CHANGES IN BRAIN OXYGEN TENSION

EVOKED BY SENSORY STIMULATION

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by

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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 relation-ships 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 relation-
ship 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 inter-
actions 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

pO_2 (Davies, McCulloch and Roseman, 1944) and the

production of CO_2 (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. Further-
more, 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. Polar-
ography 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 occured. 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 occured 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 photo-stimulator (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 proceedures 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 a 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.

RESULTS

Studies of the Lateral Geniculate Nuclei in Acute Preparations

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 occured 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 appropiate 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 quantatative 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 pre-parations 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 primarly 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
anaesthesic 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 Misrahy
(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

d.c. amplifier

10 K.

1 K.

1.3 volts

Ag/Ag Cl reference

B

signal input

0.1 mf.

1M.

0.1 mf.

1M.

1M.

d.c. amplifier

C

cathode current

microamps

4.0

3.2

2.4

1.6

1.2

0.4

C.S.F.

subcortical grey matter

volts (negative)

0.2   0.6   1.0

cathode bias
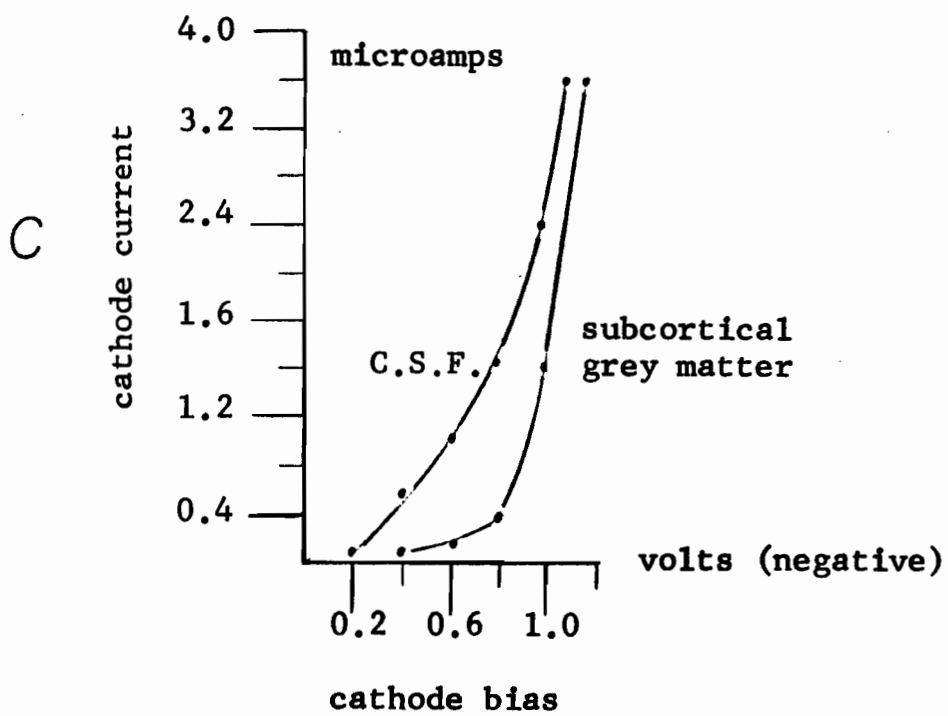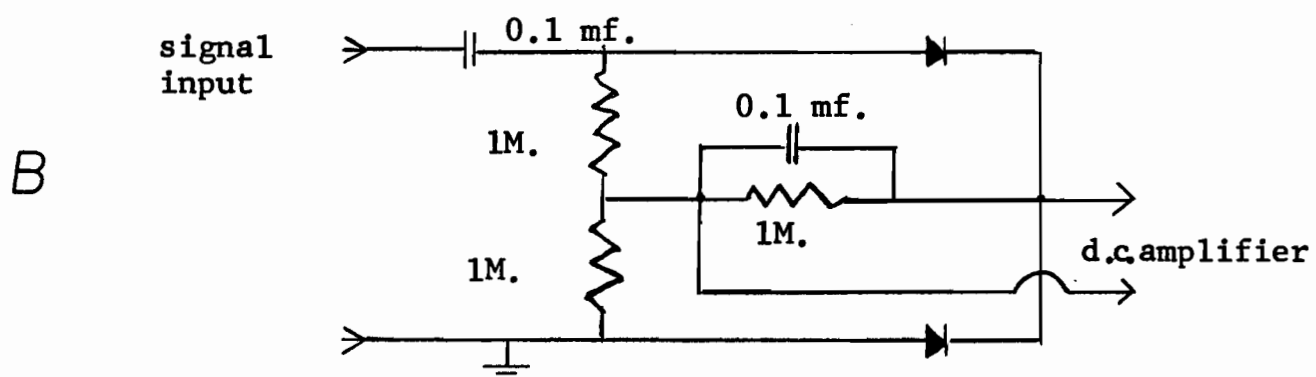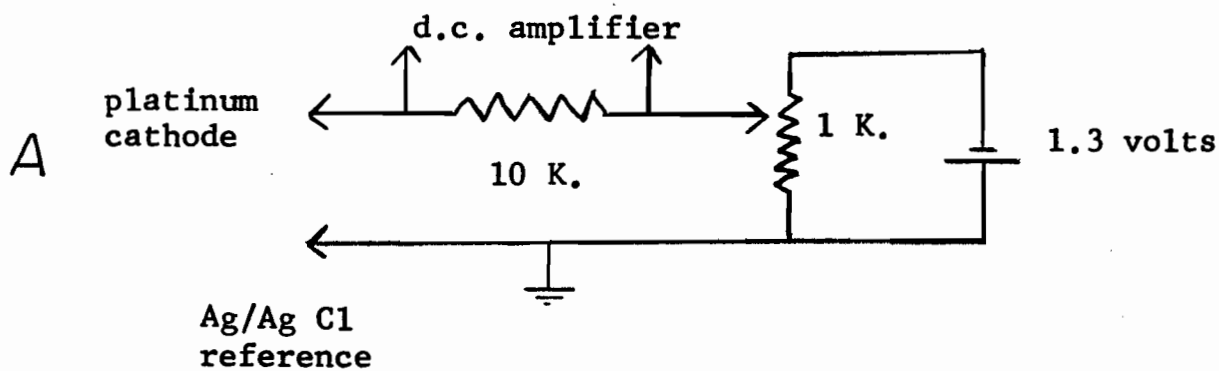
FIGURE 1

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.

A

B

2/sec. flashes

40 sec.

4%

4%

40 sec.
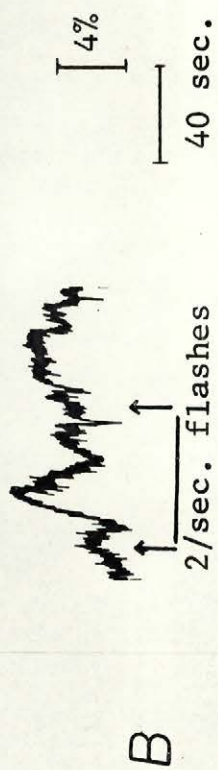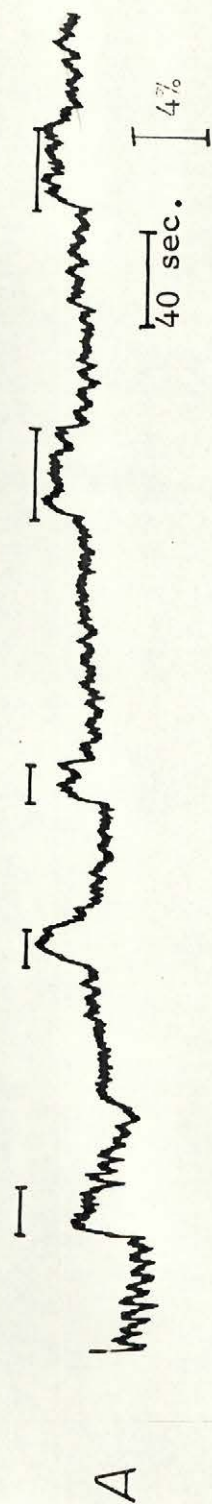
FIGURE 2

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.
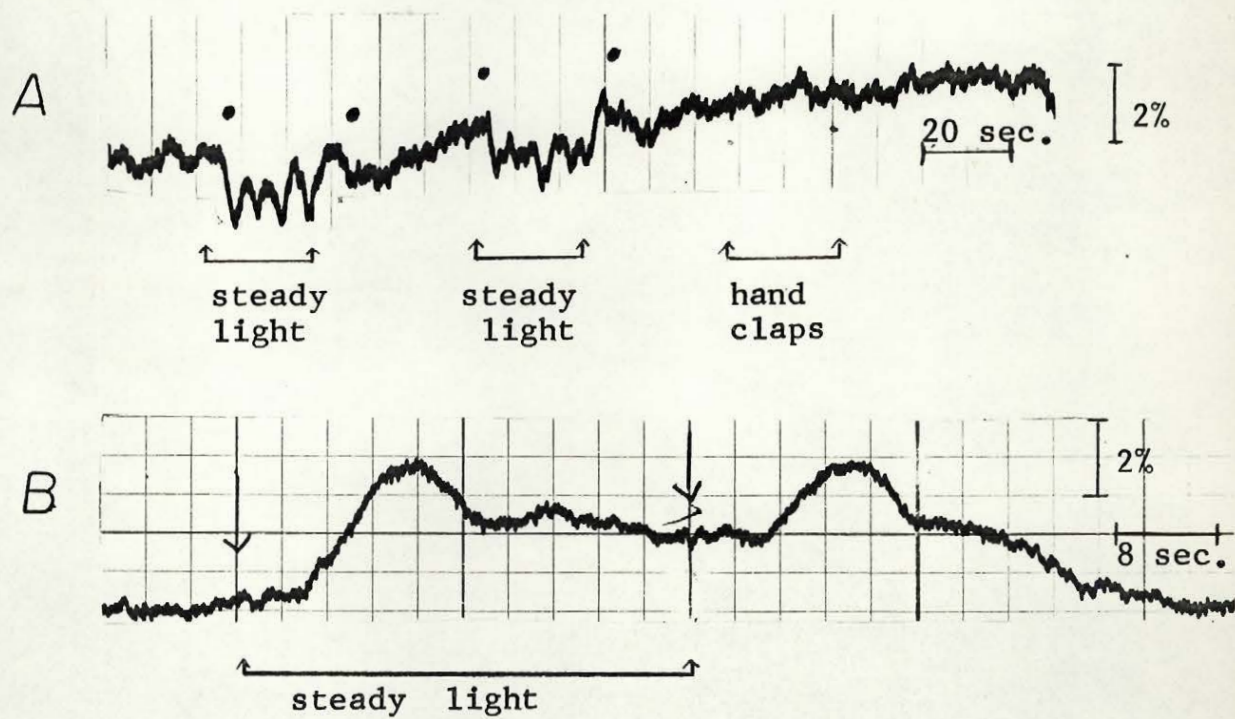
FIGURE 3

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.)
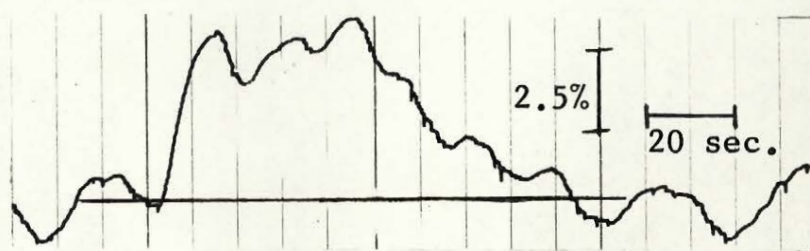
32/sec. flashes
relative intensity 8

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).
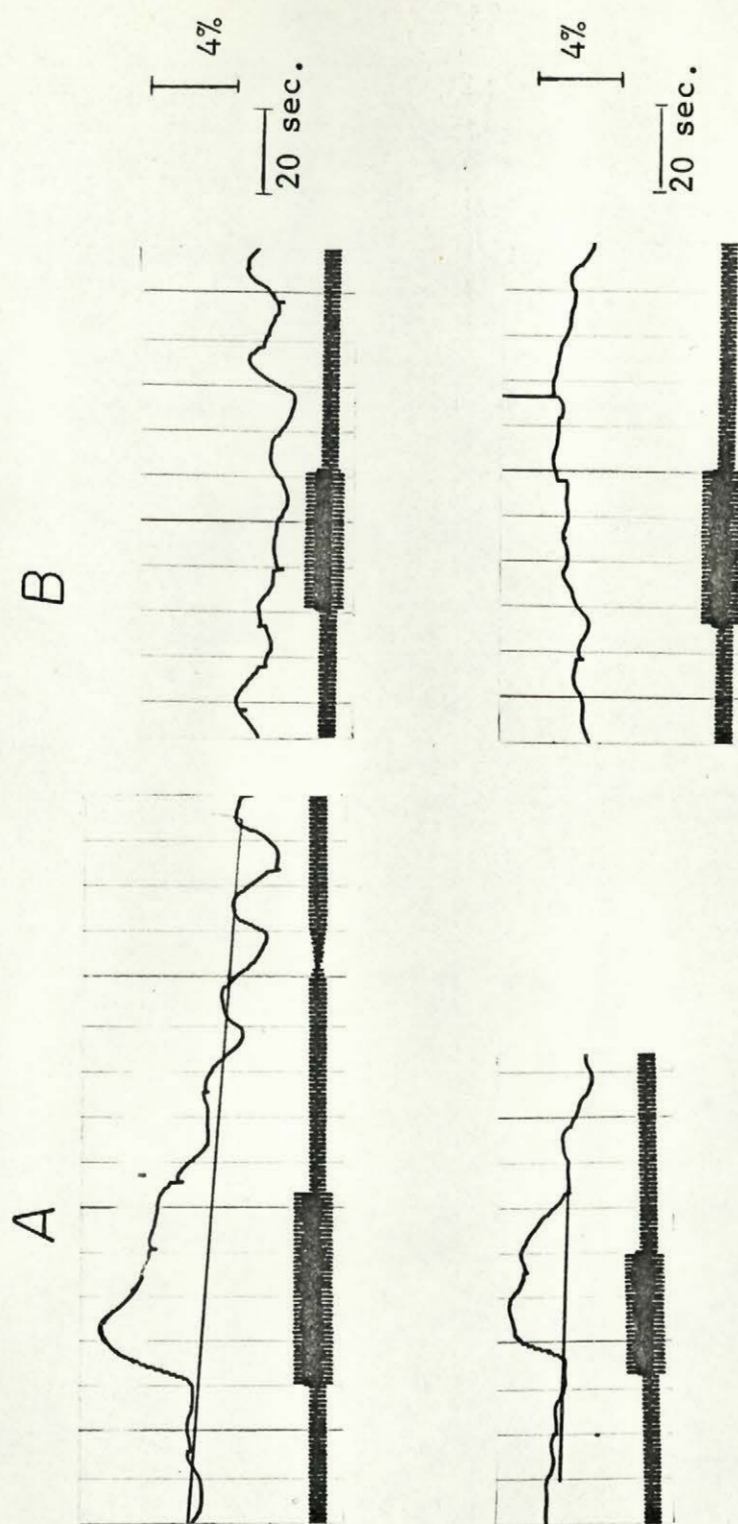
FIGURE 5

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

L.G.N.

S.C.

4%

20 sec.

B

L.G.N.

F.A.

2/sec. flashes

4%

20 sec.

L.G.N.

F.A.

Pressure to paw

C

H.6mm.

H.5mm.

H.2mm.

H.0mm.

4%

20 sec
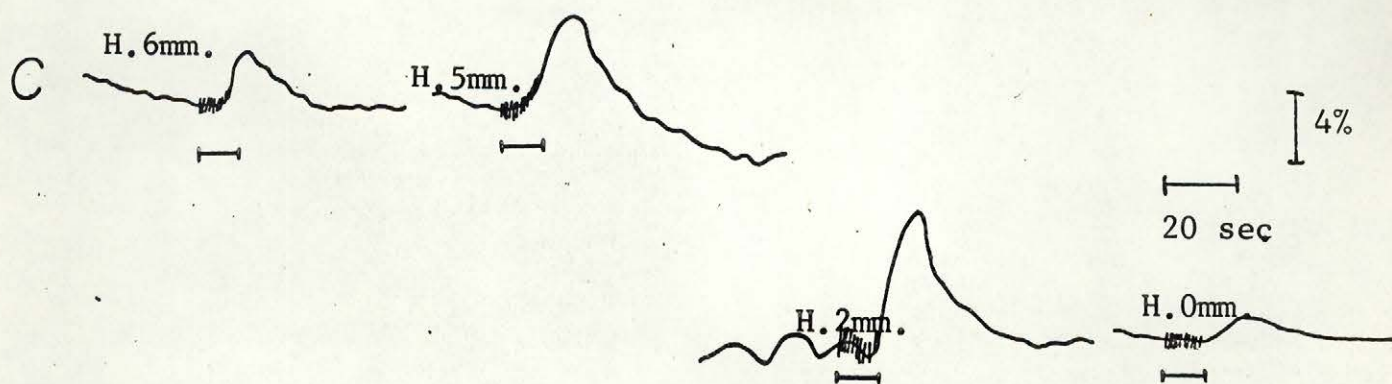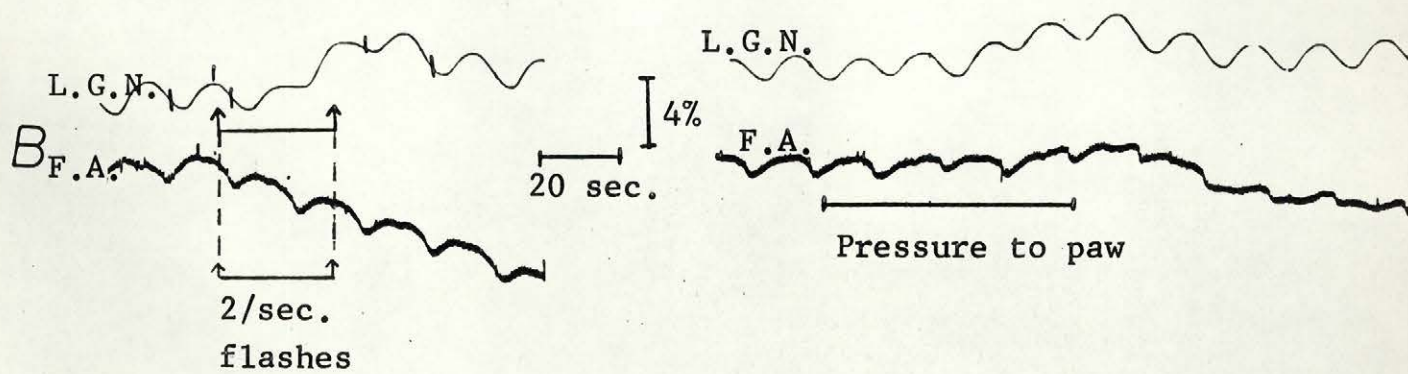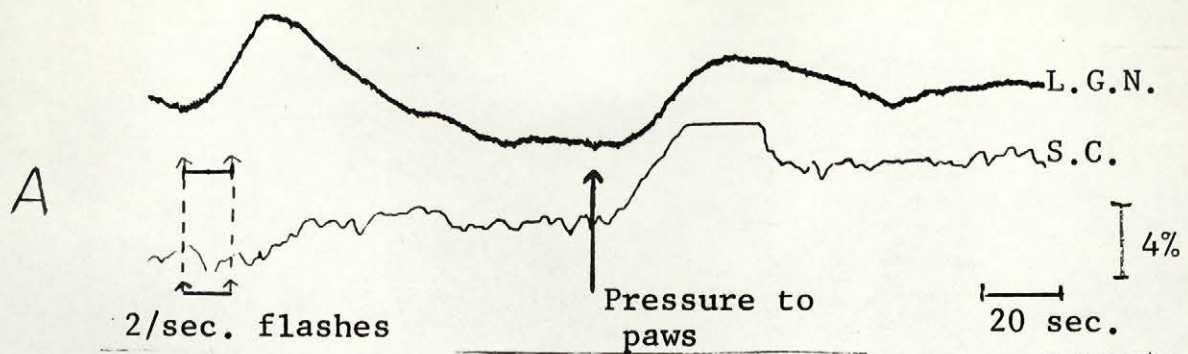
FIGURE 6

Figure 7. Diagramatic representation of two penetrations

in the lateral geniculate nucleus (L.G.N.).

O.T.: optic tract. Coordinates refer to the

atlas of the cat brain by Snider and Niemer (1961).

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
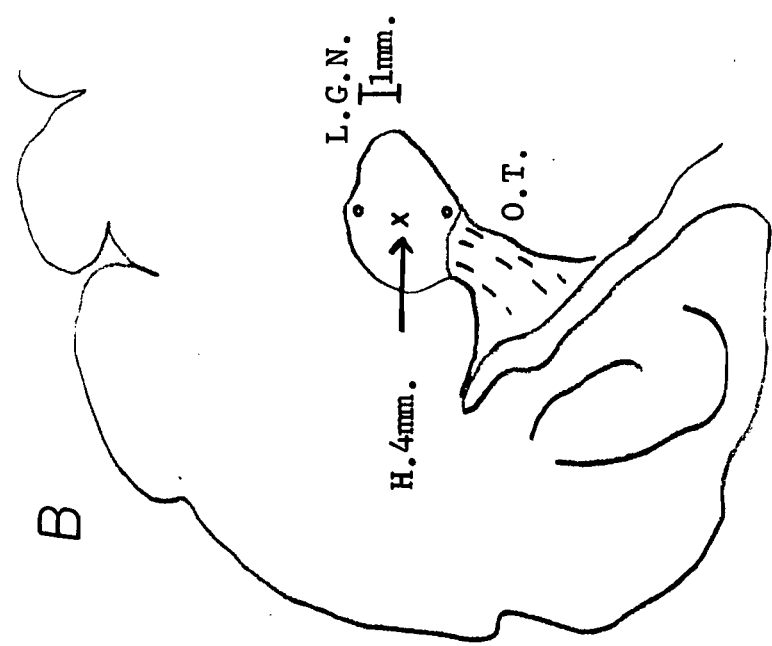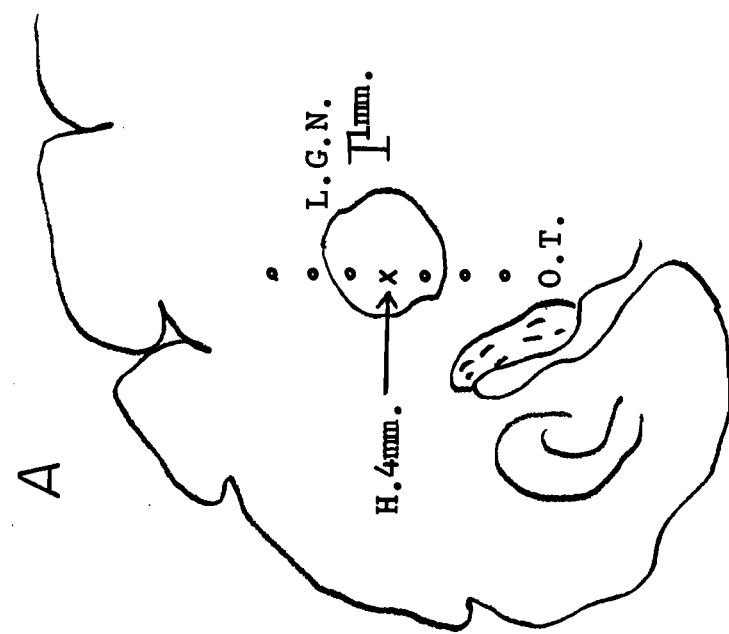
FIGURE 7

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
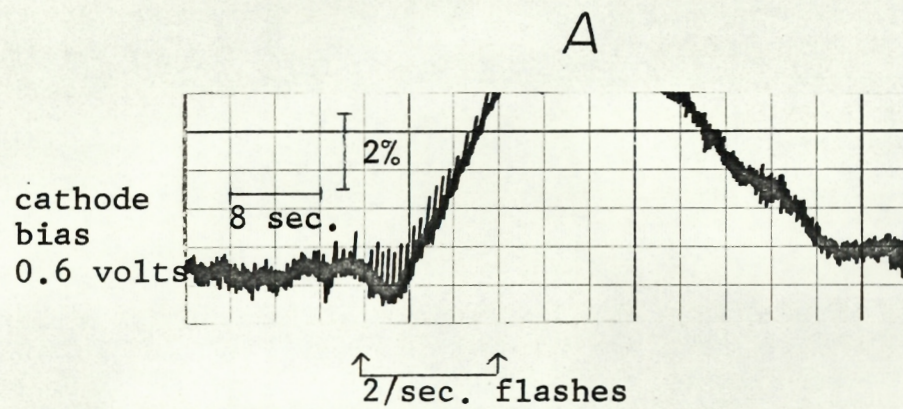   reduced to 0 volts.

cathode
bias
0.6 volts

2%

8 sec.

2/sec. flashes

cathode
bias
0 volts

2/sec. flashes

A

B

20 sec. 3%

2/sec. flashes

2/sec.
flashes

2/sec.
flashes
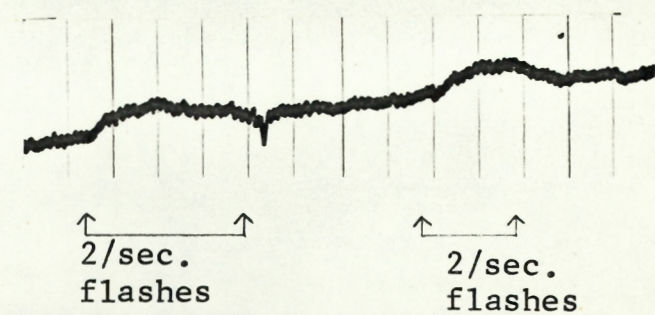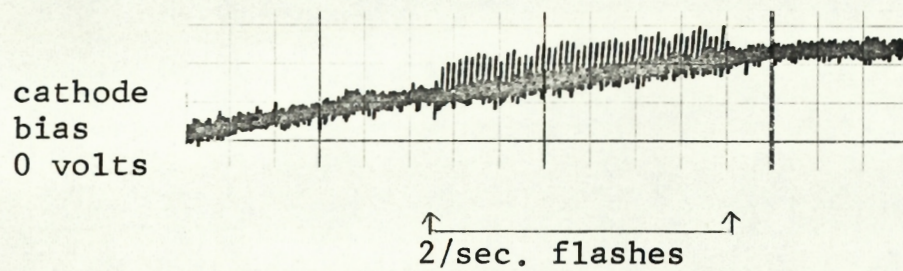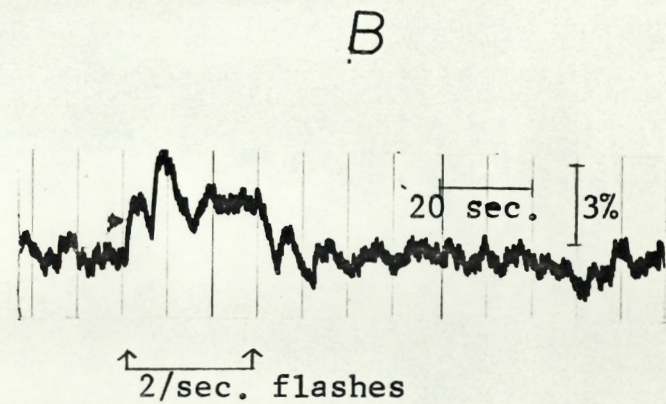
FIGURE 8

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.

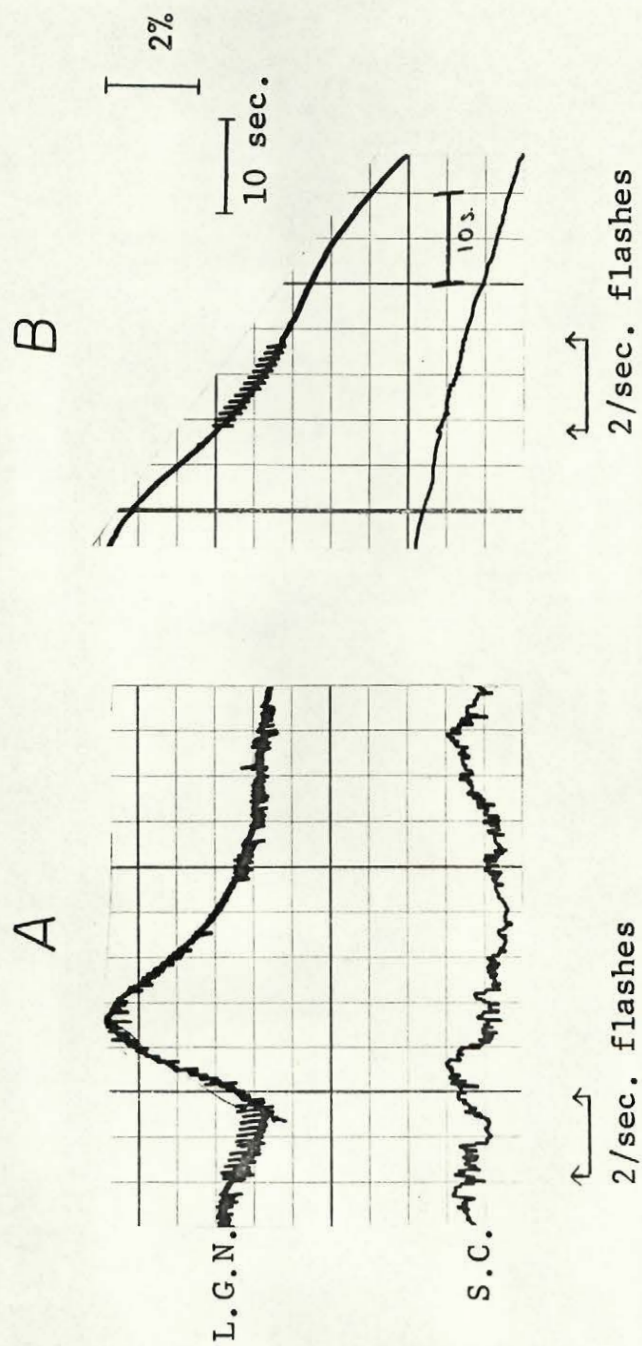B. Three minutes after the injection; mean

current 0.25 microamps.

FIGURE 9

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.

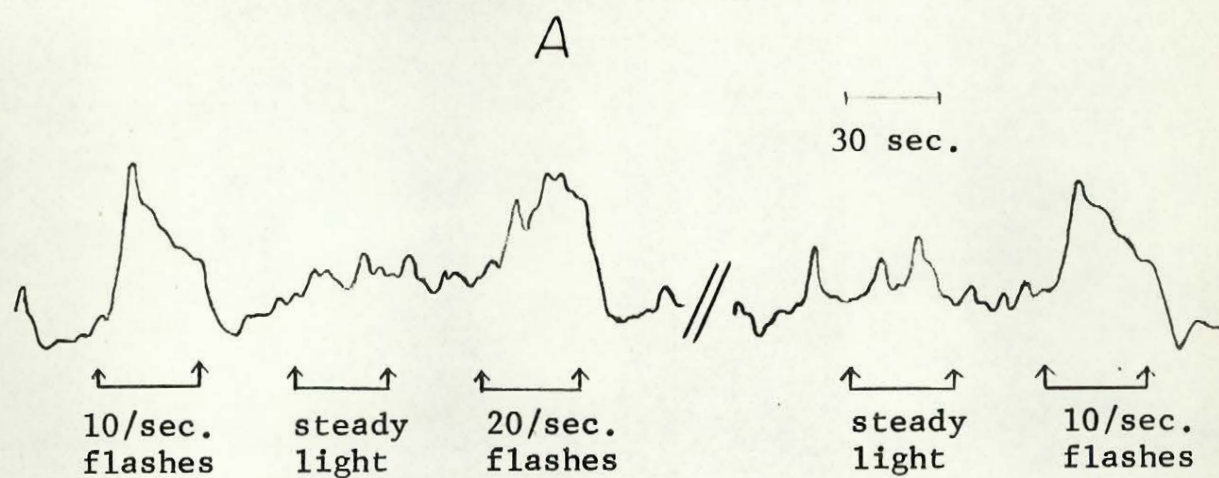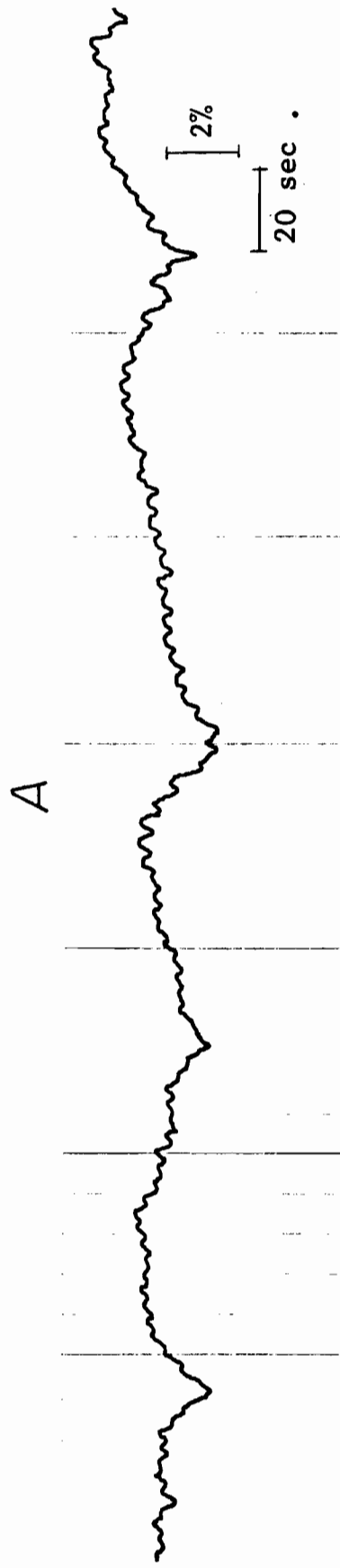(These records were retraced from

the originals.)

A

30 sec.

10/sec.
flashes

steady
light

20/sec.
flashes

steady
light

10/sec.
flashes

B

70

micro-
volts

50

30

30 sec.

10/sec.
flashes

10/sec.
flashes
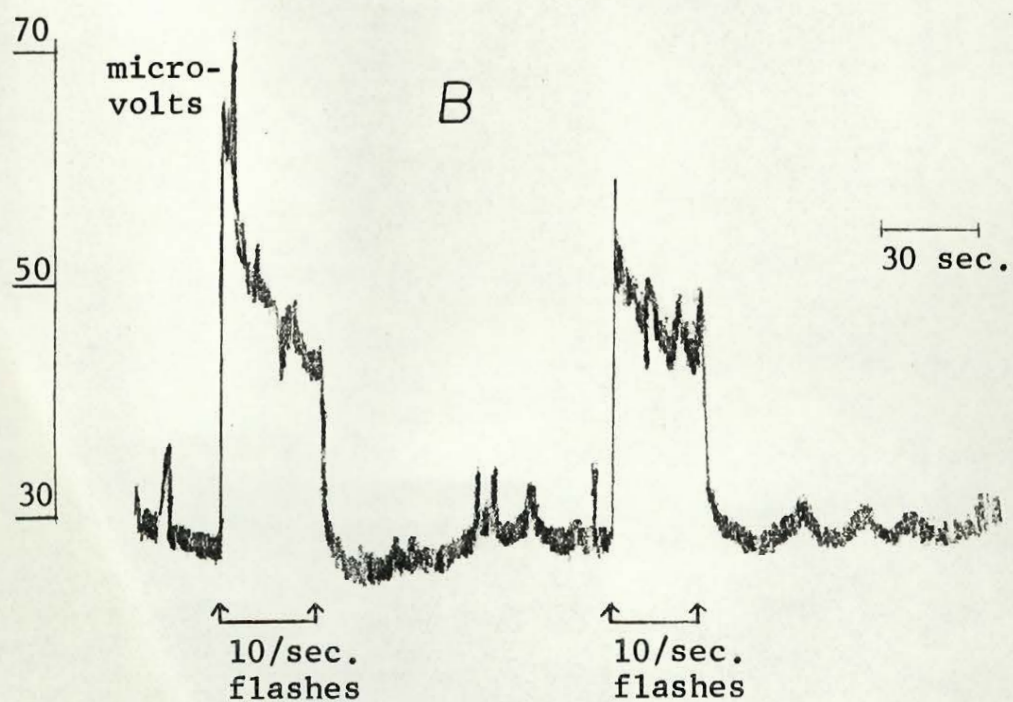
FIGURE 10

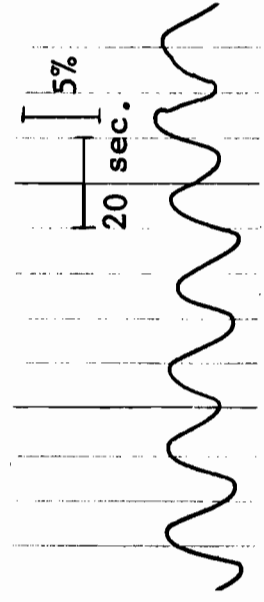Figure 11.   Rhythmic activity in the brain recorded

by the oxygen cathode.

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

B. Rhythm rate 3/min. (Breathing rate 8/min.)
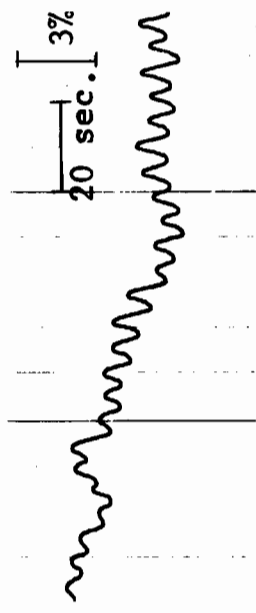
C. Rhythm rate 12.min. (Breathing rate 12/min.)

FIGURE 11