CHANGES IN BRAIN OXYGEN TENSION
EVOKED BY SENSORY STIMULATION
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EVOKED BY SENSORY STIMULATION

by
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A thesis submitted to the Faculty of Graduate Studies and Research in partial fulfilment of the requirements for the degree of Master of Science.

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August 1966
ACKNOWLEDGEMENTS

I wish to thank Dr. Ronald Melzack for his advice in the preparation of this thesis. I would also like to extend my appreciation to Mrs. Lynn Kernaghan for her skilful handling of the manuscript.
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INTRODUCTION

The use of physiological concepts in psychological theory has led to attempts by psychologists and physiologists to establish neurophysiological correlates of behaviour (Hebb, 1955; John & Killam, 1959). While studies of the effects of lesions and electrical or chemical stimulation of cerebral tissue have provided useful insights into the physiological basis of behaviour, attempts to observe the ongoing activity of the central nervous system in an awake, behaving organism have encountered serious problems. Electroencephalographic recordings are easy to obtain from animals while they are performing behavioural tasks, but their interpretation involves highly complex analysis (Creutzfeldt, 1966). Valuable and clear-cut information has been obtained by monitoring single unit activity by means of micro-electrodes (Hubel and Wiesel, 1962; Burns, Heron and Pritchard, 1962), but the animal preparations used for these experiments were either anaesthetised or otherwise immobilised, and the applicability of the data to the normal behaving animal is uncertain. The recording of unit activity in the chronic animal is, moreover, technically difficult. A third type of activity can
be recorded from the brain using conventional macroelectrodes. This activity has been called the "multi-unit" or "tonic" neural activity of the area (Arduini, 1963).

**Tonic Activity**

The "tonic" activity of an area is the number of high frequency electrical potentials that occur in that area during a specific period of integration. Arduini (1963) has defined "tonic" activity as the steady state neural activity that is not time locked to any stimulation. In contrast, gross activity that is transient and locked to a particular stimulus is referred to as "phasic". It is, however, doubtful if any activity could be termed "tonic" if these definitions were used rigorously, because changes in the level of neural activity that are long term rather than transient can also be elicited by specific stimulation. For example, a change in illumination produces changes in activity in the lateral geniculate nucleus that last as long as stimulation is maintained (Arduini and Pinneo, 1963). These responses are hardly
"phasic". For the purpose of this study, all long-term neural changes are referred to as changes in "tonic" activity.

Tonic activity provides little information on the spatial and temporal patterning of the neural firing. Its functional significance, however, is reflected in psychological theory by the general concepts of "arousal" (Hebb, 1955), and "activation" (Malmo, 1959). More recently Bindra, (1966) has given definitions of "drive" and "incentive motivation" which suggest not only functional states of general activity but also central states of greater specificity. However the neuro-physiological implications of such theories have not been fully explored.

Physiologists have typically studied tonic activity as a significant process in the sensory pathways or as a function of the non-specific systems. Studies of the sensory systems include those of Beidler (1953) and Pfaffmann (1960) on taste mechanisms, in which tonic neural activity was recorded from the chorda tympani. Pfaffmann showed that the intensity of the tonic activity produced by a given stimulus can be related to the aversive or attractive quality of that stimulus. Tonic activity has also been
studied in the cat auditory nuclei by Starr and Livingston (1963). Changes in tonic activity evoked by white noise stimulation were recorded under various conditions of anaesthesia, attention, and activity of the middle-ear musculature. The changes obtained in the medial geniculate nuclei and inferior colliculus were more complex than those in the lower brainstem. The activity in the inferior colliculus, moreover, was observed to decrease below its original level on the termination of the stimulation, and such decreases were offered as possible explanations for some auditory perceptual after-effects. Recently, Galin (1965) has elaborated on this work by showing that the tonic neural changes in the inferior colliculus can be inhibited by pairing the white noise stimulus with electric shock. In the visual system, Arduini and Pinneo (1963) have correlated the tonic activity in the lateral geniculate nucleus with the intensity and frequency of visual stimulation, and Pinneo (1966) has suggested that these relationships can be the basis of intensity discrimination.

Pinneo (1966) has recently proposed that the musculature can be controlled by varying the tonic activity in certain brainstem nuclei. Similar control over the skeletal muscles was suggested by Granit (1955) on the basis of studies showing that the tonic activity in the gamma
Efferent fibers can be excited by centers in the mesencephalic reticular formation, and inhibited by areas in the bulboreticular formation and the anterior limbic gyrus. Tonic activity, then, can be considered not only as a significant process in the sensory nuclei but also as a functional process in the motor output and in the non-specific systems. The type of relationship that exists among the tonic activities in the sensory, motor and non-specific systems has been suggested by Granit (1955). He proposes that the tonic activity of the sensory nuclei "energises" the reticular system which, in turn, activates motor efferents, and, by way of centrifugal fibers, modulates the sensory inputs, thus providing closed feedback loops.

A more detailed discussion of the possible interactions between the non-specific and sensory systems has been provided by Melzack and Wall (1965). They propose a model in which the axons from the substantia gelatinosa can presynaptically inhibit the transmission of nerve impulses from cutaneous A and C fibers to cells in the dorsal horns. The probability of the afferent fibers being modulated in this way is dependent
on the level of tonic activity in the substantia gelatinosa. This, in turn, is dependent on the tonic firing levels in the peripheral fibers, with control also being exercised by centrifugal inputs from the higher centers.

Similar interactions can occur throughout the spinal cord, brainstem, and forebrain. Rosen and Vastola (1966) have demonstrated that the sensitivity of the visual cortex is influenced by the tonic neural activity in the lateral geniculate nuclei. Since this activity is partially dependent on the activity in the tegmentum, they suggest that the sensitivity of the cortex can be controlled not only by direct innervation from the reticular system, but also by the mediation of the sensory relay nuclei.

It can be seen that these complex inter-relationships of tonic activity, revealed by physiological studies, are not fully reflected in the concepts of arousal and activation proposed by psychological theorists (Hebb, 1955; Malmo, 1959). In their conceptual nervous systems, the significance of tonic activity is restricted to a homogeneous reticular formation, and interactions between different kinds of sensory inputs, as well as
control of sensory inputs over the motor system, occurs principally in the cortex. However, it may be of greater value to the psychologist to consider tonic activity in its discrete, subcortical relationships, since the characteristics of such neural activity suggest it may be involved in the long-term control exercised by the processes of motivation and learning over the sensory input and motor output of the behaving animal.

Methods of Monitoring Tonic Neural Activity in the Brain

Studies of neural activity have been dominated by techniques for recording electrical potentials. However, changes in neural activity are also reflected by variations in the general level of metabolism, and these changes can be measured by techniques other than the conventional potential electrode. Such techniques may not only prove to be more convenient for use in behavioural studies, but also may indicate aspects of cerebral function not revealed by potential recordings. Changes in cerebral metabolism can be monitored by such indices as the heat production (Serota and Gerard, 1938), the concentration of metabolic by-products (Geiger, 1957)
or labelled amino acids (Altman 1966), the changes in pO₂ (Davies, McCulloch and Roseman, 1944) and the production of CO₂ (Meyer, Grotoh, Tazaki, Hamaguchi, Ishikawa, Nouailhat, and Symon, 1962). Moreover, Schmidt (1950) has suggested that local adjustments of cerebral blood flow accompany variations in metabolic activity. Thus, Ingvar (1958) has recorded local vascular changes in the cortex. Sokoloff (1961), moreover, using radio-active tracers, has shown preferential uptake of the tracers in the visual system after intense visual stimulation, which is interpreted (Sokoloff, 1961) to indicate increased blood flow through the system.

This evidence, taken together, indicates that the measurement of blood flow through an area also provides an index of gross neural activity in that area. However, some of the methods used for measuring local vascular and metabolic changes, such as autoradiography, involve the sacrifice of the animal and therefore are not suitable for the study of ongoing behaviour. In contrast, the technique of oxygen polarography, used by Ingvar, Lubbers, and Siejo (1960), Cross and Silver (1962), Meyer et al. (1962), and other investigators of cerebral
circulation, does not have such inadequacies. Furthermore, it has the advantage of being free from the artifact involved in conventional electrical recordings and can easily be adapted to the study of chronic preparations (Clark and Misrahy, 1957). The purpose of the present study was to assess the polarographic technique as a method for investigating functional neural activity. In particular, it was thought that the study of local vascular changes would provide a further index of tonic neural activity which has been shown above to play a key role in psychological processes.

The Recording Technique: Oxygen Polarography as a Method of Measuring Blood Flow

The principle underlying polarographic analysis of the ionic constituents in a solution is the preferential reduction of a specific ion at an electrode biased with a voltage that is characteristic to that ion. Polarography is used extensively in physical chemistry (Koltoff and Lingane, 1952), and its use in physiology, usually to detect oxygen ions, has been reviewed by Davies (1964) and Cater (1961). A typical oxygen
cathode is made of platinum and biased, with respect to a non-polarizable reference, within the range of 0.6 to 0.8 volts. Under these conditions, the current flow is dependent on the amount of oxygen being reduced at the electrode tip. If the tip is covered with a membrane permeable only to oxygen, then the current can be directly related to the oxygen concentration in the solution. Ingvar et al. (1960) have used such a device for measuring blood flow in the cerebral cortex. However, the size of the membrane and its sensitivity to mechanical deformation makes this kind of electrode unsuitable for recording from deep, subcortical tissue. Depth recordings using bare tipped electrodes have been made in anaesthetised cats by Cross and Silver (1962), in chronic preparations by Travis and Clark (1965), and in conscious human subjects by Cooper (1963). Although, bare tipped electrodes can be affected by ions other than oxygen present in cerebral tissue, in-vitro studies reported by Cater (1961) and Davies (1964) have shown that the oxygen cathode current is primarily produced by oxygen reduction even in the presence of the other ions normally found in extracellular fluid. Cater (1961)
has also reported that the electrode is insensitive to the mechanical pressures that may be exerted by the tissue on the detecting tip.

When a polarographic cathode is placed in cerebral tissue, the amount of oxygen that is reduced at its tip can be changed by three processes. Firstly, when there is an increased blood flow through the tissue the concentration of oxygen in the tissue will increase. Secondly, as Cross and Silver (1962) have shown, high oxygen concentrations exist near the surface of blood vessels, so that the displacement of a vessel towards the cathode, during vasodilation, will also increase the concentration of oxygen near the electrode tip. Thirdly, any fluid flow through the tissue will cause additional ionic movement, resulting in increased reduction of oxygen at the cathode. However, since all of these changes are the result of variations in blood flow, the oxygen cathode current can be taken as a measure of changes in the vascular condition of the tissue.
Experiments

In the first series of experiments, vascular activity was studied in the lateral geniculate nuclei of cats. Arduini and Pinneo (1963) have correlated the tonic neural activity of these nuclei with the intensity and frequency of the visual stimulation. Furthermore, McElligott (1966), using visual stimulation, has observed evoked temperature changes, which are mainly vascular in origin, in the lateral geniculate nuclei of anaesthetised and conscious cats. Because of these data, it seemed that the lateral geniculate nuclei would provide highly suitable areas for the initial testing of the recording procedures. In the second series of experiments, vascular and tonic neural activities were measured in the inferior colliculus of anaesthetised cats, McElligott (1966) has also studied evoked local vascular changes in these structures, using white noise stimulation, and the experiments of Starr and Livingston (1963) provide supporting data on the character of the tonic neural activity. Furthermore, the conditioning studies of Galin (1965) suggest that significant changes can occur in the inferior colliculus during the experimental modification.
of behaviour. A comparison of the changes in the lateral geniculate nuclei and inferior colliculi would also provide a demonstration that the responses were specific to a given sensory modality. Finally, observations were made on the vascular and tonic neural activities in chronic preparations.

METHODS

Subjects

The experiments were performed on twenty-six cats. Polarographic recordings were taken from twenty-four animals under moderate levels of anaesthesia (sodium pentobarbital). The initial doses were approximately 30 mg/kg. body weight, injected i.p., with supplementary doses given as necessary during the experiments. In twenty-one of the animals, vascular activity was observed in the lateral geniculate nuclei, and in three animals, vascular and tonic neural activity was recorded from the inferior colliculus. Recordings were also taken from two conscious animals, with electrodes permanently implanted in the lateral
geniculate nuclei.

**Apparatus**

The oxygen cathodes used in this study were made of platinum wire (containing 10% iridium), of 0.5 mm. diameter, and insulated, except for the tip, with insulex. A large area silver electrode, an Ag/AgCl electrode, or the frame of the stereotaxic instrument were all tried as the non-polarizable reference anode, and each proved to be equally effective. The control circuit is shown in Fig. 1A. The current was dropped down by means of a 10,000 ohm resistor and the voltage was measured by a Grass d.c. amplifier (model 7P1A). The steady-state currents were of the order of 0.5 microamps or less, giving minimal signal distortion. This current density is significantly lower than that usually used for cathodal stimulation, although blocking of units adjacent to the tip might have occurred. Overt behavioural responses were never observed when the polarization voltage was applied.

Cathodal currents were typically 1.5 microamps in normal saline or arterial blood, 0.5 microamps at
the cortical surface and 0.2 microamps in subcortical tissue (Fig. 1C). These relative values agree with the oxygen tension levels given by Cross and Silver (1962) for cortical and subcortical tissue. Large changes in the cathode current occurred when the preparation inhaled pure oxygen or nitrogen, and the systemic changes in the blood circulation evoked by applying pressure to the paw could also be recorded. It was considered that such changes gave adequate confirmation that the electrode was a sensitive detector of oxygen variations.

Tonic electrical activity was measured by the platinum cathode, amplified by a Tektronix differential amplifier (model 2A61), and then averaged by the integrator circuit shown in Fig. 1B. The output of the integrator was measured with a Grass d.c. amplifier (model 7P1A) having 1 megohm input impedance. The filters of the differential amplifier were set at 600 cps. (3 db. frequency) and at 6 kc. (3 db. frequency). The attenuation by these filters was 20 db./decade. Since equivalent values of tonic neural activity were obtained when data were recorded simultaneously with this integrator and a Ballantine root mean square meter (Arduini and Pinneo,
1963), it was assumed that the linearity of the integrator was satisfactory.

Visual stimulation was produced by a Grass photostimulator (PS2D), with flash rates varying from 2/sec. to 50/sec. The flash duration was 10 microseconds, and the lamp gave a blue-white light. Auditory stimulation consisted of white noise produced by a back-biased diode.

Procedure

The acute preparations were held in a standard stereotaxic instrument, and an area of cortex, about 1 cm. in diameter, was exposed by means of a trephine. The cathodes were inserted into the tissue according to the coordinates given in the atlas of Snider and Niemer (1961), and their exact positions were verified, after the experiments, by standard histological techniques. In several experiments an oxygen cathode was inserted into the femoral artery and the arterial oxygen tension was monitored simultaneously with the cathode changes in the brain. The reference anodes were placed under the temporal muscles. Hollow ear-bars were used when auditory stimulation was provided. During
visual stimulation, the pupils of the preparation were
dilated with Cyclogel (1 to 2 drops).

Essentially the same procedures were used when
electrodes were permanently implanted in the chronic
preparations. Surgery was carried out under aseptic
conditions and the holes through the skull were about
one millimeter in diameter. Before securing the electrode,
visual stimulation was presented and the electrode position
was adjusted until responses were observed. The electrode
was then secured to the skull with dental cement. The
skin was sutured, and antibiotics were administered. A
recovery period of at least one week was allowed before
the animals were tested.

Anaesthetised animals were held in the stereotaxic
instrument during testing. The chronic preparations
were placed in a restraining box (16 x 13 x 7 in.) from
which the head protruded. The animals were oriented
toward the source of visual stimulation, and were
dark-adapted for 30 minutes before being tested.
The current flow in the oxygen cathode is assumed, for reasons described above, to reflect the amount of oxygen that is reduced at the cathode tip. Changes in the cathode current, in response to flashing light (2/sec.), are shown in Fig. 2A. Displacements were in the positive direction and of the order of 3% of the base current, with latencies of 5 to 10 seconds. The maximum displacement occurred 10 to 20 seconds after the initial rise. Since the response time of the electrode is of the order of milliseconds, these periods represent the real periods of the physiological changes. The increase in current was usually maintained throughout the period of the stimulation, but responses were occasionally elicited which showed a drop in current prior to cessation of stimulation (Fig. 2B). It is possible that these latter responses resulted from a drop in the baseline occurring simultaneously with the response.

In one preparation a decrease in current was evoked by stimulation with steady light (Fig. 3A). In another
preparation however, steady light produced "on" and "off" responses, both positive in direction (Fig. 3B). These two types of response are consistent with the observations of Arduini and Pinneo (1963) on the tonic neural activity in the lateral geniculate nuclei. The difference between the two types of response may be explained in terms of the neural dark discharge in the lateral geniculate nucleus, which varies from animal to animal, and is also dependent on the background illumination, which was not strictly controlled in these experiments. Reduction in the relative intensity of the photostimulation produced an appropriate reduction in the amplitude of the response (Fig. 4). Similarly, the response amplitude decreased when the stimulation rate was increased from 2/sec. to 50/sec. (Fig. 5). It was difficult to obtain consistent results with more discrete changes in the stimulus parameters, but the variation in response amplitude as a function of gross changes in intensity and frequency agree in general with the changes in tonic neural activity reported by Arduini and Pinneo (1963).
It is important to demonstrate that the cathode responses are localised to the lateral geniculate nuclei. Simultaneous recordings were taken by cathodes placed in the lateral geniculate nucleus and superior colliculus. While equivalent current displacements were produced in both nuclei by systemic circulatory change induced by pressure applied to the paw of the cat, only the lateral geniculate nucleus responded to the visual stimulation (Fig. 6A). A similar comparison was made between the femoral arterial blood pressure and activity in the lateral geniculate nucleus with the same results (Fig. 6B). Moreover, maps of cathode current change in the lateral geniculate nucleus showed that the magnitude of the current change varies with the depth of penetration into the nucleus by the cathode (Fig. 6C). This would be expected if such changes were dependent on the gross neural firing in the cellular mass of the nucleus.

Of the 21 preparations studied, histological examination showed that the cathode has passed through the lateral geniculate nucleus in 16 animals. In 5 animals the electrode track was outside the lateral
geniculate nucleus, and responses were never obtained in these preparations. Of the 16 cats with penetrations through the lateral geniculate nucleus, reliable oxygen cathode changes were observed in 11. Although it was usually possible to obtain cathode responses over a range of several millimeters in the lateral geniculate nucleus, in two preparations the responses were restricted to the central portion of the nucleus (Fig. 7). In five preparations, cathode responses were not observed even though the cathode had passed through the central portion of the lateral geniculate nucleus. The recordings of two of these animals were difficult to interpret because of large baseline fluctuations, and were rejected from the study. No response dependence on the lateral or anterior coordinates of the recording sites was noted in these studies.

Theoretically the reduction of oxygen at the cathode occurs preferentially when the electrode is biased, with respect to the tissue, by a negative potential of 0.6 volts. Much smaller responses should be recorded when the cathode bias is 0 volts, and in practice with a cathode bias of 0 volts, responses were usually not observed (Fig. 8A). However, in one preparation, small changes were detected in
response to visual stimulation (Fig. 8B). These may perhaps be explained in terms of residual polarization on the cathode. The oxygen cathode responses could also be suppressed by dropping the metabolism of the tissue below a critical level. Gross changes in the responsiveness of the lateral geniculate nucleus occurred three minutes after the administration of a fatal dose of sodium pentobarbital (Fig. 9). The mean cathode current was then 60% of the original value. The current recorded in the dead preparation was about 25% of the original level.

**Studies of the Lateral Geniculate Nucleus in Chronic Preparations**

Platinum electrodes were permanently implanted in the lateral geniculate nuclei in two cats. A piece of silver wire (1-cm. long and 1-mm. in diameter) was inserted under the scalp and used as the non-polarizable anode. During the recordings, the animals' gross movements were restricted, but head movements were possible. The cathode responses to visual stimulation were similar to those recorded in the acute preparations,
although it was not possible to monitor generalised systemic effects, or to obtain a quantitative calibration (Fig. 10A). Tonic neural activity was recorded in these preparations with a Ballantine root-mean-square meter (Fig. 10B).

Studies of the Inferior Colliculus in Acute Preparations

Several experiments were carried out to study the cathodal and tonic neural activity elicited by white noise in the inferior colliculus. Three acute preparations were examined. Clear-cut cathodal responses to white noise stimulation were never observed, although systemic changes could be elicited. The positions of the recording sites were determined by histological examination, and they proved to be in the inferior colliculus. The tonic neural electrical changes were of the order of 5%, in contrast with the 50% changes recorded by Galin (1965) and McElligott (1966) using similar stimulation. The small amplitude of these neural responses may reflect an extremely low level of neural metabolic activity, and thus explain the absence of any vascular responses.
Rhythmic activity

Rhythmic activity was recorded by cathodes placed in sub-cortical grey matter. Similar rhythmic changes in oxygen tension have been recorded from conscious cats (Clark and Misrahy 1957), and humans (Cooper 1963) by the use of the polarographic method. Frequencies were in two ranges, 3 to 12 per minute, and about one per minute (Fig. 11). The faster waves seemed to be synchronous with respiration when the breathing was slow. But in lightly anaesthetised or conscious animals, the rhythms recorded by the cathode appeared to be unrelated to breathing, heart rate or any similar functions.

DISCUSSION

The purpose of this study was to assess the method of oxygen polarography as a means of monitoring functional cerebral activity, and to apply the technique to the study of long-term changes in tonic neural activity. Results have been obtained that allow a critical appreciation of the oxygen cathode, and give
further insight into the significance of data, reported by other investigators, on slow changes in cerebral activity.

Changes in oxygen cathode current have been evoked in the lateral geniculate nuclei by visual stimulation in both awake and anaesthetised cats. These changes were localised in the lateral geniculate nuclei. Moreover, their correlation with the intensity and rate of stimulation was similar to that observed in tonic neural electrical responses by Arduini and Pinneo (1963), who used equivalent stimulation.

In principle, the changes in the oxygen cathode current could have been produced by variations in tissue pressure, or by ionic processes other than oxygen reduction occurring at the cathode tip. Evidence minimising the significance of such activities has been discussed in the introduction. Furthermore, tissue movement over the cathode tip or the non-polarizable reference electrode would produce transient changes in the current flow, with the polarization rapidly re-establishing itself. But the responses were, in general, sustained displacements
throughout the period of the stimulation. Also, as the responses were specific to a reducing voltage of 0.6 volts, which is characteristic of the oxygen ion, interference by other ionic processes may be discounted.

It was noted in the introduction that the probable sources of change in the oxygen cathode current are (1) increases in the tissue oxygen concentration, (2) displacement of blood vessels, or (3) physical movement of oxygen ions by fluid flow through the tissue. It was not possible in these experiments to determine the relative importance of these three causal factors.

Vascular responses to auditory stimulation could not be recorded from the inferior colliculus (three preparations), and vascular responses to visual stimulation were also absent in two preparations in which the cathode tip was definitely in the lateral geniculate nucleus. Several explanations for these anomalies can be offered. First, it is possible that the changes in cathode current were in fact primarily produced by blood vessel displacement, while the cathodes in the non-responding preparations were
outside the vicinity of an appropriate blood vessel. However, the cathodes in these placements were sensitive to vasodilation caused by systemic changes in blood flow. A second explanation is that local vasodilation does not occur if the tonic neural changes are below a certain threshold level. And, in fact, in the inferior colliculus, the tonic neural electrical changes measured in these experiments were small, of the order of 5%, compared with tonic activity responses recorded in the inferior colliculus by McElligott (1966) and Galin (1965), which were of the order of 50%. A third explanation is that the anaesthetic agent interfered in some way with the process of vasodilation normally accompanying metabolic changes. It should be possible to reach a solution to this problem of response lability by carrying out further experiments in which the significant factors of blood vessel position, and levels of anaesthesia and tonic neural activity are carefully controlled or measured.

The polarographic method seems suitable for the study of functional changes in the oxygen content of
of brain tissue. Experiments can be performed without the use of extensive electrical shielding, the electrical circuit used are of the simplest kind, and because the responses are large compared with most bio-electrical phenomena, they can be measured with instruments of low sensitivity. Furthermore the cathode can be used for recording electrical activity by conventional methods and is easily adapted for studies of the freely moving animal.

Recently, Travis and Clark (1965) made polarographic measurements of cerebral activity in cats during conditioned avoidance learning in a shuttle box. They observed changes of oxygen cathode current in a number of different structures. However, their failure to show that the responses are localized specifically in these structures makes it difficult to give any functional significance to their data. The changes they observed may simply reflect general changes in body blood flow, since the oxygen cathode will detect any systemic circulatory changes that accompany autonomic activity. The method of oxygen polarography should be restricted to those studies that do not involve
autonomic reactions, or to studies in which such general changes can be controlled, or are considered to be of significance.

The responses that were recorded by the oxygen cathode in this study are best explained as modifications in the local vascular system produced by changes in the level of tonic neural firing. This interpretation is supported by the data of McElligott (1966) who, using visual stimulation, evoked localised thermal responses in the lateral geniculate nuclei of cats. Although it is possible that some part of these responses were due directly to metabolic thermal processes, a vascular component was shown to exist. The correlation of these thermal responses with the intensity and frequency of the visual stimulation is comparable to the correlation of oxygen cathode responses with the parameters of visual stimulation observed in this study.

It may be concluded from this study that slow vascular changes of functional significance occur in the brain. Such changes in the vascular system support the contention of Schmidt (1950) that the local cerebral blood flow varies according to the metabolic demand of
the tissue. Schmidt argues further that the general changes in cerebral circulation are not just passive reflections of changes in the body circulation. Thus, Cross and Silver (1962) have demonstrated that the hypothalamus exerts considerable intrinsic control over the general circulation of the forebrain, and Baust (1964) has provided evidence suggesting that cells in the lower brainstem can be directly excited by increases in cerebral blood flow. If discrete changes in blood flow reflect functional, localized changes in tonic neural activity, then the general changes in cerebral circulation may also reflect changes, of a general nature, in tonic neural electrical activity. This suggests that in addition to the localised variations already discussed, overall neural changes occur throughout the brain, which is implicit in the concept of "arousal" proposed by Hebb (1955).

Only a few studies involving the general variation in cerebral blood flow during behaviour have been reported (Hull, Buchwald, Dubrovsky, & Garcia, 1965; Kawamura & Sawyer; 1965). However, these studies on
vascular activity reveal variations that are similar to the slow potential changes in the brain, which have been studied more extensively. Thus Vastola (1955), using visual stimulation, recorded slow potential changes from the lateral geniculate nuclei of cats. The size and direction of these responses are similar to the vascular and tonic neural electrical activities recorded by McElligott (1966) and Arduini and Pinneo (1963). Wurtz (1966), and Rowland and Goldstone (1963) measured the slow potential changes that occur with different conditions of arousal. In general the cortical negative potential increased with arousal in a manner similar to the changes in systemic cerebral blood flow described in Hull et al. (1965). Also, Aladjalova (1964) and Norton and Jowett (1965) have recorded rhythmic slow potentials from the brain that have frequency ranges similar to those of the vascular rhythms reported in this study and by Clark and Misrahay (1957). If the characteristics of the slow potential changes should be shown to be highly correlated with those of the vascular activity, then the data of these investigations may also be interpreted in terms of tonic
neural activity, especially in its more general form. In fact Rowland and Goldstone (1963) have suggested that their studies provide evidence for a unitary drive similar to "arousal".

It was proposed in the introduction that the use of recording techniques other than the conventional potential electrode might reveal new aspects of cerebral function. And in fact this study shows that consideration and measurement of the vascular activity in the brain does give further insight into both psychophysiological concepts of behavioral theory and the physiological variables currently being studied as correlates of ongoing behaviour. Further use of the oxygen cathode, and equivalent techniques, in complex behavioural studies should prove fruitful.

SUMMARY

Changes in the oxygen levels in cerebral tissue of cats were measured with polarographic cathodes. Reliable responses to visual stimulation were recorded in the lateral geniculate nucleus in anaesthetised and awake
animals. The amplitudes of polarographic cathode responses are directly related to stimulus intensity and inversely related to stimulus rate. Both increases and decreases in the cathode current are produced by steady illumination. Control studies showed that the responses are localised in the lateral geniculate nucleus, and are dependent on a cathode bias of 0.6 volts. Rhythmic activity, with periods of the order of minutes, was recorded from cerebral grey matter. The cathode responses recorded in this study are similar to cerebral slow potential changes and tonic neural electrical activity observed by other investigators. The cathode responses are interpreted as variations in the vascular activity produced by changes in tonic neural activity. It is suggested that both vascular changes and cerebral slow potential changes reflect the functional significance of discrete and general variations in tonic neural activity.
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Figure 1. Circuits used in the experiments

A. Biasing circuit for the oxygen cathode.

B. Integrating circuit used for measuring tonic neural activity.

C. Variation in cathode current, for different biasing potentials, in cerebrospinal fluid (C.S.F.) at the cortex, and in subcortical grey matter.
A platinum cathode

10 K.

Ag/Ag Cl reference

signal input

0.1 mf.

1 M.

0.1 mf.

1 M.

subcortical grey matter

C.S.F.

microamps

volts (negative)

FIGURE 1
Figure 2.

A. Typical series of oxygen cathode responses evoked in the lateral geniculate nucleus by light flashes (2/sec.). The periods of stimulation are indicated by the upper bars.

B. Responses recorded from the lateral geniculate nucleus in which the current increase is not maintained throughout the stimulation. Such responses were recorded less frequently than those shown in A.
Figure 3.  

A. Decreases in the cathode current in response to steady illumination; recorded from the lateral geniculate nucleus.

B. Increases in the cathode current in response to steady illumination; recorded from the lateral geniculate nucleus.
FIGURE 3
Figure 4. Variation in the amplitude of the response as a function of the intensity of stimulation. Intensity ratio 8/1. (Horizontal lines were drawn in to provide an indication of the base line.)
32/sec. flashes
relative intensity 8

32/sec. flashes
relative intensity 1

FIGURE 4
Figure 5. Variation in the amplitude of the responses recorded by a cathode from the lateral geniculate nucleus as a function of rates of visual stimulation.

A. Stimulation rate: 2 flashes per second at relative intensities of 8 (top) and 4 (bottom).

B. Stimulation rate: 50 flashes per second at relative intensities of 8 (top) and 4 (bottom).
Figure 6. Localisation of the oxygen cathode responses.

A. Cathode responses recorded simultaneously from the lateral geniculate nucleus (L.G.N.) and superior colliculus (S.C.).

B. Cathode responses recorded simultaneously from the lateral geniculate nucleus (L.G.N.) and femoral artery (F.A.).

C. Cathode responses recorded at different heights in the lateral geniculate nucleus. The periods of stimulation are indicated by the bars.

(These records were retraced from the originals).
A 2/sec. flashes
Pressure to paws 20 sec.

B 2/sec. flashes
Pressure to paw

C H.6mm. H.5mm. H.2mm. H.0mm

FIGURE 6
Figure 7. Diagramatic representation of two penetrations in the lateral geniculate nucleus (L.G.N.).


A. Electrode track at A 7.5, L 10.0.

B. Electrode track at A 6.0, L 10.0.

O loci at which no responses were recorded

X loci at which responses were recorded
Figure 8. Effect on the responses to flashing light of different cathode biasing voltages.

A. Typical loss of response when cathode bias is reduced to 0 volts.

B. Exceptional case in which small responses are still observed when the bias is reduced to 0 volts.
FIGURE 8

A

Cathode bias 0.6 volts

B

Cathode bias 0 volts

2/sec. flashes

20 sec. 3%

2/sec. flashes

2/sec. flashes
Figure 9. Effect of overdose of nembutal on cathode responses to visual stimulation. L.G.N.: lateral geniculate nucleus, S.C.: superior colliculus.

A. Before injection; mean current 0.4 microamps.

B. Three minutes after the injection; mean current 0.25 microamps.
Figure 10.  

A. Oxygen cathode responses evoked in the lateral geniculate nucleus of an awake cat by light flashes. 

B. Tonic neural activity in the lateral geniculate nucleus corresponding to the cathode responses shown in A. 

(These records were retraced from the originals.)
FIGURE 10
Figure 11. Rhythmic activity in the brain recorded by the oxygen cathode.

A. Rhythm rate 0.8/min. (Breathing rate 12/min.)

B. Rhythm rate 3/min. (Breathing rate 8/min.)

C. Rhythm rate 12/min. (Breathing rate 12/min.)