 1st and 6th heartbeat after the minimum. Thus, the maximum increase in CBFV was usually seen as early as about 8 to 10 seconds after the beginning of the strain (as seen in Fig 1), whereas a possible $CO_2$ retention should show its maximum effect toward the end of the strain. Moreover, blood gas analysis during studies with a longer period of VM (20 seconds) found either no change or a slight decrease in $Paco_2$.[32] To further substantiate this, in five anesthetized patients undergoing the VM to check for surgical hemostasis, we obtained arterial blood gases immediately before and after the maneuver and found similar results (35±2 versus 34±3 mm Hg). Therefore, a change in $CO_2$ is unlikely to confound our results.

Because autoregulation does not act instantaneously, the resistance vessels continue to be dilated after the sudden release of intrathoracic pressure in phase III.

**TABLE 5. Possible Indexes of Autoregulation**

| | Side | AI-II | 95% Confidence Interval | AI-IV | 95% Confidence Interval |
|---|---|---|---|---|---|
| 20 mm Hg | Left | 3.00±1.41 | 1.99-4.01 | 1.18±0.14 | 1.08-1.28 |
| | Right | 2.71±1.41 | 1.76-3.72 | 1.16±0.15 | 1.06-1.27 |
| 40 mm Hg | Left | 2.87±1.3 | 1.86-3.87 | 1.36±0.25 | 1.18-1.54 |
| | Right | 3.36±2.18 | 1.68-5.03 | 1.35±0.33 | 1.11-1.58 |

AI indicates autoregulatory index.

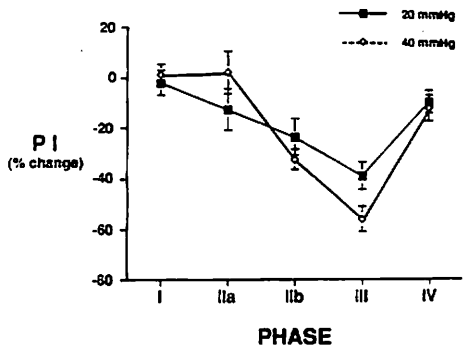


FIG 3. Graph shows percentage changes from baseline in PI during the VM at 20 mm Hg and 40 mm Hg of intrathoracic pressure. I through IV indicate phases of the VM. All values are mean±SD.

This offers a good explanation for the level of the observed overshoot in CBFV in phase IV.

Therefore, our AI-IV (see Table 4), which is derived from the velocity changes between phases I and IV relative to corresponding changes in ABP, might be a more reliable marker for intact autoregulation than our AI-II, which reflects relative rises of CBFV versus ABP in phase II. The latter changes were nonlinear and occurred at different starting points among the subjects. As shown in Table 4, the narrow normal 95% confidence intervals of AI-IV may allow detection of patients with impaired cerebral autoregulatory capacity. However, it should be noted that our study was performed in young subjects, and generalization to older individuals may not be appropriate and must await further studies.

Because few or no side-to-side differences were seen in response to the VM, another potentially useful tool for the detection of unilateral pathological autoregulatory capacity (eg, in severe unilateral carotid stenosis) may be the detection of marked side-to-side differences.

Testing autoregulation by means of the VM may prove to be clinically useful, because qualitative and quantitative measurements (eg, the AIs) can be easily obtained noninvasively in a short time. In our series they were reproducible. If the VM is applied at moderate pressure levels below 40 mm Hg, and is not performed on patients with potential contraindications such as retinopathy,[33,34] unclipped cerebral aneurysm, or known severe autonomic failure, it can be conducted safely and conveniently. Because the VM can be simulated by keeping the ventilator at a given pressure during an inspiratory pause, it may also be suitable for use in ventilated patients in the intensive care unit or the operating room. Moreover, the VM with simultaneous TCD and arterial pressure monitoring allows documentation of both the sympathetic and cerebral autoregulatory responses.

In conclusion, we suggest that TCD is well suited to analysis of changes in CBF and CVR during the VM. We demonstrated for the first time in normal adults that the changes in CBFV as an index of CBF during the VM are marked and that they exceed the concomitant relative ABP changes significantly. These changes are associated with changes in pulsatility reflecting altering CVR. Although cerebral autoregulation cannot fully compensate for the rapid challenges in the VM, these phenomena may be used as convenient tools in the study of the autoregulatory responses in normal and altered brain.

Further research is under way to investigate whether the VM and the proposed derived indexes may detect and quantify impairment in autoregulatory capacity in patients with cerebrovascular disease.

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