Regional Cerebral Blood Flow During Stimulation of Seventh Cranial Nerve

BY VIRGILIO D. SALANGA, M.D., AND ARTHUR G. WALTZ, M.D.*

Abstract:
The right seventh cranial nerve (n. VII) was exposed intracranially via a suboccipital approach in each of eight cats. Measurements of cerebral blood flow (CBF) were made from superficial cortex, sulcal cortex, basal cortex, the basal ganglia, and the centrum semiovale of each cerebral hemisphere of each cat by autoradiography using 14C-antipyrine. In six cats, measurements of CBF were made during electric stimulation of n. VII; in two of these, the nerve was sectioned before stimulation. In the remaining two cats, measurements were made after exposure but without stimulation of n. VII; in these cats, there were no side-to-side differences of CBF. In each of the four cats with n. VII intact, CBF values were lower on the stimulated side. In each of the two cats with n. VII sectioned, CBF values were higher on the stimulated side. Thus, stimulation of n. VII causes regional increases of CBF only when centripetal effects of stimulation are prevented. Cerebral vasodilatation has been observed by others during stimulation of a sectioned or an intact n. VII. When an intact nerve is stimulated, vasodilatation apparently is unable to compensate for decreases of CBF mediated centripetally through brain stem structures and extracranial or basal cerebral vessels; moreover, such vasodilatation may be due in part to regulatory responses of vessels to decreases of perfusion pressure.

Additional Key Words: experimental cerebral blood flow in cats, cerebral circulation, basal ganglia, 14C-antipyrine, vasodilatation, perfusion pressure

Numerous anatomical studies have shown that arterial blood vessels on the surface and in the depths of the brain are invested by nerve fibers. Neuromuscular contacts, synaptic vesicles with adrenergic or cholinergic characteristics, and fluorescent catecholamine products have been described for arteries at the base and over the convexity of the brain, suggesting that the vascular nerves are capable of efferent functional activity. However, the functions of the intracranial vascular nerves are as yet unknown.

Although cerebral blood vessels are less responsive to vasoactive agents and neurogenic influences than are vessels of other organs, adequate stimulation of sympathetic nerves can cause constriction of superficial cortical arterial blood vessels and decreases of blood flow in brain tissue and in cervical arteries and veins. Stimulation of the intracranial portion of the seventh cranial nerve (n. VII) can cause cerebral vasodilatation, thought to be related to the presence of parasympathetic vasodilator nerves; effects on cerebral blood flow (CBF) have been inconsistent and inconsistent. Stimulation or section of sympathetic or parasympathetic nervous structures can modify the regulatory responses of the cerebral vasculature to changes of perfusion pressure and arterial carbon dioxide tension (Paco2), although regulatory responses persist despite sympathetic denervation.

Regional changes of blood flow in brain tissue can remain undetected by methods commonly used for measurement of CBF. Therefore, to help determine the nature of parasympathetic influences on the cerebral circulation, regional measurements of CBF were made in cats by an autoradiographical method, during stimulation of the intracranial portion of n. VII.
Methods

Each of eight adult cats was anesthetized lightly with pentobarbital (25 mg/kg) injected intrapleurally, and a tracheostomy was made. With the use of an operation microscope, the right n. VII was exposed in the posterior fossa between the brain stem and the internal auditory meatus by a posterior suboccipital craniectomy and retraction of the cerebellum. For positive identification of n. VII, the reaction of the ipsilateral facial muscles and ipsilateral lacrimation was noted during electric stimulation. In two of the eight cats, the exposed n. VII was sectioned at its point of exit from the brain stem.

In each cat, an arterial catheter was passed transfemorally into the abdominal aorta for monitoring mean systemic arterial blood pressure (MABP) with a strain gauge and polygraph, and for drawing blood samples for measurement of $P_aO_2$, $P_aCO_2$, pH, and hematocrit. A catheter was passed transfemorally to the inferior vena cava for the injection of $^{14}$C-antipyrine, a diffusible radioactive indicator. In addition, an arteriovenous shunt was established by connecting, through a three-way stopcock, a catheter placed transfemorally in the abdominal aorta to a catheter placed transfemorally in the inferior vena cava. Blood pressure in the shunt was monitored with a strain gauge and polygraph. Each cat then was paralyzed with a minimal dose of tubocurarine injected intravenously and was ventilated mechanically with a respirator. The ventilating mixture consisted of air to which were added small amounts of carbon dioxide and oxygen. $P_aCO_2$ was maintained constant, between 32 and 37 torr (normal to slightly high for a cat); $P_aO_2$ was between 97 and 140 torr; and pH was between 7.38 and 7.44. The hematocrit value was determined to be normal (between 37% and 45%), and MABP was stable and within normal limits before stimulation of n. VII began.

In six of the eight cats, including the two in which n. VII was sectioned, the exposed nerve was stimulated by square-wave, direct-current impulses of 2 v, at 30 Hertz and 1-msec duration, using a metallic monopolar stimulating electrode insulated except at its tip. The position of the electrode was verified with the operation microscope. In the other two cats, the electrode was placed around the exposed n. VII, but no stimulating current was applied. Once begun, stimulation was continued until the cat was killed.

After one minute of stimulation, or after placement of the electrode in the two cats not stimulated, $^{14}$C-labeled antipyrine was injected intravenously for measurements of regional CBF. Approximately 375 $\mu$Ci in 5-ml physiological saline was injected into the inferior vena cava at a constant rate for one minute. During the injection, 0.2 ml of blood was withdrawn every ten seconds from the stopcock in the arteriovenous shunt, for measurement of the arterial concentration of the indicator. The circulation of blood then was stopped by the rapid intravenous injection of a saturated solution of potassium chloride. The brain was removed quickly (within ten minutes) and frozen at $-100^\circ$ to $-150^\circ$C in 2-methylbutane cooled with liquid nitrogen. After warming to $-20^\circ$C in a freezer for two to four days, the frozen brain was cut coronally into six to eight slices. Two serial sections, 20 $\mu$ thick, were made from each slice in a cryostat, placed on glass slides, and dried on a hot plate.

The slides were put into a cassette so that the sections of brain faced the emulsion of x-ray film. Plastic disks containing known amounts of $^{14}$C-antipyrine also were put into the cassette. After exposure for approximately ten weeks, the film was developed and the optical densities of the autoradiographic images were measured with a densitometer. The amounts of $^{14}$C-antipyrine in various regions of the brain were determined from a standard curve prepared from the density values for the plastic disks. Values for regional CBF were calculated by digital computer from the equation:

$$C_t(T) = \lambda k \int_0^T C_a e^{-k(t-T)} dt,$$

where $C_t(T)$ is the concentration of $^{14}$C-antipyrine in the region of tissue at time T (one minute), $\lambda$ is the blood-tissue partition coefficient ($\lambda = 1$ for antipyrine), $C_a$ is the arterial concentration of the indicator, and $k_1$ (with $\lambda = 1$) is the CBF value in ml/gm/min.

Measurements of CBF were made from multiple sites in five regions of each of the two cerebral hemispheres: (1) superficial (exposed) cortex of the convexity of the hemisphere, excluding the temporal lobe and the inferior surface; (2) cortex from the same part of the hemisphere but lying deep in sulci; (3) superficial and sulcal cortex from the temporal lobe and inferior surface of the hemisphere; (4) gray matter from the basal ganglia, largely the caudate and lenticular nuclei; and (5) white matter from the centrum semiovale. Fifteen to 35 individual measurements were obtained from each of the regions in each cerebral hemisphere. The mean value and standard deviation for each region were compared with the mean value and standard deviation for the corresponding region of the opposite cerebral hemisphere by statistical analysis (Student's $t$ test), to be certain that differences of CBF values were not likely due to random variability of individual measurements caused by observer error, or to variations of true CBF.

Results

There were no consistent side-to-side differences between the CBF values obtained from the various regions of the left and the right hemispheres of cats 1 and 2, in which n. VII was exposed but not stimulated (table 1, fig. 1). The differences that were noted were inconsistent as to direction: the regional CBF values from the hemisphere on the side of the exposed nerve could be either higher or lower than the values from the opposite hemisphere. Side-to-side differences between regional CBF values did not exceed 0.01 ml/gm/min, with two exceptions (basal cortex and basal ganglia of cat 2).

In cats 3, 4, 5, and 6, which had stimulation of an intact n. VII, regional CBF values were consistently lower on the stimulated side (table, fig. 214 Stroke, Vol. 4, March-April 1973
FIGURE 1

Autoradiograph of section of brain from cat 1, in which right cranial nerve VII was exposed but not stimulated. Cerebral blood flow (CBF) (indicated in ml/gm/min X 100) is directly related to density of autoradiographical image: darker regions are those with greater CBF. There were no consistent side-to-side differences of CBF.

2). Although not all differences were statistically significant at the 95% level of confidence, there were no instances in which regional CBF was greater on the stimulated side.

In cats 7 and 8, in which the exposed n. VII was sectioned and its distal end stimulated, opposite results were obtained (table, fig. 3). Consistently higher values for regional CBF were obtained from the hemisphere on the side of the stimulated nerve. Most of the differences were of statistical significance.

No changes of MABP were noted during stimulation.

Discussion

Although measurements of regional CBF could not be made both before and during stimulation of n. VII because of the requirements of the autoradiographical method, the results show clearly that the stimulation of n. VII influenced the cerebral circulation. Side-to-side differences of regional CBF values were unidirectional: values were lower on the stimulated side in cats with intact n. VIIs and higher on the stimulated side in cats with sectioned n. VIIs. No such consistent side-to-side differences were found in the cats in which n. VII was not stimulated.

The finding of opposite effects from stimulation of intact and sectioned n. VIIs was surprising, in view of the work of Chorobski and Penfield,13 who found that dilatation of the surface arterial vessels of the brain occurred with stimulation of n. VII whether sectioned or not. In the present study, direct observations of the surface vessels of the brain were not made. However, from the results of the measurements of regional CBF, the cerebral vasodilatation observed by Chorobski and Penfield may have been caused by two separate mechanisms working together when an intact n. VII was stimulated:

1. The primary effect of stimulation of the vasomotor fibers, presumably parasympathetic, accompanying the intracranial portion of n. VII appears to be dilatation of the regulatory cerebral arterial blood vessels, causing an increase of CBF. Regional differences in degrees of vasodilatation and

<table>
<thead>
<tr>
<th>Cat</th>
<th>Status of right n. VII</th>
<th>Hemisphere</th>
<th>Superior cortex</th>
<th>Sural cortex</th>
<th>Basal cortex</th>
<th>Basal ganglia</th>
<th>Centrum semiovale</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Exposed, not stimulated</td>
<td>Left</td>
<td>0.59</td>
<td>0.55</td>
<td>0.45</td>
<td>0.42</td>
<td>0.19</td>
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<tr>
<td></td>
<td></td>
<td>Right</td>
<td>0.60</td>
<td>0.54</td>
<td>0.46</td>
<td>0.43</td>
<td>0.18</td>
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<tr>
<td>2</td>
<td>Exposed, not stimulated</td>
<td>Left</td>
<td>1.79</td>
<td>1.72</td>
<td>1.70</td>
<td>1.79</td>
<td>0.52</td>
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<tr>
<td></td>
<td></td>
<td>Right</td>
<td>1.78</td>
<td>1.72</td>
<td>1.64*</td>
<td>1.81</td>
<td>0.52</td>
</tr>
<tr>
<td>3</td>
<td>Intact, stimulated</td>
<td>Left</td>
<td>0.72</td>
<td>0.77</td>
<td>0.70</td>
<td>0.70</td>
<td>0.27</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Right</td>
<td>0.70*</td>
<td>0.74*</td>
<td>0.64*</td>
<td>0.66*</td>
<td>0.26*</td>
</tr>
<tr>
<td>4</td>
<td>Intact, stimulated</td>
<td>Left</td>
<td>0.88</td>
<td>0.97</td>
<td>0.68</td>
<td>0.75</td>
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</tr>
<tr>
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<td></td>
<td>Right</td>
<td>0.87</td>
<td>0.95*</td>
<td>0.65*</td>
<td>0.72</td>
<td>0.28</td>
</tr>
<tr>
<td>5</td>
<td>Intact, stimulated</td>
<td>Left</td>
<td>0.67</td>
<td>0.69</td>
<td>0.58</td>
<td>0.72</td>
<td>0.28</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Right</td>
<td>0.62*</td>
<td>0.64*</td>
<td>0.52*</td>
<td>0.70</td>
<td>0.26</td>
</tr>
<tr>
<td>6</td>
<td>Intact, stimulated</td>
<td>Left</td>
<td>0.54</td>
<td>0.55</td>
<td>0.46</td>
<td>0.50</td>
<td>0.19</td>
</tr>
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<td></td>
<td></td>
<td>Right</td>
<td>0.53*</td>
<td>0.54*</td>
<td>0.46</td>
<td>0.49*</td>
<td>0.19</td>
</tr>
<tr>
<td>7</td>
<td>Sectioned, stimulated</td>
<td>Left</td>
<td>0.77</td>
<td>0.77</td>
<td>0.60</td>
<td>0.64</td>
<td>0.28</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Right</td>
<td>0.79*</td>
<td>0.81*</td>
<td>0.63*</td>
<td>0.65</td>
<td>0.29*</td>
</tr>
<tr>
<td>8</td>
<td>Sectioned, stimulated</td>
<td>Left</td>
<td>0.85</td>
<td>0.96</td>
<td>0.81</td>
<td>0.84</td>
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<tr>
<td></td>
<td></td>
<td>Right</td>
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<td>0.99*</td>
<td>0.85*</td>
<td>0.88*</td>
<td>0.50*</td>
</tr>
</tbody>
</table>

*Significantly different (P <0.05) from left side.
increases of CBF occur, but CBF increases both on the surface and in the depths of the brain.

2. Centripetal effects of stimulation of an intact n. VII appear to prevent increases of regional CBF despite cerebral vasodilatation. Presumably, other vasoactive influences, such as activation of sympathetic pathways with resulting constriction of blood vessels in the neck and at the base of the brain, lead to regional decreases of CBF that cannot be compensated for by vasodilatation caused by the centrifugal effects of stimulation. Moreover, regional decreases of perfusion pressure from centripetal effects may cause additional dilatation of regulatory cerebral arterial vessels, as a response to maintain CBF ("autoregulation"). Measurements of CBF during stimulation of an intact n. VII in animals with sympathetic denervation would help elucidate the role of sympathetic pathways in the decreases of regional CBF that occur when an intact n. VII is stimulated. Although the present study does not delineate definitively the function of the parasympathetic nervous system in the normal regulatory responses of the cerebral vasculature, it provides further evidence that the autonomic nervous system can influence the cerebral circulation, and that the primary effect of stimulation of the parasympathetic fibers that accompany the intracranial portion of n. VII is cerebral vascular dilatation.

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Dr. Thoralf M. Sundt, Jr., Department of Neurologic Surgery, Mayo Clinic, advised and demonstrated the operative approach to n. VII; Dr. Takenori Yamaguchi assisted in the early phases of the study; and technical, instrumentation, and analytic assistance was provided by Robert E. Anderson, Robert D. Ostrom, and the Mayo Clinic Computer Facility, Mayo Clinic and Mayo Foundation, Rochester, Minnesota.

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rCBF DURING STIMULATION OF n. VII


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