A New Technique of Recording Cortical Blood Flow in Cats, Suitable for Measurement of Arterio-Venous Concentration Differences

In an attempt at measuring cortical blood flow by collecting the venous blood from the caudal end of the superior sagittal sinus, INGVAR and SÖDERBERG[1] found that the majority of other venous communications from the region studied could be eliminated by replacing the top of the skull-bone with dental cement. This procedure interrupted the diploic vessels that anastomose with the veins on the cortical surface. If the frontal end of the sagittal sinus was then ligated and large superficial veins at the margin of the cortical area to be recorded from were destroyed, the only anastomoses left were the communicating vessels between the superior and inferior sagittal sinuses. INGVAR and SÖDERBERG[1] did not eliminate these vessels but made a check of their functional importance and discarded those experiments in which the anastomoses proved to be extensive. Recently, JÖBSIS and SÖDERBERG[2] have applied this technique of recording cortical blood flow on a neuronally isolated cortical slab of nearly the same size as the cortical region recorded from by INGVAR and SÖDERBERG (Figure 1 B). During the preparation of the slab, the inferior sinus could easily be removed, and the venous outflow from the superior sagittal sinus was therefore identical with the total outflow from the slab. However, the electrical activity of the isolated cortex differed greatly from that of the intact brain. For that reason, probably, the blood flow was also found to have a lower rate than one would expect from other measurements[1,3]. The autoregulation of the blood vessels in response to changes in arterial blood pressure was also found to be poor.

In order to compare the vasomotor activity in the isolated cortex with that of a more intact brain, a new preparation has now been developed that occupies an intermediate position between the isolated slab and the intact cortex used by INGVAR and SÖDERBERG[1].

Methods. The operation, which is performed in two stages, starts in a way similar to that described by JÖBSIS and SÖDERBERG[2] by sucking a wedge-shaped cavity in one hemisphere along the entire length of the sagittal sinus (Figure 1 A and 2). The groove serves two purposes: the inferior sagittal sinus can be destroyed, and blood flow will only be collected from part of one hemisphere. This is a great advantage. It is easier to manage a small venous outflow and replace the blood loss caused by it by intravenous infusion at a rate equal to the outflow, and the cats will therefore live longer. In addition, in many cats the superior sagittal sinus is so narrow that it cannot serve as the sole venous outflow from both hemispheres after the other venous exits have been interrupted. Great vasodilatations in the cortex will then cause brain oedema, or signs of it, and such experiments will have to be discarded. The rostral end of the superior sinus is then ligated and a longitudinal, curved groove is drilled in the skull-bone approximately along the lateral border of the cortical region to be recorded from (see Figure 2, broken line), thereby interrupting the venous communications through diploic veins.

The end of the operation is also similar to that described by JÖBSIS and SÖDERBERG[2]: the groove in the brain is washed with H_2O_2 and filled with Gelfoam and the bony defects are covered with dental cement that will also fix the silver ball electrodes used for EEG recording. The animal is allowed to recover for several hours to permit closure of damaged blood vessels before the second stage of the operation begins when large doses of heparin are

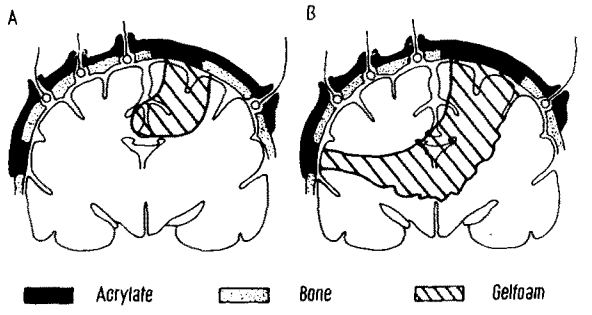

Fig. 1. Cross sections of animals operated with the new technique (A) and for preparing an isolated slab according to JÖBSIS and SÖDERBERG[2] (B).

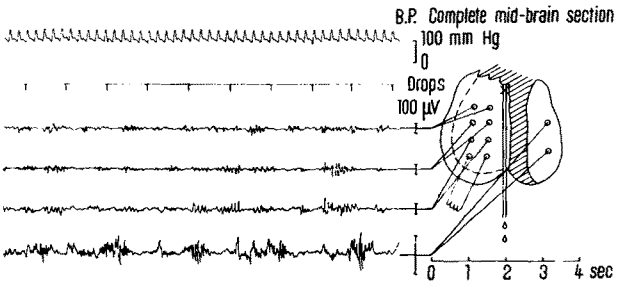

Fig. 2. Original record of blood pressure, drop signals and EEG from three areas on the side from which the blood flow was recorded and from one on the contralateral hemisphere. The cat was prepared on the day before the experiment when the mid-brain was also transected. Calibrations and top view of recording situation on the right. Broken line on the cortical surface indicates the groove in the skull-bone.

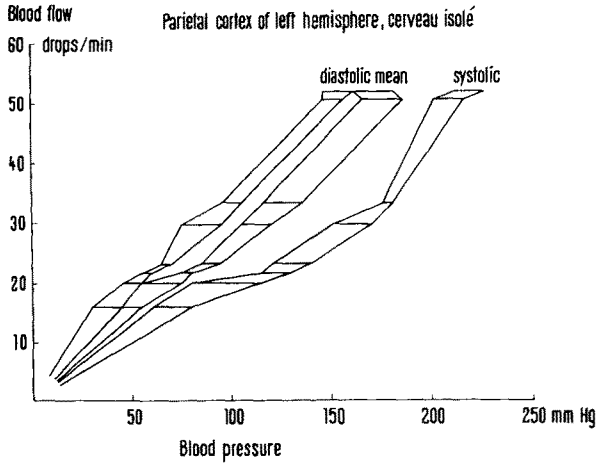

Fig. 3. Pressure-flow diagram of one cat experiment. Each horizontal line represents the range of measurements at each flow level.

[1] D. H. INGVAR and U. SÖDERBERG, EEG Clin. Neurophysiol. *8*, 403 (1956); Acta physiol. scand. *42*, 130 (1958).

[2] F. F. JÖBSIS and U. SÖDERBERG, Verh. deutsch. Ges. Kreislaufforschung, Bad Nauheim, 27. Tagung (D. Steinkopff, Darmstadt 1961), p. 301; to be published.—U. SÖDERBERG, Proc. XXII Int. Physiol. Congr., Leiden (1962), in press.

[3] C. F. SCHMIDT, *The Cerebral Circulation in Health and Disease* (Thomas, Springfield 1950).—N. A. LASSEN and O. MUNCK, Acta physiol. scand. *33*, 30 (1955).—S. S. KETY in *Neurophysiology* (FIELD, MAGOUN, and HALL, Ed., Amer. Physiol. Soc., Washington 1960), section 1, vol. III, p. 1751.

given to stop coagulation and the superior sinus is cannulated. The venous outflow is recorded as drop rate and the blood is collected for future chemical analysis. Afterwards the brain is fixed in formalin and the cortical region recorded from is dissected free and weighed.

Results. As expected, the preparations were found to be more stable and could be used for longer recording periods than those obtained with the technique of INGVAR and SÖDERBERG. In the animals tested, the rate of blood flow per unit weight of cortex recorded from usually exceeded that of the isolated slab and varied between 0.17 and 0.50 ml/g/min at a systolic blood pressure level of 100 to 120 mm Hg and at resting conditions (synchronized EEG activity in the cerveau isolé preparation). A sample of an original record is given in Figure 2 that also shows the recording situation on the right. Note the abnormal EEG record from the right hemisphere that is damaged by the operation.

The blood vessels were dilated in response to what is generally believed to be increased activity. They also possessed the ability of autoregulation, buffering to some extent the effects of changes in blood pressure on the flow rate (Figure 3). As can be seen in the Figure, the strongest buffer activity occurred in the range of normal pressures. Autoregulation could be demonstrated also during inadequate ventilation.

Glucose uptake was also measured from rate of blood flow and the arteriovenous concentration difference. In resting conditions, 30 to 70 μg were taken up per g/min, a figure that is comparable to the uptake of 44 to 62 μg/g/min that has been reported for the whole human brain[4], and exceeds the uptake by the slab by about 50%.

Comments. When cerebral blood flow is measured, the choice of method is determined by the actual problem. This is because each technique described in the literature suffers from its individual draw-backs. In those cases where the exchange of substances between blood and brain are to be measured, it is of great importance to collect all the blood that has passed through the part of brain that is investigated and also that the blood samples do not contain blood that has perfused other tissues. The present technique seems to fulfil these requirements better than methods previously presented for recording blood flow from a largely intact part of the brain. Furthermore, because of the long time that is allowed for the recovery after the first stage of operation, a cerveau isolé preparation can be used and anaesthetics avoided.

The autoregulation is evidently better preserved in this preparation than in the isolated slab as reported by JÖBSIS and SÖDERBERG[2]. This suggests that most of the vascular response to changes in blood pressure is a result of the action of vessels within the region recorded from, because vessels outside this area will not be disturbed by any of the described operations. The arteries on the surface of the temporal and parietal lobes of the cat's brain are always thinner than 0.5 mm in diameter. The assumption that only small vessels are responsible for the autoregulation is in agreement with the findings of, for example, TEXTER et al.[5], who observed a change in resistance in small intestinal blood vessels similar to that seen in the cerebral vascular bed in the present experiments when the blood pressure was altered. Since autoregulation could be demonstrated also during inadequate ventilation, the whole effect cannot be a result of changes in pCO_2 in the brain such as are also known to influence the cerebral vascular resistance[6].

Zusammenfassung. Der Blutstrom in der Hirnrinde der Katze wurde mit einer neuen Methode quantitativ gemessen und die Resultate mit früheren Untersuchungen über die Durchblutung eines nervös isolierten Rindenlappens verglichen. Bei normalen Druckverhältnissen war die Strömungsgeschwindigkeit 0,17 bis 0,50 ml/g/min. Selbststeuerung des Strömungswiderstandes war deutlich vorhanden. Die Aufnahme von Glykose, die aus Durchblutung und arteriovenöser Differenz berechnet wurde, betrug 30 bis 70 μg/g Hirngewebe/min.

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[4] S. S. KETY in *Metabolism of the Nervous System* (D. RICHTER, Ed., Pergamon Press, London 1957), p. 221.—U. SÖDERBERG, Proc. XXII Int. Physiol. Congr., Leiden (1962), in press.

[5] E. C. TEXTER Jr., S. MERRIL, M. SCHWARTZ, G. VAN DERSTAPPEN, and F. J. HADDY, Amer. J. Physiol. *202*, 253 (1962).

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