A Method for Serial Measurement of Regional Cortical Metabolism and Blood Flow

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Abstract: A Method for Serial Measurement of Regional Cortical Metabolism and Blood Flow

There is a practical way to measure metabolism, flow, and function in a localized area of brain serially in the same animal. Our preliminary anatomical and angiographical studies have indicated that certain paired cerebral veins drain only blood from cortex supplied by easily identified cerebral arteries. These veins have been cannulated bilaterally without altering flow in their territory of distribution. When compared to the arterial concentrations of the substances and the regional blood flow, one can calculate the regional metabolic rate of the tissue in this inflow-outflow system (vascular-metabolic unit). This system can be subjected to ischemia, trauma, and pharmacological and neurophysiological alterations. In addition, it is accessible for measurement of electrical activity, surface fluorometry, and sampling for histological and cortical biochemical analysis.

Additional Key Words: electrical activity, ischemia, angiography, physiological alterations

Introduction

In an effort to measure nutrient requirements of the brain and to correlate these with clinical phenomena such as stroke, ingenious techniques to measure cerebral blood flow were devised and perfected. Initial studies on total cerebral blood flow proved too gross to detect many pathophysiological entities, and methods which measure flow in specific regions of brain were devised. Although there was frequent correlation of neurological symptoms with reduction in blood flow, certain inconsistencies were observed. Frequently, neurologically inactive portions of brain seemed to demonstrate near normal blood flow; often, increased flow was noted near infarcted brain. Investigators realized that the physical presence of adequate blood supply gave insufficient information about neuron function or potential for recovery if the metabolic activity of glial and nerve cells was altered. This led to preliminary studies in total brain metabolism and interesting observations about the utilization of oxygen, glucose, and other metabolically active products in normal and damaged brain. Again, the majority of these studies analyzed the metabolic activity of the brain or a cerebral hemisphere as a whole. A requirement for the measurement of local metabolism in an area of brain surrounded by normal tissue has led to the development of the experimental model described herein.

Methods

ANATOMICAL

Incident to a large series of experimental subarachnoid hemorrhage experiments in monkeys, our laboratory has accumulated numerous serial cerebral angiograms and formaldehyde-fixed monkey brains. Twenty-five of these brains underwent intra-arterial injection of micropulverized barium chloride at the time of sacrifice. Examination of these brains and angiograms revealed that certain cortical veins drain only the territory of distribution of other easily recognized cerebral arteries. Most obvious of these are the paired veins in the parietal region which accept two large tributaries approximately 9 mm before entering the superior sagittal sinus. There are no proximal tributaries or other evidence of drainage from the parasagittal cortex. The territory of drainage of these veins is somewhat analogous to the Rolandic veins in man. In brains whose arterial tree was filled with barium, it was possible to identify the surface arteries which bore relationship to this vein, and to trace them back to their parent artery. These dissections and angiograms revealed certain characteristics of this vein and its branches: (1) At its bifurcation, the vein accepts only drainage from the convexity surface of a portion of the frontal and parietal lobes; (2) Both right and left veins have a markedly similar course and distribution and they enter the...
sagittal sinus directly opposite one another; (3) This vein drains only blood from the cortex supplied by branches of the superior division of the middle cerebral artery as it leaves the Sylvian fissure (see figs. 1 and 2). Branches of the anterior cerebral artery supply a portion of the frontal pole of the monkey brain, as well as most of the interhemispheric surface of the parasagittal cortex. Fine branches of this artery extend approximately 4 mm onto the convexity surface of the brain in the region of the parietal vein. At this point, middle cerebral artery circulation dominates the convexity blood supply and extends somewhat more medial than the cortex drained by the parietal vein and its branches. We concluded, therefore, that anterior cerebral artery blood did not ultimately drain into the parietal vein. The posterior cerebral artery supplies the inferior surface of the temporal and occipital lobes and extends onto the convexity of the occipital pole. Again, its territory of distribution is remote from cortex drained by the parietal vein. Retrograde injection at venous pressure of micropulverized barium suspension into the parietal vein demonstrated filling of cortex predicted by the anatomical dissection (fig. 3).

Slices of brain taken through the area of these retrograde barium injections were examined under the dissecting microscope. The finest branches of the cortical veins could be followed almost to the cortex-white matter junction. Their distribution was fairly uniform in a plane 0.1 mm to 0.3 mm superficial to this junction, and in no instance did the injected barium cross into the white matter.

**Physiological Data**

The following experiments were performed on a series of ten monkeys weighing 5 to 7 kg. These animals were anesthetized by an intramuscular injection of phencyclidine, a cataleptic agent which renders the animal unresponsive to pain, but preserves pupillary and corneal reflexes. The animals were intubated and maintained on control respiration with 40% nitrous oxide-60% oxygen, and periodic injections of d-tubocurarine. By the time the various surgical procedures were completed, it was assumed that the effect of phencyclidine was exhausted, and analgesia was maintained principally by the light nitrous oxide inhalation. Blood pressure was monitored via a femoral artery catheter. End-tidal Pco₂ was recorded with each respiration by an infrared gas analyzer. A slow intravenous drip of 5% dextrose and water was administered according to the animal's calculated fluid requirements. Both carotid arteries were exposed in the neck and the external carotid artery was cannulated by a fine polyethylene catheter advanced near the orifice of the internal carotid artery. Utilizing a 0.3 mm focal spot magnification x-ray tube, serial angiography was performed through each carotid artery, and arterial structure and venous drainage were identified. The small parasagittal craniectomy, which exposes each parietal vein near the midline, was performed. Separate small craniectomies were made over the cortex drained by these veins on each side. The margin of the craniectomy was tailored so that a fitted "washer" with a mylar membrane could be fixed to lie in the plane of the now-excised dura. Lithium dioxide radioisotope recording crystals attached to a flexible arm were placed 0.5 mm from the surface of the membrane. These crystals are capable of accurately recording beta emission from the immediately underlying cortex. Because of the short penetrance of beta particles, radioactivity from any other part of the brain was not measured. The output from these crystals was amplified and recorded on a Harshaw count ratemeter and analyzing system. This output was displayed on a strip chart recorder and fed into a computer interface, which was in turn connected by data access line to a PDP 11 computer for on-line instantaneous analysis of the isotope washout curve. Permanent punch paper tape recording of this output was also made for subsequent restudy. The computer was programmed to statistically examine isotope washout data following the intracarotid injection of 2 mc of Krypton 85. The data were analyzed for a very quick (shunt-peak) comp-

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**Diagram 1**

The parietal vein and its branches are within the cortical distribution of the middle cerebral artery. The transcortical portion of the vein in the parasagittal region crosses the territory of supply of the anterior cerebral artery where it has no branches.

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**Diagram 2**

Barium-injected monkey brains indicate the territory of supply of the anterior, middle, and posterior cerebral arteries. In this view the interhemispheric fissure has been opened and the parietal vein ligated as it enters the superior sagittal sinus.
Radiograph of a monkey brain, in vitro, after retrograde injection of barium suspension into the parietal vein. This view shows the lateral extent of its branches. These merge with a single vein which enters the superior sagittal sinus as shown in figure 2.

ponent and a slower component which represents the mean flow in the gray matter. Statistical analysis of each curve was determined by error-matrix, chi-square deviation, extended deviation according to the method of Kassell and Reivich. The animal was then heavily heparinized, and a series of control blood flow determinations were made over each cortex. With each determination, the hemoglobin, Pco, and Po, were measured by a blood gas analyzer. Two sets of EEG electrodes were fixed across the craniectomy and recorded in bipolar fashion on a Grass electroencephalograph. The animal's body temperature was maintained stable by a heat lamp servoed through a rectal thermistor. After baseline regional blood flows were determined, the parietal vein on each side was exposed by a transdural incision. Utilizing the operating microscope a polyethylene catheter, whose inner diameter approximated that of the parietal vein, was fashioned. The vein was tied as it entered the sagittal sinus, and the distal end was opened. With microsurgical technique, the vein was catheterized a distance of 7 mm. This catheter, with an appropriate fitting, was plugged into one limb of a Y-connector whose outflow had been fed previously to the left internal jugular vein by a common tubing. The contralateral vein was similarly cannulated and connected to the other limb of the Y-connector. The Y-assembly was fixed at the level of the torcular herophile so that normal outflow resistance was maintained. A series of regional blood flow determinations was again made to ascertain the effect, if any, of this cannulation. The drip rate of blood from each parietal vein was easily seen in the glass connector. Because the drops were of very uniform size, accurate measurement of the venous flow rate was simplified. With periodic heparinization, it was possible to keep the system patent throughout the duration of the experiment, which in some cases was as long as two days. Each limb of the Y-assembly was connected by a stopcock to a collecting chamber through which periodic sampling of the venous blood for biochemical determinations could be made. The samples were collected under mineral oil and approximately 0.7 ml was required for each determination. Oxygen content and hemoglobin were measured within ten minutes by an IL Co-oximeter, pH, Pco, and Po, were measured also within ten minutes by an IL Blood Gas Analyzer. During this ten-minute interval, despite occlusion from the atmosphere by the mineral oil, it was possible that the metabolites in the sample might change their values from the moment of collection. Serial oxygen content, hemoglobin, pH, Pco, and Po, determinations were made at three minutes, ten minutes and 15 minutes after sampling, and there was no statistically significant variation. In-the-room co-oximeter and blood gas analyzer were required for these experiments. Cerebral blood flow was increased with epinephrine-induced hypertension and with hypercarbia, and decreased by elevating the head of the operating table. At the end of the experiments, retrograde injection of micropulverized barium at venous pressure was made, and the excised brain was x-rayed in vitro.

In five monkeys, the craniectomy was extended on each side to expose the entire convexity surface of each cerebral hemisphere. A series of reference points was arbitrarily mapped on the surface of the convexity. Dissolved in a volume of 0.2 ml, 0.2 mc of Krypton 85 was injected 1 mm deep into cortex at each reference point. One minute after
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each injection, 0.5 ml of blood was sampled from the parietal vein. A simultaneous sample from the femoral venous catheter was collected. The beta emission of these samples was counted for two minutes in a Baird-Atomic well-counter scintillation spectrometer.

Results

For convenience, this intracerebral artery inflow system, cortex of venous drainage, and cortical vein outflow system will be called a vascular-metabolic unit (VMU).

Anatomical justification of the VMU has been described and is illustrated (figs. 1, 2, and 3).

Cannulation of the parietal vein did not alter flow in the cortex of the VMU. Beta emission washout techniques were considered more accurate than any other form of flow measurement in a specific area of cortex. Because of the short penetration of beta particles, radioisotope emission from gray matter immediately beneath the detector was recorded. Gamma recording methods were not used for this purpose because the possibility of stray counts from areas of brain not in the VMU was unacceptable. Perhaps highly collimated gamma recording methods could be devised. This modification would require extremely large isotope doses in order to achieve statistically reliable curves. In the control preparation, the rate of venous outflow from each Rolandic vein was 8 to 16 drops per minute. These drops of blood were 0.0527 ± 0.00012 ml yielding a typical venous outflow rate of 0.6 to 1.2 ml per minute.

THE EFFECT OF CHANGES IN THE VENOUS OUTFLOW SYSTEM PRESSURE ON FLOW RATE

A Statham pressure transducer was connected to one end of the Y-tube to record venous pressure in the system. In addition, direct pressure measurements from the parietal vein were made. In the normal preparation, venous blood pressure fluctuated between 6 and 8 mm Hg with sinusoidal variations during respiration. With the venous outflow occluded, venous pressure increased to vary between 12 and 18 mm/H2O, and returned promptly to the previous level when the jugular venous outflow was opened. The jugular venous pressure was near zero when the system was open to air. Elevation and lowering of the Y-tube throughout a reasonable range did not significantly alter the venous outflow pressure. This pressure is apparently maintained by the cortical flow and is great enough to overcome small changes produced by the position of the outflow apparatus. Similarly, lowering or elevating the Y-tube did not significantly change the rate of the venous outflow. This suggests that within reasonable ranges of catheter positioning, resistance or "sucking" artifact would not be significant. The Y-tubing is placed at the level of the torcula herophile which would represent the average pressure level between the sagittal sinus and the jugular vein. This observation was made by Rapela and Green3 with flow and pressure measurements in the lateral sinus of dogs. Autoregulatory responses to small changes in blood pressure were demonstrated both in the cortical regional blood flow and the regional venous outflow, with results similar to Symon's who cannulated the vein of Labbé.4

CORRELATION OF VENOUS FLOW RATE FROM PARIEtal VEIN WITH REGIONAL CORTICAL BLOOD FLOW THROUGH VMU

Blood pressure was lowered by changing the animal's position, and was raised with epinephrine. In addition, 20% mixtures of CO2 were administered through the respirator. After each of these variables which might be expected to alter cerebral blood flow, venous outflow rate and regional cerebral blood flow were measured.

Theoretically, by dividing the venous outflow by the regional cerebral blood flow (which is expressed in volume per weight of brain per minute), one can arrive at a figure which may represent the weight of brain which the parietal vein drains. In the experiment outlined in graph 1, this value was about 1.25 gm. Although this figure probably does not represent the actual weight of the brain in the VMU, one can see that the slope of the charted line depends on this weight. In one experiment, we altered the position of the catheter so that it then drained only one branch of the parietal vein. In this instance, the regional blood flow-venous outflow relationship was still linear, though the curve was much flatter since the rate of venous outflow was now reduced. With further experimentation, it may be possible to actually determine the weight of brain in the VMU, and therefore absolute values for the volume of metabolites utilized may be calculated rather than simply metabolic rates.

Graph 1 correlates the results in one animal dur-
ing ten variations in flow. The venous outflow and regional cerebral blood flow bore a linear relationship throughout blood flow ranges from 28.34 ml per 100 gm of brain per minute through 142.95 ml per 100 gm per minute. This simply indicates that changes in overall cerebral blood flow are reflected in the venous outflow through a wide range and disproportionate venous shunting to other areas is unlikely.

**CORTICAL MAPPING OF VENOUS DRAINAGE OF THE PARIETAL VEIN**

In order to map the cortex drained by the parietal vein, an effort was made to inject isotope into individual branches of the middle cerebral artery. This is impossible because this procedure would require occlusion of branches of the artery, which therefore would alter the pattern of flow because of collateralization. Nilsson demonstrated that a superficial intracortical injection of Krypton 85 would be washed out by blood flow, and the isotope recording of this washout curve was quite similar to an intra-arterial injection. We confirmed this by injecting 0.2 ml of Krypton, dissolved in 0.2 ml of saline, a depth of 1 mm into the cortex through a fine needle. Over this cortex, a Geiger-Mueller tube recorded the beta emission of this isotope. This curve was virtually identical to washout curves achieved by intra-arterial injection and measurement through the same device over the cortex. Subsequently, a series of similar injections was made at various points along the cortex as shown in figure 4. One minute after each injection, 0.5 ml of blood was collected from the parietal vein of the ipsilateral hemisphere. Simultaneously, 0.5 ml of blood was extracted from the femoral vein as a control. The beta emission of these paired samples was counted. These data indicate that the venous drainage of each major branch of the parietal vein includes only the adjacent gyrus. Injections along the origin of these tributaries near the Sylvian fissure, and in the low parietal area, did not drain into the parietal vein. Injection into the parasagittal cortex (in the distribution of the anterior cerebral artery) also did not drain into the parietal vein which has no branches in this region. The territory of drainage of the parietal vein in the monkey seems to be entirely within the distribution of the superior divisions of the middle cerebral artery. Although these 0.2 ml injections obviously damaged the cortex to some extent, their purpose was to map the territory of drainage rather than to accurately reflect local flow. When Evans blue was added to the Krypton solution, one could observe that the injected bolus remained rather circumscribed and did not diffuse significantly beyond the injection site.

**Discussion**

As mentioned earlier, research in cerebral circulation has progressed from measurement of total cerebral

![FIGURE 4](http://stroke.ahajournals.org/figure4.jpg)

**Photograph of monkey brain after removal of right hemicranium and excision of dura. The number points refer to sites of injection of Krypton 85. The large arrow indicates the parietal vein which was subsequently cannulated and sampled for beta activity 30 seconds after each injection. Only points 7, 8, 11, 12, and 13 showed significant beta activity after injection.**
blood flow to regional blood flow, and more recently to total cerebral metabolism. Techniques to measure regional brain metabolism now seem necessary. Most serial studies on cerebral metabolism involve the simultaneous measurement of the metabolite in the arterial circulation and jugular venous blood. Difference between these two, when multiplied by the total cerebral blood flow, is an index of the metabolic rate of this substance (CMR). The jugular venous blood, however, contains an admixture of metabolites from both cerebral hemispheres and perhaps extracerebral tissue. Therefore, only relatively gross alterations in metabolism can be measured. Thus, blood from cerebral infarction is soon diluted by drainage from more normal tissue. Significant alterations in the metabolism of glucose, oxygen, and certain ions have been observed in coma, severe head injury, etc. To our knowledge, AV differences across a localized area of brain have not been recorded serially.

Other techniques to measure regional cerebral metabolism have certain serious disadvantages. Some of these techniques are capable of measuring only one metabolite. Others require rapid freezing of the cortex and, therefore, cannot be performed serially in the same animal. These will be summarized briefly.

**POLAROGRAPHIC OXIMETER**

Through the use of a polarographic electrode inserted into the cortex, local partial pressure of oxygen has been measured (Po). This device measures oxygen "availability" which may be a rather passive index of metabolism. Calculations for metabolism require a volumetric determination of oxygen content. This cannot be extrapolated accurately from Po, particularly in the lower (venous) ranges. The artifact induced by inserting the probe in the cortex could be significant.

**CHEMICAL ANALYSIS OF THE CORTEX**

Portions of cerebral cortex may be excised and subjected to biochemical analysis. To stop metabolism at the point of sample-taking, the surface and depths of the brain are often quick frozen. At present, this is the only technique by which one may measure the activity of high energy phosphates (ATP-ADP-AMP-phosphocreatine) in the brain. When the entire exposed cortex is frozen, the preparation cannot be used for serial studies. The artifacts induced by freezing are as yet unknown.

**SURFACE FLUOROMETRY**

One stage in glycolytic metabolism can be measured serially in focal areas of brain by newly perfected techniques. The exposed cortex is subjected to a beam of ultraviolet light in the 340 to 370 nm range, which causes NADH to fluoresce in the 420 to 480 nm range. This fluorescence can be detected by sophisticated photoelectronic recording. Throughout the glycolytic cycle, NAD+ is reduced to NADH in the presence of cerebral hypoxia. Reduction in oxygen to critical levels, therefore, is associated with increased fluorescence which emanates from increasing proportions of NADH. Accurate quantitation of this anaerobic glycolysis is not possible at present. A disadvantage of this technique is that it measures only one aspect of metabolism. Artifacts induced by brain pulsation and spectral absorption by hemoglobin must be obviated to enhance the accuracy of this attractive laboratory technique.

**GAS SAMPLING FROM MEMBRANE-FITTED BRAIN PROBES**

Certain artificial membranes will permit the selective passage of gases from brain substance. Gases aspirated from membrane-tipped probes have been analyzed, usually by mass spectrometry. This technique is restricted to the study of certain gaseous metabolic by-products and the volume of brain from which these gases are extracted has not been determined. An artifact induced by insertion of such a probe into the brain is worrisome.

**MEASUREMENT OF REGIONAL METABOLISM OF RADIOACTIVE OXYGEN**

Ter-Pogossian, Eichling et al. measured regional oxygen consumption with a series of externally placed scintillation probes following the intracarotid injection of oxygen-15 tagged hemoglobin. The washout curve from these probes is compared to similar curves after 15.0-carboxyhemoglobin and 15.0-water. From these three curves, oxygen utilization and cerebral blood flow can be measured and, ultimately, regional oxygen consumption can be calculated. Unfortunately, the short half-life of these isotopes requires that a generating cyclotron be nearby, and thereby renders this study impractical for most laboratories.

**Comment**

Certain criticisms of this technique may come to mind if the basic premise is not understood. Simply stated, it is presumed that all of the blood draining into the parietal vein emanates from a known cortical vascular bed. If vascular occlusion experiments are to be considered among the uses of the VMU, it is known that this cortex is supplied entirely by the middle cerebral artery. Of course, the middle cerebral artery supplies a greater volume of cortex than is drained by the parietal vein. Nonetheless, the main requisite appears to be that the parietal vein drains only cortex in the middle cerebral artery territory. The data from intracortical injection of Krypton 85 suggest that the territory of drainage of this vein can be "mapped" with reasonable accuracy. The ideal experiment would be a selective injection of an indicator substance into each major cerebral artery with examination of the subsequent cortical distribution of this indicator. Unfortunately, we know of no way in which a cerebral artery can be selectively injected without first occluding that vessel. Proximal occlusion of a cerebral
artery would promote collateral flow from the remaining vessels of the circle of Willis, and this altered physiology would render the test of little value. Similarly, injection into the internal carotid artery with the anterior and posterior cerebral arteries occluded would selectively fill the middle cerebral artery, but its territory of distribution would now be increased by collateralization to the occluded vessels. Meldrum and Brierley demonstrated "boundary zones" between the major cerebral arteries on the cortex by perfusion of the carotid artery in the heparinized animal immediately postmortem with an indicator agent. The boundary zones were visualized because the cortical vessels near the circle of Willis tend to fill first, and the fine vessels in the boundary zones last. They showed that the anterior cerebral artery-middle cerebral boundary zone lay in the depths of the intraparietal sulcus posteriorly, and extended 10 mm to 20 mm along the convexity of the cortex in the frontal pole. On their illustrations, the cortex of drainage of the parietal vein was filled by branches of the middle cerebral artery. Because of its posterior location, this cortex did not seem to be significantly supplied by branches of the anterior cerebral artery which extend only a few millimeters into the convexity. In our experiments the catheter is passed into the vein well beyond this parasagittal cortex.

Because of an effective collateral flow mechanism, when the middle cerebral artery is occluded, blood still flows into the parietal vein, though at a much reduced rate. This does not represent a disadvantage of the technique, since knowledge of the effects of collateral circulation should be considered in studies of regional brain blood flow and metabolism. Experiments could be designed, in fact, which would test the role of collateralization in nourishing the cortex of the VMU. If desired, however, total isolation of the VMU cortex can be effected by occlusion of the anterior and posterior cerebral arteries which can be done through the transorbital approach. Under these circumstances, one would expect the venous drainage from the VMU to stop when the middle cerebral artery was occluded. An alternative method of isolation from collateral flow would be separation of the cortex adjacent to the VMU from the surrounding circulation by anatomical dissection or cauterization of surface blood supply. Effectively then, one could restrict all arterial input to vessels leaving the Sylvian fissure. Significant artifact could be introduced, however, by such manipulation.

Under conditions of altered physiology, venous blood from other areas of the brain may enter the parietal vein through transcortical veno-venous anastomoses. To test the extent of these anastomoses, a retrograde injection of angiographical contrast material at greater than venous pressure was made through the catheter in the parietal vein. Figure 5 is a lateral angiogram taken during the injection. Note that the parietal vein and its branches fill throughout the cortex of the VMU. In addition, their branches anastomose with branches of a laterally placed vein in the temporal region, which is anatomically analogous to the vein of Labbé in man. This vein traverses the cortex to empty into the transverse sinus. There are no other cortical venous anastomoses, and when this single alternate exit channel is occluded, major venous inflow and outflow to the cortex of the VMU is restricted to the parietal vein. Occlusion of this vein is routine in ischemia experiments. Symon was able to cannulate this vein for his serial blood flow studies of regional autoregulation. Venous flow rate in the vein of Labbé was similar to those described above for the parietal vein.

An important issue concerns whether the cortical venous effluent drains the same depth of brain tissue which is seen by the beta counter. The following background information confirms a fortunate coincidence, and indicates why this method is likely to be more accurate than whole brain gamma-emitting regional techniques. Horstmann and Lierse have examined histological sections of the brains of mammals especially stained to demonstrate capillaries. They were able subsequently to calculate the area of capillaries per given area of gray matter and white matter. In the cerebral convexities, 1.3% of gray matter is composed entirely of capillaries. In the underlying white matter in the same region, only 0.5% of each tissue unit is represented by capillaries. They concluded that brain capillary density is an anatomical expression for topical demand of metabolic products.

Nilsson was able to inject microliter amounts of Krypton 85 at various depths into the gray and white matter of the brain. He subsequently measured the beta emission of this isotope which correlated nicely with cortical recordings when the same substance was given by the ordinary intra-arterial route. He found that isotope injected at a depth of over 6 mm produced no recordable beta emissions from the surface counter. In his experience, calculated flows for gray matter were on the average 5.1 times higher than those for white matter. Espagno and Lazorthes, utilizing the same measured cortical and subcortical injection technique in man, were able to measure a greater depth through use of gamma-emitting isotopes. Immediately after each local intracerebral injection of a saline solution of Xenon 133, they resected various depths of cortical and subcortical white matter. Flow in the gray matter was three times that of the subcortical white matter and six times that of the central white matter. The above studies indicate that the beta emission of Krypton 85 used in these experiments derives entirely from the first 4 to 5 mm of cerebral cortex. Any flow from deeper layers (central white matter) is likely to be "slower" and of minor metabolic significance.

In our monkeys, the cortical gray matter...
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FIGURE 5
Lateral radiograph of parieto-occipital portion of the head in a monkey following the retrograde injection of angiographical contrast material at greater than venous pressure through a catheter in the parietal vein (upper arrow). Note that the "overflow" contrast material enters branches of the laterally placed vein of Labbe (lower arrow) which in turn empties into the transverse sinus.

Our anatomical studies, confirming those of Gillilan,\(^1\) indicate that a superficial cortical vein drains only the cortex. Subcortical and deeper white matter drains into the central veins. Fortuitously, the depth of the superficial venous system drainage corresponds anatomically with the penetration of beta emissions of Krypton 85 through the brain (fig. 6). Furthermore, its intercommunication with the deep venous system is negligible. Gleichmann et al.\(^\text{17}\) proposed a similar concept when they sought to measure cortical metabolism by the insertion of a catheter in the anterior end of the superior sagittal sinus in dogs. Thereby, the cortical venous drainage from both frontal lobes could be sampled. They observed the above described anatomical and physiological coincidence by which the beta emission from an intra-arterially injected isotope correlates with the superficial cortex drained by cortical veins. Their method was limited by lack of anatomical studies to indicate the exact areas of drainage. Since this technique measures both frontal lobes symmetrically, no "control" cortex was available for comparative studies. As might be expected, their values for cortical metabolic rates were significantly

FIGURE 6
Diagrammatic representation of the area of drainage of the cortical venous system which, coincidentally, covers a depth approximate to the penetrance of beta particles through the brain. Thus, flow calculated by beta emission measurements from intra-arterial Krypton-85 derives from the same cortex drained by the superficial vein from which blood is sampled.
higher than cerebral metabolic rates described by others. Their cortical metabolic rate of oxygen, for instance, was 7.0/100 gm/min ± SD 2.3 (a value which is similar to that achieved in our controls).

The effects on cerebral metabolism and flow of light nitrous oxide anesthesia are least among the available humane ways to produce analgesia. Nonetheless, the anesthesia likely influences cerebral metabolism, and experimental alterations in metabolism, when compared to the controls, must consider these effects. The electroencephalogram under light nitrous oxide anesthesia appears to have a well-organized alpha rhythm of appropriate amplitude which suggests that this method would not mask experimentally induced metabolic alterations.

Studies are underway to determine baseline metabolic rates for glucose and oxygen in this preparation. Regional cortical metabolic rates are determined by measuring the arteriovenous blood difference of the substance and multiplying this by the regional cortical blood flow. These can be correlated with bipolar EEG across the VMU, surface fluorometry, cortical temperature, etc. Other metabolites which enter the venous system in proportion to their production or utilization can be similarly sampled.

References
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