Impaired Neurogenic Cerebrovascular Control and Dysautoregulation After Stroke

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Abstract:
Cerebral autoregulation was tested in 32 patients with various anatomical locations and stages of ischemic cerebrovascular disease. Cerebral perfusion pressure (CPP) was raised or lowered in a standard manner by the use of head-up tilting (induced hypotension) and head-down tilting (induced hypertension). Any impairment of cerebral autoregulation was analyzed quantitatively by the ratio of the change in cerebral blood flow (CBF) over the change in CPP. There was significant correlation between the degree of dysautoregulation whether CPP was increased or decreased. An inverse correlation was shown between the degree of dysautoregulation and the duration after the ischemic episode during both induced hypotension and hypertension. Patients with brainstem lesions including those with transient ischemic attacks (TIAs) showed a greater impairment of autoregulation which persisted longer than those with hemispheric lesions. Patients with severe cerebral hemispheric infarction showed greater impairment of autoregulation than those with minor hemispheric lesions. Dysautoregulation also was greater in patients with subcortical lesions compared to those with cortical lesions.

Hypertensive patients showed significantly greater decreases in CBF and effective MABP during induced hypotension than normotensive patients although autoregulation index was the same. Thus, symptoms are more frequent in hypertensives because of greater changes in CPP.

Paradoxical responses in CBF to changes in CPP occurred in six patients. These were noted in moderately severe lesions in relatively young patients with hypertension and deeply located cerebral or brainstem lesions in the subacute stage. The mechanisms which control cerebral autoregulation were discussed and the nervous structures situated in the deep cerebral regions and brainstem, possibly the central structures of the autonomic nervous system, were proposed to control autoregulation of CBF.

Additional Key Words
vertebrobasilar insufficiency
autoregulation
stroke
TIA

Recent studies of the pathogenesis of cerebrovascular disease have shown impairment of autoregulation of the cerebral vessels in addition to the damage of the cerebral parenchyma. For instance, in areas of infarcted or damaged brain the vasomotor capacitance to changes in arterial carbon dioxide tension \( \text{PaCO}_2 \) and/or perfusion pressure is impaired so that usually in a severely ischemic region the cerebral blood flow (CBF) passively follows changes in the systemic blood pressure and becomes less responsive to changes in \( \text{PaCO}_2 \).

Differences in the severity of neurological symptoms from one patient to another when a major cerebral vessel has become occluded as well as fluctuations in the neurological status from day to day have been attributed to the functional capacitance of the collateral circulation. It was hypothesized that the collateral circulation becomes impaired by dysautoregulation and/or impaired chemical regulation during the acute stages of cerebral infarction but improves with the passage of time.

Up to the present time extensive studies of cerebral vasomotor responses in patients with cerebrovascular disease have not been correlated with the site, degree and severity of the lesion due to the lack of a simple and rapid method for measuring the degree of impaired vasomotor response to changes in \( \text{PaCO}_2 \) or cerebral perfusion pressure. Some studies have been published on the effect of

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drug-induced hypertension and hypotension in patients with cerebrovascular disease, although the drugs commonly used to manipulate systemic blood pressure may themselves alter cerebral vasomotor tone and hence distort natural responses of the cerebral vessels.

In reviewing the available literature on cerebral dysautoregulation in men it became evident that cases so far reported lacked an orderly correlation of information concerning the severity and localization of the cerebral infarction as well as other key information such as duration of the lesion and association of hypertension.

Meanwhile evidence has been accumulating rapidly concerning the possible importance of neurogenic control of the cerebral circulation in autoregulatory responses, although the mechanisms controlling cerebral autoregulation have long been assumed to be myogenic and metabolic.

The present study was designed in a prospective manner to investigate and compare in a quantitative manner cerebral dysautoregulation in patients with carefully categorized types of cerebrovascular disease at various intervals of time after the ischemic episode. The cerebral perfusion pressure was increased or decreased by tilting the body head up or head down by use of a tilt-table while monitoring cerebral arteriovenous differences for blood gases.

Case Material

Cerebral dysautoregulation was studied in 32 patients with various types of cerebral ischemia and infarction classified according to clinical, angiographical, EEG, CSF and brain scan findings. Age, sex, clinical diagnosis, clinical severity and interval of time between the ischemic episode and the time of study, and any associated hypertension are shown in table 1.

There were 19 males and 13 females ranging in age from 42 to 83 years with a mean age of 64 years. Twenty-one patients had cerebral infarction and 11 patients had brainstem ischemia or infarction. Six patients of the latter group had transient ischemic attacks referable to the vertebrobasilar system.

The clinical course and severity of the attack were arbitrarily classified according to severity into grades 1 through 4 as follows:

Grade 1—Transient ischemic attacks where the duration of localized neurological deficits did not exceed 24 hours and recovery was complete.

Grade 2—Reversible ischemic neurological deficits where the neurological deficits consisted of hemiparesis, monoparesis, dysphasia, etc., and persisted longer than 24 hours but recovery was virtually complete within three weeks.

Grade 3—Presumed cerebral infarction with moderate residual disabilities where recovery was steadily progressive, but moderate residual disability persisted after three weeks.

Grade 4—Presumed cerebral infarction with severe neurological deficits where severe neurological deficits persisted after three weeks with little or no evidence of recovery.

There were six patients in Grade 1, ten patients in Grade 2, 11 patients in Grade 3 and five patients in Grade 4. The interval of time between measurements and the cerebral ischemic episode ranged from 1 to 44 days with a mean of 16 days. Twenty-two patients had associated hypertension classified as essential hypertension after cardiovascular evaluation. Cerebral autoregulation was measured in 29 patients by both head-up and head-down tilting; in the remaining three patients satisfactory data were obtained in only one of these two maneuvers. Prior to the study, all patients were examined by a cardiologist in consultation in order to gain assurance that the cardiac status was satisfactory to withstand the measurements. Informed consent was obtained in writing for the procedure.

Methods

A detailed description and citation of the relevant references for the present study have been reported. In brief, each patient was given 50 mg of meperidine hydrochloride intramuscularly prior to the study. One percent procaine hydrochloride was applied to all puncture sites.

Under fluoroscopic control, catheters were placed via the antecubital veins into each cerebral transverse sinus and the superior vena cava. Other catheters were placed at the origin of the left vertebral artery, in the right brachial artery and in the femoral vein.

By means of a peristaltic pump, blood was drawn at a constant rate from the right brachial artery and transverse sinus. Arterial and cerebral venous blood samples were propelled through cuvettes containing electrodes and sensors for monitoring hydrogen clearance curves, oxygen tension (P02), carbon dioxide tension (PCO2), pH and oxygen saturation (SO2). The blood was returned to the circulation by means of an indwelling catheter in the femoral vein. Each parameter was recorded on a polygraph.

To measure hemispheric blood flow (HBF), an 8 to 10 ml bolus of hydrogen-saturated saline was injected into the carotid artery. HBF was calculated from the clearance curve for hydrogen obtained from the transverse sinus.

Arterial and cerebral venous differences for oxygen content (A-V)O2 was calculated from measurements of oxygen saturation, P02 and oxygen capacity. After measuring HBF, any changes in cerebral blood flow (CBF) induced by body tilting were calculated from the (A-V)O2 differences since the cerebral metabolic rate for oxygen is regarded as constant during tilting. The HBF measurements were carried out on the same side as the hemispheric lesion in patients with unilateral cerebral infarction.

Arterial blood pressure was monitored by the use of a strain gauge connected to the arterial catheter whose tip was placed at the origin of the vertebral artery from the left subclavian artery. The degree of tilting was measured with a goniometer. The strain gauge sensor was taped to the tilt-table at the level of the external ear.
### TABLE 1
Clinical Classification of Case Material

<table>
<thead>
<tr>
<th>Case no.</th>
<th>Age</th>
<th>Sex</th>
<th>Diagnosis</th>
<th>Duration (days)</th>
<th>Severity of neurological deficit</th>
<th>Clinical and laboratory data</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>75</td>
<td>M</td>
<td>R-cerebral infarction (cortical), hypertension</td>
<td>6</td>
<td>2</td>
<td>L-hemiparesis with dysphasia, no sensory loss, no ataxia; EEG: asynchronous R-temporal slow waves, brain scan: R-MCA regional slowed flow, CSF: normal, angiogram: diffuse intracranial arteriosclerosis</td>
</tr>
<tr>
<td>2</td>
<td>71</td>
<td>M</td>
<td>R-cerebral infarction (subcortical), hypertension</td>
<td>8</td>
<td>4</td>
<td>Sudden unconsciousness with L-hemiplegia and hypesthesia, eyes deviated to R; EEG: diffuse slow activity, brain scan: normal, angiogram: generalized arteriosclerosis, stenoses L-ICA, L-VA</td>
</tr>
<tr>
<td>3</td>
<td>69</td>
<td>M</td>
<td>R-cerebral infarction (cortical)</td>
<td>9</td>
<td>2</td>
<td>R-hemiparesis (leg &gt; arm) without sensory loss, complete recovery in one week; EEG: slow wave focus in R-temporal; brain scan, CSF: normal, angiogram: diffuse cerebral arteriosclerosis</td>
</tr>
<tr>
<td>4</td>
<td>56</td>
<td>M</td>
<td>R-cerebral infarction (subcortical), hypertension</td>
<td>9</td>
<td>3</td>
<td>L-hemiplegia and hypesthesia, bilaterally increased tendon reflexes; EEG: generalized slow activity with focal delta R-temporal, brain scan: increased uptake in R-hemisphere and slow flow through R-MCA, CSF: protein and pressure increased</td>
</tr>
<tr>
<td>5</td>
<td>70</td>
<td>F</td>
<td>L-cerebral infarction (cortical), hypertension</td>
<td>10</td>
<td>3</td>
<td>R-hemiparesis (leg &gt; arm), dysphasia, disorientated; EEG: slow focus L-frontotemporal, brain scan: slow flow, CSF: normal</td>
</tr>
<tr>
<td>6</td>
<td>69</td>
<td>F</td>
<td>R-cerebral infarction (cortical)</td>
<td>12</td>
<td>3</td>
<td>L-hemiplegia without sensory loss; EEG: diffuse slow activity, brain scan: slow flow through R-MCA, CSF: normal, angiogram: occlusion R-ICA and R-MCA</td>
</tr>
<tr>
<td>7</td>
<td>56</td>
<td>M</td>
<td>R-cerebral infarction (cortical)</td>
<td>12</td>
<td>3</td>
<td>L-hemiplegia without sensory loss; EEG: slow activity R-temporal, brain scan: marked reduction in flow through R-MCA and R-ICA, angiogram: R-ICA occlusion</td>
</tr>
<tr>
<td>8</td>
<td>49</td>
<td>M</td>
<td>R-cerebral infarction (cortical)</td>
<td>12</td>
<td>2</td>
<td>L-hemiparesis, transient blindness, slight sensory loss; EEG: slow focus in R-central region, brain scan: no flow through R-MCA, CSF: normal, angiogram: intracranial arteriosclerosis</td>
</tr>
<tr>
<td>9</td>
<td>66</td>
<td>M</td>
<td>R-cerebral infarction (subcortical), hypertension</td>
<td>12</td>
<td>4</td>
<td>Persistent L-hemiplegia and hemihypesthesia, eyes deviated to R, drowsy; EEG: alpha depressed on R, brain scan: increased uptake in R hemisphere, angiogram: diffuse arteriosclerotic change</td>
</tr>
<tr>
<td>10</td>
<td>67</td>
<td>F</td>
<td>R-cerebral infarction (cortical), hypertension</td>
<td>13</td>
<td>3</td>
<td>L-hemiplegia (arm &gt; leg) and sensory disturbance; EEG: focal slowing in R-temporal, brain scan: increased uptake R-temporal, angiogram: R-ICA occlusion</td>
</tr>
<tr>
<td>11</td>
<td>83</td>
<td>M</td>
<td>L-cerebral infarction (cortical)</td>
<td>14</td>
<td>2</td>
<td>R-hemiparesis with dysphasia; EEG: bilateral temporal lobe slow activity more marked in L, brain scan, CSF: normal, angiogram: L-ICA stenosis</td>
</tr>
<tr>
<td>Case no.</td>
<td>Age</td>
<td>Sex</td>
<td>Diagnosis</td>
<td>Duration (days)</td>
<td>Severity of neurological deficit</td>
<td>Clinical and laboratory data</td>
</tr>
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</tr>
<tr>
<td>12</td>
<td>42</td>
<td>M</td>
<td>L-cerebral infarction (subcortical), hypertension</td>
<td>15</td>
<td>3</td>
<td>R-hemiplegia, hypesthesia, dysarthria, headache, R-homonymous hemianopia; EEG: high voltage delta activity</td>
</tr>
<tr>
<td>13</td>
<td>67</td>
<td>M</td>
<td>R-cerebral infarction (subcortical), hypertension</td>
<td>16</td>
<td>3</td>
<td>L-hemiparesis, hypesthesia; EEG: generalized slow activity, brain scan: normal, angiogram: L-ICA stenosis</td>
</tr>
<tr>
<td>14</td>
<td>54</td>
<td>F</td>
<td>L-cerebral infarction (subcortical), hypertension</td>
<td>17</td>
<td>3</td>
<td>R-hemiparesis, hypesthesia; EEG: delta activity on left, brain scan, CSF: normal, angiogram: multiple branch occlusions of left MCA</td>
</tr>
<tr>
<td>15</td>
<td>73</td>
<td>F</td>
<td>L-cerebral infarction (subcortical), hypertension</td>
<td>18</td>
<td>3</td>
<td>R-hemiparesis, hypesthesia, confused, bilateral extensor plantar responses; CSF: normal</td>
</tr>
<tr>
<td>16</td>
<td>69</td>
<td>F</td>
<td>Bilateral cerebral infarction (subcortical), hypertension</td>
<td>18</td>
<td>4</td>
<td>L-hemiplegia, hypesthesia, coma followed by R-hemiparesis, progressive deterioration; brain scan: increased uptake in R-parietotemporal and slow flow through R-MCA, angiogram: R-ACA and L-ICA occlusion, multiple bilateral stenoses</td>
</tr>
<tr>
<td>17</td>
<td>48</td>
<td>M</td>
<td>L-cerebral infarction (cortical), hypertension</td>
<td>19</td>
<td>3</td>
<td>R-hemiparesis, hypesthesia, aphasia, R-homonymous hemianopia, sensory loss, oculomotor, agnosia, disorientation; EEG: delta activity</td>
</tr>
<tr>
<td>18</td>
<td>66</td>
<td>M</td>
<td>L-cerebral infarction (cortical)</td>
<td>25</td>
<td>3</td>
<td>R-hemiparesis, hypesthesia, aphasia, stuporous, improved; EEG: slow focus in L-occipitotemporal region, brain scan: normal, angiogram: diffuse arteriosclerosis</td>
</tr>
<tr>
<td>19</td>
<td>56</td>
<td>F</td>
<td>R-cerebral infarction (subcortical), hypertension</td>
<td>25</td>
<td>2</td>
<td>L-hemiplegia, sensory disturbance; EEG: episodic slow waves</td>
</tr>
<tr>
<td>20</td>
<td>68</td>
<td>M</td>
<td>L-cerebral infarction (subcortical), hypertension</td>
<td>42</td>
<td>4</td>
<td>R-hemiparesis, dysarthria, drowsy and confused, progressive deterioration; EEG: generalized depressed activity</td>
</tr>
<tr>
<td>21</td>
<td>68</td>
<td>F</td>
<td>R-cerebral infarction (cortical)</td>
<td>44</td>
<td>2</td>
<td>L-hemiparesis, dysphasia; EEG: independent foci of delta activity in L and R-temporal, brain scan: normal, angiogram: R-MCA, L-ICA occlusion, R-ICA stenosis</td>
</tr>
</tbody>
</table>

**Brainstem ischemia and infarction**

<table>
<thead>
<tr>
<th>Case no.</th>
<th>Age</th>
<th>Sex</th>
<th>Diagnosis</th>
<th>Duration (days)</th>
<th>Severity of neurological deficit</th>
<th>Clinical and laboratory data</th>
</tr>
</thead>
<tbody>
<tr>
<td>22</td>
<td>63</td>
<td>M</td>
<td>Vertebrobasilar insufficiency, hypertension</td>
<td>1</td>
<td>1</td>
<td>Daily attacks of dizziness, diplopia, ataxia, syncope; EEG, brain scan, CSF: normal</td>
</tr>
<tr>
<td>23</td>
<td>65</td>
<td>F</td>
<td>Vertebrobasilar insufficiency, hypertension</td>
<td>3</td>
<td>1</td>
<td>Frequent attacks of vertigo, ataxia, nausea with occipital headache; EEG, brain scan, CSF, angiogram: normal</td>
</tr>
<tr>
<td>24</td>
<td>66</td>
<td>M</td>
<td>Brainstem infarction</td>
<td>8</td>
<td>2</td>
<td>Diplopia, ataxia, vertical nystagmus; EEG: slow occipital alpha activity, CSF: normal</td>
</tr>
<tr>
<td>25</td>
<td>61</td>
<td>F</td>
<td>Vertebrobasilar insufficiency, hypertension</td>
<td>8</td>
<td>1</td>
<td>Frequent attacks of syncope, dysarthria, slurred speech, hypesthesia L-face; EEG: generalized slow alpha activity and R-temporo-occipital focus; brain scan, CSF: normal, angiogram: narrowing L-subclavian artery, generalized arteriosclerosis</td>
</tr>
<tr>
<td>Case no.</td>
<td>Age</td>
<td>Sex</td>
<td>Diagnosis</td>
<td>Duration (days)</td>
<td>Severity of neurological deficit</td>
<td>Clinical and laboratory data</td>
</tr>
<tr>
<td>---------</td>
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<td>----------------</td>
<td>----------------------------------</td>
<td>-------------------------------</td>
</tr>
<tr>
<td>26</td>
<td>59</td>
<td>F</td>
<td>Verteobasilar insufficiency, hypertension</td>
<td>10</td>
<td>1</td>
<td>Recurrent dizziness, dysesthesias and drooping of L-eye, bilateral vertical and horizontal nystagmus, ataxia, increased tendon reflexes; EEG: slowing of background activity; brain scan, CSF, angiogram: normal</td>
</tr>
<tr>
<td>27</td>
<td>77</td>
<td>M</td>
<td>Brainstem infarction, hypertension</td>
<td>12</td>
<td>2</td>
<td>Prolonged attacks of ataxia, dysarthria, diplopia with persistent cerebellar sign; EEG, brain scan: normal, angiogram: R-VA, L-ICA stenosis, generalized arteriosclerotic change</td>
</tr>
<tr>
<td>28</td>
<td>63</td>
<td>M</td>
<td>Brainstem infarction</td>
<td>15</td>
<td>2</td>
<td>Dysphagia, dysarthria, nystagmus, increased R-tendon reflexes, L-hemiparesis; EEG: bilateral slow activity; brain scan, CSF: normal</td>
</tr>
<tr>
<td>29</td>
<td>62</td>
<td>M</td>
<td>Brainstem infarction</td>
<td>16</td>
<td>4</td>
<td>Syncope followed by persistent dysarthria, ataxia, eyes deviated to L; EEG: diffuse slow activity and some focal delta waves in R-parieto-occipital; brain scan, CSF: normal, angiogram: R and L-VA stenosis</td>
</tr>
<tr>
<td>30</td>
<td>66</td>
<td>F</td>
<td>Verteobasilar insufficiency, hypertension</td>
<td>25</td>
<td>1</td>
<td>Recurrent drop attacks without loss of consciousness with transient ataxia, cerebellar tremor; EEG: bilateral slow activity in temporal regions, CSF: normal, angiogram: diffuse sclerotic change and L-VA stenosis</td>
</tr>
<tr>
<td>31</td>
<td>65</td>
<td>F</td>
<td>Verteobasilar insufficiency</td>
<td>26</td>
<td>1</td>
<td>Attacks of photopsia, ataxia and incoordination; EEG: shift slowing; brain scan, EEG: normal, angiogram: increased tortuosity of vertebral arteries</td>
</tr>
<tr>
<td>32</td>
<td>48</td>
<td>M</td>
<td>Brainstem infarction, hypertension</td>
<td>31</td>
<td>2</td>
<td>Sudden onset dysarthria and facial weakness, diplopia, vertigo, ataxia, bilateral increase of tendon reflexes; EEG, brain scan, CSF, angiogram: normal</td>
</tr>
</tbody>
</table>

M = male, F = female, R = right, L = left, ACA = anterior cerebral artery, MCA = middle cerebral artery, ICA = internal carotid artery, VA = vertebral artery.
in order to record the effective arterial blood pressure (effective BP) at the brain where the patient's position was altered. Intracranial venous pressure (ICVP) also was monitored at the level of the external ear by a strain gauge connected to the venous catheter whose tip lay in the transverse sinus. Intracranial pressure (ICP) was monitored by directing a catheter in a cephalad direction via the subarachnoid space after lumbar puncture with its sensor placed at the level of the cisterna magna. Central venous pressure (CVP) was recorded with the baseline adjusted at the level of the heart. The patient was placed on the tilt-table and the strain gauges were mounted on the table at the points described. Effective mean arterial blood pressure (effective MABP) was calculated by adding one-third of the pulse pressure to the diastolic pressure. Mean ICVP (MICVP), mean ICP (MICP) and mean CVP (MCVP) were computed as the minimum recorded pressures plus one-third of the pulse pressures. Cerebral perfusion pressure (CPP) across the brain was calculated as effective MABP minus MICVP.

Quantitative analysis of any impairment of cerebral autoregulation was computed by means of the following formula which we term the autoregulation index (A.I.):

$$A.I. = \frac{\Delta CBF}{\Delta CPP} \text{ ml/100 gm brain/min mm Hg}$$

where $\Delta CBF$ equals the change of cerebral blood flow when CPP was changed from the steady state level by head-up to head-down tilting ($\Delta CPP$).

It is well known that when cerebral autoregulation is intact, the caliber of cerebral vessels adjusts to maintain cerebral blood flow constant despite changes in perfusion pressure of as much as 180 to 200 mm Hg. Thus, when autoregulation is intact, A.I. should be zero or close to zero, and any deviation of A.I. from zero in a plus or minus direction will be in direct proportion to the degree of dysautoregulation. As far as we are aware, this is the first time that quantitative estimates of dysautoregulation have been measured in man.

The $t$-test was used to compare the differences, and for comparison of the population which had different standard deviations, the significance of the differences was calculated by Cochran's approximation. A significance level at $P < 0.05$ was used to test the validity of the results.

**Results**

**EFFECT OF TILTING ON CEREBRAL VENOUS, ARTERIAL AND INTRACRANIAL DYNAMICS**

The results of head-up tilting to $47^\circ$ and head-down tilting to $26^\circ$ are summarized in tables 2-a and 2-b, and graphically illustrated in figure 1. Examples of actual recordings are illustrated in figure 2. The tilting of the patient was carried out slowly to prevent artifactual effects of abrupt changes in CBF.

All data in which either CPP decreased below the autoregulatory range present in normal individuals or when $P_{aCO_2}$ was grossly altered by...
### TABLE 2-a
**Effect of Tilting on Cerebral Venous and Arterial Blood Gases in Stroke Patients**

<table>
<thead>
<tr>
<th></th>
<th>Steady state</th>
<th>Head-up (46.8 ± 4.8°)</th>
<th>Tilt</th>
<th>Steady state</th>
<th>Head-down (25.8 ± 3.7°)</th>
<th>Tilt</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cerebral venous blood</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$P_0_2$ (mm Hg)</td>
<td>30.1 ± 4.7</td>
<td>27.8 ± 7.8* (N = 30)</td>
<td></td>
<td>29.9 ± 4.5</td>
<td>30.7 ± 4.9* (N = 31)</td>
<td></td>
</tr>
<tr>
<td>$S_0_2$ (%)</td>
<td>54.0 ± 8.0</td>
<td>48.0 ± 9.7* (N = 30)</td>
<td></td>
<td>51.8 ± 9.0</td>
<td>53.2 ± 8.3* (N = 31)</td>
<td></td>
</tr>
<tr>
<td>$P_0_2$ (mm Hg)</td>
<td>53.5 ± 6.8</td>
<td>54.1 ± 6.6* (N = 28)</td>
<td></td>
<td>53.4 ± 7.1</td>
<td>52.9 ± 7.1* (N = 29)</td>
<td></td>
</tr>
<tr>
<td>pH</td>
<td>7.239 ± 0.039</td>
<td>7.237 ± 0.037* (N = 24)</td>
<td></td>
<td>7.243 ± 0.038</td>
<td>7.244 ± 0.038* (N = 27)</td>
<td></td>
</tr>
<tr>
<td>$O_2$ (vol %)</td>
<td>8.52 ± 1.89</td>
<td>7.58 ± 1.94* (N = 30)</td>
<td></td>
<td>8.24 ± 1.92</td>
<td>8.46 ± 1.91* (N = 31)</td>
<td></td>
</tr>
<tr>
<td><strong>Arterial blood</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$P_0_2$ (mm Hg)</td>
<td>72.8 ± 8.2</td>
<td>74.0 ± 8.4* (N = 30)</td>
<td></td>
<td>71.0 ± 10.1</td>
<td>70.9 ± 10.3* (N = 31)</td>
<td></td>
</tr>
<tr>
<td>$S_0_2$ (%)</td>
<td>94.9 ± 3.8</td>
<td>95.3 ± 3.6* (N = 30)</td>
<td></td>
<td>94.2 ± 4.0</td>
<td>94.1 ± 4.1* (N = 31)</td>
<td></td>
</tr>
<tr>
<td>$P_0_2$ (mm Hg)</td>
<td>41.3 ± 6.2</td>
<td>40.5 ± 6.9* (N = 29)</td>
<td></td>
<td>40.7 ± 6.3</td>
<td>40.9 ± 6.4* (N = 30)</td>
<td></td>
</tr>
<tr>
<td>pH</td>
<td>7.323 ± 0.044</td>
<td>7.327 ± 0.046* (N = 28)</td>
<td></td>
<td>7.318 ± 0.046</td>
<td>7.317 ± 0.042* (N = 28)</td>
<td></td>
</tr>
<tr>
<td>$O_2$ (vol %)</td>
<td>15.18 ± 2.33</td>
<td>15.22 ± 2.34* (N = 30)</td>
<td></td>
<td>15.20 ± 2.33</td>
<td>15.19 ± 2.31* (N = 31)</td>
<td></td>
</tr>
</tbody>
</table>

Values = mean ± standard deviation.  
N = number of cases.  
* = statistically significant difference compared with steady state value.

### TABLE 2-b
**Effect of Tilting on CBF and Intracranial Dynamics in Stroke Patients**

<table>
<thead>
<tr>
<th></th>
<th>Steady state</th>
<th>Head-up</th>
<th>Tilt</th>
<th>Steady state</th>
<th>Head-down</th>
<th>Tilt</th>
</tr>
</thead>
<tbody>
<tr>
<td>CBF (ml/100 gm brain/min)</td>
<td>33.7 ± 3.8</td>
<td>29.6 ± 4.7* (N = 30)</td>
<td></td>
<td>33.1 ± 4.0</td>
<td>34.1 ± 4.7* (N = 31)</td>
<td></td>
</tr>
<tr>
<td>Effective MABP (mm Hg)</td>
<td>108.6 ± 19.1</td>
<td>84.7 ± 18.4* (N = 30)</td>
<td></td>
<td>101.9 ± 17.9</td>
<td>115.7 ± 19.0* (N = 31)</td>
<td></td>
</tr>
<tr>
<td>CPP (mm Hg)</td>
<td>101.4 ± 18.7</td>
<td>82.9 ± 18.0* (N = 30)</td>
<td></td>
<td>94.4 ± 17.3</td>
<td>102.8 ± 18.2* (N = 31)</td>
<td></td>
</tr>
<tr>
<td>MICVP (mm saline)</td>
<td>98.0 ± 47.1</td>
<td>24.1 ± 49.0* (N = 30)</td>
<td></td>
<td>103.8 ± 45.8</td>
<td>178.2 ± 59.5* (N = 31)</td>
<td></td>
</tr>
<tr>
<td>MICP (mm saline)</td>
<td>156.4 ± 44.0</td>
<td>55.9 ± 51.2* (N = 28)</td>
<td></td>
<td>155.1 ± 51.9</td>
<td>253.3 ± 66.7* (N = 30)</td>
<td></td>
</tr>
<tr>
<td>MCVP (mm saline)</td>
<td>70.9 ± 54.8</td>
<td>25.3 ± 59.3* (N = 26)</td>
<td></td>
<td>69.5 ± 55.6</td>
<td>106.0 ± 69.7* (N = 30)</td>
<td></td>
</tr>
</tbody>
</table>

Values = mean ± standard deviation.  
N = number of cases.  
* = statistically significant difference compared with steady state value.  
CBF = cerebral blood flow, MABP = mean arterial blood pressure, CPP = cerebral perfusion pressure, MICVP = mean intracranial venous pressure, MIPCP = mean intracranial pressure, and MCVP = mean central venous pressure.
concomitant hyperventilation were excluded from the present study.\textsuperscript{5, 21}

During head-up tilting there was induced hypotension and cerebral venous \( P_{O_2} \) (CVP\( _{O_2} \)), CVS\( _{O_2} \), CVpH decreased significantly and CVP\( _{CO_2} \) increased significantly compared to the steady state compatible with reduced CBF and impaired autoregulation (table 2-a). Arterial \( P_{O_2} \) (Pao\( _{2} \)) and Sa\( _{O_2} \)

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{fig2a.png}
\caption{Effect of head-up tilting (induced hypotension) and head-down tilting (induced hypertension) on cerebral hemodynamics: The decreases in cerebral venous \( P_{O_2} \) (CVP\( _{O_2} \)) and saturation (CVS\( _{O_2} \)) which indicate a fall in CBF are in proportion to the decrease of effective arterial blood pressure (or cerebral perfusion pressure) displaying an impairment of autoregulation in CBF.}
\end{figure}
There is a rise in CBF with increase in effective arterial blood pressure.
increased slightly and changes in PaCO₂ and apH were minimum but significant. These changes in arterial gases and pH were believed to result from the decrease in intrathoracic pressure (decrease in CVP) and slight hyperventilation induced by the change in posture. During the head-up position CBF decreased significantly with an average decrease of 12.2%, effective MABP and CPP were reduced by 24.9 and 18.5 mm Hg, respectively, and the other pressure measurements also were significantly reduced (table 2-b).

During the head-down position (induced hypertension) there was an increase in CBF. Effective MABP and CPP increased by 13.8 and 8.4 mm Hg, respectively.

These differences in the change of CBF, effective MABP and CPP between head-up and head-down tilting were due to the degree of tilt. In both induced hypotension and hypertension, the changes in CBF were proportional to the direction and degree of change in CPP, indicating that in the group of patients as a whole, dysautoregulation was present whether CPP was raised or lowered. As shown in the left-hand panel of figure 1, there were some exceptions. Two patients during induced hypotension and four patients during induced hypertension showed an inverse response to changes in CPP (paradoxic response). The mean autoregulation index (A.I.) expressed in absolute values was 0.221 (SD ± 0.120) ml/100 gm brain/min to unit change in CPP during induced hypotension, and 0.217 (SD ± 0.206) ml/100 gm brain/min per mm Hg during induced hypertension (middle panel, fig. 1). There was no significant difference of A.I. when induced hypotension was compared to induced hypertension. In fact, there was significant correlation between the degree of dysautoregulation when cerebral perfusion pressure was altered in either direction (right-hand panel, fig. 1).

**EFFECT OF TIME INTERVAL AFTER ISCHEMIC EPISODE, AGE, AND HYPERTENSION ON DYSAUTOREGULATION**

Cerebral dysautoregulation was analyzed according to the duration after the ischemic episode and the age of the patients (fig. 3).

During both induced hypotension and hypertension there was a significant inverse correlation between the magnitude of dysautoregulation and the duration of survival following the ictus. In other

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**EFFECT OF DURATION OF SYMPTOMS AND AGE ON DYSAUTOREGULATION**

**DURATION OF SYMPTOMS**

**AGE**

![Graphs showing the effect of duration of symptoms and age on cerebral dysautoregulation.](http://stroke.ahajournals.org/)

*Effect of duration of symptoms (left-hand panel) and age (right-hand panel) on cerebral dysautoregulation. Left: There are significant inverse correlations between the degree of dysautoregulation and the duration during both induced hypotension and hypertension. Right: No significant correlations are seen between these two variables.*
words, the longer the survival after the stroke, the less was the degree of dysautoregulation. On the contrary, there was no correlation between the severity of dysautoregulation and the patients' age.

The study group of patients were divided into those with hypertension and those without. Comparison between these two groups is shown in figure 4. The degree of dysautoregulation (A.I.) was not significantly higher in hypertensive patients than in normotensive patients, while induced changes in effective MABP in either head-up or head-down position were significantly greater in the hypertensive than in the normotensive group.

**EFFECT OF SEVERITY OF SYMPTOMS AND LOCATION ON DYSAUTOREGULATION**

The study group of patients with cerebral hemispheric infarction was divided into three groups according to the severity of their neurological deficit and their clinical course. The ten cases with mild vertebrobasilar symptoms (Grades 1 and 2) were compared to the entire group of patients with cerebral hemispheric infarction. As demonstrated in Figure 5, dysautoregulation was much more severe in patients with mild brainstem lesions than in patients with moderate cerebral hemispheric infarction (Grades 2 and 3). The patients with severe cerebral hemispheric infarction (Grade 4) showed greater dysautoregulation than those with Grades 2 and 3 of cerebral hemispheric infarction during either induced hypotension or hypertension.

In addition to analyzing whether the location of the lesion within the brainstem or the cerebral hemisphere influenced autoregulation, the group with cerebral hemispheric infarction was further subdivided into those with cortical and subcortical lesions and the effect on autoregulation compared. Since the duration of the symptoms had already been shown to influence the degree of dysautoregulation, the cases also were subdivided into acute and subacute groups (table 3 and fig. 6).

While the dysautoregulation in brainstem and subcortical lesions was less in the subacute stage (15 days or more after the ictus) compared to the acute stage (within 14 days of the ictus), it was still greater than in cases with cortical lesions in both stages.

The cases with cortical lesions showed greater dysautoregulation during induced hypotension than hypertension in the acute stage. However, in cases with brainstem and subcortical lesions the degree of dysautoregulation was not significantly different whether hypotension or hypertension was induced.

**DYSAUTOREGULATION COMPARED BETWEEN HYPERTENSIVES AND NORMOTENSIVES WITH STROKE**

Comparison of cerebral dysautoregulation in hypertensive patients to normotensive patients. There is no difference in the degree of dysautoregulation between the two groups (left-hand panel). In the hypertensive patients, however, greater falls in CBF and effective MABP, and a greater rise in effective MABP are shown as compared to the normotensive patients (middle and right-hand panels).

**FIGURE 4**
MEYER, SHIMAZU, FUKUUCHI, OHUCHI, OKAMOTO, KOTO, ERICSSON

RELATIONSHIP BETWEEN SEVERITY OF SYMPTOMS
AND DYSAUTOREGULATION

INDUCED HYPOTENSION

INDUCED HYPERTENSION

Effect of clinical course and severity on cerebral dysautoregulation. The patients with severe cerebral infarction and brainstem lesions showed a higher impairment of autoregulation during both induced hypotension and hypertension.

PARADOXICAL RESPONSES OF CBF TO CHANGES IN CPP

During induced hypertension CBF decreased in four patients (marked with ++ in all figures) and when hypotension was induced CBF increased in two patients (marked + in all figures). An example of continuous measurements showing a paradoxical response is illustrated in figure 7, left panel. Of these, five occurred in cases of brainstem or subcortical lesions (fig. 6). All four cases with flow decreases during induced hypertension were found to be within the hypertensive group and also showed a marked impairment of autoregulation during induced hypotension (figs. 1 and 4).

Discussion

VALIDITY OF TILTING AS A METHOD FOR MEASURING CEREBRAL PERFUSION PRESSURE-FLOW RELATIONSHIPS

In the past, increases or decreases of cerebral perfusion pressure (CPP) have been induced by means of pressor amines or peripheral vasodilator drugs such as ganglionic blocking agents in order to evaluate the presence or absence of dysautoregulation. It is well known that such pharmacological preparations may themselves affect CBF. Thus, postural tilting is a preferable method for demonstrating any abnormality of autoregulation in CBF.

Scheinberg and Stead reported a decrease in CBF during head-up tilting to 45° to 65° in normal subjects. They measured CBF by means of the N₂O method. During head-up position, the effective MABP was reduced on the average from 84.5 to 55.1 mm Hg. CBF decreased by 20.5% as a mean and the (A-V)O₂ difference increased on an average of 23.0%. However, since values for Paco₂ were not given, hyperventilation which commonly occurs during tilting was probably responsible.

In the present study, Paco₂ and respiration were continuously monitored and, if large changes in Paco₂ occurred, the data were discarded. In addition, tilting was restricted to 47°. Patients with small cortical lesions of greater than two weeks' duration showed intact autoregulation in both head-up and head-down positions. These results suggest
### TABLE 3
Comparison of Cerebral Dysautoregulation in Brainstem Ischemia and Infarction Compared to Cerebral Infarction

<table>
<thead>
<tr>
<th></th>
<th>Brainstem ischemia and infarction</th>
<th>Subcortical</th>
<th>Cerebral Infarction</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number of cases</td>
<td>11</td>
<td>9</td>
<td>12</td>
<td>21</td>
</tr>
<tr>
<td>Grade</td>
<td>1.6 ± 0.9</td>
<td>3.3 ± 0.7</td>
<td>2.6 ± 0.5</td>
<td>2.9 ± 0.7</td>
</tr>
<tr>
<td>Duration after onset (days)</td>
<td>14.1 ± 9.7</td>
<td>18.0 ± 10.3</td>
<td>16.2 ± 10.1</td>
<td>17.0 ± 10.0</td>
</tr>
</tbody>
</table>

1. Induced hypotension
   - Acute (≤ 14 days)
     - 0.314 ± 0.078 (N = 6) vs 0.302 ± 0.008 (N = 3)
       - 0.001 < P < 0.005
     - Subacute (> 14 days)
       - 0.216 ± 0.144 (N = 4) vs 0.293 ± 0.092 (N = 5)
       - 0.01 < P < 0.005
       - Total
         - 0.275 ± 0.114 (N = 10) vs 0.296 ± 0.070 (N = 8)
         - 0.001 < P < 0.005

2. Induced hypertension
   - Acute (≤ 14 days)
     - 0.451 ± 0.185 (N = 6) vs 0.477 ± 0.266 (N = 3)
       - 0.005 < P < 0.01
     - Subacute (> 14 days)
       - 0.184 ± 0.115* (N = 5) vs 0.195 ± 0.076 (N = 5)
       - 0.005 < P < 0.01
       - Total
         - 0.330 ± 0.204 (N = 11) vs 0.301 ± 0.212 (N = 8)
         - 0.001 < P < 0.005

Values = ΔCBF/ΔCPP = mean ± standard deviation.

N = number of cases.

* = statistically significant difference compared with acute cases.
Comparison of cerebral dysautoregulation in brainstem lesions to cerebral hemispheric lesions. During both induced hypotension and hypertension, brainstem and subcortical lesions showed a higher degree of dysautoregulation than cortical lesions as total cases (left-hand panel), or in acute stage (middle) and subacute stage (right). An impairment of autoregulation in the former two groups persisted longer than the latter group, although each group had a tendency to improve as time after ictus increased.

Figures 6

Comparison of cerebral dysautoregulation in brainstem lesions to cerebral hemispheric lesions. During both induced hypotension and hypertension, brainstem and subcortical lesions showed a higher degree of dysautoregulation than cortical lesions as total cases (left-hand panel), or in acute stage (middle) and subacute stage (right). An impairment of autoregulation in the former two groups persisted longer than the latter group, although each group had a tendency to improve as time after ictus increased.

DYSAUTOREGULATION COMPARED BETWEEN BRAINSTEM AND CEREBRAL ISCHEMIA AND INFARCTION

In our experience, postural tilting is a simple, safe, rapid and useful method for objectively measuring cerebral perfusion pressure-flow relationships provided that: (1) the change of posture must be carried out slowly and carefully after explaining the procedure to prevent apprehension of the subjects, (2) that Pao2 must be monitored, and (3) that perfusion pressure must not exceed the autoregulatory pressure range present in normal individuals.

QUANTITATIVE ANALYSIS OF CEREBRAL DYSAUTOREGULATION

In this study, dysautoregulation was analyzed quantitatively by the use of the autoregulation index which revealed new information relevant to the pathogenesis of cerebral vascular symptoms and the physiological control of the CBF in man. Previous authors10 concluded arbitrarily that autoregulation was lost when CBF was reduced over 7.0 ml/100 gm brain/min as the blood pressure was lowered. They did not consider the degree of perfusion pressure changes which were lowered by the use of drugs over a wide range (14 to 57 mm Hg).

They based this arbitrary decision on statistical limitations of the reproducibility of the method used to measure CBF. Others also neglected to consider the magnitude of the changes in perfusion pressure when deciding whether autoregulation was present or absent, i.e., they used an all-or-none concept.7-9

that autoregulation is intact in normal subjects and CBF does not change if tilting is slowly carried out and does not exceed 47° in the head-up position and 26° in the head-down position and provided that Paco2 is unaltered. In addition, the procedure of tilting was fully explained to the patients and slowly carried out over a three-minute interval to prevent apprehension and to prevent hyperventilation as well as to avoid rapid changes in effective arterial blood pressure, since autoregulation takes 30 to 120 seconds to become effective even in normal subjects.26

Despite these precautions the patients observed in the present study showed a minimal but significant decrease in Pao2 due to slight hyperventilation during head-up tilting (table 2-a) which was presumably caused by gravitational forces on the diaphragm and viscera improving respiratory function, since the orthopneic position is known to improve pulmonary function.

Another factor which will invalidate measurements of the autoregulation index is when the perfusion pressure falls below 50 to 60 mm Hg in the head-up position, since autoregulation is lost even in normal individuals at CPP below this range.6, 21 In the present study whenever the effective MABP approached 60 mm Hg, the head-up tilt was lessened or discontinued.

In our experience, postural tilting is a simple, safe, rapid and useful method for objectively measuring cerebral perfusion pressure-flow relationships provided that: (1) the change of posture must be carried out slowly and carefully after explaining the procedure to prevent apprehension of the subjects, (2) that Pao2 must be monitored, and (3) that perfusion pressure must not exceed the autoregulatory pressure range present in normal individuals.

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FIGURE 7

Effect of alpha-adrenergic blockade by phenoxybenzamine on cerebral dysautoregulation. The patient showed flow decrease to induced hypertension. Following intracarotid infusion of 10 mg phenoxybenzamine (PBZ) the change in CBF became passive to the increase in effective arterial blood pressure.

In other words, in order to quantitatively assess impairment of autoregulation, changes in CBF expressed in ml/100 gm brain/min must be considered in direct proportion to changes in perfusion pressure expressed in mm Hg instead of percent change from steady state values.5,27

\[
\text{Reproducibility} = \frac{\text{Value of 1st measurement} - \text{2nd measurement}}{\text{Value of 1st measurement}}
\]

In the present study, cerebral dysautoregulation was analyzed in terms of both changes in CBF and changes in cerebral perfusion pressure (CPP). In order to validate such quantitative measurements of A.I. the accuracy of CBF measurements must be known. To determine the reproducibility of CBF measurements calculated from the continuous (A-V)O₂ differences, two measurements of the (A-V)O₂ differences at five-minute intervals were repeated in 11 patients during the steady state. The reproducibility was examined by the following formula:

The reproducibility calculated by this formula was 1.3 ± 0.9% (0.4 ± 0.3 ml/100 gm brain/min). Therefore, changes in CBF of more than 1.0 ml/100 gm brain/min (mean plus two standard deviations) compared to steady state values, or changes in A.I. of more than 0.054 during induced hypotension and
0.119 during induced hypertension (table 2-b), were considered abnormal.

It has been shown previously that cerebral oxygen consumption is constant during tilting, and this was substantiated in the present study since cerebral A-V differences for oxygen, carbon dioxide and glucose remained constant in those patients with intact autoregulation.

CEREBRAL DYSAUTOREGULATION IN CEREBRAL ISCHEMIA AND INFARCTION

The total group of all patients with cerebrovascular symptoms showed impaired autoregulation in the head-up or head-down position when considered as a mean. Analysis of the degree of dysautoregulation according to different age groups failed to show that age played any significant role.

Cerebral dysautoregulation has generally been assumed to persist for some weeks after stroke, but the duration has never been accurately defined. For example, regional CBF studies by Skinhøj et al. demonstrated a focal or diffuse loss of autoregulation “shortly” after a “cerebrovascular accident” but not between attacks in patients with transient ischemic attacks (TIA). Others reported autoregulation to be intact in patients with TIA two days after the onset. However, both of these authors studied patients with transient neurological deficits due to hemispheric ischemia.

As far as we are aware, the present investigation is the first to measure autoregulation in patients with TIAs referable to the vertebrobasilar system, and it soon became apparent that the anatomical location of the cerebral ischemia itself was of great importance in the pathogenesis of the degree and duration of cerebral dysautoregulation. In general, patients with brainstem ischemia (TIAs) and lesions near the diencephalon showed more severe dysautoregulation which persisted longer than in patients with infarction of the cerebral cortex.

Reports of the duration of dysautoregulation in patients with major cerebral infarction also are conflicting. Paulson et al. reported a diffuse loss of autoregulation which persisted for two weeks in patients with “cerebral infarction without arterial occlusion.” Other investigators commented vaguely that autoregulation was lost for a few days in most patients although it remained impaired for several months in some.

In the present study more than one-half the patients were tested for dysautoregulation 15 days or more after the onset of the stroke and marked dysautoregulation still persisted. Such differences in the duration of dysautoregulation between previous reports and ours are readily explained by differences in the location and severity of cerebral infarction as well as the methods used to measure CBF.

Let us now consider the six patients who showed paradoxical responses of CBF to CPP changes in the present study. All four patients who had decreases of CBF during induced hypertension were severely hypertensive and had subcortical and brainstem lesions. During head-down tilt, the effective MABP and effective systolic blood pressure were in the order of 120 and 190 mm Hg.

Previous investigators also observed paradoxical flow decrease during induced hypertension with abolished cerebral vasoconstrictor reactivity in cerebral infarction and brain tumors, and they interpreted these phenomena as a result of an “intracranial steal” effect. This speculation, however, does not seem to be the case in the present study because these patients showed normal or close to normal vasomotor capacitance to PaO2 changes.

Waltz reported in experimental ischemia that while dysautoregulation was the rule as MABP was raised when the MABP exceeded 120 mm Hg, CBF ceased to increase; he proposed that the arterial vessels respond to maximal stimulation by undergoing vasoconstriction or spasm. The most likely explanation in our patients is that they were hypertensive and their cerebral vessels underwent excessive vasoconstriction as the intraluminal pressure was increased, a condition known to occur in hypertension.

This view was supported by additional studies. In three of the hypertensive patients showing excessive autoregulation or paradoxical responses, cerebral dysautoregulation was reinvestigated following the intracarotid infusion of an alpha-adrenergic blocking agent (10 mg phenoxybenzamine hydrochloride). This agent blocked or reversed the fall in CBF in all cases showing that the alpha-adrenergic vasoconstrictive receptors participate in the regulatory mechanism of cerebral autoregulation and respond excessively in these paradoxical cases (fig. 7, right panel). In the two cases with a flow increase during induced hypotension there are two possible explanations. Either the decrease in intracranial pressure during head-up tilt allowed more flow of blood into the ischemic area or, less likely, the vessels in the ischemic zone were in a hyperreactive state to their parasympathetic or beta-adrenergic receptors because of the damage caused by the ischemic episode and displayed a resultant overreaction (excessive vasodilation) to induced hypotension.

Let us now consider the fact that patients with brainstem and subcortical lesions (including vertebrobasilar insufficiency) showed a greater degree and longer duration of impairment of autoregulation as compared to patients with cortical lesions. The injured sites affected by ischemic episodes in these groups were located anatomically in the deep regions of the brain such as thalamus, hypothalamus,
mesencephalon and brainstem which are known to contain centers controlling autonomic innervations of the cerebral vessels in both animals and man.12, 17 Hence, damage to these nervous structures logically would give rise to a greater loss of cerebral autoregulation.

The role of the brainstem and diencephalon in the autonomic control of CBF and metabolism has been reviewed in several studies.16-18 We have demonstrated a loss of autoregulation in three patients with Shy-Drager syndrome12 in which the central autonomic nervous system is well known to be impaired.

The pathways of the autonomic nervous system from the centers in the brainstem to the cerebral vessels are well established and the rich autonomic innervation of the cerebral vessels has been proved.31 Physiological investigations have demonstrated cerebral vasoconstriction and decreased CBF following sympathetic stimulation.4, 14, 15, 10 In addition, James et al.15 adduced that the blockade of sympathetic nervous system in the neck resulted in impaired cerebral autoregulation.

The neurogenic hypothesis has been assumed not to contribute to cerebral autoregulation by most authors,4 10, 21, 22 while others have assumed it to play a part.12, 15, 10 In the present study, the importance of neurogenic control of the cerebral circulation in man is reaffirmed since impaired autoregulation after brainstem lesions is difficult to explain by other explanations such as the myogenic or metabolic hypotheses.5, 6

In conclusion, nervous structures in the diencephalic area and brainstem appear to play an important role in cerebral autoregulation as judged by patients with cerebrovascular disorders. The observations reported here also clarify the pathogenesis of some symptoms in such patients. Hypertension is commonly associated with stroke and patients with hypertension showed a greater reduction in both CBF and effective MABP during head-up tilting and larger increases during induced hypertension when compared to normotensive patients. The present study shows that patients with vertebrobasilar insufficiency have a statistically significantly greater cerebral dysautoregulation which persists for a longer time after the initial ischemic episode than patients with cortical ischemic lesions. Such orthostatic dysautoregulation in patients with occlusive disease in the vertebrobasilar arterial system may well explain the frequent dizziness, vertigo, photopsia and symptoms of diffuse cerebral ischemia when such patients, particularly if hypertensive, stand up suddenly after lying recumbent.

References


Impaired Neurogenic Cerebrovascular Control and Dysautoregulation After Stroke
JOHN STIRLING MEYER, KUNIO SHIMAZU, YASUO FUKUUCHI, TADAO OHUCHI,
SHIGEMICHI OKAMOTO, ATSUO KOTO and ARTHUR DALE ERICSSON

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