Neurogenic Cerebral Vasodilation From Electrical Stimulation of the Cerebellum in the Monkey

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SUMMARY The effect of stimulation of fastigial nucleus (FN) on cerebral blood flow (CBF) was examined in anesthetized, paralyzed monkeys. CBF was measured with a flow transducer chronically implanted on the left common carotid artery. The left external carotid artery and its branches were ligated. Electrical stimulation of the fastigial nucleus produced rapid (within two seconds) increases in arterial pressure (AP) and heart rate. Mean carotid blood flow (MCBF) rose 77% (± 40% SEM) above control and followed the increases in mean arterial pressure (MAP). Calculated cerebrovascular resistance decreased immediately by 27% (± 14% SEM) below control. The increases in MCBF were not caused by a passively responding cerebrovascular bed (CVB) resulting from the stimulation or trauma to the vessels. Cerebral metabolism was not altered during stimulation as determined from the arteriovenous oxygen content difference. CBF autoregulation was still present with stimulation of the fastigial nucleus. The autoregulatory curve was shifted to a higher flow level. During the initial MAP changes in sympathectomized animals, MCBF increased to a greater extent than in the innervated animals, suggesting the presence of two neurogenic vasodilatory systems. It appears that electrical stimulation of the fastigial nucleus inhibits sympathetic tone and increases parasympathetic activity to the CVB, resulting in vasodilation and an increase in MCBF.

Hernandez-Perez et al. performed chronic unilateral superior cervical ganglionectomies in monkeys and found evidence for the existence of sympathetic tone in the CVB. They observed a 30% increase in CBF on the denervated side. Stone et al. bilaterally removed the SCG in a chronic monkey preparation and showed that this decreased the CBF sensitivity of the CVB. James et al. using acute unilateral superior cervical ganglionectomy in the baboon, found an impairment of autoregulation. Yoshida et al. also observed a deterioration of the autoregulatory response after chronic unilateral superior cervical ganglionectomies in the monkey.

Centrally originating neural influences on CBF have been suggested by the results of hypothermic and electrolytic lesions and electrical stimulation in certain areas in the central nervous system. Only in a few cases were these centrally induced effects associated with an identifiable autonomic response. In contrast, the CBF response from FN stimulation accompanies a specific and highly differentiated peripheral autonomic activation. It is the aim of this study to show that the specificity of the FPR involves a significant neurogenic influence on CBF and does not abolish flow-pressure cerebral autoregulation.

Methods

Surgical Preparation

Seventeen rhesus monkeys (Macaca mulatta), weighing from 3 to 8.5 kg, were utilized in these studies. Sterile surgery for implantation of a Doppler ultrasonic flow transducer around the left CCA was performed prior to experimentation. For surgery, the animals were anesthetized with a 10 mg per kilogram IM injection of ketamine hydrochloride. The left CCA and its bifurcation were exposed. The left external carotid artery and its branches were isolated by blunt dissection and ligated. A Doppler flow transducer was placed around a segment of the CCA just caudal to the bifurcation. The transducer was anchored in the skin with the leads wrapped around it and the transducer was then secured in place with a rubber band. The transducer was then connected to a flowmeter and the flow was recorded.

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the animals. In these animals, the carotid bifurcation also was exposed on the right side. The ganglion, which lies medial, superior, and posterior to the bifurcation, was dissected free from the surrounding fascia with minimal disturbance to the internal carotid artery. The entire ganglion was excised. All animals were allowed to recover for 10 to 14 days. The recovery period for sympathectomized animals permitted complete degeneration of adrenergic nerve fibers as shown previously.10, 11

EXPERIMENTAL PROCEDURE

Following recovery, the animals were anesthetized with an IM injection of 10 mg per kilogram of ketamine hydrochloride. The Doppler leads were exteriorized through a small skin incision and connected to the appropriate electronics to record the Doppler signal. A 10% solution of alpha chloralose in propylene glycol was then injected through a femoral venous catheter at a dosage of 50 mg per kilogram. A catheter tip pressure transducer (Millar Instruments) was inserted through one femoral artery and the remaining femoral artery was cannulated with a polyethylene catheter. Following cannulation, the animals were intubated with a cuffed endotracheal tube, fixed in a stereotaxic frame (Kopf Instruments), paralyzed with an IV injection of gallamine triethiodide, and mechanically ventilated on a Harvard respirator. Tidal volume and respiratory rate were adjusted to produce a moderate hyperventilation.

Electrode tracking was begun 8 mm posterior to the interaural line and 1.5 mm lateral to the midline. A 6 mm in diameter portion of the dura was exposed with a trephine. The dura was then cut and reflected to one side for entry of the electrode. The cerebellum was searched in 0.50-mm steps beginning at a point 15 to 30 mm above the horizontal plane through the interaural line. The stimulus was displayed on a cathode ray oscillograph (Tektronix 7403N) for continuous monitoring of current by measuring the voltage drop across a 10-ohm resistor at the stimulator. A Grass SD5 stimulator provided the stimulus. The electrode employed was a Kopf Instruments SNE-100 stainless steel coaxial electrode which has a shaft diameter of 0.25 mm and a tip diameter of 0.10 mm. At each 0.50-mm step, a 1.5-mA current was delivered in monopolar square wave pulses of 0.1-msec duration at a frequency of 160 Hz for ten seconds. This stimulus provided a clearly recognizable blood pressure increase in the response areas. When a response area was encountered, the electrode was lowered in 0.25-mm steps to locate the point producing the maximum blood pressure increase.

The responsiveness of the CVB was tested by two methods. The first method involved changing the MAP by exsanguination and methoxamine infusion as described previously.10, 11 With this procedure a CBF autoregulation curve was obtained by plotting CBF versus MAP. MAP was varied over a wide range from approximately 40 mm Hg to more than 200 mm Hg in some animals. Exsanguination was accomplished within five minutes and the blood returned to the animal. After the return of CBF and MAP to control levels, methoxamine was infused until the MAP rose to approximately 200 mm Hg. The infusion usually was completed in less than five minutes. The determination of CBF autoregulation was accomplished before the initiation of cerebellar stimulation and at intervals during the experiments. Upon location of the FPR, CBF autoregulation was again determined prior to any further stimulation. In this manner, the responsiveness of the CVB to changes in MAP was determined throughout the experiments. Deterioration of CVB responsiveness was not found in any of the trials. The second method used to determine the responsiveness of the CVB was exposure of the animal to a mixture of 12% CO2 and air. CBF increased 100% to 500% above the control levels in the various animals. This procedure was also done periodically during each experiment to ensure maintenance of the responsiveness of the CVB.

MEASUREMENTS

All measurements other than body temperature and blood gases were recorded on an eight-channel Beckman type RM dynograph. AP was measured with a solid-state catheter tip pressure transducer threaded through a femoral artery into the thoracic aorta. Pulsatile and mean pressures were recorded on separate channels. Heart rate was measured from the arterial pressure pulse by a cardiotachometer. The flow signal from the Doppler probe was recorded on two channels, one displaying pulsatile flow and the other mean flow. The Doppler system has been described elsewhere.10 The velocity of blood flow was directly recorded by the Doppler system and velocity of flow (cm/sec) was converted to volume flow (ml/min) by multiplying the velocity measurements by the cross-sectional areas of the vessel surrounded by the probe. A cross-sectional area was determined from acrylic casts of the vessels at autopsy. The measurement of ICA flow with the flow transducer will be referred to as CBF.

Blood gases (PCO2, PO2, pH) were determined from 1-ml arterial blood samples taken from a femoral arterial catheter. Samples were withdrawn during initial adjustments of the respirator, just prior to recording data during stimulation and during 12% CO2 administration. Saline was used to replace blood taken for these samples. Blood gases were determined on an Instrumentation Laboratory, Inc., blood gas analyzer (Model 213). The average arterial blood gas values were: 30.4 mm Hg PCO2 (± 1.4 mm Hg SEM), 121.2 mm Hg PO2 (± 2.5 mm Hg SEM), and 7.553 pH (± 0.034 SEM). Oxygen saturation and hemoglobin were determined from femoral arterial blood and posterior sagittal sinus blood on an Instrumentation Laboratory, Inc., cooximeter (Model 182). Body temperature was maintained at 37° ± 0.5°C. The Student's t test was used to analyze data statistically. A P value less than 0.05 was considered significant.

HISTOLOGY

At the end of each experiment, maximum response points were marked with a 0.5-mA direct current for 30 seconds. Animals were killed with an IV injection of KCl. The brains of innervated animals were perfused through each CCA with 50 ml of formalin and 75 ml of potassium ferrocyanide and ferricyanide for identifying lesion sites by the Prussian blue.
reaction. The cerebellum was preserved in 10% formalin. For examination, the cerebellar tissue was frozen with Dry Ice and sectioned (40 to 90 μm thick) on a sliding microtome. Sections were stained with cresyl violet. Brains of sympathectomized animals were not perfused but were immediately removed so that the cerebral vessels could be examined for adrenergic innervation by a histochemical fluorescence technique.\textsuperscript{19, 20}

Results

TYPICAL RESPONSE

Electrical stimulation in discrete areas of the deep cerebellar white matter consistently produced rapid increases in MAP and usually an increase in pulse pressure (fig. 1). AP began to increase 1.8 seconds (± 0.1 second SEM) after stimulation. This latency was independent of the stimulus current. In most cases, MAP rapidly attained a maximum value and then began to decline toward control by the end of the ten-second stimulus. With longer periods of stimulation, the MAP always remained above control during the stimulus period. In a few instances MAP continued to increase through the end of the stimulus; and, in two animals, the maximum MAP was more effectively maintained as stimulus current increased.

Mean carotid blood flow (MCBF) (fig. 1) closely paralleled MAP throughout stimulation. The latency of the two responses was virtually identical and maximum responses were attained almost simultaneously.

A tachycardia consistently accompanied the blood pressure response (fig. 1). The increase in heart rate was initiated concurrently with the AP response but rose to a maximum value at a slower rate. Cardioacceleration was more pronounced if the prestimulus heart rate was low.

HISTOLOGY

A representative line drawing of a cross section of the cerebellum can be seen in figure 2. At the end of each experiment the site of the electrode was marked with an electrolytic lesion. The symbols shown in the figure are from four representative animals showing the widest variation of location around the FN. In the other control and ganglionectomized animals, the electrolytic lesions fell within the bounds of those shown. The lesions abolished the AP and CBF response to stimulation in the area. Repositioning of the electrode into the contralateral FN would evoke a rise in AP and CBF.

MAP VERSUS STIMULUS CURRENT

Stimulus response curves were constructed for each animal. After locating the most active point in a response area, the stimulus current was lowered and then raised in small increments to determine threshold current. A current of at least 0.5 mA was required to elicit a response in AP or CBF. The increases in AP and CBF could not be dissociated by decreasing the current below 0.5 mA, so it appeared that the AP and CBF responses had identical thresholds. After determining the threshold, the stimulus current was increased in 0.5-mA steps until no increase in the response was observed. The maximum change in MAP was plotted against current in figure 3. The average prestimulus MAP was 149 mm Hg (± 11 mm Hg SEM). The maximum MAP continued to increase throughout the stimulus range. The change in maximum MAP was less with stimulus currents above 1.5 mA. At 3.5 mA the maximum increase in MAP was 45 mm Hg (± 10 mm Hg SEM) or 33% (± 11% SEM) above control.

MCBF VERSUS STIMULUS CURRENT

The stimulus response curves for the MCBF response were determined in the same manner as for MAP. The average prestimulus MCBF was 27 ml per minute (± 5 ml per minute SEM). Maximum MCBF response rose with in-
FIGURE 1. Line drawing of a coronal section approximately 8 mm posterior to the interaural line. Symbols indicate the site of electrolytic lesions which abolished the increase in MAP, MCBF, and heart rate which occurred from stimulation at these points.

increments in current to 1.5 mA (fig. 4A, solid line). Stimulating with 1.5 mA produced changes in MCBF of 3 to 31 ml per minute, representing increases above controls of 23% to 156%. The average MCBF increase was 18 ml per minute (± 8 ml per minute SEM), which represented an increase of 77% (± 40% SEM) above control. The maximum MCBF response varied only slightly with stimulus inten-

CVR VERSUS STIMULUS CURRENT

Cerebrovascular resistance (CVR) was calculated from the maximum MAP and maximum MCBF for each response to stimulation (fig. 4B). The average control CVR was $506 \times 10^3$ dynes sec cm$^{-5}$ (± $98.0 \times 10^3$ dynes sec cm$^{-5}$ SEM). CVR decreased $144 \times 10^3$ dynes sec cm$^{-5}$ (± $83 \times 10^3$ dynes sec cm$^{-5}$ SEM) below control with stimulation at 1.5 mA. This represented a reduction of 27% (± 14% SEM) in CVR. Above 2.5 mA, the decrease in CVR became less pronounced as the maximum MCBF began to decrease and the maximum MAP continued to increase.

MCBF VERSUS MAP

To examine the dynamic relationship between flow and pressure during the rapid rising phase of change with FN stimulation, curves of the MCBF versus MAP were plotted for each animal studied. At each 5 mm Hg increment in pressure, the change in MCBF was recorded and a single
curve of the change in MCBF versus the change in MAP was obtained for each animal. These individual curves were then averaged together for a single curve for the group. Analysis of each curve was stopped at the maximum increase in MAP. Figure 5 shows the average relationship between the change in MCBF and changes in MAP with FN stimulation. It should be noticed that the curve was found to be approximately linear with a slope of 0.4 ml per minute mm Hg⁻¹. At higher changes in pressure in some animals, there was a tendency for the change in flow to increase out of proportion to the remainder of the curve. It must be emphasized that figure 5 was obtained in a very dynamic state during the time of rapid changes in the cerebral vessels.

CEREBRAL OXYGEN CONSUMPTION

Cerebral oxygen consumption (CMRO₂) was calculated as an index of cerebral metabolism in four innervated animals. The arterial and venous oxygen saturation was determined from a femoral arterial blood sample and a superior sagittal sinus blood sample taken just prior to FN stimulation and during the maximum MCBF response to stimulation. Oxygen content was calculated for each sample. The prestimulus CMRO₂ averaged 4.7 ml per minute and during FN stimulation the CMRO₂ averaged 4.6 ml per minute.

AUTOREGULATION DURING STIMULATION

The ability of the animals to maintain a flow-pressure relationship was assessed during stimulation (fig. 6) to determine if the increase in MCBF was due to an abolition of autoregulation. Prior to FN stimulation a normal autoregulatory curve was obtained in the animals. The lower curve of figure 6 shows the normal response of a representative animal. MAP was increased by an infusion of methoxamine and lowered by exsanguination. The arrows from the lower control CBF and MAP points indicate the change with FN stimulation. Methoxamine infusion or exsanguination began immediately after reaching the peak response while stimulation was continued until each procedure was completed. Methoxamine infusion elevated MAP to more than 200 mm Hg while MCBF remained relatively constant at or near its maximum stimulus value. An immediate drop in MCBF back to control was observed when stimulation was discontinued even at the elevated MAP. The lower part of the autoregulatory curve was examined by exsanguinating the animal at the peak of its MCBF response to a prolonged stimulus. MAP was reduced to approximately 60 mm Hg. During stimulation MCBF remained relatively constant, maintaining its peak stimulus value down to about 80 mm Hg MAP. Terminating the stimulus produced a sharp drop in MCBF as it did at the higher pressures. These results were consistent in all animals studied.

SYMPATHECTOMIZED ANIMALS

Six animals were used in which both superior cervical ganglia were removed. Histochemical examination of cerebral vessels from bilaterally ganglionectionized animals indicated a complete elimination of monoamine containing fibers. The CVB in these animals was considered to be sympathectomized. Figure 7 illustrates the type of response elicited from sympathectomized animals during FN stimulation. Sympathectomy altered the cerebrovascular response. MCBF reached its maximum value prior to the attainment of maximum MAP rather than paralleling the increase in MAP as it did in the innervated animals. In addition, some stimulations in sympathectomized animals initiated an increase in MCBF before the MAP began to increase. The response of the CVB to changes in MAP by exsanguination or methoxamine infusion was similar to that of the control animals.

MAP AND MCBF VERSUS STIMULUS CURRENT

The MAP response curve for the sympathectomized animals (fig. 3, dotted line) was not significantly different from the response curve for the innervated animals (fig. 3,
solid line). The average control MAP for the sympathectomized animals was 140 mm Hg (± 10 mm Hg SEM).

The MCBF response curve for the sympathectomized animals (fig. 4A, dotted line) was not significantly different from the response curve for the innervated animals (fig. 4A, solid line). The average control MCBF for the sympathectomized animals was 33 ml per minute (± 6 ml per minute SEM).

**CVR VERSUS STIMULUS CURRENT**

The CVR response curve for the sympathectomized animals (fig. 4B, dotted line) was not significantly different from the CVR curve for the innervated animals (fig. 4B, solid line), except at 3 mA. At this current, the decrease in CVR in the sympathectomized animals was significantly less than in the innervated animals (P < 0.001). At 1.5 mA, CVR decreased in the sympathectomized animals by 43.9 × 10³ dynes sec cm⁻⁵ (± 19.9 × 10³ dynes sec cm⁻⁵ SEM), representing a reduction of 11% (± 4% SE). The average control CVR for the sympathectomized animals was 390 × 10³ dynes sec cm⁻⁶ (± 75.0 × 10³ dynes sec cm⁻⁶ SEM).

**MCBF VERSUS MAP**

The MCBF versus MAP curve for the sympathectomized animals (fig. 5, dotted line) was determined in the same manner as the curve for the innervated animals. The curve for the sympathectomized animals is significantly elevated above the curve for the innervated animals (P < 0.01) at 5 mm Hg, 10 mm Hg, and 15 mm Hg. This indicates that at the initial increase in MAP, MCBF is increasing more rapidly in the sympathectomized animals than in the innervated animals.

**Discussion**

The primary concern of any CBF investigation must be the accuracy of its measurements since extracranial contamination is always a possibility. In these studies, it is felt that isolation of the arterial inflow has been accomplished to the extent that extracranial flow should account for no more than 5% to 10% of the measured flow. Thus the MCBF measured in the current experiments would be synonymous with mean cerebral blood flow. Extracranial contamination around the cranium should be even further diminished due to the diffuse peripheral vasoconstriction which occurs with electrical stimulation of the FN. A second criterion which must be satisfied in CBF studies is the measurements reflect a normally functional CVB. Two particular characteristics are commonly associated with a normal CVB. One of these is the ability to autoregulate. CBF autoregulation is the ability to maintain a relatively constant flow in spite of profound fluctuations in AP. In this study, autoregulation was tested by altering MAP over a wide range with methoxamine and by exsanguination during the course of the experiments. The fact that MCBF remained relatively constant indicated that the animals were responsive and remained so throughout the experimental period. This normal response further diminishes the possibility of extracranial contamination since flow through extracranial vessels would be expected to fluctuate with AP.

The second characteristic which a normal CVB exhibits is a reactivity to increased inspired CO₂. The response consists of a substantial vasodilation in the CVB with a dramatic increase in CBF and a partial to complete abolishment of autoregulation depending upon the concentration of inspired CO₂. Administration of 12% CO₂ and air, which has been found to produce a large increase in CBF, significantly elevated MCBF in these animals and indicated that they were responsive to CO₂.

Stimulation of the FN of the cerebellum caused an increase in MCBF and a decrease in CVR (fig. 4). Several different mechanisms could explain these results: (1) a passively responding CVB due to absence of autoregulation, (2) inability of the autoregulatory phenomenon to respond to rapid changes in AP, (3) metabolically induced alterations in CBF, (4) abolition of autoregulation due to electrical stimulation, or (5) neurogenically mediated vasodilation.

**PASSIVE VASCULAR RESPONSE AND AUTOREGULATION**

Characterization of the resistance and flow changes is complicated by the rapid increase in MAP which accompanies them. The increase in MCBF and decrease in CVR could have resulted from an absence of autoregulation due to prolonged hypoxia or a high arterial Pco₂. Under these conditions, the CVB would have responded passively.
to alterations in MAP. Analysis of the blood gases in these experiments rules against hypoxia or hypercarbia being present. Trauma to the CVB is not a valid explanation since the vessels supplying the circle of Willis were not handled nor was any undue trauma associated with cranial opening and electrode placement.

The increases in AP due to cerebellar stimulation were usually more rapid than the increase induced with methoxamine. There is the possibility that these rapid increases in AP produced a passive increase in CBF prior to the initiation of the autoregulatory mechanism. Several prolonged stimulations were accomplished in which MCBF and MAP remained elevated even though an adequate period of time had been allowed for the initiation of autoregulatory control. Rapid increases in MAP were elicited also from brain stem areas and yet these increases produced minor changes in MCBF. A comparison of the dynamic response of MCBF to MAP in control and ganglionectomized animals (fig. 5) also showed that the response could not be passive to a change in pressure. If the bed responded passively the two curves would be identical and not different as shown. Yoshida et al. induced similar increases in MAP (50 to 60 mm Hg) in monkeys by clamping the thoracic aorta. MAP was elevated more rapidly than with cerebellar stimulation. Their results demonstrated an immediate increase in CVR, indicating that the autoregulatory phenomenon is almost instantaneous. In contrast, cerebellar stimulation produces a decrease in CVR which does not appear to be the result of passive distention.

**METABOLIC VASODILATION**

Evidence indicates that CBF is directly related to changes in cerebral metabolism. Cerebral metabolism and CBF have been shown to increase with electrical stimulation of the brain stem reticular formation. Characteristic of stimulation in this area is an activation of the EEG. Moruzzi and Magoun demonstrated that a similar EEG activation results from stimulation of the FN. Thus, the possibility exists that stimulation of the FN increases CBF by increasing cerebral metabolic rate. For this reason, the CMRO₂ was determined during the peak MCBF response to stimulation and just prior to stimulation. The value for CMRO₂ during stimulation was actually slightly less than the prestimulus CMRO₂, indicating that an increase in cerebral metabolic rate did not occur. This would indicate that the cerebrovascular response occurred through some other mechanism.

**ABOLITION OF AUTOREGULATION**

Doba and Reis felt that the increase in CCA flow which they observed in cats with FN stimulation was due to an abolition of CBF autoregulation. This possibility was also considered in the present study since MCBF so closely followed the changes in MAP during stimulation. To test this possibility AP was altered with methoxamine and exsanguination during the peak of the MCBF response. The relative constancy of MCBF at its peak stimulus response as MAP was varied over an extended stimulus period indicated that autoregulation was intact but functioning at a higher MCBF level during stimulation. This suggested that autoregulation was operating at a greater vascular lumen diameter which could only result from a neurogenic vasodilation. Maintenance of autoregulation following a change in MCBF has been shown in other studies with denervation and varying levels of CO₂. Both neurogenic and metabolic factors can influence the caliber of the resistance vessels in the brain. It appears that there is a family of autoregulatory curves relating MCBF to MAP in the brain. The relationship of any particular curve to resting flow will depend on the state of that vessel at any point in time.

**NEUROGENIC VASODILATION**

Because of the sympathetically mediated peripheral involvement, a reasonable assumption would be that vasodilation of intracranial vessels might occur through a change in sympathetic activity. Besides the physiological evidence mentioned earlier, there is both anatomical and pharmacological evidence for a sympathetic role in the CVB. Histochemical and ultrastructural studies have delineated an abundant adrenergic innervation of all the extraparenchymal vessels. By far the predominant source of these fibers in the monkey is the SCG. Pharmacological studies suggest the presence of a functional adrenergic innervation. Cerebrovascular vasodilation could be produced through an inhibition of sympathetic activity. This was demonstrated in the monkey in earlier studies by removal of one SCG. The flow through the denervated vessels was increased above the opposite side.

The dynamic response of blood vessels to changes in length has been investigated by Johansson and Mellander measuring both the electrical and mechanical activity of the portal vein. The results of their study indicate that small blood vessels may be more sensitive to the rate of change of pressure than to the static change in pressure under normal conditions. The implication for the current study would be that a rapid elevation in pressure brought about by stimulation of the brain should result in little, if any, change in the measured flow. As mentioned earlier, this was found to be true as bulbo spinal areas were stimulated, causing a rapid rise in arterial pressure with no change in flow. Stimulation in the FN, however, increased both flow and pressure in an almost linear fashion, as seen in figure 5. Removal of the sympathetic innervation to the cerebral vessels changed the relationship of the dynamic flow and pressure but did not abolish the response.

Comparison of the CVR changes during stimulation of the FN in the sympathectomized and innervated animals indicates a definite trend toward a reduced cerebrovascular response after ganglionectomy (fig. 4B). The change in CVR represents a change in resistance occurring at the maximum MCBF and MAP. Diminution of the cerebrovascular response to simulation rather than complete disappearance indicates the existence of another system exerting an effect on the CVB or that the sympathetics have not been entirely removed. Histochemical analysis of intracranial vessels taken from ganglionectomized animals revealed a virtual complete degeneration of adrenergic fibers at the circle of Willis and along the major vessels leaving the circle. Thus, it seems that the sympathetic nerves are functioning in con-
junction with another vasodilatory system which may be activated with FN stimulation.

Evidence supporting the existence of a cholinergic system has been accumulating over the years. Using histochemical and degeneration techniques, Chorobski and Penfield presented evidence indicating that a cerebrovascular vasodilatory system, identified by themselves and Cobb and Finesinger, left the brain stem and traveled through the facial and greater petrosal nerves to enter the internal carotid plexus. Later physiological evidence also implicated the seventh cranial nerve as a route for cerebral vasodilatory fibers. Location of the ganglia supposedly mediating the cerebral vasodilatory response, at the junction of the greater petrosal nerve with the internal carotid artery, indicates that they are parasympathetic. Recent histochemical and ultrastructural studies indicate that cholinergic fibers are present on intracranial vessels. Studies in the monkey reveal an abundant cholinergic fiber distribution over most major intracranial vessels (personal communication).

Doba and Ries have provided evidence for the participation of the FN in an orthostatic reflex. A reflex of this type should involve the CVB. The FN receives information of orthostatic changes through the vestibular apparatus. Neuronal firing in the FN would then result in an increase in AP and a cerebral vasodilation. CBF would be maintained during orthostasis which might otherwise decrease CBF, resulting in dizziness or fainting. The FPR may act as a reflex response with a shorter latency than the more classical baroreceptor reflex and the drop in MAP with changes in posture would not result in loss of CBF. Since this could be classified as a reflex, this would be the first reflex adjustment of the FN in an orthostatic reflex. A reflex of this type should involve the CVB. The FN receives information of orthostatic changes through the vestibular apparatus.

References
13. Stavraky GW: Response of cerebral blood vessels to electric stimulation of the thalamus and hypothalamic regions. Arch Neurol Psychiat (Chicago) 35(1002-1028, 1936
35. Doba N, Reis DJ: Role of the carotid body and the vestibular apparatus in regulation of orthostatic reflexes in the cat. Circulation Research 34:9-18, 1974
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